The Iodine Status of Women of Childbearing Age in an Iodine-repleted Area: An Epidemiological Study in Sengi Village on Merapi Mountain Area

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ABSTRACT

Background: *The low iodine content of daily water sources and repeated volcanic eruptions are expected to affect the iodine status and thyroid hormone profile of women of childbearing age in the Magelang regency. This study aimed to determine the iodine and thyroid profile among women of childbearing age.* ***Methods****: We used a cross-sectional descriptive study to learn about 140 women of reproductive age living in Sengi village from October 2017 to January 2018. We assessed the iodine level, dietary intake, and goitrogenic food consumption using food frequency questionnaire (FFQ), urinary iodine concentration (UIC), thyroid stimulating hormone (TSH) and free thyroxine (fT4), and total goiter rate (TGR).* ***Results****: The median UIC was 199.5 (126.0 – 264.0) µg/L. The TGR was 10.7% on palpation and 7.8% on ultrasound. The proportion of UIC levels below 100µg/L was 18.5%. The mean water iodine content was 2.03 ± 4.74 µg/L. The mean salt iodine level was 28.6±13.7ppm. There were only 35% who consumed salt with adequate iodine contents, and only 19.29% consumed >150µg iodine from daily dietary intake based on FFQ. The median TSH and FT4 levels were 1.72 and 1.51mIU/L.* ***Conclusion****: Women of childbearing age in Sengi Village generally had adequate iodine profiles and normal thyroid hormone levels but a considerable proportion of TGR and low UIC. The iodine contents within the freshwater source, table salt, and daily dietary intake were low. There are no significant association between Iodine status, daily goitrogen intake, daily iodine intake and salt iodine concentration*

Keywords*: Iodine profile, Thyroid, Women of childbearing age.*

INTRODUCTION

Iodine deficiency has been one of the major public health problems around the globe.[1,2] In Indonesia, the national Iodine Deficiency Disorders (IDD) survey showed that 8,2% were severely endemic to IDD.[3] In Central Java, the prevalence of iodine deficiency was 24.9%, in which the Magelang Regency accounts for 14.3% of the total cases.[3] The spectrum of IDD may affect any age, and the impacts include miscarriage, stillbirth, increased perinatal morbidity and mortality, goiter, and hypothyroidism.[4] Children, pregnant women, and lactating women are the most vulnerable groups.[4] Undiagnosed IDD among women of childbearing age might increase the risk of developing IDD and/ or its devastating consequences later during pregnancy and lactating period.[4,5]

The World Health Organization (WHO) and the International Council for Control of Iodine Deficiency Disorders (ICCIDD) have propagated the use of household iodized salt to manage IDD.[6] In 2020, 124 countries or around 88% of the world's population have put in place regulations about mandatory salt iodination.[7] In Indonesia, the widely used household iodized salt is potassium iodate (KIO_3), with a minimum concentration of 30-80 ppm KIO_3.[3] The national household coverage of adequately iodized salt in Indonesia is 55.1%, with higher coverage in the urban population (59.3%) than in the rural counterpart (51.4%).[8]

Geographical conditions, such as climate, topography, and land material, greatly affect the iodine availability in the area.[9] People living in the mountain area usually have a higher risk of developing IDD compared to those who live in the lowland areas.[10] In 2007, the soil in areas surrounding Merapi mountain in Central Java, Indonesia, was reported to possess low iodine content. Sengi Village is one of the villages with moderate danger; a previous study showed that the prevalence of congenital hypothyroidism was 6%, categorizing the area endemic for IDD.[11]

Women of childbearing age are one of the most vulnerable groups to suffer from IDD[4,5]. Studies from several developed and developing countries have shown that in this population, there are still areas that are iodine deficient.[12–15] Considering IDD's irreversible and significant maternofetal, neonatal, and offspring impact, it is essential to assess the iodine status in this population.[16] Therefore, this study aims to assess the iodine profile of women of childbearing age in the Sengi village from 2017 to 2018.

METHODS

We conducted this cross-sectional study in Magelang from October 2017 to January 2018. The population was women aged 18-45 years. The inclusion criteria were women living in the area for a minimum of 1 year who are willing to provide written informed consent to participate in this study. The exclusion criteria were pregnancy, severe sickness, having received iodine supplementation in the past year, or inability to complete the entire study.

