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

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Abstract

Pregnant women need an increase in 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 the 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, Indonesia. The total sample was eighty-eight pregnant women. Primary data collection was done by taking urine for Urinary Iodine Excretion (UIE) and blood serum for Thyroid Stimulating Hormone (TSH) levels, Mid-Upper Arm Circumference (MUAC) measurements for anthropometric nutritional status and filling out questionnaires related to subject characteristics and Semi Quantitative Food Frequency Questionnaire (SQ-FFQ) interviews related to food consumption. This study showed that 53.4% of pregnant women had high TSH levels and 68.2% of 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).

1. Introduction

Iodine is an essential micronutrient for the formation of thyroid hormones in the body. The 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 the thyroid gland by 10% and an increase in thyroid hormone production by 50%, causing the need for iodine in pregnant women to increase (Alexander *et al*., 2017). The need for iodine in adults is about 150 mcg/day. The World Health Organization (WHO) recommends a higher intake of iodine in pregnant women, which is 250 mcg/day. A deficiency in 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 (Kementrian Kesehatan Republik Indonesia, 2015). Based on UIE thematic map in Central Java province, Indonesia, there were 4 districts with median UIE levels of school children <100 g/L, one of which was Jepara Regency (Kartono and Moeljanto, 2008). The Indonesian government has created a salt iodization program for every household to use as a long-term program to solve the IDD problem in Indonesia. However, previous research has shown that 75% of the 76 salt brands in Jepara contain less than 30 ppm of iodine. In the Mayong, Batealit and Pakis Aji sub-districts, there was only 20-30% available iodized salt with levels of more than 30 ppm (Dunney and Murphy, 2015).

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, Indonesia showed that 17.1% of pregnant women in goitre replete areas had high TSH levels and 19.2% of pregnant women in non-replete goitre areas had high TSH levels (Kusrini *et al*., 2016). Screening to see the

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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 is 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 the 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 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, Indonesia 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 females (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 reported that hypothyroidism can occur among moderate to severe iron deficiency (El-Masry *et al*., 2018). Research in Magelang, Indonesia, showed that the prevalence of pregnant women with iodine deficiency was higher in the third trimester than in the second and first trimester in the area of IDD replete. However, the prevalence of pregnant women with iodine deficiency was higher in the second trimester than in the third and first trimester in the area of non-IDD replete (Kusrini *et al*., 2016).

IDD in pregnant women is a problem that can have an impact not only on the mother but also on the fetus. In Indonesia, studies examining IDD based on UIE and TSH levels, especially in pregnant women are still rare. Especially in Jepara Regency, Indonesia with a high IDD rate and low levels of iodized salt, there have been no studies examining factors that increase the risk of IDD in pregnant women. Based on the description above, this study aimed to investigate the risk factors of IDD among pregnant women in Jepara, Indonesia.

2. Materials and methods

This research was carried out using an observational method with a case-control study design based on UIE levels and based on TSH levels. 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, Indonesia. The sampling technique was carried out with cluster sampling and the total sample obtained was 88 pregnant women (47 cases with 41 controls for TSH levels and 60 cases with 28 controls for UIE levels). Ethical clearance was obtained by the bioethics commission of health research from the Faculty of Medicine, Diponegoro University. The subjects were willing to participate in the study by filling out the written informed consent form.

Primary data were collected by taking a 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 consumption. Prior to data collection on the subject, knowledge and attitude related to pregnancy, nutrition and IDD questionnaires, family support and media information were tested to measure its validity and reliability. The knowledge questionnaire related to pregnancy consisted of five questions, related to nutrition consisted of ten questions and related to IDD consisted of ten questions. The attitude questionnaire related to pregnancy, nutrition and IDD consists of ten questions each. The family support and media information questionnaire consisted of 6 questions each. Subjects with family support and media information score > 55 were categorized as good (Arikunto, 2010). Subjects with knowledge and attitude scores> 60 were categorized as sufficient (Goni *et al*., 2019).

The research instrument for food consumption used a Semi Quantitative Food Frequency Questionnaire (SQ-FFQ) and nutritional status used Mid-Upper Arm Circumference (MUAC) tape. Pregnant women with MUAC < 23.5 cm were included as small MUAC and pregnant women with MUAC ≥ 23.5 cm were included as normal MUAC (Tejayanti, 2020). Subjects with senior high school educational levels were categorized as sufficient education and subjects with junior high school or a less educational level were categorized as insufficient education. The food consumption of pregnant women was divided into 3 groups, namely inadequate (<80%), sufficient (80-100%) and excessive (>100%) (Yunitasari *et al*., 2019).

