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Judul : **Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45−59 years): A Cross-Sectional National Data Analysis**

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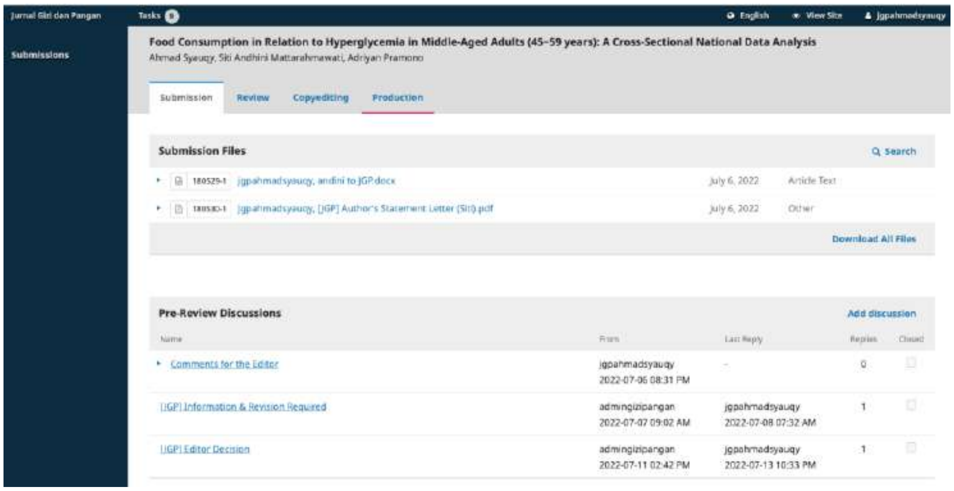
PRE REVIEW DISCUSSIONS



SUBMISSION

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Wed, Jul 6 at 8:47 PM

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ARTIKEL AWAL

Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis

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ABSTRACT

Diabetes, one of the non-communicable diseases, is the main cause of death in the world. Previous studies also found that diet was associated with the increased prevalence of diabetes. The objective of this study was to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia. This study was done using a cross-sectional design to analyze data from the 2018 Indonesia Basic Health Survey (IBHS). A total of 8477 subjects met the inclusion criteria and included in this study. Fasting blood glucose was analyzed in the laboratory using an enzymatic analysis. A food frequency questionnaire was used to assess the food intake. Multivariate analysis using multiple logistic regression was used to analyze the association of food consumption and FBG. Our results found that the prevalence of hyperglycemia was 43%. The mean FBG was 104.68 ± 31.99 for male and 110.75 ± 43.92 for female subjects. Frequent consumption of carbonated drinks (OR=1.139; CI=0.966-1.343), sweet desserts (OR=1.265; CI=1.132-1.413), beverages (OR=1.433; CI=1.263-1.626), salty foods (OR=1.189; CI=1.079-1.311), fried foods (OR=1.172; CI=1.033-1.331), and instant foods (OR=1.186; CI=1.088-1.293), and inadequate consumption of vegetable (OR=1.002; CI=0.920-1.100) were significantly associated with increased crude odds of hyperglycemia. There was a significant association between food consumption and FBG levels among middle-aged adults in Indonesia.

Keyword: diet, food consumption, hyperglycemia, fasting blood glucose, Indonesia

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Runner Title: Food consumption and hyperglycemia

INTRODUCTION

Non-communicable diseases are the leading cause of public health problems in developed and developing countries (Naghavi M, 2017). Diabetes, one of the non-communicable diseases, is the main cause of death in the world (Zheng *et al.*, 2018). Diabetes or hyperglycemia is characterized by an increase in blood sugar levels in the body. Previous studies found that the prevalence of hyperglycemia and the components of metabolic syndrome increased rapidly with age in women and men (Wu *et al.*, 2017, Jiang *et al.*, 2018). Recently, Indonesia is the fourth country after India, China, and America, with the most diabetes sufferers globally (Naghavi M, 2017). The prevalence of diabetes in Indonesia was around 6% (Mihardja *et al.*, 2014). Interestingly, based on the 2018 Indonesia Basic Health Survey (IBHS), the higher prevalence of diabetes was among middle-aged adults with almost 10% (Riskesdas, 2018).

Diabetes is caused by many factors such as lifestyle (Kufe *et al.*, 2015). Sedentary lifestyle has associated with the increasing trend of diabetes (Nurwanti *et al.*, 2018). Previous study also found that diet was associated with the increased prevalence of diabetes (Lambrinou *et al.*, 2019). Nowadays, Indonesian people tend to consume high western foods and low fruits and vegetables (Riskesdas, 2018). Western foods or unhealthy foods are correlated with an increased prevalence of hyperglycemia and metabolic syndrome (Syauqy *et al.*, 2018). Furthermore, inadequate consumption of vegetables and fruits can also escalate the diabetes prevalence (Syauqy *et al*., 2018, Schwingshackl *et al.*, 2017).

Western foods or unhealthy foods is consisted of sweet, sugar, fat, beverages, fried foods, and seasoning. Some studies have found the association between food consumption and metabolic syndrome among middle-aged adults in Taiwan (Syauqy *et al.*, 2018). Moreover, middle-aged adults who consumed high fruits and vegetables and less unhealthy foods had a better quality of life (Lo *et al.*, 2016). However, to the best of our knowledge, study investigated the association of unhealthy foods, fruits, and vegetables intakes with diabetes among middle-aged adults in Indonesia was still rare, especially using a national database that represents the Indonesian population. Therefore, the objective of this study was to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia.

METHODS

Study population and design

This study was done using a cross-sectional design to analyze data from the 2018 Indonesia Basic Health Survey (IBHS). Briefly, the IBHS used a two-stage stratified cluster sampling method survey population includes all Indonesian households, representing 26 Provinces and utilizing a sample framework from the national socio-economic survey in March 2018 (Riskesdas, 2018). The target sample included 300,000 households from 30,000 census blocks of the national socio-economic survey framework (Riskesdas, 2018). The total population data of the IBHS were 713,783 people aged ≥15 years (Riskesdas, 2018). The inclusion criteria in this study was individuals aged 45-59. While, subjects were excluded due to extreme values or missing data. Finally, a total of 8477 subjects met the inclusion criteria and included in this study. This study had received ethical approval from the Health Research Ethics Commission, Fakultas Kedokteran, Universitas 'Aisyiyah Yogyakarta No. 1415/KEP-UNISA/VI/2021.

Measurements

The independent variables in study were the consumption of foods; while, the dependent variable was FBG. Fasting blood glucose was analyzed in the laboratory using an enzymatic analysis. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dL) and normal (<125 mg/dL) (Genuth *et al.*, 2003, Riskesdas, 2018). All variables were done by the IBHS. A food frequency questionnaire was used to assess the food intake. The food consumption of unhealthy and healthy food items consumed per day was included carbonated drinks, energy drinks, sweet desserts, beverages, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods, fruits, and vegetables (Riskesdas, 2018). Consumption of unhealthy foods was categorized as frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Fruits and vegetable consumption was categorized into adequate (≥5 servings per day) and inadequate (<5 servings per day) (Riskesdas, 2018). Sociodemographic data (age, gender, education, and place of residence) and lifestyle (smoking status, alcohol intake, and physical activity) were obtained using a structured questionnaire. Smoking is categorized into yes and no. Consumption of alcoholic beverages is categorized into yes and no (Atamni *et al.*, 2016). Gender was categorized as male and female. Education level was categorized as high (completed 12-year compulsory education or bachelor/diploma/higher education graduates) and low (not completed 12-year compulsory education). Residency was categorized as urban and rural.

Smoking status was categorized as yes and no. Alcohol consumption was categorized as yes and no. Physical activity was categorized as low and moderate. Physical activity is categorized as sufficient if doing heavy physical activity and moderate activity for 150 minutes/week (Riskesdas, 2018).

Data analysis

Univariate analysis was presented using mean ± standard deviation for numerical data and frequency (percentage) for categorical data. In addition, bivariate analysis was performed using the Chi-square test. Whereas, multivariate analysis using multiple logistic regression was used to analyze the association of food consumption and FBG. Odds ratio (OR) with 95% confidence intervals was conducted in the analyze. We used unadjusted (model 1) and adjusted (model 2). Model 2 was adjusted for age, gender, residency, smoking status, alcohol consumption, and physical activity. All analyses were performed using the SPSS program 25 version with a *p*-value <0.05 considered statistically significant. We used the dichotomy variable in this study to calculate the OR value. The fasting blood glucose value was categorized as hyperglycemia (≥126 mg/dL) and normal (<125 mg/dL) (Genuth et al., 2003, Riskesdas, 2018). Consumption of unhealthy foods was categorized as frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Fruits and vegetable consumption was categorized into adequate (≥5 servings per day) and inadequate (<5 servings per day) (Riskesdas, 2018). Gender was categorized as male and female. Education level was categorized as high (completed 12-year compulsory education or bachelor/diploma/higher education graduates) and low (not completed 12-year compulsory education). Residency was categorized as urban and rural. Smoking status was categorized as yes and no. Alcohol consumption was categorized as yes and no. Physical activity was categorized as low and moderate, and (Riskesdas, 2018).

RESULTS AND DISCUSSION

Table 1 shows the characteristics of the subjects. Among 8477 subjects, 61% were female, 51.2% lived in rural areas, 32% were smokers, 1.1% consumed alcohol, and 81.7% had high physical activity. Our results also found that the prevalence of hyperglycemia was 43% (Figure 1). The mean FBG was 104.68 ± 31.99 for male and 110.75 ± 43.92 for female subjects. *Physiological changes* associated with *ageing was significantly altered glucose metabolism, which affected the ability of pancreatic β-cells to produce insulin. Insulin is a pancreatic hormone that maintains* *normal blood glucose levels by facilitating cellular glucose uptake* (Niswender, 2011). This study found that the prevalence of hyperglycemia was higher in females (44.6%) than males (40.6%). This result was in line with a previous study. Women are more risk of experiencing hyperglycemia due to the hormonal changes (Association, 2018). Moreover, physical activity in women tends to be lower than in men (Ferreira *et al.*, 2010).

Table 1. Characteristics of the subjects (n=8477).

Variabel	All subjects
Age, years	51.6 ± 4.279
Gender, n(%)	
Male	3259 (38.4)
Female	5218 (61.6)
Education levels, n(%)	
High	2930 (34.6)
Low	5547 (65.4)
Residency, n(%)	
Rural	4341 (51.2)
Urban	4136 (48.8)
Smoking status, n(%)	
No	5741 (67.7)
Yes	2736 (32.3)
Alcohol consumption, n(%)	
No	8383 (98.9)
Yes	94 (1.1)
Physical activity, n(%)	
High	6922 (81.7)
Low	1555 (18.3)
Fasting blood glucose, mg/dL	108.42 ± 39.87

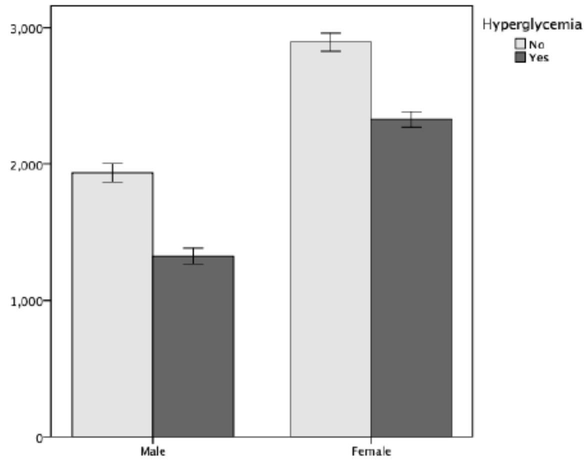

Figure 1. Prevalence of hyperglycemia across gender.

The association of food consumption and hyperglycemia are described in Table 2. The majority of the subjects with hyperglycemia were frequent consumption of carbonated drinks (93.0), sweet desserts (79.8), beverages (84.5), salty foods (71.7), fried foods (85.9), processed foods (80.4), seasonings (89.7), instant foods (51.8), and inadequate consumption of fruits (73.3), and vegetable (82.5).

Table 2. Food consumption and hyperglycemia (N = 8477).

Variables	Hyperglycemia		Total (%)	*p*
	Yes (n = 3648)	No (4829)		
Carbonated drinks, n (%)				0.050
Infrequent	254 (7.0)	379 (7.9)	633 (7.5)	
Frequent	3396 (93.0)	4448 (92.1)	7844 (92.5)	
Energy drinks, n (%)				0.300
Infrequent	187 (5.1)	261 (5.4)	448 (5.3)	
Frequent	3463 (94.9)	4566 (94.6)	8029 (94.7)	
Sweet desserts, n (%)				0.000
Infrequent	736 (20.2)	808 (16.7)	1544 (18.2)	
Frequent	2912 (79.8)	4021 (83.3)	6933 (81.8)	
Beverages, n (%)				0.000
Infrequent	564 (15.5)	546 (11.3)	1110 (13.1)	

Frequent	3086 (84.5)	4281 (88.7)	7367 (86.9)	
Salty foods, n (%)				0.000
Infrequent	1032 (28.9)	1202 (24.9)	2234 (26.4)	
Frequent	2618 (71.7)	3625 (75.1)	6243 (73.6)	
Fried foods, n (%)				0.015
Infrequent	513 (14.1)	591 (12.2)	1104 (13.0)	
Frequent	3137 (85.9)	4236 (87.8)	7373 (87.0)	
Grilled foods, n (%)				0.515
Infrequent	1056 (28.9)	1429 (29.6)	2485 (29.3)	
Frequent	2594 (71.1)	3398 (70.4)	5992 (70.7)	
Processed foods, n (%)				0.035
Infrequent	714 (19.6)	1023 (21.2)	1737 (20.5)	
Frequent	2936 (80.4)	3804 (78.8)	6740 (79.5)	
Seasonings, n (%)				0.020
Infrequent	376 (10.3)	425 (8.8)	801 (9.4)	
Frequent	3274 (89.7)	4402 (91.2)	7676 (90.6)	
Instant foods, n (%)				0.000
Infrequent	1761 (48.2)	2125 (44.0)	3886 (45.8)	
Frequent	1889 (51.8)	2702 (56.0)	4591 (54.2)	
Fruits, n (%)				0.042
Adequate	976 (26.7)	1374 (28.5)	2350 (27.7)	
Inadequate	2674 (73.3)	3453 (71.5)	6127 (72.3)	
Vegetable, n (%)				0.049
Adequate	637 (17.5)	841 (17.4)	1478 (17.4)	
Inadequate	3013 (82.5)	3986 (82.6)	6999 (82.6)	

The odds ratios (95% confidence intervals) for food consumption across hyperglycemia are presented in Table 3. Frequent consumption of carbonated drinks (OR=1.139; CI=0.966-1.343), sweet desserts (OR=1.265; CI=1.132-1.413), beverages (OR=1.433; CI=1.263-1.626), salty foods (OR=1.189; CI=1.079-1.311), fried foods (OR=1.172; CI=1.033-1.331), processed foods (OR=1.106; CI=0.993-1.230), seasonings (OR=1.190; CI=1.028-1.377), instant foods (OR=1.186; CI=1.088-1.293), and inadequate consumption of fruits (OR=1.090; CI=0.990-1.200) and vegetable (OR=1.002; CI=0.920-1.100) were significantly associated with increased crude odds (model 1) of hyperglycemia. After adjusting for age, gender, education levels, residency, smoking status, alcohol consumption, and physical activity (model 2), processed foods, seasonings, and fruits was not significantly associated with hyperglycemia.

Table 3. Odds ratios (95% confidence intervals) for food consumption across hyperglycemia

Variables	Model 1*			Model 2**		
	OR	95% CI	*p*	OR	95% CI	*p*
Carbonated drinks			0.039			0.050
Infrequent	1			1		
Frequent	1.139	0.966 - 1.343		1.073	0.908 - 1.269	
Energy drinks			0.565			0.772
Infrequent	1			1		
Frequent	1.058	0.873 - 1.284		0.971	0.798 - 1.182	
Sweet desserts			0.000	1		0.000
Infrequent	1					
Frequent	1.265	1.132 - 1.413		1.238	1.108 - 1.384	
Beverages			0.000			0.000
Infrequent	1			1		
Frequent	1.433	1.263 - 1.626		1.378	1.213 - 1.567	
Savory foods			0.000			0.000
Infrequent	1			1		
Frequent	1.189	1.079 - 1.311		1.169	1.060 - 1.289	
Fried foods			0.014			0.042
Infrequent	1			1		
Frequent	1.172	1.033 - 1.331		1.142	1.005 - 1.299	
Grilled foods			0.504			0.735
Infrequent	1			1		
Frequent	1.033	0.940 - 1.135		1.017	0.924 - 1.119	
Processed foods			0.036			0.149
Infrequent	1			1		
Frequent	1.106	0.993 - 1.230		1.083	0.972 - 1.206	
Seasonings			0.020			0.052
Infrequent	1			1		

Frequent	1.190	1.028 - 1.377		1.156	0.998 - 1.340	
Instant foods			0.000			0.008
Infrequent	1			1		
Frequent	1.186	1.088 - 1.293		1.127	1.032 - 1.229	
Fruits			0.045			0.051
Adequate	1			1		
Inadequate	1.090	0.990 – 1.200		1.085	0.977 – 1.189	
Vegetables						
Adequate	1		0.036	1		0.041
Inadequate	1.002	0.920 – 1.100		1.090	1.030 – 1.163	

*Model 1 was unadjusted. **Model 2 was adjusted for age, gender, education level, residency, smoking status, alcohol consumption, physical activity.

We found that frequent consumption of sweet desserts and beverages were significantly associated with risk of elevated FBG. Sweet desserts and beverages contained carbohydrates or simple sugars with a high glycemic index (GI) value, leading to accelerated blood sugar levels (Medina-Remón *et al.*, 2018). Other studies found a decrease in endothelial cells' micro and macro cellular function when consuming sweetened sugary beverages (Loader *et al.*, 2017). This metabolic abnormalities are due to the increased in oxidative stress and decreased in NO's (nitric oxide) bioavailability, which plays an important role in glucose metabolism in the body. The decreased in NO bioavailability is also related to risk of developing type 2 diabetes (Loader et al., 2017).

Subjects which frequently consumed salty foods were associated with risk of increased FBG. This result is in line with a previous study. High consumption of salty foods is correlated with an increased risk factor for DM (Fitria *et al.*, 2016). High intake of sodium increases the risk of hyperglycemia through the PPAR δ/adiponectin/SGLT2 mechanism in regulating sodium and glucose homeostasis (Zhao *et al.*, 2016). Furthermore, fried foods are high in fat, including saturated fat and cholesterol. Frequent consumption of fried food will lead to hyperglycemia in the pre-elderly population. A high-fat diet also significantly contributes to obesity and non-insulin-dependent diabetes mellitus (Naja *et al.*, 2013). Previous study found a positive relationship between high intake of saturated fat and cholesterol and increased hyperglycemia and type 2 diabetes in humans and rats (Cahill *et al.*, 2014). Saturated fat in the cell membrane will decrease the viscosity of the lipid bilayer of a cell membrane and lead to a decrease in the insulin receptors (Min *et al.*, 2018).

Frequent consumption of instant foods has a significant relationship with the incidence of hyperglycemia as indicated by an increase in FBG in this study. Our results are consistent with other studies that high intake of instant foods were linked to a higher risk of developing diabetes due to the high carbohydrate and fat (Huh *et al.*, 2017). Current study also found that seasonings such as monosodium glutamate had a significant effect on the incidence of hyperglycemia. However, after adjustment, there is no significant relationship. An animal trial of monosodium glutamate found a significant increase in glucose levels as evidenced by an increase in HOMA-IR value in rats. It is because of the changes in insulin binding or insulin post receptors in the target tissues (Helal *et al.*, 2019). Monosodium glutamate may trigger the degradation of neuronal membranes, allowing calcium ions to enter cells because of its permeability of sodium ions, calcium ions, and water. Then, it might damage the pancreatic gland and hyperglycemia (Jusuf *et al.*, 2020).

Consumption of fruits and vegetables reduced hyperglycemia. Fiber might delay the digestion and absorption of carbohydrates and increase satiety effect. In individuals with insulin resistance, fiber can increase peripheral insulin sensitivity through short-chain fatty acids produced by fiber fermentation in the gut (Mudgil and Samman, 2017). In addition, a diet high in fruits and vegetables is associated with high intake of magnesium and iron (Zhang *et al.*, 2015). Magnesium is an important cofactor for several enzymes in glucose metabolism, which further plays a role in the development of diabetes (Verma and Garg, 2017). In this study, individuals with inadequate consumption of vegetables and fruits were 1.002 and 1.090 times, respectively, more likely to have high FBG than those with adequate consumption of vegetables and fruits.

Some limitations should be mentioned in this study. Firstly, dietary data were taken using a frequency of intake which is no information related to nutrients. Moreover, the cross-sectional design restricts the results in maintaining the causality between the variables. Further research with a priori or a posteriori dietary pattern approach is highly recommended. Additional longitudinal study is needed to explore the mechanism between variables.

CONCLUSION

There was a significant association between food consumption and FBG levels among middle-aged adults in Indonesia. Frequent consumption of carbonated drinks, sweet desserts, beverages, salty foods, fried foods, and instant foods, and inadequate consumption of vegetable on increasing FBG levels and the incidence of hyperglycemia among middle-aged adults in Indonesia. Further research with a priori or a posteriori dietary pattern approach is highly recommended. Additional longitudinal study is needed to explore the mechanism between variables.

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AUTHOR DISCLOSURE

The authors have no conflict of interest.

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Comments for the Editor

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Participants Edit

- Ahmad Syauqy, S.Gz, MPH.,Ph.D (jgpahmadsyauqy)

Messages

Note	From

Dear Prof. Dr. Ir. Dodik Briawan, MCN, *Editor-in-Chief,*

All authors have approved and agreed to submit the manuscript entitled “Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis” to *the Indonesian Journal of Nutrition and Food*. The significance of the results is to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia using a national data analysis. The content of the manuscript is original, it has not been published or accepted for publication, and will not be submitted to any other journals while it is under consideration by *the Indonesian Journal of Nutrition and Food*. All authors read and approved the final version of the manuscript for submission.

If you have any questions, please feel free to contact me. I am looking forward to your response.

Sincerely,
Ahmad Syauqy. (corresponding author)
E-mail: syauqy@fk.undip.ac.id

[JGP] Information & Revision Required

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Participants

- Prof. Dr. Dodik Briawan, MCN (admingizipangan)
- Ahmad Syauqy, S.Gz, MPH.,Ph.D (jgpahmadsyauqy)

Messages

Note	From
Dear Ahmad Syauqy and Team Diponegoro University Good day. Thank you for the submission to our journal. Before we continue to the skimming process by the editorial team, we need you to do some revisions based on JGP format. Kindly see those comments added & track changes that we used in the manuscript. Make sure to click **"accept all changes and stop tracking"** before you do the revision in the manuscript. Reply to all comments and use **green highlight** in the revision part of the manuscript. Send back the revised manuscript by replying to this message no later than **Sunday, 10 July 2022**. Thank you. Regards, -- Secretariat of Indonesian Journal of Nutrition and Food Department of Community Nutrition, Faculty of Human Ecology IPB University, Dramaga, Bogor Indonesia, 16680 E-mail address: jgp@apps.ipb.ac.id Website: http://journal.ipb.ac.id/index.php/jgizipangan [JGP] Manuscript_checked (07072022).docx [JGP] Author Guidelines.pdf [JGP] Manuscript Template.pdf	admingizipangan 2022-07-07 09:02 AM

HASIL REVIEW

Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis

Ahmad Syauqy[1,2*], Siti Andhini Mattarahmawati[1], Adriyan Pramono[1,2]

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ABSTRACT

. The objective of this study was to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia. This study was done using a cross-sectional design to analyze data from the 2018 Indonesia Basic Health Survey (IBHS). A total of 8477 subjects met the inclusion criteria and included in this study. Fasting blood glucose was analyzed in the laboratory using an enzymatic analysis. A food frequency questionnaire was used to assess the food intake. Multivariate analysis using multiple logistic regression was used to analyze the association of food consumption and FBG. Our results found that the prevalence of hyperglycemia was 43%. The mean FBG was 104.68 ± 31.99 for male and 110.75 ± 43.92 for female subjects. Frequent consumption of carbonated drinks (OR=1.139; CI=0.966-1.343), sweet desserts (OR=1.265; CI=1.132-1.413), beverages (OR=1.433; CI=1.263-1.626), salty foods (OR=1.189; CI=1.079-1.311), fried foods (OR=1.172; CI=1.033-1.331), and instant foods (OR=1.186; CI=1.088-1.293), and inadequate consumption of vegetable (OR=1.002; CI=0.920-1.100) were significantly associated with increased crude odds of hyperglycemia. There was a significant association between food consumption and FBG levels among middle-aged adults in Indonesia.

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Keyword: diet, food consumption, hyperglycemia, fasting blood glucose, Indonesia

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Runner Title: Food consumption and hyperglycemia

INTRODUCTION

Non-communicable diseases are the leading cause of public health problems in developed and developing countries (Naghavi M 2017). Diabetes, one of the non-communicable diseases, is the main cause of death in the world (Zheng *et al.* 2018). Diabetes or hyperglycemia is characterized by an increase in blood sugar levels in the body. Previous studies found that the prevalence of hyperglycemia and the components of metabolic syndrome increased rapidly with age in women and men (Wu *et al.* 2017, Jiang *et al.* 2018). Recently, Indonesia is the fourth country after India, China, and America, with the most diabetes sufferers globally (Naghavi M 2017). The prevalence of diabetes in Indonesia was around 6% (Mihardja *et al.* 2014). Interestingly, based on the 2018 Indonesia Basic Health Survey (IBHS), the higher prevalence of diabetes was among middle-aged adults with almost 10% (Riskesdas 2018).

Diabetes is caused by many factors such as lifestyle (Kufe *et al.* 2015). Sedentary lifestyle has associated with the increasing trend of diabetes (Nurwanti *et al.* 2018). Previous study also found that diet was associated with the increased prevalence of diabetes (Lambrinou *et al.* 2019). Nowadays, Indonesian people tend to consume high western foods and low fruits and vegetables (Riskesdas, 2018). Western foods or unhealthy foods are correlated with an increased prevalence of hyperglycemia and metabolic syndrome (Syauqy *et al.* 2018). Furthermore, inadequate consumption of vegetables and fruits can also escalate the diabetes prevalence (Syauqy *et al*. 2018, Schwingshackl *et al.* 2017).

Western foods or unhealthy foods is consisted of sweet, sugar, fat, beverages, fried foods, and seasoning. Some studies have found the association between food consumption and metabolic syndrome among middle-aged adults in Taiwan (Syauqy *et al.* 2018). Moreover, middle-aged adults who consumed high fruits and vegetables and less unhealthy foods had a better quality of life (Lo *et al.* 2016). However, to the best of our knowledge, study investigated the association of unhealthy foods, fruits, and vegetables intakes with diabetes among middle-aged adults in Indonesia was still rare, especially using a national database that represents the Indonesian population. Therefore, the objective of this study was to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia.

METHODS

Design, location, and time

This study was done using a cross-sectional design to analyze data from the 2018 Indonesia Basic Health Survey (IBHS). Briefly, the IBHS used a two-stage stratified cluster sampling method survey population includes all Indonesian households, representing 26 Provinces and utilizing a sample framework from the national socio-economic survey in March 2018 (Riskesdas 2018). The target sample included 300,000 households from 30,000 census blocks of the national socio-economic survey framework (Riskesdas 2018). The total population data of the IBHS were 713,783 people aged ≥15 years (Riskesdas 2018). The inclusion criteria in this study was individuals aged 45-59. While, subjects were excluded due to extreme values or missing data. Finally, a total of 8477 subjects met the inclusion criteria and included in this study. This study had received ethical approval from the Health Research Ethics Commission, Fakultas Kedokteran, Universitas 'Aisyiyah Yogyakarta No. 1415/KEP-UNISA/VI/2021.

Measurements

The independent variables in study were the consumption of foods; while, the dependent variable was FBG. Fasting blood glucose was analyzed in the laboratory using an enzymatic analysis. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dL) and normal (<125 mg/dL) (Genuth *et al.* 2003; Riskesdas 2018). All variables were done by the IBHS. A food frequency questionnaire was used to assess the food intake. The food consumption of unhealthy and healthy food items consumed per day was included carbonated drinks, energy drinks, sweet desserts, beverages, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods, fruits, and vegetables (Riskesdas 2018). Consumption of unhealthy foods was categorized as frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Fruits and vegetable consumption was categorized into adequate (≥5 servings per day) and inadequate (<5 servings per day) (Riskesdas 2018). Sociodemographic data (age, gender, education, and place of residence) and lifestyle (smoking status, alcohol intake, and physical activity) were obtained using a structured questionnaire. Smoking is categorized into yes and no. Consumption of alcoholic beverages is categorized into yes and no (Atamni *et al.* 2016). Gender was categorized as male and female. Education level was categorized as high (completed 12-year compulsory education or bachelor/diploma/higher education graduates) and low (not completed 12-year compulsory education). Residency was categorized as urban and rural. Smoking status

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4. Data analysis

was categorized as yes and no. Alcohol consumption was categorized as yes and no. Physical activity was categorized as low and moderate. Physical activity is categorized as sufficient if doing heavy physical activity and moderate activity for 150 minutes/week (Riskesdas 2018).

Data analysis

Univariate analysis was presented using mean ± standard deviation for numerical data and frequency (percentage) for categorical data. In addition, bivariate analysis was performed using the Chi-square test. Whereas, multivariate analysis using multiple logistic regression was used to analyze the association of food consumption and FBG. Odds ratio (OR) with 95% confidence intervals was conducted in the analyze. We used unadjusted (model 1) and adjusted (model 2). Model 2 was adjusted for age, gender, residency, smoking status, alcohol consumption, and physical activity. All analyses were performed using the SPSS program 25 version with a *p*-value <0.05 considered statistically significant. We used the dichotomy variable in this study to calculate the OR value. The fasting blood glucose value was categorized as hyperglycemia (≥126 mg/dL) and normal (<125 mg/dL) (Genuth *et al.* 2003; Riskesdas 2018). Consumption of unhealthy foods was categorized as frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Fruits and vegetable consumption was categorized into adequate (≥5 servings per day) and inadequate (<5 servings per day) (Riskesdas 2018). Gender was categorized as male and female. Education level was categorized as high (completed 12-year compulsory education or bachelor/diploma/higher education graduates) and low (not completed 12-year compulsory education). Residency was categorized as urban and rural. Smoking status was categorized as yes and no. Alcohol consumption was categorized as yes and no. Physical activity was categorized as low and moderate, and (Riskesdas 2018).

RESULTS AND DISCUSSION

Table 1 shows the characteristics of the subjects. Among 8477 subjects, 61% were female, 51.2% lived in rural areas, 32% were smokers, 1.1% consumed alcohol, and 81.7% had high physical activity. Our results also found that the prevalence of hyperglycemia was 43% (Figure 1). The mean FBG was 104.68±31.99 for male and 110.75±43.92 for female subjects. *Physiological changes* associated with *ageing was significantly altered glucose metabolism, which affected the ability of pancreatic β-cells to produce insulin. Insulin is a pancreatic hormone that maintains normal blood glucose levels by facilitating cellular glucose uptake* (Niswender 2011). This study found that the prevalence of hyperglycemia was higher in females (44.6%) than males (40.6%). This result was in line with a previous study. Women are more risk of experiencing hyperglycemia due to the hormonal changes (Association 2018). Moreover, physical activity in women tends to be lower than in men (Ferreira *et al.* 2010).

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Table 1. Characteristics of the subjects (n=8477).

Variabel	All subjects
Age, years	51.6 ± 4.279
Gender, n(%)	
Male	3259 (38.4)
Female	5218 (61.6)
Education levels, n(%)	
High	2930 (34.6)
Low	5547 (65.4)
Residency, n(%)	
Rural	4341 (51.2)
Urban	4136 (48.8)
Smoking status, n(%)	
No	5741 (67.7)
Yes	2736 (32.3)
Alcohol consumption, n(%)	
No	8383 (98.9)
Yes	94 (1.1)
Physical activity, n(%)	
High	6922 (81.7)
Low	1555 (18.3)
Fasting blood glucose, mg/dL	108.42 ± 39.87

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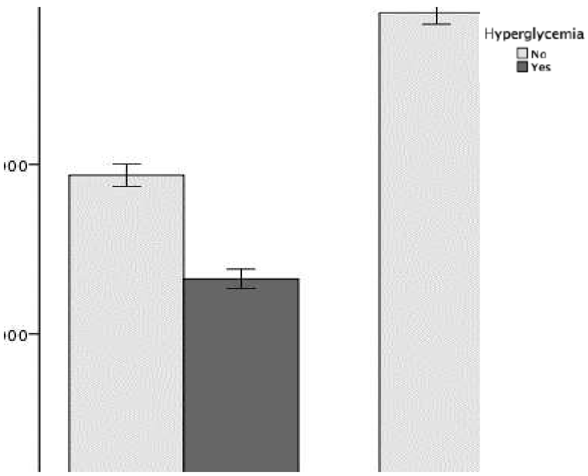

Figure 1. Prevalence of hyperglycemia across gender.

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The association of food consumption and hyperglycemia are described in Table 2. The majority of the subjects with hyperglycemia were frequent consumption of carbonated drinks (93.0), sweet desserts (79.8), beverages (84.5), salty foods (71.7), fried foods (85.9), processed foods (80.4), seasonings (89.7), instant foods (51.8), and inadequate consumption of fruits (73.3), and vegetable (82.5).

Table 2. Food consumption and hyperglycemia (N = 8477).

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Variables	Hyperglycemia		Total (%)	*p*
	Yes (n = 3648)	No (4829)		
Carbonated drinks, n (%)				0.050
Infrequent	254 (7.0)	379 (7.9)	633 (7.5)	
Frequent	3396 (93.0)	4448 (92.1)	7844 (92.5)	
Energy drinks, n (%)				0.300
Infrequent	187 (5.1)	261 (5.4)	448 (5.3)	
Frequent	3463 (94.9)	4566 (94.6)	8029 (94.7)	
Sweet desserts, n (%)				0.000
Infrequent	736 (20.2)	808 (16.7)	1544 (18.2)	
Frequent	2912 (79.8)	4021 (83.3)	6933 (81.8)	
Beverages, n (%)				0.000
Infrequent	564 (15.5)	546 (11.3)	1110 (13.1)	

Frequent	3086 (84.5)	4281 (88.7)	7367 (86.9)	
Salty foods, n (%)				0.000
Infrequent	1032 (28.9)	1202 (24.9)	2234 (26.4)	
Frequent	2618 (71.7)	3625 (75.1)	6243 (73.6)	
Fried foods, n (%)				0.015
Infrequent	513 (14.1)	591 (12.2)	1104 (13.0)	
Frequent	3137 (85.9)	4236 (87.8)	7373 (87.0)	
Grilled foods, n (%)				0.515
Infrequent	1056 (28.9)	1429 (29.6)	2485 (29.3)	
Frequent	2594 (71.1)	3398 (70.4)	5992 (70.7)	
Processed foods, n (%)				0.035
Infrequent	714 (19.6)	1023 (21.2)	1737 (20.5)	
Frequent	2936 (80.4)	3804 (78.8)	6740 (79.5)	
Seasonings, n (%)				0.020
Infrequent	376 (10.3)	425 (8.8)	801 (9.4)	
Frequent	3274 (89.7)	4402 (91.2)	7676 (90.6)	
Instant foods, n (%)				0.000
Infrequent	1761 (48.2)	2125 (44.0)	3886 (45.8)	
Frequent	1889 (51.8)	2702 (56.0)	4591 (54.2)	
Fruits, n (%)				0.042
Adequate	976 (26.7)	1374 (28.5)	2350 (27.7)	
Inadequate	2674 (73.3)	3453 (71.5)	6127 (72.3)	
Vegetable, n (%)				0.049
Adequate	637 (17.5)	841 (17.4)	1478 (17.4)	
Inadequate	3013 (82.5)	3986 (82.6)	6999 (82.6)	

The odds ratios (95% confidence intervals) for food consumption across hyperglycemia are presented in Table 3. Frequent consumption of carbonated drinks (OR=1.139; CI=0.966-1.343), sweet desserts (OR=1.265; CI=1.132-1.413), beverages (OR=1.433; CI=1.263-1.626), salty foods (OR=1.189; CI=1.079-1.311), fried foods (OR=1.172; CI=1.033-1.331), processed foods (OR=1.106; CI=0.993-1.230), seasonings (OR=1.190; CI=1.028-1.377), instant foods (OR=1.186; CI=1.088-1.293), and inadequate consumption of fruits (OR=1.090; CI=0.990-1.200) and vegetable (OR=1.002; CI=0.920-1.100) were significantly associated with increased crude odds (model 1) of hyperglycemia. After adjusting for age, gender, education levels, residency, smoking status, alcohol consumption, and physical activity (model 2), processed foods, seasonings, and fruits was not significantly associated with hyperglycemia.

Table 3. Odds ratios (95% confidence intervals) for food consumption across hyperglycemia

Variables	Model 1*			Model 2**		
	OR	95% CI	*p*	OR	95% CI	*p*
Carbonated drinks			0.039			0.050
Infrequent	1			1		
Frequent	1.139	0.966 - 1.343		1.073	0.908 - 1.269	
Energy drinks			0.565			0.772
Infrequent	1			1		
Frequent	1.058	0.873 - 1.284		0.971	0.798 - 1.182	
Sweet desserts			0.000	1		0.000
Infrequent	1					
Frequent	1.265	1.132 - 1.413		1.238	1.108 - 1.384	
Beverages			0.000			0.000
Infrequent	1			1		
Frequent	1.433	1.263 - 1.626		1.378	1.213 - 1.567	
Savory foods			0.000			0.000
Infrequent	1			1		
Frequent	1.189	1.079 - 1.311		1.169	1.060 - 1.289	
Fried foods			0.014			0.042
Infrequent	1			1		
Frequent	1.172	1.033 - 1.331		1.142	1.005 - 1.299	
Grilled foods			0.504			0.735
Infrequent	1			1		
Frequent	1.033	0.940 - 1.135		1.017	0.924 - 1.119	
Processed foods			0.036			0.149
Infrequent	1			1		
Frequent	1.106	0.993 - 1.230		1.083	0.972 - 1.206	
Seasonings			0.020			0.052
Infrequent	1			1		

Frequent	1.190	1.028 - 1.377		1.156	0.998 - 1.340	
Instant foods			0.000			0.008
Infrequent	1			1		
Frequent	1.186	1.088 - 1.293		1.127	1.032 - 1.229	
Fruits			0.045			0.051
Adequate	1			1		
Inadequate	1.090	0.990 – 1.200		1.085	0.977 – 1.189	
Vegetables						
Adequate	1		0.036	1		0.041
Inadequate	1.002	0.920 – 1.100		1.090	1.030 – 1.163	

*Model 1 was unadjusted. **Model 2 was adjusted for age, gender, education level, residency, smoking status, alcohol consumption, physical activity.

We found that frequent consumption of sweet desserts and beverages were significantly associated with risk of elevated FBG. Sweet desserts and beverages contained carbohydrates or simple sugars with a high Glycemic Index (GI) value, leading to accelerated blood sugar levels (Medina-Remón *et al.* 2018). Other studies found a decrease in endothelial cells' micro and macro cellular function when consuming sweetened sugary beverages (Loader *et al.* 2017). This metabolic abnormalities are due to the increased in oxidative stress and decreased in NO's (nitric oxide) bioavailability, which plays an important role in glucose metabolism in the body. The decreased in NO bioavailability is also related to risk of developing type 2 diabetes (Loader *et al.* 2017).

Subjects which frequently consumed salty foods were associated with risk of increased FBG. This result is in line with a previous study. High consumption of salty foods is correlated with an increased risk factor for DM (Fitria *et al.* 2016). High intake of sodium increases the risk of hyperglycemia through the PPAR δ/adiponectin/SGLT2 mechanism in regulating sodium and glucose homeostasis (Zhao *et al.* 2016). Furthermore, fried foods are high in fat, including saturated fat and cholesterol. Frequent consumption of fried food will lead to hyperglycemia in the pre-elderly population. A high-fat diet also significantly contributes to obesity and non-insulin-dependent diabetes mellitus (Naja *et al.* 2013). Previous study found a positive relationship between high intake of saturated fat and cholesterol and increased hyperglycemia and type 2 diabetes in humans and rats (Cahill *et al.* 2014). Saturated fat in the cell membrane will decrease the viscosity of the lipid bilayer of a cell membrane and lead to a decrease in the insulin receptors (Min *et al.* 2018).

Frequent consumption of instant foods has a significant relationship with the incidence of hyperglycemia as indicated by an increase in FBG in this study. Our results are consistent with other studies that high intake of instant foods were linked to a higher risk of developing diabetes due to the high carbohydrate and fat (Huh *et al.* 2017). Current study also found that seasonings such as monosodium glutamate had a significant effect on the incidence of hyperglycemia. However, after adjustment, there is no significant relationship. An animal trial of monosodium glutamate found a significant increase in glucose levels as evidenced by an increase in HOMA-IR value in rats. It is because of the changes in insulin binding or insulin post receptors in the target tissues (Helal *et al.* 2019). Monosodium glutamate may trigger the degradation of neuronal membranes, allowing calcium ions to enter cells because of its permeability of sodium ions, calcium ions, and water. Then, it might damage the pancreatic gland and hyperglycemia (Jusuf *et al.* 2020).

Consumption of fruits and vegetables reduced hyperglycemia. Fiber might delay the digestion and absorption of carbohydrates and increase satiety effect. In individuals with insulin resistance, fiber can increase peripheral insulin sensitivity through short-chain fatty acids produced by fiber fermentation in the gut (Mudgil & Samman 2017). In addition, a diet high in fruits and vegetables is associated with high intake of magnesium and iron (Zhang *et al.* 2015). Magnesium is an important cofactor for several enzymes in glucose metabolism, which further plays a role in the development of diabetes (Verma & Garg 2017). In this study, individuals with inadequate consumption of vegetables and fruits were 1.002 and 1.090 times, respectively, more likely to have high FBG than those with adequate consumption of vegetables and fruits.

Some limitations should be mentioned in this study. Firstly, dietary data were taken using a frequency of intake which is no information related to nutrients. Moreover, the cross-sectional design restricts the results in maintaining the causality between the variables. Further research with a priori or a posteriori dietary pattern approach is highly recommended. Additional longitudinal study is needed to explore the mechanism between variables.

CONCLUSION

There was a significant association between food consumption and FBG levels among middle-aged adults in Indonesia. Frequent consumption of carbonated drinks, sweet desserts, beverages, salty foods, fried foods, and instant foods, and inadequate consumption of vegetable on increasing FBG levels and the incidence of hyperglycemia among middle-aged adults in Indonesia. Further research with a priori or a posteriori dietary pattern approach is highly recommended. Additional longitudinal study is needed to explore the mechanism between variables.

ACKNOWLEDGMENT

We would like to thank Faculty of Medicine (UPPP), Diponegoro University (1149/UN7.5.4.2.1/PP/PM/2020)

DECLARATION OF INTERESTS

The authors have no conflict of interest.

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HASIL PERBAIKAN ARTIKEL

Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis

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ABSTRACT

The objective of this study was to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia. This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS). A total of 8477 subjects met the inclusion criteria and included in this study. Fasting blood glucose (FBG) was analyzed in the laboratory using an enzymatic analysis. A food frequency questionnaire was used to assess the food intake. Multivariate analysis using multiple logistic regression was used to analyze the association of food consumption and FBG. Our results found that the prevalence of hyperglycemia in this population was 43%. The mean FBG was 104.68 ± 31.99 for male and 110.75 ± 43.92 for female subjects. Frequent consumption of carbonated drinks (OR=1.139; CI=0.966-1.343), sweet desserts (OR=1.265; CI=1.132-1.413), beverages (OR=1.433; CI=1.263-1.626), salty foods (OR=1.189; CI=1.079-1.311), fried foods (OR=1.172; CI=1.033-1.331), and instant foods (OR=1.186; CI=1.088-1.293), and inadequate consumption of vegetable (OR=1.002; CI=0.920-1.100) were significantly associated with increased odds of hyperglycemia. There was a significant association between food consumption and FBG levels among middle-aged adults in Indonesia.

Keyword: diet, food consumption, hyperglycemia, fasting blood glucose, Indonesia

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Runner Title: Food consumption and hyperglycemia

INTRODUCTION

Non-communicable diseases are the leading cause of public health problems in developed and developing countries (Naghavi M 2017). Diabetes, one of the non-communicable diseases, is the main cause of death in the world (Zheng *et al.* 2018). Diabetes or hyperglycemia is characterized by an increase in blood sugar levels in the body. Previous studies found that the prevalence of hyperglycemia and the components of metabolic syndrome increased rapidly with age in women and men (Wu *et al.* 2017, Jiang *et al.* 2018). Recently, Indonesia is the fourth country after India, China, and America, with the most diabetes sufferers globally (Naghavi M 2017). The prevalence of diabetes in Indonesia was around 6% (Mihardja *et al.* 2014). Interestingly, based on the 2018 Indonesia Basic Health Survey (IBHS), the higher prevalence of diabetes was among middle-aged adults with almost 10% (MoH 2018).

Diabetes is caused by many factors such as lifestyle (Sudargo *et al.* 2018). Sedentary lifestyle has associated with the increasing trend of diabetes (Nurwanti *et al.* 2018). Previous study also found that diet was associated with the increased prevalence of diabetes (Lambrinou *et al.* 2019). Nowadays, Indonesian people tend to consume high western foods and low fruits and vegetables (MoH 2018). Western foods or unhealthy foods are correlated with an increased prevalence of hyperglycemia and metabolic syndrome (Syauqy *et al.* 2018). Furthermore, inadequate consumption of vegetables and fruits can also escalate the diabetes prevalence (Syauqy *et al*. 2018; Schwingshackl *et al.* 2017).

Western foods or unhealthy foods is consisted of sweet, sugar, fat, beverages, fried foods, and seasoning. Some studies have found the association between food consumption and metabolic syndrome among middle-aged adults in Taiwan (Syauqy *et al*. 2018). Moreover, middle-aged adults who consumed high fruits and vegetables and less unhealthy foods had a better quality of life (Lo *et al.* 2016). However, to the best of our knowledge, study investigated the association of unhealthy foods, fruits, and vegetables intakes with diabetes among middle-aged adults in Indonesia was still rare, especially using a national database that represents the Indonesian population. Therefore, the objective of this study was to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia.

METHODS

Design, location, and time

This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS). Briefly, the IBHS used a two-stage stratified cluster sampling method survey population includes all Indonesian households, representing 26 Provinces and utilizing a sample framework from the national socio-economic survey in March 2018 (MoH 2018).

Sampling

The target sample included 300,000 households from 30,000 census blocks of the national socio-economic survey framework (MoH 2018). The total population data of the IBHS were 713,783 people aged ≥15 years (MoH 2018). The inclusion criteria in this study was individuals aged 45-59. While, subjects were excluded due to extreme values or missing data. Finally, a total of 8477 subjects met the inclusion criteria and included in this study. This study had received ethical approval from the Health Research Ethics Commission, Medical Faculty, Universitas 'Aisyiyah Yogyakarta No. 1415/KEP-UNISA/VI/2021.

Data Collection

The independent variables in study were the consumption of foods; while, the dependent variable was FBG. Fasting blood glucose was analyzed in the laboratory using an enzymatic analysis. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dL) and normal (<125 mg/dL) (Genuth *et al.* 2003; MoH 2018). All variables were done by the IBHS. A food frequency questionnaire was used to assess the food intake. The food consumption of unhealthy and healthy food items consumed per day was included carbonated drinks, energy drinks, sweet desserts, beverages, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods, fruits, and vegetables (MoH 2018). Consumption of unhealthy foods was categorized as frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Fruits and vegetable consumption was categorized into adequate (≥5 servings per day) and inadequate (<5 servings per day) (MoH 2018). Sociodemographic data (age, gender, education, and place of residence) and lifestyle (smoking status, alcohol intake, and physical activity) were obtained using a structured questionnaire. Smoking is categorized into yes and no. Consumption of alcoholic beverages is categorized into yes and no (Atamni *et al.* 2016). Gender was categorized as male and female. Education level was categorized as high (completed 12-year compulsory education or bachelor/diploma/higher education graduates) and low (not completed 12-year compulsory education). Residency was categorized as urban and rural. Smoking status was categorized as yes and no. Alcohol consumption was categorized as yes and no. Physical activity was categorized as low and moderate. Physical activity is categorized as sufficient if doing heavy physical activity and moderate activity for 150 minutes/week (MoH 2018).

Data analysis

Univariate analysis was presented using mean ± standard deviation for numerical data and frequency (percentage) for categorical data. In addition, bivariate analysis was performed using the Chi-square test. Whereas, multivariate analysis using multiple logistic regression was used to analyze the association of food consumption and FBG. Odds ratio (OR) with 95% confidence intervals was conducted in the analyze. We used unadjusted (model 1) and adjusted (model 2). Model 2 was adjusted for age, gender, residency, smoking status, alcohol consumption, and physical activity. All analyses were performed using the SPSS program 25 version with a *p*-value <0.05 considered statistically significant. We used the dichotomy variable in this study to calculate the OR value. The fasting blood glucose value was categorized as hyperglycemia (≥126 mg/dL) and normal (<125 mg/dL) (Genuth et al. 2003, MoH 2018). Consumption of unhealthy foods was categorized as frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Fruits and vegetable consumption was categorized into adequate (≥5 servings per day) and inadequate (<5 servings per day) (MoH 2018). Gender was categorized as male and female. Education level was categorized as high (completed 12-year compulsory education or bachelor/diploma/higher education graduates) and low (not completed 12-year compulsory education). Residency was categorized as urban and rural. Smoking status was categorized as yes and no. Alcohol consumption was categorized as yes and no. Physical activity was categorized as low and moderate, and (MoH 2018).

RESULTS AND DISCUSSION

Table 1 shows the characteristics of the subjects. Among 8477 subjects, 61.6% were female, 51.2% lived in rural areas, 32.3% were smokers, 1.1% consumed alcohol, and 18.3% had high physical activity. Our results also found that the prevalence of hyperglycemia in the population was 43% (Figure 1). The mean FBG was 104.68±31.99 for male and 110.75±43.92 for female subjects. *Physiological change* associated with *ageing was significantly altered glucose metabolism, which affected the ability of pancreatic β-cells to produce insulin. Insulin is a* *pancreatic hormone that maintains normal blood glucose levels by facilitating cellular glucose uptake* (Niswender 2011). This study found that the prevalence of hyperglycemia was higher in females (44.6%) than males (40.6%). This result was in line with a previous study. Women are more risk of experiencing hyperglycemia due to the hormonal changes (American Diabetes Association 2018). Moreover, physical activity in women tends to be lower than in men (The Lancet Public Health 2019).

Table 1. Characteristics of the subjects (n=8,477).

Variabel	All subjects
Age, years	51.6 ± 4.279
Gender, n(%)	
Male	3,259 (38.4)
Female	5,218 (61.6)
Education levels, n(%)	
High	2,930 (34.6)
Low	5,547 (65.4)
Residency, n(%)	
Rural	4,341 (51.2)
Urban	4,136 (48.8)
Smoking status, n(%)	
No	5,741 (67.7)
Yes	2,736 (32.3)
Alcohol consumption, n(%)	
No	8,383 (98.9)
Yes	94 (1.1)
Physical activity, n(%)	
High	6,922 (81.7)
Low	1,555 (18.3)
Fasting blood glucose, mg/dL	108.42 ± 39.87

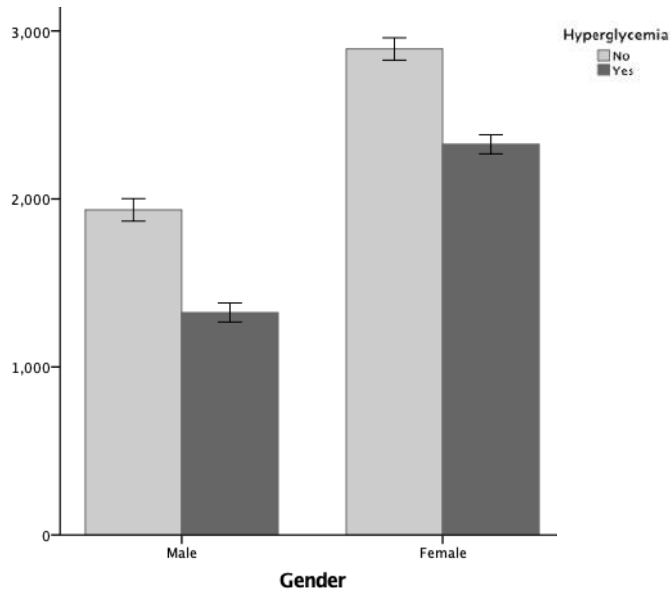

Figure 1. Prevalence of hyperglycemia across gender.

The association of food consumption and hyperglycemia are described in Table 2. The majority of the subjects with hyperglycemia were frequent consumption of carbonated drinks (93.0), sweet desserts (79.8), beverages (84.5), salty foods (71.7), fried foods (85.9), processed foods (80.4), seasonings (89.7), instant foods (51.8), and inadequate consumption of fruits (73.3), and vegetable (82.5).

Table 2. Food consumption and hyperglycemia (N = 8,477).

Variables	Hyperglycemia		Total (%)	*p*
	Yes (n = 3,648)	No (4,829)		
Carbonated drinks, n (%)				0.050
Infrequent	254 (7.0)	379 (7.9)	633 (7.5)	
Frequent	3,396 (93.0)	4,448 (92.1)	7,844 (92.5)	
Energy drinks, n (%)				0.300
Infrequent	187 (5.1)	261 (5.4)	448 (5.3)	
Frequent	3,463 (94.9)	4,566 (94.6)	8,029 (94.7)	
Sweet desserts, n (%)				0.000
Infrequent	736 (20.2)	8,08 (16.7)	1,544 (18.2)	

Frequent	2,912 (79.8)	4,021 (83.3)	6,933 (81.8)	
Beverages, n (%)				0.000
Infrequent	564 (15.5)	546 (11.3)	1,110 (13.1)	
Frequent	3,086 (84.5)	4,281 (88.7)	7,367 (86.9)	
Salty foods, n (%)				0.000
Infrequent	1,032 (28.9)	1,202 (24.9)	2,234 (26.4)	
Frequent	2,618 (71.7)	3,625 (75.1)	6,243 (73.6)	
Fried foods, n (%)				0.015
Infrequent	513 (14.1)	591 (12.2)	1,104 (13.0)	
Frequent	3,137 (85.9)	4,236 (87.8)	7,373 (87.0)	
Grilled foods, n (%)				0.515
Infrequent	1,056 (28.9)	1,429 (29.6)	2,485 (29.3)	
Frequent	2,594 (71.1)	3,398 (70.4)	5,992 (70.7)	
Processed foods, n (%)				0.035
Infrequent	714 (19.6)	1,023 (21.2)	1,737 (20.5)	
Frequent	2,936 (80.4)	3,804 (78.8)	6,740 (79.5)	
Seasonings, n (%)				0.020
Infrequent	376 (10.3)	425 (8.8)	801 (9.4)	
Frequent	3,274 (89.7)	4,402 (91.2)	7,676 (90.6)	
Instant foods, n (%)				0.000
Infrequent	1,761 (48.2)	2,125 (44.0)	3,886 (45.8)	
Frequent	1,889 (51.8)	2,702 (56.0)	4,591 (54.2)	
Fruits, n (%)				0.042
Adequate	976 (26.7)	1,374 (28.5)	2,350 (27.7)	
Inadequate	2,674 (73.3)	3,453 (71.5)	6,127 (72.3)	
Vegetable, n (%)				0.049
Adequate	637 (17.5)	841 (17.4)	1,478 (17.4)	
Inadequate	3,013 (82.5)	3,986 (82.6)	6,999 (82.6)	

The odds ratios (95% confidence intervals) for food consumption across hyperglycemia are presented in Table 3. Frequent consumption of carbonated drinks (OR=1.139; CI=0.966-1.343), sweet desserts (OR=1.265; CI=1.132-1.413), beverages (OR=1.433; CI=1.263-1.626), salty foods (OR=1.189; CI=1.079-1.311), fried foods (OR=1.172; CI=1.033-1.331), processed foods

(OR=1.106; CI=0.993-1.230), seasonings (OR=1.190; CI=1.028-1.377), instant foods (OR=1.186; CI=1.088-1.293), and inadequate consumption of fruits (OR=1.090; CI=0.990-1.200) and vegetable (OR=1.002; CI=0.920-1.100) were significantly associated with increased crude odds (model 1) of hyperglycemia. After adjusting for age, gender, education levels, residency, smoking status, alcohol consumption, and physical activity (model 2), processed foods, seasonings, and fruits were not significantly associated with hyperglycemia.