The primary outcomes were urine iodine concentration (UIC), iodine concentration within the table salt consumed by the subjects, iodine concentration within the freshwater source for daily use, estimation of daily iodine intake from diet, total goiter rate (TGR), and thyroid hormones concentration including thyroid stimulating hormone (TSH) and free thyroxine (FT_4).

The number of samples needed to estimate the UIC parameter was 140 subjects. All data were compiled, edited, tabulated, then analyzed using descriptive analysis on SPSS. This study protocol was approved by the ethical committee of the Faculty of Medicine Diponegoro University and Kariadi General Hospital (No.676/EC/FK-RSDK/XI/2017).

RESULTS

There were 140 subjects included in this study, of which 97.8% were native residents who had been living there for more than 24 years. The subjects' mean age was 33 years old. The subjects' socioeconomic status was

Table 1. Characteristics of study population.

Variables	N	%	Mean ± SD
Age (years)			33 ± 8
≤ 20	6	4.3	
21-30	54	38.6	
31-40	49	35	
>40	31	22.1	
Subvillage			
Sengi	38	27.1	
Ngampel	24	17.1	
Candi Duwur	24	17.1	
Gowok Pos	19	13.6	
Gowok Sabrang	13	9.3	
Gowok Ringin	11	7.9	
Candi Tengah	6	4.3	
Candi Pos	5	3.6	
Education Level			
Uneducated	1	0.7	
Elementary school	56	40	
Junior high school	48	34.3	
Senior high school	34	24.3	
University	1	0.7	
Occupation			
Farmer	102	72.9	

Housewife	20	14.3	
Blue collar worker	10	7.1	
Merchant	4	2.9	
Teacher	2	1.4	
Private employee	2	1.4	
Monthly income		Rp814.286 ± 657.36	
< IDR 500,000 (USD34.90)	34	24.3	
IDR 500,000 (USD34.90 - IDR 1,000,000 (USD69.81)	87	62.1	
IDR 1,000,001 (USD34.90) – IDR 2,000,000 (USD139.62)	15	10.7	
> IDR 2,000,000 (USD139.62)	4	2.9	
Duration of stay			24 ± 13
< 5 years	10	7.1	
5-10 years	25	17.9	
>10 years	105	75	

mainly lower to middle income, with an average monthly income of IDR 814,000 (USD 56.91). The baseline characteristics of the study subjects are presented in **Table 1**.

The mean Body Mass Index (BMI) is 23.67±4.82 kg/m^2. Most subjects (89.3%) did not have enlarged thyroid glands. From the thyroid ultrasound examination, the mean thyroid volume was 12.22±13.43 cc. The TGR at Sengi Village was 7.8%. Among 140 subjects, 37 (25.7%) had thyroid nodule(s). The median UIC was 199.5 µg/L. The complete data are presented in **Table 2**.

The mean KIO_3 concentration within the household salt consumed by the subjects was 28.6±13.7 ppm. Eighty-nine (63,6%) salt samples had lower KIO_3 concentration than the recommended level, and two samples (1.4%) had higher KIO_3 concentration than the recommended level. Based on the salt type, the salt block is the most common salt used (78.6%), followed by regular grains table salt (21.4%). The freshwater iodine content based on the altitude of the water source is illustrated in **Figure 1**.

Daily dietary iodine intake among the subjects was categorized as inadequate in 80.17% of subjects. The iodine profile of the freshwater source, table salt consumption, and daily iodine intake from the diet can be seen in **Table 3**. The most commonly consumed iodine-rich source was eggs (60.7%). They consumed eggs more than three times a week. The most common goitrogenic food consumed by the respondents was cabbage (37.1%). They ate it more than thrice a week. The respondents' dietary patterns are described in **Table 4**.

The median TSH and FT4 levels were 1.72 mIU/L and 1.51 mIU/L. As many as 135 subjects (97.0%) had normal TSH levels, while three subjects (2.0%) had high TSH levels, and two subjects (1.0%) had low TSH levels. All subjects had normal FT4 levels. Almost all (96,5%) of the subjects were euthyroid. The remaining three (2,1%) subjects had subclinical hypothyroidism, and two (1,4%) subjects had subclinical hyperthyroidism.

UIC is the gold standard to define iodine deficiency for a population in a region[17]. WHO

Table 2. The total goiter rate and urine iodine concentration among childbearing-age women in Sengi village.