Measurement of UIE levels used urine sample with ammonium persulfate digestion with spectrophotometric detection of the Sandell-Kolthoff reaction. A reagent that

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was used to measure UIE levels were potassium iodate, ammonium peroxydisulfate, arsenious acid, sodium chloride, ceric ammonium sulfate, sulfuric acid 5N and 3N and deionized water. Measurement of TSH levels in blood serum using the Enzyme Linked Immunosorbent Assay (ELISA) method with General Biologicals Corporation (GBC) reagent. Samples, standards and controls were each taken and put into the well. Add conjugate to all wells and incubate for 60 mins at room temperature. Then, wash the plate with wash buffer 5 times then add the substrate to all wells. Incubate for 30 mins in a dark room. Last, add stop solution to all wells and read with a microplate reader at a wavelength of 450 nm. The dynamic increase of HCG concentration in the first trimester allows TSH levels to dynamic decrease with sudden changes occurring at 7 to 9 weeks of gestation. Therefore, this study was only carried out on pregnant women in the second and third trimesters (Kim *et al*., 2015). Pregnant women in the second trimester were in the range of 13-27 weeks and the third trimester was more than 27 weeks (Wynne *et al*., 2020). UIE levels were low 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 second trimester were 0.2 -3.0 mIU/L and third trimester were 0.3-3.0 mIU/L (Green *et al*., 2011).

Univariate analysis was used on one variable to know and identify 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 a 95% confidence level. Multivariate analysis was to determine the strongest risk factors of IDD by using logistic regression analysis with a stepwise method.

3. Results

The number of subjects obtained in the study at the Mlonggo Health Center and the Pakis Aji Health Center, Jepara Regency, Indonesia, 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%). Pregnant women aged over 35 years and under 20 years had a higher percentage of high TSH levels than normal TSH levels. Pregnant women with a parity of more than 4 had high TSH levels. 61.9% of pregnant women with sufficient education had high TSH levels. 55.9% of pregnant women with normal MUAC had high TSH levels and 45% of pregnant women with low MUAC had high TSH levels. Pregnant women in the third trimester had a higher percentage of high TSH levels (54.7%). Approximately 77.8% of subjects with poor family support had high TSH levels. About 66.7% of the subject with poor media information had high TSH levels. Based on knowledge, almost all subjects had sufficient knowledge related to pregnancy. About 53.7% of subjects with insufficient knowledge related to nutrition had high TSH levels. Whereas, 56.6% of subjects with sufficient knowledge related to IDD had high TSH levels and 48.6% of subjects with insufficient knowledge related to IDD had high TSH levels. The majority of subjects with insufficient attitudes had high TSH levels, namely attitudes related to pregnancy (60%) and IDD (60%). Around 55% of pregnant women with sufficient attitudes related to nutrition had high TSH levels and 50% of pregnant women with insufficient attitudes related to nutrition had high TSH levels. Based on macro intake, 62.5% of subjects with excess energy intake had high TSH levels, 57.6% of subjects with excess carbohydrate intake had high TSH levels, 75% of subjects with excess protein intake had high TSH levels and 53.3% of subjects with excess fat intake have high TSH levels. Subjects with excess fiber intake had high TSH levels. Based on micronutrient intake, 53.8% of subjects with excess vitamin C intake had high TSH levels, 66.7% of subjects with excess magnesium intake had high TSH levels and 52.4% of subjects with excess manganese intake had high TSH levels.

Based on UIE levels, 68.2% of subjects were included as low UIE levels and 31.8% of subjects as normal UIE levels. The majority of subjects had low UIE in all age groups. Pregnant women with a parity of more than 4 had normal UIE levels. 71.74% of pregnant women with insufficient education had low UIE. 70% of pregnant women with small MUAC had low UIE levels. The majority of pregnant women had low UIE levels both in the second trimester (58.33%) and in the third trimester (71.88%). Approximately 72.2% of pregnant women with poor family support had low UIE levels. Based on knowledge related to pregnancy, subjects with insufficient knowledge had low UIE levels. Based on nutritional knowledge, 70.73% of subjects with insufficient knowledge had low UIE levels. Based on the knowledge of IDD, 82.86% of subjects with insufficient IDD knowledge had low UIE levels. The majority of subjects with insufficient attitudes had low UIE levels, namely attitudes related to pregnancy (100%) and IDD (80%). 70% of pregnant women with sufficient attitudes related to nutrition had low UIE levels and 64.3%% of pregnant women with sufficient attitudes related to nutrition had low UIE levels. Based on macronutrient intake, 65.63% of subjects with inadequate energy intake had low UIE levels, 70.37% of subjects with inadequate carbohydrate intake had low UIE levels, 72.06% of subjects with inadequate protein intake had low UIE