Table 3. Odds ratios (95% confidence intervals) for food consumption across hyperglycemia

Variables	Model 1*			Model 2**		
	OR	95% CI	*p*	OR	95% CI	*p*
Carbonated drinks			0.039			0.050
Infrequent	1			1		
Frequent	1.139	0.966 - 1.343		1.073	0.908 - 1.269	
Energy drinks			0.565			0.772
Infrequent	1			1		
Frequent	1.058	0.873 - 1.284		0.971	0.798 - 1.182	
Sweet desserts			0.000	1		0.000
Infrequent	1					
Frequent	1.265	1.132 - 1.413		1.238	1.108 - 1.384	
Beverages			0.000			0.000
Infrequent	1			1		
Frequent	1.433	1.263 - 1.626		1.378	1.213 - 1.567	
Savory foods			0.000			0.000
Infrequent	1			1		
Frequent	1.189	1.079 - 1.311		1.169	1.060 - 1.289	
Fried foods			0.014			0.042
Infrequent	1			1		
Frequent	1.172	1.033 - 1.331		1.142	1.005 - 1.299	
Grilled foods			0.504			0.735
Infrequent	1			1		
Frequent	1.033	0.940 - 1.135		1.017	0.924 - 1.119	
Processed foods			0.036			0.149

Infrequent	1			1		
Frequent	1.106	0.993 - 1.230		1.083	0.972 - 1.206	
Seasonings			0.020			0.052
Infrequent	1			1		
Frequent	1.190	1.028 - 1.377		1.156	0.998 - 1.340	
Instant foods			0.000			0.008
Infrequent	1			1		
Frequent	1.186	1.088 - 1.293		1.127	1.032 - 1.229	
Fruits			0.045			0.051
Adequate	1			1		
Inadequate	1.090	0.990 – 1.200		1.085	0.977 – 1.189	
Vegetables						
Adequate	1		0.036	1		0.041
Inadequate	1.002	0.920 – 1.100		1.090	1.030 – 1.163	

*Model 1 was unadjusted. **Model 2 was adjusted for age, gender, education level, residency, smoking status, alcohol consumption, physical activity.

We found that frequent consumption of sweet desserts and beverages were significantly associated with risk of elevated FBG. Sweet desserts and beverages contained carbohydrates or simple sugars with a high Glycemic Index (GI) value, leading to accelerated blood sugar levels (Medina-Remón *et al.* 2018). Other studies found a decrease in endothelial cells' micro and macro cellular function when consuming sweetened sugary beverages (Loader *et al.* 2017). These metabolic abnormalities are due to the increased in oxidative stress and decreased in NO's (nitric oxide) bioavailability, which plays an important role in glucose metabolism in the body. The decreased in NO bioavailability is also related to risk of developing type 2 diabetes (Loader *et al*. 2017).

Subjects which frequently consumed salty foods were associated with risk of increased FBG. This result is in line with a previous study. High consumption of salty foods is correlated with an increased risk factor for DM (Fitria *et al.* 2016). High intake of sodium increases the risk of hyperglycemia through the PPAR δ/adiponectin/SGLT2 mechanism in regulating sodium and glucose homeostasis (Zhao *et al.* 2016). Furthermore, fried foods are high in fat, including saturated fat and cholesterol. Frequent consumption of fried food will lead to hyperglycemia in the pre-elderly population. A high-fat diet also significantly contributes to obesity and non-insulin-dependent diabetes mellitus (Naja *et al.* 2013). Previous study found a positive relationship between high intake of saturated fat and cholesterol and increased hyperglycemia and type 2 diabetes in humans and rats (Cahill *et al.* 2014). Saturated fat in the cell membrane will decrease the viscosity of the lipid bilayer of a cell membrane and lead to a decrease in the insulin receptors (Min *et al.* 2018).

Frequent consumption of instant foods had a significant relationship with the incidence of hyperglycemia as indicated by an increase in FBG in this study. Our results are consistent with other studies that high intake of instant foods were linked to a higher risk of developing diabetes due to the high carbohydrate and fat (Huh *et al.* 2017). Current study also found that seasonings such as monosodium glutamate had a significant effect on the incidence of hyperglycemia. However, after adjustment, there was no significant relationship. An animal trial of monosodium glutamate found a significant increase in glucose levels as evidenced by an increase in HOMA-IR value in rats. It is because of the changes in insulin binding or insulin post receptors in the target tissues (Helal *et al.* 2019). Monosodium glutamate may trigger the degradation of neuronal membranes, allowing calcium ions to enter cells because of its permeability of sodium ions, calcium ions, and water. Then, it might damage the pancreatic gland and hyperglycemia (Jusuf *et al.* 2020).

Consumption of fruits and vegetables reduced hyperglycemia. Fiber might delay the digestion and absorption of carbohydrates and increase satiety effect. In individuals with insulin resistance, fiber can increase peripheral insulin sensitivity through short-chain fatty acids produced by fiber fermentation in the gut (Samaan 2017) . In addition, a diet high in fruits and vegetables is associated with high intake of magnesium and iron (Zhang *et al.* 2015). Magnesium is an important cofactor for several enzymes in glucose metabolism, which further plays a role in the development of diabetes (Verma & Garg 2017). In this study, individuals with inadequate consumption of vegetables and fruits were 1.002 and 1.090 times, respectively, more likely to have high FBG than those with adequate consumption of vegetables and fruits.

Some limitations should be mentioned in this study. Firstly, dietary data were taken using a frequency of intake which is no information related to nutrients. Moreover, the cross-sectional design restricts the results in maintaining the causality between the variables. Further research with a priori or a posteriori dietary pattern approach is highly recommended. Additional longitudinal study is needed to explore the mechanism between variables.

CONCLUSION

There was a significant association between food consumption and FBG levels among middle-aged adults in Indonesia. Frequent consumption of carbonated drinks, sweet desserts, beverages, salty foods, fried foods, and instant foods, and inadequate consumption of vegetable on increasing FBG levels and the incidence of hyperglycemia among middle-aged adults in Indonesia. Further research with a priori or a posteriori dietary pattern approach is highly recommended. Additional longitudinal study is needed to explore the mechanism between variables.

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DECLARATION OF INTERESTS

The authors have no conflict of interest.

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[JGP] Editor Decision

Close Panel

Participants

- Prof. Dr. Dodik Briawan, MCN (admingizipangan)
- Ahmad Syauqy, S.Gz, MPH.,Ph.D (jgpahmadsyauqy)

Messages

Note	From
Dear Ahmad Syauqy and team Good day. Herewith this, we would like to inform you that your manuscript entitled "***Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis"*** with the authors of Ahmad Syauqy, Siti Andhini Mattarahmawati, dan Adriyan Pramono has been passed the preliminary review process with major revision. First, please read all the comments added in the manuscript. Do not forget to reply to all comments both in the manuscript and the author's revision form and do revision as advised. Second, we need your help to mention **2 recommended names of reviewers** (with min. H-index 3 in Scopus) with their full names, email, and phone numbers (please do not recommend any reviewer from Dept. of Community Nutrition, IPB University). Last, fill in all the author's signatures for the author's statement letter. Send back **the revised manuscript, the author's revision form, the author's statement letter,** and **the information of the reviewers** no later than **Monday, 18 July 2022** by replying to this message. Do not hesitate to contact our secretariat for further information. Thank you for your cooperation.	admingizipangan 2022-07-11 02:42 PM

Note	From

Regards,

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Kepada Yth.
Sdr. Ahmad Syauqy dan tim penulis
Diponegoro University

Bersama ini disampaikan bahwa naskah saudara yang berjudul ***"Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis"*** dengan penulis Ahmad Syauqy, Siti Andhini Mattarahmawati, dan Adriyan Pramono telah kami terima. Dengan ini disampaikan bahwa naskah tersebut telah lolos penelahaan awal. Untuk dilakukan penelahaan lebih lanjut oleh mitra bestari, kami mohon saudara (1) dapat memperbaiki naskah tersebut sesuai saran perbaikan terlampir, dan (2) menandatangani surat pernyataan penulis.

Atas perhatian dan kerjasama yang baik disampaikan terima kasih.

Ketua Redaksi
Jurnal Gizi dan Pangan

Prof Dr Ir Dodik Briawan, MCN

SARAN PERBAIKAN

Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis

ABSTRACT

The objective of this study was to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia. This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS). A total of 8477 subjects met the inclusion criteria and included in this study. Fasting blood glucose (FBG) was analyzed in the laboratory using an enzymatic analysis. A food frequency questionnaire was used to assess the food intake. Multivariate analysis using multiple logistic regression was used to analyze the association of food consumption and FBG. Our results found that the prevalence of hyperglycemia in this population was 43%. The mean FBG was 104.68 ± 31.99 for male and 110.75 ± 43.92 for female subjects. Frequent consumption of carbonated drinks (OR=1.139; CI=0.966-1.343), sweet desserts (OR=1.265; CI=1.132-1.413), beverages (OR=1.433; CI=1.263-1.626), salty foods (OR=1.189; CI=1.079-1.311), fried foods (OR=1.172; CI=1.033-1.331), and instant foods (OR=1.186; CI=1.088-1.293), and inadequate consumption of vegetable (OR=1.002; CI=0.920-1.100) were significantly associated with increased odds of hyperglycemia. There was a significant association between food consumption and FBG levels among middle-aged adults in Indonesia.

Keyword: diet, food consumption, hyperglycemia, fasting blood glucose, Indonesia

Runner Title: Food consumption and hyperglycemia

INTRODUCTION

Non-communicable diseases are the leading cause of public health problems in developed and developing countries (Naghavi M 2017). Diabetes, one of the non-communicable diseases, is the main cause of death in the world (Zheng *et al.* 2018). Diabetes or hyperglycemia is characterized by an increase in blood sugar levels in the body. Previous studies found that the prevalence of hyperglycemia and the components of metabolic syndrome increased rapidly with

age in women and men (Wu *et al.* 2017, Jiang *et al.* 2018). Recently, Indonesia is the fourth country after India, China, and America, with the most diabetes sufferers globally (Naghavi M 2017). The prevalence of diabetes in Indonesia was around 6% (Mihardja *et al.* 2014). Interestingly, based on the 2018 Indonesia Basic Health Survey (IBHS), the higher prevalence of diabetes was among middle-aged adults with almost 10% (MoH RI 2018).

Diabetes is caused by many factors such as lifestyle (Sudargo *et al.* 2018). Sedentary lifestyle has associated with the increasing trend of diabetes (Nurwanti *et al.* 2018). Previous study also found that diet was associated with the increased prevalence of diabetes (Lambrinou *et al.* 2019). Nowadays, Indonesian people tend to consume high western foods and low fruits and vegetables (MoH 2018). Western foods or unhealthy foods are correlated with an increased prevalence of hyperglycemia and metabolic syndrome (Syauqy *et al.* 2018). Furthermore, inadequate consumption of vegetables and fruits can also escalate the diabetes prevalence (Syauqy *et al*. 2018; Schwingshackl *et al.* 2017).

Western foods or unhealthy foods is consisted of sweet, sugar, fat, beverages, fried foods, and seasoning. Some studies have found the association between food consumption and metabolic syndrome among middle-aged adults in Taiwan (Syauqy *et al*. 2018). Moreover, middle-aged adults who consumed high fruits and vegetables and less unhealthy foods had a better quality of life (Lo *et al.* 2016). However, to the best of our knowledge, study investigated the association of unhealthy foods, fruits, and vegetables intakes with diabetes among middle-aged adults in Indonesia was still rare, especially using a national database that represents the Indonesian population. Therefore, the objective of this study was to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia.

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METHODS

Design, location, and time

This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS). Briefly, the IBHS used a two-stage stratified cluster sampling method survey population includes all Indonesian households, representing 26 Provinces and utilizing a sample framework from the national socio-economic survey in March 2018 (MoH RI 2018).

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Sampling

The target sample included 300,000 households from 30,000 census blocks of the national socio-economic survey framework (MoH RI 2018). The total population data of the IBHS were 713,783 people aged ≥15 years (MoH RI 2018). The inclusion criteria in this study was individuals aged 45-59. While, subjects were excluded due to extreme values or missing data. Finally, a total of 8477 subjects met the inclusion criteria and included in this study. This study had received ethical approval from the Health Research Ethics Commission, Medical Faculty, Universitas 'Aisyiyah Yogyakarta No. 1415/KEP-UNISA/VI/2021.

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Data collection

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The independent variables in study were the consumption of foods; while, the dependent variable was FBG. Fasting blood glucose was analyzed in the laboratory using an enzymatic analysis. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dL) and normal (<125 mg/dL) (Genuth *et al.* 2003; MoH RI 2018). All variables were done by the IBHS. A food frequency questionnaire was used to assess the food intake. The food consumption of unhealthy and healthy food items consumed per day was included carbonated drinks, energy drinks, sweet desserts, beverages, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods, fruits, and vegetables (MoH RI 2018). Consumption of unhealthy foods was categorized as frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Fruits and vegetable consumption was categorized into adequate (≥5 servings per day) and inadequate (<5 servings per day) (MoH RI 2018). Sociodemographic data (age, gender, education, and place of residence) and lifestyle (smoking status, alcohol intake, and physical activity) were obtained using a structured questionnaire. Smoking is categorized into yes and no. Consumption of alcoholic beverages is categorized into yes and no (Atamni *et al.* 2016). Gender was categorized as male and female. Education level was categorized as high (completed 12-year compulsory education or bachelor/diploma/higher education graduates) and low (not completed 12-year compulsory education). Residency was categorized as urban and rural. Smoking status was categorized as yes and no. Alcohol consumption was categorized as yes and no. Physical activity was categorized as low and moderate. Physical activity is categorized as sufficient if doing heavy physical activity and moderate activity for 150 minutes/week (MoH RI 2018).

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Data analysis

Univariate analysis was presented using mean ± standard deviation for numerical data and frequency (percentage) for categorical data. In addition, bivariate analysis was performed using the Chi-square test. Whereas, multivariate analysis using multiple logistic regression was used to analyze the association of food consumption and FBG. Odds ratio (OR) with 95% confidence intervals was conducted in the analyze. We used unadjusted (model 1) and adjusted (model 2). Model 2 was adjusted for age, gender, residency, smoking status, alcohol consumption, and physical activity. All analyses were performed using the SPSS program 25 version with a *p*-value <0.05 considered statistically significant. We used the dichotomy variable in this study to calculate the OR value. The fasting blood glucose value was categorized as hyperglycemia (≥126 mg/dL) and normal (<125 mg/dL) (Genuth *et al*. 2003; MoH RI 2018). Consumption of unhealthy foods was categorized as frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Fruits and vegetable consumption was categorized into adequate (≥5 servings per day) and inadequate (<5 servings per day) (MoH RI 2018). Gender was categorized as male and female. Education level was categorized as high (completed 12-year compulsory education or bachelor/diploma/higher education graduates) and low (not completed 12-year compulsory education). Residency was categorized as urban and rural. Smoking status was categorized as yes and no. Alcohol consumption was categorized as yes and no. Physical activity was categorized as low and moderate, and (MoH RI 2018).

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RESULTS AND DISCUSSION

Table 1 shows the characteristics of the subjects. Among 8477 subjects, 61.6% were female, 51.2% lived in rural areas, 32.3% were smokers, 1.1% consumed alcohol, and 18.3% had high physical activity. Our results also found that the prevalence of hyperglycemia in the population was 43% (Figure 1). The mean FBG was 104.68±31.99 for male and 110.75±43.92 for female subjects. *Physiological change* associated with *ageing was significantly altered glucose metabolism, which affected the ability of pancreatic β-cells to produce insulin. Insulin is a pancreatic hormone that maintains normal blood glucose levels by facilitating cellular glucose uptake* (Niswender 2011). This study found that the prevalence of hyperglycemia was higher in females (44.6%) than males (40.6%). This result was in line with a previous study. Women are more risk of experiencing hyperglycemia due to the hormonal changes (American Diabetes

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Association 2018). Moreover, physical activity in women tends to be lower than in men (The Lancet Public Health 2019).

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Table 1. Characteristics of the subjects (n=8,477).

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Variabel	All subjects
Age, years	51.6 ± 4.279
Gender, n(%)	
Male	3,259 (38.4)
Female	5,218 (61.6)
Education levels, n(%)	
High	2,930 (34.6)
Low	5,547 (65.4)
Residency, n(%)	
Rural	4,341 (51.2)
Urban	4,136 (48.8)
Smoking status, n(%)	
No	5,741 (67.7)
Yes	2,736 (32.3)
Alcohol consumption, n(%)	
No	8,383 (98.9)
Yes	94 (1.1)
Physical activity, n(%)	
High	6,922 (81.7)
Low	1,555 (18.3)
Fasting blood glucose, mg/dL	108.42 ± 39.87

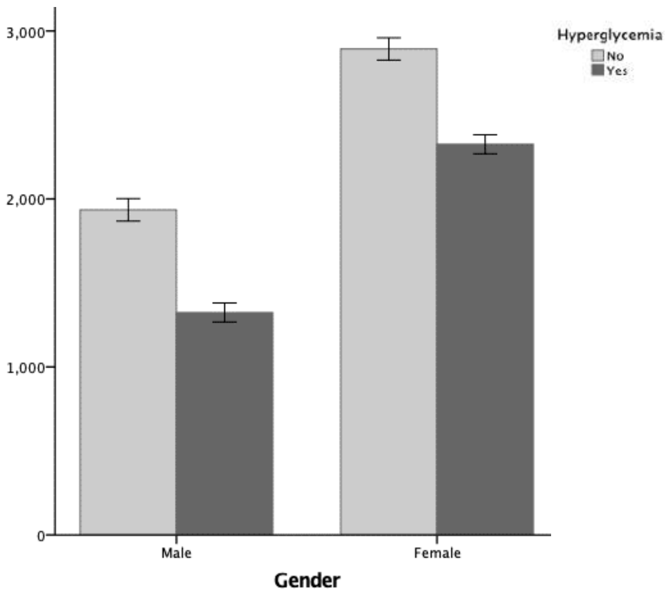

Figure 1. Prevalence of hyperglycemia across gender.

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The association of food consumption and hyperglycemia are described in Table 2. The majority of the subjects with hyperglycemia were frequent consumption of carbonated drinks (93.0), sweet desserts (79.8), beverages (84.5), salty foods (71.7), fried foods (85.9), processed foods (80.4), seasonings (89.7), instant foods (51.8), and inadequate consumption of fruits (73.3), and vegetable (82.5).

Table 2. Food consumption and hyperglycemia (N = 8,477).

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Variables	Hyperglycemia		Total (%)	*p*
	Yes (n = 3,648)	No (4,829)		
Carbonated drinks, n (%)				0.050
Infrequent	254 (7.0)	379 (7.9)	633 (7.5)	
Frequent	3,396 (93.0)	4,448 (92.1)	7,844 (92.5)	
Energy drinks, n (%)				0.300
Infrequent	187 (5.1)	261 (5.4)	448 (5.3)	
Frequent	3,463 (94.9)	4,566 (94.6)	8,029 (94.7)	
Sweet desserts, n (%)				0.000
Infrequent	736 (20.2)	8,08 (16.7)	1,544 (18.2)	

Frequent	2,912 (79.8)	4,021 (83.3)	6,933 (81.8)	
Beverages, n (%)				0.000
Infrequent	564 (15.5)	546 (11.3)	1,110 (13.1)	
Frequent	3,086 (84.5)	4,281 (88.7)	7,367 (86.9)	
Salty foods, n (%)				0.000
Infrequent	1,032 (28.9)	1,202 (24.9)	2,234 (26.4)	
Frequent	2,618 (71.7)	3,625 (75.1)	6,243 (73.6)	
Fried foods, n (%)				0.015
Infrequent	513 (14.1)	591 (12.2)	1,104 (13.0)	
Frequent	3,137 (85.9)	4,236 (87.8)	7,373 (87.0)	
Grilled foods, n (%)				0.515
Infrequent	1,056 (28.9)	1,429 (29.6)	2,485 (29.3)	
Frequent	2,594 (71.1)	3,398 (70.4)	5,992 (70.7)	
Processed foods, n (%)				0.035
Infrequent	714 (19.6)	1,023 (21.2)	1,737 (20.5)	
Frequent	2,936 (80.4)	3,804 (78.8)	6,740 (79.5)	
Seasonings, n (%)				0.020
Infrequent	376 (10.3)	425 (8.8)	801 (9.4)	
Frequent	3,274 (89.7)	4,402 (91.2)	7,676 (90.6)	
Instant foods, n (%)				0.000
Infrequent	1,761 (48.2)	2,125 (44.0)	3,886 (45.8)	
Frequent	1,889 (51.8)	2,702 (56.0)	4,591 (54.2)	
Fruits, n (%)				0.042
Adequate	976 (26.7)	1,374 (28.5)	2,350 (27.7)	
Inadequate	2,674 (73.3)	3,453 (71.5)	6,127 (72.3)	
Vegetable, n (%)				0.049
Adequate	637 (17.5)	841 (17.4)	1,478 (17.4)	
Inadequate	3,013 (82.5)	3,986 (82.6)	6,999 (82.6)	

Commented [A29]: The % should be row %

The odds ratios (95% confidence intervals) for food consumption across hyperglycemia are presented in Table 3. Frequent consumption of carbonated drinks (OR=1.139; CI=0.966-1.343), sweet desserts (OR=1.265; CI=1.132-1.413), beverages (OR=1.433; CI=1.263-1.626), salty foods (OR=1.189; CI=1.079-1.311), fried foods (OR=1.172; CI=1.033-1.331), processed foods

(OR=1.106; CI=0.993-1.230), seasonings (OR=1.190; CI=1.028-1.377), instant foods (OR=1.186; CI=1.088-1.293), and inadequate consumption of fruits (OR=1.090; CI=0.990-1.200) and vegetable (OR=1.002; CI=0.920-1.100) were significantly associated with increased crude odds (model 1) of hyperglycemia. After adjusting for age, gender, education levels, residency, smoking status, alcohol consumption, and physical activity (model 2), processed foods, seasonings, and fruits were not significantly associated with hyperglycemia.

Commented [A30]: Correct them after double check Table 3

Table 3. Odds ratios (95% confidence intervals) for food consumption across hyperglycemia

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Variables	Model 1*			Model 2**		
	OR	95% CI	*p*	OR	95% CI	*p*
Carbonated drinks			0.039			0.050
Infrequent	1			1		
Frequent	1.139	0.966 - 1.343		1.073	0.908 - 1.269	
Energy drinks			0.565			0.772
Infrequent	1			1		
Frequent	1.058	0.873 - 1.284		0.971	0.798 - 1.182	
Sweet desserts			0.000	1		0.000
Infrequent	1					
Frequent	1.265	1.132 - 1.413		1.238	1.108 - 1.384	
Beverages			0.000			0.000
Infrequent	1			1		
Frequent	1.433	1.263 - 1.626		1.378	1.213 - 1.567	
Savory foods			0.000			0.000
Infrequent	1			1		
Frequent	1.189	1.079 - 1.311		1.169	1.060 - 1.289	
Fried foods			0.014			0.042
Infrequent	1			1		
Frequent	1.172	1.033 - 1.331		1.142	1.005 - 1.299	
Grilled foods			0.504			0.735
Infrequent	1			1		
Frequent	1.033	0.940 - 1.135		1.017	0.924 - 1.119	
Processed foods			0.036			0.149

Infrequent	1			1		
Frequent	1.106	0.993 - 1.230		1.083	0.972 - 1.206	
Seasonings			0.020			0.052
Infrequent	1			1		
Frequent	1.190	1.028 - 1.377		1.156	0.998 - 1.340	
Instant foods			0.000			0.008
Infrequent	1			1		
Frequent	1.186	1.088 - 1.293		1.127	1.032 - 1.229	
Fruits			0.045			0.051
Adequate	1			1		
Inadequate	1.090	0.990 – 1.200		1.085	0.977 – 1.189	
Vegetables						
Adequate	1		0.036	1		0.041
Inadequate	1.002	0.920 – 1.100		1.090	1.030 – 1.163	

*Model 1 was unadjusted. **Model 2 was adjusted for age, gender, education level, residency, smoking status, alcohol consumption, physical activity.

We found that frequent consumption of sweet desserts and beverages were significantly associated with risk of elevated FBG. Sweet desserts and beverages contained carbohydrates or simple sugars with a high Glycemic Index (GI) value, leading to accelerated blood sugar levels (Medina-Remón *et al.* 2018). Other studies found a decrease in endothelial cells' micro and macro cellular function when consuming sweetened sugary beverages (Loader *et al.* 2017). These metabolic abnormalities are due to the increased in oxidative stress and decreased in NO's (nitric oxide) bioavailability, which plays an important role in glucose metabolism in the body. The decreased in NO bioavailability is also related to risk of developing type 2 diabetes (Loader *et al*. 2017).

Subjects which frequently consumed salty foods were associated with risk of increased FBG. This result is in line with a previous study. High consumption of salty foods is correlated with an increased risk factor for DM (Fitria *et al.* 2016). High intake of sodium increases the risk of hyperglycemia through the PPAR δ/adiponectin/SGLT2 mechanism in regulating sodium and glucose homeostasis (Zhao *et al.* 2016). Furthermore, fried foods are high in fat, including saturated fat and cholesterol. Frequent consumption of fried food will lead to hyperglycemia in the

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pre-elderly population. A high-fat diet also significantly contributes to obesity and non-insulin-dependent diabetes mellitus (Naja *et al.* 2013). Previous study found a positive relationship between high intake of saturated fat and cholesterol and increased hyperglycemia and type 2 diabetes in humans and rats (Cahill *et al.* 2014). Saturated fat in the cell membrane will decrease the viscosity of the lipid bilayer of a cell membrane and lead to a decrease in the insulin receptors (Min *et al.* 2018).

Frequent consumption of instant foods had a significant relationship with the incidence of hyperglycemia as indicated by an increase in FBG in this study. Our results are consistent with other studies that high intake of instant foods were linked to a higher risk of developing diabetes due to the high carbohydrate and fat (Huh *et al.* 2017). Current study also found that seasonings such as monosodium glutamate had a significant effect on the incidence of hyperglycemia. However, after adjustment, there was no significant relationship. An animal trial of monosodium glutamate found a significant increase in glucose levels as evidenced by an increase in HOMA-IR value in rats. It is because of the changes in insulin binding or insulin post receptors in the target tissues (Helal *et al.* 2019). Monosodium glutamate may trigger the degradation of neuronal membranes, allowing calcium ions to enter cells because of its permeability of sodium ions, calcium ions, and water. Then, it might damage the pancreatic gland and hyperglycemia (Jusuf *et al.* 2020).

Consumption of fruits and vegetables reduced hyperglycemia. Fiber might delay the digestion and absorption of carbohydrates and increase satiety effect. In individuals with insulin resistance, fiber can increase peripheral insulin sensitivity through short-chain fatty acids produced by fiber fermentation in the gut (Samaan 2017) . In addition, a diet high in fruits and vegetables is associated with high intake of magnesium and iron (Zhang *et al.* 2015). Magnesium is an important cofactor for several enzymes in glucose metabolism, which further plays a role in the development of diabetes (Verma & Garg 2017). In this study, individuals with inadequate consumption of vegetables and fruits were 1.002 and 1.090 times, respectively, more likely to have high FBG than those with adequate consumption of vegetables and fruits.

Some limitations should be mentioned in this study. Firstly, dietary data were taken using a frequency of intake which is no information related to nutrients. Moreover, the cross-sectional design restricts the results in maintaining the causality between the variables. Further research with

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CONCLUSION

There was a significant association between food consumption and FBG levels among middle-aged adults in Indonesia. Frequent consumption of carbonated drinks, sweet desserts, beverages, salty foods, fried foods, and instant foods, and inadequate consumption of vegetable on increasing FBG levels and the incidence of hyperglycemia among middle-aged adults in Indonesia. Further research with a priori or a posteriori dietary pattern approach is highly recommended. Additional longitudinal study is needed to explore the mechanism between variables.

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DECLARATION OF INTERESTS

The authors have no conflict of interest.

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JGP Technical Editor: Assessment Guideline
(Preliminary Review)

Manuscript Title : Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis

No	Guideline for Editor	Comments
1	Is the manuscript within JGP scope?	Yes
2	Is the manuscript using appropriate, clear and sufficient English language?	Still need refinement
3	Is the title suitable and does it clearly state the content of the manuscript?	Somewhat. In most the article, the author refers to FBG
4	Is the abstract concise and does it appropriately describe the following the IMRAD guideline?	Yes
5	Does the introduction describe problem(s), scope of field, and objective(s) clearly?	Need more literature on the current food consumption
6	Is the method written clearly and does it make experiment repeatable and consider ethical rules?	Need more explanation. No information about ethical consideration
7	Is the statistical method appropriate?	Yes
8	Is the content of the table(s) and figure(s) (if any) appropriate as well as easy to understand?	Figure and Table need double check
9	Does the discussion clearly explained and showed any relation to results and research questions?	Could be improved better by deeper synthesis of the findings in relation to the literature
10	Does the conclusion communicate clearly?	Yes
11.	Please attach the manuscript with comments and activate the "track changes" function.	Yes
12.	Use relatively new references (should be from the last 10 years), with the ratio of primary references of about 80%.	Yes

Your recommendation (click in one of the boxes below):

☐ a. Accepted
☐ b. Accepted pending with minor revision
☒ c. Will be reconsidered after major revision

Jakarta, 11 July 2022
Editor.

(Signed)

Settings

Dear Prof. Dr. Ir. Dodik Briawan, MCN, *Editor-in-Chief*

Many thanks for the editors' suggestions and comments. We have revised throughout the manuscript entitled "Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis" according to the editors' comments and suggestions. We also checked and revised some grammatical errors in the manuscript. Please find **the revised manuscript, the author's revision form, the author's statement letter, and the information of the reviewers** in the attachment.

If you have any questions, please feel free to call me at +6224-76402881 (syauqy@fk.undip.ac.id). I am looking forward to your response. Thank you.

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HASIL PERBAIKAN

Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis

ABSTRACT

The objective of this study was to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia. This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS). A total of 8477 subjects met the inclusion criteria and included in this study. Fasting blood glucose (FBG) was analyzed in the laboratory using an enzymatic analysis. A food frequency questionnaire was used to assess the food intake. Multivariate analysis using multiple logistic regression was used to analyze the association of food consumption and FBG. Our results found that the prevalence of hyperglycemia in this population was 43%. The mean FBG was 104.68 ± 31.99 for male and 110.75 ± 43.92 for female subjects. Frequent consumption of carbonated drinks (OR=1.139; CI=0.966-1.343), sweet desserts (OR=1.265; CI=1.132-1.413), beverages (OR=1.433; CI=1.263-1.626), salty foods (OR=1.189; CI=1.079-1.311), fried foods (OR=1.172; CI=1.033-1.331), and instant foods (OR=1.186; CI=1.088-1.293), and inadequate consumption of vegetable (OR=1.002; CI=0.920-1.100) were significantly associated with increased odds of hyperglycemia. There was a significant association between food consumption and FBG levels among middle-aged adults in Indonesia.

Keyword: diet, food consumption, hyperglycemia, fasting blood glucose, Indonesia

Runner Title: Food consumption and hyperglycemia

INTRODUCTION

Non-communicable diseases are the leading cause of public health problems in developed and developing countries (Naghavi M 2017). Diabetes, one of the non-communicable diseases, is the main cause of death in the world (Zheng *et al.* 2018). Diabetes or hyperglycemia is characterized by an increase in blood sugar levels in the body. Previous studies found that the prevalence of hyperglycemia and the components of metabolic syndrome increased rapidly with age in women and men (Wu *et al.* 2017, Jiang *et al.* 2018). Recently, Indonesia is the fourth country after India, China, and America, with the most diabetes sufferers globally (Naghavi M 2017). The prevalence of diabetes in Indonesia was around 6% (Mihardja *et al.* 2014). Interestingly, based on the 2018 Indonesia Basic Health Survey (IBHS), the higher prevalence of diabetes was among middle-aged adults with almost 10% (MoH 2018).

Diabetes is caused by many factors including lifestyle (Sudargo *et al.* 2018). Sedentary lifestyle has associated with the increasing trend of diabetes (Nurwanti *et al.* 2018). Previous study also found that diet was associated with the increased prevalence of diabetes (Lambrinou *et al.* 2019). Western foods or unhealthy foods are correlated with an increased prevalence of hyperglycemia and metabolic syndrome (Syauqy *et al.* 2018). Western foods or unhealthy foods is consisted of sweet, sugar, fat, beverages, fried foods, and seasoning; hence, the unhealthy food is high in simple carbohydrate, saturated fat, and sodium. Furthermore, inadequate consumption of vegetables and fruits can also escalate the diabetes prevalence (Syauqy *et al*. 2018, Schwingshackl *et al.* 2017).

Some studies have found the association between food consumption and metabolic syndrome among middle-aged adults in Taiwan (Syauqy *et al*. 2018). Moreover, middle-aged adults who consumed high fruits and vegetables and less unhealthy foods had a better quality of life (Lo *et al.* 2016). Nowadays, a research found that Indonesian people tend to consume high western foods and low fruits and vegetables (MoH 2018). However, to the best of our knowledge, study investigated the association of unhealthy foods, fruits, and vegetables intakes with diabetes among middle-aged adults in Indonesia was still rare, especially using a national database that represents the Indonesian population. Therefore, the objective of this study was to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia.

METHODS

Design, location, and time

This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS). Briefly, the IBHS used a two-stage stratified cluster sampling method survey population includes all Indonesian households, representing 26 Provinces and utilizing a sample framework from the national socio-economic survey in March 2018 (MoH 2018).

The target sample included 300,000 households from 30,000 census blocks of the national socio-economic survey framework (MoH 2018). The total population data of the IBHS were

713,783 people aged ≥15 years (MoH 2018). The inclusion criteria in this study were individuals aged 45-59 years, had completed data of foods consumption, had completed data on fasting blood glucose, and agreed and had given their written informed consent. While, subjects were excluded due to extreme values or missing data. Finally, a total of 8477 subjects met the inclusion criteria and included in this study. This study had received ethical approval from the Health Research Ethics Commission, Medical Faculty, Universitas 'Aisyiyah Yogyakarta No. 1415/KEP-UNISA/VI/2021.

Procedures

The independent variables in study were the consumption of foods; while, the dependent variable was hyperglycemia status. Fasting blood glucose were measured with fingertip capillary blood tests (Accu-Chek Performa, Roche Diagnostics GmbH, Mannheim, Germany). All participants were instructed to fast overnight before blood sampling. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dL) and normal (<125 mg/dL) (Genuth *et al.* 2003, MoH 2018). A food frequency questionnaire was used to assess the food intake. The food consumption of unhealthy and healthy food items consumed per day was included carbonated drinks, energy drinks, sweet desserts, beverages, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods, fruits, and vegetables (MoH 2018). Consumption of unhealthy foods was categorized as frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Fruits and vegetable consumption was categorized into adequate (≥5 servings per day) and inadequate (<5 servings per day) (MoH 2018). Sociodemographic data (age, gender, education, and place of residence) and lifestyle (smoking status, alcohol intake, and physical activity) were obtained using a structured questionnaire. Smoking is categorized into yes and no. Consumption of alcoholic beverages is categorized into yes and no (Atamni *et al.* 2016). Gender was categorized as male and female. Education level was categorized as high (completed 12-year compulsory education or bachelor/diploma/higher education graduates) and low (not completed 12-year compulsory education). Residency was categorized as urban and rural. Physical activity was categorized as low and moderate. Physical activity is categorized as sufficient if doing heavy physical activity and moderate activity for 150 minutes/week (MoH 2018).

Data analysis

Univariate analysis was presented using mean ± standard deviation for numerical data and frequency (percentage) for categorical data. In addition, bivariate analysis was performed using the Chi-square test. Whereas, multivariate analysis using multiple logistic regression was used to analyze the association of food consumption and hyperglycemia status. Odds ratio (OR) with 95% confidence intervals was conducted in the analyze. We used unadjusted (model 1) and adjusted (model 2). Model 2 was adjusted for age, gender, residency, smoking status, alcohol consumption, and physical activity. All analyses were performed using the SPSS program 25 version with a *p*-value <0.05 considered statistically significant.

RESULTS AND DISCUSSION

Table 1 shows the characteristics of the subjects. Among 8477 subjects, 61.6% were female, 51.2% lived in rural areas, 32.3% were smokers, 1.1% consumed alcohol, and 18.3% had high physical activity. Our results also found that the prevalence of hyperglycemia in the population was 43% (Figure 1). The mean FBG was 104.68±31.99 for male and 110.75±43.92 for female subjects. This study also found that the prevalence of hyperglycemia was higher in females (44.6%) than males (40.6%). This result was in line with a previous study. Women are more risk of experiencing hyperglycemia due to the hormonal changes (Association 2018). Moreover, physical activity in women tends to be lower than in men (The Lancet Public Health 2019).

Table 1. Characteristics of the subjects (n=8,477).

Variabel	All subjects
Age, years	51.6 ± 4.279
Gender, n(%)	
Male	3,259 (38.4)
Female	5,218 (61.6)
Education levels, n(%)	
High	2,930 (34.6)
Low	5,547 (65.4)
Residency, n(%)	
Rural	4,341 (51.2)
Urban	4,136 (48.8)
Smoking status, n(%)	

No	5,741 (67.7)
Yes	2,736 (32.3)
Alcohol consumption, n(%)	
No	8,383 (98.9)
Yes	94 (1.1)
Physical activity, n(%)	
High	6,922 (81.7)
Low	1,555 (18.3)
Fasting blood glucose, mg/dL	108.42 ± 39.87

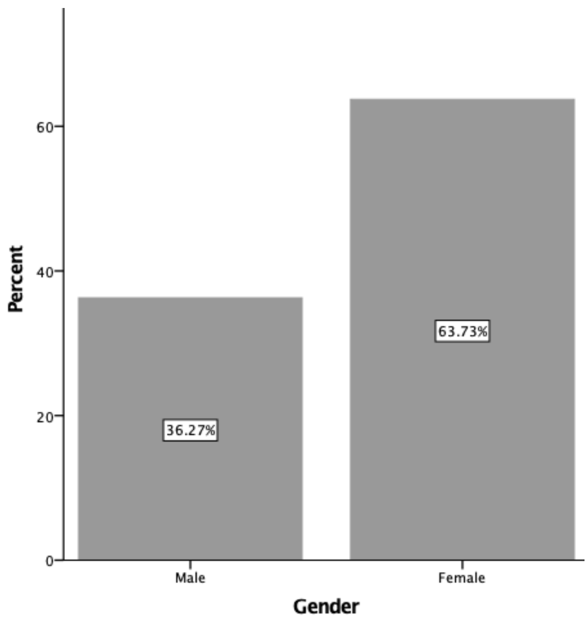

Figure 1. Prevalence of hyperglycemia across gender.

The association of food consumption and hyperglycemia are described in Table 2. The majority of the subjects with hyperglycemia were frequent consumption of carbonated drinks (43.4), sweet desserts (42.0), beverages (41.9), salty foods (41.9), fried foods (42.5), processed foods (43.6), seasonings (42.6), instant foods (41.1), and inadequate consumption of fruits (43.6), and vegetable (43.0).

Table 2. Food consumption and hyperglycemia (N = 8,477).

Variables	Hyperglycemia		Total (%)	*p*
	Yes (n = 3,648)	No (4,829)		
Carbonated drinks, n (%)				0.050
Infrequent	254 (40.1)	379 (59.9)	633 (100)	
Frequent	3,396 (43.3)	4,448 (56.7)	7,844 (100)	
Energy drinks, n (%)				0.300
Infrequent	187 (41.7)	261 (58.3)	448 (100)	
Frequent	3,463 (43.1)	4,566 (56.9)	8,029 (100)	
Sweet desserts, n (%)				0.000
Infrequent	736 (47.8)	808 (52.2)	1,544 (100)	
Frequent	2,912 (42.0)	4,021 (58.0)	6,933 (100)	
Beverages, n (%)				0.000
Infrequent	564 (50.8)	546 (49.2)	1,110 (100)	
Frequent	3,086 (41.9)	4,281 (58.1)	7,367 (100)	
Salty foods, n (%)				0.000
Infrequent	1,032 (46.2)	1,202 (53.8)	2,234 (100)	
Frequent	2,618 (41.9)	3,625 (58.1)	6,243 (100)	
Fried foods, n (%)				0.015
Infrequent	513 (46.5)	591 (53.5)	1,104 (100)	
Frequent	3,137 (42.5)	4,236 (57.5)	7,373 (100)	
Grilled foods, n (%)				0.515
Infrequent	1,056 (42.5)	1,429 (57.5)	2,485 (100)	
Frequent	2,594 (43.3)	3,398 (56.7)	5,992 (100)	
Processed foods, n (%)				0.035
Infrequent	714 (41.1)	1,023 (58.9)	1,737 (100)	
Frequent	2,936 (43.6)	3,804 (56.4)	6,740 (100)	
Seasonings, n (%)				0.020
Infrequent	376 (46.9)	425 (53.1)	801 (100)	
Frequent	3,274 (42.6)	4,402 (57.4)	7,676 (100)	
Instant foods, n (%)				0.000
Infrequent	1,761 (45.3)	2,125 (54.7)	3,886 (100)	
Frequent	1,889 (41.1)	2,702 (58.9)	4,591 (100)	
Fruits, n (%)				0.042
Adequate	976 (41.5)	1,374 (58.5)	2,350 (100)	

Inadequate	2,674 (43.6)	3,453 (56.4)	6,127 (100)	
Vegetable, n (%)				0.049
Adequate	637 (43.1)	841 (56.9)	1,478 (100)	
Inadequate	3,013 (43.0)	3,986 (57.0)	6,999 (100)	

The odds ratios (95% confidence intervals) for food consumption across hyperglycemia are presented in Table 3. Frequent consumption of carbonated drinks (OR=1.139; CI=0.966-1.343), sweet desserts (OR=1.265; CI=1.132-1.413), beverages (OR=1.433; CI=1.263-1.626), salty foods (OR=1.189; CI=1.079-1.311), fried foods (OR=1.172; CI=1.033-1.331), processed foods (OR=1.106; CI=0.993-1.230), seasonings (OR=1.190; CI=1.028-1.377), instant foods (OR=1.186; CI=1.088-1.293), and inadequate consumption of fruits (OR=1.090; CI=0.990-1.200) and vegetable (OR=1.002; CI=0.920-1.100) were significantly associated with increased crude odds (model 1) of hyperglycemia. After adjusting for age, gender, education levels, residency, smoking status, alcohol consumption, and physical activity (model 2), processed foods, seasonings, and fruits were not significantly associated with hyperglycemia.

Table 3. Odds ratios (95% confidence intervals) for food consumption across hyperglycemia

Variables	Model 1*			Model 2**		
	OR	95% CI	*p*	OR	95% CI	*p*
Carbonated drinks			0.039			0.050
Infrequent	1			1		
Frequent	1.139	0.966 - 1.343		1.073	0.908 - 1.269	
Energy drinks			0.565			0.772
Infrequent	1			1		
Frequent	1.058	0.873 - 1.284		0.971	0.798 - 1.182	
Sweet desserts			0.000	1		0.000
Infrequent	1					
Frequent	1.265	1.132 - 1.413		1.238	1.108 - 1.384	
Beverages			0.000			0.000
Infrequent	1			1		
Frequent	1.433	1.263 - 1.626		1.378	1.213 - 1.567	
Savory foods			0.000			0.000

Infrequent	1			1		
Frequent	1.189	1.079 - 1.311		1.169	1.060 - 1.289	
Fried foods			0.014			0.042
Infrequent	1			1		
Frequent	1.172	1.033 - 1.331		1.142	1.005 - 1.299	
Grilled foods			0.504			0.735
Infrequent	1			1		
Frequent	1.033	0.940 - 1.135		1.017	0.924 - 1.119	
Processed foods			0.036			0.149
Infrequent	1			1		
Frequent	1.106	0.993 - 1.230		1.083	0.972 - 1.206	
Seasonings			0.020			0.052
Infrequent	1			1		
Frequent	1.190	1.028 - 1.377		1.156	0.998 - 1.340	
Instant foods			0.000			0.008
Infrequent	1			1		
Frequent	1.186	1.088 - 1.293		1.127	1.032 - 1.229	
Fruits			0.045			0.051
Adequate	1			1		
Inadequate	1.090	0.990 – 1.200		1.085	0.977 – 1.189	
Vegetables						
Adequate	1		0.036	1		0.041
Inadequate	1.002	0.920 – 1.100		1.090	1.030 – 1.163	

*Model 1 was unadjusted. **Model 2 was adjusted for age, gender, education level, residency, smoking status, alcohol consumption, physical activity.

We found that frequent consumption of sweet desserts and beverages were significantly associated with risk of elevated FBG. Sweet desserts and beverages contained carbohydrates or simple sugars with a high Glycemic Index (GI) value, leading to accelerated blood sugar levels (Medina-Remón *et al.* 2018). Other studies found a decrease in endothelial cells' micro and macro cellular function when consuming sweetened sugary beverages (Loader *et al.* 2017). These metabolic abnormalities are due to the increased in oxidative stress and decreased in NO's (nitric oxide) bioavailability, which plays an important role in glucose metabolism in the body. The decreased in NO bioavailability is also related to risk of developing type 2 diabetes (Loader *et al*. 2017). Added sugar intake is involved in the production of reactive oxygen species (ROS). It then might increase the expression of cytokines and cell adhesion molecules (Prasad and Dhar 2014).

Subjects which frequently consumed salty foods were associated with risk of increased FBG. This result is in line with a previous study. High consumption of salty foods is correlated with an increased risk factor for DM (Fitria *et al.* 2016). High intake of sodium increases the risk of hyperglycemia through the PPAR δ/adiponectin/SGLT2 mechanism in regulating sodium and glucose homeostasis (Zhao *et al.* 2016).

Frequent consumption of fried foods were significantly associated with risk of elevated FBG in recent study. Fried foods are high in fat, including saturated fat and cholesterol. Frequent consumption of fried food will lead to hyperglycemia in the pre-elderly population. A high-fat diet also significantly contributes to obesity and non-insulin-dependent diabetes mellitus (Naja *et al.* 2013). Previous study found a positive relationship between high intake of saturated fat and cholesterol and increased hyperglycemia and type 2 diabetes in humans and rats (Cahill *et al.* 2014). Saturated fat in the cell membrane will decrease the viscosity of the lipid bilayer of a cell membrane and lead to a decrease in the insulin receptors (Min *et al.* 2018).

Frequent consumption of instant foods had a significant relationship with the incidence of hyperglycemia as indicated by an increase in FBG in this study. Our results are consistent with other studies that high intake of instant foods were linked to a higher risk of developing diabetes due to the high carbohydrate and fat (Huh *et al.* 2017). However, after adjustment, there was no significant relationship. An animal trial of monosodium glutamate found a significant increase in glucose levels as evidenced by an increase in HOMA-IR value in rats. It is because of the changes in insulin binding or insulin post receptors in the target tissues (Helal *et al.* 2019). Monosodium glutamate may trigger the degradation of neuronal membranes, allowing calcium ions to enter cells because of its permeability of sodium ions, calcium ions, and water. Then, it might damage the pancreatic gland and hyperglycemia (Jusuf *et al.* 2020).

Consumption of fruits and vegetables reduced hyperglycemia. Fiber might delay the digestion and absorption of carbohydrates and increase satiety effect. In individuals with insulin resistance, fiber can increase peripheral insulin sensitivity through short-chain fatty acids produced by fiber fermentation in the gut (Samaan 2017) . In addition, a diet high in fruits and vegetables is associated with high intake of magnesium and iron (Zhang *et al.* 2015). Magnesium is an important cofactor for several enzymes in glucose metabolism, which further plays a role in the development of diabetes (Verma & Garg 2017). In this study, individuals with inadequate consumption of vegetables and fruits were 1.002 and 1.090 times, respectively, more likely to have high FBG than those with adequate consumption of vegetables and fruits.

This study has some strengths. To the best of our knowledge, this was the first study analyzing the association of food consumption with hyperglycemia among middle-aged in Indonesia. Our study used a large sample that reflected the Indonesian population. Some limitations should be mentioned in this study. Firstly, dietary data were taken using a frequency of intake which is no information related to nutrients. Moreover, the cross-sectional design restricts the results in maintaining the causality between the variables. Further research with a priori or a posteriori dietary pattern approach is highly recommended. Additional longitudinal study is needed to explore the mechanism between variables.

CONCLUSION

There was a significant association between food consumption and hyperglycemia status among middle-aged adults in Indonesia. Frequent consumption of carbonated drinks, sweet desserts, beverages, salty foods, fried foods, and instant foods, and inadequate consumption of vegetable increased FBG levels. Further research with a priori or a posteriori dietary pattern approach is highly recommended. Additional longitudinal study is needed to explore the mechanism between variables.

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DECLARATION OF INTERESTS

The authors have no conflict of interest.

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AUTHOR'S REVISION FORM

Title	:	Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis
Author(s)	:	

No	Manuscript section	Corrected line	Suggestions	Revised line	Revisions
1	Title	-	-	-	-
2	Abstract	-	-	-	-
3	Introduction	50-51	Please be more specific on typically Western foods or unhealthy foods.	46 – 48	We added information related to the unhealthy diet: "Western foods or unhealthy foods is consisted of sweet, sugar, fat, beverages, fried foods, and seasoning; hence, the unhealthy food is high in simple carbohydrate, saturated fat, and sodium"
		56	Add literature about the situation of food consumption, especially unhealthy foods, fruits and vegetable, in general/adult population of Indonesia. It will be better if there is also literature about food consumption among diabetic population in Indonesia.	54 – 56	We added literature about the situation in Indonesia: "Nowadays, a research found that Indonesian people tend to consume high western foods and low fruits and vegetables (MoH 2018)."
4	Method	66	Are you sure 26 provinces?		Yes, there are 26 provinces. We cited the reference.
		67	Explain what type of data or variable were collected and whether	70-71, 86, 91, 107-108	We used total population (line 70-71). And we explained the type

			all data were for all population or not.		of data in 'Procedures and Data Analysis' (86, 91, 107-108).
		73	Is it only age as the inclusion criteria??	71-74	We added other inclusion criteria: "The inclusion criteria in this study were individuals aged 45-59 years, had completed data of foods consumption, had completed data on fasting blood glucose, and agreed and had given their written informed consent"
		73	What is the unit?	72	We added the unit: "Years"
		79	This is not data collection as data has been there	80	We revised "data collection" to "Procedures"
		81	it should be hyperglycemia status	82	We revised it accordingly: "Hyperglycemia status"
		81	Is this part of the IBHS or an independent analysis? What is the source of blood sample? Venous or capillary?	82-84	We added more information related to blood sample: "Fasting blood glucose were measured with fingertip capillary blood tests (Accu-Chek Performa, Roche Diagnostics GmbH, Mannheim, Germany)"
		84	What does this mean?	64-65, 87	We deleted 'All variables were done by the IBHS' to make clearly (line 87). We already

					explained it in ‘Design, location, and time’: This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS) (line 64-65).
		90	How about if the consumption is onc	91-93	We explained it: “One serving a day is grouping to ‘frequent’ (≥ 1-time per day or 1-6 times per week)”
		100	double	102	We deleted this sentence: ‘Smoking status was categorized as yes and no. Alcohol consumption was categorized as yes and no.’
		110	as above	111	We revised it accordingly: “Hyperglycemia status”
		122	double	115	We deleted this sentence: ‘We used the dichotomy variable in this study to calculate the OR value. The fasting blood glucose value was categorized as hyperglycemia (≥126 mg/dL) and normal (<125 mg/dL) (Genuth *et al*. 2003; MoH RI 2018). Consumption of unhealthy foods was categorized as

					frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Fruits and vegetable consumption was categorized into adequate (≥5 servings per day) and inadequate (<5 servings per day) (MoH RI 2018). Gender was categorized as male and female. Education level was categorized as high (completed 12-year compulsory education or bachelor/diploma/higher education graduates) and low (not completed 12-year compulsory education). Residency was categorized as urban and rural. Smoking status was categorized as yes and no. Alcohol consumption was categorized as yes and no. Physical activity was categorized as low and moderate…..’
5	Result and discussion	133-137	??? no relevance with previous sentences.	122	We deleted the sentence to make clearly
		141-142	What is the relevance with the previous sentences/	124-127	This sentence explains why women have more

					risk of hyperglycemia.
		144	Make numbering in English	Table 1	We already used English format.
		148	Is it prevalence? What does y-axis refers to?	130, Figure 1	Thank you. We revised Figure 1 to show the prevalence of hyperglycemia across gender. Y-axis is percentage and x-axis is gender
		156	As above	Table 2	We already used English format.
		156	Put the examples of foods in the methods	89	We added the examples of foods in the methods
		156	The % should be row %	141, table 2	We revised it accordingly (table 2)
		158-169	Correct them after double check Table 3	Table 3	We already checked Table 3
		171-172	Need to double check the 95%CI and p-value. Some are wrong	Table 3	We already checked Table 3
		181-185	Explain how sugar lead to oxidative stress?	170-172	We add explanation related to how sugar lead to oxidative stress: "Added sugar intake is involved in the production of reactive oxygen species (ROS). It then might increase the expression of cytokines and cell adhesion molecules"
		191	Why soddenly to fried foods?	179	We separate the sentences to make it clearly. And we also added "Frequent

					consumption of fried foods were significantly associated with risk of elevated FBG" to make clearly
		204	You do not measure this	192	We deleted the sentence: 'Current study also found that seasonings such as monosodium glutamate had a significant effect on the incidence of hyperglycemia'
		224	Add discussion on the strengths of the association	211-214	We added the strengths in discussion: " This study has some strengths. To the best of our knowledge, this was the first study analyzing the association of food consumption with hyperglycemia among middle-aged in Indonesia. Our study used a large sample that reflected the Indonesian population.
6	Conclusion and suggestion	-	-	-	-
7	References	-	-	-	-
8	Others:	-	-	-	-

* Information:

- This form is an additional file that must be attached along with the revised manuscript to make the revision easy to track **(please highlight the revised part in the revised manuscript in color).**
- The Corrected Line column is filled in according to the line number where corrected by the editor/reviewer. The Revised Line collumn is filled in according to the line number where revised by the author.

- If the author does not correct the correction for certain reasons, please inform the argument in the Revisions column.

Semarang, 14 July 2022,

Ahmad Syauqy

Overall comments :

Dear Prof. Dr. Ir. Dodik Briawan, MCN, *Editor-in-Chief*

Many thanks for the editors' suggestions and comments. We have revised throughout the manuscript entitled "Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis" according to the editors' comments and suggestions. We also checked and revised some grammatical errors in throughout the manuscript.

If you have any questions, please feel free to call me at +6224-76402881 (syauqy@fk.undip.ac.id). I am looking forward to your response. Thank you.

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AUTHORS STATEMENT LETTER

The undersigned below declare that:

Article title : **Food consumption in relation to hyperglycemia in middle-aged adults (45-59 years): a cross-sectional national data analysis**

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2. Siti Andhini Mattarahmawati
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The manuscript has been carefully examined by authors and it contains no fabrication, falsification, and plagiarism. The manuscript is not simultaneously being processed in other journals or publications during the review process.

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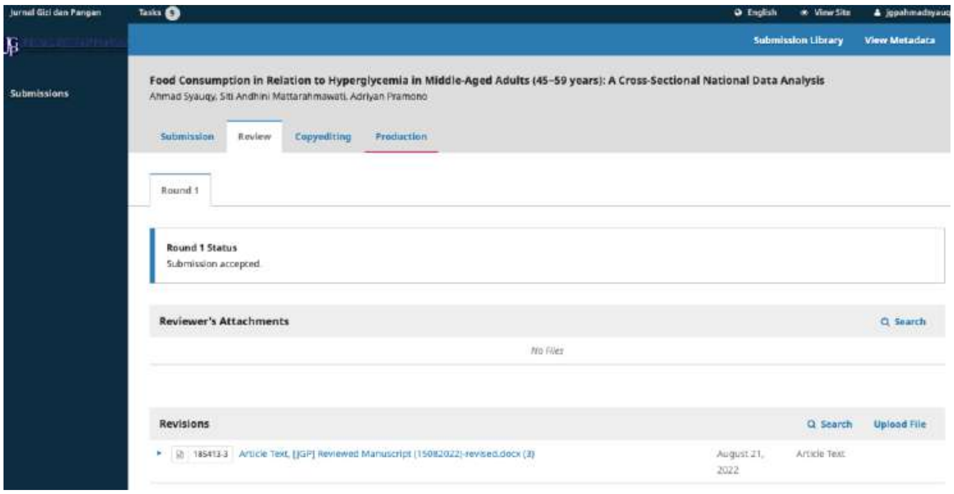
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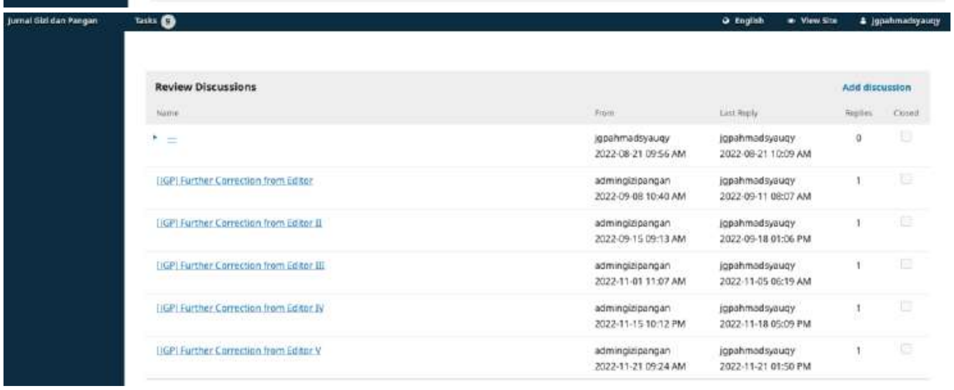
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Close Panel

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- Prof. Dr. Dodik Briawan, MCN (admingizipangan)
- Ahmad Syauqy, S.Gz, MPH.,Ph.D (jgpahmadsyauqy)

Messages

Note	From
Dear Ahmad Syauqy and Team Diponegoro University Good day. Here we attach the manuscript for further correction from our editor. Kindly check those comments & blue highlights, and do revision as advised. Make sure to reply to all comments, use highlights, and rewrite them in the author's revision form. Send back the revised manuscript & the author's revision form no later than **Thursday, 15 September 2022** by replying to this message. Thank you. Regards, -- Secretariat of Indonesian Journal of Nutrition and Food Department of Community Nutrition, Faculty of Human Ecology IPB University, Dramaga, Bogor Indonesia, 16680 E-mail address: jgp@apps.ipb.ac.id Website: http://journal.ipb.ac.id/index.php/jgizipangan [JGP] Manuscript_Checked (08092022).docx [JGP] Author's Revision Form.docx	admingizipangan 2022-09-08 10:40 AM

HASIL KOREKSI EDITOR (I)

Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis

ABSTRACT

The objective of this study was to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia. This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS). A total of 8477 subjects met the inclusion criteria and included in this study. Fasting blood glucose (FBG) was analyzed in the laboratory using an enzymatic analysis. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dL) and normal (<125 mg/dL). A food frequency questionnaire was used to assess the food intake. Multiple logistic regression was used to analyze the association of food consumption and hyperglycemia. Our results found that the prevalence of hyperglycemia in this population was 43%. The mean FBG was 104.68 ± 31.99 mg/dL for male and 110.75 ± 43.92 mg/dL for female subjects. Frequent consumption of carbonated drinks (OR=1.139; CI=0.966, 1.343), sweet desserts (OR=1.265; CI=1.132, 1.413), sugar-sweetened beverages (SSB) (OR=1.433; CI=1.263, 1.626), salty foods (OR=1.189; CI=1.079, 1.311), fried foods (OR=1.172; CI=1.033, 1.331), instant foods (OR=1.186; CI=1.088, 1.293), and inadequate consumption of vegetable (OR=1.002; CI=0.920, 1.100) were significantly associated with increased odds of hyperglycemia. There was a significant association between food consumption and hyperglycemia among middle-aged adults in Indonesia.

