KORESPONDENSI PAPER

Judul : Risk Factors for Disorders due to Iodine Deficiency (IDD) among Pregnant Women in Jepara, Indonesia
Jurnal : Food Research
Status : Jurnal Internasional Terindeks Scopus (Q3) SJR 0,23

AKTIVITAS KORESPONDENSI

No	Aktivitas	Tanggal
1	Submit Artikel	5 Oktober 2021
2	Review dan Revisi Artikel	12 November 2021
3	Accepted	3 Maret 2022

1. Submit Artikel

From: Ani Margawati <animargawati@gmail.com>
Sent: Tuesday, 5 October, 2021 12:04 PM
To: foodresearch.my@outlook.com <foodresearch.my@outlook.com>
Subject: MANUSCRIPT SUBMISSION

Dear,

Professor Dr. Son Radu

Chief Editor

Food Research

First of all, I would like to introduce my self, I am Ani Margawati as the first author of manuscript entitled ***"Risk Factors for Disorders Due to Iodine Deficiency (IDD) Among Pregnant Women in Jepara"*** would like to request you to consider the attached manuscript for publication in Food Research as an original article.

Pregnant women are known to experience an increase in the size of thyroid gland by 10% and an increase in thyroid hormone production by 50%, causing the need for iodine in the pregnant women increases. The incidence of IDD that not handled properly during pregnancy can cause premature birth, intrauterine growth disorders, fetal death, impaired fetal development, respiratory disorders and increased perinatal mortality.

Based on the 2013 data, the prevalence of pregnant women in Indonesia with Urinary Iodine Excretion (UIE) <100 g/L was 24.3%. One of the causes of the problem was 50.8% of household salt in Indonesia has a low level of iodine. However, Jepara Regency which is a producer of iodized salt, shows the phenomenon that there are still several sub-districts that endemic for IDD. Therefore, it is necessary to study other factors related to the incidence of IDD in pregnant women based on pregnant women characteristics and food intake. The results of this study showed that education and knowledge of IDD were risk factors of IDD among pregnant women.

I believe that the findings of this study are relevant to the scope of your journal and will be of interest to its readership. This manuscript has not been published or presented elsewhere in part or in entirety, and is not under consideration by another journal. Hopefully, this article can be accepted and be sources of public knowledge and sources of reading for researchers.

We suggest reviewers for our manuscript are :

1. Dr. Ahmad Syauqi. Expertise in Clinical nutrition. Email : syauqy@fk.undip.ac.id
2. Prof. Soeharyo Hadi Saputro. Expertise in Internist and epidemiologist. Email : prof_haryo@yahoo.co.id
3. Dr. Ali Rosidi. Expertise in Community nutrition. Email : alirhesa@yahoo.co.id
4. Prof. Ali Khomsan. Expertise in Public health nutrition. Email : erlangga259@yahoo.com

Thank you for your consideration of this manuscript.

Sincerely,

Dra. Ani Margawati, M.Kes, PhD

Dept of Nutrition Science, Faculty of Medicine, Diponegoro University, Semarang, Indonesia

Full Paper_Risk Factors for Disorders Due to Iodine Deficiency (IDD) Among Pregnant Women in Jepara.docx
113K

Gmail Ani Margawati <animargawati@gmail.com>

Re: MANUSCRIPT SUBMISSION

1 message

Food Research <foodresearch.my@outlook.com> Wed, Oct 6, 2021 at 2:26 AM
To: Ani Margawati <animargawati@gmail.com>

Dear Dra. Ani Margawati,

Thank you for your submission to Food Research.
Before we begin the reviewing process, kindly revise the manuscript according to the comments attached and revert at your earliest convenience.
Adhering to Food Research format is greatly appreciated.

Best regards,
Son Radu, PhD
Chief Editor

Gmail Ani Margawati <animargawati@gmail.com>

Manuscript ID: FR-2021-814

12 messages

Food Research <foodresearch.my@outlook.com> Thu, Oct 7, 2021 at 3:52 AM
To: Ani Margawati <animargawati@gmail.com>

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Your paper will be reviewed by three or more reviewers assigned by the Food Research editorial board and final decision made by the editor will be informed by email in due course. Reviewers' suggestions and editor's comments will be then made available via email attached file. You can monitor the review process for your paper by emailing us on the "Status of my manuscript".

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7th October 2021

Authors: Margawati, A., Utami, A., Nugraheni, A. and Hananingtyas, A.

Manuscript title: Risk factors for disorders due to iodine deficiency (IDD) among pregnant women in Jepara

Manuscript ID: FR-2021-814

Dear Dr. Ani Margawati,

This message is to acknowledge receipt of the above manuscript that you submitted via email to Food Research. Your manuscript has been successfully checked-in. Please refer to the assigned manuscript ID number in any correspondence with the Food Research Editorial Office or with the editor.

Your paper will be reviewed by three or more reviewers assigned by the Food Research editorial board and final decision made by the editor will be informed by email in due course. Reviewers' suggestions and editor's comments will be then made available via email attached file. You can monitor the review process for your paper by emailing us on the "Status of my manuscript".

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Chief Editor
Email: foodresearch.my@outlook.com

2. Review dan Revisi Artikel

Food Research <foodresearch.my@outlook.com> Fri, Nov 12, 2021 at 1:41 AM
To: Ani Margawati <animargawati@gmail.com>

Dear Dr. Ani Margawati,

Manuscript FR-2021-814 entitled " Risk factors for disorders due to iodine deficiency (IDD) among pregnant women in Jepara " which you submitted to Food Research, has been reviewed. The comments of the reviewer(s) are included in the attached file.

The reviewer(s) have recommended publication, but also suggest some revisions to your manuscript. Therefore, I invite you to respond to the reviewer(s)' comments and revise your manuscript. Once the revised manuscript is prepared, please send it back to me for further processing.

Because we are trying to facilitate timely publication of manuscripts submitted to Food Research, your revised manuscript should be submitted before or by 26th November 2021. If it is not possible for you to submit your revision by this date, please let us know.

Once again, thank you for submitting your manuscript to Food Research and I look forward to receiving your revised manuscript.

Sincerely,

Son Radu, PhD
Chief Editor, Food Research
foodresearch.my@outlook.com

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MANUSCRIPT EVALUATION FORM

Date : 7th October 2021

Manuscript ID : FR-2021-814

Please return by : 7th November 2021

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2. Your review should consider the article's scholarly merit including originality of the research issue and/or methodology, adequacy and rigor of the research methodology and techniques used, quality and rigor of data analysis, comprehensiveness of literature review, and the readability and presentation of the article. Please provide detailed and specific comments to all items. Also, where appropriate please provide suggestions for revision.

COMMENT SHEET

Using item 2 in page 1 as a guideline, please indicate the reasons for your recommendations. Most author(s) will appreciate frankness, combined with a modicum of tact. Even if you recommend that the manuscript be accepted for publication, please provide some general comments to the author(s).

Evaluation Criteria	Grade				
	A (Excellent)	B	C	D	E (Worst)
1. Appropriateness of Contents	v				
2. Originality of Topic	v				
3. Manuscript Format	v				
4. Research Methodology		v			
5. Data Analysis	v				
6. Relevance to the Journal	v				

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(REVIEWER'S SECTION) REVIEWER'S COMMENTS/SUGGESTIONS		(AUTHOR'S SECTION) AUTHOR'S ACTION/RESPONSE *NOTE FOR AUTHOR: Please state your response to the reviewer's comments/suggestion below
1.	**Title** *It should reflect the article* You should mention the country in the title because no one knows where is Jepara	
2.	**Abstract** *Background, Aim, Methodology and Conclusion* It is well written, concise, and informative. Please add variable MUAC for nutritional status in abstract, and SQ-FFQ as instrument for food consumption	
3.	**Keywords** *Min. 3 and Max. 6* OK, 3 keywords have been listed	
4.	**Introduction** *Concise with sufficient background* It is well written including prevalence of IDD and many factors related IDD has been discussed. Iodine RDA is microgram not gram (please revise)	
5.	**Research design/Methodology** *Clearly described and reproducible* a. Please mention if you already had the ethical clearance to conduct the survey. b. Please add information on case-control, is it based on UIE, TSH or others? c. Specify how many samples in Case group and how many in Control group? d. How did you measure knowledge and attitude? Have you tested the validity and reliability of the instrument?	

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6.	**Data Analysis** *Results well presented and discussed* In the RESULT please explain Table 1 in details, because you have so many information in Table 1. Overall the discussion is interesting and well written.	
7.	**Conclusion** *A clear summary of the study* It is OK	
8.	**References** *References should follow the journal's format* Good references	
9.	**English Proficiency** It should be proofread by professional translator	
10.	**Additional comments/suggestions by the reviewer about the article** This study is very important to reveal problem of IDD in developing country. Information that should be added are: how the government should take action on IDD problem, what intervention should be done, and how the government control production and distribution of fortified salt in the community	

Overall Evaluation

Please choose one.

Accept		**Major Revision**	
Minor Revision	**V**	**Reject**	

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COMMENT SHEET

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Evaluation Criteria	Grade				
	A (Excellent)	B	C	D	E (Worst)
1. Appropriateness of Contents	x				
2. Originality of Topic		x			
3. Manuscript Format			x		
4. Research Methodology		x			
5. Data Analysis		x			
6. Relevance to the Journal	x				

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1.	**Title** *It should reflect the article :* Acceptable	
2.	**Abstract** *Background, Aim, Methodology and Conclusion* Acceptable	
3.	**Keywords** *Min. 3 and Max. 6* Okay	
4.	**Introduction** *Concise with sufficient background* • The reason for choosing the research location is not strong. Information regarding the incidence of endemic IDD is incomplete. The prevalence rate of IDD in Jepara is not stated. Just mentioning that IDD in Jepara is high. Please complete it. • Please state the reason for choosing 2nd trimester pregnancy • Please state the novelty of this research	
5.	**Research design/Methodology** *Clearly described and reproducible* • The steps in testing UIE are not yet complete. Please complete and make sure to mention the brand and specifications of the measuring tool. • The ELISA test step for TSH testing is also not complete. Please complete and make sure to mention the brand and specifications of the measuring tool. • There is no reason for choosing the subject of pregnant women in the 2nd and 3rd trimesters. Please mention with	

	adequate references.	
6.	**Data Analysis** *Results well presented and discussed* Okay. In the discussion there is a statement that the behavior of pregnant women has nothing to do with the incidence of IDD, but the authors suggest pregnant women to maintain healthy behavior including consumption of iodine. Please mention a little discussion about the need for healthy living behavior during pregnancy.	
7.	**Conclusion** *A clear summary of the study* Fair	
8.	**References** *References should follow the journal's format* Use reference writing according to the rules of this journal. Please check and fix again	
9.	**English Proficiency** Fair	
10.	**Additional comments/suggestions by the reviewer about the article**	

Overall Evaluation

Please choose one.

Accept		**Major Revision**	
Minor Revision	**V**	**Reject**	

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2. Your review should consider the article's scholarly merit including originality of the research issue and/or methodology, adequacy and rigor of the research methodology and techniques used, quality and rigor of data analysis, comprehensiveness of literature review, and the readability and presentation of the article. Please provide detailed and specific comments to all items. Also, where appropriate please provide suggestions for revision.

COMMENT SHEET

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Evaluation Criteria	Grade				
	A (Excellent)	B	C	D	E (Worst)
1. Appropriateness of Contents		V			
2. Originality of Topic		V			
3. Manuscript Format		V			
4. Research Methodology			V		
5. Data Analysis		V			
6. Relevance to the Journal	V				

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1.	**Title** *It should reflect the article*	
2.	**Abstract** *Background, Aim, Methodology and Conclusion*	
3.	**Keywords** *Min. 3 and Max. 6*	I suggested that author(s) add "Indonesia" and "case control design" in the Keywords
4.	**Introduction** *Concise with sufficient background*	The introduction is concise with sufficient background, I have suggestion as follow: - Please added the location of the study in the study aimed (line 65-66)
5.	**Research design/Methodology** *Clearly described and reproducible*	The methods are clearly described and reproducible, I have suggestions as follow: - Please delete "This study aimed to determine the risk factors for the incidence of IDD seen from UIE and TSH status among pregnant women" (line 72-73). The aim of the study should be stated in the introduction. - please describe more about the procedures of taking urine sample (for UIE) and blood serum sample (for TSH)
6.	**Data Analysis** *Results well presented and discussed*	Please check table 2, 3, 4, and 5. 'OR' should be replaced as 'P', and 'P' should be replaced as 'OR' (P value is alpha (<0.001)). The sequence usually starts with OR, 95% CI and followed by the p value
7.	**Conclusion** *A clear summary of the study*	A conclusion is clearly describe the study

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8.	**References** *References should follow the journal's format*	the references are appropriate
9.	**English Proficiency**	Overall English is good
10.	**Additional comments/suggestions by the reviewer about the article**	Line 31. Replace 'can't' to 'cannot'

Overall Evaluation

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Minor Revision	**v**	**Reject**	

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Risk factors for disorders due to iodine deficiency (IDD) among pregnant women in Jepara

Abstract

Pregnant women need an increase for iodine intake. In 2013, 24.3% of pregnant women in Indonesia had low iodine excretion values. Iodine is known to affect thyroid hormone regulation. This study aimed to analyze risk factors of Iodine Deficiency Disease (IDD) in pregnant women. This study was conducted using an observational method with a case control design. The subjects in this study were pregnant women in the 2nd and 3rd trimesters in the Mlonggo and Pakis Aji Health Centers, Jepara Regency. The total sample was 88 pregnant women. Primary data collection was done by taking urine for Urinary Iodine Excretion (UIE) and blood serum for Thyroid Stimulating Hormone (TSH) levels, anthropometric measurements for nutritional status and filling out questionnaires related to subject characteristics and interviews related to intake. This study showed that 53.4% of pregnant women had high TSH levels and 68.2% pregnant women had low UIE levels. The results of the multivariate analysis showed that education was the strongest risk factor of IDD based on TSH levels (p value 0,020; OR *adjusted* 0,324; CI OR 0,125:0,835) and knowledge of IDD was the strongest risk factor of IDD based on UIE levels (p value 0,008; OR *adjusted* 4,776; CI OR 1,510:15,105).

