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Iodine and goitrogens intakes among menopausal women in calcareous region

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ABSTRACT

Wonogiri Regency, Indonesia, is a calcareous mountainous region which has limitations in terms of iodine content in soil and water. Kismantoro is one of the Sub-districts in the regency with severe iodine deficiency. This condition is related to the intake of iodine and factors that inhibit the intake of iodine such as goitrogens. This causal-comparative study was conducted to determine the difference of iodine and goitrogenic foods intakes among menopausal women in Kismantoro Sub-district. A total of 307 menopausal women were taken randomly. Iodine intake as well as goitrogens were measured using the semi quantitative-food frequency questionnaire (SQ-FFQ). There was no difference in the percentage of recommended dietary allowance (RDA) for iodine intake ($p=0.857$) and goitrogens intake ($p=0.084$) among the menopausal women, but there were differences in energy, protein, carbohydrate, and fat intake ($p<0.001$) respectively. In addition, the prevalence of goiter was 10.4% which did not differ in the premenopausal, perimenopausal and postmenopausal groups ($p=0.227$). However, it was found that most menopausal women had insufficient iodine intake (71.3%) and frequent goitrogenic foods intake (68.7%). Thus, a synergistic manner between stakeholders is still needed to improve the variation of iodine food sources while consume less goitrogens in the area.

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1. INTRODUCTION

Thyroid function disorders are more common in women, which is 5-20 times higher than in men and increases with age, including in the elderly [1]–[3] and in postmenopausal women [4], [5]. This is related to changes in thyroid hormones such as thyroid stimulating hormone (TSH), and free thyroxine 4 (FT4) with increasing age and changes in follicle stimulating hormone (FSH) and luteinizing hormone (LH) which affect the balance of the estrogen and progesterone hormones, thereby reducing the regularity of the menstrual cycle, even this cycle can stop altogether [6]. Menopausal symptoms are related to the decrease in the estrogen hormone which also causes the thyroid hormone to decrease [7], [8]. Previous research stated that the prevalence of thyroid disorders in women were high, with details in the premenopausal group of 8.2% [9], perimenopausal 34.5% [10] and postmenopausal 12.7% [9]. The impact of thyroid function disorders in the elderly group, especially in women, are hypothyroidism and hyperthyroidism that interferes with body physiology such as cardiovascular disorders [11]–[14], the risk of bone fractures [15], [16], and the occurrence of nodular goiter [4], [17].

The risk of thyroid dysfunction will increase in areas of iodine deficiency because the iodine intake is below the standard for individual needs and this lasts for a long time [18], [19]. Environmental factors such

as calcareous or limestone soil also contribute to the risk of iodine deficiency because the iodine content in soil and water is very low. The goiter-endemic limestone area with very low soil and water iodine content puts locally grown food at risk for low iodine content [20]. The iodine content in food depends on the amount of iodine contained in the water and soil where the food is grown [18]. When associated with the occurrence of endemic goiter in calcareous areas, this is due to the low and limited mobility, bioavailability, bioaccessibility, and transfer of iodine into the food chain, due to dependence on locally grown food as daily food intake [18], [20].

Wonogiri Regency is a calcareous mountainous region located in the eastern part of Central Java Province, Indonesia. This district is an area at risk for iodine deficiency; this is indicated by the number of people suffering from goiter by 1,308 people and cretins as many as 191 people. Kismantoro Sub-district is the sub-district with the highest goiter prevalence in Wonogiri Regency, which is 30.44% [21]. This prevalence makes Kismantoro Sub-district an endemic area of severe goiter because it is far above the WHO threshold of 5% [22]. This environment condition make people in endemic areas have low intake of iodine below the recommended dietary allowance (RDA) for women aged 30-80 years in Indonesia, which is 150 μg/day [23]. The low intake of iodine in endemic areas of goiter that occurs continuously will cause thyroid function disorders that are increasingly widespread with various clinical manifestations [19], [24].

In addition, the intake of goitrogens also play a very important role in the occurrence of thyroid function disorders. Goitrogens are a diverse group of chemical compounds that can interfere with the absorption or utilization of iodine by the thyroid gland [24], [25]. If goitrogens are often consumed in a state of insufficient iodine intake, then thyroid function will be increasingly disrupted, due to the inhibition of the absorption of iodine needed by the thyroid gland, so that thyroid hormone production cannot be formed properly [26]. High intakes of goitrogens can cause minimal iodine intake to be inadequate for the physiological demands of the thyroid gland and in some circumstances contribute to the development of endemic goiter [24], [27]. Types of goitrogens that play an important role in problems in endemic areas of goiter come from foods such as cassava (cyanogenic glucoside), vegetables from the Brassica family (glucosinolates), nuts and tubers (flavonoids). It is also classified as a source of sulfurated organics, such as thiocyanates, isothiocyanates, goitrin and disulfides, and flavonoids [19], [27], [28].