Keyword: diet, food consumption, hyperglycemia, fasting blood glucose, Indonesia

Runner Title: Food consumption and hyperglycemia

INTRODUCTION

Non-communicable diseases are the leading cause of public health problems in developed and developing countries (Naghavi M 2017). Diabetes, one of the non-communicable diseases, is the main cause of death in the world (Zheng *et al.* 2018). Diabetes or hyperglycemia is characterized by an increase in blood sugar levels in the body. Previous studies found that the

prevalence of hyperglycemia and the components of metabolic syndrome increased rapidly with age in women and men (Wu *et al.* 2017, Jiang *et al.* 2018). Recently, Indonesia is the fourth country after India, China, and America, with the most diabetes sufferers globally (Naghavi M 2017). The prevalence of diabetes in Indonesia was around 6% (Mihardja *et al.* 2014). Interestingly, based on the 2018 Indonesia Basic Health Survey (IBHS), the higher prevalence of diabetes was among middle-aged adults with almost 10% (MoH 2018).

Diabetes is caused by many factors including lifestyle (Sudargo *et al.* 2018). Sedentary lifestyle has associated with the increasing trend of diabetes (Nurwanti *et al.* 2018). Previous study also found that diet was associated with the increased prevalence of diabetes (Lambrinou *et al.* 2019). Western foods or unhealthy foods are correlated with an increased prevalence of hyperglycemia and metabolic syndrome (Syauqy *et al.* 2018). Western foods or unhealthy foods is consisted of sweet, sugar, fat, sugar-sweetened beverages (SSB), fried foods, and seasoning; hence, the unhealthy food is high in simple carbohydrate, saturated fat, and sodium. Furthermore, inadequate consumption of vegetables and fruits can also escalate the diabetes prevalence (Syauqy *et al*. 2018, Schwingshackl *et al.* 2017).

Some studies have found the association between food consumption and metabolic syndrome among middle-aged adults in Taiwan (Syauqy *et al*. 2018). Moreover, middle-aged adults who consumed high fruits and vegetables and less unhealthy foods had a better quality of life (Lo *et al.* 2016). Nowadays, a research found that Indonesian people tend to consume high western foods and low fruits and vegetables (MoH 2018). However, to the best of our knowledge, study investigated the association of unhealthy foods, fruits, and vegetables intakes with diabetes among middle-aged adults in Indonesia was still rare, especially using a national database that represents the Indonesian population. Therefore, the objective of this study was to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia.

METHODS

Design, location, and time

This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS). Briefly, the IBHS used a two-stage stratified cluster sampling method survey population includes all Indonesian households, representing 26 Provinces and utilizing a sample framework from the national socio-economic survey in March 2018 (MoH 2018). This study had received ethical approval from the Health Research Ethics Commission, Medical Faculty, Universitas 'Aisyiyah Yogyakarta No. 1415/KEP-UNISA/VI/2021.

Sampling

The target sample included 300,000 households from 30,000 census blocks of the national socio-economic survey framework (MoH 2018). The total population data of the IBHS were 713,783 people aged ≥15 years (MoH 2018). The inclusion criteria in this study were individuals aged 45-59 years, had completed data of foods consumption, had completed data on fasting blood glucose, and agreed and had given their written informed consent. While, subjects were excluded due to extreme values or missing data. Finally, a total of 8477 subjects met the inclusion criteria and included in this study.

Commented [A36]: Explain how many of the 713,783 people had blood samples. Why from 713,783 remains 8,477 people? It is impossible that >700,000 people had missing data.

Data collection

The independent variables in this study were the consumption of foods; while, the dependent variable was hyperglycemia status. Fasting blood glucose were measured with fingertip capillary blood tests (Accu-Chek Performa, Roche Diagnostics GmbH, Mannheim, Germany). All participants were instructed to fast overnight (8-10 hours) before blood sampling. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dL) and normal (<125 mg/dL) (Genuth *et al.* 2003, MoH 2018). A validated food frequency questionnaire (FFQ) was used to assess the daily food consumption. The FFQ was validated by the IBHS prior the study (MoH 2018). The FFQ includes carbonated drinks, energy drinks, sweet desserts, SSB, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods, fruits, and vegetables (MoH 2018). Consumption of unhealthy foods (carbonated drinks, energy drinks, sweet desserts, SSB, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods) was categorized as frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Fruits and vegetable consumption was categorized into adequate (≥5 servings per day) and inadequate (<5 servings per day) (MoH 2018). Sociodemographic data (age, gender, education,

Commented [A37]: What happed to those who have blood glucose of 125?

and place of residence) and lifestyle (smoking status, alcohol intake, and physical activity) were obtained using a structured questionnaire. Smoking is categorized into yes and no. Consumption of alcoholic beverages is categorized into yes and no (Atamni *et al.* 2016). Gender was categorized as male and female. Education level was categorized as high (completed 12-year compulsory education or bachelor/diploma/higher education graduates) and low (not completed 12-year compulsory education). Residency was categorized as urban and rural. Physical activity was categorized as low (doing heavy physical activity for <150 minutes/week) and high (doing heavy physical activity for ≥150 minutes/week (MoH 2018).

Data analysis

Univariate analysis was presented using mean±standard deviation for numerical data and frequency (percentage) for categorical data. In addition, bivariate analysis was performed using independent samples t-test for continuous variables and the Chi-square test for categorical variables. Whereas, multivariate analysis using multiple logistic regression was used to analyze the association of food consumption and hyperglycemia status. Odds ratio (OR) with 95% confidence intervals was conducted in the analyze. We used unadjusted (model 1) and adjusted (model 2). Model 2 was adjusted for demographic data (age, gender, residency) and lifestyle (smoking status, alcohol consumption, and physical activity). We selected demographic data and lifestyle because they have potential association with hyperglycemia that might interfere the results. All analyses were performed using the SPSS program 25 version with a *p*-value <0.05 considered statistically significant.

RESULTS AND DISCUSSION

Table 1 shows the characteristics of the subjects. Among 8477 subjects, 61.6% were female, 51.2% lived in rural areas, 32.3% were smokers, 1.1% consumed alcohol, and 18.3% had high physical activity. Our results also found that the prevalence of hyperglycemia in the population was 43% (Figure 1). The mean FBG was 104.68±31.99 mg/dL for male and 110.75±43.92 mg/dL for female subjects. This study also found that the prevalence of hyperglycemia was higher in females (44.6%) than males (40.6%). This result was in line with a previous study in the United State (ADA 2018). Women are more risk of experiencing hyperglycemia due to the hormonal changes (ADA 2018). Moreover, physical activity in women tends to be lower than in men (The Lancet Public Health 2019).

Table 1. Characteristics of the subjects (n=8,477).

Variables	Hyperglycemia		*P*	All subjects
	Yes (n = 3,648)	No (4,829)		
Age, years	52.05±4.29	41.27±4.24	<0.001*	51.6 ± 4.28
Gender, n(%)			<0.001**	
Male	1,323 (36.3)	1,935 (40.1)		3,258 (38.4)
Female	2,325 (63.7)	2,894 (59.9)		5,219 (61.6)
Education levels, n (%)			0.310**	
High	1,239 (34.0)	1,691 (35.0)		2,930 (34.6)
Low	2,409 (66.0)	3,138 (65.0)		5,547 (65.4)
Residency, n (%)			0.188**	
Rural	1,837 (50.4)	2,502 (51.8)		4,339 (51.2)
Urban	1,811 (49.6)	2,325 (48.2)		4,136 (48.8)
Smoking status, n (%)			<0.001**	
No	2,546 (69.8)	3,195 (66.2)		5,741 (67.7)
Yes	1,102 (30.2)	1,634 (33.8)		2,736 (32.3)
Alcohol consumption, n (%)			0.465**	
No	3,604 (98.8)	4,779 (99.0)		8,383 (98.9)
Yes	44 (1.2)	50 (1.0)		94 (1.1)
Physical activity, n (%)			0.019**	
High	1,684 (46.2)	2,355 (48.8)		4,039 (47.6)
Low	1,964 (53,8)	2,474 (51,2)		4,438 (52.4)
Fasting blood glucose, mg/dL	130.84±52.65	91.47±5.43	<0.001*	108.42 ± 39.87

*Comparison between continuous variables and hyperglycemia were performed using independent samples t-test

**Comparison between categorical variables and hyperglycemia were performed using Chi-square test

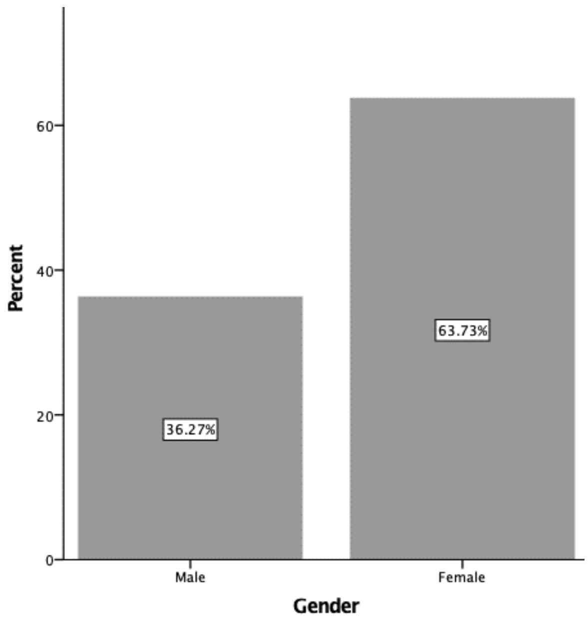

Figure 1. Prevalence of hyperglycemia across gender.

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The association of food consumption and hyperglycemia are described in Table 2. The majority of the subjects with hyperglycemia were significantly frequent consumption of carbonated drinks (43.4), sweet desserts (42.0), SSB (41.9), salty foods (41.9), fried foods (42.5), processed foods (43.6), seasonings (42.6), instant foods (41.1), and inadequate consumption of fruits (43.6), and vegetable (43.0).

Table 2. Food consumption and hyperglycemia (N = 8,477)*.

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Variables	Hyperglycemia		P^{**}	Total (%)
	Yes (n = 3,648)	No (4,829)		
Carbonated drinks, n (%)			0.050	
Infrequent	254 (40.1)	379 (59.9)		633 (100)
Frequent	3,396 (43.3)	4,448 (56.7)		7,844 (100)
Energy drinks, n (%)			0.300	
Infrequent	187 (41.7)	261 (58.3)		448 (100)
Frequent	3,463 (43.1)	4,566 (56.9)		8,029 (100)
Sweet desserts, n (%)			<0.001	
Infrequent	736 (47.8)	808 (52.2)		1,544 (100)

Frequent	2,912 (42.0)	4,021 (58.0)		6,933 (100)
Sugar-sweetened beverages, n (%)			<0.001	
Infrequent	564 (50.8)	546 (49.2)		1,110 (100)
Frequent	3,086 (41.9)	4,281 (58.1)		7,367 (100)
Salty foods, n (%)			<0.001	
Infrequent	1,032 (46.2)	1,202 (53.8)		2,234 (100)
Frequent	2,618 (41.9)	3,625 (58.1)		6,243 (100)
Fried foods, n (%)			0.015	0.015
Infrequent	513 (46.5)	591 (53.5)		1,104 (100)
Frequent	3,137 (42.5)	4,236 (57.5)		7,373 (100)
Grilled foods, n (%)			0.515	
Infrequent	1,056 (42.5)	1,429 (57.5)		2,485 (100)
Frequent	2,594 (43.3)	3,398 (56.7)		5,992 (100)
Processed foods, n (%)			0.035	0.035
Infrequent	714 (41.1)	1,023 (58.9)		1,737 (100)
Frequent	2,936 (43.6)	3,804 (56.4)		6,740 (100)
Seasonings, n (%)			0.020	
Infrequent	376 (46.9)	425 (53.1)		801 (100)
Frequent	3,274 (42.6)	4,402 (57.4)		7,676 (100)
Instant foods, n (%)			<0.001	<0.001
Infrequent	1,761 (45.3)	2,125 (54.7)		3,886 (100)
Frequent	1,889 (41.1)	2,702 (58.9)		4,591 (100)
Fruits, n (%)			0.042	0.042
Adequate	976 (41.5)	1,374 (58.5)		2,350 (100)
Inadequate	2,674 (43.6)	3,453 (56.4)		6,127 (100)
Vegetable, n (%)			0.049	
Adequate	637 (43.1)	841 (56.9)		1,478 (100)
Inadequate	3,013 (43.0)	3,986 (57.0)		6,999 (100)

*Frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Adequate (≥5 servings per day) and inadequate (<5 servings per day)

**Comparison between food consumption and hyperglycemia were performed using Chi-square test

The odds ratios (95% confidence intervals) for food consumption across hyperglycemia are presented in Table 3. Frequent consumption of carbonated drinks (OR=1.139; CI=0.966, 1.343),

sweet desserts (OR=1.265; CI=1.132, 1.413), SSB (OR=1.433; CI=1.263, 1.626), salty foods (OR=1.189; CI=1.079, 1.311), fried foods (OR=1.172; CI=1.033, 1.331), processed foods (OR=1.106; CI=0.993, 1.230), seasonings (OR=1.190; CI=1.028, 1.377), instant foods (OR=1.186; CI=1.088, 1.293), and inadequate consumption of fruits (OR=1.090; CI=0.990, 1.200) and vegetable (OR=1.002; CI=0.920, 1.100) were significantly associated with increased crude odds (model 1) of hyperglycemia. After adjusting for age, gender, education levels, residency, smoking status, alcohol consumption, and physical activity (model 2), processed foods, seasonings, and fruits were not significantly associated with hyperglycemia.

Table 3. Odds ratios (95% confidence intervals) for food consumption across hyperglycemia

Variables	Model 1**			Model 2***		
	OR	95% CI	*p*	OR	95% CI	*p**
Carbonated drinks			0.039			0.050
Infrequent	1			1		
Frequent	1.139	0.966, 1.343		1.073	0.908, 1.269	
Energy drinks			0.565			0.772
Infrequent	1			1		
Frequent	1.058	0.873, 1.284		0.971	0.798, 1.182	
Sweet desserts			<0.001	1		<0.001
Infrequent	1					
Frequent	1.265	1.132, 1.413		1.238	1.108, 1.384	
Sugar-sweetened beverages			<0.001			<0.001
Infrequent	1			1		
Frequent	1.433	1.263, 1.626		1.378	1.213, 1.567	
Salty foods			<0.001			<0.001
Infrequent	1			1		
Frequent	1.189	1.079, 1.311		1.169	1.060, 1.289	

Fried foods			0.014			0.042
Infrequent	1			1		
Frequent	1.172	1.033, 1.331		1.142	1.005, 1.299	
Grilled foods			0.504			0.735
Infrequent	1			1		
Frequent	1.033	0.940, 1.135		1.017	0.924, 1.119	
Processed foods			0.036			0.149
Infrequent	1			1		
Frequent	1.106	0.993, 1.230		1.083	0.972, 1.206	
Seasonings			0.020			0.052
Infrequent	1			1		
Frequent	1.190	1.028, 1.377		1.156	0.998, 1.340	
Instant foods			<0.001			0.008
Infrequent	1			1		
Frequent	1.186	1.088, 1.293		1.127	1.032, 1.229	
Fruits			0.045			0.051
Adequate	1			1		
Inadequate	1.090	0.990, 1.200		1.085	0.977, 1.189	
Vegetables						
Adequate	1		0.036	1		0.041
Inadequate	1.002	0.920, 1.100		1.090	1.030, 1.163	

*Differences between food consumption and hyperglycemia were analyzed using multiple logistic regression. **Model 1 was unadjusted. ***Model 2 was adjusted for age, gender, education level, residency, smoking status, alcohol consumption, physical activity.

We found that frequent consumption of sweet desserts and SSB were significantly associated with risk of hyperglycemia. Sweet desserts and SSB contained carbohydrates or simple sugars with a high Glycemic Index (GI) value, leading to accelerated blood sugar levels (Medina-Remón *et al.* 2018). Other studies found a decrease in endothelial cells' micro and macro cellular function when consuming sweetened sugary beverages (Loader *et al.* 2017). These metabolic abnormalities are due to the increased in oxidative stress and decreased in NO's (nitric oxide) bioavailability, which plays an important role in glucose metabolism in the body. The decreased in NO bioavailability is also related to risk of developing type 2 diabetes (Loader *et al*. 2017). Added sugar intake is involved in the production of reactive oxygen species (ROS). It then might increase the expression of cytokines and cell adhesion molecules (Prasad and Dhar 2014).

Participants which frequently consumed salty foods were associated with risk of hyperglycemia. This result is in line with a previous study. High consumption of salty foods is correlated with an increased risk factor for DM (Fitria *et al.* 2016). High intake of sodium increases the risk of hyperglycemia through the PPAR δ/adiponectin/SGLT2 mechanism in regulating sodium and glucose homeostasis (Zhao *et al.* 2016).

Frequent consumption of fried foods were significantly associated with risk of hyperglycemia in recent study. Fried foods are high in fat, including saturated fat and cholesterol. Frequent consumption of fried food will lead to hyperglycemia in the pre-elderly population. A high-fat diet also significantly contributes to obesity and non-insulin-dependent diabetes mellitus (Naja *et al.* 2013). Previous study found a positive relationship between high intake of saturated fat and cholesterol and increased hyperglycemia and type 2 diabetes in humans and rats (Cahill *et al.* 2014). Saturated fat in the cell membrane will decrease the viscosity of the lipid bilayer of a cell membrane and lead to a decrease in the insulin receptors (Min *et al.* 2018).

Frequent consumption of instant foods had a significant relationship with the incidence of hyperglycemia as indicated by an increase in FBG in this study. Our results are consistent with other studies that high intake of instant foods were linked to a higher risk of developing diabetes due to the high carbohydrate and fat (Huh *et al.* 2017). However, after adjustment, there was no significant relationship. An animal trial of monosodium glutamate found a significant increase in glucose levels as evidenced by an increase in HOMA-IR value in rats. It is because of the changes in insulin binding or insulin post receptors in the target tissues (Helal *et al.* 2019). Monosodium glutamate may trigger the degradation of neuronal membranes, allowing calcium ions to enter cells because of its permeability of sodium ions, calcium ions, and water. Then, it might damage the pancreatic gland and hyperglycemia (Jusuf *et al.* 2020).

Consumption of fruits and vegetables reduced hyperglycemia. Fiber might delay the digestion and absorption of carbohydrates and increase satiety effect. In individuals with insulin resistance, fiber can increase peripheral insulin sensitivity through short-chain fatty acids produced by fiber fermentation in the gut (Samaan 2017) . In addition, a diet high in fruits and vegetables is associated with high intake of magnesium and iron (Zhang *et al.* 2015). Magnesium is an important cofactor for several enzymes in glucose metabolism, which further plays a role in the development of diabetes (Verma & Garg 2017). In this study, individuals with inadequate consumption of vegetables and fruits were 1.002 and 1.090 times, respectively, more likely to have high FBG than those with adequate consumption of vegetables and fruits.

This study has some strengths. To the best of our knowledge, this was the first study analyzing the association of food consumption with hyperglycemia among middle-aged in Indonesia. Our study used a large sample that reflected the Indonesian population. Some limitations should be mentioned in this study. Firstly, dietary data were taken using a frequency of intake which is no information related to nutrients. Moreover, the cross-sectional design restricts the results in maintaining the causality between the variables. Further research with a priori or a posteriori dietary pattern approach is highly recommended. Additional longitudinal study is needed to explore the mechanism between variables.

CONCLUSION

There was a significant association between food consumption and hyperglycemia status among middle-aged adults in Indonesia. Frequent consumption of carbonated drinks, sweet desserts, SSB, salty foods, fried foods, and instant foods, and inadequate consumption of vegetable increased the odds (chance) to have hyperglycemia. Further research with a priori or a posteriori dietary pattern approach is highly recommended. Additional longitudinal study is needed to explore the mechanism between variables.

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We would like to thank Faculty of Medicine (name), (university name) (registration number).

DECLARATION OF INTERESTS

The authors have no conflict of interest.

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Settings

Dear Prof. Dr. Dodik Briawan, MCN,

Many thanks for the reviewers' suggestions and comments. We have revised throughout the manuscript entitled "Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis" according to the reviewers' comments and suggestions.

If you have any questions, please feel free to call me at +6224-76402881 (email: syauqy@fk.undip.ac.id). I am looking forward to your response.

Best Regards,

Ahmad Syauqy

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HASIL PERBAIKAN EDITOR (I)

Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis

ABSTRACT

The objective of this study was to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia. This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS). A total of 8477 subjects met the inclusion criteria and included in this study. Fasting blood glucose (FBG) was analyzed in the laboratory using an enzymatic analysis. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dL) and normal (<126 mg/dL). A food frequency questionnaire was used to assess the food intake. Multiple logistic regression was used to analyze the association of food consumption and hyperglycemia. Our results found that the prevalence of hyperglycemia in this population was 43%. The mean FBG was 104.68 ± 31.99 mg/dL for male and 110.75 ± 43.92 mg/dL for female subjects. Frequent consumption of carbonated drinks (OR=1.139; CI=0.966, 1.343), sweet desserts (OR=1.265; CI=1.132, 1.413), sugar-sweetened beverages (SSB) (OR=1.433; CI=1.263, 1.626), salty foods (OR=1.189; CI=1.079, 1.311), fried foods (OR=1.172; CI=1.033, 1.331), instant foods (OR=1.186; CI=1.088, 1.293), and inadequate consumption of vegetable (OR=1.002; CI=0.920, 1.100) were significantly associated with increased odds of hyperglycemia. There was a significant association between food consumption and hyperglycemia among middle-aged adults in Indonesia.

Keyword: diet, food consumption, hyperglycemia, fasting blood glucose, Indonesia

Runner Title: Food consumption and hyperglycemia

INTRODUCTION

Non-communicable diseases are the leading cause of public health problems in developed and developing countries (Naghavi M 2017). Diabetes, one of the non-communicable diseases, is the main cause of death in the world (Zheng *et al.* 2018). Diabetes or hyperglycemia is characterized by an increase in blood sugar levels in the body. Previous studies found that the

prevalence of hyperglycemia and the components of metabolic syndrome increased rapidly with age in women and men (Wu *et al.* 2017, Jiang *et al.* 2018). Recently, Indonesia is the fourth country after India, China, and America, with the most diabetes sufferers globally (Naghavi M 2017). The prevalence of diabetes in Indonesia was around 6% (Mihardja *et al.* 2014). Interestingly, based on the 2018 Indonesia Basic Health Survey (IBHS), the higher prevalence of diabetes was among middle-aged adults with almost 10% (MoH 2018).

Diabetes is caused by many factors including lifestyle (Sudargo *et al.* 2018). Sedentary lifestyle has associated with the increasing trend of diabetes (Nurwanti *et al.* 2018). Previous study also found that diet was associated with the increased prevalence of diabetes (Lambrinou *et al.* 2019). Western foods or unhealthy foods are correlated with an increased prevalence of hyperglycemia and metabolic syndrome (Syauqy *et al.* 2018). Western foods or unhealthy foods consisted of sweet, sugar, fat, sugar-sweetened beverages (SSB), fried foods, and seasoning; hence, the unhealthy food is high in simple carbohydrate, saturated fat, and sodium. Furthermore, inadequate consumption of vegetables and fruits can also escalate the diabetes prevalence (Syauqy *et al*. 2018, Schwingshackl *et al.* 2017).

Some studies have found the association between food consumption and metabolic syndrome among middle-aged adults in Taiwan (Syauqy *et al*. 2018). Moreover, middle-aged adults who consumed high fruits and vegetables and less unhealthy foods had a better quality of life (Lo *et al.* 2016). A research found that Indonesian people tend to consume high western foods and low fruits and vegetables (MoH 2018). However, to the best of our knowledge, study investigated the association of unhealthy foods, fruits, and vegetables intakes with diabetes among middle-aged adults in Indonesia was still rare, especially using a national database that represents the Indonesian population. Therefore, the objective of this study was to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia.

METHODS

Design, location, and time

This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS). Briefly, the IBHS used a two-stage stratified cluster sampling method survey population includes all Indonesian households, representing 26 Provinces and utilizing a sample framework from the national socio-economic survey in March 2018 (MoH 2018). This study had received ethical approval from the Health Research Ethics Commission, Medical Faculty, Universitas 'Aisyiyah Yogyakarta No. 1415/KEP-UNISA/VI/2021.

Sampling

The target sample included 300,000 households from 30,000 census blocks of the national socio-economic survey framework (MoH 2018). The total population data of the IBHS were 713,783 people aged ≥15 years (MoH 2018). The inclusion criteria in this study were individuals aged 45-59 years, had completed data of foods consumption, had completed data on fasting blood glucose, and agreed and had given their written informed consent (n=8,481). While, subjects were excluded due to extreme values or missing data (n=4). Finally, a total of 8,477 subjects met the inclusion criteria and included in this study.

Data collection

The independent variables in this study were the consumption of foods; while, the dependent variable was hyperglycemia status. Fasting blood glucose were measured with fingertip capillary blood tests (Accu-Chek Performa, Roche Diagnostics GmbH, Mannheim, Germany). All participants were instructed to fast overnight (8-10 hours) before blood sampling. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dL) and normal (<126 mg/dL) (Genuth *et al.* 2003, MoH 2018). A validated food frequency questionnaire (FFQ) was used to assess the daily food consumption. The FFQ was validated by the IBHS prior the study (MoH 2018). The FFQ includes carbonated drinks, energy drinks, sweet desserts, SSB, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods, fruits, and vegetables (MoH 2018). Consumption of unhealthy foods (carbonated drinks, energy drinks, sweet desserts, SSB, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods) was categorized as frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Fruits and vegetable consumption was categorized into adequate (≥5 servings per day) and inadequate (<5 servings per day) (MoH 2018). Sociodemographic data (age, gender, education,

and place of residence) and lifestyle (smoking status, alcohol intake, and physical activity) were obtained using a structured questionnaire. Smoking is categorized into yes and no. Consumption of alcoholic beverages is categorized into yes and no (Atamni *et al*. 2016). Gender was categorized as male and female. Education level was categorized as high (completed 12-year compulsory education or bachelor/diploma/higher education graduates) and low (not completed 12-year compulsory education). Residency was categorized as urban and rural. Physical activity was categorized as low (doing heavy physical activity for <150 minutes/week) and high (doing heavy physical activity for ≥150 minutes/week (MoH 2018).

Data analysis

Univariate analysis was presented using mean±standard deviation for numerical data and frequency (percentage) for categorical data. In addition, bivariate analysis was performed using independent samples t-test for continuous variables and the Chi-square test for categorical variables. Whereas, multivariate analysis using multiple logistic regression was used to analyze the association of food consumption and hyperglycemia status. Odds ratio (OR) with 95% confidence intervals was conducted in the analyze. We used unadjusted (model 1) and adjusted (model 2). Model 2 was adjusted for demographic data (age, gender, residency) and lifestyle (smoking status, alcohol consumption, and physical activity). We selected demographic data and lifestyle because they have potential association with hyperglycemia that might interfere the results. All analyses were performed using the SPSS program 25 version with a *p*-value <0.05 considered statistically significant.

RESULTS AND DISCUSSION

Table 1 shows the characteristics of the subjects. The majority of the subjects with hyperglycemia were older (52.05±4.29), female (44.6), not smoking (44.3), and had low physical activity (44.3). Our results also found that the prevalence of hyperglycemia in the population was 43% (Figure 1). The mean FBG was 104.68±31.99 mg/dL for male and 110.75±43.92 mg/dL for female subjects. This study also found that the prevalence of hyperglycemia was higher in females (63.7) than males (36.3). This result was in line with a previous study in the United State (ADA 2018). Women are more risk of experiencing hyperglycemia due to the hormonal changes (ADA 2018). Moreover, physical activity in women tends to be lower than in men (The Lancet Public Health 2019).

Table 1. Characteristics of the subjects (n=8,477).

Variables	Hyperglycemia		*P*	All subjects
	Yes (n = 3,648)	No (4,829)		
Age, years	52.05±4.29	41.27±4.24	<0.001*	51.6 ± 4.28
Gender, n(%)			<0.001**	
Male	1,323 (40.6)	1,935 (59.4)		3,258 (100)
Female	2,325 (44.6)	2,894 (55.4)		5,219 (100)
Education levels, n (%)			0.310**	
High	1,239 (42.3)	1,691 (57.7)		2,930 (100)
Low	2,409 (43.4)	3,138 (56.6)		5,547 (100)
Residency, n (%)			0.188**	
Rural	1,837 (42.3)	2,502 (57.7)		4,339 (100)
Urban	1,811 (43.8)	2,325 (56.2)		4,136 (100)
Smoking status, n (%)			<0.001**	
No	2,546 (44.3)	3,195 (55.7)		5,741 (100)
Yes	1,102 (40.3)	1,634 (59.7)		2,736 (100)
Alcohol consumption, n (%)			0.465**	
No	3,604 (43.0)	4,779 (57.0)		8,383 (100)
Yes	44 (46.8)	50 (53.2)		94 (100)
Physical activity, n (%)			0.019**	
High	1,684 (41.7)	2,355 (58.3)		4,039 (100)
Low	1,964 (44.3)	2,474 (55,7)		4,438 (100)
Fasting blood glucose, mg/dL	130.84±52.65	91.47±5.43	<0.001*	108.42 ± 39.87

*Comparison between continuous variables and hyperglycemia were performed using independent samples t-test

**Comparison between categorical variables and hyperglycemia were performed using Chi-square test

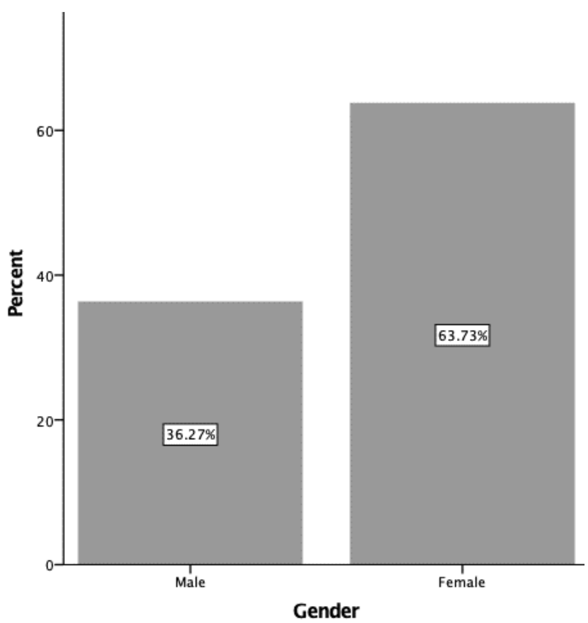

Figure 1. Prevalence of hyperglycemia across gender.

The association of food consumption and hyperglycemia are described in Table 2. The majority of the subjects with hyperglycemia were significantly frequent consumption of carbonated drinks (43.4), sweet desserts (42.0), SSB (41.9), salty foods (41.9), fried foods (42.5), processed foods (43.6), seasonings (42.6), instant foods (41.1), and inadequate consumption of fruits (43.6), and vegetable (43.0).

Table 2. Food consumption and hyperglycemia (N = 8,477)*.

Variables	Hyperglycemia		P^{**}	Total (%)
	Yes (n = 3,648)	No (4,829)		
Carbonated drinks, n (%)			0.050	
Infrequent	254 (40.1)	379 (59.9)		633 (100)
Frequent	3,396 (43.3)	4,448 (56.7)		7,844 (100)
Energy drinks, n (%)			0.300	
Infrequent	187 (41.7)	261 (58.3)		448 (100)
Frequent	3,463 (43.1)	4,566 (56.9)		8,029 (100)
Sweet desserts, n (%)			<0.001	
Infrequent	736 (47.8)	808 (52.2)		1,544 (100)

Frequent	2,912 (42.0)	4,021 (58.0)		6,933 (100)
Sugar-sweetened beverages, n (%)			<0.001	
Infrequent	564 (50.8)	546 (49.2)		1,110 (100)
Frequent	3,086 (41.9)	4,281 (58.1)		7,367 (100)
Salty foods, n (%)			<0.001	
Infrequent	1,032 (46.2)	1,202 (53.8)		2,234 (100)
Frequent	2,618 (41.9)	3,625 (58.1)		6,243 (100)
Fried foods, n (%)			0.015	0.015
Infrequent	513 (46.5)	591 (53.5)		1,104 (100)
Frequent	3,137 (42.5)	4,236 (57.5)		7,373 (100)
Grilled foods, n (%)			0.515	
Infrequent	1,056 (42.5)	1,429 (57.5)		2,485 (100)
Frequent	2,594 (43.3)	3,398 (56.7)		5,992 (100)
Processed foods, n (%)			0.035	0.035
Infrequent	714 (41.1)	1,023 (58.9)		1,737 (100)
Frequent	2,936 (43.6)	3,804 (56.4)		6,740 (100)
Seasonings, n (%)			0.020	
Infrequent	376 (46.9)	425 (53.1)		801 (100)
Frequent	3,274 (42.6)	4,402 (57.4)		7,676 (100)
Instant foods, n (%)			<0.001	<0.001
Infrequent	1,761 (45.3)	2,125 (54.7)		3,886 (100)
Frequent	1,889 (41.1)	2,702 (58.9)		4,591 (100)
Fruits, n (%)			0.042	0.042
Adequate	976 (41.5)	1,374 (58.5)		2,350 (100)
Inadequate	2,674 (43.6)	3,453 (56.4)		6,127 (100)
Vegetable, n (%)			0.049	
Adequate	637 (43.1)	841 (56.9)		1,478 (100)
Inadequate	3,013 (43.0)	3,986 (57.0)		6,999 (100)

*Frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Adequate (≥5 servings per day) and inadequate (<5 servings per day)

**Comparison between food consumption and hyperglycemia were performed using Chi-square test

The odds ratios (95% confidence intervals) for food consumption across hyperglycemia are presented in Table 3. Frequent consumption of carbonated drinks (OR=1.139; CI=0.966, 1.343),

sweet desserts (OR=1.265; CI=1.132, 1.413), SSB (OR=1.433; CI=1.263, 1.626), salty foods (OR=1.189; CI=1.079, 1.311), fried foods (OR=1.172; CI=1.033, 1.331), processed foods (OR=1.106; CI=0.993, 1.230), seasonings (OR=1.190; CI=1.028, 1.377), instant foods (OR=1.186; CI=1.088, 1.293), and inadequate consumption of fruits (OR=1.090; CI=0.990, 1.200) and vegetable (OR=1.002; CI=0.920, 1.100) were significantly associated with increased crude odds (model 1) of hyperglycemia. After adjusting for age, gender, education levels, residency, smoking status, alcohol consumption, and physical activity (model 2), processed foods, seasonings, and fruits were not significantly associated with hyperglycemia.

Table 3. Odds ratios (95% confidence intervals) for food consumption across hyperglycemia

Variables	Model 1**			Model 2***		
	OR	95% CI	*p*	OR	95% CI	*p**
Carbonated drinks			0.039			0.050
Infrequent	1			1		
Frequent	1.139	0.966, 1.343		1.073	0.908, 1.269	
Energy drinks			0.565			0.772
Infrequent	1			1		
Frequent	1.058	0.873, 1.284		0.971	0.798, 1.182	
Sweet desserts			<0.001	1		<0.001
Infrequent	1					
Frequent	1.265	1.132, 1.413		1.238	1.108, 1.384	
Sugar-sweetened beverages			<0.001			<0.001
Infrequent	1			1		
Frequent	1.433	1.263, 1.626		1.378	1.213, 1.567	
Salty foods			<0.001			<0.001
Infrequent	1			1		
Frequent	1.189	1.079, 1.311		1.169	1.060, 1.289	
Fried foods			0.014			0.042

Infrequent	1			1		
Frequent	1.172	1.033, 1.331		1.142	1.005, 1.299	
Grilled foods			0.504			0.735
Infrequent	1			1		
Frequent	1.033	0.940, 1.135		1.017	0.924, 1.119	
Processed foods			0.036			0.149
Infrequent	1			1		
Frequent	1.106	0.993, 1.230		1.083	0.972, 1.206	
Seasonings			0.020			0.052
Infrequent	1			1		
Frequent	1.190	1.028, 1.377		1.156	0.998, 1.340	
Instant foods			<0.001			0.008
Infrequent	1			1		
Frequent	1.186	1.088, 1.293		1.127	1.032, 1.229	
Fruits			0.045			0.051
Adequate	1			1		
Inadequate	1.090	0.990, 1.200		1.085	0.977, 1.189	
Vegetables						
Adequate	1		0.036	1		0.041
Inadequate	1.002	0.920, 1.100		1.090	1.030, 1.163	

*Differences between food consumption and hyperglycemia were analyzed using multiple logistic regression. **Model 1 was unadjusted. ***Model 2 was adjusted for age, gender, education level, residency, smoking status, alcohol consumption, physical activity.

We found that frequent consumption of sweet desserts and SSB were significantly associated with risk of hyperglycemia. Sweet desserts and SSB contained carbohydrates or simple sugars with a high Glycemic Index (GI) value, leading to accelerated blood sugar levels (Medina-Remón *et al.* 2018). Other studies found a decrease in endothelial cells' micro and macro cellular function when consuming sweetened sugary beverages (Loader *et al.* 2017). These metabolic abnormalities are due to the increased in oxidative stress and decreased in NO's (nitric oxide) bioavailability, which plays an important role in glucose metabolism in the body. The decreased in NO bioavailability is also related to risk of developing type 2 diabetes (Loader *et al*. 2017). Added sugar intake is involved in the production of reactive oxygen species (ROS). It then might increase the expression of cytokines and cell adhesion molecules (Prasad and Dhar 2014).

Participants which frequently consumed salty foods were associated with risk of hyperglycemia. This result is in line with a previous study. High consumption of salty foods is correlated with an increased risk factor for DM (Fitria *et al.* 2016). High intake of sodium increases the risk of hyperglycemia through the PPAR δ/adiponectin/SGLT2 mechanism in regulating sodium and glucose homeostasis (Zhao *et al.* 2016).

Frequent consumption of fried foods were significantly associated with risk of hyperglycemia in recent study. Fried foods are high in fat, including saturated fat and cholesterol. Frequent consumption of fried food will lead to hyperglycemia in the pre-elderly population. A high-fat diet also significantly contributes to obesity and non-insulin-dependent diabetes mellitus (Naja *et al.* 2013). Previous study found a positive relationship between high intake of saturated fat and cholesterol and increased hyperglycemia and type 2 diabetes in humans and rats (Cahill *et al.* 2014). Saturated fat in the cell membrane will decrease the viscosity of the lipid bilayer of a cell membrane and lead to a decrease in the insulin receptors (Min *et al.* 2018).

Frequent consumption of instant foods had a significant relationship with the incidence of hyperglycemia as indicated by an increase in FBG in this study. Our results are consistent with other studies that high intake of instant foods were linked to a higher risk of developing diabetes due to the high carbohydrate and fat (Huh *et al.* 2017). However, after adjustment, there was no significant relationship. An animal trial of monosodium glutamate found a significant increase in glucose levels as evidenced by an increase in HOMA-IR value in rats. It is because of the changes in insulin binding or insulin post receptors in the target tissues (Helal *et al.* 2019). Monosodium glutamate may trigger the degradation of neuronal membranes, allowing calcium ions to enter cells because of its permeability of sodium ions, calcium ions, and water. Then, it might damage the pancreatic gland and hyperglycemia (Jusuf *et al.* 2020).

Consumption of fruits and vegetables reduced hyperglycemia. Fiber might delay the digestion and absorption of carbohydrates and increase satiety effect. In individuals with insulin resistance, fiber can increase peripheral insulin sensitivity through short-chain fatty acids produced by fiber fermentation in the gut (Samaan 2017) . In addition, a diet high in fruits and vegetables is associated with high intake of magnesium and iron (Zhang *et al.* 2015). Magnesium is an important cofactor for several enzymes in glucose metabolism, which further plays a role in the development of diabetes (Verma & Garg 2017). In this study, individuals with inadequate consumption of vegetables and fruits were 1.002 and 1.090 times, respectively, more likely to have high FBG than those with adequate consumption of vegetables and fruits.

This study has some strengths. To the best of our knowledge, this was the first study analyzing the association of food consumption with hyperglycemia among middle-aged in Indonesia. Our study used a large sample that reflected the Indonesian population. Some limitations should be mentioned in this study. Firstly, dietary data were taken using a frequency of intake which is no information related to nutrients. Moreover, the cross-sectional design restricts the results in maintaining the causality between the variables. Further research with a priori or a posteriori dietary pattern approach is highly recommended. Additional longitudinal study is needed to explore the mechanism between variables.

CONCLUSION

There was a significant association between food consumption and hyperglycemia status among middle-aged adults in Indonesia. Frequent consumption of carbonated drinks, sweet desserts, SSB, salty foods, fried foods, and instant foods, and inadequate consumption of vegetable increased the odds (chance) to have hyperglycemia. Further research with a priori or a posteriori dietary pattern approach is highly recommended. Additional longitudinal study is needed to explore the mechanism between variables.

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DECLARATION OF INTERESTS

The authors have no conflict of interest.

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AUTHOR'S REVISION FORM

Title	:	**Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis**
Author(s)	:	Ahmad Syauqy, Siti Andhini Mattarahmawati, Adriyan Pramono

No	Manuscript section	Corrected line	Suggestions	Revised line	Revisions
1	Title	-	-	-	-
2	Abstract	-	-	-	-
3	Introduction	-	-	-	-
4	Method	76-79	Explain how many of the 713,783 people had blood samples. Why from 713,783 remains 8,477 people? It is impossible that >700,000 people had missing data.	79, 80	Thank you. 713,783 people were total population aged ≥15 years. 8,481 people were included in this study (the inclusion criteria: individuals aged 45-59 years, had completed data of foods consumption, had completed data on fasting blood glucose, and agreed and had given their written informed consent. We revise the sentence to make more clear. "The inclusion criteria in this study were individuals aged 45-59 years, had completed data of foods consumption, had completed data on fasting blood glucose, and agreed and had given their written informed consent (n=8,481). While, subjects were excluded due to extreme values or missing data (n=4)."
		88-89	What happed to those who have blood glucose of 125?	11, 88	Thank you. It should be <126. We revised it accordingly

5	Result and discussion	144	This has to be 5 of males (or females) with hyperglycemia over all males (or females)	131	Thank you. I revise the percentage in the sentence according to Figure 1. The figure means that 3,648 subjects were hyperglycemia. Among 3,648 subjects with hyperglycemia, 2,325 (63.7) were female and 1,323 (36.3) were male.
		152	Why do you present your data differently from Tabel 1?	Table 1. line 125-127	Thank you. We revise it accordingly. We change Table 1
6	Conclusion and suggestion	-	-	-	-
7	References	-	-	-	-
8	Others:		Blue highlight: Need correction in English	48, 56	Thank you. We revise consisted and a research. The rest words with blue highlight are correct

* Information:

- This form is an additional file that must be attached along with the revised manuscript to make the revision easy to track **(please highlight the revised part in the revised manuscript in color).**
- The Corrected Line column is filled in according to the line number where corrected by the editor/reviewer. The Revised Line collumn is filled in according to the line number where revised by the author.
- If the author does not correct the correction for certain reasons, please inform the argument in the Revisions column.

Semarang, 11 September 2022,

Ahmad Syauqy

Overall comments :

[JGP] Further Correction from Editor II

Close Panel

Participants

- Prof. Dr. Dodik Briawan, MCN (admingizipangan)
- Ahmad Syauqy, S.Gz, MPH.,Ph.D (jgpahmadsyauqy)

Messages

Note	From
Dear Ahmad Syauqy and Team Diponegoro University Good day. Here we attach the manuscript for the 2nd further correction from our editor. Kindly check those comments & yellow highlights in the manuscript. Make sure to reply to all comments in the manuscript, use highlights for the revision part, and write your response in the author's revision form. Kindly do revision as advised. Send back the revised manuscript & the author's revision form no later than **Thursday, 22 September 2022** by replying to this message. Thank you. Regards, -- Secretariat of Indonesian Journal of Nutrition and Food Department of Community Nutrition, Faculty of Human Ecology IPB University, Dramaga, Bogor Indonesia, 16680 E-mail address: jgp@apps.ipb.ac.id Website: http://journal.ipb.ac.id/index.php/jgizipangan [JGP] Manuscript_Checked (15092022).docx [JGP] Author's Revision Form.docx	admingizipangan 2022-09-15 09:13 AM

HASIL KOREKSI EDITOR (II)

Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis

ABSTRACT

The objective of this study was to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia. This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS). A total of 8477 subjects met the inclusion criteria and included in this study. Fasting blood glucose (FBG) was analyzed in the laboratory using an enzymatic analysis. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dL) and normal (<126 mg/dL). A food frequency questionnaire was used to assess the food intake. Multiple logistic regression was used to analyze the association of food consumption and hyperglycemia. Our results found that the prevalence of hyperglycemia in this population was 43%. The mean FBG was 104.68 ± 31.99 mg/dL for male and 110.75 ± 43.92 mg/dL for female subjects. Frequent consumption of carbonated drinks (OR=1.139; CI=0.966, 1.343), sweet desserts (OR=1.265; CI=1.132, 1.413), sugar-sweetened beverages (SSB) (OR=1.433; CI=1.263, 1.626), salty foods (OR=1.189; CI=1.079, 1.311), fried foods (OR=1.172; CI=1.033, 1.331), instant foods (OR=1.186; CI=1.088, 1.293), and inadequate consumption of vegetable (OR=1.002; CI=0.920, 1.100) were significantly associated with increased odds of hyperglycemia. There was a significant association between food consumption and hyperglycemia among middle-aged adults in Indonesia.

Keyword: diet, food consumption, hyperglycemia, fasting blood glucose, Indonesia

Runner Title: Food consumption and hyperglycemia

INTRODUCTION

Non-communicable diseases are the leading cause of public health problems in developed and developing countries (Naghavi M 2017). Diabetes, one of the non-communicable diseases, is the main cause of death in the world (Zheng *et al.* 2018). Diabetes or hyperglycemia is characterized by an increase in blood sugar levels in the body. Previous studies found that the

prevalence of hyperglycemia and the components of metabolic syndrome increased rapidly with age in women and men (Wu *et al.* 2017, Jiang *et al.* 2018). Recently, Indonesia is the fourth country after India, China, and America, with the most diabetes sufferers globally (Naghavi M 2017). The prevalence of diabetes in Indonesia was around 6% (Mihardja *et al.* 2014). Interestingly, based on the 2018 Indonesia Basic Health Survey (IBHS), the higher prevalence of diabetes was among middle-aged adults with almost 10% (MoH 2018).

Diabetes is caused by many factors including lifestyle (Sudargo *et al.* 2018). Sedentary lifestyle has been associated with the increasing trend of diabetes (Nurwanti *et al.* 2018). Previous study also found that diet was associated with the increased prevalence of diabetes (Lambrinou *et al.* 2019). Western foods or unhealthy foods are correlated with an increased prevalence of hyperglycemia and metabolic syndrome (Syauqy *et al.* 2018). Western foods or unhealthy foods consisted of sweet, sugar, fat, sugar-sweetened beverages (SSB), fried foods, and seasoning; hence, the unhealthy food is high in simple carbohydrate, saturated fat, and sodium. Furthermore, inadequate consumption of vegetables and fruits can also escalate the diabetes prevalence (Syauqy *et al*. 2018, Schwingshackl *et al.* 2017).

Some studies have found the association between food consumption and metabolic syndrome among middle-aged adults in Taiwan (Syauqy *et al*. 2018). Moreover, middle-aged adults who consumed high fruits and vegetables and less unhealthy foods had a better quality of life (Lo *et al.* 2016). A research found that Indonesian people tend to consume high western foods and low fruits and vegetables (MoH 2018). However, to the best of our knowledge, study investigated the association of unhealthy foods, fruits, and vegetables intakes with diabetes among middle-aged adults in Indonesia was still rare, especially using a national database that represents the Indonesian population. Therefore, the objective of this study was to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia.

METHODS

Design, location, and time

This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS). Briefly, the IBHS used a two-stage stratified cluster sampling method survey population includes all Indonesian households, representing 26 Provinces and utilizing a sample framework from the national socio-economic survey in March 2018 (MoH 2018). This study had received ethical approval from the Health Research Ethics Commission, Medical Faculty, Universitas 'Aisyiyah Yogyakarta No. 1415/KEP-UNISA/VI/2021.

Sampling

The target sample included 300,000 households from 30,000 census blocks of the national socio-economic survey framework (MoH 2018). The total population data of the IBHS were 713,783 people aged ≥15 years (MoH 2018). The inclusion criteria in this study were individuals aged 45-59 years, had completed data of foods consumption, had completed data on fasting blood glucose, and agreed and had given their written informed consent (n=8,481). While, subjects were excluded due to extreme values or missing data (n=4). Finally, a total of 8,477 subjects met the inclusion criteria and included in this study.

Data collection

The independent variables in this study were the consumption of foods; while, the dependent variable was hyperglycemia status. Fasting blood glucose were measured with fingertip capillary blood tests (Accu-Chek Performa, Roche Diagnostics GmbH, Mannheim, Germany). All participants were instructed to fast overnight (8-10 hours) before blood sampling. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dL) and normal (<126 mg/dL) (Genuth *et al.* 2003, MoH 2018). A validated food frequency questionnaire (FFQ) was used to assess the daily food consumption. The FFQ was validated by the IBHS prior the study (MoH 2018). The FFQ includes carbonated drinks, energy drinks, sweet desserts, SSB, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods, fruits, and vegetables (MoH 2018). Consumption of unhealthy foods (carbonated drinks, energy drinks, sweet desserts, SSB, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods) was categorized as frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Fruits and vegetable consumption was categorized into adequate (≥5 servings per day) and inadequate (<5 servings per day) (MoH 2018). Sociodemographic data (age, gender, education, and place of residence) and lifestyle (smoking status, alcohol intake, and physical activity) were obtained using a structured questionnaire. Smoking is categorized into yes and no. Consumption of alcoholic beverages is categorized into yes and no (Atamni *et al.* 2016). Gender was categorized as male and female. Education level was categorized as high (completed 12-year compulsory education or bachelor/diploma/higher education graduates) and low (not completed 12-year compulsory education). Residency was categorized as urban and rural. Physical activity was categorized as low (doing heavy physical activity for <150 minutes/week) and high (doing heavy physical activity for ≥150 minutes/week (MoH 2018).

Data analysis

Univariate analysis was presented using mean±standard deviation for numerical data and frequency (percentage) for categorical data. In addition, bivariate analysis was performed using independent samples t-test for continuous variables and the Chi-square test for categorical variables. Whereas, multivariate analysis using multiple logistic regression was used to analyze the association of food consumption and hyperglycemia status. Odds ratio (OR) with 95% confidence intervals was conducted in the analyze. We used unadjusted (model 1) and adjusted (model 2). Model 2 was adjusted for demographic data (age, gender, residency) and lifestyle (smoking status, alcohol consumption, and physical activity). We selected demographic data and lifestyle because they have potential association with hyperglycemia that might interfere the results. All analyses were performed using the SPSS program 25 version with a *p*-value <0.05 considered statistically significant.

RESULTS AND DISCUSSION

Table 1 shows the characteristics of the subjects. The majority of the subjects with hyperglycemia were older (52.05±4.29), female (44.6), not smoking (44.3), and had low physical activity (44.3). Our results also found that the prevalence of hyperglycemia in the population was 43% (Figure 1). The mean FBG was 104.68±31.99 mg/dL for male and 110.75±43.92 mg/dL for female subjects. This study also found that the prevalence of hyperglycemia was higher in females (63.7) than males (36.3). This result was in line with a previous study in the United State (ADA 2018). Women are more risk of experiencing hyperglycemia due to the hormonal changes (ADA 2018). Moreover, physical activity in women tends to be lower than in men (The Lancet Public Health 2019).

Commented [A40]: The prevalence should be 40.6% in males and 44.6% in females.
But among all diabetics, 63.7% were females.

Table 1. Characteristics of the subjects (n=8,477).

Variables	Hyperglycemia		*P*	All subjects
	Yes (n = 3,648)	No (4,829)		
Age, years	52.05±4.29	41.27±4.24	<0.001*	51.6 ± 4.28
Gender, n(%)			<0.001**	
Male	1,323 (40.6)	1,935 (59.4)		3,258 (100)
Female	2,325 (44.6)	2,894 (55.4)		5,219 (100)

Education levels, n (%)			0.310**	
High	1,239 (42.3)	1,691 (57.7)		2,930 (100)
Low	2,409 (43.4)	3,138 (56.6)		5,547 (100)
Residency, n (%)			0.188**	
Rural	1,837 (42.3)	2,502 (57.7)		4,339 (100)
Urban	1,811 (43.8)	2,325 (56.2)		4,136 (100)
Smoking status, n (%)			<0.001**	
No	2,546 (44.3)	3,195 (55.7)		5,741 (100)
Yes	1,102 (40.3)	1,634 (59.7)		2,736 (100)
Alcohol consumption, n (%)			0.465**	
No	3,604 (43.0)	4,779 (57.0)		8,383 (100)
Yes	44 (46.8)	50 (53.2)		94 (100)
Physical activity, n (%)			0.019**	
High	1,684 (41.7)	2,355 (58.3)		4,039 (100)
Low	1,964 (44.3)	2,474 (55,7)		4,438 (100)
Fasting blood glucose, mg/dL	130.84±52.65	91.47±5.43	<0.001*	108.42 ± 39.87

*Comparison between continuous variables and hyperglycemia were performed using independent samples t-test

**Comparison between categorical variables and hyperglycemia were performed using Chi-square test

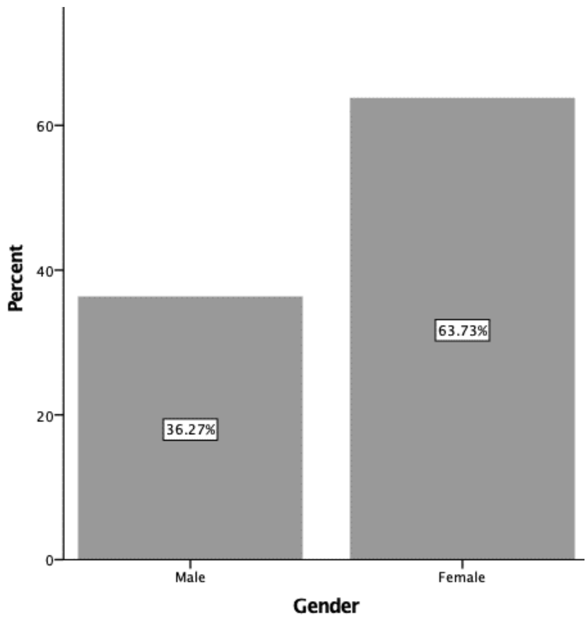

Figure 1. Prevalence of hyperglycemia across gender.

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The association of food consumption and hyperglycemia are described in Table 2. The majority of the subjects with hyperglycemia were significantly frequent consumption of carbonated drinks (43.4), sweet desserts (42.0), SSB (41.9), salty foods (41.9), fried foods (42.5), processed foods (43.6), seasonings (42.6), instant foods (41.1), and inadequate consumption of fruits (43.6), and vegetable (43.0).

Commented [A42]: Correct this sentence. Also should reflects the results of the table. Frequent consumption of some risky foods were associated with lower hyperglycemia

Table 2. Food consumption and hyperglycemia (N = 8,477)*.