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Table 1. Distribution of subject characteristics

Variables	N	%	Thyroid Stimulating Hormone (TSH)				Urinary Iodine Excretion (UIE)			
			High		Normal		Low		Normal	
			n	%	n	%	n	%	n	%
Age										
>35 years old	15	17	10	66.7	5	33.3	8	53.33	7	46.67
20-35 years old	70	79.5	34	48.6	36	51.4	50	71.43	20	28.57
<20 years	3	3.4	3	100	0	0	2	66.67	1	33.33
Parity										
P<4	87	98.9	46	52.9	41	47.1	60	68.97	27	31.03
P≥4	1	1	1	100	0	0	0	0	1	100
Mother's education										
Sufficient	42	47.7	26	61.9	16	38.1	27	64.29	15	35.71
Insufficient	46	52.3	21	45.65	25	54.35	33	71.74	13	28.26
Mid-Upper Arm Circumference										
Normal	68	77.3	38	55.9	30	44.1	46	67.65	22	32.35
Small	20	22.7	9	45	11	55	14	70	6	30
Gestational age										
Third trimester	64	72.7	35	54.7	29	45.3	46	71.88	18	28.13
Second trimester	24	27.3	12	50	12	50	14	58.33	10	41.67
Family's support										
Good	79	89.8	40	50.6	39	49.4	3	33.3	6	66.7
Poor	9	10.2	7	77.8	2	22.2	57	72.2	22	27.8
Media information										
Good	55	62.5	25	45.5	30	54.5	37	67.3	18	32.7
Bad	33	37.5	22	66.7	11	33.3	23	69.7	10	30.3
Pregnancy knowledge										
Sufficient	86	97.7	46	53.5	40	46.5	58	67.4	28	32.6
Insufficient	2	2.3	1	50	1	50	2	100	0	0
Nutrition knowledge										
Sufficient	47	53.4	25	53.2	22	46.8	31	65.96	16	34.04
Insufficient	41	46.6	22	53.7	19	46.3	29	70.73	12	29.27
Iodine Deficiency Disease Knowledge										
Sufficient	53	60.2	30	56.6	23	43.4	31	58.49	22	41.51
Insufficient	35	39.8	17	48.6	18	51.4	29	82.86	6	17.14
Pregnancy attitude										
Sufficient	83	94.3	44	53	39	47	55	66.4	28	33.7
Insufficient	5	5.7	3	60	2	40	5	100	0	0
Nutrition attitude										
Sufficient	60	68.2	33	55	27	45	42	70	18	30
Insufficient	28	31.8	14	50	14	50	18	64.3	10	35.7
Iodine Deficiency Disease attitude										
Sufficient	73	83	38	52	35	48	48	65.8	25	34.2
Insufficient	15	17	9	60	6	40	12	80	3	20
Energy intake										
Excessive (>100%)	8	9.1	5	62.5	3	37.5	4	50	4	50
Adequate (80-100%)	48	54.5	26	54.2	22	45.8	35	72.92	13	27.08
Inadequate (<80%)	32	36.4	16	50	16	50	21	65.63	11	34.38
Carbohydrate intake										
Excessive (>100%)	33	37.5	19	57.6	14	42.4	21	63.64	12	36.36
Adequate (80-100%)	28	31.8	13	46.4	15	53.6	20	71.43	8	28.57
Inadequate (<80%)	27	30.7	15	55.6	12	44.4	19	70.37	8	29.63

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Table 1 (Cont.). Distribution of subject characteristics