Keywords: Pregnant women, Iodine, Thyroid stimulating hormone

1. Introduction

Iodine is an essential micronutrient for the formation of thyroid hormones in the body. Thyroid hormone plays an important role in various functions such as basal metabolism, heart rate and bone growth and the central nervous system (González-Martínez *et al*., 2021). Pregnant women are known to experience an increase in the size of thyroid gland by 10% and an increase in thyroid hormone production by 50%, causing the need for iodine in the pregnant women increases (Alexander *et al*.,

2017). The need for iodine in adults is about 150 g/day. The World Health Organization (WHO) recommends a higher intake of iodine in pregnant women, which is 250 g/day. Deficiency of iodine intake is thought to be the main cause of hypothyroidism and Iodine Deficiency Disorders (IDD) (Taylor and Lazarus, 2019).

Based on the 2013 RISKESDAS data, the prevalence of pregnant women in Indonesia with Urinary Iodine Excretion (UIE) <100 g/L was 24.3%. One of the causes of the problem was 50.8% of household salt in Indonesia has a low level of iodine. Therefore, household coverage with iodized salt consumption can't be an indicator of the fulfilment of iodine intake (Kementrian Kesehatan Republik Indonesia, 2015).

Examination of urinary iodine excretion (UIE) in 2007 until 2012 in Jepara Regency showed that several sub-districts including as IDD endemic areas such as Mayong, Batealit and Pakis Aji (Widiyatni and Subagio, 2016). Apart from UIE levels, IDD status can also be seen from Thyroid Stimulating Hormone (TSH) levels. If thyroid hormone production is insufficient, there will be an increase in TSH production (Kementrian Kesehatan Republik Indonesia, 2015). Research in Magelang showed 17.1% of pregnant women in goiter replete areas had high TSH levels and 19.2% of pregnant women in non-replete goiter areas had high TSH levels (Kusrini *et al*., 2016). Screening to see the adequacy of iodine in the body is very important for pregnant women as an indicator to detect the occurrence of IDD.

Commented [A1]: • The reason for choosing the research location is not strong. Information regarding the incidence of endemic IDD is incomplete. The prevalence rate of IDD in Jepara is not stated. Just mentioning that IDD in Jepara is high. Please complete it.

The incidence of IDD that not handled properly during pregnancy can cause premature birth, intrauterine growth disorders, fetal death, impaired fetal development, respiratory disorders and increased perinatal mortality. This is because iodine is needed by thyroid hormone for the growth and formation of vital organs of the fetus (Animal Welfare Branch, 2007). Adequacy of iodine in the mother is very important to prevent hypothyroidism in the fetus. During the early stages of pregnancy, the fetus is still dependent on the mother's thyroid hormone production. During midterm pregnancy, the fetus begins to produce its own thyroid hormone but still requires iodine intake from the mother

(Khadilkar, 2019). Based on data from Cipto Mangunkusumo Hospital in Jakarta and Hasan Sadikin Hospital in Bandung around 2014, 1 from 2513 newborns had congenital hypothyroidism. This prevalence was higher than global data, which is 1 in 3000 newborns (Kementrian Kesehatan Republik Indonesia, 2015).

Apart from iodine, many other nutrients are risk factors for IDD. Malnutrition is known to cause thyroid disorders. Research in 2017 showed that there was a positive correlation between TSH and Body Mass Index (BMI) in female (Singh *et al*., 2020). However, other studies stated that there was no significant difference in BMI in hypothyroid patients (Ranabir *et al*., 2019). Deficiency of macronutrient elements such as protein and micronutrient elements such as iron, selenium and zinc are known to interfere with thyroid gland function. Previous studies have stated that hypothyroidism can occur among moderate to severe iron deficient (El-Masry *et al*., 2018). Research in Magelang showed that the prevalence of pregnant women with iodine deficiency was higher in the third trimester than in the previous trimester (Kusrini *et al*., 2016). However, another study in Korea showed that the lowest TSH levels occurred in women in third trimester of pregnancy (Kim *et al*., 2015).

IDD in pregnant women is a problem that can have an impact not only on the mother but also on the fetus. Fetuses with mothers who have IDD are at risk of inhibiting fetal development. Based on the description above, researchers are interested in knowing the risk factors of IDD among pregnant women.

Commented [A2]: •Please state the reason for choosing 2nd trimester pregnancy

Commented [A3]: • Please state the novelty of this research

2. Materials and methods

This research was carried out using an observational method with a case control study design. The subjects in this study were pregnant women in the second and third trimesters in the Mlonggo Health Center and Pakis Aji Health Center, Jepara Regency. The sampling technique was carried out with cluster sampling and total sample obtained was 88 pregnant women. The subjects were willing to

participate in the study by filling the informed consent form. This study aimed to determine the risk factors for the incidence of IDD seen from UIE and TSH status among pregnant women.

Primary data were collected by taking urine sample for UIE levels, blood serum for TSH levels, anthropometric measurements for nutritional status, filling out questionnaires related to subject characteristics and interviewing subjects related to food intake. The research instrument used a Semi Quantitative Food Frequency Questionnaire (SQ-FFQ) for food intake, Mid-Upper Arm Circumference (MUAC) tape to measure nutritional status, measurement of UIE levels using urine sample with Acid Digestion method and measurement of TSH levels using whole blood serum with Enzyme Linked Immunosorbent Assay (ELISA) method. Pregnant women with MUAC < 23.5 cm included as poor nutritional status and pregnant women with MUAC ≥ 23.5 cm included as normal nutritional status (Tejayanti, 2020). The food intake of pregnant women was divided into 3 groups, namely inadequate (<80%), sufficient (80-100%) and excessive (>100%) (Yunitasari *et al*., 2019). Pregnant women in the second trimester were in the range of 13-27 weeks and the third trimester were more than 27 weeks. UIE levels were less if < 150 g/L and normal if 150 g/L (WHO (World Health Organization), 2013). Categorization of TSH levels based on gestational age, normal category if TSH values in the first trimester were 0.1-2.5 mIU/L, second trimester were 0.2 -3.0 mIU/L and third trimester were 0.3-3.0mIU/L (Green *et al*., 2011).

Univariate analysis was used on one variable with the aim of knowing and identifying the frequency distribution and characteristics of each variable. Bivariate analysis was to determine the risk (odds ratio) of exposure to cases by using the Chi Square test formula with 95% confidence level. Multivariate analysis was to determine the strongest risk factors of IDD by using logistic regression analysis.

3. Results

Commented [A4]: • The steps in testing UIE are not yet complete. Please complete and make sure to mention the brand and specifications of the measuring tool

Commented [A5]: • The ELISA test step for TSH testing is also not complete. Please complete and make sure to mention the brand and specifications of the measuring tool.

Commented [A6]: • There is no reason for choosing the subject of pregnant women in the 2nd and 3rd trimesters. Please mention with adequate references.

The number of subjects obtained in the study at the Mlonggo Health Center and the Pakis Aji Health Center, Jepara Regency, as many as 88 subjects with varying ages from 18 to 41 years. The following characteristics of the subject were shown in table 1.

This study showed that the number of subjects with high TSH levels was more than subjects with normal TSH (53.4%). While based on UEI levels, 68.2% of subjects was included as low UEI levels and 31.8% of subjects as normal UEI levels.

Based on table 2, this study provides findings that education was a risk factor for IDD seen from TSH levels (p value 0,015; OR 0,169; CI OR 0,040:0,709). The results of multivariate analysis in table 3 showed that education was the strongest risk factor for the incidence of IDD seen from TSH levels (p value 0,020; OR adjusted 0,324; CI OR 0,125:0,835).

Risk factors of IDD based on UEI levels can be seen in tables 4 and 5. Based on table 4, this study provided that there were no independent variables as risk factors of IDD. However, after adjusted of age, education, MUAC, gestational age, media information, pregnancy knowledge, nutritional knowledge, nutritional attitudes, IDD attitudes and food intake variables with multivariate analysis, table 5 showed that IDD knowledge was the strongest risk factor for IDD based on UEI (p value 0,008; OR adjusted 4,776; CI OR 1,510:15,105).

4. Discussion

Iodine is an essential element that the body needs to produce thyroid hormone. Iodine deficiency can cause thyroid swelling, hypothyroidism and intellectual disability in infants and children whose mothers were deficient in iodine during pregnancy. Measurement of UIE levels is one method for measuring the adequacy of iodine in the blood because about 90% of the iodine in the body will be excreted through urine (Mutalazimah *et al*., 2013). This study in second and third trimester pregnant women showed that 68.2% of pregnant women had low UIE levels. In addition, the clinical diagnosis of IDD can be seen by the level of thyroid stimulating hormone (TSH) (Chaker *et al*., 2017). This study

showed 53.4% of pregnant women had high TSH levels and 46.6% of pregnant women had low TSH levels. The percentage of pregnant women with IDD in this study was much higher than the previous study in Magelang which showed that 17.1% of pregnant women in endemic areas of goiter experienced hypothyroidism and 19.2% of pregnant women in non-endemic areas of goiter experienced hypothyroidism (Kusrini *et al*., 2016). Although this study was conducted in the coastal area of Jepara which is a salt-producing area, but the prevalence of pregnant women with low iodine adequacy is still high. This is in contrast to previous studies which showed the prevalence of low UIE levels in coastal areas only 5.9% of subjects (Kurniangga, 2016). However, previous studies in the same area such as Mayong, Batealit and Pakis Aji, Jepara Regency, mentioned the availability of iodized salt with levels of 30 ppm is only 20 – 30% (Widiyatni *et al*., 2016). This may be the reason for low iodine adequacy in subjects.

This study was dominated by the age of 20-35 years, about 79.5% of the total subjects. Previous literature showed that the age of pregnant women with the lowest risk is when the mother is 20 – 30 years old compared to younger or older ages (Bellieni, 2016). Previous research has shown that pregnant women giving birth at the age of <20 years or >34 years have a higher risk of having a child born with low birth weight compared to 20-34 years old (Mubasyiroh *et al*., 2016). This study shows that age has not been a risk factor for IDD either based on UIE levels or TSH levels because $p > 0.05$. Although not yet a significant risk factor, all pregnant women aged < 20 years had high TSH levels and 66.7% of pregnant women aged > 35 years had high TSH levels. This is in line with previous studies showing age was not a risk factor for hypothyroidism in pregnancy. That study also showed that the peak of the increase in TSH levels occurred in pregnant women aged over 35 years (Potlukova *et al*., 2012). IDD can strike at various ages, genders and races. However, IDD is known to be most common in women after menopause due to various hormonal changes in the body (Sharma, 2018).

Based on this study, parity has not been a risk factor for IDD status based on UIE levels and TSH levels in pregnant women. This study is in line with research in Lithuania which showed that parity had no relationship with hypothyroidism (Dauksiene *et al*., 2017). However, this study contradicted previous studies which stated that there was an association between parity and an increase in thyroid volume. However, the study stated that the relationship only occurred in pregnant women who smoked. Smoking may affect the thyroid by inhibiting the absorption of iodine (Knudsen *et al*., 2002). Therefore, there is a need for further research that examines the risk of pregnant women who smoke both passively and actively with the incidence of IDD.

Measurement of the nutritional status of pregnant women in this study used Mid-Upper Arm Circumference (MUAC). Previous research has shown that MUAC is a good predictor of the risk of low birth weight compared to other anthropometric measurements. Pregnant women with MUAC < 23.5 cm have a risk of experiencing chronic energy deficiency (Tejayanti, 2020). This study showed that 77.3% of pregnant women had normal nutritional status. However, this study has not shown that nutritional status is a risk factor for the incidence of IDD based on UIE levels and TSH levels in pregnant women. This is contrary to previous studies which stated that MUAC had a negative relationship with the size of the thyroid gland. The study raised concerns about the impact of chronic energy deficiency not on the development of the thyroid gland, but on the brain development of the fetus and neonate. Although in this study did not directly being measured, the risk of small MUAC being left unchecked would have the potential to have an impact on fetal and new born brain development (Brahmbhatt *et al*., 2001).

This study was dominated by the third trimester of pregnancy, which was 79.5% of the total subjects. This study has not shown gestational age to be a risk factor for IDD, both in terms of UIE levels and TSH levels in pregnant women. Although not yet a significant risk factor, the percentage of pregnant women with IDD status based on TSH levels was higher in the third trimester than in the second

trimester, which was 54.7%. IDD status based on UIE levels also shows that the percentage of pregnant women in the third trimester was more IDD than second trimester. Previous research in Mexico showed that the average TSH level was higher in third trimester pregnant women compared to first and second trimester (Bocos-Terraz *et al*., 2009). During the first trimester, there was an increase blood flow and glomerular filtration so that iodine in the urine is lost. During the second trimester, TSH levels return to normal and the fetus begins to produce its own thyroid hormone. However, during the third trimester of pregnancy, thyroid hormone-dependent neurogenesis is still ongoing, so iodine deficiency that occurs early in pregnancy may be difficult to treat. Previous studies have shown that pregnant women with iodine deficiency in the third trimester are more at risk of premature birth and low birth weight babies due to restriction of fetal growth and low thyroid hormone production (Candido *et al*., 2020).