Variables	N	%
Thyroid gland grade by palpation		
No palpable or visible goiter	125	89.29
Palpable goiter	9	6.43
Visible goiter	6	4.29
Thyroid gland volume by ultrasound examination		
≤18.6 cc	129	92.2
>18.6 cc	11	7.8
UIC (µg/L)		
<20 (severe iodine deficiency)	1	0.7
20-49 (moderate iodine deficiency)	10	7.1
50-99 (mild iodine deficiency)	15	10.7
100-199 (adequate iodine intake)	45	32.1
200-299 (excessive iodine intake)	53	37.9
>300 (iodine-induced hyperthyroidism. thyroid autoimmune)	16	11.4

Table 3. Iodine profile and daily iodine and goitrogenic intake of childbearing women in Sengi village.

Variable	Value
Urinary iodine concentration (mcg/L)	199.5 (126.0 – 264.0[a]
Thyroid volume (cc)	9.1 (3.5-128.3)[b]
Iodine concentration in salt (ppm)	26.5 (5.3-100.5)[b]
Daily salt consumption (gr)	2.5 (0.5-13.3)[b]
Daily iodine intake from salt (mcg/L)	74.0 (74.0-394.6)[b]
Daily iodine intake from food (mcg/L)	12.8 (0.0-100.1)[b]
Daily total iodine intake (mcgg)	91.7 (14.3-456.8)[b]
Daily goitrogen intake (mg)	1.1 (0.0-8.3)[b]

Note: [a]Median (interquartile range), [b]Median (minimum - maximum

Table 4. Dietary pattern of iodine-rich and goitrogenic foods of childbearing-age women in Sengi village in the last 1 month.

Type of Food	Frequency					
	≥ 3 times/ week		< 3 times/ week		Never	
	n	%	n	%	n	%
Iodine-rich foods						
Pindang	7	5	105	75	28	20
Salted fish	5	3.6	83	59.3	52	37.1
Saltwater fish	2	1.4	39	27.9	99	70.7
Shrimp	0	0	4	2.2	136	97.1
Oyster	0	0	1	0.7	139	99.3
Egg	85	60.7	48	34.3	7	5
Milk	20	14.3	19	13.6	101	72.1
Beef liver	0	0	3	2.1	137	97.9
Spinach	24	17.1	64	45.7	52	37.1
Jelly	8	5.7	88	62.9	44	31.4
Goitrogenic foods						
Cassava	30	21.4	99	70.7	11	7.9
Sweet potato	29	20.7	91	65	20	14.3
Mustard greens	52	37.1	70	50	18	12.9
Cabbage	23	16.4	71	50.7	46	32.9
Cassava leaf	21	15	79	56.4	40	28.6

cut-off for IDD in the adult population is when the median UIC of the population is less than 100 mcg/L, and >50% of the population has UIC of less than 100 µg/L or <20% of the population has UIC of less than 50 mcg/L. Among the women of childbearing age in Sengi village, the median UIC was 199.5, with 81.4% of subjects having a UIC value of > 100 mcg/L. Therefore, considering the UIC parameter, the women of childbearing age in Sengi village had adequate iodine status. As many as 10% of subjects had UIC levels of 50.1 - 99,9 mcg/L, and 8.8% of other subjects had UIC levels of <50 mcg/L. Based on palpation and thyroid ultrasound, the IDD prevalence from the TGR parameter was 10.7% and 7.8%. Goiter prevalence in this study was 7.8% by thyroid ultrasound examination. No evaluation of either de novo/residual goiter or thyroiditis goiter was performed in this study; hence the TGR value of this study may not truly represent the IDD problem in the region. Therefore, based on the UIC parameter, women of childbearing age in Sengi village were still considered to possess adequate iodine levels.

Table 5 demonstrates the relationship between iodine intake from the daily consumed table salt and the UIC. This study showed that those with normal UIC mostly consumed salt with >40 ppm of KIO_3. As many as 88.9% of subjects with normal UIC consumed salt with 10-40 ppm of KIO_3, and 8.9% consumed salt with >40 ppm of KIO_3.

The study shows that despite the difference in iodine status based on IUC levels, there are no

Table 5. The distribution of salt iodine concentration consumed by childbearing-age women in sengi village based on their urine iodine concentration level.

Urine Iodine Concentration (µg/L)	Salt Iodine Concentration					
	<10 ppm	10-20 ppm	20.1-30 ppm	30.1-40 ppm	>40 ppm	N
<100	0	26.9	50	11.5	11.5	26
100-199	2.2	22.2	46.7	20	8.9	45
>199	2.9	18.8	31.9	23.2	23.2	69

Table 6. Association between iodine status, daily goitrogen intake, daily iodine intake and salt iodine concentration.