Variables	N	%	Thyroid Stimulating Hormone (TSH)				Urinary Iodine Excretion (UIE)			
			High		Normal		Low		Normal	
			n	%	n	%	n	%	n	%
Protein intake										
Excessive (>100%)	4	4.5	3	75	1	25	2	50	2	50
Adequate (80-100%)	16	18.2	9	56.3	7	43.8	9	56.25	7	43.75
Inadequate (<80%)	68	77.3	35	51.5	33	48.5	49	72.06	19	27.94
Fat intake										
Excessive (>100%)	15	17	8	53.3	7	46.7	10	66.67	5	33.33
Adequate (80-100%)	32	36.4	20	62.5	12	37.5	22	68.75	10	31.25
Inadequate (<80%)	41	46.6	19	46.3	22	53.7	28	68.29	13	31.71
Fiber intake										
Excessive (>100%)	1	1.1	1	100	0	0	1	100	0	0
Inadequate (<80%)	87	98.9	46	52.9	41	47.1	59	67.82	28	32.18
Vitamin C intake										
Excessive (>100%)	26	29.5	14	53.8	12	46.2	18	69.23	8	30.77
Adequate (80-100%)	16	18.2	10	62.5	6	37.5	10	62.5	6	37.5
Inadequate (<80%)	46	52.3	23	50	23	50	32	69.57	14	30.43
Magnesium intake										
Excessive (>100%)	18	20.5	12	66.7	6	33.3	11	61.11	7	38.89
Adequate (80-100%)	33	37.5	17	51.5	16	48.5	23	69.7	10	30.3
Inadequate (<80%)	37	42	18	48.6	19	51.4	26	70.27	11	29.73
Mangan intake										
Excessive (>100%)	82	93.2	43	52.4	39	47.6	57	69.5	25	30.5
Adequate (80-100%)	6	6.8	4	66.7	2	33.3	3	50	3	50

levels and 68.29 % of subjects with inadequate fat intake had low UIE levels. Subjects with excess fibre intake had low UIE levels. Based on micronutrient intake, 69.57% of subjects with inadequate vitamin C intake had low UIE levels, 70.27% of subjects with inadequate magnesium intake had low UIE levels and 69.5% of subjects with excess manganese intake had low UIE 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 the 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 UIE 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 consumption variables with multivariate analysis, Table 5 showed that IDD knowledge was the strongest risk factor for IDD based on UIE (p-value 0.008; OR adjusted 4.776; CI OR 1.510:15.105) and family's support was a risk factor for IDD based on UIE (p-value 0.037; OR adjusted 0.185; CI OR 0.038:0.906).

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 normal TSH levels. The percentage of pregnant women with IDD in this study was much higher than the previous study in Magelang, Indonesia which showed that 17.1% of pregnant women in endemic areas of goitre experienced hypothyroidism and 19.2% of pregnant women in non-endemic areas of goitre experienced hypothyroidism (Kusrini *et al*., 2016). Although this study was conducted in the coastal area of

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

Variables	OR	95% CI for OR		p
		Lower	Upper	
Age				
>35 years old	Reference			
20-35 years old	0.264	0.054	1.29	0.1
<20 years	671017006437299580	<0.001	<0.001	0.999
Parity				
P<4	Reference			
P≥4	2699389903.446	<0.001	<0.001	1
Mother's education				
Sufficient	Reference			
Insufficient	0.169	0.04	0.709	0.015
Mid-Upper Arm Circumference				
Normal	Reference			
Small	0.63	0.14	2.837	0.547
Gestational age				
Third trimester	Reference			
Second trimester	0.242	0.057	1.022	0.054
Family's support				
Good	Reference			
Bad	2.475	0.297	20.634	0.402
Media information				
Good	Reference			
Bad	1.548	0.444	5.403	0.493
Pregnancy knowledge				
Sufficient	Reference			
Insufficient	<0.001	<0.001	<0.001	0.999
Nutrition knowledge				
Sufficient	Reference			
Insufficient	1.493	0.431	5.177	0.527
Iodine Deficiency Disease Knowledge				
Sufficient	Reference			
Insufficient	1.475	0.407	5.346	0.554
Pregnancy attitude				
Sufficient	Reference			
Insufficient	1.069	0.094	12.175	0.957
Nutrition attitude				
Sufficient	Reference			
Insufficient	0.637	0.186	2.18	0.473
Iodine Deficiency Disease attitude				
Sufficient	Reference			
Insufficient	1.361	0.287	6.443	0.698
Energy intake				
Excessive (>100%)	Reference			
Adequate (80-100%)	0.876	0.051	15.16	0.927
Inadequate (<80%)	0.913	0.025	33.404	0.96
Carbohydrate intake				
Excessive (>100%)	Reference			
Adequate (80-100%)	0.502	0.085	2.967	0.447
Inadequate (<80%)	0.437	0.025	7.517	0.569
Protein intake				
Excessive (>100%)	Reference			
Adequate (80-100%)	0.297	0.01	8.882	0.484
Inadequate (<80%)	0.377	0.006	24.557	0.647