Variables	Hyperglycemia		P**	Total (%)
	Yes (n = 3,648)	No (4,829)		
Carbonated drinks, n (%)			0.050	
Infrequent	254 (40.1)	379 (59.9)		633 (100)
Frequent	3,396 (43.3)	4,448 (56.7)		7,844 (100)
Energy drinks, n (%)			0.300	
Infrequent	187 (41.7)	261 (58.3)		448 (100)
Frequent	3,463 (43.1)	4,566 (56.9)		8,029 (100)
Sweet desserts, n (%)			<0.001	
Infrequent	736 (47.8)	808 (52.2)		1,544 (100)

Frequent	2,912 (42.0)	4,021 (58.0)		6,933 (100)
Sugar-sweetened beverages, n (%)			<0.001	
Infrequent	564 (50.8)	546 (49.2)		1,110 (100)
Frequent	3,086 (41.9)	4,281 (58.1)		7,367 (100)
Salty foods, n (%)			<0.001	
Infrequent	1,032 (46.2)	1,202 (53.8)		2,234 (100)
Frequent	2,618 (41.9)	3,625 (58.1)		6,243 (100)
Fried foods, n (%)			0.015	0.015
Infrequent	513 (46.5)	591 (53.5)		1,104 (100)
Frequent	3,137 (42.5)	4,236 (57.5)		7,373 (100)
Grilled foods, n (%)			0.515	
Infrequent	1,056 (42.5)	1,429 (57.5)		2,485 (100)
Frequent	2,594 (43.3)	3,398 (56.7)		5,992 (100)
Processed foods, n (%)			0.035	0.035
Infrequent	714 (41.1)	1,023 (58.9)		1,737 (100)
Frequent	2,936 (43.6)	3,804 (56.4)		6,740 (100)
Seasonings, n (%)			0.020	
Infrequent	376 (46.9)	425 (53.1)		801 (100)
Frequent	3,274 (42.6)	4,402 (57.4)		7,676 (100)
Instant foods, n (%)			<0.001	<0.001
Infrequent	1,761 (45.3)	2,125 (54.7)		3,886 (100)
Frequent	1,889 (41.1)	2,702 (58.9)		4,591 (100)
Fruits, n (%)			0.042	0.042
Adequate	976 (41.5)	1,374 (58.5)		2,350 (100)
Inadequate	2,674 (43.6)	3,453 (56.4)		6,127 (100)
Vegetable, n (%)			0.049	
Adequate	637 (43.1)	841 (56.9)		1,478 (100)
Inadequate	3,013 (43.0)	3,986 (57.0)		6,999 (100)

*Frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Adequate (≥5 servings per day) and inadequate (<5 servings per day)

**Comparison between food consumption and hyperglycemia were performed using Chi-square test

The odds ratios (95% confidence intervals) for food consumption across hyperglycemia are presented in Table 3. Frequent consumption of carbonated drinks (OR=1.139; CI=0.966, 1.343),

sweet desserts (OR=1.265; CI=1.132, 1.413), SSB (OR=1.433; CI=1.263, 1.626), salty foods (OR=1.189; CI=1.079, 1.311), fried foods (OR=1.172; CI=1.033, 1.331), processed foods (OR=1.106; CI=0.993, 1.230), seasonings (OR=1.190; CI=1.028, 1.377), instant foods (OR=1.186; CI=1.088, 1.293), and inadequate consumption of fruits (OR=1.090; CI=0.990, 1.200) and vegetable (OR=1.002; CI=0.920, 1.100) were significantly associated with increased crude odds (model 1) of hyperglycemia. After adjusting for age, gender, education levels, residency, smoking status, alcohol consumption, and physical activity (model 2), processed foods, seasonings, and fruits were not significantly associated with hyperglycemia.

Table 3. Odds ratios (95% confidence intervals) for food consumption across hyperglycemia

Variables	Model 1**			Model 2***		
	OR	95% CI	*p*	OR	95% CI	*p**
Carbonated drinks			0.039			0.050
Infrequent	1			1		
Frequent	1.139	0.966, 1.343		1.073	0.908, 1.269	
Energy drinks			0.565			0.772
Infrequent	1			1		
Frequent	1.058	0.873, 1.284		0.971	0.798, 1.182	
Sweet desserts			<0.001	1		<0.001
Infrequent	1					
Frequent	1.265	1.132, 1.413		1.238	1.108, 1.384	
Sugar-sweetened beverages			<0.001			<0.001
Infrequent	1			1		
Frequent	1.433	1.263, 1.626		1.378	1.213, 1.567	
Salty foods			<0.001			<0.001
Infrequent	1			1		

Commented [A43]: Check the p-value in relation to the 95% CI. Some are wrong

Frequent	1.189	1.079, 1.311		1.169	1.060, 1.289	
Fried foods			0.014			0.042
Infrequent	1			1		
Frequent	1.172	1.033, 1.331		1.142	1.005, 1.299	
Grilled foods			0.504			0.735
Infrequent	1			1		
Frequent	1.033	0.940, 1.135		1.017	0.924, 1.119	
Processed foods			0.036			0.149
Infrequent	1			1		
Frequent	1.106	0.993, 1.230		1.083	0.972, 1.206	
Seasonings			0.020			0.052
Infrequent	1			1		
Frequent	1.190	1.028, 1.377		1.156	0.998, 1.340	
Instant foods			<0.001			0.008
Infrequent	1			1		
Frequent	1.186	1.088, 1.293		1.127	1.032, 1.229	
Fruits			0.045			0.051
Adequate	1			1		
Inadequate	1.090	0.990, 1.200		1.085	0.977, 1.189	
Vegetables						
Adequate	1		0.036	1		0.041
Inadequate	1.002	0.920, 1.100		1.090	1.030, 1.163	

*Differences between food consumption and hyperglycemia were analyzed using multiple logistic regression. **Model 1 was unadjusted. ***Model 2 was adjusted for age, gender, education level, residency, smoking status, alcohol consumption, physical activity.

We found that frequent consumption of sweet desserts and SSB were significantly associated with risk of hyperglycemia. Sweet desserts and SSB contained carbohydrates or simple sugars with a high Glycemic Index (GI) value, leading to accelerated blood sugar levels (Medina-Remón *et al.* 2018). Other studies found a decrease in endothelial cells' micro and macro cellular function when consuming sweetened sugary beverages (Loader *et al.* 2017). These metabolic abnormalities are due to the increased in oxidative stress and decreased in NO's (nitric oxide) bioavailability, which plays an important role in glucose metabolism in the body. The decreased in NO bioavailability is also related to risk of developing type 2 diabetes (Loader *et al*. 2017). Added sugar intake is involved in the production of reactive oxygen species (ROS). It then might increase the expression of cytokines and cell adhesion molecules (Prasad and Dhar 2014).

Participants who frequently consumed salty foods were associated with risk of hyperglycemia. This result is in line with a previous study. High consumption of salty foods is correlated with an increased risk factor for DM (Fitria *et al.* 2016). High intake of sodium increases the risk of hyperglycemia through the PPAR δ/adiponectin/SGLT2 mechanism in regulating sodium and glucose homeostasis (Zhao *et al.* 2016).

Frequent consumption of fried foods were significantly associated with risk of hyperglycemia in recent study. Fried foods are high in fat, including saturated fat and cholesterol. Frequent consumption of fried food will lead to hyperglycemia in the pre-elderly population. A high-fat diet also significantly contributes to obesity and non-insulin-dependent diabetes mellitus (Naja *et al.* 2013). Previous study found a positive relationship between high intake of saturated fat and cholesterol and increased hyperglycemia and type 2 diabetes in humans and rats (Cahill *et al.* 2014). Saturated fat in the cell membrane will decrease the viscosity of the lipid bilayer of a cell membrane and lead to a decrease in the insulin receptors (Min *et al.* 2018).

Frequent consumption of instant foods had a significant relationship with the incidence of hyperglycemia as indicated by an increase in FBG in this study. Our results are consistent with other studies that high intake of instant foods were linked to a higher risk of developing diabetes due to the high carbohydrate and fat (Huh *et al.* 2017). However, after adjustment, there was no significant relationship. An animal trial of monosodium glutamate found a significant increase in glucose levels as evidenced by an increase in HOMA-IR value in rats. It is because of the changes in insulin binding or insulin post receptors in the target tissues (Helal *et al.* 2019). Monosodium glutamate may trigger the degradation of neuronal membranes, allowing calcium ions to enter cells because of its permeability of sodium ions, calcium ions, and water. Then, it might damage the pancreatic gland and hyperglycemia (Jusuf *et al.* 2020).

Consumption of fruits and vegetables reduced hyperglycemia. Fiber might delay the digestion and absorption of carbohydrates and increase satiety effect. In individuals with insulin

Commented [A44]: Could the discussion add explanation why there are an opposite direction of association between bivariate (Table 2) and multivariate (Table 3). For example for instant foods; in bivariate, infrequent consumption are associated with higher prevalence of hyperglycemia, but not in multivariate analysis. These also for sweet desert, sugar-sweetened beverages, salty foods and fried foods

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Commented [A47]: Not as shown in table 2.

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resistance, fiber can increase peripheral insulin sensitivity through short-chain fatty acids produced by fiber fermentation in the gut (Samaan 2017) . In addition, a diet high in fruits and vegetables is associated with high intake of magnesium and iron (Zhang *et al.* 2015). Magnesium is an important cofactor for several enzymes in glucose metabolism, which further plays a role in the development of diabetes (Verma & Garg 2017). In this study, individuals with inadequate consumption of vegetables and fruits were 1.002 and 1.090 times, respectively, more likely to have high FBG than those with adequate consumption of vegetables and fruits.

Commented [A49]: Check again the discussion. It has to be in line with the results presented in the tables.

This study has some strengths. To the best of our knowledge, this was the first study analyzing the association of food consumption with hyperglycemia among middle-aged in Indonesia. Our study used a large sample that reflected the Indonesian population. Some limitations should be mentioned in this study. Firstly, dietary data were taken using a frequency of intake which is no information related to nutrients. Moreover, the cross-sectional design restricts the results in maintaining the causality between the variables. Further research with a priori or a posteriori dietary pattern approach is highly recommended. Additional longitudinal study is needed to explore the mechanism between variables.

CONCLUSION

There was a significant association between food consumption and hyperglycemia status among middle-aged adults in Indonesia. Frequent consumption of carbonated drinks, sweet desserts, SSB, salty foods, fried foods, and instant foods, and inadequate consumption of vegetable increased the odds (chance) to have hyperglycemia. Further research with a priori or a posteriori dietary pattern approach is highly recommended. Additional longitudinal study is needed to explore the mechanism between variables.

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ACKNOWLEDGMENT

We would like to thank Faculty of Medicine (name), (university name) (registration number).

DECLARATION OF INTERESTS

The authors have no conflict of interest.

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Settings

Dear Prof. Dr. Dodik Briawan, MCN, Editor-in-Chief,

Many thanks for the editors' suggestions and comments. We have revised throughout the manuscript entitled "Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis" according to the editors' comments and suggestions.

If you have any questions, please feel free to call me at +6224-76402881 (email: syauqy@fk.undip.ac.id). I am looking forward to your response.

Best Regards,

Ahmad Syauqy

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HASIL PERBAIKAN EDITOR (II)

Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis

ABSTRACT

The objective of this study was to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia. This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS). A total of 8477 subjects met the inclusion criteria and included in this study. Fasting blood glucose (FBG) was analyzed in the laboratory using an enzymatic analysis. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dL) and normal (<126 mg/dL). A food frequency questionnaire was used to assess the food intake. Multiple logistic regression was used to analyze the association of food consumption and hyperglycemia. Our results found that the prevalence of hyperglycemia in this population was 43%. The mean FBG was 104.68 ± 31.99 mg/dL for male and 110.75 ± 43.92 mg/dL for female subjects. Frequent consumption of sweet desserts (OR=1.265; CI=1.132, 1.413), sugar-sweetened beverages (SSB) (OR=1.433; CI=1.263, 1.626), salty foods (OR=1.189; CI=1.079, 1.311), fried foods (OR=1.172; CI=1.033, 1.331), and instant foods (OR=1.186; CI=1.088, 1.293) were significantly associated with increased odds of hyperglycemia. There was a significant association between food consumption and hyperglycemia among middle-aged adults in Indonesia.

Keyword: diet, food consumption, hyperglycemia, fasting blood glucose, Indonesia

Runner Title: Food consumption and hyperglycemia

INTRODUCTION

Non-communicable diseases are the leading cause of public health problems in developed and developing countries (Naghavi M 2017). Diabetes, one of the non-communicable diseases, is the main cause of death in the world (Zheng *et al.* 2018). Diabetes or hyperglycemia is characterized by an increase in blood sugar levels in the body. Previous studies found that the prevalence of hyperglycemia and the components of metabolic syndrome increased rapidly with

age in women and men (Wu *et al.* 2017, Jiang *et al.* 2018). Recently, Indonesia is the fourth country after India, China, and America, with the most diabetes sufferers globally (Naghavi M 2017). The prevalence of diabetes in Indonesia was around 6% (Mihardja *et al.* 2014). Interestingly, based on the 2018 Indonesia Basic Health Survey (IBHS), the higher prevalence of diabetes was among middle-aged adults with almost 10% (MoH 2018).

Diabetes is caused by many factors including lifestyle (Sudargo *et al.* 2018). Sedentary lifestyle has been associated with the increasing trend of diabetes (Nurwanti *et al.* 2018). Previous study also found that diet was associated with the increased prevalence of diabetes (Lambrinou *et al.* 2019). Western foods or unhealthy foods are correlated with an increased prevalence of hyperglycemia and metabolic syndrome (Syauqy *et al.* 2018). Western foods or unhealthy foods consisted of sweet, sugar, fat, sugar-sweetened beverages (SSB), fried foods, and seasoning; hence, the unhealthy food is high in simple carbohydrate, saturated fat, and sodium. Furthermore, inadequate consumption of vegetables and fruits can also escalate the diabetes prevalence (Syauqy *et al*. 2018, Schwingshackl *et al.* 2017).

Some studies have found the association between food consumption and metabolic syndrome among middle-aged adults in Taiwan (Syauqy *et al*. 2018). Moreover, middle-aged adults who consumed high fruits and vegetables and less unhealthy foods had a better quality of life (Lo *et al.* 2016). A research found that Indonesian people tend to consume high western foods and low fruits and vegetables (MoH 2018). However, to the best of our knowledge, study investigated the association of unhealthy foods, fruits, and vegetables intakes with diabetes among middle-aged adults in Indonesia was still rare, especially using a national database that represents the Indonesian population. Therefore, the objective of this study was to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia.

METHODS

Design, location, and time

This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS). Briefly, the IBHS used a two-stage stratified cluster sampling method survey population includes all Indonesian households, representing 26 Provinces and utilizing a sample framework from the national socio-economic survey in March 2018 (MoH 2018). This study had received ethical approval from the Health Research Ethics Commission, Medical Faculty, Universitas 'Aisyiyah Yogyakarta No. 1415/KEP-UNISA/VI/2021.

Sampling

The target sample included 300,000 households from 30,000 census blocks of the national socio-economic survey framework (MoH 2018). The total population data of the IBHS were 713,783 people aged ≥15 years (MoH 2018). The inclusion criteria in this study were individuals aged 45-59 years, had completed data of foods consumption, had completed data on fasting blood glucose, and agreed and had given their written informed consent (n=8,481). While, subjects were excluded due to extreme values or missing data (n=4). Finally, a total of 8,477 subjects met the inclusion criteria and included in this study.

Data collection

The independent variables in this study were the consumption of foods; while, the dependent variable was hyperglycemia status. Fasting blood glucose were measured with fingertip capillary blood tests (Accu-Chek Performa, Roche Diagnostics GmbH, Mannheim, Germany). All participants were instructed to fast overnight (8-10 hours) before blood sampling. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dL) and normal (<126 mg/dL) (Genuth *et al.* 2003, MoH 2018). A validated food frequency questionnaire (FFQ) was used to assess the daily food consumption. The FFQ was validated by the IBHS prior the study (MoH 2018). The FFQ includes carbonated drinks, energy drinks, sweet desserts, SSB, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods, fruits, and vegetables (MoH 2018). Consumption of unhealthy foods (carbonated drinks, energy drinks, sweet desserts, SSB, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods) was categorized as frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Fruits and vegetable consumption was categorized into adequate (≥5 servings per day) and inadequate (<5 servings per day) (MoH 2018). Sociodemographic data (age, gender, education, and place of residence) and lifestyle (smoking status, alcohol intake, and physical activity) were obtained using a structured questionnaire. Smoking is categorized into yes and no. Consumption of alcoholic beverages is categorized into yes and no (Atamni *et al.* 2016). Gender was categorized as male and female. Education level was categorized as high (completed 12-year compulsory education or bachelor/diploma/higher education graduates) and low (not completed 12-year compulsory education). Residency was categorized as urban and rural. Physical activity was categorized as low (doing heavy physical activity for <150 minutes/week) and high (doing heavy physical activity for ≥150 minutes/week (MoH 2018).

Data analysis

Univariate analysis was presented using mean±standard deviation for numerical data and frequency (percentage) for categorical data. In addition, bivariate analysis was performed using independent samples t-test for continuous variables and the Chi-square test for categorical variables. Whereas, multivariate analysis using multiple logistic regression was used to analyze the association of food consumption and hyperglycemia status. Odds ratio (OR) with 95% confidence intervals was conducted in the analyze. We used unadjusted (model 1) and adjusted (model 2). Model 2 was adjusted for demographic data (age, gender, residency) and lifestyle (smoking status, alcohol consumption, and physical activity). We selected demographic data and lifestyle because they have potential association with hyperglycemia that might interfere the results. All analyses were performed using the SPSS program 25 version with a *p*-value <0.05 considered statistically significant.

RESULTS AND DISCUSSION

Table 1 shows the characteristics of the subjects. The majority of the subjects with hyperglycemia were older (52.05±4.29), female (63.7), not smoking (69.8), and had low physical activity (53.3). Our results also found that the prevalence of hyperglycemia in the population was 43%. The mean FBG was 104.68±31.99 mg/dL for male and 110.75±43.92 mg/dL for female subjects. This study also found that the prevalence of hyperglycemia was higher in females (44.6) than males (40.6) (Figure 1). This result was in line with a previous study in the United State (ADA 2018). Women are more risk of experiencing hyperglycemia due to the hormonal changes (ADA 2018). Moreover, physical activity in women tends to be lower than in men (The Lancet Public Health 2019).

Table 1. Characteristics of the subjects.

Variables	Hyperglycemia		*P*	All subjects
	Yes (n = 3,648)	No (4,829)		(n=8,477)
Age, years	52.05±4.29	41.27±4.24	<0.001*	51.6 ± 4.28
Gender, n(%)			<0.001**	
Male	1,323 (36.3)	1,935 (40.1)		3,258 (38.4)

Female	2,325 (63.7)	2,894 (59.9)		5,219 (61.6)
Education levels, n (%)			0.310**	
High	1,239 (34.0)	1,691 (35.0)		2,930 (34.6)
Low	2,409 (66.0)	3,138 (65.0)		5,547 (65.4)
Residency, n (%)			0.188**	
Rural	1,837 (50.4)	2,502 (51.8)		4,339 (51.2)
Urban	1,811 (49.8)	2,325 (48.2)		4,136 (48.8)
Smoking status, n (%)			<0.001**	
No	2,546 (69.8)	3,195 (66.2)		5,741 (67.7)
Yes	1,102 (30.2)	1,634 (33.8)		2,736 (32.3)
Alcohol consumption, n (%)			0.465**	
No	3,604 (98.8)	4,779 (99.0)		8,383 (98.9)
Yes	44 (1.2)	50 (1.0)		94 (1.1)
Physical activity, n (%)			0.019**	
High	1,684 (46.2)	2,355 (48.8)		4,039 (47.6)
Low	1,964 (53.3)	2,474 (51.2)		4,438 (52.4)
Fasting blood glucose, mg/dL	130.84±52.65	91.47±5.43	<0.001*	108.42 ± 39.87

*Comparison between continuous variables and hyperglycemia were performed using independent samples t-test

**Comparison between categorical variables and hyperglycemia were performed using Chi-square test

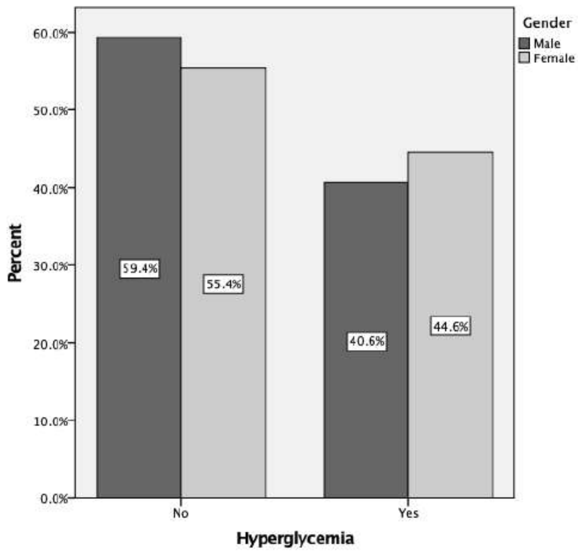

Figure 1. Prevalence of hyperglycemia among gender male and female among subjects with hyperglycemia.

The association of food consumption and hyperglycemia are described in Table 2. Among subjects with hyperglycemia, 79.8%, 84.5%, 71.7%, 85.9%, 80.4%, 89.7%, and 51.7% frequently consumed sweet desserts, SSB, salty foods, fried foods, processed foods, seasonings, and instant foods, respectively. Moreover, among subjects with hyperglycemia, 73.2% inadequate consumed fruits.

Table 2. Food consumption and hyperglycemia*.

Variables	Hyperglycemia		P**	Total (%)
	Yes (n = 3,648)	No (4,829)		(N = 8,477)
Carbonated drinks, n (%)			0.050	
Infrequent	254 (7.0)	379 (7.8)		633 (7.5)
Frequent	3,396 (93.0)	4,448 (92.2)		7,844 (92.5)
Energy drinks, n (%)			0.300	
Infrequent	187 (5.1)	261 (5.4)		448 (5.3)
Frequent	3,463 (94.9)	4,566 (94.6)		8,029 (94.7)
Sweet desserts, n (%)			<0.001	
Infrequent	736 (20.2)	808 (17.7)		1,544 (18.2)
Frequent	2,912 (79.8)	4,021 (82.3)		6,933 (81.8)

Sugar-sweetened beverages, n (%)			<0.001	
Infrequent	564 (15.5)	546 (11.3)		1,110 (13.1)
Frequent	3,086 (84.5)	4,281 (88.7)		7,367 (86.9)
Salty foods, n (%)			<0.001	
Infrequent	1,032 (28.3)	1,202 (24.9)		2,234 (26.4)
Frequent	2,618 (71.7)	3,625 (75.1)		6,243 (73.6)
Fried foods, n (%)			0.015	0.015
Infrequent	513 (14.1)	591 (12.2)		1,104 (13.0)
Frequent	3,137 (85.9)	4,236 (87.8)		7,373 (87.0)
Grilled foods, n (%)			0.515	
Infrequent	1,056 (28.9)	1,429 (29.6)		2,485 (29.3)
Frequent	2,594 (71.1)	3,398 (70.4)		5,992 (70.7)
Processed foods, n (%)			0.035	0.035
Infrequent	714 (19.6)	1,023 (21.2)		1,737 (20.5)
Frequent	2,936 (80.4)	3,804 (78.8)		6,740 (79.5)
Seasonings, n (%)			0.020	
Infrequent	376 (10.3)	425 (8.8)		801 (9.5)
Frequent	3,274 (89.7)	4,402 (91.2)		7,676 (90.5)
Instant foods, n (%)			<0.001	<0.001
Infrequent	1,761 (48.3)	2,125 (44.0)		3,886 (45.8)
Frequent	1,889 (51.7)	2,702 (56.0)		4,591 (54.2)
Fruits, n (%)			0.042	0.042
Adequate	976 (26.8)	1,374 (28.5)		2,350 (27.7)
Inadequate	2,674 (73.2)	3,453 (71.5)		6,127 (72.3)
Vegetable, n (%)			0.495	
Adequate	637 (17.5)	841 (17.4)		1,478 (17.4)
Inadequate	3,013 (82.5)	3,986 (82.6)		6,999 (82.6)

*Frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Adequate (≥5 servings per day) and inadequate (<5 servings per day)

**Comparison between food consumption and hyperglycemia were performed using Chi-square test

The odds ratios (95% confidence intervals) for food consumption across hyperglycemia are presented in Table 3. Frequent consumption of sweet desserts (OR=1.265; CI=1.132, 1.413), SSB (OR=1.433; CI=1.263, 1.626), salty foods (OR=1.189; CI=1.079, 1.311), fried foods (OR=1.172;

CI=1.033, 1.331), and instant foods (OR=1.186; CI=1.088, 1.293) were significantly associated with increased crude odds (model 1) of hyperglycemia. After adjusting for age, gender, education levels, residency, smoking status, alcohol consumption, and physical activity (model 2), frequent consumption of seasonings was not significantly associated with hyperglycemia.

Table 3. Odds ratios (95% confidence intervals) for food consumption across hyperglycemia

Variables	Model 1**			Model 2***		
	OR	95% CI	*p*	OR	95% CI	*p**
Carbonated drinks			0.122			0.419
Infrequent	1			1		
Frequent	1.139	0.966, 1.343		1.071	0.907, 1.266	
Energy drinks			0.565			0.772
Infrequent	1			1		
Frequent	1.058	0.873, 1.284		0.971	0.798, 1.182	
Sweet desserts			<0.001	1		<0.001
Infrequent	1					
Frequent	1.265	1.132, 1.413		1.238	1.108, 1.384	
Sugar-sweetened beverages			<0.001			<0.001
Infrequent	1			1		
Frequent	1.433	1.263, 1.626		1.378	1.213, 1.567	
Salty foods			<0.001			<0.001
Infrequent	1			1		
Frequent	1.189	1.079, 1.311		1.169	1.060, 1.289	
Fried foods			0.014			0.042
Infrequent	1			1		
Frequent	1.172	1.033, 1.331		1.142	1.005, 1.299	
Grilled foods			0.504			0.735
Infrequent	1			1		
Frequent	1.033	0.940, 1.135		1.017	0.924, 1.119	
Processed foods			0.066			0.167
Infrequent	1			1		
Frequent	1.106	0.993, 1.230		1.079	0.969, 1.202	

Seasonings			0.020			0.052
Infrequent	1			1		
Frequent	1.190	1.028, 1.377		1.156	0.998, 1.340	
Instant foods			<0.001			0.008
Infrequent	1			1		
Frequent	1.186	1.088, 1.293		1.127	1.032, 1.229	
Fruits			0.080			0.098
Adequate	1			1		
Inadequate	1.090	0.990, 1.200		1.086	0.985, 1.197	
Vegetables						
Adequate	1		0.969	1		0.983
Inadequate	1.002	0.895, 1.123		1.001	1.893, 1.123	

[*]Differences between food consumption and hyperglycemia were analyzed using multiple logistic regression. [**]Model 1 was unadjusted. [***]Model 2 was adjusted for age, gender, education level, residency, smoking status, alcohol consumption, physical activity.

We found that frequent consumption of sweet desserts and SSB were significantly associated with risk of hyperglycemia. Sweet desserts and SSB contained carbohydrates or simple sugars with a high Glycemic Index (GI) value, leading to accelerated blood sugar levels (Medina-Remón *et al.* 2018). Other studies found a decrease in endothelial cells' micro and macro cellular function when consuming sweetened sugary beverages (Loader *et al.* 2017). These metabolic abnormalities are due to the increased in oxidative stress and decreased in NO's (nitric oxide) bioavailability, which plays an important role in glucose metabolism in the body. The decreased in NO bioavailability is also related to risk of developing type 2 diabetes (Loader *et al*. 2017). Added sugar intake is involved in the production of reactive oxygen species (ROS). It then might increase the expression of cytokines and cell adhesion molecules (Prasad and Dhar 2014).

Participants who frequently consumed salty foods were associated with risk of hyperglycemia. This result is in line with a previous study. High consumption of salty foods is correlated with an increased risk factor for DM (Fitria *et al.* 2016). High intake of sodium increases the risk of hyperglycemia through the PPAR δ/adiponectin/SGLT2 mechanism in regulating sodium and glucose homeostasis (Zhao *et al.* 2016).

Frequent consumption of fried foods were significantly associated with risk of hyperglycemia in recent study. Fried foods are high in fat, including saturated fat and cholesterol. Frequent consumption of fried food will lead to hyperglycemia in the pre-elderly population. A high-fat diet also significantly contributes to obesity and non-insulin-dependent diabetes mellitus (Naja *et al.* 2013). Previous study found a positive relationship between high intake of saturated fat and cholesterol and increased hyperglycemia and type 2 diabetes in humans and rats (Cahill *et al.* 2014). Saturated fat in the cell membrane will decrease the viscosity of the lipid bilayer of a cell membrane and lead to a decrease in the insulin receptors (Min *et al.* 2018).

Frequent consumption of instant foods had a significant relationship with the incidence of hyperglycemia as indicated by an increase in FBG in this study. Our results are consistent with other studies that high intake of instant foods were linked to a higher risk of developing diabetes due to the high carbohydrate and fat (Huh *et al.* 2017). An animal trial of monosodium glutamate found a significant increase in glucose levels as evidenced by an increase in HOMA-IR value in rats. It is because of the changes in insulin binding or insulin post receptors in the target tissues (Helal *et al.* 2019). Monosodium glutamate may trigger the degradation of neuronal membranes, allowing calcium ions to enter cells because of its permeability of sodium ions, calcium ions, and water. Then, it might damage the pancreatic gland and hyperglycemia (Jusuf *et al.* 2020).

Consumption of fruits and vegetables reduced hyperglycemia. Fiber might delay the digestion and absorption of carbohydrates and increase satiety effect. In individuals with insulin resistance, fiber can increase peripheral insulin sensitivity through short-chain fatty acids produced by fiber fermentation in the gut (Samaan 2017) . In addition, a diet high in fruits and vegetables is associated with high intake of magnesium and iron (Zhang *et al.* 2015). Magnesium is an important cofactor for several enzymes in glucose metabolism, which further plays a role in the development of diabetes (Verma & Garg 2017). In this study, individuals with inadequate consumption of vegetables and fruits were 1.002 and 1.090 times, respectively, more likely to have high FBG than those with adequate consumption of vegetables and fruits, but these association were not statistically significant.

This study has some strengths. To the best of our knowledge, this was the first study analyzing the association of food consumption with hyperglycemia among middle-aged in Indonesia. Our study used a large sample that reflected the Indonesian population. Some limitations should be mentioned in this study. Firstly, dietary data were taken using a frequency of intake which is no information related to nutrients. Moreover, the cross-sectional design restricts the results in maintaining the causality between the variables. Further research with a priori or a posteriori dietary pattern approach is highly recommended. Additional longitudinal study is needed to explore the mechanism between variables.

CONCLUSION

There was a significant association between food consumption and hyperglycemia status among middle-aged adults in Indonesia. Frequent consumption of sweet desserts, SSB, salty foods, fried foods, and instant foods increased the odds (chance) to have hyperglycemia. Further research with a priori or a posteriori dietary pattern approach is highly recommended. Additional longitudinal study is needed to explore the mechanism between variables.

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We would like to thank Faculty of Medicine (name), (university name) (registration number).

DECLARATION OF INTERESTS

The authors have no conflict of interest.

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AUTHOR'S REVISION FORM

Title	:	**Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis**
Author(s)	:	Ahmad Syauqy, Siti Andhini Mattarahmawati, Adriyan Pramono

No	Manuscript section	Corrected line	Suggestions	Revised line	Revisions
1	Title	-	-	-	-
2	Abstract	-	-	-	-
3	Introduction	-	-	-	-
4	Method	-	-	-	-
5	Result and discussion	130-131	The prevalence should be 40.6% in males and 44.6% in females. But among all diabetics, 63.7% were females.	128-129	Thank you. We revised it accordingly. The prevalence should be 40.6% in males and 44.6% in females.
		144 (Figure 1)	This figure is not correct	Figure 1 (139)	Thank you. We revised Figure 1 according to the previous suggestion; the prevalence should be 40.6% and 44.6% in male and female, respectively.
		147-148	Correct this sentence. Also should reflects the results of the table. Frequent consumption of some risky foods were associated with lower hyperglycemia	145-148; Table 2	Thank you. We corrected the sentence according to the Table 2. We described the consumption of the food only among subjects with hyperglycemia: "Among subjects with hyperglycemia, 79.8%, 84.5%, 71.7%, 85.9%, 80.4%, 89.7%, and 51.7% frequently consumed sweet desserts, SSB, salty foods, fried foods, processed foods, seasonings, and instant foods, respectively. Moreover, among subjects with

					hyperglycemia, 73.2% inadequate consumed fruits." We also revised the percentage in Table 2 to make it clear.
		173 (Table 3)	Check the p-value in relation to the 95% CI. Some are wrong	Table 3; 157-160 (results); 16-19 (abstract); 235-237 (conclusion)	Thank you. We checked and revised the OR, CI and p-value in Table 3 and the abstract and the conclusion
		179	Could the discussion add explanation why there are an opposite direction of association between bivariate (Table 2) and multivariate (Table 3). For example for instant foods; in bivariate, infrequent consumption are associated with higher prevalence of hyperglycemia, but not in multivariate analysis. These also for sweet desert, sugar-sweetened beverages, salty foods and fried foods	145-148; Table 2	Thank you. The data are in the same direction. But, due to the unbalanced number of subjects with hyperglycemia and subjects without hyperglycemia; therefore, the number of subjects who frequent and infrequent consumption of risk foods in without hyperglycemia group is higher than those in with hyperglycemia group. We revise Table 2 and the explanation to make it clear.
		179-229	Check again the discussion. It has to be in line with the results presented in the tables.	203-204; 219-222	Thank you. We revised the discussion accordingly.
		192	Not in table 2. But need more explanation why the direction change in table 3.	145-148; Table 2	Thank you. The data are in the same direction. But, it could be due to the unbalanced number of subjects with hyperglycemia and subjects without hyperglycemia; therefore, the number

					of subjects who frequent and infrequent consumption of risk foods in without hyperglycemia group is higher than those in with hyperglycemia group. We revised Table 2 and the explanation to make it clear.
		197-198	As above		Thank you. We already explained previously.
		209-210	Not as shown in table 2.		Thank you. We already explained previously.
		211	Still significant	204	Thank you. We deleted it accordingly.
6	Conclusion and suggestion	243-245	Check again (see notes in results and discussion)		Thank you. We already revised and explained previously.
7	References	-	-	-	-
8	Others:		The editor gave highlight in the manuscript (yellow)		Thank you

* Information:

- This form is an additional file that must be attached along with the revised manuscript to make the revision easy to track **(please highlight the revised part in the revised manuscript in color).**
- The Corrected Line column is filled in according to the line number where corrected by the editor/reviewer. The Revised Line collumn is filled in according to the line number where revised by the author.
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Semarang, 18 September 2022,

(Ahmad Syauqy)

Overall comments :

[JGP] Further Correction from Editor III

Close Panel

Participants

- Prof. Dr. Dodik Briawan, MCN (admingizipangan)
- Ahmad Syauqy, S.Gz, MPH.,Ph.D (jgpahmadsyauqy)

Messages

Note	From
Dear Ahmad Syauqy and Team Diponegoro University Good day. Here we attach the manuscript for the 3rd further correction from our editor. Kindly check those comments & blue highlights in the manuscript. Make sure to reply to all comments in the manuscript, use highlights for the revision part, and write your response in the author's revision form. Kindly do the revision as advised. Send back the revised manuscript & the author's revision form no later than **Sunday, 6 November 2022** by replying to this message. Thank you. Regards, -- Secretariat of Indonesian Journal of Nutrition and Food Department of Community Nutrition, Faculty of Human Ecology IPB University, Dramaga, Bogor Indonesia, 16680 E-mail address: jgp@apps.ipb.ac.id Website: http://journal.ipb.ac.id/index.php/jgizipangan [JGP] Manuscript_checked (01112022).docx [JGP] Author's Revision Form.docx	admingizipangan 2022-11-01 11:07 AM

HASIL REVISI EDITOR (III)

Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis

ABSTRACT

The objective of this study was to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia. This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS). A total of 8477 subjects met the inclusion criteria and included in this study. Fasting blood glucose (FBG) was analyzed in the laboratory using an enzymatic analysis. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dL) and normal (<126 mg/dL). A food frequency questionnaire was used to assess the food intake. Multiple logistic regression was used to analyze the association of food consumption and hyperglycemia. Our results found that the prevalence of hyperglycemia in this population was 43%. The mean FBG was 104.68 ± 31.99 mg/dL for male and 110.75 ± 43.92 mg/dL for female subjects. Frequent consumption of sweet desserts (OR=1.265; CI=1.132, 1.413), sugar-sweetened beverages (SSB) (OR=1.433; CI=1.263, 1.626), salty foods (OR=1.189; CI=1.079, 1.311), fried foods (OR=1.172; CI=1.033, 1.331), and instant foods (OR=1.186; CI=1.088, 1.293) were significantly associated with increased odds of hyperglycemia. There was a significant association between food consumption and hyperglycemia among middle-aged adults in Indonesia.

Keyword: diet, food consumption, hyperglycemia, fasting blood glucose, Indonesia

Runner Title: Food consumption and hyperglycemia

INTRODUCTION

Non-communicable diseases are the leading cause of public health problems in developed and developing countries (Naghavi M 2017). Diabetes, one of the non-communicable diseases, is the main cause of death in the world (Zheng *et al.* 2018). Diabetes or hyperglycemia is characterized by an increase in blood sugar levels in the body. Previous studies found that the prevalence of hyperglycemia and the components of metabolic syndrome increased rapidly with

age in women and men (Wu *et al.* 2017, Jiang *et al.* 2018). Recently, Indonesia is the fourth country after India, China, and America, with the most diabetes sufferers globally (Naghavi M 2017). The prevalence of diabetes in Indonesia was around 6% (Mihardja *et al.* 2014). Interestingly, based on the 2018 Indonesia Basic Health Survey (IBHS), the higher prevalence of diabetes was among middle-aged adults with almost 10% (MoH 2018).

Diabetes is caused by many factors including lifestyle (Sudargo *et al.* 2018). Sedentary lifestyle has been associated with the increasing trend of diabetes (Nurwanti *et al.* 2018). Previous study also found that diet was associated with the increased prevalence of diabetes (Lambrinou *et al.* 2019). Western foods or unhealthy foods are correlated with an increased prevalence of hyperglycemia and metabolic syndrome (Syauqy *et al.* 2018). Western foods or unhealthy foods consisted of sweet, sugar, fat, sugar-sweetened beverages (SSB), fried foods, and seasoning; hence, the unhealthy food is high in simple carbohydrate, saturated fat, and sodium. Furthermore, inadequate consumption of vegetables and fruits can also escalate the diabetes prevalence (Syauqy *et al*. 2018, Schwingshackl *et al.* 2017).

Some studies have found the association between food consumption and metabolic syndrome among middle-aged adults in Taiwan (Syauqy *et al*. 2018). Moreover, middle-aged adults who consumed high fruits and vegetables and less unhealthy foods had a better quality of life (Lo *et al.* 2016). A research found that Indonesian people tend to consume high western foods and low fruits and vegetables (MoH 2018). However, to the best of our knowledge, study investigated the association of unhealthy foods, fruits, and vegetables intakes with diabetes among middle-aged adults in Indonesia was still rare, especially using a national database that represents the Indonesian population. Therefore, the objective of this study was to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia.

METHODS

Design, location, and time

This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS). Briefly, the IBHS used a two-stage stratified cluster sampling method survey population includes all Indonesian households, representing 26 Provinces and utilizing a sample framework from the national socio-economic survey in March 2018 (MoH 2018). This study had received ethical approval from the Health Research Ethics Commission, Medical Faculty, Universitas 'Aisyiyah Yogyakarta No. 1415/KEP-UNISA/VI/2021.

Sampling

The target sample included 300,000 households from 30,000 census blocks of the national socio-economic survey framework (MoH 2018). The total population data of the IBHS were 713,783 people aged ≥15 years (MoH 2018). The inclusion criteria in this study were individuals aged 45-59 years, had completed data of foods consumption, had completed data on fasting blood glucose, and agreed and had given their written informed consent (n=8,481). While, subjects were excluded due to extreme values or missing data (n=4). Finally, a total of 8,477 subjects met the inclusion criteria and included in this study.

Data collection

The independent variables in this study were the consumption of foods; while, the dependent variable was hyperglycemia status. Fasting blood glucose were measured with fingertip capillary blood tests (Accu-Chek Performa, Roche Diagnostics GmbH, Mannheim, Germany). All participants were instructed to fast overnight (8-10 hours) before blood sampling. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dL) and normal (<126 mg/dL) (Genuth *et al.* 2003, MoH 2018). A validated food frequency questionnaire (FFQ) was used to assess the daily food consumption. The FFQ was validated by the IBHS prior the study (MoH 2018). The FFQ includes carbonated drinks, energy drinks, sweet desserts, SSB, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods, fruits, and vegetables (MoH 2018). Consumption of unhealthy foods (carbonated drinks, energy drinks, sweet desserts, SSB, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods) was categorized as frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Fruits and vegetable consumption was categorized into adequate (≥5 servings per day) and inadequate (<5 servings per day) (MoH 2018). Sociodemographic data (age, gender, education,

and place of residence) and lifestyle (smoking status, alcohol intake, and physical activity) were obtained using a structured questionnaire. Smoking is categorized into yes and no. Consumption of alcoholic beverages is categorized into yes and no (Atamni *et al*. 2016). Gender was categorized as male and female. Education level was categorized as high (completed 12-year compulsory education or bachelor/diploma/higher education graduates) and low (not completed 12-year compulsory education). Residency was categorized as urban and rural. Physical activity was categorized as low (doing heavy physical activity for <150 minutes/week) and high (doing heavy physical activity for ≥150 minutes/week (MoH 2018).

Data analysis

Univariate analysis was presented using mean±standard deviation for numerical data and frequency (percentage) for categorical data. In addition, bivariate analysis was performed using independent samples t-test for continuous variables and the Chi-square test for categorical variables. Whereas, multivariate analysis using multiple logistic regression was used to analyze the association of food consumption and hyperglycemia status. Odds ratio (OR) with 95% confidence intervals was conducted in the analyze. We used unadjusted (model 1) and adjusted (model 2). Model 2 was adjusted for demographic data (age, gender, residency) and lifestyle (smoking status, alcohol consumption, and physical activity). We selected demographic data and lifestyle because they have potential association with hyperglycemia that might interfere the results. All analyses were performed using the SPSS program 25 version with a *p*-value <0.05 considered statistically significant.

RESULTS AND DISCUSSION

Table 1 shows the characteristics of the subjects. The majority of the subjects with hyperglycemia were older (52.05±4.29), female (63.7), not smoking (69.8), and had low physical activity (53.3). Our results also found that the prevalence of hyperglycemia in the population was 43%. The mean FBG was 104.68±31.99 mg/dL for male and 110.75±43.92 mg/dL for female subjects. This study also found that the prevalence of hyperglycemia was higher in females (44.6) than males (40.6) (Figure 1). This result was in line with a previous study in the United State (ADA 2018). Women are more risk of experiencing hyperglycemia due to the hormonal changes (ADA 2018). Moreover, physical activity in women tends to be lower than in men (The Lancet Public Health 2019).

Table 1. Characteristics of the subjects.

Variables	n	Hyperglycemia		*P*
		Yes (n = 3,648)	No (4,829)	
Age, years	8,477	52.05±4.29	41.27±4.24	<0.001*
Gender, n(%)				<0.001**
Male	3,258	1,323 (40.6)	1,935 (59.4)	
Female	5,219	2,325 (44.6)	2,894 (55.4)	

Continue with the other variables

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Table 1. Characteristics of the subjects.

Variables	Hyperglycemia		*P*	All subjects
	Yes (n = 3,648)	No (4,829)		(n=8,477)
Age, years	52.05±4.29	41.27±4.24	<0.001*	51.6 ± 4.28
Gender, n(%)			<0.001**	
Male	1,323 (36.3)	1,935 (40.1)		3,258 (38.4)
Female	2,325 (63.7)	2,894 (59.9)		5,219 (61.6)
Education levels, n (%)			0.310**	
High	1,239 (34.0)	1,691 (35.0)		2,930 (34.6)
Low	2,409 (66.0)	3,138 (65.0)		5,547 (65.4)
Residency, n (%)			0.188**	
Rural	1,837 (50.4)	2,502 (51.8)		4,339 (51.2)
Urban	1,811 (49.8)	2,325 (48.2)		4,136 (48.8)
Smoking status, n (%)			<0.001**	
No	2,546 (69.8)	3,195 (66.2)		5,741 (67.7)
Yes	1,102 (30.2)	1,634 (33.8)		2,736 (32.3)
Alcohol consumption, n (%)			0.465**	
No	3,604 (98.8)	4,779 (99.0)		8,383 (98.9)
Yes	44 (1.2)	50 (1.0)		94 (1.1)
Physical activity, n (%)			0.019**	
High	1,684 (46.2)	2,355 (48.8)		4,039 (47.6)
Low	1,964 (53.3)	2,474 (51.2)		4,438 (52.4)
Fasting blood glucose, mg/dL	130.84±52.65	91.47±5.43	<0.001*	108.42 ± 39.87

*Comparison between continuous variables and hyperglycemia were performed using independent samples t-test

**Comparison between categorical variables and hyperglycemia were performed using Chi-square test

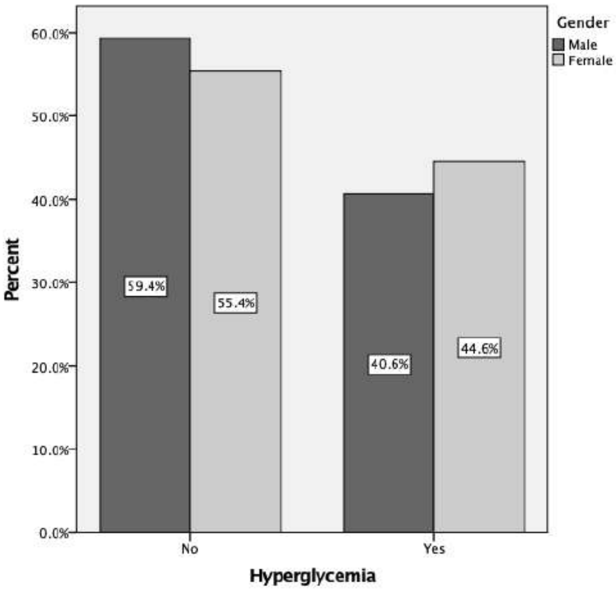

Figure 1. Prevalence of hyperglycemia among gender male and female among subjects with hyperglycemia.

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The association of food consumption and hyperglycemia are described in Table 2. Among subjects with hyperglycemia, 79.8%, 84.5%, 71.7%, 85.9%, 80.4%, 89.7%, and 51.7% frequently consumed sweet desserts, SSB, salty foods, fried foods, processed foods, seasonings, and instant foods, respectively. Moreover, among subjects with hyperglycemia, 73.2% inadequate consumed fruits.

Commented [A53]: You need to explain according to the findings in the table.
Your table shows an association between hyperglycemic vs. non-glycemic. Your sentences should figure out whether there is association or not. And if yes, to which direction. Whether the association is according to your hypothesis or the theory that you have found.

Table 2. Food consumption and hyperglycemia*.

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Variables	Hyperglycemia		P^{**}	Total (%)
	Yes (n = 3,648)	No (4,829)		(N = 8,477)
Carbonated drinks, n (%)			0.050	
Infrequent	254 (7.0)	379 (7.8)		633 (7.5)
Frequent	3,396 (93.0)	4,448 (92.2)		7,844 (92.5)
Energy drinks, n (%)			0.300	
Infrequent	187 (5.1)	261 (5.4)		448 (5.3)
Frequent	3,463 (94.9)	4,566 (94.6)		8,029 (94.7)
Sweet desserts, n (%)			<0.001	
Infrequent	736 (20.2)	808 (17.7)		1,544 (18.2)
Frequent	2,912 (79.8)	4,021 (82.3)		6,933 (81.8)
Sugar-sweetened beverages, n (%)			<0.001	
Infrequent	564 (15.5)	546 (11.3)		1,110 (13.1)

Frequent	3,086 (84.5)	4,281 (88.7)		7,367 (86.9)
Salty foods, n (%)			<0.001	
Infrequent	1,032 (28.3)	1,202 (24.9)		2,234 (26.4)
Frequent	2,618 (71.7)	3,625 (75.1)		6,243 (73.6)
Fried foods, n (%)			0.015	0.015
Infrequent	513 (14.1)	591 (12.2)		1,104 (13.0)
Frequent	3,137 (85.9)	4,236 (87.8)		7,373 (87.0)
Grilled foods, n (%)			0.515	
Infrequent	1,056 (28.9)	1,429 (29.6)		2,485 (29.3)
Frequent	2,594 (71.1)	3,398 (70.4)		5,992 (70.7)
Processed foods, n (%)			0.035	0.035
Infrequent	714 (19.6)	1,023 (21.2)		1,737 (20.5)
Frequent	2,936 (80.4)	3,804 (78.8)		6,740 (79.5)
Seasonings, n (%)			0.020	
Infrequent	376 (10.3)	425 (8.8)		801 (9.5)
Frequent	3,274 (89.7)	4,402 (91.2)		7,676 (90.5)
Instant foods, n (%)			<0.001	<0.001
Infrequent	1,761 (48.3)	2,125 (44.0)		3,886 (45.8)
Frequent	1,889 (51.7)	2,702 (56.0)		4,591 (54.2)
Fruits, n (%)			0.042	0.042
Adequate	976 (26.8)	1,374 (28.5)		2,350 (27.7)
Inadequate	2,674 (73.2)	3,453 (71.5)		6,127 (72.3)
Vegetable, n (%)			0.495	
Adequate	637 (17.5)	841 (17.4)		1,478 (17.4)
Inadequate	3,013 (82.5)	3,986 (82.6)		6,999 (82.6)

*Frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Adequate (≥5 servings per day) and inadequate (<5 servings per day)

**Comparison between food consumption and hyperglycemia were performed using Chi-square test

Commented [A55]:

Commented [A56]: You could use the odd ratio here because you have separated between those with disease (hyperglycemia) and non-disease (no hyperglycemia)

The odds ratios (95% confidence intervals) for food consumption across hyperglycemia are presented in Table 3. Frequent consumption of sweet desserts (OR=1.265; CI=1.132, 1.413), SSB (OR=1.433; CI=1.263, 1.626), salty foods (OR=1.189; CI=1.079, 1.311), fried foods (OR=1.172; CI=1.033, 1.331), and instant foods (OR=1.186; CI=1.088, 1.293) were significantly associated with increased crude odds (model 1) of hyperglycemia. After adjusting for age, gender, education levels, residency, smoking status, alcohol consumption, and physical activity (model 2), frequent consumption of seasonings was not significantly associated with hyperglycemia.

Table 3. Odds ratios (95% confidence intervals) for food consumption across hyperglycemia

Variables	Model 1**			Model 2***		
	OR	95% CI	*p*	OR	95% CI	*p**
Carbonated drinks			0.122			0.419
Infrequent	1			1		
Frequent	1.139	0.966, 1.343		1.071	0.907, 1.266	
Energy drinks			0.565			0.772
Infrequent	1			1		
Frequent	1.058	0.873, 1.284		0.971	0.798, 1.182	
Sweet desserts			<0.001	1		<0.001
Infrequent	1					
Frequent	1.265	1.132, 1.413		1.238	1.108, 1.384	
Sugar-sweetened beverages			<0.001			<0.001
Infrequent	1			1		
Frequent	1.433	1.263, 1.626		1.378	1.213, 1.567	
Salty foods			<0.001			<0.001
Infrequent	1			1		
Frequent	1.189	1.079, 1.311		1.169	1.060, 1.289	
Fried foods			0.014			0.042
Infrequent	1			1		
Frequent	1.172	1.033, 1.331		1.142	1.005, 1.299	
Grilled foods			0.504			0.735
Infrequent	1			1		
Frequent	1.033	0.940, 1.135		1.017	0.924, 1.119	
Processed foods			0.066			0.167
Infrequent	1			1		
Frequent	1.106	0.993, 1.230		1.079	0.969, 1.202	
Seasonings			0.020			0.052
Infrequent	1			1		
Frequent	1.190	1.028, 1.377		1.156	0.998, 1.340	
Instant foods			<0.001			0.008
Infrequent	1			1		

Frequent	1.186	1.088, 1.293		1.127	1.032, 1.229	
Fruits			0.080			0.098
Adequate	1			1		
Inadequate	1.090	0.990, 1.200		1.086	0.985, 1.197	
Vegetables						
Adequate	1		0.969	1		0.983
Inadequate	1.002	0.895, 1.123		1.001	1.893, 1.123	

*Differences between food consumption and hyperglycemia were analyzed using multiple logistic regression. **Model 1 was unadjusted. ***Model 2 was adjusted for age, gender, education level, residency, smoking status, alcohol consumption, physical activity.

We found that frequent consumption of sweet desserts and SSB were significantly associated with risk of hyperglycemia. Sweet desserts and SSB contained carbohydrates or simple sugars with a high Glycemic Index (GI) value, leading to accelerated blood sugar levels (Medina-Remón *et al.* 2018). Other studies found a decrease in endothelial cells' micro and macro cellular function when consuming sweetened sugary beverages (Loader *et al.* 2017). These metabolic abnormalities are due to the increased in oxidative stress and decreased in NO's (nitric oxide) bioavailability, which plays an important role in glucose metabolism in the body. The decreased in NO bioavailability is also related to risk of developing type 2 diabetes (Loader *et al*. 2017). Added sugar intake is involved in the production of reactive oxygen species (ROS). It then might increase the expression of cytokines and cell adhesion molecules (Prasad and Dhar 2014).

Commented [A57]: Could you add explanation why the direction of association from bivariate analysis (Table 2) is different from multivariate analysis (Table 3). I have asked this before.

To be clear, as an example,
In Table 2, frequent SSB consumption is associated with a lower proportion of hyperglycemia.
But in Table 3, frequent SSB consumption has a higher odd (1.378 in model 20 of being hyperglycemic.

Other variables are also on that direction.

Could you explain what are the factors or that? Or I wrongly interpret your table?

Participants who frequently consumed salty foods were associated with risk of hyperglycemia. This result is in line with a previous study. High consumption of salty foods is correlated with an increased risk factor for DM (Fitria *et al.* 2016). High intake of sodium increases the risk of hyperglycemia through the PPAR δ/adiponectin/SGLT2 mechanism in regulating sodium and glucose homeostasis (Zhao *et al.* 2016).

Frequent consumption of fried foods were significantly associated with risk of hyperglycemia in recent study. Fried foods are high in fat, including saturated fat and cholesterol. Frequent consumption of fried food will lead to hyperglycemia in the pre-elderly population. A high-fat diet also significantly contributes to obesity and non-insulin-dependent diabetes mellitus (Naja *et al.* 2013). Previous study found a positive relationship between high intake of saturated fat and cholesterol and increased hyperglycemia and type 2 diabetes in humans and rats (Cahill *et al.* 2014). Saturated fat in the cell membrane will decrease the viscosity of the lipid bilayer of a cell membrane and lead to a decrease in the insulin receptors (Min *et al.* 2018).

Frequent consumption of instant foods had a significant relationship with the incidence of hyperglycemia as indicated by an increase in FBG in this study. Our results are consistent with other studies that high intake of instant foods were linked to a higher risk of developing diabetes due to the high carbohydrate and fat (Huh *et al.* 2017). An animal trial of monosodium glutamate found a significant increase in glucose levels as evidenced by an increase in HOMA-IR value in rats. It is because of the changes in insulin binding or insulin post receptors in the target tissues (Helal *et al.* 2019). Monosodium glutamate may trigger the degradation of neuronal membranes, allowing calcium ions to enter cells because of its permeability of sodium ions, calcium ions, and water. Then, it might damage the pancreatic gland and hyperglycemia (Jusuf *et al.* 2020).

Consumption of fruits and vegetables reduced hyperglycemia. Fiber might delay the digestion and absorption of carbohydrates and increase satiety effect. In individuals with insulin resistance, fiber can increase peripheral insulin sensitivity through short-chain fatty acids produced by fiber fermentation in the gut (Samaan 2017) . In addition, a diet high in fruits and vegetables is associated with high intake of magnesium and iron (Zhang *et al.* 2015). Magnesium is an important cofactor for several enzymes in glucose metabolism, which further plays a role in the development of diabetes (Verma & Garg 2017). In this study, individuals with inadequate consumption of vegetables and fruits were 1.002 and 1.090 times, respectively, more likely to have high FBG than those with adequate consumption of vegetables and fruits, but these association were not statistically significant.

This study has some strengths. To the best of our knowledge, this was the first study analyzing the association of food consumption with hyperglycemia among middle-aged in Indonesia. Our study used a large sample that reflected the Indonesian population. Some limitations should be mentioned in this study. Firstly, dietary data were taken using a frequency of intake which is no information related to nutrients. Moreover, the cross-sectional design restricts the results in maintaining the causality between the variables. Further research with a priori or a posteriori dietary pattern approach is highly recommended. Additional longitudinal study is needed to explore the mechanism between variables.

Commented [A58]: Use a consistent terminology. Do you want to use hyperglycemic or high FBG?

Commented [A59]: You need to add explanation that the food consumption practice might be as a result of their disease condition.
For example; as you know you have diabetic, you change your dietary practice. But that change dietary practice may not change yet your disease status

Commented [A60]: Your discussion here is aligned with Table 3; but not in table 2.

Commented [A61]: You need to put more explanation why do you recommend this (what are the advantages in taking the study conclusion by having a priori or posteriori hypothesis in the study design).

CONCLUSION

There was a significant association between food consumption and hyperglycemia status among middle-aged adults in Indonesia. Frequent consumption of sweet desserts, SSB, salty foods, fried foods, and instant foods increased the odds (chance) to have hyperglycemia. Further research with a priori or a posteriori dietary pattern approach is highly recommended. Additional longitudinal study is needed to explore the mechanism between variables.

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We would like to thank Faculty of Medicine (name), (university name) (registration number).

DECLARATION OF INTERESTS

The authors have no conflict of interest.

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Settings

Dear Prof. Dr. Dodik Briawan, MCN, Editor-in-Chief,

Many thanks for the editors' suggestions and comments. We have revised throughout the manuscript entitled "Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis" according to the editors' comments and suggestions.