Iodine Status	Daily Goitrogen intake[a] (mg)	p-value	Daily Iodine Intake[a] (μg)	p-value	Salt Iodine Concentration[a] (ppm)	p-value
Deficient	1.09 (0.01-7.95)		87.46 (22.85-276.80)		23.25 (10.6-47.6)	
Adequate	1.05 (0.08-8.11)		86.93 (143-253.93)		26.5 (5.3-63.5)	
Excessive	1.09 (0-8.33)	0.981[b]	93.50 (16.60-456.77)	0.499[b]	28.6 (7.4-106.5	0.109[b]

Note: [a]Median (minimum - maximum), [b]Kruskal-Wallis test

significant association between daily goitrogen intake, daily iodine intake and salt iodine concentration (**Table 6**).

DISCUSSION

The TGR based on the USG examination was 8.6%. It declined significantly from 20% in 2015. Using the WHO epidemiological criteria, Dukun Subdistrict had been categorized as moderately endemic for IDD in 2015 and became mildly deficient of iodine in 2017-2018.[18] The median UIC among women of reproductive age in Indonesia was 189.0 mcg/L in 2013. In Central Java, the value was higher; 240 mcg/L. The higher provincial median UIC was possibly due to several coastal regions where daily water sources contain a much higher level of iodine; hence higher UICs.[18]

Another large-scale survey involving 106,825 pregnant women in Central Java in 2011 showed that the median UIC was 156 mcg/L, and the percentage of pregnant women with UIC lower than 100 mcg/L was 33.87%. There were four districts with mild iodine deficiency found in the study mentioned above. That study further assessed that 18 neonates (0.03%) were suspected of having cretinism, and 174 (0.18%) had TGR degrees of 1 – 2.[17]

Kusrini's study showed that the mean UIC reached 221$\pm$88 mcg/L among pregnant women in Magelang. But in the general population in Magelang, it was 244 $\pm$ 92 mcg/L.[15] This marked difference was caused by the difference in urine samples used. Kusrini's study measured both spot urine and three days 24-hour urine samples for the mean UIC measurement. In our study, only spot urine samples were used. WHO stated that spot urine is already a reliable representation of an individual's iodine status.[19] Therefore, it is conclusive that the iodine status of both women of reproductive age and pregnant women of Magelang regency, including Sengi village is adequate.

The iodine status of this study was determined by UIC instead of TGR. Total goiter rate (TGR) was a reliable predictor of moderate-to-severe iodine insufficiency when endemic goiter caused by iodine shortage was common. A significant drawback of the usage of TGR is that goiter resolution takes a long time to occur after iodine intake improves. In adults, TGR may represent past IDDs rather than current ones. A change in the TGR may not correctly reflect the possible contribution of IDDs to a decline in intelligence quotient (IQ) and cognitive impairment[20]. The WHO goiter rate criteria were meant to be applied to school-age children[18] . There were other causes that contributes to TGR, such as residual goiters or goiters due to autoimmune thyroiditis. Thus, the TGR data had to be interpreted carefully.

The median TSH and FT_4 levels were within the normal range (median TSH 1.72 mIU/L and median FT_4 1.51 mIU/L), and almost all subjects in this study were categorized as euthyroid (96.5%). Kusrini's study showed an increasing trend of median TSH along with an increase in gestational age. The median TSH level for all subjects from the rural area was 1.30 mIU/L. The median FT_4 level in that study was 1.27 mIU/L among all the subjects.[15] This difference might be caused by the increased maternal thyroid hormone production during pregnancy; hence there were higher subclinical hyperthyroidism cases in that study. Another cohort study reported that lower TSH and greater FT_3 and FT_4 concentrations were linked to lower iodine availability throughout pregnancy and postpartum. The thyroid function improves after iodine supplementation before pregnancy and throughout pregnancy[21].