Based on this study, 52.3% of the subjects had low education. Multivariate analysis on this study showed that education was the strongest risk factor for IDD as seen from the TSH level of pregnant women. This study also showed that mothers with insufficient education were 0.324x more at risk experiencing IDD than mothers with sufficient education. This is in contrast to previous research which showed that households with highly educated heads and wives were more likely to use iodized salt than families with low levels of education. That study stated that individual education can affect behavior in society, including consumption of iodized salt (Nadimin, 2015). Although the majority of pregnant women in this study had low education, 97.7% of pregnant women had sufficient knowledge related to pregnancy, 53.4% of pregnant women had sufficient knowledge related to nutrition and 60.2% of pregnant women have sufficient IDD knowledge. This study showed that 62.5% of pregnant women had good media information and 89.9% had good family support. Previous research showed that watching the media and sources of information both shown risk to knowledge and perception of the disease (Karasneh *et al*., 2020). Multivariate analysis on this study also showed that knowledge of

IDD was the strongest risk factor for IDD based on UIE levels. Pregnant women with insufficient knowledge of IDD were 4,776x more at risk of experiencing IDD that pregnant women with sufficient knowledge of IDD. This study showed that 82.9% of pregnant women with insufficient IDD knowledge had less UIE levels. Knowledge is a factor from within to shape one's actions. Sufficient knowledge related to IDD in pregnant women is known to increase awareness of iodized salt intake and how to store iodized salt properly (Sudarto, 2017).

Sufficient knowledge from pregnant women must be balanced with good attitudes both in pregnancy and family health. This study showed that the majority of pregnant women had good attitudes during pregnancy (94.3%), nutritional attitudes (68.2%) and IDD attitudes (83%). However, this study did not show mother's attitude to be a risk factor for IDD. This is in line with research in Iran which showed that attitude is not a risk factor for IDD based on UEI levels. The study also mentioned that the mother's practices related to the fulfillment of low iodine 2.5 times the risk of IDD (Mirmiran *et al*., 2013). Although it has not been statistically proven, this study showed that the percentage of pregnant women experience IDD was higher in pregnant women with less attitudes. Therefore, the mother's attitude towards pregnancy, nutrition and IDD needs to be followed by good daily practices as well.

This study showed that the overall intake of macronutrients and micronutrients has not been a risk factor for IDD both based on TSH levels and UIE levels. This is contrary to research in Brazil which stated that a gluten-free diet with the provision of minerals and vitamins can increase thyroid level and reverting subclinical hypothyroidism. Hypothyroidism itself can cause disturbances in the intestinal tract, which causes problems with bowel movements (Mezzomo and Nadal, 2016). Therefore, adequate intake of water and fiber is necessary for pregnant women. In addition, stress management and behavioral interventions such as weight management, a balanced diet and a healthy home environment are known to aid in recovery from thyroid disease (Ihnatowicz *et al*., 2020).

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5. Conclusion

There were 53.4% of pregnant women from all research subjects in the Mlonggo Health Center and Pakis Aji Health Center, Jepara who had high TSH levels and 68.2% of pregnant women had low UIE levels. This study showed that education was the strongest risk factor for IDD (TSH level) and knowledge of IDD was the strongest risk factor for IDD (UIE level).

Conflict of interest

The authors declare no conflict of interest.

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Tables

Table 1. Distribution of subject characteristics

Variables	Frequency	
	n	%
TSH* levels (mIU/ L)		
Normal	41	46.6
High	47	53.4
UIE** levels (µg/L)		
Nomal	28	31.8
Low	60	68.2
Age		
>35 years old	15	17.0
20-35 years old	70	79.5
<20 years	3	3.4
Parity		
P<4	87	98.9
P=>4	1	1.0
Mother's education		
Sufficient	42	47.7
Insufficient	46	52.3
Mid-Upper Arm Circumference		
Normal	68	77.3
Small	20	22.7
Gestational age		
Third trimester	64	72.7
Second trimester	24	27.3
Family's support		
Good	79	89.8
Bad	9	10.2
Media information		
Good	55	62.5
Bad	33	37.5
Pregnancy knowledge		
Sufficient	86	97.7
Insufficient	2	2.3
Nutrition knowledge		
Sufficient	47	53.4
Insufficient	41	46.6
Iodine Deficiency Disease Knowledge		
Sufficient	53	60.2
Insufficient	35	39.8
Pregnancy attitude		
Sufficient	83	94.3
Insufficient	5	5.7
Nutrition attitude		

Sufficient	60	68.2
Insufficient	28	31.8
Iodine Deficiency Disease attitude		
Sufficient	73	83.0
Insufficient	15	17.0
Energy intake		
Excessive (>100%)	8	9.1
Adequate (80-100%)	48	54.5
Inadequate (<80%)	32	36.4
Carbohydrate intake		
Excessive (>100%)	33	37.5
Adequate (80-100%)	28	31.8
Inadequate (<80%)	27	30.7
Protein intake		
Excessive (>100%)	4	4.5
Adequate (80-100%)	16	18.2
Inadequate (<80%)	68	77.3
Fat intake		
Excessive (>100%)	15	17.0
Adequate (80-100%)	32	36.4
Inadequate (<80%)	41	46.6
Fiber intake		
Excessive (>100%)	1	1.1
Inadequate (<80%)	87	98.9
Vitamin C intake		
Excessive (>100%)	26	29.5
Adequate (80-100%)	16	18.2
Inadequate (<80%)	46	52.3
Magnesium intake		
Excessive (>100%)	18	20.5
Adequate (80-100%)	33	37.5
Inadequate (<80%)	37	42.0
Mangan intake		
Excessive (>100%)	82	93.2
Adequate (80-100%)	6	6.8

*TSH = Thyroid Stimulating Hormone

**UIE = Urinary Iodine Excretion

337 Table 2. Full models of risk factors for Iodine Deficiency Disease (IDD) based on Thyroid Stimulating
338 Hormone (TSH) levels

Variables	Thyroid Stimulating Hormone (TSH)				p	OR	95% CI for OR	
	High		Normal					
	n	%	n	%			Lower	Upper
Age								
>35 years old	10	66.7	5	33.3	Reference			
20-35 years old	34	48.6	36	51.4	0.100	0.264	0.054	1.290
<20 years	3	100	0	0	0.999	67101 70064 37299 580	<0.001	<0.001
Parity								
P<4	46	52.9	41	47.1	Reference			
P=>4	1	100	0	0	1	26993 89903. 446	<0.001	<0.001
Mother's education								
Sufficient	26	61.90	16	38.10	Reference			
Insufficient	21	45.65	25	54.35	0.015	0.169	0.040	0.709
Mid-Upper Arm Circumference								
Normal	38	55.9	30	44.1	Reference			
Small	9	45	11	55	0.547	0.630	0.140	2.837
Gestational age								
Third trimester	35	54.7	29	45.3	Reference			
Second trimester	12	50	12	50	0.054	0.242	0.057	1.022
Family's support								
Good	40	50.6	39	49.4	Reference			
Bad	7	77.8	2	22.2	0.402	2.475	0.297	20.634
Media information								
Good	25	45.5	30	54.5	Reference			
Bad	22	66.7	11	33.3	0.493	1.548	0.444	5.403
Pregnancy knowledge								
Sufficient	46	53.5	40	46.5	Reference			
Insufficient	1	50	1	50	0.999	<0.001	<0.001	<0.001
Nutrition knowledge								
Sufficient	25	53.2	22	46.8	Reference			
Insufficient	22	53.7	19	46.3	0.527	1.493	0.431	5.177
Iodine Deficiency Disease Knowledge								
Sufficient	30	56.6	23	43.4	Reference			
Insufficient	17	48.6	18	51.4	0.554	1.475	0.407	5.346
Pregnancy attitude								
Sufficient	44	53	39	47	Reference			
Insufficient	3	60	2	40	0.957	1.069	0.094	12.175

Nutrition attitude								
Sufficient	33	55	27	45	Reference			
Insufficient	14	50	14	50	0.473	0.637	0.186	2.180
Iodine Deficiency Disease attitude								
Sufficient	38	52	35	48	Reference			
Insufficient	9	60	6	40	0.698	1.361	0.287	6.443
Energy intake								
Excessive (>100%)	5	62.5	3	37.5	Reference			
Adequate (80-100%)	26	54.2	22	45.8	0.927	0.876	0.051	15.160
Inadequate (<80%)	16	50	16	50	0.960	0.913	0.025	33.404
Carbohydrate intake								
Excessive (>100%)	19	57.6	14	42.4	Reference			
Adequate (80-100%)	13	46.4	15	53.6	0.447	0.502	0.085	2.967
Inadequate (<80%)	15	55.6	12	44.4	0.569	0.437	0.025	7.517
Protein intake								
Excessive (>100%)	3	75	1	25	Reference			
Adequate (80-100%)	9	56.3	7	43.8	0.484	0.297	0.010	8.882
Inadequate (<80%)	35	51.5	33	48.5	0.647	0.377	0.006	24.557
Fat intake								
Excessive (>100%)	8	53.3	7	46.7	Reference			
Adequate (80-100%)	20	62.5	12	37.5	0.582	1.657	0.257	9.999
Inadequate (<80%)	19	46.3	22	53.7	0.764	1.335	0.203	8.784
Fiber intake								
Excessive (>100%)	1	100	0	0	Reference			
Inadequate (<80%)	46	52.9	41	47.1	1	<0.001	<0.001	<0.001
Vitamin C intake								
Excessive (>100%)	14	53.8	12	46.2	Reference			
Adequate (80-100%)	10	62.5	6	37.5	0.058	5.944	0.938	37.657
Inadequate (<80%)	23	50	23	50	0.272	2.441	0.496	12.014
Magnesium intake								
Excessive (>100%)	12	66.7	6	33.3	Reference			
Adequate (80-100%)	17	51.5	16	48.5	0.766	1.441	0.130	15.987
Inadequate (<80%)	18	48.6	19	51.4	0.833	0.752	0.053	10.644
Mangan intake								
Excessive (>100%)	43	52.4	39	47.6	Reference			
Adequate (80-100%)	4	66.7	2	33.3	0.345	2.935	0.315	27.361

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340

341 Table 3. Fix models of risk factors for Iodine Deficiency Disease (IDD) based on Thyroid Stimulating
342 Hormone (TSH) levels

Variables	p	OR adjusted	95% CI for OR	
			Lower	Upper
Age				
>35 years old	Reference			
20-35 years old	0.164	0.419	0.123	1.426
<20 years	0.999	702462842.485	<0.001	<0.001
Mother's education				
Sufficient	Reference			
Insufficient	0.020	0.324	0.125	0.835
Media information				
Good	Reference			
Bad	0.066	2.533	0.941	6.760

343

344

345 Table 4. Full models of risk factors for Iodine Deficiency Disease (IDD) based on Urinary Iodine Excretion
346 (UIE)

Variables	Urinary Iodine Excretion (UIE)				p	OR	95% CI for OR	
	Low		Normal					
	n	%	n	%			Lower	Upper
Age								
>35 years old	8	53.33	7	46.67	Reference			
20-35 years old	50	71.43	20	28.57	0.753	1.345	0.212	8.544
<20 years	2	66.67	1	33.33	0.343	0.153	0.003	7.386
Parity								
P<4	60	68.97	27	31.03	Reference			
P=>4	0	0.00	1	100.0	1	<0.001	<0.001	<0.001
Mother's education								
Sufficient	27	64.29	15	35.71	Reference			
Insufficient	33	71.74	13	28.26	0.518	1.685	0.346	8.202
Mid-Upper Arm Circumference								
Normal	46	67.65	22	32.35	Reference			
Small	14	70.00	6	30.00	0.551	1.666	0.311	8.923
Gestational age								
Third trimester	46	71.88	18	28.13	Reference			
Second trimester	14	58.33	10	41.67	0.223	0.378	0.079	1.806
Family's support								
Good	3	33.3	6	66.7	Reference			
Bad	57	72.2	22	27.8	0.067	0.133	0.015	1.151
Media information								
Good	37	67.3	18	32.7	Reference			
Bad	23	69.7	10	30.3	0.252	2.361	0.543	10.257
Pregnancy knowledge								
Sufficient	58	67.4	28	32.6	Reference			
Insufficient	2	100	0	0	0.999	32254 23349.734	<0.001	<0.001
Nutrition knowledge								
Sufficient	31	65.96	16	34.04	Reference			
Insufficient	29	70.73	12	29.27	0.911	1.088	0.249	4.747
Iodine Deficiency Disease Knowledge								
Sufficient	31	58.49	22	41.51	Reference			
Insufficient	29	82.86	6	17.14	0.078	4.602	0.841	25.168
Pregnancy attitude								
Sufficient	55	66.4	28	33.7	Reference			
Insufficient	5	100	0	0	0.999	<0.001	<0.001	<0.001
Nutrition attitude								
Sufficient	42	70	18	30	Reference			
Insufficient	18	64.3	10	35.7	0.216	0.378	0.081	1.764