If you have any questions, please feel free to call me at +6224-76402881 (email: syauqy@fk.undip.ac.id). I am looking forward to your response.

Best Regards,

Ahmad Syauqy

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HASIL PERBAIKAN EDITOR (III)

Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis

ABSTRACT

The objective of this study was to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia. This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS). A total of 8477 subjects met the inclusion criteria and included in this study. Fasting blood glucose (FBG) was analyzed in the laboratory using an enzymatic analysis. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dL) and normal (<126 mg/dL). A food frequency questionnaire was used to assess the food intake. Multiple logistic regression was used to analyze the association of food consumption and hyperglycemia. Our results found that the prevalence of hyperglycemia in this population was 43%. The mean FBG was 104.68 ± 31.99 mg/dL for male and 110.75 ± 43.92 mg/dL for female subjects. Frequent consumption of sweet desserts (OR=1.265; CI=1.132, 1.413), sugar-sweetened beverages (SSB) (OR=1.433; CI=1.263, 1.626), salty foods (OR=1.189; CI=1.079, 1.311), fried foods (OR=1.172; CI=1.033, 1.331), and instant foods (OR=1.186; CI=1.088, 1.293) were significantly associated with increased odds of hyperglycemia. There was a significant association between food consumption and hyperglycemia among middle-aged adults in Indonesia.

Keyword: diet, food consumption, hyperglycemia, fasting blood glucose, Indonesia

Runner Title: Food consumption and hyperglycemia

INTRODUCTION

Non-communicable diseases are the leading cause of public health problems in developed and developing countries (Naghavi M 2017). Diabetes, one of the non-communicable diseases, is the main cause of death in the world (Zheng *et al.* 2018). Diabetes or hyperglycemia is characterized by an increase in blood sugar levels in the body. Previous studies found that the prevalence of hyperglycemia and the components of metabolic syndrome increased rapidly with

age in women and men (Wu *et al.* 2017, Jiang *et al.* 2018). Recently, Indonesia is the fourth country after India, China, and America, with the most diabetes sufferers globally (Naghavi M 2017). The prevalence of diabetes in Indonesia was around 6% (Mihardja *et al.* 2014). Interestingly, based on the 2018 Indonesia Basic Health Survey (IBHS), the higher prevalence of diabetes was among middle-aged adults with almost 10% (MoH 2018).

Diabetes is caused by many factors including lifestyle (Sudargo *et al.* 2018). Sedentary lifestyle has been associated with the increasing trend of diabetes (Nurwanti *et al.* 2018). Previous study also found that diet was associated with the increased prevalence of diabetes (Lambrinou *et al.* 2019). Western foods or unhealthy foods are correlated with an increased prevalence of hyperglycemia and metabolic syndrome (Syauqy *et al.* 2018). Western foods or unhealthy foods consisted of sweet, sugar, fat, sugar-sweetened beverages (SSB), fried foods, and seasoning; hence, the unhealthy food is high in simple carbohydrate, saturated fat, and sodium. Furthermore, inadequate consumption of vegetables and fruits can also escalate the diabetes prevalence (Syauqy *et al*. 2018, Schwingshackl *et al.* 2017).

Some studies have found the association between food consumption and metabolic syndrome among middle-aged adults in Taiwan (Syauqy *et al*. 2018). Moreover, middle-aged adults who consumed high fruits and vegetables and less unhealthy foods had a better quality of life (Lo *et al.* 2016). A research found that Indonesian people tend to consume high western foods and low fruits and vegetables (MoH 2018). However, to the best of our knowledge, study investigated the association of unhealthy foods, fruits, and vegetables intakes with diabetes among middle-aged adults in Indonesia was still rare, especially using a national database that represents the Indonesian population. Therefore, the objective of this study was to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia.

METHODS

Design, location, and time

This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS). Briefly, the IBHS used a two-stage stratified cluster sampling method survey population includes all Indonesian households, representing 26 Provinces and utilizing a sample framework from the national socio-economic survey in March 2018 (MoH 2018). This study had received ethical approval from the Health Research Ethics Commission, Medical Faculty, Universitas 'Aisyiyah Yogyakarta No. 1415/KEP-UNISA/VI/2021.

Sampling

The target sample included 300,000 households from 30,000 census blocks of the national socio-economic survey framework (MoH 2018). The total population data of the IBHS were 713,783 people aged ≥15 years (MoH 2018). The inclusion criteria in this study were individuals aged 45-59 years, had completed data of foods consumption, had completed data on fasting blood glucose, and agreed and had given their written informed consent (n=8,481). While, subjects were excluded due to extreme values or missing data (n=4). Finally, a total of 8,477 subjects met the inclusion criteria and included in this study.

Data collection

The independent variables in this study were the consumption of foods; while, the dependent variable was hyperglycemia status. Fasting blood glucose were measured with fingertip capillary blood tests (Accu-Chek Performa, Roche Diagnostics GmbH, Mannheim, Germany). All participants were instructed to fast overnight (8-10 hours) before blood sampling. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dL) and normal (<126 mg/dL) (Genuth *et al.* 2003, MoH 2018). A validated food frequency questionnaire (FFQ) was used to assess the daily food consumption. The FFQ was validated by the IBHS prior the study (MoH 2018). The FFQ includes carbonated drinks, energy drinks, sweet desserts, SSB, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods, fruits, and vegetables (MoH 2018). Consumption of unhealthy foods (carbonated drinks, energy drinks, sweet desserts, SSB, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods) was categorized as frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Fruits and vegetable consumption was categorized into adequate (≥5 servings per day) and inadequate (<5 servings per day) (MoH 2018). Sociodemographic data (age, gender, education,

and place of residence) and lifestyle (smoking status, alcohol intake, and physical activity) were obtained using a structured questionnaire. Smoking is categorized into yes and no. Consumption of alcoholic beverages is categorized into yes and no (Atamni *et al.* 2016). Gender was categorized as male and female. Education level was categorized as high (completed 12-year compulsory education or bachelor/diploma/higher education graduates) and low (not completed 12-year compulsory education). Residency was categorized as urban and rural. Physical activity was categorized as low (doing heavy physical activity for <150 minutes/week) and high (doing heavy physical activity for ≥150 minutes/week (MoH 2018).

Data analysis

Univariate analysis was presented using mean±standard deviation for numerical data and frequency (percentage) for categorical data. In addition, bivariate analysis was performed using independent samples t-test for continuous variables and the Chi-square test for categorical variables. Whereas, multivariate analysis using multiple logistic regression was used to analyze the association of food consumption and hyperglycemia status. Odds ratio (OR) with 95% confidence intervals was conducted in the analyze. We used unadjusted (model 1) and adjusted (model 2). Model 2 was adjusted for demographic data (age, gender, residency) and lifestyle (smoking status, alcohol consumption, and physical activity). We selected demographic data and lifestyle because they have potential association with hyperglycemia that might interfere the results. All analyses were performed using the SPSS program 25 version with a *p*-value <0.05 considered statistically significant.

RESULTS AND DISCUSSION

Table 1 shows the characteristics of the subjects. The majority of the subjects with hyperglycemia were older (52.05±4.29), female (63.7), not smoking (69.8), and had low physical activity (53.3). Our results also found that the prevalence of hyperglycemia in the population was 43%. The mean FBG was 104.68±31.99 mg/dL for male and 110.75±43.92 mg/dL for female subjects. This study also found that the prevalence of hyperglycemia was higher in females (44.6) than males (40.6) (Figure 1). This result was in line with a previous study in the United State (ADA 2018). Women are more risk of experiencing hyperglycemia due to the hormonal changes (ADA 2018). Moreover, physical activity in women tends to be lower than in men (The Lancet Public Health 2019).

Table 1. Characteristics of the subjects.

Variables	n	Hyperglycemia		*P*
		Yes (3,648)	No (4,829)	
Age, mean±SD	8,477 (100)	52.05±4.29	41.27±4.24	<0.001*
Gender, n (%)				<0.001**
Male	3,258 (38.4)	1,323 (36.3)	1,935 (40.1)	
Female	5,219 (61.6)	2,325 (63.7)	2,894 (59.9)	
Education levels, n (%)				0.310**
High	2,930 (34.6)	1,239 (34.0)	1,691 (35.0)	
Low	5,547 (65.4)	2,409 (66.0)	3,138 (65.0)	
Residency, n (%)				0.188**
Rural	4,339 (51.2)	1,837 (50.4)	2,502 (51.8)	
Urban	4,136 (48.8)	1,811 (49.6)	2,325 (48.2)	
Smoking status, n (%)				<0.001**
No	5,741 (67.7)	2,546 (69.8)	3,195 (66.2)	
Yes	2,736 (32.3)	1,102 (30.2)	1,634 (33.8)	
Alcohol consumption, n (%)				0.465**
No	8,383 (98.9)	3,604 (98.8)	4,779 (99.0)	
Yes	94 (1.1)	44 (1.2)	50 (1.0)	
Physical activity, n (%)				0.019**
High	4,039 (47.6)	1,684 (46.2)	2,355 (48.8)	
Low	4,438 (52.4)	1,964 (53.8)	2,474 (51.2)	
Fasting blood glucose, mean±SD	8,477 (100%)	130.84±52.65	91.47±5.43	<0.001*

*Comparison between continuous variables and hyperglycemia were performed using independent samples t-test

**Comparison between categorical variables and hyperglycemia were performed using Chi-square test

The association of food consumption and hyperglycemia are described in Table 2. Among subjects with hyperglycemia, 20.2%, 15.5%, 28.3%, 14.1%, 10.3%, and 48.3% frequently consumed sweet desserts, SSB, salty foods, fried foods, seasonings, and instant foods, respectively. Moreover, among subjects with hyperglycemia, 73.2% inadequate consumed fruits.

Table 2. Food consumption and hyperglycemia*.

Variables	n	Hyperglycemia		OR (95% CI)	*P***
		Yes (3,648)	No (4,829)		
Carbonated drinks, n (%)					
Infrequent	7,844 (92.5)	3,396 (93.0)	4,448 (92.2)	0.877	0.123
Frequent	633 (7.5)	254 (7.0)	379 (7.8)	(0.966, 1.343)	
Energy drinks, n (%)					
Infrequent	8,029 (94.7)	3,463 (94.9)	4,566 (94.6)		0.300

Frequent	448 (5.3)	187 (5.1)	261 (5.4)	0.944 (0.873, 1.284)	
Sweet desserts, n (%)					
Infrequent	6,933 (81.8)	2,912 (79.8)	4,021 (82.3)	1.265	<0.001
Frequent	1,544 (18.2)	736 (20.2)	808 (17.7)	(1.132, 1.413)	
Sugar-sweetened beverages, n (%)					
Infrequent	7,367 (86.9)	3,086 (84.5)	4,281 (88.7)	1.433	<0.001
Frequent	1,110 (13.1)	564 (15.5)	546 (11.3)	(1.263, 1.626)	
Salty foods, n (%)					
Infrequent	6,243 (73.6)	2,618 (71.7)	3,625 (75.1)	1.189	<0.001
Frequent	2,234 (26.4)	1,032 (28.3)	1,202 (24.9)	(1.079, 1.311)	
Fried foods, n (%)					
Infrequent	7,373 (87.0)	3,137 (85.9)	4,236 (87.8)	1.172	0.015
Frequent	1,104 (13.0)	513 (14.1)	591 (12.2)	(1.033, 1.331)	
Grilled foods, n (%)					
Infrequent	5,992 (70.7)	2,594 (71.1)	3,398 (70.4)	1.033	0.515
Frequent	2,485 (29.3)	1,056 (28.9)	1,429 (29.6)	(0.940, 1.135)	
Processed foods, n (%)					
Infrequent	1,737 (20.5)	2,936 (80.4)	3,804 (78.8)	0.905	0.069
Frequent	6,740 (79.5)	714 (19.6)	1,023 (21.2)	(0.813, 1.007)	
Seasonings, n (%)					
Infrequent	7,676 (90.5)	3,274 (89.7)	4,402 (91.2)	1.190	0.020
Frequent	801 (9.5)	376 (10.3)	425 (8.8)	(1.028, 1.377)	
Instant foods, n (%)					
Infrequent	4,591 (54.2)	1,889 (51.7)	2,702 (56.0)	1.186	<0.001
Frequent	3,886 (45.8)	1,761 (48.3)	2,125 (44.0)	(1.088, 1.293)	
Fruits, n (%)					
Adequate	2,350 (27.7)	976 (26.8)	1,374 (28.5)	1.090	0.042
Inadequate	6,127 (72.3)	2,674 (73.2)	3,453 (71.5)	(0.990, 1.200)	
Vegetable, n (%)					
Adequate	1,478 (17.4)	637 (17.5)	841 (17.4)	1.002	0.495
Inadequate	6,999 (82.6)	3,013 (82.5)	3,986 (82.6)	(0.895, 1.123)	

*Frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Adequate (≥5 servings per day) and inadequate (<5 servings per day)

**Comparison between food consumption and hyperglycemia were performed using Chi-square test

The odds ratios (95% confidence intervals) for food consumption across hyperglycemia are presented in Table 3. Frequent consumption of sweet desserts (OR=1.168; CI=1.035, 1.315), SSB (OR=1.306; CI=1.137, 1.600), salty foods (OR=1.159; CI=1.049, 1.281), fried foods (OR=1.153; CI=1.014, 1.312), seasoning (OR=1.119; CI=1.007, 1.356), and instant foods (OR=1.116; CI=1.020, 1.221) were significantly associated with increased crude odds (model 1) of hyperglycemia. After adjusting for age, gender, education levels, residency, smoking status, alcohol consumption, and physical activity (model 2), frequent consumption of seasonings was not significantly associated with hyperglycemia.

Table 3. Odds ratios (95% confidence intervals) for food consumption across hyperglycemia

Variables	Model 1[**]			Model 2[***]		
	OR	95% CI	*p*	OR	95% CI	*p*[*]
Carbonated drinks			0.122			0.419
Infrequent	1			1		
Frequent	1.066	0.889, 1.279		1.071	0.907, 1.266	
Energy drinks			0.565			0.772
Infrequent	1			1		
Frequent	0.961	0.778, 1.187		0.971	0.798, 1.182	
Sweet desserts			<0.001	1		<0.001
Infrequent	1					
Frequent	1.168	1.035, 1.315		1.135	1.005, 1.281	
Sugar-sweetened beverages			<0.001			<0.001
Infrequent	1			1		
Frequent	1.306	1.137, 1.600		1.284	1.116, 1.477	
Salty foods			<0.001			<0.001
Infrequent	1			1		
Frequent	1.159	1.049, 1.281		1.140	1.031, 1.260	
Fried foods			0.014			0.042
Infrequent	1			1		
Frequent	1.153	1.014, 1.312		1.137	1.000, 1.294	
Grilled foods			0.504			0.735
Infrequent	1			1		0.495
Frequent	0.980	0.888, 1.082		0.964	0.872, 1.065	
Processed foods			0.410			0.167
Infrequent	1			1		
Frequent	1.048	0.937, 1.173		1.079	0.969, 1.202	
Seasonings			0.040			0.052
Infrequent	1			1		
Frequent	1.119	1.007, 1.356		1.156	0.998, 1.340	
Instant foods			0.016			0.008
Infrequent	1			1		
Frequent	1.116	1.020, 1.221		1.127	1.032, 1.229	
Fruits			0.080			0.098
Adequate	1			1		
Inadequate	1.038	0.937, 1.149		1.086	0.985, 1.197	

Vegetables						
Adequate	1		0.969	1		0.883
Inadequate	0.953	0.846, 1.074		1.001	1.893, 1.123	

*Differences between food consumption and hyperglycemia were analyzed using multiple logistic regression. **Model 1 was unadjusted. ***Model 2 was adjusted for age, gender, education level, residency, smoking status, alcohol consumption, physical activity.

We found that frequent consumption of sweet desserts and SSB were significantly associated with risk of hyperglycemia. Sweet desserts and SSB contained carbohydrates or simple sugars with a high Glycemic Index (GI) value, leading to accelerated blood sugar levels (Medina-Remón *et al.* 2018). Other studies found a decrease in endothelial cells' micro and macro cellular function when consuming sweetened sugary beverages (Loader *et al.* 2017). These metabolic abnormalities are due to the increased in oxidative stress and decreased in NO's (nitric oxide) bioavailability, which plays an important role in glucose metabolism in the body. The decreased in NO bioavailability is also related to risk of developing type 2 diabetes (Loader *et al*. 2017). Added sugar intake is involved in the production of reactive oxygen species (ROS). It then might increase the expression of cytokines and cell adhesion molecules (Prasad and Dhar 2014).

Participants who frequently consumed salty foods were associated with risk of hyperglycemia. This result is in line with a previous study. High consumption of salty foods is correlated with an increased risk factor for DM (Fitria *et al.* 2016). High intake of sodium increases the risk of hyperglycemia through the PPAR δ/adiponectin/SGLT2 mechanism in regulating sodium and glucose homeostasis (Zhao *et al.* 2016).

Frequent consumption of fried foods were significantly associated with risk of hyperglycemia in recent study. Fried foods are high in fat, including saturated fat and cholesterol. Frequent consumption of fried food will lead to hyperglycemia in the pre-elderly population. A high-fat diet also significantly contributes to obesity and non-insulin-dependent diabetes mellitus (Naja *et al.* 2013). Previous study found a positive relationship between high intake of saturated fat and cholesterol and increased hyperglycemia and type 2 diabetes in humans and rats (Cahill *et al.* 2014). Saturated fat in the cell membrane will decrease the viscosity of the lipid bilayer of a cell membrane and lead to a decrease in the insulin receptors (Min *et al.* 2018).

Frequent consumption of instant foods had a significant relationship with the incidence of hyperglycemia as indicated by an increase in FBG in this study. Our results are consistent with other studies that high intake of instant foods were linked to a higher risk of developing diabetes due to the high carbohydrate and fat (Huh *et al.* 2017). An animal trial of monosodium glutamate found a significant increase in glucose levels as evidenced by an increase in HOMA-IR value in rats. It is because of the changes in insulin binding or insulin post receptors in the target tissues (Helal *et al.* 2019). Monosodium glutamate may trigger the degradation of neuronal membranes, allowing calcium ions to enter cells because of its permeability of sodium ions, calcium ions, and water. Then, it might damage the pancreatic gland and hyperglycemia (Jusuf *et al.* 2020).

Consumption of fruits and vegetables reduced hyperglycemia. Fiber might delay the digestion and absorption of carbohydrates and increase satiety effect. In individuals with insulin resistance, fiber can increase peripheral insulin sensitivity through short-chain fatty acids produced by fiber fermentation in the gut (Samaan 2017) . In addition, a diet high in fruits and vegetables is associated with high intake of magnesium and iron (Zhang *et al.* 2015). Magnesium is an important cofactor for several enzymes in glucose metabolism, which further plays a role in the development of diabetes (Verma & Garg 2017). In this study, individuals with inadequate consumption of fruits and vegetables were 1.086 and 1.001, respectively, more likely to have hyperglycemia than those with adequate consumption of vegetables and fruits, but these association were not statistically significant. Diabetes is a chronic disease. People with diabetes might change their diet, and eat more healthy food; however, it cannot change immediately the condition of the disease.

This study has some strengths. To the best of our knowledge, this was the first study analyzing the association of food consumption with hyperglycemia among middle-aged in Indonesia. Our study used a large sample that reflected the Indonesian population. Some limitations should be mentioned in this study. Firstly, dietary data were taken using a frequency of intake which is no information related to nutrients. Moreover, the cross-sectional design restricts the results in maintaining the causality between the variables. Further research with a priori or a posteriori method is highly recommended. By using a priori or a posteriori method, researchers may derive the dietary patterns consisting of complex foods with many nutrients that represent the diet intake among population of interest. Moreover, additional longitudinal study is needed to explore the mechanism between variables.

CONCLUSION

There was a significant association between food consumption and hyperglycemia status among middle-aged adults in Indonesia. Frequent consumption of sweet desserts, SSB, salty foods, fried foods, and instant foods increased the odds (chance) to have hyperglycemia. Further research with a priori or a posteriori dietary pattern approach is highly recommended. Additional longitudinal study is needed to explore the mechanism between variables.

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DECLARATION OF INTERESTS

The authors have no conflict of interest.

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AUTHOR'S REVISION FORM

Title	:	**Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis**
Author(s)	:	Ahmad Syauqy, Siti Andhini Mattarahmawati, Adriyan Pramono

No	Manuscript section	Corrected line	Suggestions	Revised line	Revisions
1	Title	-	-	-	-
2	Abstract	-	-	-	-
3	Introduction	-	-	-	-
4	Method	-	-	-	-
5	Result and discussion	Table 1	Convert the table into this type; so not confusing	Table 1	We revised it accordingly
		Figure 1	No need this figure, redundant (info has been available in Table 1)	Figure 1	We deleted Figure 1
		149	You need to explain according to the findings in the table. Your table shows an association between hyperglycemic vs. non-glycemic. Your sentences should figure out whether there is association or not. And if yes, to which direction. Whether the association is according to your hypothesis or the theory that you have found.	141-144	We revised Table 2. And, we revised the explanation according to the Table 2. "Among subjects with hyperglycemia, 20.2%, 15.5%, 28.3%, 14.1%, 10.3%, and 48.3% frequently consumed sweet desserts, SSB, salty foods, fried foods, seasonings, and instant foods, respectively. Moreover, among subjects with hyperglycemia, 73.2% inadequate consumed fruits." We revised Table 2. We made a mistake when input the data between frequent and infrequent in Table 2. Now, the data are correct.

		Table 2	Also change as Table 1 in example.	Table 2	We revised it accordingly
		157	You could use the odd ratio here because you have separated between those with disease (hyperglycemia) and non-disease (no hyperglycemia)	Table 2	We added the "OR (95% CI)" in Table 2
		177	Your discussion here is aligned with Table 3; but not in table 2.		We revised Table 2. We made a mistake when input the data between frequent and infrequent in Table 2. Now, the data are correct.
		178	Could you add explanation why the direction of association from bivariate analysis (Table 2) is different from multivariate analysis (Table 3). I have asked this before. To be clear, as an example, In Table 2, frequent SSB consumption is associated with a lower proportion of hyperglycemia. But in Table 3, frequent SSB consumption has a higher odd (1.378 in model 20 of being hyperglycemic. Other variables are also on that direction. Could you explain what are the factors or that? Or I wrongly interpret your table?		We revised Table 2. We made a mistake when input the data between frequent and infrequent in Table 2. Now, the data are correct.
		225	Use a consistent terminology. Do you want to use hyperglycemic or high FBG?	218	We revised it accordingly

		226	You need to add explanation that the food consumption practice might be as a result of their disease condition. For example; as you know you have diabetic, you change your dietary practice. But that change dietary practice may not change yet your disease status	220-222	We added explanation: " Diabetes is a chronic disease. People with diabetes might change their diet and eat more healthy food; however, it cannot immediately change the condition of the disease."
		233-235	You need to put more explanation why do you recommend this (what are the advantages in taking the study conclusion by having a priori or posteriori hypothesis in the study design).		We added more explanation: "By using a priori and a posteriori method, researchers may derive the dietary patterns consisting of complex foods with many nutrients that represent the diet intake among population of interest."
6	Conclusion and suggestion	-	-	-	-
7	References	-	-	-	-
8	Others:	-	-	-	-

* Information:

- This form is an additional file that must be attached along with the revised manuscript to make the revision easy to track **(please highlight the revised part in the revised manuscript in color).**
- The Corrected Line column is filled in according to the line number where corrected by the editor/reviewer. The Revised Line collumn is filled in according to the line number where revised by the author.
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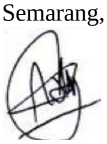
Semarang, 5 November 2022,



(Ahmad Syauqy)

Overall comments :

[JGP] Further Correction from Editor IV

Close Panel

Participants

- Prof. Dr. Dodik Briawan, MCN (admingizipangan)
- Ahmad Syauqy, S.Gz, MPH.,Ph.D (jgpahmadsyauqy)

Messages

Note	From
Dear Ahmad Syauqy and Team Diponegoro University Good day. Here we attach the manuscript for the 4th further correction from our editor. Kindly check those comments in the manuscript. Make sure to reply to all comments in the manuscript, use highlights for the revision part, and write your response in the author's revision form. Kindly do the revision as advised. Send back the revised manuscript & the author's revision form no later than **Saturday, 19 November 2022** by replying to this message. Thank you. Regards, -- Secretariat of Indonesian Journal of Nutrition and Food Department of Community Nutrition, Faculty of Human Ecology IPB University, Dramaga, Bogor Indonesia, 16680 E-mail address: jgp@apps.ipb.ac.id Website: http://journal.ipb.ac.id/index.php/jgizipangan [JGP] Manuscript_checked (15112022).docx [JGP] Author's Revision Form.docx	admingizipangan 2022-11-15 10:12 PM

HASIL REVISI EDITOR (IV)

Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis

ABSTRACT

The objective of this study was to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia. This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS). A total of 8477 subjects met the inclusion criteria and included in this study. Fasting blood glucose (FBG) was analyzed in the laboratory using an enzymatic analysis. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dL) and normal (<126 mg/dL). A food frequency questionnaire was used to assess the food intake. Multiple logistic regression was used to analyze the association of food consumption and hyperglycemia. Our results found that the prevalence of hyperglycemia in this population was 43%. The mean FBG was 104.68 ± 31.99 mg/dL for male and 110.75 ± 43.92 mg/dL for female subjects. Frequent consumption of sweet desserts (OR=1.265; CI=1.132, 1.413), sugar-sweetened beverages (SSB) (OR=1.433; CI=1.263, 1.626), salty foods (OR=1.189; CI=1.079, 1.311), fried foods (OR=1.172; CI=1.033, 1.331), and instant foods (OR=1.186; CI=1.088, 1.293) were significantly associated with increased odds of hyperglycemia. There was a significant association between food consumption and hyperglycemia among middle-aged adults in Indonesia.

Keyword: diet, food consumption, hyperglycemia, fasting blood glucose, Indonesia

Runner Title: Food consumption and hyperglycemia

INTRODUCTION

Non-communicable diseases are the leading cause of public health problems in developed and developing countries (Naghavi M 2017). Diabetes, one of the non-communicable diseases, is the main cause of death in the world (Zheng *et al.* 2018). Diabetes or hyperglycemia is characterized by an increase in blood sugar levels in the body. Previous studies found that the prevalence of hyperglycemia and the components of metabolic syndrome increased rapidly with

age in women and men (Wu *et al.* 2017, Jiang *et al.* 2018). Recently, Indonesia is the fourth country after India, China, and America, with the most diabetes sufferers globally (Naghavi M 2017). The prevalence of diabetes in Indonesia was around 6% (Mihardja *et al.* 2014). Interestingly, based on the 2018 Indonesia Basic Health Survey (IBHS), the higher prevalence of diabetes was among middle-aged adults with almost 10% (MoH 2018).

Diabetes is caused by many factors including lifestyle (Sudargo *et al.* 2018). Sedentary lifestyle has been associated with the increasing trend of diabetes (Nurwanti *et al.* 2018). Previous study also found that diet was associated with the increased prevalence of diabetes (Lambrinou *et al.* 2019). Western foods or unhealthy foods are correlated with an increased prevalence of hyperglycemia and metabolic syndrome (Syauqy *et al.* 2018). Western foods or unhealthy foods consisted of sweet, sugar, fat, sugar-sweetened beverages (SSB), fried foods, and seasoning; hence, the unhealthy food is high in simple carbohydrate, saturated fat, and sodium. Furthermore, inadequate consumption of vegetables and fruits can also escalate the diabetes prevalence (Syauqy *et al*. 2018, Schwingshackl *et al.* 2017).

Some studies have found the association between food consumption and metabolic syndrome among middle-aged adults in Taiwan (Syauqy *et al*. 2018). Moreover, middle-aged adults who consumed high fruits and vegetables and less unhealthy foods had a better quality of life (Lo *et al.* 2016). A research found that Indonesian people tend to consume high western foods and low fruits and vegetables (MoH 2018). However, to the best of our knowledge, study investigated the association of unhealthy foods, fruits, and vegetables intakes with diabetes among middle-aged adults in Indonesia was still rare, especially using a national database that represents the Indonesian population. Therefore, the objective of this study was to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia.

METHODS

Design, location, and time

This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS). Briefly, the IBHS used a two-stage stratified cluster sampling method survey population includes all Indonesian households, representing 26 Provinces and utilizing a sample framework from the national socio-economic survey in March 2018 (MoH 2018). This study had received ethical approval from the Health Research Ethics Commission, Medical Faculty, Universitas 'Aisyiyah Yogyakarta No. 1415/KEP-UNISA/VI/2021.

Sampling

The target sample included 300,000 households from 30,000 census blocks of the national socio-economic survey framework (MoH 2018). The total population data of the IBHS were 713,783 people aged ≥15 years (MoH 2018). The inclusion criteria in this study were individuals aged 45-59 years, had completed data of foods consumption, had completed data on fasting blood glucose, and agreed and had given their written informed consent (n=8,481). While, subjects were excluded due to extreme values or missing data (n=4). Finally, a total of 8,477 subjects met the inclusion criteria and included in this study.

Data collection

The independent variables in this study were the consumption of foods; while, the dependent variable was hyperglycemia status. Fasting blood glucose were measured with fingertip capillary blood tests (Accu-Chek Performa, Roche Diagnostics GmbH, Mannheim, Germany). All participants were instructed to fast overnight (8-10 hours) before blood sampling. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dL) and normal (<126 mg/dL) (Genuth *et al.* 2003, MoH 2018). A validated food frequency questionnaire (FFQ) was used to assess the daily food consumption. The FFQ was validated by the IBHS prior the study (MoH 2018). The FFQ includes carbonated drinks, energy drinks, sweet desserts, SSB, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods, fruits, and vegetables (MoH 2018). Consumption of unhealthy foods (carbonated drinks, energy drinks, sweet desserts, SSB, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods) was categorized as frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Fruits and vegetable consumption was categorized into adequate (≥5 servings per day) and inadequate (<5 servings per day) (MoH 2018). Sociodemographic data (age, gender, education,

and place of residence) and lifestyle (smoking status, alcohol intake, and physical activity) were obtained using a structured questionnaire. Smoking was categorized into yes and no. Consumption of alcoholic beverages was categorized into yes and no (Atamni *et al.* 2016). Gender was categorized as male and female. Education level was categorized as high (completed 12-year compulsory education or bachelor/diploma/higher education graduates) and low (not completed 12-year compulsory education). Residency was categorized as urban and rural. Physical activity was categorized as low (doing heavy physical activity for <150 minutes/week) and high (doing heavy physical activity for ≥150 minutes/week (MoH 2018).

Data analysis

Univariate analysis was presented using mean±standard deviation for numerical data and frequency (percentage) for categorical data. In addition, bivariate analysis was performed using independent samples t-test for continuous variables and the Chi-square test for categorical variables. Whereas, multivariate analysis using multiple logistic regression was used to analyze the association of food consumption and hyperglycemia status. Odds ratio (OR) with 95% confidence intervals was conducted in the analyze. We used unadjusted (model 1) and adjusted (model 2). Model 2 was adjusted for demographic data (age, gender, residency) and lifestyle (smoking status, alcohol consumption, and physical activity). We selected demographic data and lifestyle because they have potential association with hyperglycemia that might interfere the results. All analyses were performed using the SPSS program 25 version with a *p*-value <0.05 considered statistically significant.

RESULTS AND DISCUSSION

Table 1 shows the characteristics of the subjects. The majority of the subjects with hyperglycemia were older (52.05±4.29), female (63.7), not smoking (69.8), and had low physical activity (53.3). Our results also found that the prevalence of hyperglycemia in the population was 43%. The mean FBG was 104.68±31.99 mg/dL for male and 110.75±43.92 mg/dL for female subjects. This study also found that the prevalence of hyperglycemia was higher in females (44.6%) than males (40.6%) ~~(Figure 1~~). This result was in line with a previous study in the United State (ADA 2018). Women are more risk of experiencing hyperglycemia due to the hormonal changes (ADA 2018). Moreover, physical activity in women tends to be lower than in men (The Lancet Public Health 2019).

Table 1. Characteristics of the subjects.

Variables	n	Hyperglycemia		P
		Yes (3,648)	No (4,829)	
Age, mean±SD	8,477 (100)	52.05±4.29	41.27±4.24	<0.001*
Gender, n (%)				<0.001**
Male	3,258 (38.4)	1,323 (36.3)	1,935 (40.1)	
Female	5,219 (61.6)	2,325 (63.7)	2,894 (59.9)	
Education levels, n (%)				0.310**
High	2,930 (34.6)	1,239 (34.0)	1,691 (35.0)	
Low	5,547 (65.4)	2,409 (66.0)	3,138 (65.0)	
Residency, n (%)				0.188**
Rural	4,339 (51.2)	1,837 (50.4)	2,502 (51.8)	
Urban	4,136 (48.8)	1,811 (49.6)	2,325 (48.2)	
Smoking status, n (%)				<0.001**
No	5,741 (67.7)	2,546 (69.8)	3,195 (66.2)	
Yes	2,736 (32.3)	1,102 (30.2)	1,634 (33.8)	
Alcohol consumption, n (%)				0.465**
No	8,383 (98.9)	3,604 (98.8)	4,779 (99.0)	
Yes	94 (1.1)	44 (1.2)	50 (1.0)	
Physical activity, n (%)				0.019**
High	4,039 (47.6)	1,684 (46.2)	2,355 (48.8)	
Low	4,438 (52.4)	1,964 (53.8)	2,474 (51.2)	
Fasting blood glucose, mean±SD	8,477 (100%)	130.84±52.65	91.47±5.43	<0.001*

*Comparison between continuous variables and hyperglycemia were performed using independent samples t-test

**Comparison between categorical variables and hyperglycemia were performed using Chi-square test

Commented [A62]: Delete this column

The association of food consumption and hyperglycemia are described in Table 2. Among subjects with hyperglycemia, 20.2%, 15.5%, 28.3%, 14.1%, 10.3%, and 48.3% frequently consumed sweet desserts, SSB, salty foods, fried foods, seasonings, and instant foods, respectively. Moreover, among subjects with hyperglycemia, 73.2% consumed inadequate fruits.

Commented [A63]: Discuss how these numbers compared to other references? Is it typical?

Also, why these practices were worse compared to non-hyperglycemia?

Table 2. Food consumption and hyperglycemia*.

Variables	n	Hyperglycemia		OR	P^{**}
		Yes (3,648)	No (4,829)	(95% CI)	
Carbonated drinks, n (%)					
Infrequent	7,844 (92.5)	3,396 (93.0)	4,448 (92.2)	0.877	0.123
Frequent	633 (7.5)	254 (7.0)	379 (7.8)	(0.966, 1.343)	
Energy drinks, n (%)					
Infrequent	8,029 (94.7)	3,463 (94.9)	4,566 (94.6)	0.944	0.300
Frequent	448 (5.3)	187 (5.1)	261 (5.4)	(0.873, 1.284)	
Sweet desserts, n (%)					
Infrequent	6,933 (81.8)	2,912 (79.8)	4,021 (82.3)	1.265	<0.001
Frequent	1,544 (18.2)	736 (20.2)	808 (17.7)	(1.132, 1.413)	
Sugar-sweetened beverages, n (%)					
Infrequent	7,367 (86.9)	3,086 (84.5)	4,281 (88.7)	1.433	<0.001
Frequent	1,110 (13.1)	564 (15.5)	546 (11.3)	(1.263, 1.626)	
Salty foods, n (%)					
Infrequent	6,243 (73.6)	2,618 (71.7)	3,625 (75.1)	1.189	<0.001
Frequent	2,234 (26.4)	1,032 (28.3)	1,202 (24.9)	(1.079, 1.311)	
Fried foods, n (%)					
Infrequent	7,373 (87.0)	3,137 (85.9)	4,236 (87.8)	1.172	0.015
Frequent	1,104 (13.0)	513 (14.1)	591 (12.2)	(1.033, 1.331)	
Grilled foods, n (%)					
Infrequent	5,992 (70.7)	2,594 (71.1)	3,398 (70.4)	1.033	0.515
Frequent	2,485 (29.3)	1,056 (28.9)	1,429 (29.6)	(0.940, 1.135)	
Processed foods, n (%)					
Infrequent	1,737 (20.5)	2,936 (80.4)	3,804 (78.8)	0.905	0.069
Frequent	6,740 (79.5)	714 (19.6)	1,023 (21.2)	(0.813, 1.007)	
Seasonings, n (%)					
Infrequent	7,676 (90.5)	3,274 (89.7)	4,402 (91.2)	1.190	0.020
Frequent	801 (9.5)	376 (10.3)	425 (8.8)	(1.028, 1.377)	
Instant foods, n (%)					
Infrequent	4,591 (54.2)	1,889 (51.7)	2,702 (56.0)	1.186	<0.001
Frequent	3,886 (45.8)	1,761 (48.3)	2,125 (44.0)	(1.088, 1.293)	

Fruits, n (%)					
Adequate	~~2,350 (27.7)~~	976 (26.8)	1,374 (28.5)	1.090	0.042
Inadequate	~~6,127 (72.3)~~	2,674 (73.2)	3,453 (71.5)	(0.990, 1.200)	
Vegetable, n (%)					
Adequate	~~1,478 (17.4)~~	637 (17.5)	841 (17.4)	1.002	0.495
Inadequate	~~6,999 (82.6)~~	3,013 (82.5)	3,986 (82.6)	(0.895, 1.123)	

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*Frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Adequate (≥5 servings per day) and inadequate (<5 servings per day)

**Comparison between food consumption and hyperglycemia were performed using Chi-square test

The odds ratios (95% confidence intervals) for food consumption across hyperglycemia are presented in Table 3. Frequent consumption of sweet desserts (OR=1.168; CI=1.035, 1.315), SSB (OR=1.306; CI=1.137, 1.600), salty foods (OR=1.159; CI=1.049, 1.281), fried foods (OR=1.153; CI=1.014, 1.312), seasoning (OR=1.119; CI=1.007, 1.356), and instant foods (OR=1.116; CI=1.020, 1.221) were significantly associated with increased crude odds (model 1) of hyperglycemia. After adjusting for age, gender, education levels, residency, smoking status, alcohol consumption, and physical activity (model 2), frequent consumption of seasonings was not significantly associated with hyperglycemia.

Table 3. Odds ratios (95% confidence intervals) for food consumption across hyperglycemia

Variables	Model 1**			Model 2***		
	OR	95% CI	*p*	OR	95% CI	*p**
Carbonated drinks			0.122			0.419
Infrequent	1			1		
Frequent	1.066	0.889, 1.279		1.071	0.907, 1.266	
Energy drinks			0.565			0.772
Infrequent	1			1		
Frequent	0.961	0.778, 1.187		0.971	0.798, 1.182	
Sweet desserts			<0.001	1		<0.001
Infrequent	1					
Frequent	1.168	1.035, 1.315		1.135	1.005, 1.281	
Sugar-sweetened beverages			<0.001			<0.001

Infrequent	1			1		
Frequent	1.306	1.137, 1.600		1.284	1.116, 1.477	
Salty foods			<0.001			<0.001
Infrequent	1			1		
Frequent	1.159	1.049, 1.281		1.140	1.031, 1.260	
Fried foods			0.014			0.042
Infrequent	1			1		
Frequent	1.153	1.014, 1.312		1.137	1.000, 1.294	
Grilled foods			0.504			0.735
Infrequent	1			1		0.495
Frequent	0.980	0.888, 1.082		0.964	0.872, 1.065	
Processed foods			0.410			0.167
Infrequent	1			1		
Frequent	1.048	0.937, 1.173		1.079	0.969, 1.202	
Seasonings			0.040			0.052
Infrequent	1			1		
Frequent	1.119	1.007, 1.356		1.156	0.998, 1.340	
Instant foods			0.016			0.008
Infrequent	1			1		
Frequent	1.116	1.020, 1.221		1.127	1.032, 1.229	
Fruits			0.080			0.098
Adequate	1			1		
Inadequate	1.038	0.937, 1.149		1.086	0.985, 1.197	
Vegetables						
Adequate	1		0.969	1		0.883
Inadequate	0.953	0.846, 1.074		1.001	1.893, 1.123	

*Differences between food consumption and hyperglycemia were analyzed using multiple logistic regression. **Model 1 was unadjusted. ***Model 2 was adjusted for age, gender, education level, residency, smoking status, alcohol consumption, physical activity.

We found that frequent consumption of sweet desserts and SSB were significantly associated with risk of hyperglycemia. Sweet desserts and SSB contained carbohydrates or simple sugars with a high Glycemic Index (GI) value, leading to accelerated blood sugar levels (Medina-Remón *et al.* 2018). Other studies found a decrease in endothelial cells' micro and macro cellular function when consuming sweetened sugary beverages (Loader *et al.* 2017). These metabolic abnormalities are due to the increased in oxidative stress and decreased in NO's (nitric oxide) bioavailability, which plays an important role in glucose metabolism in the body. The decreased in NO bioavailability is also related to risk of developing type 2 diabetes (Loader *et al*. 2017). Added sugar intake is involved in the production of reactive oxygen species (ROS). It then might increase the expression of cytokines and cell adhesion molecules (Prasad and Dhar 2014).

Participants who frequently consumed salty foods were associated with risk of hyperglycemia. This result is in line with a previous study. High consumption of salty foods is correlated with an increased risk factor for DM (Fitria *et al.* 2016). High intake of sodium increases the risk of hyperglycemia through the PPAR δ/adiponectin/SGLT2 mechanism in regulating sodium and glucose homeostasis (Zhao *et al.* 2016).

Frequent consumption of fried foods was significantly associated with risk of hyperglycemia in recent study. Fried foods are high in fat, including saturated fat and cholesterol. Frequent consumption of fried food will lead to hyperglycemia in the pre-elderly population. A high-fat diet also significantly contributes to obesity and non-insulin-dependent diabetes mellitus (Naja *et al.* 2013). Previous study found a positive relationship between high intake of saturated fat and cholesterol and increased hyperglycemia and type 2 diabetes in humans and rats (Cahill *et al.* 2014). Saturated fat in the cell membrane will decrease the viscosity of the lipid bilayer of a cell membrane and lead to a decrease in the insulin receptors (Min *et al.* 2018).

Frequent consumption of instant foods had a significant relationship with the incidence of hyperglycemia as indicated by an increase in FBG in this study. Our results are consistent with other studies that high intake of instant foods were linked to a higher risk of developing diabetes due to the high carbohydrate and fat (Huh *et al.* 2017). An animal trial of monosodium glutamate found a significant increase in glucose levels as evidenced by an increase in HOMA-IR value in rats. It is because of the changes in insulin binding or insulin post receptors in the target tissues (Helal *et al.* 2019). Monosodium glutamate may trigger the degradation of neuronal membranes, allowing calcium ions to enter cells because of its permeability of sodium ions, calcium ions, and water. Then, it might damage the pancreatic gland and hyperglycemia (Jusuf *et al.* 2020).

In this study, individuals with inadequate consumption of fruits and vegetables were 1.086 and 1.001, respectively, more likely to have hyperglycemia than those with adequate consumption of vegetables and fruits, but these associations were not statistically significant. Consumption of fruits and vegetables reduced hyperglycemia. Fiber might delay the digestion and absorption of carbohydrates and increase satiety effect. In individuals with insulin resistance, fiber can increase peripheral insulin sensitivity through short-chain fatty acids produced by fiber fermentation in the gut (Samaan 2017) . In addition, a diet high in fruits and vegetables is associated with high intake of magnesium and iron (Zhang *et al.* 2015). Magnesium is an important cofactor for several enzymes in glucose metabolism, which further plays a role in the development of diabetes (Verma & Garg 2017). Diabetes is a chronic disease. People with diabetes might change their diet, and eat more healthy food; however, it cannot change immediately the condition of the disease.

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Commented [A66]: What is the overall risk of hyperglycemia in this study? How many % are able to be explained by these variables and how many % for the unexplained one? You did multiple regression, so you should be able to answer this.

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This study has some strengths. To the best of our knowledge, this was the first study analyzing the association of food consumption with hyperglycemia among middle-aged in Indonesia. Our study used a large sample that reflected the Indonesian population. Some limitations should be mentioned in this study. Firstly, dietary data were taken using a frequency of intake which is no information related to nutrients. Moreover, the cross-sectional design restricts the results in maintaining the causality between the variables. Further research with a priori or a posteriori method is highly recommended. By using a priori or a posteriori method, researchers may derive the dietary patterns consisting of complex foods with many nutrients that represent the diet intake among population of interest. Moreover, additional longitudinal study is needed to explore the mechanism between variables.

CONCLUSION

There was a significant association between food consumption and hyperglycemia status among middle-aged adults in Indonesia. Frequent consumption of sweet desserts, SSB, salty foods, fried foods, and instant foods increased the odds (chance) to have hyperglycemia. Further research with a priori or a posteriori dietary pattern approach is highly recommended. Additional longitudinal study is needed to explore the mechanism between variables.

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DECLARATION OF INTERESTS

The authors have no conflict of interest.

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Settings

Dear Prof. Dr. Dodik Briawan, MCN, Editor-in-Chief,

Many thanks for the editors' suggestions and comments. We have revised throughout the manuscript entitled "Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis" according to the editors' comments and suggestions.

If you have any questions, please feel free to call me at +6224-76402881 (email: syauqy@fk.undip.ac.id). I am looking forward to your response.

Best Regards,

Ahmad Syauqy

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HASIL PERBAIKAN EDITOR (IV)

Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis

ABSTRACT

The objective of this study was to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia. This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS). A total of 8477 subjects met the inclusion criteria and included in this study. Fasting blood glucose (FBG) was analyzed in the laboratory using an enzymatic analysis. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dL) and normal (<126 mg/dL). A food frequency questionnaire was used to assess the food intake. Multiple logistic regression was used to analyze the association of food consumption and hyperglycemia. Our results found that the prevalence of hyperglycemia in this population was 43%. The mean FBG was 104.68 ± 31.99 mg/dL for male and 110.75 ± 43.92 mg/dL for female subjects. Frequent consumption of sweet desserts (OR=1.265; CI=1.132, 1.413), sugar-sweetened beverages (SSB) (OR=1.433; CI=1.263, 1.626), salty foods (OR=1.189; CI=1.079, 1.311), fried foods (OR=1.172; CI=1.033, 1.331), and instant foods (OR=1.186; CI=1.088, 1.293) were significantly associated with increased odds of hyperglycemia. There was a significant association between food consumption and hyperglycemia among middle-aged adults in Indonesia.

Keyword: diet, food consumption, hyperglycemia, fasting blood glucose, Indonesia

Runner Title: Food consumption and hyperglycemia

INTRODUCTION

Non-communicable diseases are the leading cause of public health problems in developed and developing countries (Naghavi M 2017). Diabetes, one of the non-communicable diseases, is the main cause of death in the world (Zheng *et al.* 2018). Diabetes or hyperglycemia is characterized by an increase in blood sugar levels in the body. Previous studies found that the prevalence of hyperglycemia and the components of metabolic syndrome increased rapidly with

age in women and men (Wu *et al.* 2017, Jiang *et al.* 2018). Recently, Indonesia is the fourth country after India, China, and America, with the most diabetes sufferers globally (Naghavi M 2017). The prevalence of diabetes in Indonesia was around 6% (Mihardja *et al.* 2014). Interestingly, based on the 2018 Indonesia Basic Health Survey (IBHS), the higher prevalence of diabetes was among middle-aged adults with almost 10% (MoH 2018).

Diabetes is caused by many factors including lifestyle (Sudargo *et al.* 2018). Sedentary lifestyle has been associated with the increasing trend of diabetes (Permatasari & Syauqy 2022). Previous study also found that diet was associated with the increased prevalence of diabetes (Lambrinou *et al.* 2019). Western foods or unhealthy foods are correlated with an increased prevalence of hyperglycemia and metabolic syndrome (Syauqy *et al.* 2018). Western foods or unhealthy foods consisted of sweet, sugar, fat, sugar-sweetened beverages (SSB), fried foods, and seasoning; hence, the unhealthy food is high in simple carbohydrate, saturated fat, and sodium. Furthermore, inadequate consumption of vegetables and fruits can also escalate the diabetes prevalence (Syauqy *et al*. 2018, Schwingshackl *et al.* 2017).

Some studies have found the association between food consumption and metabolic syndrome among middle-aged adults in Taiwan (Syauqy *et al*. 2018). Moreover, middle-aged adults who consumed high fruits and vegetables and less unhealthy foods had a better quality of life (Lo *et al.* 2016). A research found that Indonesian people tend to consume high western foods and low fruits and vegetables (MoH 2018). However, to the best of our knowledge, study investigated the association of unhealthy foods, fruits, and vegetables intakes with diabetes among middle-aged adults in Indonesia was still rare, especially using a national database that represents the Indonesian population. Therefore, the objective of this study was to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia.

METHODS

Design, location, and time

This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS). Briefly, the IBHS used a two-stage stratified cluster sampling method survey population includes all Indonesian households, representing 26 Provinces and utilizing a sample framework from the national socio-economic survey in March 2018 (MoH 2018). This study had received ethical approval from the Health Research Ethics Commission, Medical Faculty, Universitas 'Aisyiyah Yogyakarta No. 1415/KEP-UNISA/VI/2021.

Sampling

The target sample included 300,000 households from 30,000 census blocks of the national socio-economic survey framework (MoH 2018). The total population data of the IBHS were 713,783 people aged ≥15 years (MoH 2018). The inclusion criteria in this study were individuals aged 45-59 years, had completed data of foods consumption, had completed data on fasting blood glucose, and agreed and had given their written informed consent (n=8,481). While, subjects were excluded due to extreme values or missing data (n=4). Finally, a total of 8,477 subjects met the inclusion criteria and included in this study.

Data collection

The independent variables in this study were the consumption of foods; while, the dependent variable was hyperglycemia status. Fasting blood glucose were measured with fingertip capillary blood tests (Accu-Chek Performa, Roche Diagnostics GmbH, Mannheim, Germany). All participants were instructed to fast overnight (8-10 hours) before blood sampling. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dL) and normal (<126 mg/dL) (Genuth *et al.* 2003, MoH 2018). A validated food frequency questionnaire (FFQ) was used to assess the daily food consumption. The FFQ was validated by the IBHS prior the study (MoH 2018). The FFQ includes carbonated drinks, energy drinks, sweet desserts, SSB, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods, fruits, and vegetables (MoH 2018). Consumption of unhealthy foods (carbonated drinks, energy drinks, sweet desserts, SSB, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods) was categorized as frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Fruits and vegetable consumption was categorized into adequate (≥5 servings per day) and inadequate (<5 servings per day) (MoH 2018). Sociodemographic data (age, gender, education,

and place of residence) and lifestyle (smoking status, alcohol intake, and physical activity) were obtained using a structured questionnaire. Smoking was categorized into yes and no. Consumption of alcoholic beverages was categorized into yes and no (Atamni *et al.* 2016). Gender was categorized as male and female. Education level was categorized as high (completed 12-year compulsory education or bachelor/diploma/higher education graduates) and low (not completed 12-year compulsory education). Residency was categorized as urban and rural. Physical activity was categorized as low (doing heavy physical activity for <150 minutes/week) and high (doing heavy physical activity for ≥150 minutes/week (MoH 2018).

Data analysis

Univariate analysis was presented using mean±standard deviation for numerical data and frequency (percentage) for categorical data. In addition, bivariate analysis was performed using independent samples t-test for continuous variables and the Chi-square test for categorical variables. Whereas, multivariate analysis using multiple logistic regression was used to analyze the association of food consumption and hyperglycemia status. Odds ratio (OR) with 95% confidence intervals was conducted in the analyze. We used unadjusted (model 1) and adjusted (model 2). Model 2 was adjusted for demographic data (age, gender, residency) and lifestyle (smoking status, alcohol consumption, and physical activity). We selected demographic data and lifestyle because they have potential association with hyperglycemia that might interfere the results. All analyses were performed using the SPSS program 25 version with a *p*-value <0.05 considered statistically significant.

RESULTS AND DISCUSSION

Table 1 shows the characteristics of the subjects. The majority of the subjects with hyperglycemia were older (52.05±4.29), female (63.7), not smoking (69.8), and had low physical activity (53.3). Our results also found that the prevalence of hyperglycemia in the population was 43%. The mean FBG was 104.68±31.99 mg/dL for male and 110.75±43.92 mg/dL for female subjects. This study also found that the prevalence of hyperglycemia was higher in females (44.6%) than males (40.6%). This result was in line with a previous study in the United State (ADA 2018). Women are more risk of experiencing hyperglycemia due to the hormonal changes (ADA 2018). Moreover, physical activity in women tends to be lower than in men (The Lancet Public Health 2019).

Table 1. Characteristics of the subjects.

Variables	Hyperglycemia		*P*
	Yes (3,648)	No (4,829)	
Age, mean±SD	52.05±4.29	41.27±4.24	<0.001*
Gender, n (%)			<0.001**
Male	1,323 (36.3)	1,935 (40.1)	
Female	2,325 (63.7)	2,894 (59.9)	
Education levels, n (%)			0.310**
High	1,239 (34.0)	1,691 (35.0)	
Low	2,409 (66.0)	3,138 (65.0)	
Residency, n (%)			0.188**
Rural	1,837 (50.4)	2,502 (51.8)	
Urban	1,811 (49.6)	2,325 (48.2)	
Smoking status, n (%)			<0.001**
No	2,546 (69.8)	3,195 (66.2)	
Yes	1,102 (30.2)	1,634 (33.8)	
Alcohol consumption, n (%)			0.465**
No	3,604 (98.8)	4,779 (99.0)	
Yes	44 (1.2)	50 (1.0)	
Physical activity, n (%)			0.019**
High	1,684 (46.2)	2,355 (48.8)	
Low	1,964 (53.8)	2,474 (51.2)	
Fasting blood glucose, mean±SD	130.84±52.65	91.47±5.43	<0.001*

*Comparison between continuous variables and hyperglycemia were performed using independent samples t-test

**Comparison between categorical variables and hyperglycemia were performed using Chi-square test

The association of food consumption and hyperglycemia are described in Table 2. Among subjects with hyperglycemia, 20.2%, 15.5%, 28.3%, 14.1%, 10.3%, and 48.3% frequently consumed sweet desserts, SSB, salty foods, fried foods, seasonings, and instant foods, respectively. Moreover, among subjects with hyperglycemia, 73.2% consumed inadequate fruits.

Table 2. Food consumption and hyperglycemia*.

Variables	Hyperglycemia		OR	P^{**}
	Yes (3,648)	No (4,829)	(95% CI)	
Carbonated drinks, n (%)				
Infrequent	3,396 (93.0)	4,448 (92.2)	0.877	0.123
Frequent	254 (7.0)	379 (7.8)	(0.966, 1.343)	
Energy drinks, n (%)				
Infrequent	3,463 (94.9)	4,566 (94.6)	0.944	0.300
Frequent	187 (5.1)	261 (5.4)	(0.873, 1.284)	
Sweet desserts, n (%)				
Infrequent	2,912 (79.8)	4,021 (82.3)	1.265	<0.001
Frequent	736 (20.2)	808 (17.7)	(1.132, 1.413)	
Sugar-sweetened beverages, n (%)				
Infrequent	3,086 (84.5)	4,281 (88.7)	1.433	<0.001
Frequent	564 (15.5)	546 (11.3)	(1.263, 1.626)	
Salty foods, n (%)				
Infrequent	2,618 (71.7)	3,625 (75.1)	1.189	<0.001
Frequent	1,032 (28.3)	1,202 (24.9)	(1.079, 1.311)	
Fried foods, n (%)				
Infrequent	3,137 (85.9)	4,236 (87.8)	1.172	0.015
Frequent	513 (14.1)	591 (12.2)	(1.033, 1.331)	
Grilled foods, n (%)				
Infrequent	2,594 (71.1)	3,398 (70.4)	1.033	0.515
Frequent	1,056 (28.9)	1,429 (29.6)	(0.940, 1.135)	
Processed foods, n (%)				
Infrequent	2,936 (80.4)	3,804 (78.8)	0.905	0.069
Frequent	714 (19.6)	1,023 (21.2)	(0.813, 1.007)	
Seasonings, n (%)				
Infrequent	3,274 (89.7)	4,402 (91.2)	1.190	0.020
Frequent	376 (10.3)	425 (8.8)	(1.028, 1.377)	
Instant foods, n (%)				
Infrequent	1,889 (51.7)	2,702 (56.0)		<0.001

Frequent	1,761 (48.3)	2,125 (44.0)	1.186 (1.088, 1.293)	
Fruits, n (%)				
Adequate	976 (26.8)	1,374 (28.5)	1.090	0.042
Inadequate	2,674 (73.2)	3,453 (71.5)	(0.990, 1.200)	
Vegetable, n (%)				
Adequate	637 (17.5)	841 (17.4)	1.002	0.495
Inadequate	3,013 (82.5)	3,986 (82.6)	(0.895, 1.123)	

*Frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Adequate (≥5 servings per day) and inadequate (<5 servings per day)

**Comparison between food consumption and hyperglycemia were performed using Chi-square test

The odds ratios (95% confidence intervals) for food consumption across hyperglycemia are presented in Table 3. Frequent consumption of sweet desserts (OR=1.168; CI=1.035, 1.315), SSB (OR=1.306; CI=1.137, 1.600), salty foods (OR=1.159; CI=1.049, 1.281), fried foods (OR=1.153; CI=1.014, 1.312), seasoning (OR=1.119; CI=1.007, 1.356), and instant foods (OR=1.116; CI=1.020, 1.221) were significantly associated with increased crude odds (model 1) of hyperglycemia (R^2=2%). After adjusting for age, gender, education levels, residency, smoking status, alcohol consumption, and physical activity (model 2), frequent consumption of seasonings was not significantly associated with hyperglycemia (R^2=9%).