Previous program in the Kismantoro area carried out by the government related to iodine deficiency disorder (IDD), countermeasure through IDD screening and food intake still focuses on the group of women of childbearing age. Meanwhile, this research focuses on menopausal women who have a higher risk both in terms of increasing age and in terms of hormones. From the background mentioned above, it can be summarized that with increasing age in the menopausal group of women there will be changes in hormonal profiles which will affect macronutrient intake. Apart from that, in calcareous mountainous areas, this condition will also affect the intake of iodine and goitrogenic substances which influence the enlargement of goiters. We hypothesized that there were differences in iodine and goitrogens intake between groups of menopausal women in Kismantoro Sub-district. This study will compare the intake of iodine and goitrogens in premenopausal, perimenopausal and postmenopausal women. In addition, this study analyzes the changes in energy and macronutrients intake characteristics and the risk of goiter in each group. Previous studies indicate that women who live in calcareous mountains, who have frequent intake of goitrogens but having insufficient iodine intake, experiencing the risk of thyroid function disorders. This is due to at their age, the estrogen hormone declines and the menstrual cycle decreases or even stops.

2. METHOD

This causal-comparative study was conducted in Kismantoro Sub-district, Wonogiri Regency, Central Java, Indonesia from July to December 2019. The population in the menopausal women (premenopausal, perimenopausal, and postmenopausal groups) 30-74 years old in Kismantoro Sub-district was 7,857 women, and 307 women were taken as samples using simple random sampling method. In this study, premenopausal women are defined as women who still have regular menstrual cycles in the past year. Perimenopausal women are those who have experienced irregular menstrual cycles in the past year (experienced significant changes in length, duration or blood volume). Meanwhile, postmenopausal women are defined as women who have not experienced menstruation in the past year or more [29]. Research ethics were obtained from the Faculty of Medicine, Universitas Muhammadiyah Surakarta No.2265/B.1/KEPK-FKUMS/VII/2019. Each respondent has also signed an informed consent form.

Iodine and goitrogens intake data were taken using the semi quantitative-food frequency questionnaire (SQ-FFQ) method for the last three months. The list of foods in the FFQ Form consists of foods containing iodine and goitrogens that are often consumed in Kismantoro Sub-district according to the results of the initial survey through focus group discussion (FGD) activities with health cadres. The list of foods containing iodine consists of 15 types and the list of goitrogenic foods consists of 24 types (consisting

of staple foods, animal protein, plant protein, vegetables, and beverages). The 24-hour food recall was carried out for 3 non-consecutive days, to complete the SQ-FFQ results. Iodine intake per individual was expressed in μg/day and percentage of RDA. Iodine intake was categorized into sufficient and insufficient based on the the previous research used a cut-off point of 77% for the vitamins and minerals group [30]. Meanwhile, goitrogens intake was expressed in daily, weekly and monthly scores. The goitrogens scoring method was based on the Indonesian Ministry of Health standard which states that the intake frequency was devided to ≥ 3 times/day (score 50); 1-2 times/day (score 25); 3-6 times/week (score 15); 1-2 times/week (score 10); 2 times/month (score 5) and never (score 0). The total goitrogens score was categorized into Rare (score < median) and Frequent (score≥median) [31]. This study also presented the intake of energy, carbohydrates, protein, and fat. Nutrient intake requirement was based on the RDA for Indonesia in 2019. All macronutrient intakes were categorized as Low (< 80%); Moderate (80-110%) and High (>110%) [32].

The goiter status of menopausal women was determined by palpation of the thyroid gland by a trained health personnel, with the criteria of "Yes" (if a lump is seen and/or palpable in the thyroid gland) and "No" (if there is no palpable lump in the thyroid gland) [22]. Kismantoro Sub-district is an endemic area of severe goiter (30.4%) so that representative palpation measurements were used for areas with moderate and severe goiter prevalence [22], [33], [34]. Socio-demographic data of menopausal women who were described and analyzed were age, educational level, occupation, and family income level.

The software used in data processing and analysis was Microsoft Excel and IBM SPSS Statistics version 23. Nutrient intake data was processed using Nutrisurvey 2007. This study analyzed both univariate and bivariate data. The normality test of the data was carried out by Kolmogorov-Smirnov. Analysis of differences in the groups of premenopausal, perimenopausal and postmenopausal women age were carried out using one way ANOVA test. Meanwhile, the Kruskal-Wallis test was carried out on energy and macronutrients, iodine, and goitrogens intake data. Analysis of frequency differences of goiter in menopausal women was carried out using the Chi-square test. All statistical tests used a significance level of 5% (0.05).