Iodine Deficiency Disease attitude								
Sufficient	48	65.8	25	34.2	Reference			
Insufficient	12	80	3	20	0.879	1.168	0.158	8.636
Energy intake								
Excessive (>100%)	4	50.00	4	50.00	Reference			
Adequate (80-100%)	35	72.92	13	27.08	0.510	2.798	0.131	59.842
Inadequate (<80%)	21	65.63	11	34.38	0.554	0.301	0.006	16.021
Carbohydrate intake								
Excessive (>100%)	21	63.64	12	36.36	Reference			
Adequate (80-100%)	20	71.43	8	28.57	0.922	0.903	0.117	7.002
Inadequate (<80%)	19	70.37	8	29.63	0.464	3.572	0.118	108.079
Protein intake								
Excessive (>100%)	2	50.00	2	50.00	Reference			
Adequate (80-100%)	9	56.25	7	43.75	0.913	1.277	0.016	103.689
Inadequate (<80%)	49	72.06	19	27.94	0.646	3.294	0.020	531.651
Fat intake								
Excessive (>100%)	10	66.67	5	33.33	Reference			
Adequate (80-100%)	22	68.75	10	31.25	0.736	0.666	0.063	7.074
Inadequate (<80%)	28	68.29	13	31.71	0.321	0.279	0.023	3.459
Fiber intake								
Excessive (>100%)	1	100.0	0	0.00	Reference			
Inadequate (<80%)	59	67.82	28	32.18	1	<0.001	<0.001	<0.001
Vitamin C intake								
Excessive (>100%)	18	69.23	8	30.77	Reference			
Adequate (80-100%)	10	62.50	6	37.50	0.241	0.306	0.042	2.217
Inadequate (<80%)	32	69.57	14	30.43	0.804	1.265	0.199	8.054
Magnesium intake								
Excessive (>100%)	11	61.11	7	38.89	Reference			
Adequate (80-100%)	23	69.70	10	30.30	0.754	1.582	0.089	27.962
Inadequate (<80%)	26	70.27	11	29.73	0.691	1.881	0.063	42.427
Mangan intake								
Excessive (>100%)	57	69.5	25	30.5	Reference			
Adequate (80-100%)	3	50	3	50	0.347	0.279	0.020	3.988

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Table 5. Fix models of risk factors for Iodine Deficiency Disease (IDD) based on Urinary Iodine Excretion (UIE)

Variables	p	OR adjusted	95% CI for OR	
			Lower	Upper
Parity				
P<4	*Reference*			
P=>4	1	<0.001	<0.001	<0.001
Family's support				
Good	*Reference*			
Bad	0.037	0.185	0.038	0.906
Iodine Deficiency Disease Knowledge				
Sufficient	*Reference*			
Insufficient	0.008	4.776	1.510	15.105
Pregnancy attitude				
Sufficient	*Reference*			
Insufficient	0.999	<0.001	<0.001	<0.001

Risk factors for disorders due to iodine deficiency (IDD) among pregnant women in Jepara

Abstract

Pregnant women need an increase for iodine intake. In 2013, 24.3% of pregnant women in Indonesia had low iodine excretion values. Iodine is known to affect thyroid hormone regulation. This study aimed to analyze risk factors of Iodine Deficiency Disease (IDD) in pregnant women. This study was conducted using an observational method with a case control design. The subjects in this study were pregnant women in the 2nd and 3rd trimesters in the Mlonggo and Pakis Aji Health Centers, Jepara Regency. The total sample was 88 pregnant women. Primary data collection was done by taking urine for Urinary Iodine Excretion (UIE) and blood serum for Thyroid Stimulating Hormone (TSH) levels, anthropometric measurements for nutritional status and filling out questionnaires related to subject characteristics and interviews related to intake. This study showed that 53.4% of pregnant women had high TSH levels and 68.2% pregnant women had low UIE levels. The results of the multivariate analysis showed that education was the strongest risk factor of IDD based on TSH levels (p value 0,020; OR *adjusted* 0,324; CI OR 0,125:0,835) and knowledge of IDD was the strongest risk factor of IDD based on UIE levels (p value 0,008; OR *adjusted* 4,776; CI OR 1,510:15,105).

Keywords: Pregnant women, Iodine, Thyroid stimulating hormone

1. Introduction

Iodine is an essential micronutrient for the formation of thyroid hormones in the body. Thyroid hormone plays an important role in various functions such as basal metabolism, heart rate and bone growth and the central nervous system (González-Martínez *et al.*, 2021). Pregnant women are known to experience an increase in the size of thyroid gland by 10% and an increase in thyroid hormone production by 50%, causing the need for iodine in the pregnant women increases (Alexander *et al.*,

Commented [U1]: Please add what country is Jepara

Commented [U2]: Mention the country

Commented [U3]: Add MUAC as the variable

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2017). The need for iodine in adults is about 150 g/day. The World Health Organization (WHO) recommends a higher intake of iodine in pregnant women, which is 250 g/day. Deficiency of iodine intake is thought to be the main cause of hypothyroidism and Iodine Deficiency Disorders (IDD) (Taylor and Lazarus, 2019).

Based on the 2013 RISKESDAS data, the prevalence of pregnant women in Indonesia with Urinary Iodine Excretion (UIE) <100 g/L was 24.3%. One of the causes of the problem was 50.8% of household salt in Indonesia has a low level of iodine. Therefore, household coverage with iodized salt consumption can't be an indicator of the fulfilment of iodine intake (Kementrian Kesehatan Republik Indonesia, 2015).

Examination of urinary iodine excretion (UIE) in 2007 until 2012 in Jepara Regency showed that several sub-districts including as IDD endemic areas such as Mayong, Batealit and Pakis Aji (Widiyatni and Subagio, 2016). Apart from UIE levels, IDD status can also be seen from Thyroid Stimulating Hormone (TSH) levels. If thyroid hormone production is insufficient, there will be an increase in TSH production (Kementrian Kesehatan Republik Indonesia, 2015). Research in Magelang showed 17.1% of pregnant women in goiter replete areas had high TSH levels and 19.2% of pregnant women in non-replete goiter areas had high TSH levels (Kusrini *et al*., 2016). Screening to see the adequacy of iodine in the body is very important for pregnant women as an indicator to detect the occurrence of IDD.

The incidence of IDD that not handled properly during pregnancy can cause premature birth, intrauterine growth disorders, fetal death, impaired fetal development, respiratory disorders and increased perinatal mortality. This is because iodine is needed by thyroid hormone for the growth and formation of vital organs of the fetus (Animal Welfare Branch, 2007). Adequacy of iodine in the mother is very important to prevent hypothyroidism in the fetus. During the early stages of pregnancy, the fetus is still dependent on the mother's thyroid hormone production. During midterm pregnancy, the fetus begins to produce its own thyroid hormone but still requires iodine intake from the mother

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(Khadilkar, 2019). Based on data from Cipto Mangunkusumo Hospital in Jakarta and Hasan Sadikin Hospital in Bandung around 2014, 1 from 2513 newborns had congenital hypothyroidism. This prevalence was higher than global data, which is 1 in 3000 newborns (Kementrian Kesehatan Republik Indonesia, 2015).

Apart from iodine, many other nutrients are risk factors for IDD. Malnutrition is known to cause thyroid disorders. Research in 2017 showed that there was a positive correlation between TSH and Body Mass Index (BMI) in female (Singh *et al*., 2020). However, other studies stated that there was no significant difference in BMI in hypothyroid patients (Ranabir *et al*., 2019). Deficiency of macronutrient elements such as protein and micronutrient elements such as iron, selenium and zinc are known to interfere with thyroid gland function. Previous studies have stated that hypothyroidism can occur among moderate to severe iron deficient (El-Masry *et al*., 2018). Research in Magelang showed that the prevalence of pregnant women with iodine deficiency was higher in the third trimester than in the previous trimester (Kusrini *et al*., 2016). However, another study in Korea showed that the lowest TSH levels occurred in women in third trimester of pregnancy (Kim *et al*., 2015).

IDD in pregnant women is a problem that can have an impact not only on the mother but also on the fetus. Fetuses with mothers who have IDD are at risk of inhibiting fetal development. Based on the description above, researchers are interested in knowing the risk factors of IDD among pregnant women.

2. Materials and methods

This research was carried out using an observational method with a case control study design. The subjects in this study were pregnant women in the second and third trimesters in the Mlonggo Health Center and Pakis Aji Health Center, Jepara Regency. The sampling technique was carried out with cluster sampling and total sample obtained was 88 pregnant women. The subjects were willing to

Commented [U7]: Please explain the ethical clearance to conduct this survey

Commented [U8]: explain case control based on UIE, TSH or others?

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participate in the study by filling the informed consent form. This study aimed to determine the risk factors for the incidence of IDD seen from UIE and TSH status among pregnant women.

Primary data were collected by taking urine sample for UIE levels, blood serum for TSH levels, anthropometric measurements for nutritional status, filling out questionnaires related to subject characteristics and interviewing subjects related to food intake. The research instrument used a Semi Quantitative Food Frequency Questionnaire (SQ-FFQ) for food intake, Mid-Upper Arm Circumference (MUAC) tape to measure nutritional status, measurement of UIE levels using urine sample with Acid Digestion method and measurement of TSH levels using whole blood serum with Enzyme Linked Immunosorbent Assay (ELISA) method. Pregnant women with MUAC < 23.5 cm included as poor nutritional status and pregnant women with MUAC ≥ 23.5 cm included as normal nutritional status (Tejayanti, 2020). The food intake of pregnant women was divided into 3 groups, namely inadequate (<80%), sufficient (80-100%) and excessive (>100%) (Yunitasari *et al*., 2019). Pregnant women in the second trimester were in the range of 13-27 weeks and the third trimester were more than 27 weeks. UIE levels were less if < 150 g/L and normal if 150 g/L (WHO (World Health Organization), 2013). Categorization of TSH levels based on gestational age, normal category if TSH values in the first trimester were 0.1-2.5 mIU/L, second trimester were 0.2 -3.0 mIU/L and third trimester were 0.3-3.0mIU/L (Green *et al*., 2011).

Univariate analysis was used on one variable with the aim of knowing and identifying the frequency distribution and characteristics of each variable. Bivariate analysis was to determine the risk (odds ratio) of exposure to cases by using the Chi Square test formula with 95% confidence level. Multivariate analysis was to determine the strongest risk factors of IDD by using logistic regression analysis.

3. Results

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Commented [U12]: Use food consumption instead of intake

The number of subjects obtained in the study at the Mlonggo Health Center and the Pakis Aji Health Center, Jepara Regency, as many as 88 subjects with varying ages from 18 to 41 years. The following characteristics of the subject were shown in table 1.

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This study showed that the number of subjects with high TSH levels was more than subjects with normal TSH (53.4%). While based on UEI levels, 68.2% of subjects was included as low UEI levels and 31.8% of subjects as normal UEI levels.

Based on table 2, this study provides findings that education was a risk factor for IDD seen from TSH levels (p value 0,015; OR 0,169; CI OR 0,040:0,709). The results of multivariate analysis in table 3 showed that education was the strongest risk factor for the incidence of IDD seen from TSH levels (p value 0,020; OR adjusted 0,324; CI OR 0,125:0,835).

Risk factors of IDD based on UEI levels can be seen in tables 4 and 5. Based on table 4, this study provided that there were no independent variables as risk factors of IDD. However, after adjusted of age, education, MUAC, gestational age, media information, pregnancy knowledge, nutritional knowledge, nutritional attitudes, IDD attitudes and food intake variables with multivariate analysis, table 5 showed that IDD knowledge was the strongest risk factor for IDD based on UEI (p value 0,008; OR adjusted 4,776; CI OR 1,510:15,105).

4. Discussion

Iodine is an essential element that the body needs to produce thyroid hormone. Iodine deficiency can cause thyroid swelling, hypothyroidism and intellectual disability in infants and children whose mothers were deficient in iodine during pregnancy. Measurement of UIE levels is one method for measuring the adequacy of iodine in the blood because about 90% of the iodine in the body will be excreted through urine (Mutalazimah *et al*., 2013). This study in second and third trimester pregnant women showed that 68.2% of pregnant women had low UIE levels. In addition, the clinical diagnosis of IDD can be seen by the level of thyroid stimulating hormone (TSH) (Chaker *et al*., 2017). This study

showed 53.4% of pregnant women had high TSH levels and 46.6% of pregnant women had low TSH levels. The percentage of pregnant women with IDD in this study was much higher than the previous study in Magelang which showed that 17.1% of pregnant women in endemic areas of goiter experienced hypothyroidism and 19.2% of pregnant women in non-endemic areas of goiter experienced hypothyroidism (Kusrini *et al*., 2016). Although this study was conducted in the coastal area of Jepara which is a salt-producing area, but the prevalence of pregnant women with low iodine adequacy is still high. This is in contrast to previous studies which showed the prevalence of low UIE levels in coastal areas only 5.9% of subjects (Kurniangga, 2016). However, previous studies in the same area such as Mayong, Batealit and Pakis Aji, Jepara Regency, mentioned the availability of iodized salt with levels of 30 ppm is only 20 – 30% (Widiyatni *et al*., 2016). This may be the reason for low iodine adequacy in subjects.

This study was dominated by the age of 20-35 years, about 79.5% of the total subjects. Previous literature showed that the age of pregnant women with the lowest risk is when the mother is 20 – 30 years old compared to younger or older ages (Bellieni, 2016). Previous research has shown that pregnant women giving birth at the age of <20 years or >34 years have a higher risk of having a child born with low birth weight compared to 20-34 years old (Mubasyiroh *et al*., 2016). This study shows that age has not been a risk factor for IDD either based on UIE levels or TSH levels because $p > 0.05$. Although not yet a significant risk factor, all pregnant women aged < 20 years had high TSH levels and 66.7% of pregnant women aged > 35 years had high TSH levels. This is in line with previous studies showing age was not a risk factor for hypothyroidism in pregnancy. That study also showed that the peak of the increase in TSH levels occurred in pregnant women aged over 35 years (Potlukova *et al*., 2012). IDD can strike at various ages, genders and races. However, IDD is known to be most common in women after menopause due to various hormonal changes in the body (Sharma, 2018).