Table 3. Odds ratios (95% confidence intervals) for food consumption across hyperglycemia

Variables	Model 1**			Model 2***		
	OR	95% CI	*p*	OR	95% CI	*p**
Carbonated drinks			0.122			0.419
Infrequent	1			1		
Frequent	1.066	0.889, 1.279		1.071	0.907, 1.266	
Energy drinks			0.565			0.772
Infrequent	1			1		

Frequent	0.961	0.778, 1.187		0.971	0.798, 1.182	
Sweet desserts			<0.001	1		<0.001
Infrequent	1					
Frequent	1.168	1.035, 1.315		1.135	1.005, 1.281	
Sugar-sweetened beverages			<0.001			<0.001
Infrequent	1			1		
Frequent	1.306	1.137, 1.600		1.284	1.116, 1.477	
Salty foods			<0.001			<0.001
Infrequent	1			1		
Frequent	1.159	1.049, 1.281		1.140	1.031, 1.260	
Fried foods			0.014			0.042
Infrequent	1			1		
Frequent	1.153	1.014, 1.312		1.137	1.000, 1.294	
Grilled foods			0.504			0.735
Infrequent	1			1		0.495
Frequent	0.980	0.888, 1.082		0.964	0.872, 1.065	
Processed foods			0.410			0.167
Infrequent	1			1		
Frequent	1.048	0.937, 1.173		1.079	0.969, 1.202	
Seasonings			0.040			0.052
Infrequent	1			1		
Frequent	1.119	1.007, 1.356		1.156	0.998, 1.340	
Instant foods			0.016			0.008
Infrequent	1			1		
Frequent	1.116	1.020, 1.221		1.127	1.032, 1.229	
Fruits			0.080			0.098
Adequate	1			1		
Inadequate	1.038	0.937, 1.149		1.086	0.985, 1.197	
Vegetables						
Adequate	1		0.969	1		0.883
Inadequate	0.953	0.846, 1.074		1.001	1.893, 1.123	

[*]Differences between food consumption and hyperglycemia were analyzed using multiple logistic regression. [**]Model 1 was unadjusted. [***]Model 2 was adjusted for age, gender, education level, residency, smoking status, alcohol consumption, physical activity.

We found that frequent consumption of sweet desserts and SSB were significantly associated with risk of hyperglycemia. Our result was in line with another cross-sectional study that subjects with metabolic disorders were higher intake of desserts and beverage than those without metabolic disorders (Permatasari & Syauqy 2022). Sweet desserts and SSB contained carbohydrates or simple sugars with a high Glycemic Index (GI) value, leading to accelerated blood sugar levels (Medina-Remón *et al.* 2018). Other studies found a decrease in endothelial cells' micro and macro cellular function when consuming sweetened sugary beverages (Loader *et al.* 2017). These metabolic abnormalities are due to the increased in oxidative stress and decreased in NO's (nitric oxide) bioavailability, which plays an important role in glucose metabolism in the body. The decreased in NO bioavailability is also related to risk of developing type 2 diabetes (Loader *et al*. 2017). Added sugar intake is involved in the production of reactive oxygen species (ROS). It then might increase the expression of cytokines and cell adhesion molecules (Prasad and Dhar 2014).

Participants who frequently consumed salty foods were associated with risk of hyperglycemia. This result is in line with a previous study (*Fitria* et al. 2016). High consumption of salty foods is correlated with an increased risk factor for DM (Fitria *et al.* 2016). High intake of sodium increases the risk of hyperglycemia through the PPAR δ/adiponectin/SGLT2 mechanism in regulating sodium and glucose homeostasis (Zhao *et al.* 2016).

Frequent consumption of fried foods was significantly associated with risk of hyperglycemia in recent study. Fried foods are high in fat, including saturated fat and cholesterol. Frequent consumption of fried food will lead to hyperglycemia in the pre-elderly population. A high-fat diet also significantly contributes to obesity and non-insulin-dependent diabetes mellitus (Naja *et al.* 2013). Previous study found a positive relationship between high intake of saturated fat and cholesterol and increased hyperglycemia and type 2 diabetes in humans and rats (Cahill *et al.* 2014). Saturated fat in the cell membrane will decrease the viscosity of the lipid bilayer of a cell membrane and lead to a decrease in the insulin receptors (Min *et al.* 2018).

Frequent consumption of instant foods had a significant relationship with the incidence of hyperglycemia as indicated by an increase in FBG in this study. Our results are consistent with other studies that high intake of instant foods were linked to a higher risk of developing diabetes due to the high carbohydrate and fat (Huh *et al.* 2017). An animal trial of monosodium glutamate found a significant increase in glucose levels as evidenced by an increase in HOMA-IR value in rats. It is because of the changes in insulin binding or insulin post receptors in the target tissues (Helal *et al.* 2019). Monosodium glutamate may trigger the degradation of neuronal membranes, allowing calcium ions to enter cells because of its permeability of sodium ions, calcium ions, and water. Then, it might damage the pancreatic gland and hyperglycemia (Jusuf *et al.* 2020).

In this study, individuals with inadequate consumption of fruits and vegetables were 1.086 and 1.001, respectively, more likely to have hyperglycemia than those with adequate consumption of vegetables and fruits, but these associations were not statistically significant. In contrast, another study found that more intakes of fruits and vegetables can reduce hyperglycemia (Samaan 2017). Fiber might delay the digestion and absorption of carbohydrates and increase satiety effect. In individuals with insulin resistance, fiber can increase peripheral insulin sensitivity through short-chain fatty acids produced by fiber fermentation in the gut (Samaan 2017) . In addition, a diet high in fruits and vegetables is associated with high intake of magnesium and iron (Zhang *et al.* 2015). Magnesium is an important cofactor for several enzymes in glucose metabolism, which further plays a role in the development of diabetes (Verma & Garg 2017). Diabetes is a chronic disease. People with diabetes might change their diet, and eat more healthy food; however, it cannot change immediately the condition of the disease.

The bivariate analysis in this study was in line with a previous study conducted in Indonesia (Permatasari & Syauqy 2022). Among subjects with metabolic disorders, 8.8%, 6.3%, and 21.2% frequently consumed soft drink, energy drinks, and processed meat. Moreover, among subjects with metabolic disorders, 91.9% and 88.4% consumed inadequate fruits and vegetables, respectively.

This study has some strengths. To the best of our knowledge, this was the first study analyzing the association of food consumption with hyperglycemia among middle-aged in Indonesia. Our study used a large sample that reflected the Indonesian population. Some limitations should be mentioned in this study. Firstly, dietary data were taken using a frequency of intake which is no information related to nutrients. Further research with a priori or a posteriori method is highly recommended. By using a priori or a posteriori method, researchers may derive the dietary patterns consisting of complex foods with many nutrients that represent the diet intake among population of interest. Moreover, the R^2 of logistic regression analyses in this study was relatively low; suggesting other factors outside the model still explain the incidence of hyperglycemia in middle-aged adults. Finally, the cross-sectional design restricts the results in maintaining the causality between the variables. Additional longitudinal study is needed to explore the mechanism between variables.

CONCLUSION

There was a significant association between food consumption and hyperglycemia status among middle-aged adults in Indonesia. Frequent consumption of sweet desserts, SSB, salty foods, fried foods, and instant foods increased the odds (chance) to have hyperglycemia. Further research with a priori or a posteriori dietary pattern approach is highly recommended. Additional longitudinal study is needed to explore the mechanism between variables.

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DECLARATION OF INTERESTS

The authors have no conflict of interest.

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AUTHOR'S REVISION FORM

Title	:	**Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis**
Author(s)	:	Ahmad Syauqy, Siti Andhini Mattarahmawati, Adriyan Pramono

No	Manuscript section	Corrected line	Suggestions	Revised line	Revisions
1	Title				
2	Abstract				
3	Introduction				
4	Method				
5	Result and discussion	Table 1	Delete this column	Table 1	We revised it accordingly
		140-144	Discuss how these numbers compared to other references? Is it typical? Also, why these practices were worse compared to non-hyperglycemia?	line 226-231 Line 171-176 Line 186-190 Line 195-198 Line 203-205	We revised and added the discussion section "The bivariate analysis in this study was in line with a previous study conducted in Indonesia (Permatasari & Syauqy 2022). Among subjects with metabolic disorders, 8.8%, 6.3%, and 21.2% frequently consumed soft drink, energy drinks, and processed meat. Moreover, among subjects with metabolic disorders, 91.9% and 88.4% consumed inadequate fruits and vegetables, respectively." (line 226-231)" "Our result was in line with another cross-sectional study that subjects with metabolic disorders were higher intake of desserts and beverage than those without

					metabolic disorders (Permatasari & Syauqy 2022). Sweet desserts and SSB contained carbohydrates or simple sugars with a high Glycemic Index (GI) value, leading to accelerated blood sugar levels (Medina-Remón *et al.* 2018)." Line 171-176 This result is in line with a previous study (*Fitria* et al. 2016). High consumption of salty foods is correlated with an increased risk factor for DM (Fitria *et al.* 2016). High intake of sodium increases the risk of hyperglycemia through the PPAR δ/adiponectin/SGLT2 mechanism in regulating sodium and glucose homeostasis (Zhao *et al.* 2016). Line 186-190 Previous study found a positive relationship between high intake of saturated fat and cholesterol and increased hyperglycemia and type 2 diabetes in humans and rats (Cahill *et al.* 2014). Line 195-198 Our results are consistent with other studies that high intake of instant

					foods were linked to a higher risk of developing diabetes due to the high carbohydrate and fat (Huh *et al.* 2017). Line 203-205
		Table 2	Delete this column	Table 2	We revised it accordingly
		212-213	Add bridging sentence to connect the opposite facts	215-217	We added a sentence "In contrast, another study found that more intakes of fruits and vegetables can reduce hyperglycemia"
		219	What is the overall risk of hyperglycemia in this study? How many % are able to be explained by these variables and how many % for the unexplained one? You did multiple regression, so you should be able to answer this.	Line 158 & 160; Line 239-241	We calculated the R^2. We added it in the results and discussion (R^2=2%).(line 158) (R^2=2%). (line 160) Moreover, the R^2 of logistic regression analyses in this study was relatively low; suggesting other factors outside the model still explain the incidence of hyperglycemia in middle-aged adults. (line 239-241)
		220-222	Add more explanation on the findings in relation to study design/type of study	Line 241-244	We added the explanation in discussion section Finally, the cross-sectional design restricts the results in maintaining the causality between the variables. Additional longitudinal study is needed to explore the mechanism between variables.
6	Conclusion and suggestion				
7	References				

8	Others:				

* Information:

- This form is an additional file that must be attached along with the revised manuscript to make the revision easy to track **(please highlight the revised part in the revised manuscript in color).**
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Semarang, 18 November 2022,

Ahmad Syauqy

Overall comments :

[JGP] Further Correction from Editor V

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- Ahmad Syauqy, S.Gz, MPH.,Ph.D (jgpahmadsyauqy)

Messages

Note	From
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HASIL REVISI EDITOR (V)

Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis

ABSTRACT

The objective of this study was to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia. This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS). A total of 8477 subjects met the inclusion criteria and included in this study. Fasting Blood Glucose (FBG) was analyzed in the laboratory using an enzymatic analysis. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dL) and normal (<126 mg/dL). A food frequency questionnaire was used to assess the food intake. Multiple logistic regression was used to analyze the association of food consumption and hyperglycemia. Our results found that the prevalence of hyperglycemia in this population was 43%. The mean FBG was 104.68 ± 31.99 mg/dL for male and 110.75 ± 43.92 mg/dL for female subjects. Frequent consumption of sweet desserts (OR=1.265; CI=1.132, 1.413), sugar-sweetened beverages (SSB) (OR=1.433; CI=1.263, 1.626), salty foods (OR=1.189; CI=1.079, 1.311), fried foods (OR=1.172; CI=1.033, 1.331), and instant foods (OR=1.186; CI=1.088, 1.293) were significantly associated with increased odds of hyperglycemia. There was a significant association between food consumption and hyperglycemia among middle-aged adults in Indonesia.

Keyword: diet, food consumption, hyperglycemia, fasting blood glucose, Indonesia

Runner Title: Food consumption and hyperglycemia

INTRODUCTION

Non-communicable diseases are the leading cause of public health problems in developed and developing countries (Naghavi M 2017). Diabetes, one of the non-communicable diseases, is the main cause of death in the world (Zheng *et al.* 2018). Diabetes or hyperglycemia is characterized by an increase in blood sugar levels in the body. Previous studies found that the prevalence of hyperglycemia and the components of metabolic syndrome increased rapidly with

age in women and men (Wu *et al.* 2017; Jiang *et al.* 2018). Recently, Indonesia is the fourth country after India, China, and America, with the most diabetes sufferers globally (Naghavi M 2017). The prevalence of diabetes in Indonesia was around 6% (Mihardja *et al.* 2014). Interestingly, based on the 2018 Indonesia Basic Health Survey (IBHS), the higher prevalence of diabetes was among middle-aged adults with almost 10% (MoH RI 2018).

Diabetes is caused by many factors including lifestyle (Sudargo *et al.* 2018). Sedentary lifestyle has been associated with the increasing trend of diabetes (Permatasari & Syauqy 2022). Previous study also found that diet was associated with the increased prevalence of diabetes (Lambrinou *et al.* 2019). Western foods or unhealthy foods are correlated with an increased prevalence of hyperglycemia and metabolic syndrome (Syauqy *et al.* 2018). Western foods or unhealthy foods consisted of sweet, sugar, fat, Sugar-Sweetened Beverages (SSB), fried foods, and seasoning; hence, the unhealthy food is high in simple carbohydrate, saturated fat, and sodium. Furthermore, inadequate consumption of vegetables and fruits can also escalate the diabetes prevalence (Syauqy *et al*. 2018; Schwingshackl *et al.* 2017).

Some studies have found the association between food consumption and metabolic syndrome among middle-aged adults in Taiwan (Syauqy *et al*. 2018). Moreover, middle-aged adults who consumed high fruits and vegetables and less unhealthy foods had a better quality of life (Lo *et al.* 2016). A research found that Indonesian people tend to consume high western foods and low fruits and vegetables (MoH RI 2018). However, to the best of our knowledge, study investigated the association of unhealthy foods, fruits, and vegetables intakes with diabetes among middle-aged adults in Indonesia was still rare, especially using a national database that represents the Indonesian population. Therefore, the objective of this study was to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia.

METHODS

Design, location, and time

This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS). Briefly, the IBHS used a two-stage stratified cluster sampling method survey population includes all Indonesian households, representing 26 Provinces and utilizing a sample framework from the national socio-economic survey in March 2018 (MoH RI 2018). This study had received ethical approval from the Health Research Ethics Commission, Medical Faculty, Universitas 'Aisyiyah Yogyakarta No. 1415/KEP-UNISA/VI/2021.

Sampling

The target sample included 300,000 households from 30,000 census blocks of the national socio-economic survey framework (MoH RI 2018). The total population data of the IBHS were 713,783 people aged ≥15 years (MoH RI 2018). The inclusion criteria in this study were individuals aged 45-59 years, had completed data of foods consumption, had completed data on fasting blood glucose, and agreed and had given their written informed consent (n=8,481). While, subjects were excluded due to extreme values or missing data (n=4). Finally, a total of 8,477 subjects met the inclusion criteria and included in this study.

Data collection

The independent variables in this study were the consumption of foods; while, the dependent variable was hyperglycemia status. Fasting blood glucose were measured with fingertip capillary blood tests (Accu-Chek Performa, Roche Diagnostics GmbH, Mannheim, Germany). All participants were instructed to fast overnight (8-10 hours) before blood sampling. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dL) and normal (<126 mg/dL) (Genuth *et al.* 2003; MoH RI 2018). A validated food frequency questionnaire (FFQ) was used to assess the daily food consumption. The FFQ was validated by the IBHS prior the study (MoH 2018). The FFQ includes carbonated drinks, energy drinks, sweet desserts, SSB, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods, fruits, and vegetables (MoH RI 2018). Consumption of unhealthy foods (carbonated drinks, energy drinks, sweet desserts, SSB, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods) was categorized as frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Fruits and vegetable consumption was categorized into adequate (≥5 servings per day) and inadequate (<5 servings per day) (MoH RI 2018). Sociodemographic data (age, gender, education, and place of residence) and lifestyle (smoking status, alcohol intake, and physical activity) were obtained using a structured questionnaire. Smoking was categorized into yes and no. Consumption of alcoholic beverages was categorized into yes and no (Atamni *et al*. 2016). Gender was categorized as male and female. Education level was categorized as high (completed 12-year compulsory education or bachelor/diploma/higher education graduates) and low (not completed 12-year compulsory education). Residency was categorized as urban and rural. Physical activity was categorized as low (doing heavy physical activity for <150 minutes/week) and high (doing heavy physical activity for ≥150 minutes/week (MoH RI 2018).

Data analysis

Univariate analysis was presented using mean±standard deviation for numerical data and frequency (percentage) for categorical data. In addition, bivariate analysis was performed using independent samples t-test for continuous variables and the Chi-square test for categorical variables. Whereas, multivariate analysis using multiple logistic regression was used to analyze the association of food consumption and hyperglycemia status. Odds Ratio (OR) with 95% confidence intervals was conducted in the analyze. We used unadjusted (model 1) and adjusted (model 2). Model 2 was adjusted for demographic data (age, gender, residency) and lifestyle (smoking status, alcohol consumption, and physical activity). We selected demographic data and lifestyle because they have potential association with hyperglycemia that might interfere the results. All analyses were performed using the SPSS program 25 version with a *p*-value <0.05 considered statistically significant.

RESULTS AND DISCUSSION

Table 1 shows the characteristics of the subjects. The majority of the subjects with hyperglycemia were older (52.05±4.29), female (63.7), not smoking (69.8), and had low physical activity (53.3). Our results also found that the prevalence of hyperglycemia in the population was 43%. The mean FBG was 104.68±31.99 mg/dL for male and 110.75±43.92 mg/dL for female subjects. This study also found that the prevalence of hyperglycemia was higher in females (44.6%) than males (40.6%). This result was in line with a previous study in the United State (ADA 2018). Women are more risk of experiencing hyperglycemia due to the hormonal changes (ADA 2018). Moreover, physical activity in women tends to be lower than in men (The Lancet Public Health 2019).

Table 1. Characteristics of the subjects.

Variables	Hyperglycemia Yes (n=3,648)	Hyperglycemia No (n=4,829)	*P*
Age, mean±SD	52.05±4.29	41.27±4.24	<0.001*
Gender, n (%)			<0.001**
Male	1,323 (36.3)	1,935 (40.1)	
Female	2,325 (63.7)	2,894 (59.9)	
Education levels, n (%)			0.310**
High	1,239 (34.0)	1,691 (35.0)	
Low	2,409 (66.0)	3,138 (65.0)	
Residency, n (%)			0.188**
Rural	1,837 (50.4)	2,502 (51.8)	
Urban	1,811 (49.6)	2,325 (48.2)	
Smoking status, n (%)			<0.001**
No	2,546 (69.8)	3,195 (66.2)	
Yes	1,102 (30.2)	1,634 (33.8)	
Alcohol consumption, n (%)			0.465**
No	3,604 (98.8)	4,779 (99.0)	
Yes	44 (1.2)	50 (1.0)	
Physical activity, n (%)			0.019**
High	1,684 (46.2)	2,355 (48.8)	
Low	1,964 (53.8)	2,474 (51.2)	
Fasting blood glucose, mean±SD	130.84±52.65	91.47±5.43	<0.001*

*Comparison between continuous variables and hyperglycemia were performed using independent samples t-test

**Comparison between categorical variables and hyperglycemia were performed using Chi-square test

The association of food consumption and hyperglycemia are described in Table 2. Among subjects with hyperglycemia, 20.2%, 15.5%, 28.3%, 14.1%, 10.3%, and 48.3% frequently consumed sweet desserts, SSB, salty foods, fried foods, seasonings, and instant foods, respectively. Moreover, among subjects with hyperglycemia, 73.2% consumed inadequate fruits.

Table 2. Food consumption and hyperglycemia*.

Variables	Hyperglycemia		OR	P^{**}
	Yes (n=3,648)	No (n=4,829)	(95% CI)	
Carbonated drinks, n (%)				
Infrequent	3,396 (93.0)	4,448 (92.2)	0.877	0.123
Frequent	254 (7.0)	379 (7.8)	(0.966, 1.343)	
Energy drinks, n (%)				
Infrequent	3,463 (94.9)	4,566 (94.6)	0.944	0.300
Frequent	187 (5.1)	261 (5.4)	(0.873, 1.284)	
Sweet desserts, n (%)				
Infrequent	2,912 (79.8)	4,021 (82.3)	1.265	<0.001
Frequent	736 (20.2)	808 (17.7)	(1.132, 1.413)	
Sugar-sweetened beverages, n (%)				
Infrequent	3,086 (84.5)	4,281 (88.7)	1.433	<0.001
Frequent	564 (15.5)	546 (11.3)	(1.263, 1.626)	
Salty foods, n (%)				
Infrequent	2,618 (71.7)	3,625 (75.1)	1.189	<0.001
Frequent	1,032 (28.3)	1,202 (24.9)	(1.079, 1.311)	
Fried foods, n (%)				
Infrequent	3,137 (85.9)	4,236 (87.8)	1.172	0.015
Frequent	513 (14.1)	591 (12.2)	(1.033, 1.331)	
Grilled foods, n (%)				
Infrequent	2,594 (71.1)	3,398 (70.4)	1.033	0.515
Frequent	1,056 (28.9)	1,429 (29.6)	(0.940, 1.135)	
Processed foods, n (%)				
Infrequent	2,936 (80.4)	3,804 (78.8)	0.905	0.069
Frequent	714 (19.6)	1,023 (21.2)	(0.813, 1.007)	
Seasonings, n (%)				
Infrequent	3,274 (89.7)	4,402 (91.2)	1.190	0.020
Frequent	376 (10.3)	425 (8.8)	(1.028, 1.377)	
Instant foods, n (%)				
Infrequent	1,889 (51.7)	2,702 (56.0)	1.186	<0.001
Frequent	1,761 (48.3)	2,125 (44.0)	(1.088, 1.293)	

Fruits, n (%)				
Adequate	976 (26.8)	1,374 (28.5)	1.090	0.042
Inadequate	2,674 (73.2)	3,453 (71.5)	(0.990, 1.200)	
Vegetable, n (%)				
Adequate	637 (17.5)	841 (17.4)	1.002	0.495
Inadequate	3,013 (82.5)	3,986 (82.6)	(0.895, 1.123)	

*Frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Adequate (≥5 servings per day) and inadequate (<5 servings per day)

**Comparison between food consumption and hyperglycemia were performed using Chi-square test

The odds ratios (95% confidence intervals) for food consumption across hyperglycemia are presented in Table 3. Frequent consumption of sweet desserts (OR=1.168; CI=1.035, 1.315), SSB (OR=1.306; CI=1.137, 1.600), salty foods (OR=1.159; CI=1.049, 1.281), fried foods (OR=1.153; CI=1.014, 1.312), seasoning (OR=1.119; CI=1.007, 1.356), and instant foods (OR=1.116; CI=1.020, 1.221) were significantly associated with increased crude odds (model 1) of hyperglycemia (R^2=2%). After adjusting for age, gender, education levels, residency, smoking status, alcohol consumption, and physical activity (model 2), frequent consumption of seasonings was not significantly associated with hyperglycemia (R^2=9%).

Commented [A68]: The R2 should be explained in such a way that prior to adjustment, the R2 is 2% and after the adjustment, it become 9%.

Table 3. Odds ratios (95% confidence intervals) for food consumption across hyperglycemia

Variables	Model 1**			Model 2***		
	OR	95% CI	*p*	OR	95% CI	*p**
Carbonated drinks			0.122			0.419
Infrequent	1			1		
Frequent	1.066	0.889, 1.279		1.071	0.907, 1.266	
Energy drinks			0.565			0.772
Infrequent	1			1		
Frequent	0.961	0.778, 1.187		0.971	0.798, 1.182	
Sweet desserts			<0.001	1		<0.001
Infrequent	1					
Frequent	1.168	1.035, 1.315		1.135	1.005, 1.281	
Sugar-sweetened beverages			<0.001			<0.001
Infrequent	1			1		
Frequent	1.306	1.137, 1.600		1.284	1.116, 1.477	
Salty foods			<0.001			<0.001
Infrequent	1			1		
Frequent	1.159	1.049, 1.281		1.140	1.031, 1.260	
Fried foods			0.014			0.042
Infrequent	1			1		
Frequent	1.153	1.014, 1.312		1.137	1.000, 1.294	
Grilled foods			0.504			0.735
Infrequent	1			1		0.495
Frequent	0.980	0.888, 1.082		0.964	0.872, 1.065	
Processed foods			0.410			0.167
Infrequent	1			1		
Frequent	1.048	0.937, 1.173		1.079	0.969, 1.202	
Seasonings			0.040			0.052
Infrequent	1			1		
Frequent	1.119	1.007, 1.356		1.156	0.998, 1.340	
Instant foods			0.016			0.008
Infrequent	1			1		

Frequent	1.116	1.020, 1.221		1.127	1.032, 1.229	
Fruits			0.080			0.098
Adequate	1			1		
Inadequate	1.038	0.937, 1.149		1.086	0.985, 1.197	
Vegetables						
Adequate	1		0.969	1		0.883
Inadequate	0.953	0.846, 1.074		1.001	1.893, 1.123	

*Differences between food consumption and hyperglycemia were analyzed using multiple logistic regression. **Model 1 was unadjusted. ***Model 2 was adjusted for age, gender, education level, residency, smoking status, alcohol consumption, physical activity.

We found that frequent consumption of sweet desserts and SSB were significantly associated with risk of hyperglycemia. Our result was in line with another cross-sectional study that subjects with metabolic disorders had higher intake of desserts and beverage than those without metabolic disorders (Permatasari & Syauqy 2022). Sweet desserts and SSB contained carbohydrates or simple sugars with a high Glycemic Index (GI) value, leading to accelerated blood sugar levels (Medina-Remón *et al.* 2018). Other studies found a decrease in endothelial cells' micro and macro cellular function when consuming sweetened sugary beverages (Loader *et al.* 2017). These metabolic abnormalities are due to the increased in oxidative stress and decreased in NO's (nitric oxide) bioavailability, which plays an important role in glucose metabolism in the body. The decreased in NO bioavailability is also related to risk of developing type 2 diabetes (Loader *et al*. 2017). Added sugar intake is involved in the production of reactive oxygen species (ROS). It then might increase the expression of cytokines and cell adhesion molecules (Prasad & Dhar 2014).

Participants who frequently consumed salty foods were associated with risk of hyperglycemia. This result is in line with a previous study (*Fitria et al.* 2016). High consumption of salty foods is correlated with an increased risk factor for DM (Fitria *et al.* 2016). High intake of sodium increases the risk of hyperglycemia through the PPAR δ/adiponectin/SGLT2 mechanism in regulating sodium and glucose homeostasis (Zhao *et al.* 2016).

Frequent consumption of fried foods was significantly associated with risk of hyperglycemia in recent study. Fried foods are high in fat, including saturated fat and cholesterol. Frequent consumption of fried food will lead to hyperglycemia in the pre-elderly population. A high-fat diet also significantly contributes to obesity and non-insulin-dependent diabetes mellitus

(Naja *et al.* 2013). Previous study found a positive relationship between high intake of saturated fat and cholesterol and increased hyperglycemia and type 2 diabetes in humans and rats (Cahill *et al.* 2014). Saturated fat in the cell membrane will decrease the viscosity of the lipid bilayer of a cell membrane and lead to a decrease in the insulin receptors (Min *et al.* 2018).

Frequent consumption of instant foods had a significant relationship with the incidence of hyperglycemia as indicated by an increase in FBG in this study. Our results are consistent with other studies that high intake of instant foods were linked to a higher risk of developing diabetes due to the high carbohydrate and fat (Huh *et al.* 2017). An animal trial of monosodium glutamate found a significant increase in glucose levels as evidenced by an increase in HOMA-IR value in rats. It is because of the changes in insulin binding or insulin post receptors in the target tissues (Helal *et al.* 2019). Monosodium glutamate may trigger the degradation of neuronal membranes, allowing calcium ions to enter cells because of its permeability of sodium ions, calcium ions, and water. Then, it might damage the pancreatic gland and hyperglycemia (Jusuf *et al.* 2020).

In this study, individuals with inadequate consumption of fruits and vegetables were 1.086 and 1.001, respectively, more likely to have hyperglycemia than those with adequate consumption of vegetables and fruits, but these associations were not statistically significant. In contrast, another study found that more intakes of fruits and vegetables can reduce hyperglycemia (Samaan 2017). Fiber might delay the digestion and absorption of carbohydrates and increase satiety effect. In individuals with insulin resistance, fiber can increase peripheral insulin sensitivity through short-chain fatty acids produced by fiber fermentation in the gut (Samaan 2017) . In addition, a diet high in fruits and vegetables is associated with high intake of magnesium and iron (Zhang *et al.* 2015). Magnesium is an important cofactor for several enzymes in glucose metabolism, which further plays a role in the development of diabetes (Verma & Garg 2017). Diabetes is a chronic disease. People with diabetes might change their diet, and eat more healthy food; however, it cannot change immediately the condition of the disease.

The bivariate analysis in this study was in line with a previous study conducted in Indonesia (Permatasari & Syauqy 2022). Among subjects with metabolic disorders, 8.8%, 6.3%, and 21.2% frequently consumed soft drink, energy drinks, and processed meat. Moreover, among subjects with metabolic disorders, 91.9% and 88.4% consumed inadequate fruits and vegetables, respectively.

This study has some strengths. To the best of our knowledge, this was the first study analyzing the association of food consumption with hyperglycemia among middle-aged in Indonesia. Our study used a large sample that reflected the Indonesian population. Some limitations should be mentioned in this study. Firstly, dietary data were taken using a frequency of intake which is no information related to nutrients. Further research with a priori or a posteriori method is highly recommended. By using a priori or a posteriori method, researchers may derive the dietary patterns consisting of complex foods with many nutrients that represent the diet intake among population of interest. Moreover, the R^2 of logistic regression analyses in this study was relatively low; suggesting other factors outside the model still explain the incidence of hyperglycemia in middle-aged adults. Finally, the cross-sectional design restricts the results in maintaining the causality between the variables. Additional longitudinal study is needed to explore the mechanism between variables.

CONCLUSION

There was a significant association between food consumption and hyperglycemia status among middle-aged adults in Indonesia. Frequent consumption of sweet desserts, SSB, salty foods, fried foods, and instant foods increased the odds (chance) to have hyperglycemia. Further research with a priori or a posteriori dietary pattern approach is highly recommended. Additional longitudinal study is needed to explore the mechanism between variables.

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DECLARATION OF INTERESTS

The authors have no conflict of interest.

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Settings

Dear Prof. Dr. Dodik Briawan, MCN, Editor-in-Chief,

Many thanks for the editors' suggestions and comments. We have revised throughout the manuscript entitled "Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis" according to the editors' comments and suggestions.

If you have any questions, please feel free to call me at +6224-76402881 (email: syauqy@fk.undip.ac.id). I am looking forward to your response.

Best Regards,

Ahmad Syauqy

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HASIL PERBAIKAN EDITOR (V)

Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis

ABSTRACT

The objective of this study was to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia. This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS). A total of 8477 subjects met the inclusion criteria and included in this study. Fasting Blood Glucose (FBG) was analyzed in the laboratory using an enzymatic analysis. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dL) and normal (<126 mg/dL). A food frequency questionnaire was used to assess the food intake. Multiple logistic regression was used to analyze the association of food consumption and hyperglycemia. Our results found that the prevalence of hyperglycemia in this population was 43%. The mean FBG was 104.68 ± 31.99 mg/dL for male and 110.75 ± 43.92 mg/dL for female subjects. Frequent consumption of sweet desserts (OR=1.265; CI=1.132, 1.413), sugar-sweetened beverages (SSB) (OR=1.433; CI=1.263, 1.626), salty foods (OR=1.189; CI=1.079, 1.311), fried foods (OR=1.172; CI=1.033, 1.331), and instant foods (OR=1.186; CI=1.088, 1.293) were significantly associated with increased odds of hyperglycemia. There was a significant association between food consumption and hyperglycemia among middle-aged adults in Indonesia.

Keyword: diet, food consumption, hyperglycemia, fasting blood glucose, Indonesia

Runner Title: Food consumption and hyperglycemia

INTRODUCTION

Non-communicable diseases are the leading cause of public health problems in developed and developing countries (Naghavi M 2017). Diabetes, one of the non-communicable diseases, is the main cause of death in the world (Zheng *et al.* 2018). Diabetes or hyperglycemia is characterized by an increase in blood sugar levels in the body. Previous studies found that the prevalence of hyperglycemia and the components of metabolic syndrome increased rapidly with

age in women and men (Wu *et al.* 2017; Jiang *et al.* 2018). Recently, Indonesia is the fourth country after India, China, and America, with the most diabetes sufferers globally (Naghavi M 2017). The prevalence of diabetes in Indonesia was around 6% (Mihardja *et al.* 2014). Interestingly, based on the 2018 Indonesia Basic Health Survey (IBHS), the higher prevalence of diabetes was among middle-aged adults with almost 10% (MoH RI 2018).

Diabetes is caused by many factors including lifestyle (Sudargo *et al.* 2018). Sedentary lifestyle has been associated with the increasing trend of diabetes (Permatasari & Syauqy 2022). Previous study also found that diet was associated with the increased prevalence of diabetes (Lambrinou *et al.* 2019). Western foods or unhealthy foods are correlated with an increased prevalence of hyperglycemia and metabolic syndrome (Syauqy *et al.* 2018). Western foods or unhealthy foods consisted of sweet, sugar, fat, Sugar-Sweetened Beverages (SSB), fried foods, and seasoning; hence, the unhealthy food is high in simple carbohydrate, saturated fat, and sodium. Furthermore, inadequate consumption of vegetables and fruits can also escalate the diabetes prevalence (Syauqy *et al*. 2018; Schwingshackl *et al.* 2017).

Some studies have found the association between food consumption and metabolic syndrome among middle-aged adults in Taiwan (Syauqy *et al*. 2018). Moreover, middle-aged adults who consumed high fruits and vegetables and less unhealthy foods had a better quality of life (Lo *et al.* 2016). A research found that Indonesian people tend to consume high western foods and low fruits and vegetables (MoH RI 2018). However, to the best of our knowledge, study investigated the association of unhealthy foods, fruits, and vegetables intakes with diabetes among middle-aged adults in Indonesia was still rare, especially using a national database that represents the Indonesian population. Therefore, the objective of this study was to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia.

METHODS

Design, location, and time

This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS). Briefly, the IBHS used a two-stage stratified cluster sampling method survey population includes all Indonesian households, representing 26 Provinces and utilizing a sample framework from the national socio-economic survey in March 2018 (MoH RI 2018). This study had received ethical approval from the Health Research Ethics Commission, Medical Faculty, Universitas 'Aisyiyah Yogyakarta No. 1415/KEP-UNISA/VI/2021.

Sampling

The target sample included 300,000 households from 30,000 census blocks of the national socio-economic survey framework (MoH RI 2018). The total population data of the IBHS were 713,783 people aged ≥15 years (MoH RI 2018). The inclusion criteria in this study were individuals aged 45-59 years, had completed data of foods consumption, had completed data on fasting blood glucose, and agreed and had given their written informed consent (n=8,481). While, subjects were excluded due to extreme values or missing data (n=4). Finally, a total of 8,477 subjects met the inclusion criteria and included in this study.

Data collection

The independent variables in this study were the consumption of foods; while, the dependent variable was hyperglycemia status. Fasting blood glucose were measured with fingertip capillary blood tests (Accu-Chek Performa, Roche Diagnostics GmbH, Mannheim, Germany). All participants were instructed to fast overnight (8-10 hours) before blood sampling. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dL) and normal (<126 mg/dL) (Genuth *et al.* 2003; MoH RI 2018). A validated food frequency questionnaire (FFQ) was used to assess the daily food consumption. The FFQ was validated by the IBHS prior the study (MoH 2018). The FFQ includes carbonated drinks, energy drinks, sweet desserts, SSB, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods, fruits, and vegetables (MoH RI 2018). Consumption of unhealthy foods (carbonated drinks, energy drinks, sweet desserts, SSB, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods) was categorized as frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Fruits and vegetable consumption was categorized into adequate (≥5 servings per day) and inadequate (<5 servings per day) (MoH RI 2018). Sociodemographic data (age, gender, education, and place of residence) and lifestyle (smoking status, alcohol intake, and physical activity) were obtained using a structured questionnaire. Smoking was categorized into yes and no. Consumption of alcoholic beverages was categorized into yes and no (Atamni *et al.* 2016). Gender was categorized as male and female. Education level was categorized as high (completed 12-year compulsory education or bachelor/diploma/higher education graduates) and low (not completed 12-year compulsory education). Residency was categorized as urban and rural. Physical activity was categorized as low (doing heavy physical activity for <150 minutes/week) and high (doing heavy physical activity for ≥150 minutes/week (MoH RI 2018).

Data analysis

Univariate analysis was presented using mean±standard deviation for numerical data and frequency (percentage) for categorical data. In addition, bivariate analysis was performed using independent samples t-test for continuous variables and the Chi-square test for categorical variables. Whereas, multivariate analysis using multiple logistic regression was used to analyze the association of food consumption and hyperglycemia status. Odds Ratio (OR) with 95% confidence intervals was conducted in the analyze. We used unadjusted (model 1) and adjusted (model 2). Model 2 was adjusted for demographic data (age, gender, residency) and lifestyle (smoking status, alcohol consumption, and physical activity). We selected demographic data and lifestyle because they have potential association with hyperglycemia that might interfere the results. All analyses were performed using the SPSS program 25 version with a *p*-value <0.05 considered statistically significant.

RESULTS AND DISCUSSION

Table 1 shows the characteristics of the subjects. The majority of the subjects with hyperglycemia were older (52.05±4.29), female (63.7), not smoking (69.8), and had low physical activity (53.3). Our results also found that the prevalence of hyperglycemia in the population was 43%. The mean FBG was 104.68±31.99 mg/dL for male and 110.75±43.92 mg/dL for female subjects. This study also found that the prevalence of hyperglycemia was higher in females (44.6%) than males (40.6%). This result was in line with a previous study in the United State (ADA 2018). Women are more risk of experiencing hyperglycemia due to the hormonal changes (ADA 2018). Moreover, physical activity in women tends to be lower than in men (The Lancet Public Health 2019).

Table 1. Characteristics of the subjects.

Variables	Hyperglycemia		*P*
	Yes (n=3,648)	No (n=4,829)	
Age, mean±SD	52.05±4.29	41.27±4.24	<0.001*
Gender, n (%)			<0.001**
Male	1,323 (36.3)	1,935 (40.1)	
Female	2,325 (63.7)	2,894 (59.9)	
Education levels, n (%)			0.310**
High	1,239 (34.0)	1,691 (35.0)	
Low	2,409 (66.0)	3,138 (65.0)	
Residency, n (%)			0.188**
Rural	1,837 (50.4)	2,502 (51.8)	
Urban	1,811 (49.6)	2,325 (48.2)	
Smoking status, n (%)			<0.001**
No	2,546 (69.8)	3,195 (66.2)	
Yes	1,102 (30.2)	1,634 (33.8)	
Alcohol consumption, n (%)			0.465**
No	3,604 (98.8)	4,779 (99.0)	
Yes	44 (1.2)	50 (1.0)	
Physical activity, n (%)			0.019**
High	1,684 (46.2)	2,355 (48.8)	
Low	1,964 (53.8)	2,474 (51.2)	
Fasting blood glucose, mean±SD	130.84±52.65	91.47±5.43	<0.001*

*Comparison between continuous variables and hyperglycemia were performed using independent samples t-test

**Comparison between categorical variables and hyperglycemia were performed using Chi-square test

The association of food consumption and hyperglycemia are described in Table 2. Among subjects with hyperglycemia, 20.2%, 15.5%, 28.3%, 14.1%, 10.3%, and 48.3% frequently consumed sweet desserts, SSB, salty foods, fried foods, seasonings, and instant foods, respectively. Moreover, among subjects with hyperglycemia, 73.2% consumed inadequate fruits.

Table 2. Food consumption and hyperglycemia*.

Variables	Hyperglycemia		OR	P^{**}
	Yes (n=3,648)	No (n=4,829)	(95% CI)	
Carbonated drinks, n (%)				
Infrequent	3,396 (93.0)	4,448 (92.2)	0.877	0.123
Frequent	254 (7.0)	379 (7.8)	(0.966, 1.343)	
Energy drinks, n (%)				
Infrequent	3,463 (94.9)	4,566 (94.6)	0.944	0.300
Frequent	187 (5.1)	261 (5.4)	(0.873, 1.284)	
Sweet desserts, n (%)				
Infrequent	2,912 (79.8)	4,021 (82.3)	1.265	<0.001
Frequent	736 (20.2)	808 (17.7)	(1.132, 1.413)	
Sugar-sweetened beverages, n (%)				
Infrequent	3,086 (84.5)	4,281 (88.7)	1.433	<0.001
Frequent	564 (15.5)	546 (11.3)	(1.263, 1.626)	
Salty foods, n (%)				
Infrequent	2,618 (71.7)	3,625 (75.1)	1.189	<0.001
Frequent	1,032 (28.3)	1,202 (24.9)	(1.079, 1.311)	
Fried foods, n (%)				
Infrequent	3,137 (85.9)	4,236 (87.8)	1.172	0.015
Frequent	513 (14.1)	591 (12.2)	(1.033, 1.331)	
Grilled foods, n (%)				
Infrequent	2,594 (71.1)	3,398 (70.4)	1.033	0.515
Frequent	1,056 (28.9)	1,429 (29.6)	(0.940, 1.135)	
Processed foods, n (%)				
Infrequent	2,936 (80.4)	3,804 (78.8)	0.905	0.069
Frequent	714 (19.6)	1,023 (21.2)	(0.813, 1.007)	
Seasonings, n (%)				
Infrequent	3,274 (89.7)	4,402 (91.2)	1.190	0.020
Frequent	376 (10.3)	425 (8.8)	(1.028, 1.377)	
Instant foods, n (%)				
Infrequent	1,889 (51.7)	2,702 (56.0)		<0.001

Frequent	1,761 (48.3)	2,125 (44.0)	1.186 (1.088, 1.293)	
Fruits, n (%)				
Adequate	976 (26.8)	1,374 (28.5)	1.090	0.042
Inadequate	2,674 (73.2)	3,453 (71.5)	(0.990, 1.200)	
Vegetable, n (%)				
Adequate	637 (17.5)	841 (17.4)	1.002	0.495
Inadequate	3,013 (82.5)	3,986 (82.6)	(0.895, 1.123)	

*Frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Adequate (≥5 servings per day) and inadequate (<5 servings per day)

**Comparison between food consumption and hyperglycemia were performed using Chi-square test

The odds ratios (95% confidence intervals) for food consumption across hyperglycemia are presented in Table 3. Frequent consumption of sweet desserts (OR=1.168; CI=1.035, 1.315), SSB (OR=1.306; CI=1.137, 1.600), salty foods (OR=1.159; CI=1.049, 1.281), fried foods (OR=1.153; CI=1.014, 1.312), seasoning (OR=1.119; CI=1.007, 1.356), and instant foods (OR=1.116; CI=1.020, 1.221) were significantly associated with increased crude odds (model 1) of hyperglycemia (R^2=2%). After adjusting for age, gender, education levels, residency, smoking status, alcohol consumption, and physical activity (model 2), frequent consumption of seasonings was not significantly associated with hyperglycemia (R^2=9%, it increased after adjusting for confounders).

Commented [A69]: The R2 should be explained in such a way that prior to adjustment, the R2 is 2% and after the adjustment, it become 9%.

ANSWER:
We added 'it increased after adjusting for confounders'

Table 3. Odds ratios (95% confidence intervals) for food consumption across hyperglycemia

Variables	Model 1**			Model 2***		
	OR	95% CI	*p*	OR	95% CI	*p**
Carbonated drinks			0.122			0.419
Infrequent	1			1		
Frequent	1.066	0.889, 1.279		1.071	0.907, 1.266	
Energy drinks			0.565			0.772
Infrequent	1			1		
Frequent	0.961	0.778, 1.187		0.971	0.798, 1.182	
Sweet desserts			<0.001	1		<0.001
Infrequent	1					
Frequent	1.168	1.035, 1.315		1.135	1.005, 1.281	
Sugar-sweetened beverages			<0.001			<0.001
Infrequent	1			1		
Frequent	1.306	1.137, 1.600		1.284	1.116, 1.477	
Salty foods			<0.001			<0.001
Infrequent	1			1		
Frequent	1.159	1.049, 1.281		1.140	1.031, 1.260	
Fried foods			0.014			0.042
Infrequent	1			1		
Frequent	1.153	1.014, 1.312		1.137	1.000, 1.294	
Grilled foods			0.504			0.735
Infrequent	1			1		0.495
Frequent	0.980	0.888, 1.082		0.964	0.872, 1.065	
Processed foods			0.410			0.167
Infrequent	1			1		
Frequent	1.048	0.937, 1.173		1.079	0.969, 1.202	
Seasonings			0.040			0.052
Infrequent	1			1		
Frequent	1.119	1.007, 1.356		1.156	0.998, 1.340	
Instant foods			0.016			0.008
Infrequent	1			1		

Frequent	1.116	1.020, 1.221		1.127	1.032, 1.229	
Fruits			0.080			0.098
Adequate	1			1		
Inadequate	1.038	0.937, 1.149		1.086	0.985, 1.197	
Vegetables						
Adequate	1		0.969	1		0.883
Inadequate	0.953	0.846, 1.074		1.001	1.893, 1.123	

*Differences between food consumption and hyperglycemia were analyzed using multiple logistic regression. **Model 1 was unadjusted. ***Model 2 was adjusted for age, gender, education level, residency, smoking status, alcohol consumption, physical activity.

We found that frequent consumption of sweet desserts and SSB were significantly associated with risk of hyperglycemia. Our result was in line with another cross-sectional study that subjects with metabolic disorders had higher intake of desserts and beverage than those without metabolic disorders (Permatasari & Syauqy 2022). Sweet desserts and SSB contained carbohydrates or simple sugars with a high Glycemic Index (GI) value, leading to accelerated blood sugar levels (Medina-Remón *et al.* 2018). Other studies found a decrease in endothelial cells' micro and macro cellular function when consuming sweetened sugary beverages (Loader *et al.* 2017). These metabolic abnormalities are due to the increased in oxidative stress and decreased in NO's (nitric oxide) bioavailability, which plays an important role in glucose metabolism in the body. The decreased in NO bioavailability is also related to risk of developing type 2 diabetes (Loader *et al*. 2017). Added sugar intake is involved in the production of reactive oxygen species (ROS). It then might increase the expression of cytokines and cell adhesion molecules (Prasad & Dhar 2014).

Participants who frequently consumed salty foods were associated with risk of hyperglycemia. This result is in line with a previous study (*Fitria et al.* 2016). High consumption of salty foods is correlated with an increased risk factor for DM (Fitria *et al.* 2016). High intake of sodium increases the risk of hyperglycemia through the PPAR δ/adiponectin/SGLT2 mechanism in regulating sodium and glucose homeostasis (Zhao *et al.* 2016).

Frequent consumption of fried foods was significantly associated with risk of hyperglycemia in recent study. Fried foods are high in fat, including saturated fat and cholesterol. Frequent consumption of fried food will lead to hyperglycemia in the pre-elderly population. A high-fat diet also significantly contributes to obesity and non-insulin-dependent diabetes mellitus

(Naja *et al.* 2013). Previous study found a positive relationship between high intake of saturated fat and cholesterol and increased hyperglycemia and type 2 diabetes in humans and rats (Cahill *et al.* 2014). Saturated fat in the cell membrane will decrease the viscosity of the lipid bilayer of a cell membrane and lead to a decrease in the insulin receptors (Min *et al.* 2018).

Frequent consumption of instant foods had a significant relationship with the incidence of hyperglycemia as indicated by an increase in FBG in this study. Our results are consistent with other studies that high intake of instant foods were linked to a higher risk of developing diabetes due to the high carbohydrate and fat (Huh *et al.* 2017). An animal trial of monosodium glutamate found a significant increase in glucose levels as evidenced by an increase in HOMA-IR value in rats. It is because of the changes in insulin binding or insulin post receptors in the target tissues (Helal *et al.* 2019). Monosodium glutamate may trigger the degradation of neuronal membranes, allowing calcium ions to enter cells because of its permeability of sodium ions, calcium ions, and water. Then, it might damage the pancreatic gland and hyperglycemia (Jusuf *et al.* 2020).

In this study, individuals with inadequate consumption of fruits and vegetables were 1.086 and 1.001, respectively, more likely to have hyperglycemia than those with adequate consumption of vegetables and fruits, but these associations were not statistically significant. In contrast, another study found that more intakes of fruits and vegetables can reduce hyperglycemia (Samaan 2017). Fiber might delay the digestion and absorption of carbohydrates and increase satiety effect. In individuals with insulin resistance, fiber can increase peripheral insulin sensitivity through short-chain fatty acids produced by fiber fermentation in the gut (Samaan 2017) . In addition, a diet high in fruits and vegetables is associated with high intake of magnesium and iron (Zhang *et al.* 2015). Magnesium is an important cofactor for several enzymes in glucose metabolism, which further plays a role in the development of diabetes (Verma & Garg 2017). Diabetes is a chronic disease. People with diabetes might change their diet, and eat more healthy food; however, it cannot change immediately the condition of the disease.

The bivariate analysis in this study was in line with a previous study conducted in Indonesia (Permatasari & Syauqy 2022). Among subjects with metabolic disorders, 8.8%, 6.3%, and 21.2% frequently consumed soft drink, energy drinks, and processed meat. Moreover, among subjects with metabolic disorders, 91.9% and 88.4% consumed inadequate fruits and vegetables, respectively.

This study has some strengths. To the best of our knowledge, this was the first study analyzing the association of food consumption with hyperglycemia among middle-aged in Indonesia. Our study used a large sample that reflected the Indonesian population. Some limitations should be mentioned in this study. Firstly, dietary data were taken using a frequency of intake which is no information related to nutrients. Further research with a priori or a posteriori method is highly recommended. By using a priori or a posteriori method, researchers may derive the dietary patterns consisting of complex foods with many nutrients that represent the diet intake among population of interest. Moreover, the R^2 of logistic regression analyses in this study was relatively low; suggesting other factors outside the model still explain the incidence of hyperglycemia in middle-aged adults. Finally, the cross-sectional design restricts the results in maintaining the causality between the variables. Additional longitudinal study is needed to explore the mechanism between variables.

CONCLUSION

There was a significant association between food consumption and hyperglycemia status among middle-aged adults in Indonesia. Frequent consumption of sweet desserts, SSB, salty foods, fried foods, and instant foods increased the odds (chance) to have hyperglycemia. Further research with a priori or a posteriori dietary pattern approach is highly recommended. Additional longitudinal study is needed to explore the mechanism between variables.

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DECLARATION OF INTERESTS

The authors have no conflict of interest.

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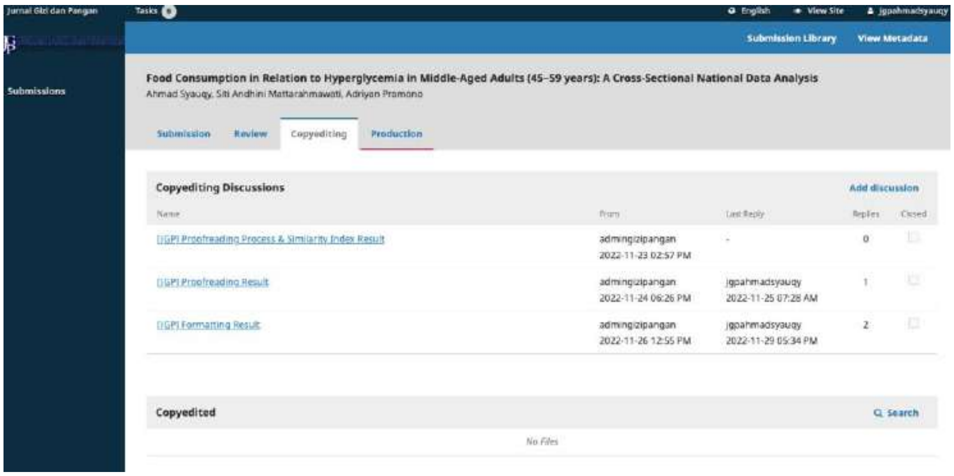

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Bersama dengan ini disampaikan bahwa naskah dengan judul ***"Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis"*** dengan penulis Ahmad Syauqy, Siti Andhini Mattarahmawati, dan Adriyan Pramono telah ditelaah oleh mitra bestari dan sudah masuk ke tahap koreksi bahasa sebelum dipublikasikan. Hal-hal yang berkaitan dengan perkembangan naskah Saudara akan kami informasikan kemudian.

Atas perhatian dan kerja samanya, kami sampaikan terima kasih.

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Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis

ABSTRACT

The study aimed to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia. This cross-sectional study utilized secondary data from the 2018 Indonesia Basic Health Survey (IBHS). A total of 8477 data met the inclusion criteria and included in this study. Fasting Blood Glucose (FBG) was analyzed in the laboratory using an enzymatic analysis. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dL) and normal (<126 mg/dL). A food frequency questionnaire was used to assess the food intake. Multiple logistic regression was used to analyze the association of food consumption and hyperglycemia. Our results found that the prevalence of hyperglycemia in this population was 43%. The mean FBG was 104.68 ± 31.99 mg/dL for male and 110.75 ± 43.92 mg/dL for female subjects. Frequent consumption of sweet desserts (OR=1.265; CI=1.132, 1.413), sugar-sweetened beverages (SSB) (OR=1.433; CI=1.263, 1.626), salty foods (OR=1.189; CI=1.079, 1.311), fried foods (OR=1.172; CI=1.033, 1.331), and instant foods (OR=1.186; CI=1.088, 1.293) were significantly associated with increased odds of hyperglycemia. There was a significant association between food consumption and hyperglycemia among middle-aged adults in Indonesia.

Keyword: diet, food consumption, hyperglycemia, fasting blood glucose, Indonesia

Runner Title: Food consumption and hyperglycemia

INTRODUCTION

Non-communicable diseases are the leading cause of public health problems in developed and developing countries (Naghavi M 2017). Diabetes, one of the non-communicable diseases, is the main cause of death in the world (Zheng *et al.* 2018). Diabetes or hyperglycemia is characterized by an increase in blood sugar levels. Previous studies found that prevalence of hyperglycemia and the components of metabolic syndrome increased rapidly with age in women and men (Wu *et al.* 2017; Jiang *et al.* 2018). Indonesia is count as fourth globally after India,

China, and America, in the number of people with diabetes (Naghavi M 2017). The prevalence of diabetes in Indonesia was around 6% (Mihardja *et al.* 2014) and based on the 2018 Indonesia Basic Health Survey (IBHS), higher prevalence of around 10% was found among middle-aged adults (MoH RI 2018).

Diabetes is caused by many factors including lifestyle (Sudargo *et al.* 2018). Sedentary lifestyle has been associated with the increasing risk for diabetes (Permatasari & Syauqy 2022). Previous study also found that diet was strongly associated with increased prevalence of diabetes (Lambrinou *et al.* 2019). Consumption of western foods or unhealthy foods is correlated with an increased prevalence of hyperglycemia and metabolic syndrome (Syauqy *et al.* 2018). Western foods or unhealthy foods are often high in simple carbohydrate, saturated fat, and sodium. In addition to increased consumption of this unhealthy food, there is also an increasing trend of inadequate consumption of vegetables and fruits which can also contribute to increase in diabetes prevalence (Syauqy *et al*. 2018; Schwingshackl *et al.* 2017).

Studies have found significant association between food consumption and metabolic syndrome among middle-aged adults in Taiwan (Syauqy *et al*. 2018). Middle-aged adults with high fruits and vegetables consumptions and lower unhealthy foods consumptions had better quality of life (Lo *et al.* 2016). However, Indonesian people tend to have high consumption of western foods and low fruits and vegetables (MoH RI 2018). However, to the best of our knowledge, study investigated the association of unhealthy foods, fruits, and vegetables intakes with diabetes among middle-aged adults in Indonesia is limited, especially using a national database that can represents the Indonesian population. Therefore, this study aimed to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia utilizing the 2018 Indonesia Basic Health Survey (IBHS)..

METHODS

Design, location, and time

This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS). The IBHS used a two-stage stratified cluster sampling method survey population includes all Indonesian households, representing 26 Provinces and utilizing a sample framework from the national socio-economic survey in March 2018 (MoH RI 2018). This study had received ethical approval from the Health Research Ethics Commission, Medical Faculty, Universitas 'Aisyiyah Yogyakarta No. 1415/KEP-UNISA/VI/2021.

Sampling

The target sample included 300,000 households from 30,000 census blocks of the national socio-economic survey framework (MoH RI 2018). The total population data of the IBHS were 713,783 people aged ≥15 years (MoH RI 2018). The inclusion criteria in this study were individuals aged 45-59 years, had complete data of foods consumption, had complete data on fasting blood glucose, and agreed and had given their written informed consent (n=8,481). While, subjects were excluded due to extreme values or missing data (n=4). Finally, a total of 8,477 subjects met the inclusion criteria and included in this study.