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

Variables	OR	95% CI for OR		p
		Lower	Upper	
Fat intake				
Excessive (>100%)	Reference			
Adequate (80-100%)	1.657	0.257	9.999	0.582
Inadequate (<80%)	1.335	0.203	8.784	0.764
Fiber intake				
Excessive (>100%)	Reference			
Inadequate (<80%)	<0.001	<0.001	<0.001	1
Vitamin C intake				
Excessive (>100%)	Reference			
Adequate (80-100%)	5.944	0.938	37.657	0.058
Inadequate (<80%)	2.441	0.496	12.014	0.272
Magnesium intake				
Excessive (>100%)	Reference			
Adequate (80-100%)	1.441	0.13	15.987	0.766
Inadequate (<80%)	0.752	0.053	10.644	0.833
Mangan intake				
Excessive (>100%)	Reference			
Adequate (80-100%)	2.935	0.315	27.361	0.345

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

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

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

Variables	OR	95% CI for OR		p
		Lower	Upper	
Age				
>35 years old	Reference			
20-35 years old	1.345	0.212	8.544	0.753
<20 years	0.153	0.003	7.386	0.343
Parity				
P<4	Reference			
P≥4	<0.001	<0.001	<0.001	1
Mother's education				
Sufficient	Reference			
Insufficient	1.685	0.346	8.202	0.518
Mid-Upper Arm Circumference				
Normal	Reference			
Small	1.666	0.311	8.923	0.551
Gestational age				
Third trimester	Reference			
Second trimester	0.378	0.079	1.806	0.223
Family's support				
Good	Reference			
Bad	0.133	0.015	1.151	0.067

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

Variables	OR	95% CI for OR		p
		Lower	Upper	
Media information				
Good	Reference			
Bad	2.361	0.543	10.257	0.252
Pregnancy knowledge				
Sufficient	Reference			
Insufficient	3225423350	<0.001	<0.001	0.999
Nutrition knowledge				
Sufficient	Reference			
Insufficient	1.088	0.249	4.747	0.911
Iodine Deficiency Disease Knowledge				
Sufficient	Reference			
Insufficient	4.602	0.841	25.168	0.078
Pregnancy attitude				
Sufficient	Reference			
Insufficient	<0.001	<0.001	<0.001	0.999
Nutrition attitude				
Sufficient	Reference			
Insufficient	0.378	0.081	1.764	0.216
Iodine Deficiency Disease attitude				
Sufficient	Reference			
Insufficient	1.168	0.158	8.636	0.879
Energy intake				
Excessive (>100%)	Reference			
Adequate (80-100%)	2.798	0.131	59.842	0.51
Inadequate (<80%)	0.301	0.006	16.021	0.554
Carbohydrate intake				
Excessive (>100%)	Reference			
Adequate (80-100%)	0.903	0.117	7.002	0.922
Inadequate (<80%)	3.572	0.118	108.079	0.464
Protein intake				
Excessive (>100%)	Reference			
Adequate (80-100%)	1.277	0.016	103.689	0.913
Inadequate (<80%)	3.294	0.02	531.651	0.646
Fat intake				
Excessive (>100%)	Reference			
Adequate (80-100%)	0.666	0.063	7.074	0.736
Inadequate (<80%)	0.279	0.023	3.459	0.321
Fiber intake				
Excessive (>100%)	Reference			
Inadequate (<80%)	<0.001	<0.001	<0.001	1
Vitamin C intake				
Excessive (>100%)	Reference			
Adequate (80-100%)	0.306	0.042	2.217	0.241
Inadequate (<80%)	1.265	0.199	8.054	0.804
Magnesium intake				
Excessive (>100%)	Reference			
Adequate (80-100%)	1.582	0.089	27.962	0.754
Inadequate (<80%)	1.881	0.063	42.427	0.691
Mangan intake				
Excessive (>100%)	Reference			
Adequate (80-100%)	0.279	0.02	3.988	0.347