Based on this study, parity has not been a risk factor for IDD status based on UIE levels and TSH levels in pregnant women. This study is in line with research in Lithuania which showed that parity had no relationship with hypothyroidism (Dauksiene *et al*., 2017). However, this study contradicted previous studies which stated that there was an association between parity and an increase in thyroid volume. However, the study stated that the relationship only occurred in pregnant women who smoked. Smoking may affect the thyroid by inhibiting the absorption of iodine (Knudsen *et al*., 2002). Therefore, there is a need for further research that examines the risk of pregnant women who smoke both passively and actively with the incidence of IDD.

Measurement of the nutritional status of pregnant women in this study used Mid-Upper Arm Circumference (MUAC). Previous research has shown that MUAC is a good predictor of the risk of low birth weight compared to other anthropometric measurements. Pregnant women with MUAC < 23.5 cm have a risk of experiencing chronic energy deficiency (Tejayanti, 2020). This study showed that 77.3% of pregnant women had normal nutritional status. However, this study has not shown that nutritional status is a risk factor for the incidence of IDD based on UIE levels and TSH levels in pregnant women. This is contrary to previous studies which stated that MUAC had a negative relationship with the size of the thyroid gland. The study raised concerns about the impact of chronic energy deficiency not on the development of the thyroid gland, but on the brain development of the fetus and neonate. Although in this study did not directly being measured, the risk of small MUAC being left unchecked would have the potential to have an impact on fetal and new born brain development (Brahmbhatt *et al*., 2001).

This study was dominated by the third trimester of pregnancy, which was 79.5% of the total subjects. This study has not shown gestational age to be a risk factor for IDD, both in terms of UIE levels and TSH levels in pregnant women. Although not yet a significant risk factor, the percentage of pregnant women with IDD status based on TSH levels was higher in the third trimester than in the second

trimester, which was 54.7%. IDD status based on UIE levels also shows that the percentage of pregnant women in the third trimester was more IDD than second trimester. Previous research in Mexico showed that the average TSH level was higher in third trimester pregnant women compared to first and second trimester (Bocos-Terraz *et al*., 2009). During the first trimester, there was an increase blood flow and glomerular filtration so that iodine in the urine is lost. During the second trimester, TSH levels return to normal and the fetus begins to produce its own thyroid hormone. However, during the third trimester of pregnancy, thyroid hormone-dependent neurogenesis is still ongoing, so iodine deficiency that occurs early in pregnancy may be difficult to treat. Previous studies have shown that pregnant women with iodine deficiency in the third trimester are more at risk of premature birth and low birth weight babies due to restriction of fetal growth and low thyroid hormone production (Candido *et al*., 2020).

Based on this study, 52.3% of the subjects had low education. Multivariate analysis on this study showed that education was the strongest risk factor for IDD as seen from the TSH level of pregnant women. This study also showed that mothers with insufficient education were 0.324x more at risk experiencing IDD than mothers with sufficient education. This is in contrast to previous research which showed that households with highly educated heads and wives were more likely to use iodized salt than families with low levels of education. That study stated that individual education can affect behavior in society, including consumption of iodized salt (Nadimin, 2015). Although the majority of pregnant women in this study had low education, 97.7% of pregnant women had sufficient knowledge related to pregnancy, 53.4% of pregnant women had sufficient knowledge related to nutrition and 60.2% of pregnant women have sufficient IDD knowledge. This study showed that 62.5% of pregnant women had good media information and 89.9% had good family support. Previous research showed that watching the media and sources of information both shown risk to knowledge and perception of the disease (Karasneh *et al*., 2020). Multivariate analysis on this study also showed that knowledge of

IDD was the strongest risk factor for IDD based on UIE levels. Pregnant women with insufficient knowledge of IDD were 4,776x more at risk of experiencing IDD that pregnant women with sufficient knowledge of IDD. This study showed that 82.9% of pregnant women with insufficient IDD knowledge had less UIE levels. Knowledge is a factor from within to shape one's actions. Sufficient knowledge related to IDD in pregnant women is known to increase awareness of iodized salt intake and how to store iodized salt properly (Sudarto, 2017).

Sufficient knowledge from pregnant women must be balanced with good attitudes both in pregnancy and family health. This study showed that the majority of pregnant women had good attitudes during pregnancy (94.3%), nutritional attitudes (68.2%) and IDD attitudes (83%). However, this study did not show mother's attitude to be a risk factor for IDD. This is in line with research in Iran which showed that attitude is not a risk factor for IDD based on UEI levels. The study also mentioned that the mother's practices related to the fulfillment of low iodine 2.5 times the risk of IDD (Mirmiran *et al*., 2013). Although it has not been statistically proven, this study showed that the percentage of pregnant women experience IDD was higher in pregnant women with less attitudes. Therefore, the mother's attitude towards pregnancy, nutrition and IDD needs to be followed by good daily practices as well.

This study showed that the overall intake of macronutrients and micronutrients has not been a risk factor for IDD both based on TSH levels and UIE levels. This is contrary to research in Brazil which stated that a gluten-free diet with the provision of minerals and vitamins can increase thyroid level and reverting subclinical hypothyroidism. Hypothyroidism itself can cause disturbances in the intestinal tract, which causes problems with bowel movements (Mezzomo and Nadal, 2016). Therefore, adequate intake of water and fiber is necessary for pregnant women. In addition, stress management and behavioral interventions such as weight management, a balanced diet and a healthy home environment are known to aid in recovery from thyroid disease (Ihnatowicz *et al*., 2020).

5. Conclusion

There were 53.4% of pregnant women from all research subjects in the Mlonggo Health Center and Pakis Aji Health Center, Jepara who had high TSH levels and 68.2% of pregnant women had low UIE levels. This study showed that education was the strongest risk factor for IDD (TSH level) and knowledge of IDD was the strongest risk factor for IDD (UIE level).

Conflict of interest

The authors declare no conflict of interest.

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332 **Tables**

333 Table 1. Distribution of subject characteristics

Variables	Frequency	
	n	%
TSH* levels (mIU/ L)		
Normal	41	46.6
High	47	53.4
UIE** levels (µg/L)		
Nomal	28	31.8
Low	60	68.2
Age		
>35 years old	15	17.0
20-35 years old	70	79.5
<20 years	3	3.4
Parity		
P<4	87	98.9
P=>4	1	1.0
Mother's education		
Sufficient	42	47.7
Insufficient	46	52.3
Mid-Upper Arm Circumference		
Normal	68	77.3
Small	20	22.7
Gestational age		
Third trimester	64	72.7
Second trimester	24	27.3
Family's support		
Good	79	89.8
Bad	9	10.2
Media information		
Good	55	62.5
Bad	33	37.5
Pregnancy knowledge		
Sufficient	86	97.7
Insufficient	2	2.3
Nutrition knowledge		
Sufficient	47	53.4
Insufficient	41	46.6
Iodine Deficiency Disease Knowledge		
Sufficient	53	60.2
Insufficient	35	39.8
Pregnancy attitude		
Sufficient	83	94.3
Insufficient	5	5.7
Nutrition attitude		

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Sufficient	60	68.2
Insufficient	28	31.8
Iodine Deficiency Disease attitude		
Sufficient	73	83.0
Insufficient	15	17.0
Energy intake		
Excessive (>100%)	8	9.1
Adequate (80-100%)	48	54.5
Inadequate (<80%)	32	36.4
Carbohydrate intake		
Excessive (>100%)	33	37.5
Adequate (80-100%)	28	31.8
Inadequate (<80%)	27	30.7
Protein intake		
Excessive (>100%)	4	4.5
Adequate (80-100%)	16	18.2
Inadequate (<80%)	68	77.3
Fat intake		
Excessive (>100%)	15	17.0
Adequate (80-100%)	32	36.4
Inadequate (<80%)	41	46.6
Fiber intake		
Excessive (>100%)	1	1.1
Inadequate (<80%)	87	98.9
Vitamin C intake		
Excessive (>100%)	26	29.5
Adequate (80-100%)	16	18.2
Inadequate (<80%)	46	52.3
Magnesium intake		
Excessive (>100%)	18	20.5
Adequate (80-100%)	33	37.5
Inadequate (<80%)	37	42.0
Mangan intake		
Excessive (>100%)	82	93.2
Adequate (80-100%)	6	6.8

*TSH = Thyroid Stimulating Hormone

**UIE = Urinary Iodine Excretion

Commented [U23]: Same as above

337 Table 2. Full models of risk factors for Iodine Deficiency Disease (IDD) based on Thyroid Stimulating
338 Hormone (TSH) levels

Variables	Thyroid Stimulating Hormone (TSH)				p	OR	95% CI for OR	
	High		Normal					
	n	%	n	%			Lower	Upper
Age								
>35 years old	10	66.7	5	33.3	Reference			
20-35 years old	34	48.6	36	51.4	0.100	0.264	0.054	1.290
<20 years	3	100	0	0	0.999	67101 70064 37299 580	<0.001	<0.001
Parity								
P<4	46	52.9	41	47.1	Reference			
P=>4	1	100	0	0	1	26993 89903. 446	<0.001	<0.001
Mother's education								
Sufficient	26	61.90	16	38.10	Reference			
Insufficient	21	45.65	25	54.35	0.015	0.169	0.040	0.709
Mid-Upper Arm Circumference								
Normal	38	55.9	30	44.1	Reference			
Small	9	45	11	55	0.547	0.630	0.140	2.837
Gestational age								
Third trimester	35	54.7	29	45.3	Reference			
Second trimester	12	50	12	50	0.054	0.242	0.057	1.022
Family's support								
Good	40	50.6	39	49.4	Reference			
Bad	7	77.8	2	22.2	0.402	2.475	0.297	20.634
Media information								
Good	25	45.5	30	54.5	Reference			
Bad	22	66.7	11	33.3	0.493	1.548	0.444	5.403
Pregnancy knowledge								
Sufficient	46	53.5	40	46.5	Reference			
Insufficient	1	50	1	50	0.999	<0.001	<0.001	<0.001
Nutrition knowledge								
Sufficient	25	53.2	22	46.8	Reference			
Insufficient	22	53.7	19	46.3	0.527	1.493	0.431	5.177
Iodine Deficiency Disease Knowledge								
Sufficient	30	56.6	23	43.4	Reference			
Insufficient	17	48.6	18	51.4	0.554	1.475	0.407	5.346
Pregnancy attitude								
Sufficient	44	53	39	47	Reference			
Insufficient	3	60	2	40	0.957	1.069	0.094	12.175

Nutrition attitude								
Sufficient	33	55	27	45	Reference			
Insufficient	14	50	14	50	0.473	0.637	0.186	2.180
Iodine Deficiency Disease attitude								
Sufficient	38	52	35	48	Reference			
Insufficient	9	60	6	40	0.698	1.361	0.287	6.443
Energy intake								
Excessive (>100%)	5	62.5	3	37.5	Reference			
Adequate (80-100%)	26	54.2	22	45.8	0.927	0.876	0.051	15.160
Inadequate (<80%)	16	50	16	50	0.960	0.913	0.025	33.404
Carbohydrate intake								
Excessive (>100%)	19	57.6	14	42.4	Reference			
Adequate (80-100%)	13	46.4	15	53.6	0.447	0.502	0.085	2.967
Inadequate (<80%)	15	55.6	12	44.4	0.569	0.437	0.025	7.517
Protein intake								
Excessive (>100%)	3	75	1	25	Reference			
Adequate (80-100%)	9	56.3	7	43.8	0.484	0.297	0.010	8.882
Inadequate (<80%)	35	51.5	33	48.5	0.647	0.377	0.006	24.557
Fat intake								
Excessive (>100%)	8	53.3	7	46.7	Reference			
Adequate (80-100%)	20	62.5	12	37.5	0.582	1.657	0.257	9.999
Inadequate (<80%)	19	46.3	22	53.7	0.764	1.335	0.203	8.784
Fiber intake								
Excessive (>100%)	1	100	0	0	Reference			
Inadequate (<80%)	46	52.9	41	47.1	1	<0.001	<0.001	<0.001
Vitamin C intake								
Excessive (>100%)	14	53.8	12	46.2	Reference			
Adequate (80-100%)	10	62.5	6	37.5	0.058	5.944	0.938	37.657
Inadequate (<80%)	23	50	23	50	0.272	2.441	0.496	12.014
Magnesium intake								
Excessive (>100%)	12	66.7	6	33.3	Reference			
Adequate (80-100%)	17	51.5	16	48.5	0.766	1.441	0.130	15.987
Inadequate (<80%)	18	48.6	19	51.4	0.833	0.752	0.053	10.644
Mangan intake								
Excessive (>100%)	43	52.4	39	47.6	Reference			
Adequate (80-100%)	4	66.7	2	33.3	0.345	2.935	0.315	27.361

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341 Table 3. Fix models of risk factors for Iodine Deficiency Disease (IDD) based on Thyroid Stimulating
342 Hormone (TSH) levels

Variables	p	OR adjusted	95% CI for OR	
			Lower	Upper
Age				
>35 years old	Reference			
20-35 years old	0.164	0.419	0.123	1.426
<20 years	0.999	702462842.485	<0.001	<0.001
Mother's education				
Sufficient	Reference			
Insufficient	0.020	0.324	0.125	0.835
Media information				
Good	Reference			
Bad	0.066	2.533	0.941	6.760

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345 Table 4. Full models of risk factors for Iodine Deficiency Disease (IDD) based on Urinary Iodine Excretion
346 (UIE)