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Data collection

The independent variables in this study were foods consumption; while, the dependent variable was blood glucose level grouped into hyperglycemia and normal. Fasting blood glucose were measured with fingertip capillary blood tests (Accu-Chek Performa, Roche Diagnostics GmbH, Mannheim, Germany). All participants were instructed to fast overnight (8-10 hours) before blood sampling. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dL) and normal (<126 mg/dL) (Genuth *et al.* 2003; MoH RI 2018). A validated food frequency questionnaire (FFQ) was used to assess the daily food consumption. The FFQ was validated by the IBHS prior the study (MoH 2018). The FFQ includes carbonated drinks, energy drinks, sweet desserts, SSB, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods, fruits, and vegetables (MoH RI 2018). Consumption of unhealthy foods (carbonated drinks, energy drinks, sweet desserts, SSB, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods) was categorized as frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Fruits and vegetable consumption was categorized into adequate (≥5 servings per day) and inadequate (<5 servings per day) (MoH RI 2018). Sociodemographic

data (age, gender, education, and place of residence) and lifestyle (smoking status, alcohol intake, and physical activity) were obtained using a structured questionnaire. Smoking was categorized into yes and no. Consumption of alcoholic beverages was categorized into yes and no (Atamni *et al.* 2016). Gender was categorized as male and female. Education level was categorized as high (completed 12-year compulsory education or bachelor/diploma/higher education graduates) and low (not completed 12-year compulsory education). Residency was categorized as urban and rural. Physical activity was categorized as low (doing heavy physical activity for <150 minutes/week) and high (doing heavy physical activity for ≥150 minutes/week (MoH RI 2018).

Data analysis

Univariate analysis was presented using mean±standard deviation for numerical data and frequency (percentage) for categorical data. In addition, bivariate analysis was performed using independent samples t-test for continuous variables and the Chi-square test for categorical variables. Whereas, multivariate analysis using multiple logistic regression was used to analyze the association of food consumption and hyperglycemia. Odds Ratio (OR) with 95% confidence intervals was used. We used unadjusted (model 1) and adjusted (model 2). Model 2 was adjusted for demographic data (age, gender, residency) and lifestyle (smoking status, alcohol consumption, and physical activity). Adjustment for demographic data and lifestyle were done due to their potential association with hyperglycemia. All analyses were performed using the SPSS program 25 version with a *p*-value <0.05 considered statistically significant.

RESULTS AND DISCUSSION

Table 1 shows the characteristics of the subjects, the majority of the subjects with hyperglycemia were older (52.05±4.29), female (63.7), not smoking (69.8), and had low physical activity (53.3). Our results also found that the prevalence of hyperglycemia in the population was 43%. The mean FBG was 104.68±31.99 mg/dL for male and 110.75±43.92 mg/dL for female subjects. The prevalence of hyperglycemia was higher in females (44.6%) than males (40.6%). This result was in line with a previous study in the United State (ADA 2018). Women are more risk of experiencing hyperglycemia due to the hormonal changes (ADA 2018). Moreover, physical activity in women tends to be lower than in men (The Lancet Public Health 2019).

Table 1. Characteristics of the subjects.

Variables	Hyperglycemia		*P*
	Yes (n=3,648)	No (n=4,829)	
Age, mean±SD	52.05±4.29	41.27±4.24	<0.001*
Gender, n (%)			<0.001**
Male	1,323 (36.3)	1,935 (40.1)	
Female	2,325 (63.7)	2,894 (59.9)	
Education levels, n (%)			0.310**
High	1,239 (34.0)	1,691 (35.0)	
Low	2,409 (66.0)	3,138 (65.0)	
Residency, n (%)			0.188**
Rural	1,837 (50.4)	2,502 (51.8)	
Urban	1,811 (49.6)	2,325 (48.2)	
Smoking status, n (%)			<0.001**
No	2,546 (69.8)	3,195 (66.2)	
Yes	1,102 (30.2)	1,634 (33.8)	
Alcohol consumption, n (%)			0.465**
No	3,604 (98.8)	4,779 (99.0)	
Yes	44 (1.2)	50 (1.0)	
Physical activity, n (%)			0.019**
High	1,684 (46.2)	2,355 (48.8)	
Low	1,964 (53.8)	2,474 (51.2)	
Fasting blood glucose, mean±SD	130.84±52.65	91.47±5.43	<0.001*

*Comparison between continuous variables and hyperglycemia were performed using independent samples t-test

**Comparison between categorical variables and hyperglycemia were performed using Chi-square test

The association of food consumption and hyperglycemia are described in Table 2. Among subjects with hyperglycemia, 20.2%, 15.5%, 28.3%, 14.1%, 10.3%, and 48.3% frequently consumed sweet desserts, SSB, salty foods, fried foods, seasonings, and instant foods, respectively. Moreover, among subjects with hyperglycemia, 73.2% consumed inadequate amount of fruits.

Table 2. Food consumption and hyperglycemia*.

Variables	Hyperglycemia		OR	*P***
	Yes (n=3,648)	No (n=4,829)	(95% CI)	

Carbonated drinks, n (%)				
Infrequent	3,396 (93.0)	4,448 (92.2)	0.877	0.123
Frequent	254 (7.0)	379 (7.8)	(0.966, 1.343)	
Energy drinks, n (%)				
Infrequent	3,463 (94.9)	4,566 (94.6)	0.944	0.300
Frequent	187 (5.1)	261 (5.4)	(0.873, 1.284)	
Sweet desserts, n (%)				
Infrequent	2,912 (79.8)	4,021 (82.3)	1.265	<0.001
Frequent	736 (20.2)	808 (17.7)	(1.132, 1.413)	
Sugar-sweetened beverages, n (%)				
Infrequent	3,086 (84.5)	4,281 (88.7)	1.433	<0.001
Frequent	564 (15.5)	546 (11.3)	(1.263, 1.626)	
Salty foods, n (%)				
Infrequent	2,618 (71.7)	3,625 (75.1)	1.189	<0.001
Frequent	1,032 (28.3)	1,202 (24.9)	(1.079, 1.311)	
Fried foods, n (%)				
Infrequent	3,137 (85.9)	4,236 (87.8)	1.172	0.015
Frequent	513 (14.1)	591 (12.2)	(1.033, 1.331)	
Grilled foods, n (%)				
Infrequent	2,594 (71.1)	3,398 (70.4)	1.033	0.515
Frequent	1,056 (28.9)	1,429 (29.6)	(0.940, 1.135)	
Processed foods, n (%)				
Infrequent	2,936 (80.4)	3,804 (78.8)	0.905	0.069
Frequent	714 (19.6)	1,023 (21.2)	(0.813, 1.007)	
Seasonings, n (%)				
Infrequent	3,274 (89.7)	4,402 (91.2)	1.190	0.020
Frequent	376 (10.3)	425 (8.8)	(1.028, 1.377)	
Instant foods, n (%)				
Infrequent	1,889 (51.7)	2,702 (56.0)	1.186	<0.001
Frequent	1,761 (48.3)	2,125 (44.0)	(1.088, 1.293)	
Fruits, n (%)				
Adequate	976 (26.8)	1,374 (28.5)		0.042

Inadequate	2,674 (73.2)	3,453 (71.5)	1.090 (0.990, 1.200)	
Vegetable, n (%)				
Adequate	637 (17.5)	841 (17.4)	1.002	0.495
Inadequate	3,013 (82.5)	3,986 (82.6)	(0.895, 1.123)	

*Frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Adequate (≥5 servings per day) and inadequate (<5 servings per day)

**Comparison between food consumption and hyperglycemia were performed using Chi-square test

The odds ratios (95% confidence intervals) for food consumption across hyperglycemia are presented in Table 3. Frequent consumption of sweet desserts (OR=1.168; CI=1.035, 1.315), SSB (OR=1.306; CI=1.137, 1.600), salty foods (OR=1.159; CI=1.049, 1.281), fried foods (OR=1.153; CI=1.014, 1.312), seasoning (OR=1.119; CI=1.007, 1.356), and instant foods (OR=1.116; CI=1.020, 1.221) were significantly associated with increased crude odds (model 1) of hyperglycemia (R^2=2%). After adjusting for age, gender, education levels, residency, smoking status, alcohol consumption, and physical activity (model 2), frequent consumption of seasonings was not significantly associated with hyperglycemia (R^2=9%, it increased after adjusting for confounders).

Table 3. Odds ratios (95% confidence intervals) for food consumption across hyperglycemia

Variables	Model 1**			Model 2***		
	OR	95% CI	*p*	OR	95% CI	p^*
Carbonated drinks			0.122			0.419
Infrequent	1			1		
Frequent	1.066	0.889, 1.279		1.071	0.907, 1.266	
Energy drinks			0.565			0.772
Infrequent	1			1		
Frequent	0.961	0.778, 1.187		0.971	0.798, 1.182	
Sweet desserts			<0.001	1		<0.001
Infrequent	1					
Frequent	1.168	1.035, 1.315		1.135	1.005, 1.281	
Sugar-sweetened beverages			<0.001			<0.001
Infrequent	1			1		
Frequent	1.306	1.137, 1.600		1.284	1.116, 1.477	
Salty foods			<0.001			<0.001
Infrequent	1			1		
Frequent	1.159	1.049, 1.281		1.140	1.031, 1.260	
Fried foods			0.014			0.042
Infrequent	1			1		
Frequent	1.153	1.014, 1.312		1.137	1.000, 1.294	
Grilled foods			0.504			0.735
Infrequent	1			1		0.495
Frequent	0.980	0.888, 1.082		0.964	0.872, 1.065	
Processed foods			0.410			0.167
Infrequent	1			1		
Frequent	1.048	0.937, 1.173		1.079	0.969, 1.202	
Seasonings			0.040			0.052
Infrequent	1			1		
Frequent	1.119	1.007, 1.356		1.156	0.998, 1.340	
Instant foods			0.016			0.008
Infrequent	1			1		

Frequent	1.116	1.020, 1.221		1.127	1.032, 1.229	
Fruits			0.080			0.098
Adequate	1			1		
Inadequate	1.038	0.937, 1.149		1.086	0.985, 1.197	
Vegetables						
Adequate	1		0.969	1		0.883
Inadequate	0.953	0.846, 1.074		1.001	1.893, 1.123	

*Differences between food consumption and hyperglycemia were analyzed using multiple logistic regression. **Model 1 was unadjusted. ***Model 2 was adjusted for age, gender, education level, residency, smoking status, alcohol consumption, physical activity.

We found that frequent consumption of sweet desserts and SSB were significantly associated with risk of hyperglycemia. Our result was in line with another cross-sectional study where subjects with metabolic disorders also had higher intake of desserts and beverage than those without metabolic disorders (Permatasari & Syauqy 2022). Sweet desserts and SSB contained carbohydrates or simple sugars with a high Glycemic Index (GI) value, leading to accelerated increase in blood sugar levels (Medina-Remón *et al.* 2018). In addition, study also found that consuming sweetened sugary beverages decreases the endothelial cells' micro and macro cellular function (Loader *et al.* 2017). These metabolic abnormalities are due to the increased in oxidative stress and decreased in NO's (nitric oxide) bioavailability, which plays an important role in glucose metabolism. The decreased in NO bioavailability is also related to risk of developing type 2 diabetes (Loader *et al*. 2017). Added sugar intake is involved in the production of reactive oxygen species (ROS). This increases the expression of cytokines and cell adhesion molecules (Prasad & Dhar 2014).

Participants who frequently consumed salty foods were also associated with increased risk of hyperglycemia. This result is in line with a previous study (*Fitria et al.* 2016). High consumption of salty foods is correlated with an increased risk factor for DM (Fitria *et al.* 2016). High intake of sodium increases the risk of hyperglycemia through the PPAR δ/adiponectin/SGLT2 mechanism in regulating sodium and glucose homeostasis (Zhao *et al.* 2016).

We also found frequent consumption of fried foods was significantly associated with risk of hyperglycemia. Fried foods are high in saturated fat and cholesterol. A high-fat diet significantly contributes to obesity and non-insulin-dependent diabetes mellitus (Naja *et al.* 2013). Previous study found a positive relationship between high intake of saturated fat and cholesterol and increased hyperglycemia and type 2 diabetes in humans and rats (Cahill *et al.* 2014). Saturated fat in the cell membrane will decrease the viscosity of the lipid bilayer of a cell membrane and lead to a decrease in the insulin receptors (Min *et al.* 2018).

Frequent consumption of instant foods also had a significant relationship with the incidence of hyperglycemia as indicated by an increase in FBG in this study. Our results are consistent with other studies that high intake of instant foods were linked to a higher risk of developing diabetes due to the high carbohydrate and fat (Huh *et al.* 2017). An animal trial of monosodium glutamate found a significant increase in glucose levels as evidenced by an increase in HOMA-IR value in rats. It is due to the changes in insulin binding or insulin post receptors in the target tissues (Helal *et al.* 2019). Monosodium glutamate may trigger the degradation of neuronal membranes, allowing calcium ions to enter cells because of its permeability of sodium ions, calcium ions, and water. Then, it might damage the pancreatic gland and hyperglycemia (Jusuf *et al.* 2020).

In this study, individuals with inadequate consumption of fruits and vegetables had a 1.086 and 1.001 times risk for hyperglycemia than those with adequate consumption of vegetables and fruits, but these associations were not statistically significant. In contrast, other study found that higher intakes of fruits and vegetables can reduce hyperglycemia (Samaan 2017). Fiber might delay the digestion and absorption of carbohydrates and increase satiety effect. In individuals with insulin resistance, fiber can increase peripheral insulin sensitivity through short-chain fatty acids produced by fiber fermentation in the gut (Samaan 2017) . In addition, a diet high in fruits and vegetables is associated with high intake of magnesium and iron (Zhang *et al.* 2015). Magnesium is an important cofactor for several enzymes in glucose metabolism, which further plays a role in the development of diabetes (Verma & Garg 2017). Diabetes is a chronic disease. People with diabetes might change their diet, and eat more healthy food; however, it cannot change immediately the condition of the disease.

Result from bivariate analysis was in line with a previous study conducted in Indonesia (Permatasari & Syauqy 2022). Among subjects with metabolic disorders, 8.8%, 6.3%, and 21.2% frequently consumed soft drink, energy drinks, and processed meat. Moreover, among subjects with metabolic disorders, 91.9% and 88.4% consumed inadequate fruits and vegetables, respectively.

To the best of our knowledge, this study is the first study analyzing the association of food consumption with hyperglycemia among middle-aged in Indonesia. Our study used a large sample that reflected the Indonesian population. However, despite its strength this study also has several limitations. Firstly, dietary data were taken using a frequency of intake which contain no information related to the nutrients. Further research with a priori or a posteriori method is highly recommended. By using a priori or a posteriori method, researchers may derive the dietary patterns consisting of complex foods with many nutrients that represent the diet intake among population of interest. Moreover, the R^2 of logistic regression analyses in this study was relatively low; suggesting other factors outside the model can explain the incidence of hyperglycemia in middle-aged adults. Finally, the cross-sectional design restricts the results in maintaining the causality between the variables. Additional longitudinal study is needed to explore the mechanism between variables to established causality.

CONCLUSION

There was a significant association between food consumption and hyperglycemia status among middle-aged adults in Indonesia. Frequent consumption of sweet desserts, SSB, salty foods, fried foods, and instant foods are all increased the odds (chance) for hyperglycemia. Further research with a priori or a posteriori dietary pattern approach is highly recommended. Additional longitudinal study is needed to explore the mechanism between variables.

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DECLARATION OF INTERESTS

The authors have no conflict of interest.

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Settings

Dear Prof. Dr. Dodik Briawan, MCN, Editor-in-Chief,

Many thanks for the editors' suggestions and comments. We have revised the manuscript entitled "Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis" according to the editors' comments and suggestions.

If you have any questions, please feel free to call me at +6224-76402881 (email: syauqy@fk.undip.ac.id). I am looking forward to your response.

Best Regards,

Ahmad Syauqy

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Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis

ABSTRACT

The study aimed to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia. This cross-sectional study utilized secondary data from the 2018 Indonesia Basic Health Survey (IBHS). A total of 8477 subjects met the inclusion criteria and included in this study. Fasting Blood Glucose (FBG) was analyzed in the laboratory using an enzymatic analysis. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dL) and normal (<126 mg/dL). A food frequency questionnaire was used to assess the food intake. Multiple logistic regression was used to analyze the association of food consumption and hyperglycemia. Our results found that the prevalence of hyperglycemia in this population was 43%. The mean FBG was 104.68 ± 31.99 mg/dL for male and 110.75 ± 43.92 mg/dL for female subjects. Frequent consumption of sweet desserts (OR=1.265; CI=1.132, 1.413), sugar-sweetened beverages (SSB) (OR=1.433; CI=1.263, 1.626), salty foods (OR=1.189; CI=1.079, 1.311), fried foods (OR=1.172; CI=1.033, 1.331), and instant foods (OR=1.186; CI=1.088, 1.293) were significantly associated with increased odds of hyperglycemia. There was a significant association between food consumption and hyperglycemia among middle-aged adults in Indonesia.

Keyword: diet, food consumption, hyperglycemia, fasting blood glucose, Indonesia

Runner Title: Food consumption and hyperglycemia

INTRODUCTION

Non-communicable diseases are the leading cause of public health problems in developed and developing countries (Naghavi M 2017). Diabetes, one of the non-communicable diseases, is the main cause of death in the world (Zheng *et al.* 2018). Diabetes or hyperglycemia is characterized by an increase in blood sugar levels. Previous studies found that prevalence of hyperglycemia and the components of metabolic syndrome increased rapidly with age in women and men (Wu *et al.* 2017; Jiang *et al.* 2018). Indonesia is count as fourth globally after India,

China, and America, in the number of people with diabetes (Naghavi M 2017). The prevalence of diabetes in Indonesia was around 6% (Mihardja *et al.* 2014) and based on the 2018 Indonesia Basic Health Survey (IBHS), higher prevalence of around 10% was found among middle-aged adults (MoH RI 2018).

Diabetes is caused by many factors including lifestyle (Sudargo *et al.* 2018). Sedentary lifestyle has been associated with the increasing risk for diabetes (Permatasari & Syauqy 2022). Previous study also found that diet was strongly associated with increased prevalence of diabetes (Lambrinou *et al.* 2019). Consumption of western foods or unhealthy foods is correlated with an increased prevalence of hyperglycemia and metabolic syndrome (Syauqy *et al.* 2018). Western foods or unhealthy foods are often high in simple carbohydrate, saturated fat, and sodium. In addition to increased consumption of this unhealthy food, there is also an increasing trend of inadequate consumption of vegetables and fruits which can also contribute to increase in diabetes prevalence (Syauqy *et al*. 2018; Schwingshackl *et al.* 2017).

Studies have found significant association between food consumption and metabolic syndrome among middle-aged adults in Taiwan (Syauqy *et al*. 2018). Middle-aged adults with high fruits and vegetables consumptions and lower unhealthy foods consumptions had better quality of life (Lo *et al.* 2016). However, Indonesian people tend to have high consumption of western foods and low fruits and vegetables (MoH RI 2018). However, to the best of our knowledge, study investigated the association of unhealthy foods, fruits, and vegetables intakes with diabetes among middle-aged adults in Indonesia is limited, especially using a national database that can represents the Indonesian population. Therefore, this study aimed to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia utilizing the 2018 Indonesia Basic Health Survey (IBHS)..

METHODS

Design, location, and time

This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS). The IBHS used a two-stage stratified cluster sampling method survey population includes all Indonesian households, representing 26 Provinces and utilizing a sample framework from the national socio-economic survey in March 2018 (MoH RI 2018). This study had received ethical approval from the Health Research Ethics Commission, Medical Faculty, Universitas 'Aisyiyah Yogyakarta No. 1415/KEP-UNISA/VI/2021.

Sampling

The target sample included 300,000 households from 30,000 census blocks of the national socio-economic survey framework (MoH RI 2018). The total population data of the IBHS were 713,783 people aged ≥15 years (MoH RI 2018).. The inclusion criteria in this study were individuals aged 45-59 years, had complete data of foods consumption, and had complete data on fasting blood glucose (n=8,481). While, subjects were excluded due to extreme values or missing data (n=4). Finally, a total of 8,477 subjects met the inclusion criteria and included in this study.

Commented [A72]: Regarding the method, is this study utilized secondary data or the study was done in parallel with Riskesdas therefore separate consents are needed?

Thank you. This study used secondary data; therefore, the informed consent was done by Riskesdas. We consider to delete it.

Commented [A73]: Subjects OR data?

Thank you. Usually, we call it ‘Subjects’ not ‘Data’. Hence, we still use ‘subjects’.

Data collection

The independent variables in this study were foods consumption; while, the dependent variable was blood glucose level grouped into hyperglycemia and normal. Fasting blood glucose were measured with fingertip capillary blood tests (Accu-Chek Performa, Roche Diagnostics GmbH, Mannheim, Germany). All participants were instructed to fast overnight (8-10 hours) before blood sampling. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dL) and normal (<126 mg/dL) (Genuth *et al.* 2003; MoH RI 2018). A validated food frequency questionnaire (FFQ) was used to assess the daily food consumption. The FFQ was validated by the IBHS prior the study (MoH 2018). The FFQ includes carbonated drinks, energy drinks, sweet desserts, SSB, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods, fruits, and vegetables (MoH RI 2018). Consumption of unhealthy foods (carbonated drinks, energy drinks, sweet desserts, SSB, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods) was categorized as frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Fruits and vegetable consumption was categorized into adequate (≥5 servings per day) and inadequate (<5 servings per day) (MoH RI 2018). Sociodemographic

data (age, gender, education, and place of residence) and lifestyle (smoking status, alcohol intake, and physical activity) were obtained using a structured questionnaire. Smoking was categorized into yes and no. Consumption of alcoholic beverages was categorized into yes and no (Atamni *et al.* 2016). Gender was categorized as male and female. Education level was categorized as high (completed 12-year compulsory education or bachelor/diploma/higher education graduates) and low (not completed 12-year compulsory education). Residency was categorized as urban and rural. Physical activity was categorized as low (doing heavy physical activity for <150 minutes/week) and high (doing heavy physical activity for ≥150 minutes/week (MoH RI 2018).

Data analysis

Univariate analysis was presented using mean±standard deviation for numerical data and frequency (percentage) for categorical data. In addition, bivariate analysis was performed using independent samples t-test for continuous variables and the Chi-square test for categorical variables. Whereas, multivariate analysis using multiple logistic regression was used to analyze the association of food consumption and hyperglycemia. Odds Ratio (OR) with 95% confidence intervals was used. We used unadjusted (model 1) and adjusted (model 2). Model 2 was adjusted for demographic data (age, gender, residency) and lifestyle (smoking status, alcohol consumption, and physical activity). Adjustment for demographic data and lifestyle were done due to their potential association with hyperglycemia. All analyses were performed using the SPSS program 25 version with a *p*-value <0.05 considered statistically significant.

RESULTS AND DISCUSSION

Table 1 shows the characteristics of the subjects, the majority of the subjects with hyperglycemia were older (52.05±4.29), female (63.7), not smoking (69.8), and had low physical activity (53.3). Our results also found that the prevalence of hyperglycemia in the population was 43%. The mean FBG was 104.68±31.99 mg/dL for male and 110.75±43.92 mg/dL for female subjects. The prevalence of hyperglycemia was higher in females (44.6%) than males (40.6%). This result was in line with a previous study in the United State (ADA 2018). Women are more risk of experiencing hyperglycemia due to the hormonal changes (ADA 2018). Moreover, physical activity in women tends to be lower than in men (The Lancet Public Health 2019).

Table 1. Characteristics of the subjects.

Variables	Hyperglycemia		P
	Yes (n=3,648)	No (n=4,829)	
Age, mean±SD	52.05±4.29	41.27±4.24	<0.001*
Gender, n (%)			<0.001**
Male	1,323 (36.3)	1,935 (40.1)	
Female	2,325 (63.7)	2,894 (59.9)	
Education levels, n (%)			0.310**
High	1,239 (34.0)	1,691 (35.0)	
Low	2,409 (66.0)	3,138 (65.0)	
Residency, n (%)			0.188**
Rural	1,837 (50.4)	2,502 (51.8)	
Urban	1,811 (49.6)	2,325 (48.2)	
Smoking status, n (%)			<0.001**
No	2,546 (69.8)	3,195 (66.2)	
Yes	1,102 (30.2)	1,634 (33.8)	
Alcohol consumption, n (%)			0.465**
No	3,604 (98.8)	4,779 (99.0)	
Yes	44 (1.2)	50 (1.0)	
Physical activity, n (%)			0.019**
High	1,684 (46.2)	2,355 (48.8)	
Low	1,964 (53.8)	2,474 (51.2)	
Fasting blood glucose, mean±SD	130.84±52.65	91.47±5.43	<0.001*

*Comparison between continuous variables and hyperglycemia were performed using independent samples t-test

**Comparison between categorical variables and hyperglycemia were performed using Chi-square test

The association of food consumption and hyperglycemia are described in Table 2. Among subjects with hyperglycemia, 20.2%, 15.5%, 28.3%, 14.1%, 10.3%, and 48.3% frequently consumed sweet desserts, SSB, salty foods, fried foods, seasonings, and instant foods, respectively. Moreover, among subjects with hyperglycemia, 73.2% consumed inadequate amount of fruits.

Table 2. Food consumption and hyperglycemia*.

Variables	Hyperglycemia		OR	P**
	Yes (n=3,648)	No (n=4,829)	(95% CI)	

Carbonated drinks, n (%)				
Infrequent	3,396 (93.0)	4,448 (92.2)	0.877	0.123
Frequent	254 (7.0)	379 (7.8)	(0.966, 1.343)	
Energy drinks, n (%)				
Infrequent	3,463 (94.9)	4,566 (94.6)	0.944	0.300
Frequent	187 (5.1)	261 (5.4)	(0.873, 1.284)	
Sweet desserts, n (%)				
Infrequent	2,912 (79.8)	4,021 (82.3)	1.265	<0.001
Frequent	736 (20.2)	808 (17.7)	(1.132, 1.413)	
Sugar-sweetened beverages, n (%)				
Infrequent	3,086 (84.5)	4,281 (88.7)	1.433	<0.001
Frequent	564 (15.5)	546 (11.3)	(1.263, 1.626)	
Salty foods, n (%)				
Infrequent	2,618 (71.7)	3,625 (75.1)	1.189	<0.001
Frequent	1,032 (28.3)	1,202 (24.9)	(1.079, 1.311)	
Fried foods, n (%)				
Infrequent	3,137 (85.9)	4,236 (87.8)	1.172	0.015
Frequent	513 (14.1)	591 (12.2)	(1.033, 1.331)	
Grilled foods, n (%)				
Infrequent	2,594 (71.1)	3,398 (70.4)	1.033	0.515
Frequent	1,056 (28.9)	1,429 (29.6)	(0.940, 1.135)	
Processed foods, n (%)				
Infrequent	2,936 (80.4)	3,804 (78.8)	0.905	0.069
Frequent	714 (19.6)	1,023 (21.2)	(0.813, 1.007)	
Seasonings, n (%)				
Infrequent	3,274 (89.7)	4,402 (91.2)	1.190	0.020
Frequent	376 (10.3)	425 (8.8)	(1.028, 1.377)	
Instant foods, n (%)				
Infrequent	1,889 (51.7)	2,702 (56.0)	1.186	<0.001
Frequent	1,761 (48.3)	2,125 (44.0)	(1.088, 1.293)	
Fruits, n (%)				
Adequate	976 (26.8)	1,374 (28.5)		0.042

Inadequate	2,674 (73.2)	3,453 (71.5)	1.090 (0.990, 1.200)	
Vegetable, n (%)				
Adequate	637 (17.5)	841 (17.4)	1.002	0.495
Inadequate	3,013 (82.5)	3,986 (82.6)	(0.895, 1.123)	

*Frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Adequate (≥5 servings per day) and inadequate (<5 servings per day)

**Comparison between food consumption and hyperglycemia were performed using Chi-square test

The odds ratios (95% confidence intervals) for food consumption across hyperglycemia are presented in Table 3. Frequent consumption of sweet desserts (OR=1.168; CI=1.035, 1.315), SSB (OR=1.306; CI=1.137, 1.600), salty foods (OR=1.159; CI=1.049, 1.281), fried foods (OR=1.153; CI=1.014, 1.312), seasoning (OR=1.119; CI=1.007, 1.356), and instant foods (OR=1.116; CI=1.020, 1.221) were significantly associated with increased crude odds (model 1) of hyperglycemia (R^2=2%). After adjusting for age, gender, education levels, residency, smoking status, alcohol consumption, and physical activity (model 2), frequent consumption of seasonings was not significantly associated with hyperglycemia (R^2=9%, it increased after adjusting for confounders).

Table 3. Odds ratios (95% confidence intervals) for food consumption across hyperglycemia

Variables	Model 1**			Model 2***		
	OR	95% CI	*p*	OR	95% CI	*p**
Carbonated drinks			0.122			0.419
Infrequent	1			1		
Frequent	1.066	0.889, 1.279		1.071	0.907, 1.266	
Energy drinks			0.565			0.772
Infrequent	1			1		
Frequent	0.961	0.778, 1.187		0.971	0.798, 1.182	
Sweet desserts			<0.001	1		<0.001
Infrequent	1					
Frequent	1.168	1.035, 1.315		1.135	1.005, 1.281	
Sugar-sweetened beverages			<0.001			<0.001
Infrequent	1			1		
Frequent	1.306	1.137, 1.600		1.284	1.116, 1.477	
Salty foods			<0.001			<0.001
Infrequent	1			1		
Frequent	1.159	1.049, 1.281		1.140	1.031, 1.260	
Fried foods			0.014			0.042
Infrequent	1			1		
Frequent	1.153	1.014, 1.312		1.137	1.000, 1.294	
Grilled foods			0.504			0.735
Infrequent	1			1		0.495
Frequent	0.980	0.888, 1.082		0.964	0.872, 1.065	
Processed foods			0.410			0.167
Infrequent	1			1		
Frequent	1.048	0.937, 1.173		1.079	0.969, 1.202	
Seasonings			0.040			0.052
Infrequent	1			1		
Frequent	1.119	1.007, 1.356		1.156	0.998, 1.340	
Instant foods			0.016			0.008
Infrequent	1			1		

Frequent	1.116	1.020, 1.221		1.127	1.032, 1.229	
Fruits			0.080			0.098
Adequate	1			1		
Inadequate	1.038	0.937, 1.149		1.086	0.985, 1.197	
Vegetables						
Adequate	1		0.969	1		0.883
Inadequate	0.953	0.846, 1.074		1.001	1.893, 1.123	

*Differences between food consumption and hyperglycemia were analyzed using multiple logistic regression. **Model 1 was unadjusted. ***Model 2 was adjusted for age, gender, education level, residency, smoking status, alcohol consumption, physical activity.

We found that frequent consumption of sweet desserts and SSB were significantly associated with risk of hyperglycemia. Our result was in line with another cross-sectional study where subjects with metabolic disorders also had higher intake of desserts and beverage than those without metabolic disorders (Permatasari & Syauqy 2022). Sweet desserts and SSB contained carbohydrates or simple sugars with a high Glycemic Index (GI) value, leading to accelerated increase in blood sugar levels (Medina-Remón *et al.* 2018). In addition, study also found that consuming sweetened sugary beverages decreases the endothelial cells' micro and macro cellular function (Loader *et al.* 2017). These metabolic abnormalities are due to the increased in oxidative stress and decreased in NO's (nitric oxide) bioavailability, which plays an important role in glucose metabolism. The decreased in NO bioavailability is also related to risk of developing type 2 diabetes (Loader *et al*. 2017). Added sugar intake is involved in the production of reactive oxygen species (ROS). This increases the expression of cytokines and cell adhesion molecules (Prasad & Dhar 2014).

Participants who frequently consumed salty foods were also associated with increased risk of hyperglycemia. This result is in line with a previous study (*Fitria et al.* 2016). High consumption of salty foods is correlated with an increased risk factor for DM (Fitria *et al.* 2016). High intake of sodium increases the risk of hyperglycemia through the PPAR δ/adiponectin/SGLT2 mechanism in regulating sodium and glucose homeostasis (Zhao *et al.* 2016).

We also found frequent consumption of fried foods was significantly associated with risk of hyperglycemia. Fried foods are high in saturated fat and cholesterol. A high-fat diet significantly contributes to obesity and non-insulin-dependent diabetes mellitus (Naja *et al.* 2013). Previous study found a positive relationship between high intake of saturated fat and cholesterol and increased hyperglycemia and type 2 diabetes in humans and rats (Cahill *et al.* 2014). Saturated fat in the cell membrane will decrease the viscosity of the lipid bilayer of a cell membrane and lead to a decrease in the insulin receptors (Min *et al.* 2018).

Frequent consumption of instant foods also had a significant relationship with the incidence of hyperglycemia as indicated by an increase in FBG in this study. Our results are consistent with other studies that high intake of instant foods were linked to a higher risk of developing diabetes due to the high carbohydrate and fat (Huh *et al.* 2017). An animal trial of monosodium glutamate found a significant increase in glucose levels as evidenced by an increase in HOMA-IR value in rats. It is due to the changes in insulin binding or insulin post receptors in the target tissues (Helal *et al.* 2019). Monosodium glutamate may trigger the degradation of neuronal membranes, allowing calcium ions to enter cells because of its permeability of sodium ions, calcium ions, and water. Then, it might damage the pancreatic gland and hyperglycemia (Jusuf *et al.* 2020).

In this study, individuals with inadequate consumption of fruits and vegetables had a 1.086 and 1.001 times risk for hyperglycemia than those with adequate consumption of vegetables and fruits, but these associations were not statistically significant. In contrast, other study found that higher intakes of fruits and vegetables can reduce hyperglycemia (Samaan 2017). Fiber might delay the digestion and absorption of carbohydrates and increase satiety effect. In individuals with insulin resistance, fiber can increase peripheral insulin sensitivity through short-chain fatty acids produced by fiber fermentation in the gut (Samaan 2017) . In addition, a diet high in fruits and vegetables is associated with high intake of magnesium and iron (Zhang *et al.* 2015). Magnesium is an important cofactor for several enzymes in glucose metabolism, which further plays a role in the development of diabetes (Verma & Garg 2017). Diabetes is a chronic disease. People with diabetes might change their diet, and eat more healthy food; however, it cannot change immediately the condition of the disease.

Result from bivariate analysis was in line with a previous study conducted in Indonesia (Permatasari & Syauqy 2022). Among subjects with metabolic disorders, 8.8%, 6.3%, and 21.2% frequently consumed soft drink, energy drinks, and processed meat. Moreover, among subjects with metabolic disorders, 91.9% and 88.4% consumed inadequate fruits and vegetables, respectively.

To the best of our knowledge, this study is the first study analyzing the association of food consumption with hyperglycemia among middle-aged in Indonesia. Our study used a large sample that reflected the Indonesian population. However, despite its strength this study also has several limitations. Firstly, dietary data were taken using a frequency of intake which contain no information related to the nutrients. Further research with a priori or a posteriori method is highly recommended. By using a priori or a posteriori method, researchers may derive the dietary patterns consisting of complex foods with many nutrients that represent the diet intake among population of interest. Moreover, the R^2 of logistic regression analyses in this study was relatively low; suggesting other factors outside the model can explain the incidence of hyperglycemia in middle-aged adults. Finally, the cross-sectional design restricts the results in maintaining the causality between the variables. Additional longitudinal study is needed to explore the mechanism between variables to established causality.

CONCLUSION

There was a significant association between food consumption and hyperglycemia status among middle-aged adults in Indonesia. Frequent consumption of sweet desserts, SSB, salty foods, fried foods, and instant foods are all increased the odds (chance) for hyperglycemia. Further research with a priori or a posteriori dietary pattern approach is highly recommended. Additional longitudinal study is needed to explore the mechanism between variables.

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We would like to thank Faculty of Medicine (name), (university name) (registration number).

DECLARATION OF INTERESTS

The authors have no conflict of interest.

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Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45–59 years): A Cross-Sectional National Data Analysis

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ABSTRACT

The study aimed to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia. This cross-sectional study utilized secondary data from the 2018 Indonesia Basic Health Survey (IBHS). A total of 8,477 subjects met the inclusion criteria and included in this study. Fasting Blood Glucose (FBG) was analyzed in the laboratory using an enzymatic analysis. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dl) and normal (<126 mg/dl). A food frequency questionnaire was used to assess the food intake. Multiple logistic regression was used to analyze the association of food consumption and hyperglycemia. Our results found that the prevalence of hyperglycemia in this population was 43%. The mean FBG was 104.68 ± 31.99 mg/dL for male and 110.75±43.92 mg/dl for female subjects. Frequent consumption of sweet desserts (OR=1.265; CI=1.132, 1.413), Sugar-Sweetened Beverages (SSB) (OR=1.433; CI=1.263, 1.626), salty foods (OR=1.189; CI=1.079, 1.311), fried foods (OR=1.172; CI=1.033, 1.331), and instant foods (OR=1.186; CI=1.088, 1.293) were significantly associated with increased odds of hyperglycemia. There was a significant association between food consumption and hyperglycemia among middle-aged adults in Indonesia.

Keywords: diet, food consumption, hyperglycemia, fasting blood glucose, Indonesia

INTRODUCTION

Non-communicable diseases are the leading cause of public health problems in developed and developing countries (Naghavi M 2017). Diabetes, one of the non-communicable diseases, is the main cause of death in the world (Zheng *et al.* 2018). Diabetes or hyperglycemia is characterized by an increase in blood sugar levels. Previous studies found that prevalence of hyperglycemia and the components of metabolic syndrome increased rapidly with age in women and men (Wu *et al.* 2017; Jiang *et al.* 2018). Indonesia is count as fourth globally after India, China, and America, in the number of people with diabetes (Naghavi M 2017). The prevalence of diabetes in Indonesia was around 6% (Mihardja *et al.* 2014) and based on the 2018 Indonesia Basic Health Survey (IBHS), higher prevalence of around 10% was found among middle-aged adults (MoH RI 2018).

Diabetes is caused by many factors including lifestyle (Sudargo *et al.* 2018). Sedentary lifestyle has been associated with the increasing risk for diabetes (Permatasari & Syauqy 2022). Previous study also found that diet was strongly associated with increased prevalence of diabetes (Lambrinou *et al.* 2019). Consumption of western foods or unhealthy foods is correlated with an increased prevalence of hyperglycemia and metabolic syndrome (Syauqy *et al.* 2018). Western foods or unhealthy foods are often high in simple carbohydrate, saturated fat, and sodium. In addition to increased consumption of this unhealthy food, there is also an increasing trend of inadequate consumption of vegetables and fruits which can also contribute to increase in diabetes prevalence (Syauqy *et al.* 2018; Schwingshackl *et al.* 2017).

Studies have found significant association between food consumption and metabolic syndrome among middle-aged adults in Taiwan (Syauqy *et al.* 2018). Middle-aged adults with high fruits and vegetables consumptions and lower unhealthy foods consumptions had better quality of life (Lo *et al.* 2016). However, Indonesian people tend to have high consumption of western foods and low fruits and vegetables (MoH RI 2018). However, to the best of our knowledge, study investigated the association of unhealthy

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foods, fruits, and vegetables intakes with diabetes among middle-aged adults in Indonesia is limited, especially using a national database that can represents the Indonesian population. Therefore, this study aimed to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia utilizing the 2018 Indonesia Basic Health Survey (IBHS).

METHODS

Design, location, and time

This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS). The IBHS used a two-stage stratified cluster sampling method survey population includes all Indonesian households, representing 26 Provinces and utilizing a sample framework from the national socio-economic survey in March 2018 (MoH RI 2018). This study had received ethical approval from the Health Research Ethics Commission, Medical Faculty, Universitas 'Aisyiyah Yogyakarta No. 1415/KEP-UNISA/VI/2021.

Sampling

The target sample included 300,000 households from 30,000 census blocks of the national socio-economic survey framework (MoH RI 2018). The total population data of the IBHS were 713,783 people aged ≥15 years (MoH RI 2018). The inclusion criteria in this study were individuals aged 45–59 years, had complete data of foods consumption, and had complete data on fasting blood glucose (n=8,481). While, subjects were excluded due to extreme values or missing data (n=4). Finally, a total of 8,477 subjects met the inclusion criteria and included in this study.

Data collection

The independent variables in this study were foods consumption; while, the dependent variable was blood glucose level grouped into hyperglycemia and normal. Fasting blood glucose were measured with fingertip capillary blood tests (Accu-Chek Performa, Roche Diagnostics GmbH, Mannheim, Germany). All participants were instructed to fast overnight (8–10 hours) before blood sampling. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dl) and normal (<126 mg/dl) (Kahn 2003; MoH RI 2018). A validated Food Frequency Questionnaire (FFQ) was used to assess the daily food consumption. The FFQ was validated by the IBHS prior the study (MoH RI 2018). The FFQ includes carbonated drinks, energy drinks, sweet desserts, SSB, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods, fruits, and vegetables (MoH RI 2018). Consumption of unhealthy foods (carbonated drinks, energy drinks, sweet desserts, SSB, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods) was categorized as frequent (≥ 1-time per day or 1–6 times per week) and infrequent (≤3 times per month or never). Fruits and vegetable consumption was categorized into adequate (≥5 servings per day) and inadequate (<5 servings per day) (MoH RI 2018). Sociodemographic data (age, gender, education, and place of residence) and lifestyle (smoking status, alcohol intake, and physical activity) were obtained using a structured questionnaire. Smoking was categorized into yes and no. Consumption of alcoholic beverages was categorized into yes and no (Atamni *et al.* 2016). Gender was categorized as male and female. Education level was categorized as high (completed 12-year compulsory education or bachelor/diploma/higher education graduates) and low (not completed 12-year compulsory education). Residency was categorized as urban and rural. Physical activity was categorized as low (doing heavy physical activity for <150 minutes/week) and high (doing heavy physical activity for ≥150 minutes/week (MoH RI 2018)

Data analysis

Univariate analysis was presented using mean±standard deviation for numerical data and frequency (percentage) for categorical data. In addition, bivariate analysis was performed using independent samples t-test for continuous variables and the Chi-square test for categorical variables. Whereas, multivariate analysis using multiple logistic regression was used to analyze the association of food consumption and hyperglycemia. Odds Ratio (OR) with 95% confidence intervals was used. We used unadjusted (model 1) and adjusted (model 2). Model 2 was adjusted for demographic data (age, gender, residency) and lifestyle (smoking status, alcohol consumption, and physical activity). Adjustment for demographic data and lifestyle were done due to their potential association with hyperglycemia. All analyses were performed using the SPSS program 25 version with a p-value <0.05 considered statistically significant.

RESULTS AND DISCUSSION

Table 1 shows the characteristics of the subjects, the majority of the subjects with hyperglycemia were older (52.05±4.29), female (63.7), not smoking (69.8), and had low physical activity (53.3). Our results also found that the prevalence of hyperglycemia in the population was 43%. The mean FBG was 104.68±31.99 mg/dl for male and 110.75±43.92 mg/dl for female subjects. The prevalence of hyperglycemia was higher in females (44.6%) than males (40.6%). This result was in line with a previous study in the United State (ADA 2018). Women are more risk of experiencing hyperglycemia due to the hormonal changes (ADA 2018). Moreover, physical activity in women tends to be lower than in men (The Lancet Public Health 2019).

The association of food consumption and hyperglycemia are described in Table 2. Among subjects with hyperglycemia, 20.2%, 15.5%, 28.3%, 14.1%, 10.3%, and 48.3% frequently consumed sweet desserts, SSB, salty foods, fried foods, seasonings, and instant foods, respectively. Moreover, among subjects with hyperglycemia, 73.2% consumed inadequate amount of fruits.

The odds ratios (95% confidence intervals) for food consumption across hyperglycemia are presented in Table 3. Frequent consumption of sweet desserts (OR=1.168; CI=1.035, 1.315), SSB (OR=1.306; CI=1.137, 1.600), salty foods (OR=1.159; CI=1.049, 1.281), fried foods (OR=1.153; CI=1.014, 1.312), seasoning (OR=1.119; CI=1.007, 1.356), and instant foods (OR=1.116; CI=1.020, 1.221) were significantly associated with increased crude odds (model 1) of hyperglycemia (R2=2%). After adjusting for age, gender, education levels, residency, smoking status, alcohol consumption, and physical activity (model 2), frequent consumption of

Table 1. Characteristics of the subjects

Variables	Hyperglycemia		*P*
	Yes (n=3,648)	No (n=4,829)	
Age (mean±SD)	52.05±4.29	41.27±4.24	<0.001*
Gender (n%)			<0.001**
Male	1,323 (36.3)	1,935 (40.1)	
Female	2,325 (63.7)	2,894 (59.9)	
Education levels (n%)			0.310**
High	1,239 (34.0)	1,691 (35.0)	
Low	2,409 (66.0)	3,138 (65.0)	
Residency (n%)			0.188**
Rural	1,837 (50.4)	2,502 (51.8)	
Urban	1,811 (49.6)	2,325 (48.2)	
Smoking status (n%)			<0.001**
No	2,546 (69.8)	3,195 (66.2)	
Yes	1,102 (30.2)	1,634 (33.8)	
Alcohol consumption (n%)			0.465**
No	3,604 (98.8)	4,779 (99.0)	
Yes	44 (1.2)	50 (1.0)	
Physical activity (n%)			0.019**
High	1,684 (46.2)	2,355 (48.8)	
Low	1,964 (53.8)	2,474 (51.2)	
Fasting blood glucose (mean±SD)	130.84±52.65	91.47±5.43	<0.001*

*Comparison between continuous variables and hyperglycemia were performed using independent samples t-test

Table 2. Food consumption and hyperglycemia

Variables	Hyperglycemia Yes (n=3,648)	Hyperglycemia No (n=4,829)	OR (95% CI)	P
Carbonated drinks (n%)				
Infrequent	3,396 (93.0)	4,448 (92.2)	0.877	0.123
Frequent	254 (7.0)	379 (7.8)	(0.966, 1.343)	
Energy drinks (n%)				
Infrequent	3,463 (94.9)	4,566 (94.6)	0.944	0.300
Frequent	187 (5.1)	261 (5.4)	(0.873, 1.284)	
Sweet desserts (n%)				
Infrequent	2,912 (79.8)	4,021 (82.3)	1.265	<0.001
Frequent	736 (20.2)	808 (17.7)	(1.132, 1.413)	
Sugar-sweetened beverages (n%)				
Infrequent	3,086 (84.5)	4,281 (88.7)	1.433	<0.001
Frequent	564 (15.5)	546 (11.3)	(1.263, 1.626)	
Salty foods (n%)				
Infrequent	2,618 (71.7)	3,625 (75.1)	1.189	<0.001
Frequent	1,032 (28.3)	1,202 (24.9)	(1.079, 1.311)	
Fried foods (n%)				
Infrequent	3,137 (85.9)	4,236 (87.8)	1.172	0.015
Frequent	513 (14.1)	591 (12.2)	(1.033, 1.331)	
Grilled foods (n%)				
Infrequent	2,594 (71.1)	3,398 (70.4)	1.033	0.515
Frequent	1,056 (28.9)	1,429 (29.6)	(0.940, 1.135)	
Processed foods (n%)				
Infrequent	2,936 (80.4)	3,804 (78.8)	0.905	0.069
Frequent	714 (19.6)	1,023 (21.2)	(0.813, 1.007)	
Seasonings (n%)				
Infrequent	3,274 (89.7)	4,402 (91.2)	1.190	0.020
Frequent	376 (10.3)	425 (8.8)	(1.028, 1.377)	
Instant foods (n%)				
Infrequent	1,889 (51.7)	2,702 (56.0)	1.186	<0.001
Frequent	1,761 (48.3)	2,125 (44.0)	(1.088, 1.293)	
Fruits (n%)				
Adequate	976 (26.8)	1,374 (28.5)	1.090	0.042
Inadequate	2,674 (73.2)	3,453 (71.5)	(0.990, 1.200)	
Vegetable (n%)				
Adequate	637 (17.5)	841 (17.4)	1.002	0.495
Inadequate	3,013 (82.5)	3,986 (82.6)	(0.895, 1.123)	

*Frequent (≥ 1-time per day or 1–6 times per week) and infrequent (≤3 times per month or never); Adequate (≥5 servings per day) and inadequate (<5 servings per day)

**Comparison between food consumption and hyperglycemia were performed using Chi-square test

seasonings was not significantly associated with hyperglycemia (R2=9%, it increased after adjusting for confounders).

We found that frequent consumption of sweet desserts and SSB were significantly associated with risk of hyperglycemia. Our result was in line with another cross-sectional study where subjects with metabolic disorders also had higher intake of desserts and beverage than those without metabolic disorders (Permatasari

Table 3. **Odds** ratios **(95% confidence intervals) for food consumption across hyperglycemia**

Variables	Model 1**			Model 2***		
	OR	95% CI	*p*	OR	95% CI	*p**
Carbonated drinks			0.122			0.419
Infrequent	1			1		
Frequent	1.066	0.889, 1.279		1.071	0.907, 1.266	
Energy drinks			0.565			0.772
Infrequent	1			1		
Frequent	0.961	0.778, 1.187		0.971	0.798, 1.182	
Sweet desserts			<0.001	1		<0.001
Infrequent	1					
Frequent	1.168	1.035, 1.315		1.135	1.005, 1.281	
Sugar-sweetened beverages			<0.001			<0.001
Infrequent	1			1		
Frequent	1.306	1.137, 1.600		1.284	1.116, 1.477	
Salty foods			<0.001			<0.001
Infrequent	1			1		
Frequent	1.159	1.049, 1.281		1.140	1.031, 1.260	
Fried foods			0.014			0.042
Infrequent	1			1		
Frequent	1.153	1.014, 1.312		1.137	1.000, 1.294	
Grilled foods			0.504			0.735
Infrequent	1			1		
Frequent	0.980	0.888, 1.082		0.964	0.872, 1.065	
Processed foods			0.410			0.495
Infrequent	1			1		
Frequent	1.048	0.937, 1.173		1.079	0.969, 1.202	
Seasonings			0.040			0.167
Infrequent	1			1		
Frequent	1.119	1.007, 1.356		1.156	0.998, 1.340	
Instant foods			0.016			0.052
Infrequent	1			1		
Frequent	1.116	1.020, 1.221		1.127	1.032, 1.229	
Fruits			0.080			0.008
Adequate	1			1		
Inadequate	1.038	0.937, 1.149		1.086	0.985, 1.197	
Vegetable			0.969			0.098
Adequate	1			1		
Inadequate	0.953	0.846, 1.074		1.001	1.893, 1.123	0.883

*Differences between food consumption and hyperglycemia were analyzed using multiple logistic regression

**Model 1 was unadjusted.

***Model 2 was adjusted for age, gender, education level, residency, smoking status, alcohol consumption, physical activity.

& Syauqy 2022). Sweet desserts and SSB contained carbohydrates or simple sugars with a high Glycemic Index (GI) value, leading to accelerated increase in blood sugar levels (Medina-Remón *et al.* 2018). In addition, study also found that consuming sweetened sugary beverages decreases the endothelial cells' micro and macro cellular function (Loader *et al.* 2017). These metabolic abnormalities are due to the increased in oxidative stress and decreased in

NO's (nitric oxide) bioavailability, which plays an important role in glucose metabolism. The decreased in NO bioavailability is also related to risk of developing type 2 diabetes (Loader *et al.* 2017). Added sugar intake is involved in the production of reactive oxygen species (ROS). This increases the expression of cytokines and cell adhesion molecules (Prasad & Dhar 2014).

Participants who frequently consumed salty foods were also associated with increased risk of hyperglycemia. This result is in line with a previous study (Nur *et al.* 2016). High consumption of salty foods is correlated with an increased risk factor for DM (Nur *et al.* 2016). High intake of sodium increases the risk of hyperglycemia through the PPAR δ/adiponectin/ SGLT2 mechanism in regulating sodium and glucose homeostasis (Zhao *et al.* 2016).

We also found frequent consumption of fried foods was significantly associated with risk of hyperglycemia. Fried foods are high in saturated fat and cholesterol. A high-fat diet significantly contributes to obesity and non-insulin-dependent diabetes mellitus (Naja *et al.* 2013). Previous study found a positive relationship between high intake of saturated fat and cholesterol and increased hyperglycemia and type 2 diabetes in humans and rats (Cahill *et al.* 2014). Saturated fat in the cell membrane will decrease the viscosity of the lipid bilayer of a cell membrane and lead to a decrease in the insulin receptors (Min *et al.* 2018).

Frequent consumption of instant foods also had a significant relationship with the incidence of hyperglycemia as indicated by an increase in FBG in this study. Our results are consistent with other studies that high intake of instant foods were linked to a higher risk of developing diabetes due to the high carbohydrate and fat (Huh *et al.* 2017). An animal trial of monosodium glutamate found a significant increase in glucose levels as evidenced by an increase in HOMA-IR value in rats. It is due to the changes in insulin binding or insulin post receptors in the target tissues (Helal *et al.* 2019). Monosodium glutamate may trigger the degradation of neuronal membranes, allowing calcium ions to enter cells because of its permeability of sodium ions, calcium ions, and water. Then, it might damage the pancreatic gland and hyperglycemia (Jusuf *et al.* 2020).

In this study, individuals with inadequate consumption of fruits and vegetables had a 1.086 and 1.001 times risk for hyperglycemia than those with adequate consumption of vegetables and fruits, but these associations were not statistically significant. In contrast, other study found that higher intakes of fruits and vegetables can reduce hyperglycemia (Samaan 2017). Fiber might delay the digestion and absorption of carbohydrates and increase satiety effect. In individuals with insulin resistance, fiber can increase peripheral insulin sensitivity through short-chain fatty acids produced by fiber fermentation in the gut (Samaan 2017) . In addition, a diet high in fruits and vegetables is associated with high intake of magnesium and iron (Zhang *et al.* 2015). Magnesium is an important cofactor for several enzymes in glucose metabolism, which further plays a role in the development of diabetes (Verma & Garg 2017). Diabetes is a chronic disease. People with diabetes might change their diet, and eat more healthy food; however, it cannot change immediately the condition of the disease.

Result from bivariate analysis was in line with a previous study conducted in Indonesia (Permatasari & Syauqy 2022). Among subjects with metabolic disorders, 8.8%, 6.3%, and 21.2% frequently consumed soft drink, energy drinks, and processed meat. Moreover, among subjects with metabolic disorders, 91.9% and 88.4% consumed inadequate fruits and vegetables, respectively.

To the best of our knowledge, this study is the first study analyzing the association of food consumption with hyperglycemia among middle-aged in Indonesia. Our study used a large sample that reflected the Indonesian population. However, despite its strength this study also has several limitations. Firstly, dietary data were taken using a frequency of intake which contain no information related to the nutrients. Further research with a priori or a posteriori method is highly recommended. By using a priori or a posteriori method, researchers may derive the dietary patterns consisting of complex foods with many nutrients that represent the diet intake among population of interest. Moreover, the R2 of logistic regression analyses in this study was relatively low; suggesting other factors outside the model can explain the incidence of hyperglycemia in middle-aged adults. Finally, the cross-sectional design restricts the results in maintaining the causality between the variables. Additional longitudinal study is needed to explore the mechanism between variables to established causality.

CONCLUSION

There was a significant association between food consumption and hyperglycemia status among middle-aged adults in Indonesia. Frequent consumption of sweet desserts, SSB, salty foods, fried foods, and instant foods are all increased the odds (chance) for hyperglycemia. Further research with a priori or a posteriori dietary pattern approach is highly recommended. Additional longitudinal study is needed to explore the mechanism between variables.

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DECLARATION OF INTERESTS

The authors have no conflict of interest.

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Settings

Dear Prof. Dr. Dodik Briawan, MCN, Editor-in-Chief,

Many thanks. Please refers to the manuscript entitled “Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis” in the attachment. We already deleted some sentences (using strikethrough text).

If you have any questions, please feel free to call me at +6224-76402881 (email: syauqy@fk.undip.ac.id). I am looking forward to your response.

Best Regards,

Ahmad Syauqy

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Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45–59 years): A Cross-Sectional National Data Analysis

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ABSTRACT

The study aimed to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia. This cross-sectional study utilized secondary data from the 2018 Indonesia Basic Health Survey (IBHS). A total of 8,477 subjects met the inclusion criteria and included in this study. Fasting Blood Glucose (FBG) was analyzed in the laboratory using an enzymatic analysis. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dl) and normal (<126 mg/dl). A food frequency questionnaire was used to assess the food intake. Multiple logistic regression was used to analyze the association of food consumption and hyperglycemia. Our results found that the prevalence of hyperglycemia in this population was 43%. The mean FBG was 104.68 ± 31.99 mg/dL for male and 110.75±43.92 mg/dl for female subjects. Frequent consumption of sweet desserts (OR=1.265; CI=1.132, 1.413), Sugar-Sweetened Beverages (SSB) (OR=1.433; CI=1.263, 1.626), salty foods (OR=1.189; CI=1.079, 1.311), fried foods (OR=1.172; CI=1.033, 1.331), and instant foods (OR=1.186; CI=1.088, 1.293) were significantly associated with increased odds of hyperglycemia. There was a significant association between food consumption and hyperglycemia among middle-aged adults in Indonesia.

Keywords: diet, food consumption, hyperglycemia, fasting blood glucose, Indonesia

INTRODUCTION

Non-communicable diseases are the leading cause of public health problems in developed and developing countries (Naghavi M 2017). Diabetes, one of the non-communicable diseases, is the main cause of death in the world (Zheng *et al.* 2018). Diabetes or hyperglycemia is characterized by an increase in blood sugar levels. Previous studies found that prevalence of hyperglycemia and the components of metabolic syndrome increased rapidly with age in women and men (Wu *et al.* 2017; Jiang *et al.* 2018). Indonesia is count as fourth globally after India, China, and America, in the number of people with diabetes (Naghavi M 2017). The prevalence of diabetes in Indonesia was around 6% (Mihardja *et al.* 2014) and based on the 2018 Indonesia Basic Health Survey (IBHS), higher prevalence of around 10% was found among middle-aged adults (MoH RI 2018).