WHO recommended the minimum daily iodine intake for non-pregnant women of reproductive age to be 150 µg. Iodine can be obtained from salt, foods, and drinks. The mean iodine intake in this study was lower than the recommendation (108.4 mcg/day).[1] The women of childbearing age in this study are at risk of developing IDD. The average iodine concentration of household table salt in all studied samples was 28.6±13.7 ppm, and only 35% of the subjects consumed salt with adequate iodine content. It was significantly lower than Kusrini's study, in which the mean salt iodine content across both areas (rural and urban) was 40.5±20.6 ppm.[22]

There were seven salt brands used by the subjects; each brand displays its iodine content, except for one brand. Each brand stated that the iodine content was within the recommended range (30-80 ppm). This suggested a possible reduction of iodine content in salt during packaging, storing, and/or transportation. The WHO reported that the iodine content in salt is reduced by 50% by the time it reaches consumers due to poor iodine quality, mishandling during packaging, poor storage conditions (high humidity and temperature), and long storage time[6]. Iodized salt is best stored in closed storage to keep the salt dry.[1,6]

The mean salt consumption among respondents was only 3.3 g/day, much lower than the WHO recommendation.[1,6] It might be caused by the food cooking method. The people of Sengi Village usually cook once daily in the morning, and the food will be eaten throughout the day. The food was cooked long before consumption, leading to several episodes of reheating before consumption, lowering the iodine content. Moreover, some participants were cautious of salt usage due to the risk of developing hypertension from consuming too much salt. Other than salt, iodine also can be obtained from food. From the Food Frequency Questionnaire (FFQ), the documented mean iodine consumption was 16.1 µg/ day. Egg was the most frequent iodine-rich food consumed by the respondents because it is affordable and readily available at all times. Saltwater fish, shrimp, and oysters are also rich in iodine, but the respondents rarely consumed them due to their high price and low availability. Almost all respondents did not consume shrimp and oysters during the one-month observation.

Based on the FFQ, the most frequent goitrogenic foods consumed by the respondents were cassava, sweet potato, mustard green, cabbage, and cassava leaf. In this study, the mean cyanide intake among respondents was 1.9 mg/ day, significantly lower than the 10 mg/ day limit set by the FAO/WHO. This goitrogenic food often contains cyanide derivates (thiocyanate and isothiocyanate) that inhibit thyroid hormone synthesis.[19] Exceeding the daily cyanide intake limit might cause health complications, such as acute intoxication, chronic toxicity, neurological disorders, growth retardation, and goiter.[23] Although cassava and sweet potato, which contain a high level of cyanide, are frequently consumed in the sample population, the cyanide intakes of the respondents are within the standard limit. The processing method might also modify the cyanide content in goitrogenic foods. Steaming and boiling cassavas, the most common processing method in Sengi Village were known ways to reduce the cyanide content.[24] Therefore, this might lower the actual cyanide consumption among respondents than predicted.

No significant associations were observed between iodine status, as determined by IUC levels, and daily iodine intake, daily goitrogen intake, and salt iodine concentration in our research. These findings imply that additional factors likely play a role in influencing iodine status within this specific region. The average iodine concentration in the water of Sengi Village was measured at 2.03 mcg/L. Nearly all participants (98.6%) consumed water with insufficient iodine content, indicating a potential heightened risk for inadequate iodine intake and the subsequent development of ID) among residents in the area.The mean water iodine concentration in Sengi Village was 2.03 mcg/L. Almost all respondents (98.6%) consumed water with poor iodine content. Hypothetically, respondents had a high chance of not getting enough iodine and eventually acquiring IDD.

There are several limitations of this study. This study did not employ three days of 24-hour urine collection for a more precise measurement of UIC. No further laboratory examination, including thyroid peroxidase (anti-TPO), was conducted for possible autoimmune causes in the presence of goiter for any subjects examined. The non-randomized sampling method employed in this study might lead to a selection bias.

CONCLUSION

In summary, women of childbearing age living in the Sengi Village possess adequate iodine status and normal thyroid hormones. Nevertheless, the iodine content within the freshwater sources, the household table salt, and daily dietary iodine intake were still deficient. Accordingly, strenuous public health intervention is required to overcome and supervise the low iodine concentration of the daily consumed salt and low dietary iodine intake.[25] The lack of association between dietary iodine intake, goitrogen intake, iodine salt concentration and iodine status may suggest that other factors such as water iodine content may play a significant role. Despite adequate iodine status in the population, there is a substantial TGR, which may indicates residual goiter from previous severe endemic IDD, or the presence of autoimmune thyroiditis. Further evaluations are needed for the exact cause of high TGR.

Continuous monitoring and public health intervention to optimize iodine intake from household salt and daily dietary intake are essential for eradicating IDD in Sengi village and Magelang regency, especially for women of reproductive age. [25] Further studies are required to re-evaluate the potential cause of high TGR in this area. The implementation of universal hypothyroid newborn screening in several urban areas in Indonesia must be extended to areas previously or currently endemic for IDD to detect, treat and prevent further disabilities.

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