Variables	Urinary Iodine Excretion (UIE)				p	OR	95% CI for OR	
	Low		Normal					
	n	%	n	%			Lower	Upper
Age								
>35 years old	8	53.33	7	46.67	Reference			
20-35 years old	50	71.43	20	28.57	0.753	1.345	0.212	8.544
<20 years	2	66.67	1	33.33	0.343	0.153	0.003	7.386
Parity								
P<4	60	68.97	27	31.03	Reference			
P=>4	0	0.00	1	100.0	1	<0.001	<0.001	<0.001
Mother's education								
Sufficient	27	64.29	15	35.71	Reference			
Insufficient	33	71.74	13	28.26	0.518	1.685	0.346	8.202
Mid-Upper Arm Circumference								
Normal	46	67.65	22	32.35	Reference			
Small	14	70.00	6	30.00	0.551	1.666	0.311	8.923
Gestational age								
Third trimester	46	71.88	18	28.13	Reference			
Second trimester	14	58.33	10	41.67	0.223	0.378	0.079	1.806
Family's support								
Good	3	33.3	6	66.7	Reference			
Bad	57	72.2	22	27.8	0.067	0.133	0.015	1.151
Media information								
Good	37	67.3	18	32.7	Reference			
Bad	23	69.7	10	30.3	0.252	2.361	0.543	10.257
Pregnancy knowledge								
Sufficient	58	67.4	28	32.6	Reference			
Insufficient	2	100	0	0	0.999	32254 23349.734	<0.001	<0.001
Nutrition knowledge								
Sufficient	31	65.96	16	34.04	Reference			
Insufficient	29	70.73	12	29.27	0.911	1.088	0.249	4.747
Iodine Deficiency Disease Knowledge								
Sufficient	31	58.49	22	41.51	Reference			
Insufficient	29	82.86	6	17.14	0.078	4.602	0.841	25.168
Pregnancy attitude								
Sufficient	55	66.4	28	33.7	Reference			
Insufficient	5	100	0	0	0.999	<0.001	<0.001	<0.001
Nutrition attitude								
Sufficient	42	70	18	30	Reference			
Insufficient	18	64.3	10	35.7	0.216	0.378	0.081	1.764

Iodine Deficiency Disease attitude								
Sufficient	48	65.8	25	34.2	Reference			
Insufficient	12	80	3	20	0.879	1.168	0.158	8.636
Energy intake								
Excessive (>100%)	4	50.00	4	50.00	Reference			
Adequate (80-100%)	35	72.92	13	27.08	0.510	2.798	0.131	59.842
Inadequate (<80%)	21	65.63	11	34.38	0.554	0.301	0.006	16.021
Carbohydrate intake								
Excessive (>100%)	21	63.64	12	36.36	Reference			
Adequate (80-100%)	20	71.43	8	28.57	0.922	0.903	0.117	7.002
Inadequate (<80%)	19	70.37	8	29.63	0.464	3.572	0.118	108.079
Protein intake								
Excessive (>100%)	2	50.00	2	50.00	Reference			
Adequate (80-100%)	9	56.25	7	43.75	0.913	1.277	0.016	103.689
Inadequate (<80%)	49	72.06	19	27.94	0.646	3.294	0.020	531.651
Fat intake								
Excessive (>100%)	10	66.67	5	33.33	Reference			
Adequate (80-100%)	22	68.75	10	31.25	0.736	0.666	0.063	7.074
Inadequate (<80%)	28	68.29	13	31.71	0.321	0.279	0.023	3.459
Fiber intake								
Excessive (>100%)	1	100.0	0	0.00	Reference			
Inadequate (<80%)	59	67.82	28	32.18	1	<0.001	<0.001	<0.001
Vitamin C intake								
Excessive (>100%)	18	69.23	8	30.77	Reference			
Adequate (80-100%)	10	62.50	6	37.50	0.241	0.306	0.042	2.217
Inadequate (<80%)	32	69.57	14	30.43	0.804	1.265	0.199	8.054
Magnesium intake								
Excessive (>100%)	11	61.11	7	38.89	Reference			
Adequate (80-100%)	23	69.70	10	30.30	0.754	1.582	0.089	27.962
Inadequate (<80%)	26	70.27	11	29.73	0.691	1.881	0.063	42.427
Mangan intake								
Excessive (>100%)	57	69.5	25	30.5	Reference			
Adequate (80-100%)	3	50	3	50	0.347	0.279	0.020	3.988

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Table 5. Fix models of risk factors for Iodine Deficiency Disease (IDD) based on Urinary Iodine Excretion (UIE)

Variables	p	OR adjusted	95% CI for OR	
			Lower	Upper
Parity				
P<4	*Reference*			
P=>4	1	<0.001	<0.001	<0.001
Family's support				
Good	*Reference*			
Bad	0.037	0.185	0.038	0.906
Iodine Deficiency Disease Knowledge				
Sufficient	*Reference*			
Insufficient	0.008	4.776	1.510	15.105
Pregnancy attitude				
Sufficient	*Reference*			
Insufficient	0.999	<0.001	<0.001	<0.001

From: Ani Margawati <animargawati@gmail.com>
Sent: Thursday, 18 November, 2021 2:43 PM
To: Food Research <foodresearch.my@outlook.com>
Subject: Re: Manuscript ID: FR-2021-814

November 18th 2021
Dear,

Professor Dr. Son Radu

Chief Editor

Food Research

I am Ani Margawati as the first author of manuscript entitled ***"Risk factors for disorders due to iodine deficiency (IDD) among pregnant women in Jepara, Indonesia"***. The following is revised of my manuscript based on reviewer(s) comments. Hopefully, this article can be accepted and be sources of public knowledge and sources of reading for researchers.

Thank you for your consideration of this manuscript.

Sincerely,

Dra. Ani Margawati, M.Kes, PhD

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==========
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Risk Factors for Disorders Due [acer1]to Iodine Deficiency (IDD) Among Pregnant Women [acer2]in Jepara

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Abstract

Pregnant women need an increase for iodine intake. In 2013, 24.3% of pregnant women in Indonesia had low iodine excretion values. Iodine is known to affect thyroid hormone regulation. This study aimed to analyze risk factors of Iodine Deficiency Disease (IDD) in pregnant women. This study was conducted using an observational method with a case control design. The subjects in this study were pregnant women in the 2nd and 3rd trimesters in the Mlonggo and Pakis Aji Health Centers, Jepara Regency. The total sample was 88 pregnant women. Primary data collection was done by taking urine for Urinary Iodine Excretion (UIE) and blood serum for Thyroid Stimulating Hormone (TSH) levels, anthropometric measurements for nutritional status and filling out questionnaires related to subject characteristics and interviews related to intake. This study showed that 53.4% of pregnant women had high TSH levels and 68.2% pregnant women had low UIE levels. The results of the multivariate analysis showed that education was the

strongest risk factor of IDD based on TSH levels (p value 0,020; OR *adjusted* 0,324; CI OR 0,125:0,835) and knowledge of IDD was the strongest risk factor of IDD based on UIE levels (p value 0,008; OR *adjusted* 4,776; CI OR 1,510:15,105).

Keywords: pregnant women, iodine, thyroid stimulating hormone[acer4]

1. Introduction

Iodine is an essential micronutrient for the formation of thyroid hormones in the body. Thyroid hormone plays an important role in various functions such as basal metabolism, heart rate and bone growth and the central nervous system (González-Martínez et al., 2021)[acer5]. Pregnant women are known to experience an increase in the size of thyroid gland by 10% and an increase in thyroid hormone production by 50%, causing the need for iodine in the pregnant women increases (Alexander et al., 2017). The need for iodine in adults is about 150 g/day. The World Health Organization (WHO) recommends a higher intake of iodine in pregnant women, which is 250 g/day. Deficiency of iodine intake is thought to be the main cause of hypothyroidism and Iodine Deficiency Disorders (IDD) (Taylor and Lazarus, 2019).

Based on the 2013 RISKESDAS data, the prevalence of pregnant women in Indonesia with Urinary Iodine Excretion (UIE) <100 g/L was 24.3%. One of the causes of the problem was 50.8% of household salt in Indonesia has a low level of iodine. Therefore, household coverage with iodized salt consumption can't be an indicator of the fulfilment of iodine intake (Kementrian Kesehatan Republik Indonesia, 2015).

Examination of urinary iodine excretion (UIE) in 2007 until 2012 in Jepara Regency showed that several sub-districts including as IDD endemic areas such as Mayong, Batealit and Pakis Aji (Widiyatni and Subagio, 2016). Apart from UIE levels, IDD status can also be seen from Thyroid Stimulating Hormone (TSH) levels. If thyroid hormone production is insufficient, there will be an increase in TSH production (Kementrian Kesehatan Republik Indonesia, 2015). Research in Magelang showed 17.1% of pregnant

46 women in goiter replete areas had high TSH levels and 19.2% of pregnant women in non-replete goiter
47 areas had high TSH levels (Kusrini et al., 2016). Screening to see the adequacy of iodine in the body is
48 very important for pregnant women as an indicator to detect the occurrence of IDD.
49 The incidence of IDD that not handled properly during pregnancy can cause premature birth,
50 intrauterine growth disorders, fetal death, impaired fetal development, respiratory disorders and
51 increased perinatal mortality. This is because iodine is needed by thyroid hormone for the growth and
52 formation of vital organs of the fetus (Animal Welfare Branch, 2007). Adequacy of iodine in the mother
53 is very important to prevent hypothyroidism in the fetus. During the early stages of pregnancy, the
54 fetus is still dependent on the mother's thyroid hormone production. During midterm pregnancy, the
55 fetus begins to produce its own thyroid hormone but still requires iodine intake from the mother
56 (Khadilkar, 2019). Based on data from Cipto Mangunkusumo Hospital in Jakarta and Hasan Sadikin
57 Hospital in Bandung around 2014, 1 from 2513 newborns had congenital hypothyroidism. This
58 prevalence was higher than global data, which is 1 in 3000 newborns (Kementrian Kesehatan Republik
59 Indonesia, 2015).
60 Apart from iodine, many other nutrients are risk factors for IDD. Malnutrition is known to cause
61 thyroid disorders. Research in 2017 showed that TSH levels were higher in subjects with protein
62 energy deficiency than in the control group (Kawicka and Regulska-Ilow, 2015). However, other
63 studies stated that there was no significant difference in Body Mass Index (BMI) in hypothyroid
64 patients (Ranabir et al., 2019). Deficiency of macronutrient elements such as protein and
65 micronutrient elements such as iron, selenium and zinc are known to interfere with thyroid gland
66 function. Previous studies have stated that 60% of patients with hypothyroidism are iron deficient
67 (Kawicka and Regulska-Ilow, 2015). Research in Magelang showed that the prevalence of pregnant
68 women with iodine deficiency was higher in the third trimester than in the previous trimester (Kusrini

et al., 2016). However, another study in Korea showed that the lowest TSH levels occurred in women in third trimester of pregnancy (Kim et al., 2015).

IDD in pregnant women is a problem that can have an impact not only on the mother but also on the fetus. Fetuses with mothers who have IDD are at risk of inhibiting fetal development. Based on the description above, researchers are interested in knowing the risk factors of IDD among pregnant women.

2. Materials and methods

This research was carried out using an observational method with a case control study design. The subjects in this study were pregnant women in the second and third trimesters in the Mlonggo Health Center and Pakis Aji Health Center, Jepara Regency. The sampling technique was carried out with cluster sampling and total sample obtained was 88 pregnant women. The subjects were willing to participate in the study by filling the informed consent form. This study aimed to determine the risk factors for the incidence of IDD seen from UIE and TSH status among pregnant women.

Primary data were collected by taking urine sample for UIE levels, blood serum for TSH levels, anthropometric measurements for nutritional status, filling out questionnaires related to subject characteristics and interviewing subjects related to food intake. The research instrument used a Semi Quantitative Food Frequency Questionnaire (SQ-FFQ) for food intake, Mid-Upper Arm Circumference (MUAC) tape to measure nutritional status, measurement of UIE levels using urine sample with Acid Digestion method and measurement of TSH levels using whole blood serum with Enzyme Linked Immunosorbent Assay (ELISA) method. Pregnant women with MUAC < 23.5 cm included as poor nutritional status and pregnant women with MUAC ≥ 23.5 cm included as normal nutritional status (Tejayanti, 2020). The food intake of pregnant women was divided into 3 groups, namely inadequate (<80%), sufficient (80-100%) and excessive (>100%) (Yunitasari et al., 2019). Pregnant women in the second trimester were in the range of 13-27 weeks and the third trimester were more than 27 weeks.

UIE levels were less if < 150 g/L and normal if 150 g/L (WHO (World Health Organization), 2013). Categorization of TSH levels based on gestational age, normal category if TSH values in the first trimester were 0.1-2.5 mIU/L, second trimester were 0.2 -3.0 mIU/L and third trimester were 0.3-3.0mIU/L (Green et al., 2011).

Univariate analysis was used on one variable with the aim of knowing and identifying the frequency distribution and characteristics of each variable. Bivariate analysis was to determine the risk (odds ratio) of exposure to cases by using the Chi Square test formula with 95% confidence level. Multivariate analysis was to determine the strongest risk factors of IDD by using logistic regression analysis.

3. Results

The number of subjects obtained in the study at the Mlonggo Health Center and the Pakis Aji Health Center, Jepara Regency, as many as 88 subjects with varying ages from 18 to 41 years. The following characteristics of the subject were shown in table 1.

This study showed that the number of subjects with high TSH levels was more than subjects with normal TSH (53.4%). While based on UEI levels, 68.2% of subjects was included as low UEI levels and 31.8% of subjects as normal UEI levels.

Based on table 2, this study provides findings that education was a risk factor for IDD seen from TSH levels (p value 0,015; OR 0,169; CI OR 0,040:0,709). The results of multivariate analysis in table 3 showed that education was the strongest risk factor for the incidence of IDD seen from TSH levels (p value 0,020; OR adjusted 0,324; CI OR 0,125:0,835).