Diabetes is caused by many factors including lifestyle (Sudargo *et al.* 2018). Sedentary lifestyle has been associated with the increasing risk for diabetes (Permatasari & Syauqy 2022). Previous study also found that diet was strongly associated with increased prevalence of diabetes (Lambrinou *et al.* 2019). Consumption of western foods or unhealthy foods is correlated with an increased prevalence of hyperglycemia and metabolic syndrome (Syauqy *et al.* 2018). Western foods or unhealthy foods are often high in simple carbohydrate, saturated fat, and sodium. In addition to increased consumption of this unhealthy food, there is also an increasing trend of inadequate consumption of vegetables and fruits which can also contribute to increase in diabetes prevalence (Syauqy *et al.* 2018; Schwingshackl *et al.* 2017).

Studies have found significant association between food consumption and metabolic syndrome among middle-aged adults in Taiwan (Syauqy *et al.* 2018). Middle-aged adults with high fruits and vegetables consumptions and lower unhealthy foods consumptions had better quality of life (Lo *et al.* 2016). However, Indonesian people tend to have high consumption of western foods and low fruits and vegetables (MoH RI 2018). However, to the best of our knowledge, study investigated the association of unhealthy

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foods, fruits, and vegetables intakes with diabetes among middle-aged adults in Indonesia is limited, especially using a national database that can represents the Indonesian population. Therefore, this study aimed to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia utilizing the 2018 Indonesia Basic Health Survey (IBHS).

METHODS

Design, location, and time

This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS). The IBHS used a two-stage stratified cluster sampling method survey population includes all Indonesian households, representing 26 Provinces and utilizing a sample framework from the national socio-economic survey in March 2018 (MoH RI 2018). This study had received ethical approval from the Health Research Ethics Commission, Medical Faculty, Universitas 'Aisyiyah Yogyakarta No. 1415/KEP-UNISA/VI/2021.

Sampling

The target sample included 300,000 households from 30,000 census blocks of the national socio-economic survey framework (MoH RI 2018). The total population data of the IBHS were 713,783 people aged ≥15 years (MoH RI 2018). The inclusion criteria in this study were individuals aged 45–59 years, had complete data of foods consumption, and had complete data on fasting blood glucose (n=8,481). While, subjects were excluded due to extreme values or missing data (n=4). Finally, a total of 8,477 subjects met the inclusion criteria and included in this study.

Data collection

The independent variables in this study were foods consumption; while, the dependent variable was blood glucose level grouped into hyperglycemia and normal. Fasting blood glucose were measured with fingertip capillary blood tests (Accu-Chek Performa, Roche Diagnostics GmbH, Mannheim, Germany). All participants were instructed to fast overnight (8–10 hours) before blood sampling. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dl) and normal (<126 mg/dl) (Kahn 2003; MoH RI 2018). A validated Food Frequency Questionnaire (FFQ) was used to assess the daily food consumption. The FFQ was validated by the IBHS prior the study (MoH RI 2018). The FFQ includes carbonated drinks, energy drinks, sweet desserts, SSB, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods, fruits, and vegetables (MoH RI 2018). Consumption of unhealthy foods (carbonated drinks, energy drinks, sweet desserts, SSB, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods) was categorized as frequent (≥ 1-time per day or 1–6 times per week) and infrequent (≤3 times per month or never). Fruits and vegetable consumption was categorized into adequate (≥5 servings per day) and inadequate (<5 servings per day) (MoH RI 2018). Sociodemographic data (age, gender, education, and place of residence) and lifestyle (smoking status, alcohol intake, and physical activity) were obtained using a structured questionnaire. Smoking was categorized into yes and no. Consumption of alcoholic beverages was categorized into yes and no (Atamni *et al.* 2016). Gender was categorized as male and female. Education level was categorized as high (completed 12-year compulsory education or bachelor/diploma/higher education graduates) and low (not completed 12-year compulsory education). Residency was categorized as urban and rural. Physical activity was categorized as low (doing heavy physical activity for <150 minutes/week) and high (doing heavy physical activity for ≥150 minutes/week (MoH RI 2018)

Data analysis

Univariate analysis was presented using mean±standard deviation for numerical data and frequency (percentage) for categorical data. In addition, bivariate analysis was performed using independent samples t-test for continuous variables and the Chi-square test for categorical variables. Whereas, multivariate analysis using multiple logistic regression was used to analyze the association of food consumption and hyperglycemia. Odds Ratio (OR) with 95% confidence intervals was used. We used unadjusted (model 1) and adjusted (model 2). Model 2 was adjusted for demographic data (age, gender, residency) and lifestyle (smoking status, alcohol consumption, and physical activity). Adjustment for demographic data and lifestyle were done due to their potential association with hyperglycemia. All analyses were performed using the SPSS program 25 version with a p-value <0.05 considered statistically significant.

RESULTS AND DISCUSSION

Table 1 shows the characteristics of the subjects, the majority of the subjects with hyperglycemia were older (52.05±4.29), female (63.7), not smoking (69.8), and had low physical activity (53.3). Our results also found that the prevalence of hyperglycemia in the population was 43%. The mean FBG was 104.68±31.99 mg/dl for male and 110.75±43.92 mg/dl for female subjects. The prevalence of hyperglycemia was higher in females (44.6%) than males (40.6%). ~~This result was in line with a previous study in the United State (ADA 2018). Women are more risk of experiencing hyperglycemia due to the hormonal changes (ADA 2018). Moreover, physical activity in women tends to be lower than in men (The Lancet Public Health 2019).~~

The association of food consumption and hyperglycemia are described in Table 2. Among subjects with hyperglycemia, 20.2%, 15.5%, 28.3%, 14.1%, 10.3%, and 48.3% frequently consumed sweet desserts, SSB, salty foods, fried foods, seasonings, and instant foods, respectively. Moreover, among subjects with hyperglycemia, 73.2% consumed inadequate amount of fruits.

The odds ratios (95% confidence intervals) for food consumption across hyperglycemia are presented in Table 3. Frequent consumption of sweet desserts (OR=1.168; CI=1.035, 1.315), SSB (OR=1.306; CI=1.137, 1.600), salty foods (OR=1.159; CI=1.049, 1.281), fried foods (OR=1.153; CI=1.014, 1.312), seasoning (OR=1.119; CI=1.007, 1.356), and instant foods (OR=1.116; CI=1.020, 1.221) were significantly associated with increased crude odds (model 1) of hyperglycemia (R2=2%). After adjusting for age, gender, education levels, residency, smoking status, alcohol consumption, and physical activity (model 2), frequent consumption of

Table 1. Characteristics of the subjects

Variables	Hyperglycemia: Yes (n=3,648)	Hyperglycemia: No (n=4,829)	*P*
Age (mean±SD)	52.05±4.29	41.27±4.24	<0.001*
Gender (n%)			<0.001**
Male	1,323 (36.3)	1,935 (40.1)	
Female	2,325 (63.7)	2,894 (59.9)	
Education levels (n%)			0.310**
High	1,239 (34.0)	1,691 (35.0)	
Low	2,409 (66.0)	3,138 (65.0)	
Residency (n%)			0.188**
Rural	1,837 (50.4)	2,502 (51.8)	
Urban	1,811 (49.6)	2,325 (48.2)	
Smoking status (n%)			<0.001**
No	2,546 (69.8)	3,195 (66.2)	
Yes	1,102 (30.2)	1,634 (33.8)	
Alcohol consumption (n%)			0.465**
No	3,604 (98.8)	4,779 (99.0)	
Yes	44 (1.2)	50 (1.0)	
Physical activity (n%)			0.019**
High	1,684 (46.2)	2,355 (48.8)	
Low	1,964 (53.8)	2,474 (51.2)	
Fasting blood glucose (mean±SD)	130.84±52.65	91.47±5.43	<0.001*

*Comparison between continuous variables and hyperglycemia were performed using independent samples t-test

Table 2. Food consumption and hyperglycemia

Variables	Hyperglycemia		OR (95% CI)	P
	Yes (n=3,648)	No (n=4,829)		
Carbonated drinks (n%)				
Infrequent	3,396 (93.0)	4,448 (92.2)	0.877	0.123
Frequent	254 (7.0)	379 (7.8)	(0.966, 1.343)	
Energy drinks (n%)				
Infrequent	3,463 (94.9)	4,566 (94.6)	0.944	0.300
Frequent	187 (5.1)	261 (5.4)	(0.873, 1.284)	
Sweet desserts (n%)				
Infrequent	2,912 (79.8)	4,021 (82.3)	1.265	<0.001
Frequent	736 (20.2)	808 (17.7)	(1.132, 1.413)	
Sugar-sweetened beverages (n%)				
Infrequent	3,086 (84.5)	4,281 (88.7)	1.433	<0.001
Frequent	564 (15.5)	546 (11.3)	(1.263, 1.626)	
Salty foods (n%)				
Infrequent	2,618 (71.7)	3,625 (75.1)	1.189	<0.001
Frequent	1,032 (28.3)	1,202 (24.9)	(1.079, 1.311)	
Fried foods (n%)				
Infrequent	3,137 (85.9)	4,236 (87.8)	1.172	0.015
Frequent	513 (14.1)	591 (12.2)	(1.033, 1.331)	
Grilled foods (n%)				
Infrequent	2,594 (71.1)	3,398 (70.4)	1.033	0.515
Frequent	1,056 (28.9)	1,429 (29.6)	(0.940, 1.135)	
Processed foods (n%)				
Infrequent	2,936 (80.4)	3,804 (78.8)	0.905	0.069
Frequent	714 (19.6)	1,023 (21.2)	(0.813, 1.007)	
Seasonings (n%)				
Infrequent	3,274 (89.7)	4,402 (91.2)	1.190	0.020
Frequent	376 (10.3)	425 (8.8)	(1.028, 1.377)	
Instant foods (n%)				
Infrequent	1,889 (51.7)	2,702 (56.0)	1.186	<0.001
Frequent	1,761 (48.3)	2,125 (44.0)	(1.088, 1.293)	
Fruits (n%)				
Adequate	976 (26.8)	1,374 (28.5)	1.090	0.042
Inadequate	2,674 (73.2)	3,453 (71.5)	(0.990, 1.200)	
Vegetable (n%)				
Adequate	637 (17.5)	841 (17.4)	1.002	0.495
Inadequate	3,013 (82.5)	3,986 (82.6)	(0.895, 1.123)	

*Frequent (≥ 1-time per day or 1–6 times per week) and infrequent (≤3 times per month or never); Adequate (≥5 servings per day) and inadequate (<5 servings per day)

**Comparison between food consumption and hyperglycemia were performed using Chi-square test

seasonings was not significantly associated with hyperglycemia (R2=9%, it increased after adjusting for confounders).

We found that frequent consumption of sweet desserts and SSB were significantly associated with risk of hyperglycemia. Our result was in line with another cross-sectional study where subjects with metabolic disorders also had higher intake of desserts and beverage than those without metabolic disorders (Permatasari

Table 3. Odds ratios (95% confidence intervals) for food consumption across hyperglycemia

Variables	Model 1**			Model 2***		
	OR	95% CI	*p*	OR	95% CI	*p**
Carbonated drinks			0.122			0.419
Infrequent	1			1		
Frequent	1.066	0.889, 1.279		1.071	0.907, 1.266	
Energy drinks			0.565			0.772
Infrequent	1			1		
Frequent	0.961	0.778, 1.187		0.971	0.798, 1.182	
Sweet desserts			<0.001	1		<0.001
Infrequent	1					
Frequent	1.168	1.035, 1.315		1.135	1.005, 1.281	
Sugar-sweetened beverages			<0.001			<0.001
Infrequent	1			1		
Frequent	1.306	1.137, 1.600		1.284	1.116, 1.477	
Salty foods			<0.001			<0.001
Infrequent	1			1		
Frequent	1.159	1.049, 1.281		1.140	1.031, 1.260	
Fried foods			0.014			0.042
Infrequent	1			1		
Frequent	1.153	1.014, 1.312		1.137	1.000, 1.294	
Grilled foods			0.504			0.735
Infrequent	1			1		
Frequent	0.980	0.888, 1.082		0.964	0.872, 1.065	
Processed foods			0.410			0.495
Infrequent	1			1		
Frequent	1.048	0.937, 1.173		1.079	0.969, 1.202	
Seasonings			0.040			0.167
Infrequent	1			1		
Frequent	1.119	1.007, 1.356		1.156	0.998, 1.340	
Instant foods			0.016			0.052
Infrequent	1			1		
Frequent	1.116	1.020, 1.221		1.127	1.032, 1.229	
Fruits			0.080			0.008
Adequate	1			1		
Inadequate	1.038	0.937, 1.149		1.086	0.985, 1.197	
Vegetable			0.969			0.098
Adequate	1			1		
Inadequate	0.953	0.846, 1.074		1.001	1.893, 1.123	0.883

*Differences between food consumption and hyperglycemia were analyzed using multiple logistic regression

**Model 1 was unadjusted.

***Model 2 was adjusted for age, gender, education level, residency, smoking status, alcohol consumption, physical activity.

& Syauqy 2022). Sweet desserts and SSB contained carbohydrates or simple sugars with a high Glycemic Index (GI) value, leading to accelerated increase in blood sugar levels (Medina-Remón *et al.* 2018). In addition, study also found that consuming sweetened sugary beverages decreases the endothelial cells' micro and macro cellular function (Loader *et al.* 2017). These metabolic abnormalities are due to the increased in oxidative stress and decreased in

NO's (nitric oxide) bioavailability, which plays an important role in glucose metabolism. The decreased in NO bioavailability is also related to risk of developing type 2 diabetes (Loader *et al.* 2017). Added sugar intake is involved in the production of reactive oxygen species (ROS). This increases the expression of cytokines and cell adhesion molecules (Prasad & Dhar 2014).

Participants who frequently consumed salty foods were also associated with increased risk of hyperglycemia. This result is in line with a previous study (Nur *et al.* 2016). High consumption of salty foods is correlated with an increased risk factor for DM (Nur *et al.* 2016). High intake of sodium increases the risk of hyperglycemia through the PPAR δ/adiponectin/ SGLT2 mechanism in regulating sodium and glucose homeostasis (Zhao *et al.* 2016).

We also found frequent consumption of fried foods was significantly associated with risk of hyperglycemia. Fried foods are high in saturated fat and cholesterol. A high-fat diet significantly contributes to obesity and non-insulin-dependent diabetes mellitus (Naja *et al.* 2013). Previous study found a positive relationship between high intake of saturated fat and cholesterol and increased hyperglycemia and type 2 diabetes in humans and rats (Cahill *et al.* 2014). Saturated fat in the cell membrane will decrease the viscosity of the lipid bilayer of a cell membrane and lead to a decrease in the insulin receptors (Min *et al.* 2018).

Frequent consumption of instant foods also had a significant relationship with the incidence of hyperglycemia as indicated by an increase in FBG in this study. Our results are consistent with other studies that high intake of instant foods were linked to a higher risk of developing diabetes due to the high carbohydrate and fat (Huh *et al.* 2017). An animal trial of monosodium glutamate found a significant increase in glucose levels as evidenced by an increase in HOMA-IR value in rats. It is due to the changes in insulin binding or insulin post receptors in the target tissues (Helal *et al.* 2019). Monosodium glutamate may trigger the degradation of neuronal membranes, allowing calcium ions to enter cells because of its permeability of sodium ions, calcium ions, and water. Then, it might damage the pancreatic gland and hyperglycemia (Jusuf *et al.* 2020).

In this study, individuals with inadequate consumption of fruits and vegetables had a 1.086 and 1.001 times risk for hyperglycemia than those with adequate consumption of vegetables and fruits, but these associations were not statistically significant. In contrast, other study found that higher intakes of fruits and vegetables can reduce hyperglycemia (Samaan 2017). Fiber might delay the digestion and absorption of carbohydrates and increase satiety effect. In individuals with insulin resistance, fiber can increase peripheral insulin sensitivity through short-chain fatty acids produced by fiber fermentation in the gut (Samaan 2017) . In addition, a diet high in fruits and vegetables is associated with high intake of magnesium and iron (Zhang *et al.* 2015). Magnesium is an important cofactor for several enzymes in glucose metabolism, which further plays a role in the development of diabetes (Verma & Garg 2017). Diabetes is a chronic disease. People with diabetes might change their diet, and eat more healthy food; however, it cannot change immediately the condition of the disease.

Result from bivariate analysis was in line with a previous study conducted in Indonesia (Permatasari & Syauqy 2022). Among subjects with metabolic disorders, 8.8%, 6.3%, and 21.2% frequently consumed soft drink, energy drinks, and processed meat. Moreover, among subjects with metabolic disorders, 91.9% and 88.4% consumed inadequate fruits and vegetables, respectively.

To the best of our knowledge, this study is the first study analyzing the association of food consumption with hyperglycemia among middle-aged in Indonesia. Our study used a large sample that reflected the Indonesian population. However, despite its strength this study also has several limitations. Firstly, dietary data were taken using a frequency of intake which contain no information related to the nutrients. Further research with a priori or a posteriori method is highly recommended. By using a priori or a posteriori method, researchers may derive the dietary patterns consisting of complex foods with many nutrients that represent the diet intake among population of interest. Moreover, the R2 of logistic regression analyses in this study was relatively low; suggesting other factors outside the model can explain the incidence of hyperglycemia in middle-aged adults. Finally, the cross-sectional design restricts the results in maintaining the causality between the variables. Additional longitudinal study is needed to explore the mechanism between variables to established causality.

CONCLUSION

There was a significant association between food consumption and hyperglycemia status among middle-aged adults in Indonesia. Frequent consumption of sweet desserts, SSB, salty foods, fried foods, and instant foods are all increased the odds (chance) for hyperglycemia. Further research with a priori or a posteriori dietary pattern approach is highly recommended. Additional longitudinal study is needed to explore the mechanism between variables.

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DECLARATION OF INTERESTS

The authors have no conflict of interest.

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HASIL PERBAIKAN FORMAT (II)

Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45-59 years): A Cross-Sectional National Data Analysis

ABSTRACT

The study aimed to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia. This cross-sectional study utilized secondary data from the 2018 Indonesia Basic Health Survey (IBHS). A total of 8477 subjects met the inclusion criteria and included in this study. Fasting Blood Glucose (FBG) was analyzed in the laboratory using an enzymatic analysis. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dL) and normal (<126 mg/dL). A food frequency questionnaire was used to assess the food intake. Multiple logistic regression was used to analyze the association of food consumption and hyperglycemia. Our results found that the prevalence of hyperglycemia in this population was 43%. The mean FBG was 104.68 ± 31.99 mg/dL for male and 110.75 ± 43.92 mg/dL for female subjects. Frequent consumption of sweet desserts (OR=1.265; CI=1.132, 1.413), sugar-sweetened beverages (SSB) (OR=1.433; CI=1.263, 1.626), salty foods (OR=1.189; CI=1.079, 1.311), fried foods (OR=1.172; CI=1.033, 1.331), and instant foods (OR=1.186; CI=1.088, 1.293) were significantly associated with increased odds of hyperglycemia. There was a significant association between food consumption and hyperglycemia among middle-aged adults in Indonesia.

Keyword: diet, food consumption, hyperglycemia, fasting blood glucose, Indonesia

Runner Title: Food consumption and hyperglycemia

INTRODUCTION

Non-communicable diseases are the leading cause of public health problems in developed and developing countries (Naghavi M 2017). Diabetes, one of the non-communicable diseases, is the main cause of death in the world (Zheng *et al.* 2018). Diabetes or hyperglycemia is characterized by an increase in blood sugar levels. Previous studies found that prevalence of hyperglycemia and the components of metabolic syndrome increased rapidly with age in women and men (Wu *et al.* 2017; Jiang *et al.* 2018). Indonesia is count as fourth globally after India,

China, and America, in the number of people with diabetes (Naghavi M 2017). The prevalence of diabetes in Indonesia was around 6% (Mihardja *et al.* 2014) and based on the 2018 Indonesia Basic Health Survey (IBHS), higher prevalence of around 10% was found among middle-aged adults (MoH RI 2018).

Diabetes is caused by many factors including lifestyle (Sudargo *et al.* 2018). Sedentary lifestyle has been associated with the increasing risk for diabetes (Permatasari & Syauqy 2022). Previous study also found that diet was strongly associated with increased prevalence of diabetes (Lambrinou *et al.* 2019). Consumption of western foods or unhealthy foods is correlated with an increased prevalence of hyperglycemia and metabolic syndrome (Syauqy *et al.* 2018). Western foods or unhealthy foods are often high in simple carbohydrate, saturated fat, and sodium. In addition to increased consumption of this unhealthy food, there is also an increasing trend of inadequate consumption of vegetables and fruits which can also contribute to increase in diabetes prevalence (Syauqy *et al*. 2018; Schwingshackl *et al.* 2017).

Studies have found significant association between food consumption and metabolic syndrome among middle-aged adults in Taiwan (Syauqy *et al*. 2018). Middle-aged adults with high fruits and vegetables consumptions and lower unhealthy foods consumptions had better quality of life (Lo *et al.* 2016). However, Indonesian people tend to have high consumption of western foods and low fruits and vegetables (MoH RI 2018). However, to the best of our knowledge, study investigated the association of unhealthy foods, fruits, and vegetables intakes with diabetes among middle-aged adults in Indonesia is limited, especially using a national database that can represents the Indonesian population. Therefore, this study aimed to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia utilizing the 2018 Indonesia Basic Health Survey (IBHS)..

METHODS

Design, location, and time

This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS). The IBHS used a two-stage stratified cluster sampling method survey population includes all Indonesian households, representing 26 Provinces and utilizing a sample framework from the national socio-economic survey in March 2018 (MoH RI 2018). This study had received ethical approval from the Health Research Ethics Commission, Medical Faculty, Universitas 'Aisyiyah Yogyakarta No. 1415/KEP-UNISA/VI/2021.

Sampling

The target sample included 300,000 households from 30,000 census blocks of the national socio-economic survey framework (MoH RI 2018). The total population data of the IBHS were 713,783 people aged ≥15 years (MoH RI 2018).. The inclusion criteria in this study were individuals aged 45-59 years, had complete data of foods consumption, and had complete data on fasting blood glucose (n=8,481). While, subjects were excluded due to extreme values or missing data (n=4). Finally, a total of 8,477 subjects met the inclusion criteria and included in this study.

Data collection

The independent variables in this study were foods consumption; while, the dependent variable was blood glucose level grouped into hyperglycemia and normal. Fasting blood glucose were measured with fingertip capillary blood tests (Accu-Chek Performa, Roche Diagnostics GmbH, Mannheim, Germany). All participants were instructed to fast overnight (8-10 hours) before blood sampling. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dL) and normal (<126 mg/dL) (Genuth *et al.* 2003; MoH RI 2018). A validated food frequency questionnaire (FFQ) was used to assess the daily food consumption. The FFQ was validated by the IBHS prior the study (MoH 2018). The FFQ includes carbonated drinks, energy drinks, sweet desserts, SSB, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods, fruits, and vegetables (MoH RI 2018). Consumption of unhealthy foods (carbonated drinks, energy drinks, sweet desserts, SSB, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods) was categorized as frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Fruits and vegetable consumption was categorized into adequate (≥5 servings per day) and inadequate (<5 servings per day) (MoH RI 2018). Sociodemographic

data (age, gender, education, and place of residence) and lifestyle (smoking status, alcohol intake, and physical activity) were obtained using a structured questionnaire. Smoking was categorized into yes and no. Consumption of alcoholic beverages was categorized into yes and no (Atamni *et al.* 2016). Gender was categorized as male and female. Education level was categorized as high (completed 12-year compulsory education or bachelor/diploma/higher education graduates) and low (not completed 12-year compulsory education). Residency was categorized as urban and rural. Physical activity was categorized as low (doing heavy physical activity for <150 minutes/week) and high (doing heavy physical activity for ≥150 minutes/week (MoH RI 2018).

Data analysis

Univariate analysis was presented using mean±standard deviation for numerical data and frequency (percentage) for categorical data. In addition, bivariate analysis was performed using independent samples t-test for continuous variables and the Chi-square test for categorical variables. Whereas, multivariate analysis using multiple logistic regression was used to analyze the association of food consumption and hyperglycemia. Odds Ratio (OR) with 95% confidence intervals was used. We used unadjusted (model 1) and adjusted (model 2). Model 2 was adjusted for demographic data (age, gender, residency) and lifestyle (smoking status, alcohol consumption, and physical activity). Adjustment for demographic data and lifestyle were done due to their potential association with hyperglycemia. All analyses were performed using the SPSS program 25 version with a *p*-value <0.05 considered statistically significant.

RESULTS AND DISCUSSION

Table 1 shows the characteristics of the subjects, the majority of the subjects with hyperglycemia were older (52.05±4.29), female (63.7), not smoking (69.8), and had low physical activity (53.3). Our results also found that the prevalence of hyperglycemia in the population was 43%. The mean FBG was 104.68±31.99 mg/dL for male and 110.75±43.92 mg/dL for female subjects. The prevalence of hyperglycemia was higher in females (44.6%) than males (40.6%). This result was in line with a previous study in the United State (ADA 2018). Women are more risk of experiencing hyperglycemia due to the hormonal changes (ADA 2018). Moreover, physical activity in women tends to be lower than in men (The Lancet Public Health 2019).

Table 1. Characteristics of the subjects.

Variables	Hyperglycemia		P
	Yes (n=3,648)	No (n=4,829)	
Age, mean±SD	52.05±4.29	41.27±4.24	<0.001*
Gender, n (%)			<0.001**
Male	1,323 (36.3)	1,935 (40.1)	
Female	2,325 (63.7)	2,894 (59.9)	
Education levels, n (%)			0.310**
High	1,239 (34.0)	1,691 (35.0)	
Low	2,409 (66.0)	3,138 (65.0)	
Residency, n (%)			0.188**
Rural	1,837 (50.4)	2,502 (51.8)	
Urban	1,811 (49.6)	2,325 (48.2)	
Smoking status, n (%)			<0.001**
No	2,546 (69.8)	3,195 (66.2)	
Yes	1,102 (30.2)	1,634 (33.8)	
Alcohol consumption, n (%)			0.465**
No	3,604 (98.8)	4,779 (99.0)	
Yes	44 (1.2)	50 (1.0)	
Physical activity, n (%)			0.019**
High	1,684 (46.2)	2,355 (48.8)	
Low	1,964 (53.8)	2,474 (51.2)	
Fasting blood glucose, mean±SD	130.84±52.65	91.47±5.43	<0.001*

*Comparison between continuous variables and hyperglycemia were performed using independent samples t-test

**Comparison between categorical variables and hyperglycemia were performed using Chi-square test

The association of food consumption and hyperglycemia are described in Table 2. Among subjects with hyperglycemia, 20.2%, 15.5%, 28.3%, 14.1%, 10.3%, and 48.3% frequently consumed sweet desserts, SSB, salty foods, fried foods, seasonings, and instant foods, respectively. Moreover, among subjects with hyperglycemia, 73.2% consumed inadequate amount of fruits.

Table 2. Food consumption and hyperglycemia*.

Variables	Hyperglycemia Yes (n=3,648)	Hyperglycemia No (n=4,829)	OR (95% CI)	P^{**}
Carbonated drinks, n (%)				
Infrequent	3,396 (93.0)	4,448 (92.2)	0.877	0.123
Frequent	254 (7.0)	379 (7.8)	(0.966, 1.343)	
Energy drinks, n (%)				
Infrequent	3,463 (94.9)	4,566 (94.6)	0.944	0.300
Frequent	187 (5.1)	261 (5.4)	(0.873, 1.284)	
Sweet desserts, n (%)				
Infrequent	2,912 (79.8)	4,021 (82.3)	1.265	<0.001
Frequent	736 (20.2)	808 (17.7)	(1.132, 1.413)	
Sugar-sweetened beverages, n (%)				
Infrequent	3,086 (84.5)	4,281 (88.7)	1.433	<0.001
Frequent	564 (15.5)	546 (11.3)	(1.263, 1.626)	
Salty foods, n (%)				
Infrequent	2,618 (71.7)	3,625 (75.1)	1.189	<0.001
Frequent	1,032 (28.3)	1,202 (24.9)	(1.079, 1.311)	
Fried foods, n (%)				
Infrequent	3,137 (85.9)	4,236 (87.8)	1.172	0.015
Frequent	513 (14.1)	591 (12.2)	(1.033, 1.331)	
Grilled foods, n (%)				
Infrequent	2,594 (71.1)	3,398 (70.4)	1.033	0.515
Frequent	1,056 (28.9)	1,429 (29.6)	(0.940, 1.135)	
Processed foods, n (%)				
Infrequent	2,936 (80.4)	3,804 (78.8)	0.905	0.069
Frequent	714 (19.6)	1,023 (21.2)	(0.813, 1.007)	
Seasonings, n (%)				
Infrequent	3,274 (89.7)	4,402 (91.2)	1.190	0.020
Frequent	376 (10.3)	425 (8.8)	(1.028, 1.377)	
Instant foods, n (%)				
Infrequent	1,889 (51.7)	2,702 (56.0)		<0.001

Frequent	1,761 (48.3)	2,125 (44.0)	1.186 (1.088, 1.293)	
Fruits, n (%)				
Adequate	976 (26.8)	1,374 (28.5)	1.090	0.042
Inadequate	2,674 (73.2)	3,453 (71.5)	(0.990, 1.200)	
Vegetable, n (%)				
Adequate	637 (17.5)	841 (17.4)	1.002	0.495
Inadequate	3,013 (82.5)	3,986 (82.6)	(0.895, 1.123)	

*Frequent (≥ 1-time per day or 1-6 times per week) and infrequent (≤3 times per month or never). Adequate (≥5 servings per day) and inadequate (<5 servings per day)

**Comparison between food consumption and hyperglycemia were performed using Chi-square test

The odds ratios (95% confidence intervals) for food consumption across hyperglycemia are presented in Table 3. Frequent consumption of sweet desserts (OR=1.168; CI=1.035, 1.315), SSB (OR=1.306; CI=1.137, 1.600), salty foods (OR=1.159; CI=1.049, 1.281), fried foods (OR=1.153; CI=1.014, 1.312), seasoning (OR=1.119; CI=1.007, 1.356), and instant foods (OR=1.116; CI=1.020, 1.221) were significantly associated with increased crude odds (model 1) of hyperglycemia (R^2=2%). After adjusting for age, gender, education levels, residency, smoking status, alcohol consumption, and physical activity (model 2), frequent consumption of seasonings was not significantly associated with hyperglycemia (R^2=9%, it increased after adjusting for confounders).

Table 3. Odds ratios (95% confidence intervals) for food consumption across hyperglycemia

Variables	Model 1**			Model 2***		
	OR	95% CI	*p*	OR	95% CI	*p**
Carbonated drinks			0.122			0.419
Infrequent	1			1		
Frequent	1.066	0.889, 1.279		1.071	0.907, 1.266	
Energy drinks			0.565			0.772
Infrequent	1			1		
Frequent	0.961	0.778, 1.187		0.971	0.798, 1.182	
Sweet desserts			<0.001	1		<0.001
Infrequent	1					

Frequent	1.168	1.035, 1.315		1.135	1.005, 1.281	
Sugar-sweetened beverages			<0.001			<0.001
Infrequent	1			1		
Frequent	1.306	1.137, 1.600		1.284	1.116, 1.477	
Salty foods			<0.001			<0.001
Infrequent	1			1		
Frequent	1.159	1.049, 1.281		1.140	1.031, 1.260	
Fried foods			0.014			0.042
Infrequent	1			1		
Frequent	1.153	1.014, 1.312		1.137	1.000, 1.294	
Grilled foods			0.504			0.735
Infrequent	1			1		0.495
Frequent	0.980	0.888, 1.082		0.964	0.872, 1.065	
Processed foods			0.410			0.167
Infrequent	1			1		
Frequent	1.048	0.937, 1.173		1.079	0.969, 1.202	
Seasonings			0.040			0.052
Infrequent	1			1		
Frequent	1.119	1.007, 1.356		1.156	0.998, 1.340	
Instant foods			0.016			0.008
Infrequent	1			1		
Frequent	1.116	1.020, 1.221		1.127	1.032, 1.229	
Fruits			0.080			0.098
Adequate	1			1		
Inadequate	1.038	0.937, 1.149		1.086	0.985, 1.197	
Vegetables						
Adequate	1		0.969	1		0.883
Inadequate	0.953	0.846, 1.074		1.001	1.893, 1.123	

*Differences between food consumption and hyperglycemia were analyzed using multiple logistic regression. **Model 1 was unadjusted. ***Model 2 was adjusted for age, gender, education level, residency, smoking status, alcohol consumption, physical activity.

We found that frequent consumption of sweet desserts and SSB were significantly associated with risk of hyperglycemia. Our result was in line with another cross-sectional study where subjects with metabolic disorders also had higher intake of desserts and beverage than those without metabolic disorders (Permatasari & Syauqy 2022). Sweet desserts and SSB contained carbohydrates or simple sugars with a high Glycemic Index (GI) value, leading to accelerated increase in blood sugar levels (Medina-Remón *et al.* 2018). In addition, study also found that consuming sweetened sugary beverages decreases the endothelial cells' micro and macro cellular function (Loader *et al.* 2017). These metabolic abnormalities are due to the increased in oxidative stress and decreased in NO's (nitric oxide) bioavailability, which plays an important role in glucose metabolism. The decreased in NO bioavailability is also related to risk of developing type 2 diabetes (Loader *et al*. 2017). Added sugar intake is involved in the production of reactive oxygen species (ROS). This increases the expression of cytokines and cell adhesion molecules (Prasad & Dhar 2014).

Participants who frequently consumed salty foods were also associated with increased risk of hyperglycemia. This result is in line with a previous study (*Fitria et al.* 2016). High consumption of salty foods is correlated with an increased risk factor for DM (Fitria *et al.* 2016). High intake of sodium increases the risk of hyperglycemia through the PPAR δ/adiponectin/SGLT2 mechanism in regulating sodium and glucose homeostasis (Zhao *et al.* 2016).

We also found frequent consumption of fried foods was significantly associated with risk of hyperglycemia. Fried foods are high in saturated fat and cholesterol. A high-fat diet significantly contributes to obesity and non-insulin-dependent diabetes mellitus (Naja *et al.* 2013). Previous study found a positive relationship between high intake of saturated fat and cholesterol and increased hyperglycemia and type 2 diabetes in humans and rats (Cahill *et al.* 2014). Saturated fat in the cell membrane will decrease the viscosity of the lipid bilayer of a cell membrane and lead to a decrease in the insulin receptors (Min *et al.* 2018).

Frequent consumption of instant foods also had a significant relationship with the incidence of hyperglycemia as indicated by an increase in FBG in this study. Our results are consistent with other studies that high intake of instant foods were linked to a higher risk of developing diabetes due to the high carbohydrate and fat (Huh *et al.* 2017). An animal trial of monosodium glutamate found a significant increase in glucose levels as evidenced by an increase in HOMA-IR value in rats. It is due to the changes in insulin binding or insulin post receptors in the target tissues (Helal *et al.* 2019). Monosodium glutamate may trigger the degradation of neuronal membranes, allowing calcium ions to enter cells because of its permeability of sodium ions, calcium ions, and water. Then, it might damage the pancreatic gland and hyperglycemia (Jusuf *et al.* 2020).

In this study, individuals with inadequate consumption of fruits and vegetables had a 1.086 and 1.001 times risk for hyperglycemia than those with adequate consumption of vegetables and fruits, but these associations were not statistically significant. In contrast, other study found that higher intakes of fruits and vegetables can reduce hyperglycemia (Samaan 2017). Fiber might delay the digestion and absorption of carbohydrates and increase satiety effect. In individuals with insulin resistance, fiber can increase peripheral insulin sensitivity through short-chain fatty acids produced by fiber fermentation in the gut (Samaan 2017) . In addition, a diet high in fruits and vegetables is associated with high intake of magnesium and iron (Zhang *et al.* 2015). Magnesium is an important cofactor for several enzymes in glucose metabolism, which further plays a role in the development of diabetes (Verma & Garg 2017). Diabetes is a chronic disease. People with diabetes might change their diet, and eat more healthy food; however, it cannot change immediately the condition of the disease.

Result from bivariate analysis was in line with a previous study conducted in Indonesia (Permatasari & Syauqy 2022). Among subjects with metabolic disorders, 8.8%, 6.3%, and 21.2% frequently consumed soft drink, energy drinks, and processed meat. Moreover, among subjects with metabolic disorders, 91.9% and 88.4% consumed inadequate fruits and vegetables, respectively.

To the best of our knowledge, this study is the first study analyzing the association of food consumption with hyperglycemia among middle-aged in Indonesia. Our study used a large sample that reflected the Indonesian population. However, despite its strength this study also has several limitations. Firstly, dietary data were taken using a frequency of intake which contain no information related to the nutrients. Further research with a priori or a posteriori method is highly recommended. By using a priori or a posteriori method, researchers may derive the dietary patterns consisting of complex foods with many nutrients that represent the diet intake among population of interest. Moreover, the R^2 of logistic regression analyses in this study was relatively low; suggesting other factors outside the model can explain the incidence of hyperglycemia in middle-aged adults. Finally, the cross-sectional design restricts the results in maintaining the causality between the variables. Additional longitudinal study is needed to explore the mechanism between variables to established causality.

CONCLUSION

There was a significant association between food consumption and hyperglycemia status among middle-aged adults in Indonesia. Frequent consumption of sweet desserts, SSB, salty foods, fried foods, and instant foods are all increased the odds (chance) for hyperglycemia. Further research with a priori or a posteriori dietary pattern approach is highly recommended. Additional longitudinal study is needed to explore the mechanism between variables.

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DECLARATION OF INTERESTS

The authors have no conflict of interest.

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Food Consumption in Relation to Hyperglycemia in Middle-Aged Adults (45–59 years): A Cross-Sectional National Data Analysis

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ABSTRACT

The study aimed to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia. This cross-sectional study utilized secondary data from the 2018 Indonesia Basic Health Survey (IBHS). A total of 8,477 subjects met the inclusion criteria and included in this study. Fasting Blood Glucose (FBG) was analyzed in the laboratory using an enzymatic analysis. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dl) and normal (<126 mg/dl). A food frequency questionnaire was used to assess the food intake. Multiple logistic regression was used to analyze the association of food consumption and hyperglycemia. Our results found that the prevalence of hyperglycemia in this population was 43%. The mean FBG was 104.68±31.99 mg/dL for male and 110.75±43.92 mg/dl for female subjects. Frequent consumption of sweet desserts (OR=1.265; CI=1.132, 1.413), Sugar-Sweetened Beverages (SSB) (OR=1.433; 95% CI:1.263−1.626), salty foods (OR=1.189; 95% CI=1.079−1.311), fried foods (OR=1.172; 95% CI=1.033−1.331), and instant foods (OR=1.186; 95% CI=1.088−1.293) were significantly associated with increased odds of hyperglycemia. There was a significant association between food consumption and hyperglycemia among middle-aged adults in Indonesia.

Keywords: diet, food consumption, hyperglycemia, fasting blood glucose, Indonesia

INTRODUCTION

Non-communicable diseases are the leading cause of public health problems in developed and developing countries (Naghavi M 2017). Diabetes, one of the non-communicable diseases, is the main cause of death in the world (Zheng *et al.* 2018). Diabetes or hyperglycemia is characterized by an increase in blood sugar levels. Previous studies found that prevalence of hyperglycemia and the components of metabolic syndrome increased rapidly with age in women and men (Wu *et al.* 2017; Jiang *et al.* 2018). Indonesia is count as fourth globally after India, China, and America, in the number of people with diabetes (Naghavi M 2017). The prevalence of diabetes in Indonesia was around 6% (Mihardja *et al.* 2014) and based on the 2018 Indonesia Basic Health Survey (IBHS), higher prevalence of around 10% was found among middle-aged adults (MoH RI 2018).

Diabetes is caused by many factors including lifestyle (Sudargo *et al.* 2018). Sedentary lifestyle has been associated with the increasing risk for diabetes (Permatasari & Syauqy 2022). Previous study also found that diet was strongly associated with increased prevalence of diabetes (Lambrinou *et al.* 2019). Consumption of western foods or unhealthy foods is correlated with an increased prevalence of hyperglycemia and metabolic syndrome (Syauqy *et al.* 2018). Western foods or unhealthy foods are often high in simple carbohydrate, saturated fat, and sodium. In addition to increased consumption of this unhealthy food, there is also an increasing trend of inadequate consumption of vegetables and fruits which can also contribute to increase in diabetes prevalence (Syauqy *et al.* 2018; Schwingshackl *et al.* 2017).

Studies have found significant association between food consumption and metabolic syndrome among middle-aged adults in Taiwan (Syauqy *et al.* 2018). Middle-aged adults with high fruits and vegetables consumptions and lower unhealthy foods consumptions had better quality of life (Lo *et al.* 2016). However, Indonesian people tend to have high consumption of western foods and low fruits and vegetables (MoH RI

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2018). However, to the best of our knowledge, study investigated the association of unhealthy foods, fruits, and vegetables intakes with diabetes among middle-aged adults in Indonesia is limited, especially using a national database that can represents the Indonesian population. Therefore, this study aimed to investigate the association between food consumption with hyperglycemia among middle-aged adults in Indonesia utilizing the 2018 Indonesia Basic Health Survey (IBHS).

METHODS

Design, location, and time

This cross-sectional study was done using data from the 2018 Indonesia Basic Health Survey (IBHS). The IBHS used a two-stage stratified cluster sampling method survey population includes all Indonesian households, representing 26 Provinces and utilizing a sample framework from the national socio-economic survey in March 2018 (MoH RI 2018). This study had received ethical approval from the Health Research Ethics Commission, Medical Faculty, Universitas 'Aisyiyah Yogyakarta No. 1415/KEP-UNISA/VI/2021.

Sampling

The target sample included 300,000 households from 30,000 census blocks of the national socio-economic survey framework (MoH RI 2018). The total population data of the IBHS were 713,783 people aged ≥15 years (MoH RI 2018). The inclusion criteria in this study were individuals aged 45–59 years, had complete data of foods consumption, and had complete data on fasting blood glucose (n=8,481). While, subjects were excluded due to extreme values or missing data (n=4). Finally, a total of 8,477 subjects met the inclusion criteria and included in this study.

Data collection

The independent variables in this study were foods consumption; while, the dependent variable was blood glucose level grouped into hyperglycemia and normal. Fasting blood glucose were measured with fingertip capillary blood tests (Accu-Chek Performa, Roche Diagnostics GmbH, Mannheim, Germany). All participants were instructed to fast overnight (8–10 hours) before blood sampling. The fasting blood glucose was categorized as hyperglycemia (≥126 mg/dl) and normal (<126 mg/dl) (Kahn 2003; MoH RI 2018). A validated Food Frequency Questionnaire (FFQ) was used to assess the daily food consumption. The FFQ was validated by the IBHS prior the study (MoH RI 2018). The FFQ includes carbonated drinks, energy drinks, sweet desserts, SSB, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods, fruits, and vegetables (MoH RI 2018). Consumption of unhealthy foods (carbonated drinks, energy drinks, sweet desserts, SSB, salty foods, fried foods, grilled foods, processed foods, seasonings, instant foods) was categorized as frequent (≥ 1-time per day or 1–6 times per week) and infrequent (≤3 times per month or never). Fruits and vegetable consumption was categorized into adequate (≥5 servings per day) and inadequate (<5 servings per day) (MoH RI 2018). Sociodemographic data (age, gender, education, and place of residence) and lifestyle (smoking status, alcohol intake, and physical activity) were obtained using a structured questionnaire. Smoking was categorized into yes and no. Consumption of alcoholic beverages was categorized into yes and no (Atamni *et al.* 2016). Gender was categorized as male and female. Education level was categorized as high (completed 12-year compulsory education or bachelor/diploma/higher education graduates) and low (not completed 12-year compulsory education). Residency was categorized as urban and rural. Physical activity was categorized as low (doing heavy physical activity for <150 minutes/week) and high (doing heavy physical activity for ≥150 minutes/week (MoH RI 2018)

Data analysis

Univariate analysis was presented using mean±standard deviation for numerical data and frequency (percentage) for categorical data. In addition, bivariate analysis was performed using independent samples t-test for continuous variables and the Chi-square test for categorical variables. Whereas, multivariate analysis using multiple logistic regression was used to analyze the association of food consumption and hyperglycemia. Odds Ratio (OR) with 95% confidence intervals was used. We used unadjusted (model 1) and adjusted (model 2). Model 2 was adjusted for demographic data (age, gender, residency) and lifestyle (smoking status, alcohol consumption, and physical activity).

Adjustment for demographic data and lifestyle were done due to their potential association with hyperglycemia. All analyses were performed using the SPSS program 25 version with a p-value <0.05 considered statistically significant.

RESULTS AND DISCUSSION

Table 1 shows the characteristics of the subjects, the majority of the subjects with hyperglycemia were older (52.05±4.29), female (63.7), not smoking (69.8), and had low physical activity (53.3). Our results also found that the prevalence of hyperglycemia in the population was 43%. The mean FBG was 104.68±31.99 mg/dl for male and 110.75±43.92 mg/dl for female subjects. The prevalence of hyperglycemia was higher in females (44.6%) than males (40.6%).

The association of food consumption and hyperglycemia are described in Table 2. Among subjects with hyperglycemia, 20.2%, 15.5%, 28.3%, 14.1%, 10.3%, and 48.3% frequently consumed sweet desserts, SSB, salty foods, fried foods, seasonings, and instant foods, respectively. Moreover, among subjects with hyperglycemia, 73.2% consumed inadequate amount of fruits.

The odds ratios (95% confidence intervals) for food consumption across hyperglycemia are presented in Table 3. Frequent consumption of sweet desserts (OR=1.168; CI=1.035, 1.315), SSB (OR=1.306; CI=1.137, 1.600), salty foods (OR=1.159; CI=1.049, 1.281), fried foods (OR=1.153; CI=1.014, 1.312), seasoning (OR=1.119; CI=1.007, 1.356), and instant foods (OR=1.116; CI=1.020, 1.221) were significantly associated with increased crude odds (model 1) of hyperglycemia (R2=2%). After adjusting for age, gender, education levels, residency, smoking status, alcohol consumption, and physical activity (model 2), frequent consumption of seasonings was not significantly associated with hyperglycemia (R2=9%, it increased after adjusting for confounders).

Table 1. Characteristics of the subjects

Variables	Hyperglycemia		*p*
	Yes (n=3,648)	No (n=4,829)	
Age (mean±SD)	52.05±4.29	41.27±4.24	<0.001*
Gender (n%)			<0.001**
Male	1,323 (36.3)	1,935 (40.1)	
Female	2,325 (63.7)	2,894 (59.9)	
Education levels (n%)			0.310**
High	1,239 (34.0)	1,691 (35.0)	
Low	2,409 (66.0)	3,138 (65.0)	
Residency (n%)			0.188**
Rural	1,837 (50.4)	2,502 (51.8)	
Urban	1,811 (49.6)	2,325 (48.2)	
Smoking status (n%)			<0.001**
No	2,546 (69.8)	3,195 (66.2)	
Yes	1,102 (30.2)	1,634 (33.8)	
Alcohol consumption (n%)			0.465**
No	3,604 (98.8)	4,779 (99.0)	
Yes	44 (1.2)	50 (1.0)	
Physical activity (n%)			0.019**
High	1,684 (46.2)	2,355 (48.8)	
Low	1,964 (53.8)	2,474 (51.2)	
Fasting blood glucose (mean±SD)	130.84±52.65	91.47±5.43	<0.001*

*Comparison between continuous variables and hyperglycemia were performed using independent samples t-test
**Comparison between food consumption and hyperglycemia were performed using Chi-square test
SD: Standard Deviation

Table 2. Food consumption and hyperglycemia*

Variables	Hyperglycemia		OR (95% CI)	p^{**}
	Yes (n=3,648)	No (n=4,829)		
Carbonated drinks (n%)				
Infrequent	3,396 (93.0)	4,448 (92.2)	0.877	0.123
Frequent	254 (7.0)	379 (7.8)	(0.966, 1.343)	
Energy drinks (n%)				
Infrequent	3,463 (94.9)	4,566 (94.6)	0.944	0.300
Frequent	187 (5.1)	261 (5.4)	(0.873, 1.284)	
Sweet desserts (n%)				
Infrequent	2,912 (79.8)	4,021 (82.3)	1.265	<0.001
Frequent	736 (20.2)	808 (17.7)	(1.132, 1.413)	
Sugar-sweetened beverages (n%)				
Infrequent	3,086 (84.5)	4,281 (88.7)	1.433	<0.001
Frequent	564 (15.5)	546 (11.3)	(1.263, 1.626)	
Salty foods (n%)				
Infrequent	2,618 (71.7)	3,625 (75.1)	1.189	<0.001
Frequent	1,032 (28.3)	1,202 (24.9)	(1.079, 1.311)	
Fried foods (n%)				
Infrequent	3,137 (85.9)	4,236 (87.8)	1.172	0.015
Frequent	513 (14.1)	591 (12.2)	(1.033, 1.331)	
Grilled foods (n%)				
Infrequent	2,594 (71.1)	3,398 (70.4)	1.033	0.515
Frequent	1,056 (28.9)	1,429 (29.6)	(0.940, 1.135)	
Processed foods (n%)				
Infrequent	2,936 (80.4)	3,804 (78.8)	0.905	0.069
Frequent	714 (19.6)	1,023 (21.2)	(0.813, 1.007)	
Seasonings (n%)				
Infrequent	3,274 (89.7)	4,402 (91.2)	1.190	0.020
Frequent	376 (10.3)	425 (8.8)	(1.028, 1.377)	
Instant foods (n%)				
Infrequent	1,889 (51.7)	2,702 (56.0)	1.186	<0.001
Frequent	1,761 (48.3)	2,125 (44.0)	(1.088, 1.293)	
Fruits (n%)				
Adequate	976 (26.8)	1,374 (28.5)	1.090	0.042
Inadequate	2,674 (73.2)	3,453 (71.5)	(0.990, 1.200)	
Vegetable (n%)				
Adequate	637 (17.5)	841 (17.4)	1.002	0.495
Inadequate	3,013 (82.5)	3,986 (82.6)	(0.895, 1.123)	

*Frequent (≥ 1-time per day or 1–6 times per week) and infrequent (≤3 times per month or never); Adequate (≥5 servings per day) and inadequate (<5 servings per day)

**Comparison between food consumption and hyperglycemia were performed using Chi-square test

We found that frequent consumption of sweet desserts and SSB were significantly associated with risk of hyperglycemia. Our result was in line with another cross-sectional study where subjects with metabolic disorders also had higher intake of desserts and beverage than those without metabolic disorders (Permatasari & Syauqy 2022). Sweet desserts and SSB contained carbohydrates or simple sugars with a high Glycemic Index (GI) value, leading

Table 3. Odds ratios (95% confidence intervals) for food consumption across hyperglycemia

Variables	Model 1**			Model 2***		
	OR	95% CI	p	OR	95% CI	p^*
Carbonated drinks			0.122			0.419
Infrequent	1			1		
Frequent	1.066	0.889, 1.279		1.071	0.907, 1.266	
Energy drinks			0.565			0.772
Infrequent	1			1		
Frequent	0.961	0.778, 1.187		0.971	0.798, 1.182	
Sweet desserts			<0.001	1		<0.001
Infrequent	1					
Frequent	1.168	1.035, 1.315		1.135	1.005, 1.281	
Sugar-sweetened beverages			<0.001			<0.001
Infrequent	1			1		
Frequent	1.306	1.137, 1.600		1.284	1.116, 1.477	
Salty foods			<0.001			<0.001
Infrequent	1			1		
Frequent	1.159	1.049, 1.281		1.140	1.031, 1.260	
Fried foods			0.014			0.042
Infrequent	1			1		
Frequent	1.153	1.014, 1.312		1.137	1.000, 1.294	
Grilled foods			0.504			0.735
Infrequent	1			1		
Frequent	0.980	0.888, 1.082		0.964	0.872, 1.065	
Processed foods			0.410			0.495
Infrequent	1			1		
Frequent	1.048	0.937, 1.173		1.079	0.969, 1.202	
Seasonings			0.040			0.167
Infrequent	1			1		
Frequent	1.119	1.007, 1.356		1.156	0.998, 1.340	
Instant foods			0.016			0.052
Infrequent	1			1		
Frequent	1.116	1.020, 1.221		1.127	1.032, 1.229	
Fruits			0.080			0.008
Adequate	1			1		
Inadequate	1.038	0.937, 1.149		1.086	0.985, 1.197	
Vegetable			0.969			0.098
Adequate	1			1		
Inadequate	0.953	0.846, 1.074		1.001	1.893, 1.123	0.883

*Differences between food consumption and hyperglycemia were analyzed using multiple logistic regression

**Model 1 was unadjusted.

***Model 2 was adjusted for age, gender, education level, residency, smoking status, alcohol consumption, physical activity.

to accelerated increase in blood sugar levels (Medina-Remón *et al.* 2018). In addition, study also found that consuming sweetened sugary beverages decreases the endothelial cells' micro and macro cellular function (Loader *et al.* 2017). These metabolic abnormalities are due to the increased in oxidative stress and decreased in NO's (nitric oxide) bioavailability, which plays an important role in glucose metabolism. The decreased in NO bioavailability is also related to risk of developing type 2 diabetes (Loader *et al.* 2017). Added sugar intake is involved in the production of reactive oxygen species (ROS). This increases the expression of cytokines and cell adhesion molecules (Prasad & Dhar 2014).

Participants who frequently consumed salty foods were also associated with increased risk of hyperglycemia. This result is in line with a previous study (Nur *et al.* 2016). High consumption of salty foods is correlated with an increased risk factor for DM (Nur *et al.* 2016). High intake of sodium increases the risk of hyperglycemia through the PPAR δ/adiponectin/ SGLT2 mechanism in regulating sodium and glucose homeostasis (Zhao *et al.* 2016).

We also found frequent consumption of fried foods was significantly associated with risk of hyperglycemia. Fried foods are high in saturated fat and cholesterol. A high-fat diet significantly contributes to obesity and non-insulin-dependent diabetes mellitus (Naja *et al.* 2013). Previous study found a positive relationship between high intake of saturated fat and cholesterol and increased hyperglycemia and type 2 diabetes in humans and rats (Cahill *et al.* 2014). Saturated fat in the cell membrane will decrease the viscosity of the lipid bilayer of a cell membrane and lead to a decrease in the insulin receptors (Min *et al.* 2018).

Frequent consumption of instant foods also had a significant relationship with the incidence of hyperglycemia as indicated by an increase in FBG in this study. Our results are consistent with other studies that high intake of instant foods were linked to a higher risk of developing diabetes due to the high carbohydrate and fat (Huh *et al.* 2017). An animal trial of monosodium glutamate found a significant increase in glucose levels as evidenced by an increase in HOMA-IR value in rats. It is due to the changes in insulin binding or insulin post receptors in the target tissues (Helal *et al.* 2019). Monosodium glutamate may trigger the degradation of neuronal membranes, allowing calcium ions to enter cells because of its permeability of sodium ions, calcium ions, and water. Then, it might damage the pancreatic gland and hyperglycemia (Jusuf *et al.* 2020).

In this study, individuals with inadequate consumption of fruits and vegetables had a 1.086 and 1.001 times risk for hyperglycemia than those with adequate consumption of vegetables and fruits, but these associations were not statistically significant. In contrast, other study found that higher intakes of fruits and vegetables can reduce hyperglycemia (Samaan 2017). Fiber might delay the digestion and absorption of carbohydrates and increase satiety effect. In individuals with insulin resistance, fiber can increase peripheral insulin sensitivity through short-chain fatty acids produced by fiber fermentation in the gut (Samaan 2017) . In addition, a diet high in fruits and vegetables is associated with high intake of magnesium and iron (Zhang *et al.* 2015). Magnesium is an important cofactor for several enzymes in glucose metabolism, which further plays a role in the development of diabetes (Verma & Garg 2017). Diabetes is a chronic disease. People with diabetes might change their diet, and eat more healthy food; however, it cannot change immediately the condition of the disease.

Result from bivariate analysis was in line with a previous study conducted in Indonesia (Permatasari & Syauqy 2022). Among subjects with metabolic disorders, 8.8%, 6.3%, and 21.2% frequently consumed soft drink, energy drinks, and processed meat. Moreover, among subjects with metabolic disorders, 91.9% and 88.4% consumed inadequate fruits and vegetables, respectively.

To the best of our knowledge, this study is the first study analyzing the association of food consumption with hyperglycemia among middle-aged in Indonesia. Our study used a large sample that reflected the Indonesian population. However, despite its strength this study also has several limitations. Firstly, dietary data were taken using a frequency of intake which contain no information related to the nutrients. Further research with a priori or a posteriori method is highly recommended. By using a priori or a posteriori method, researchers may derive the dietary patterns consisting of complex foods with many nutrients that represent the diet intake among population of interest. Moreover, the R2 of logistic regression analyses in this study was relatively low; suggesting other factors outside the model can explain the incidence of hyperglycemia in middle-aged adults. Finally, the cross-sectional design restricts the results in maintaining the causality between the variables. Additional longitudinal study is needed to explore the mechanism between variables to established causality.

CONCLUSION

There was a significant association between food consumption and hyperglycemia status among middle-aged adults in Indonesia. Frequent consumption of sweet desserts, SSB, salty foods, fried foods, and instant foods are all increased the odds (chance) for hyperglycemia. Further research with a priori or a posteriori dietary pattern approach is highly recommended. Additional longitudinal study is needed to explore the mechanism between variables.

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DECLARATION OF INTERESTS

The authors have no conflict of interest.

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