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

Variables	OR adjusted	95% CI for OR		p
		Lower	Upper	
Parity				
P<4	Reference			
P≥4	<0.001	<0.001	<0.001	1
Family's support				
Good	Reference			
Bad	0.185	0.038	0.906	0.037
Iodine Deficiency Disease Knowledge				
Sufficient	Reference			
Insufficient	4.776	1.51	15.105	0.008
Pregnancy attitude				
Sufficient	Reference			
Insufficient	<0.001	<0.001	<0.001	0.999

Jepara, Indonesia which is a salt-producing area, the prevalence of pregnant women with low iodine adequacy was still high. This is in contrast to previous studies which showed the prevalence of low UIE levels in coastal areas in only 5.9% of subjects (Kurniangga, 2016). However, previous studies in the same area such as Mayong, Batealit and Pakis Aji, Jepara, Indonesia mentioned the availability of iodized salt with levels of 30 ppm was 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). This study showed that age has not been a risk factor for IDD either based on UIE levels or TSH levels because of 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 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). 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 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 newborn brain development (Brahmbhatt *et al*., 2001).

This study was dominated by the third trimester of pregnancy, which was 72.7% 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 showed that the percentage of pregnant women in the third trimester was more IDD than in the second trimester, which was 71.88%. Previous research in Mexico showed that the average TSH level was higher in third-trimester pregnant

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women compared to the first and second trimester (Bocos-Terraz *et al*., 2009). During the third trimester of pregnancy, thyroid hormone-dependent neurogenesis is still ongoing, and 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).

Multivariate analysis of 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 0.324× more at risk of experiencing IDD than mothers with the 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 behaviour in society, including the consumption of iodized salt (Nadimin, 2015). Multivariate analysis of 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 4,776× more at risk of experiencing IDD than pregnant women with sufficient knowledge of IDD. This study showed that 82.86% of pregnant women with insufficient IDD knowledge had low 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).

This study showed that 62.5% of pregnant women had good media information and 89.9% had good family support. This study has not shown that media information is a risk factor for IDD. This is in contrast with previous research which showed that watching the media and sources of information both show risk to knowledge and perception of the disease (Karasneh *et al*., 2020). This study showed that family support was the risk factor for IDD based on UIE levels after adjustment for some variables. Pregnant women with bad family support were 0.185x more at risk of experiencing IDD. This is in contrast to previous research which showed that family support can improve the health status of family members. The role of family support in the IDD problem can be in the form of procuring and storing iodized salt properly (Chahyanto *et al*., 2017; Michaelson *et al*., 2021).

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 the 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 UIE levels. The study also mentioned that the mother's practices related to the fulfilment of low iodine 2.5 times the risk of IDD (Mirmiran *et al*., 2013). This study showed that the percentage of pregnant women who experience IDD was higher in pregnant women with fewer attitudes. Therefore, the mother's attitude towards pregnancy, nutrition and IDD needs to be followed by good daily practices as well. Although it has not been a risk factor for IDD, having healthy daily practices both in pregnancy, nutrition and prevention of IDD during pregnancy can improve the quality of pregnancy, fetal development and avoid miscarriage (Dunney and Murphy, 2015).

This study showed that the overall consumption 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 levels and revert subclinical hypothyroidism. Hypothyroidism itself can cause disturbances in the intestinal tract, which causes problems with bowel movements (Mezzomo and Nadal, 2016). Therefore, adequate consumption of water and fibre is necessary for pregnant women. In addition, stress management and behavioural 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).

Since 2009, long-term prevention of IDD in Indonesia has been carried out by iodine fortification in salt and drinking water. In Jepara Regency, Indonesia, the local government made a regional regulation of Jepara Regency number 2 of 2009 concerning the regulation and control of the circulation of iodized salt. However, a previous study in 2015 showed that 57 of 75 brands of iodized salt in Jepara had an iodine content of less than 30 ppm. In addition, short-term measures are also taken when IDD was a major nutritional problem in Indonesia, especially in moderate and severe endemic areas, namely iodized oil and lipiodol solutions, which are then replaced with iodized oil capsules (Widiyatni *et al*., 2016; Yunawati and Rabbani Karimuna, 2021).

4. Conclusion

There were 53.4% of pregnant women from all

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research subjects in the Mlonggo Health Center and Pakis Aji Health Center, Jepara, Indonesia 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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