Risk factors of IDD based on UEI levels can be seen in tables 4 and 5. Based on table 4, this study provided that there were no independent variables as risk factors of IDD. However, after adjusted of age, education, MUAC, gestational age, media information, pregnancy knowledge, nutritional knowledge, nutritional attitudes, IDD attitudes and food intake variables with multivariate analysis,

table 5 showed that IDD knowledge was the strongest risk factor for IDD based on UEI (p value 0,008; OR adjusted 4,776; CI OR 1,510:15,105).

4. Discussion

Iodine is an essential element that the body needs to produce thyroid hormone. Iodine deficiency can cause thyroid swelling, hypothyroidism and intellectual disability in infants and children whose mothers were deficient in iodine during pregnancy. Measurement of UIE levels is one method for measuring the adequacy of iodine in the blood because about 90% of the iodine in the body will be excreted through urine (Mutalazimah et al., 2013). This study in second and third trimester pregnant women showed that 68.2% of pregnant women had low UIE levels. In addition, the clinical diagnosis of IDD can be seen by the level of thyroid stimulating hormone (TSH) (Chaker et al., 2017). This study showed 53.4% of pregnant women had high TSH levels and 46.6% of pregnant women had low TSH levels. The percentage of pregnant women with IDD in this study was much higher than the previous study in Magelang which showed that 17.1% of pregnant women in endemic areas of goiter experienced hypothyroidism and 19.2% of pregnant women in non-endemic areas of goiter experienced hypothyroidism (Kusrini et al., 2016). Although this study was conducted in the coastal area of Jepara which is a salt-producing area, but the prevalence of pregnant women with low iodine adequacy is still high. This is in contrast to previous studies which showed the prevalence of low UIE levels in coastal areas only 5.9% of subjects (Kurniangga, 2016). However, previous studies in the same area such as Mayong, Batealit and Pakis Aji, Jepara Regency, mentioned the availability of iodized salt with levels of 30 ppm is only 20 – 30% (Widiyatni et al., 2016). This may be the reason for low iodine adequacy in subjects.

This study was dominated by the age of 20-35 years, about 79.5% of the total subjects. Previous literature showed that the age of pregnant women with the lowest risk is when the mother is 20 – 30 years old compared to younger or older ages (Bellieni, 2016). Previous research has shown that

pregnant women giving birth at the age of <20 years or >34 years have a higher risk of having a child born with low birth weight compared to 20-34 years old (Mubasyiroh et al., 2016). This study shows that age has not been a risk factor for IDD either based on UIE levels or TSH levels because p> 0.05. Although not yet a significant risk factor, all pregnant women aged < 20 years had high TSH levels and 66.7% of pregnant women aged > 35 years had high TSH levels. This is in line with previous studies showing age was not a risk factor for hypothyroidism in pregnancy. That study also showed that the peak of the increase in TSH levels occurred in pregnant women aged over 35 years (Potlukova et al., 2012). IDD can strike at various ages, genders and races. However, IDD is known to be most common in women after menopause due to various hormonal changes in the body (Sharma, 2018).

Based on this study, parity has not been a risk factor for IDD status based on UIE levels and TSH levels in pregnant women. This study is in line with research in Lithuania which showed that parity had no relationship with hypothyroidism (Dauksiene et al., 2017). However, this study contradicted previous studies which stated that there was an association between parity and an increase in thyroid volume. However, the study stated that the relationship only occurred in pregnant women who smoked. Smoking may affect the thyroid by inhibiting the absorption of iodine (Knudsen et al., 2002). Therefore, there is a need for further research that examines the risk of pregnant women who smoke both passively and actively with the incidence of IDD.

Measurement of the nutritional status of pregnant women in this study used Mid-Upper Arm Circumference (MUAC). Previous research has shown that MUAC is a good predictor of the risk of low birth weight compared to other anthropometric measurements. Pregnant women with MUAC < 23.5 cm have a risk of experiencing chronic energy deficiency (Tejayanti, 2020). This study showed that 77.3% of pregnant women had normal nutritional status. However, this study has not shown that nutritional status is a risk factor for the incidence of IDD based on UIE levels and TSH levels in pregnant women. This is contrary to previous studies which stated that MUAC had a negative relationship with

the size of the thyroid gland. The study raised concerns about the impact of chronic energy deficiency not on the development of the thyroid gland, but on the brain development of the fetus and neonate. Although in this study did not directly being measured, the risk of small MUAC being left unchecked would have the potential to have an impact on fetal and new born brain development (Brahmbhatt et al., 2001).

This study was dominated by the third trimester of pregnancy, which was 79.5% of the total subjects. This study has not shown gestational age to be a risk factor for IDD, both in terms of UIE levels and TSH levels in pregnant women. Although not yet a significant risk factor, the percentage of pregnant women with IDD status based on TSH levels was higher in the third trimester than in the second trimester, which was 54.7%. IDD status based on UIE levels also shows that the percentage of pregnant women in the third trimester was more IDD than second trimester. Previous research in Mexico showed that the average TSH level was higher in third trimester pregnant women compared to first and second trimester (Bocos-Terraz et al., 2009). During the first trimester, there was an increase blood flow and glomerular filtration so that iodine in the urine is lost. During the second trimester, TSH levels return to normal and the fetus begins to produce its own thyroid hormone. However, during the third trimester of pregnancy, thyroid hormone-dependent neurogenesis is still ongoing, so iodine deficiency that occurs early in pregnancy may be difficult to treat. Previous studies have shown that pregnant women with iodine deficiency in the third trimester are more at risk of premature birth and low birth weight babies due to restriction of fetal growth and low thyroid hormone production (Candido et al., 2020).

Based on this study, 52.3% of the subjects had low education. Multivariate analysis on this study showed that education was the strongest risk factor for IDD as seen from the TSH level of pregnant women. This study also showed that mothers with insufficient education were 0.324x more at risk experiencing IDD than mothers with sufficient education. This is in contrast to previous research which

showed that households with highly educated heads and wives were more likely to use iodized salt than families with low levels of education. That study stated that individual education can affect behavior in society, including consumption of iodized salt (Nadimin, 2015). Although the majority of pregnant women in this study had low education, 97.7% of pregnant women had sufficient knowledge related to pregnancy, 53.4% of pregnant women had sufficient knowledge related to nutrition and 60.2% of pregnant women have sufficient IDD knowledge. This study showed that 62.5% of pregnant women had good media information and 89.9% had good family support. Previous research showed that watching the media and sources of information both shown risk to knowledge and perception of the disease (Karasneh et al., 2020). Multivariate analysis on this study also showed that knowledge of IDD was the strongest risk factor for IDD based on UIE levels. Pregnant women with insufficient knowledge of IDD were 4,776x more at risk of experiencing IDD that pregnant women with sufficient knowledge of IDD. This study showed that 82.9% of pregnant women with insufficient IDD knowledge had less UIE levels. Knowledge is a factor from within to shape one's actions. Sufficient knowledge related to IDD in pregnant women is known to increase awareness of iodized salt intake and how to store iodized salt properly (Sudarto, 2017).

Sufficient knowledge from pregnant women must be balanced with good attitudes both in pregnancy and family health. This study showed that the majority of pregnant women had good attitudes during pregnancy (94.3%), nutritional attitudes (68.2%) and IDD attitudes (83%). However, this study did not show mother's attitude to be a risk factor for IDD. This is in line with research in Iran which showed that attitude is not a risk factor for IDD based on UEI levels. The study also mentioned that the mother's practices related to the fulfillment of low iodine 2.5 times the risk of IDD (Mirmiran et al., 2013). Although it has not been statistically proven, this study showed that the percentage of pregnant women experience IDD was higher in pregnant women with less attitudes. Therefore, the

mother's attitude towards pregnancy, nutrition and IDD needs to be followed by good daily practices as well.

This study showed that the overall intake of macronutrients and micronutrients has not been a risk factor for IDD both based on TSH levels and UIE levels. This is contrary to research in Brazil which stated that a gluten-free diet with the provision of minerals and vitamins can increase thyroid level and reverting subclinical hypothyroidism. Hypothyroidism itself can cause disturbances in the intestinal tract, which causes problems with bowel movements (Mezzomo and Nadal, 2016). Therefore, adequate intake of water and fiber is necessary for pregnant women. In addition, stress management and behavioral interventions such as weight management, a balanced diet and a healthy home environment are known to aid in recovery from thyroid disease (Ihnatowicz et al., 2020).

5. Conclusion

There were 53.4% of pregnant women from all research subjects in the Mlonggo Health Center and Pakis Aji Health Center, Jepara who had high TSH levels and 68.2% of pregnant women had low UIE levels. This study showed that education was the strongest risk factor for IDD (TSH level) and knowledge of IDD was the strongest risk factor for IDD (UIE level).

Conflict of interest

The authors declare no conflict of interest.

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332 **Tables**

333 Table 1. Distribution of subject characteristics

Variables	Frequency	
	n	%
TSH* levels (mIU/ L)		
Normal	41	46.6
High	47	53.4
UIE** levels (µg/L)		
Nomal	28	31.8
Low	60	68.2
Age		
>35 years old	15	17.0
20-35 years old	70	79.5
<20 years	3	3.4
Parity		
P<4	87	98.9
P=>4	1	1.0
Mother's education		
Sufficient	42	47.7
Insufficient	46	52.3
Mid-Upper Arm Circumference		
Normal	68	77.3
Small	20	22.7
Gestational age		
Third trimester	64	72.7
Second trimester	24	27.3
Family's support		
Good	79	89.8
Bad	9	10.2
Media information		
Good	55	62.5
Bad	33	37.5
Pregnancy knowledge		
Sufficient	86	97.7
Insufficient	2	2.3
Nutrition knowledge		
Sufficient	47	53.4
Insufficient	41	46.6
Iodine Deficiency Disease Knowledge		
Sufficient	53	60.2
Insufficient	35	39.8
Pregnancy attitude		
Sufficient	83	94.3
Insufficient	5	5.7
Nutrition attitude		

Sufficient	60	68.2
Insufficient	28	31.8
Iodine Deficiency Disease attitude		
Sufficient	73	83.0
Insufficient	15	17.0
Energy intake		
Excessive (>100%)	8	9.1
Adequate (80-100%)	48	54.5
Inadequate (<80%)	32	36.4
Carbohydrate intake		
Excessive (>100%)	33	37.5
Adequate (80-100%)	28	31.8
Inadequate (<80%)	27	30.7
Protein intake		
Excessive (>100%)	4	4.5
Adequate (80-100%)	16	18.2
Inadequate (<80%)	68	77.3
Fat intake		
Excessive (>100%)	15	17.0
Adequate (80-100%)	32	36.4
Inadequate (<80%)	41	46.6
Fiber intake		
Excessive (>100%)	1	1.1
Inadequate (<80%)	87	98.9
Vitamin C intake		
Excessive (>100%)	26	29.5
Adequate (80-100%)	16	18.2
Inadequate (<80%)	46	52.3
Magnesium intake		
Excessive (>100%)	18	20.5
Adequate (80-100%)	33	37.5
Inadequate (<80%)	37	42.0
Mangan intake		
Excessive (>100%)	82	93.2
Adequate (80-100%)	6	6.8

*TSH = Thyroid Stimulating Hormone

**UIE = Urinary Iodine Excretion

Table 2. Full models of risk factors for Iodine Deficiency Disease (IDD) based on Thyroid Stimulating Hormone (TSH) levels

Variables	Thyroid Stimulating Hormone (TSH)				p	OR	95% CI for OR	
	High		Normal					
	n	%	n	%			Lower	Upper
Age								
>35 years old	10	66.7	5	33.3	Reference			
20-35 years old	34	48.6	36	51.4	0.100	0.264	0.054	1.290

<20 years	3	100	0	0	0.999	67101 70064 37299 580	<0.001	<0.001
Parity								
P<4	46	52.9	41	47.1	Reference			
P=>4	1	100	0	0	1	26993 89903. 446	<0.001	<0.001
Mother's education								
Sufficient	26	61.90	16	38.10	Reference			
Insufficient	21	45.65	25	54.35	0.015	0.169	0.040	0.709
Mid-Upper Arm Circumference								
Normal	38	55.9	30	44.1	Reference			
Small	9	45	11	55	0.547	0.630	0.140	2.837
Gestational age								
Third trimester	35	54.7	29	45.3	Reference			
Second trimester	12	50	12	50	0.054	0.242	0.057	1.022
Family’s support								
Good	40	50.6	39	49.4	Reference			
Bad	7	77.8	2	22.2	0.402	2.475	0.297	20.634
Media information								
Good	25	45.5	30	54.5	Reference			
Bad	22	66.7	11	33.3	0.493	1.548	0.444	5.403
Pregnancy knowledge								
Sufficient	46	53.5	40	46.5	Reference			
Insufficient	1	50	1	50	0.999	<0.001	<0.001	<0.001
Nutrition knowledge								
Sufficient	25	53.2	22	46.8	Reference			
Insufficient	22	53.7	19	46.3	0.527	1.493	0.431	5.177
Iodine Deficiency Disease Knowledge								
Sufficient	30	56.6	23	43.4	Reference			
Insufficient	17	48.6	18	51.4	0.554	1.475	0.407	5.346
Pregnancy attitude								
Sufficient	44	53	39	47	Reference			
Insufficient	3	60	2	40	0.957	1.069	0.094	12.175
Nutrition attitude								
Sufficient	33	55	27	45	Reference			
Insufficient	14	50	14	50	0.473	0.637	0.186	2.180
Iodine Deficiency Disease attitude								
Sufficient	38	52	35	48	Reference			
Insufficient	9	60	6	40	0.698	1.361	0.287	6.443
Energy intake								
Excessive (>100%)	5	62.5	3	37.5	Reference			
Adequate (80-100%)	26	54.2	22	45.8	0.927	0.876	0.051	15.160

Inadequate (<80%)	16	50	16	50	0.960	0.913	0.025	33.404
Carbohydrate intake								
Excessive (>100%)	19	57.6	14	42.4	Reference			
Adequate (80-100%)	13	46.4	15	53.6	0.447	0.502	0.085	2.967
Inadequate (<80%)	15	55.6	12	44.4	0.569	0.437	0.025	7.517
Protein intake								
Excessive (>100%)	3	75	1	25	Reference			
Adequate (80-100%)	9	56.3	7	43.8	0.484	0.297	0.010	8.882
Inadequate (<80%)	35	51.5	33	48.5	0.647	0.377	0.006	24.557
Fat intake								
Excessive (>100%)	8	53.3	7	46.7	Reference			
Adequate (80-100%)	20	62.5	12	37.5	0.582	1.657	0.257	9.999
Inadequate (<80%)	19	46.3	22	53.7	0.764	1.335	0.203	8.784
Fiber intake								
Excessive (>100%)	1	100	0	0	Reference			
Inadequate (<80%)	46	52.9	41	47.1	1	<0.001	<0.001	<0.001
Vitamin C intake								
Excessive (>100%)	14	53.8	12	46.2	Reference			
Adequate (80-100%)	10	62.5	6	37.5	0.058	5.944	0.938	37.657
Inadequate (<80%)	23	50	23	50	0.272	2.441	0.496	12.014
Magnesium intake								
Excessive (>100%)	12	66.7	6	33.3	Reference			
Adequate (80-100%)	17	51.5	16	48.5	0.766	1.441	0.130	15.987
Inadequate (<80%)	18	48.6	19	51.4	0.833	0.752	0.053	10.644
Mangan intake								
Excessive (>100%)	43	52.4	39	47.6	Reference			
Adequate (80-100%)	4	66.7	2	33.3	0.345	2.935	0.315	27.361

Table 3. Fix models of risk factors for Iodine Deficiency Disease (IDD) based on Thyroid Stimulating Hormone (TSH) levels

Variables	p	OR adjusted	95% CI for OR	
			Lower	Upper
Age				
>35 years old	Reference			
20-35 years old	0.164	0.419	0.123	1.426
<20 years	0.999	702462842.485	<0.001	<0.001
Mother's education				
Sufficient	Reference			
Insufficient	0.020	0.324	0.125	0.835
Media information				
Good	Reference			
Bad	0.066	2.533	0.941	6.760

342 Table 4. Full models of risk factors for Iodine Deficiency Disease (IDD) based on Urinary Iodine Excretion
343 (UIE)

Variables	Urinary Iodine Excretion (UIE)				p	OR	95% CI for OR	
	Low		Normal					
	n	%	n	%			Lower	Upper
Age								
>35 years old	8	53.33	7	46.67	Reference			
20-35 years old	50	71.43	20	28.57	0.753	1.345	0.212	8.544
<20 years	2	66.67	1	33.33	0.343	0.153	0.003	7.386
Parity								
P<4	60	68.97	27	31.03	Reference			
P=>4	0	0.00	1	100.0	1	<0.001	<0.001	<0.001
Mother's education								
Sufficient	27	64.29	15	35.71	Reference			
Insufficient	33	71.74	13	28.26	0.518	1.685	0.346	8.202
Mid-Upper Arm Circumference								
Normal	46	67.65	22	32.35	Reference			
Small	14	70.00	6	30.00	0.551	1.666	0.311	8.923
Gestational age								
Third trimester	46	71.88	18	28.13	Reference			
Second trimester	14	58.33	10	41.67	0.223	0.378	0.079	1.806
Family's support								
Good	3	33.3	6	66.7	Reference			
Bad	57	72.2	22	27.8	0.067	0.133	0.015	1.151
Media information								
Good	37	67.3	18	32.7	Reference			
Bad	23	69.7	10	30.3	0.252	2.361	0.543	10.257
Pregnancy knowledge								
Sufficient	58	67.4	28	32.6	Reference			
Insufficient	2	100	0	0	0.999	32254 23349.734	<0.001	<0.001
Nutrition knowledge								
Sufficient	31	65.96	16	34.04	Reference			
Insufficient	29	70.73	12	29.27	0.911	1.088	0.249	4.747
Iodine Deficiency Disease Knowledge								
Sufficient	31	58.49	22	41.51	Reference			
Insufficient	29	82.86	6	17.14	0.078	4.602	0.841	25.168
Pregnancy attitude								
Sufficient	55	66.4	28	33.7	Reference			
Insufficient	5	100	0	0	0.999	<0.001	<0.001	<0.001
Nutrition attitude								
Sufficient	42	70	18	30	Reference			
Insufficient	18	64.3	10	35.7	0.216	0.378	0.081	1.764

Iodine Deficiency Disease								
attitude								
Sufficient	48	65.8	25	34.2	Reference			
Insufficient	12	80	3	20	0.879	1.168	0.158	8.636
Energy intake								
Excessive (>100%)	4	50.00	4	50.00	Reference			
Adequate (80-100%)	35	72.92	13	27.08	0.510	2.798	0.131	59.842
Inadequate (<80%)	21	65.63	11	34.38	0.554	0.301	0.006	16.021
Carbohydrate intake								
Excessive (>100%)	21	63.64	12	36.36	Reference			
Adequate (80-100%)	20	71.43	8	28.57	0.922	0.903	0.117	7.002
Inadequate (<80%)	19	70.37	8	29.63	0.464	3.572	0.118	108.079
Protein intake								
Excessive (>100%)	2	50.00	2	50.00	Reference			
Adequate (80-100%)	9	56.25	7	43.75	0.913	1.277	0.016	103.689
Inadequate (<80%)	49	72.06	19	27.94	0.646	3.294	0.020	531.651
Fat intake								
Excessive (>100%)	10	66.67	5	33.33	Reference			
Adequate (80-100%)	22	68.75	10	31.25	0.736	0.666	0.063	7.074
Inadequate (<80%)	28	68.29	13	31.71	0.321	0.279	0.023	3.459
Fiber intake								
Excessive (>100%)	1	100.0	0	0.00	Reference			
Inadequate (<80%)	59	67.82	28	32.18	1	<0.001	<0.001	<0.001
Vitamin C intake								
Excessive (>100%)	18	69.23	8	30.77	Reference			
Adequate (80-100%)	10	62.50	6	37.50	0.241	0.306	0.042	2.217
Inadequate (<80%)	32	69.57	14	30.43	0.804	1.265	0.199	8.054
Magnesium intake								
Excessive (>100%)	11	61.11	7	38.89	Reference			
Adequate (80-100%)	23	69.70	10	30.30	0.754	1.582	0.089	27.962
Inadequate (<80%)	26	70.27	11	29.73	0.691	1.881	0.063	42.427
Mangan intake								
Excessive (>100%)	57	69.5	25	30.5	Reference			
Adequate (80-100%)	3	50	3	50	0.347	0.279	0.020	3.988

Table 5. Fix models of risk factors for Iodine Deficiency Disease (IDD) based on Urinary Iodine Excretion (UIE)

Variables	p	OR adjusted	95% CI for OR	
			Lower	Upper
Parity				
P<4	*Reference*			
P=>4	1	<0.001	<0.001	<0.001
Family's support				

Good	*Reference*			
Bad	0.037	0.185	0.038	0.906
Iodine Deficiency Disease Knowledge				
Sufficient	*Reference*			
Insufficient	0.008	4.776	1.510	15.105
Pregnancy attitude				
Sufficient	*Reference*			
Insufficient	0.999	<0.001	<0.001	<0.001

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Food Research <foodresearch.my@outlook.com> Fri, Nov 19, 2021 at 3:44 PM
To: Ani Margawati <animargawati@gmail.com>

Dear Dra Ani Margawati

Thank you for the revised copy of your manuscript. We will contact you again for further processing.

Best regards,
Son Radu, PhD
Chief Editor

From: Ani Margawati <animargawati@gmail.com>
Sent: Wednesday, 5 January, 2022 10:13 AM
To: Food Research <foodresearch.my@outlook.com>
Subject: Re: Manuscript ID: FR-2021-814

January 5th 2022

Dear,
Professor Dr. Son Radu
Chief Editor
Food Research

I am Ani Margawati as the first author of manuscript entitled "Risk factors for disorders due to iodine deficiency (IDD) among pregnant women in Jepara, Indonesia". I have submitted a revision manuscript on November 19th, 2021. Since it has been more than one month since my submission, I was wondering if the status is not getting updated due to a technical error. It would be great if you could let me know when I can expect the update status of our revision manuscript. I'm sorry for the inconvenience.

Thank you for your consideration.

Sincerely,

Dra. Ani Margawati, M.Kes, PhD
[Quoted text hidden]

Food Research <foodresearch.my@outlook.com> Wed, Jan 5, 2022 at 2:56 PM
To: Ani Margawati <animargawati@gmail.com>

Dear Dra. Ani Margawati,

It is still in queue for technical review.
Please expect some delay as we are experiencing high volumes of publication at this time
Thank you for your understanding.

Best regards,

From: Ani Margawati <animargawati@gmail.com>
Sent: Tuesday, 1 March, 2022 10:16 AM
To: Food Research <foodresearch.my@outlook.com>
Subject: Re: Manuscript ID: FR-2021-814

March 1st 2022

Dear,
Professor Dr. Son Radu
Chief Editor
Food Research

I am Ani Margawati as the first author of manuscript entitled "Risk factors for disorders due to iodine deficiency (IDD) among pregnant women in Jepara, Indonesia". I have submitted a revision manuscript on November 19th, 2021 and requested an update on January 5th 2022. Your update stated that our article is still in queue for technical review. Since it has been more than three months from my submission and 2 months from the update status, I was

wondering the update status of our manuscript. Do you have any good news for us regarding the status of my submission? I'm sorry for the inconvenience.

Thank you for your consideration and I am looking forward to hear from you

Sincerely,

Dra. Ani Margawati, M.Kes, PhD
[Quoted text hidden]

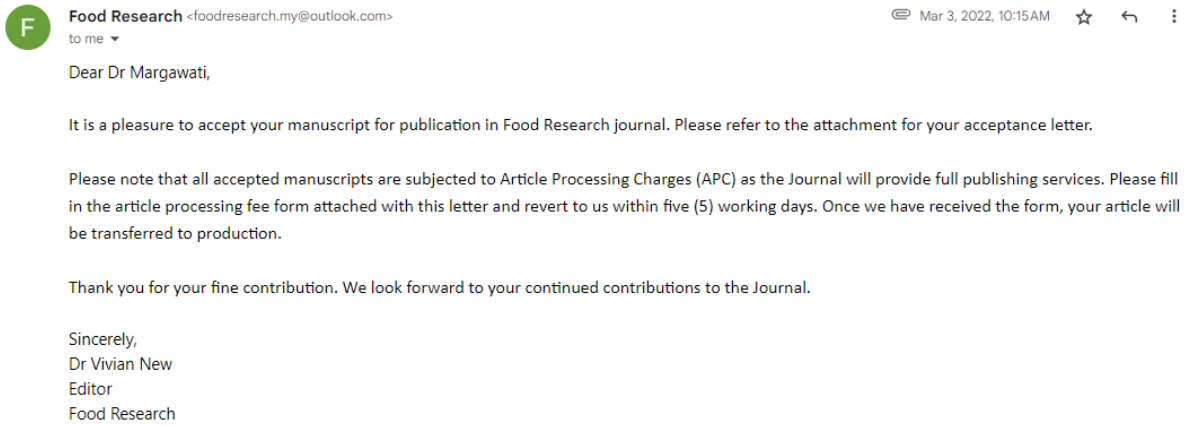
Food Research <foodresearch.my@outlook.com> Wed, Mar 2, 2022 at 12:47 AM
To: Ani Margawati <animargawati@gmail.com>

Dear Dra. Ani Margawati,

It is still being processed, due to the high volume of publication, there will be a delay in processing.
It would usually take up to 6 months after receiving the revised manuscript as many are in the queue prior to yours.
We thank you for your patience and understanding. Nonetheless, we will be in touch when it is ready.

Best regards,
Son Radu, PhD
Chief Editor

1. ACCEPTED



Food Research <foodresearch.my@outlook.com>
to me

Mar 3, 2022, 10:15 AM

Dear Dr Margawati,

It is a pleasure to accept your manuscript for publication in Food Research journal. Please refer to the attachment for your acceptance letter.

Please note that all accepted manuscripts are subjected to Article Processing Charges (APC) as the Journal will provide full publishing services. Please fill in the article processing fee form attached with this letter and revert to us within five (5) working days. Once we have received the form, your article will be transferred to production.

Thank you for your fine contribution. We look forward to your continued contributions to the Journal.

Sincerely,
Dr Vivian New
Editor
Food Research

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CORRESPONDING AUTHOR INFORMATION			
Name	Margawati, A.,	**Manuscript ID**	FR-2021-814
Manuscript Title	Risk factors for disorders due to iodine deficiency (IDD) among pregnant women in Jepara, Indonesia		
Authors	Margawati, A., Utami, A., Nugraheni, A. and Hananingtyas, A.		

INVOICE RECIPIENT			
Name		**Salutation**	
Address			
Email			

FOOD
RESEARCH

3rd March 2022

Dear Dr Margawati,

ACCEPTANCE LETTER

Food Research is pleased to inform you that the following manuscript has been accepted for publication in Food Research journal.

Manuscript Title	:	Risk factors for disorders due to iodine deficiency (IDD) among pregnant women in Jepara, Indonesia
Authors	:	Margawati, A., Utami, A., Nugraheni, A. and Hananingtyas, A.

We thank you for your fine contribution to the Food Research journal and encourage you to submit other articles to the Journal.

Yours sincerely,

Professor Dr. Son Radu
Chief Editor
Food Research