3. RESULTS AND DISCUSSION

3.1. Socio-demographic characteristics

The general characteristics of all research respondents in Kismantoro Sub-district can be seen descriptively in Table 1. In general, the perimenopausal women group had the highest percentage of 45.6%, followed by postmenopausal women 32.2% and premenopausal women 22.2%. Overall, the educational level of respondents was still relatively low, namely 27.4% uneducated and 35.8% with primary education. Most of the respondents' occupations were farmers (47.2%), followed by housewives (39.4%), merchant (8.8%) and employee (4.6%). With this very limited type of work, 95.8% of respondents had monthly family incomes below the Wonogiri Regency regional minimum wage in 2019, which was IDR 1,665,000 [35].

Table 1. Socio-demographic characteristics of respondents

Characteristics	n	%
Menopausal status		
Premenopausal	68	22.2
Perimenopausal	140	45.6
Postmenopausal	99	32.2
Educational level		
Uneducated	84	27.4
Primary education	110	35.8
Secondary education	113	36.8
Occupation		
Housewife	121	39.4
Farmer	145	47.2
Merchant	27	8.8
Employee	14	4.6
Family income		
< Regional minimum wage	294	95.8
≥ Regional minimum wage	13	4.2

Calcareaous soil contribute to the risk of iodine deficiency. Geographically, Kismantoro Sub-district, Wonogiri Regency is located at an altitude of 300-400 m above sea level. In general, calcareous soil conditions have very low organic matter content characteristics, so treatment was needed to enrich their nutrients [36]. Watts *et al*. [37] found that in calcareous areas of Malawi the soil iodine levels is 2.06 ppm. Iodine content in soil and water in Agadir mountain area of Morocco is also low at 2.05 ppm and 0.12 ppb [38]. This soil iodine level is relatively low when compared to the results of a research in China with a range

of 1.55-12.93 mg/kg [39]. Likewise, the iodine content in water in Kismantoro Sub-district is classified as iodine deficiency because it is lower than 10 g/L [40]. Previous study found that plants grown in iodine-poor soils contain very low iodine, only up to 10 μg/kg, whereas growing in iodine-rich areas can reach 1 mg/kg [41]. The type of soil in Kismantoro Sub-district, which is mostly grumosol (from weathering limestone), causing not all agricultural crops and vegetables to grow. The most widely grown agricultural crops were cassava, peanut, and sweet potato. In addition, this limestone soil condition risk low bioavailability, bioaccessibility and transfer of iodine from soil, water and air to plants and animals that live in that environment [20]. The results of previous research in Indonesia, found that the average iodine content in 5 foodstuffs in previously affected by severe iodine deficiency areas was highest (0.6-8.1μg/g) compared to iodine sufficient areas (0.1-7.5μg/g) [42]. Thus, soils in mountainous areas, especially those formed from weathering limestone such as the grumosol type, have a lower organic matter content and fertility [43].

From a socio-demographic point of view, this study found that the highest percentage of menopausal status were perimenopausal women (45.60%) followed by postmenopausal women (32.20%). This finding is different from the study of Du *et al*. [29] who found the highest percentage of postmenopausal women (52.35%) and the lowest perimenopausal women (14.52%). The average age of menopausal women in this study was 50.01 years, almost the same as the results of the studies of 49.40 and 51.20 years respectively [44], [29]. There was a difference in mean age in the premenopausal, perimenopausal and postmenopausal groups. This was due to a fairly wide age range with a minimum age of 26 years in the premenopausal women group and a maximum age of 79 years in the postmenopausal women group.

Most menopausal women had low education (primary education or below) was 63.2%, much higher than the results of previous study was 18.5% [45]. Further education in menopausal women was 36.8%, almost the same as the results of previous studies by 32.25% and 36.6% respectively [29], [45]. Due to the inadequate education, most menopausal women in Kismantoro Sub-district became farmers and housewives. There were differences in education and occupation in the three groups of menopausal women. In terms of family income, 95.8% of menopausal women had incomes below the average minimum wage, as most of them being housewives or farmers. In addition, the large number of families with low incomes caused the percentage of poor families to be quite high in Wonogiri Regency, 10.25% in 2019 and increased to 10.86% in 2020 [46]. There was no difference in family income between premenopausal, perimenopausal and postmenopausal women. This study is not in line with the previous research which found differences in family income in groups of perimenopausal and postmenopausal women [47]. Although the types of occupation of menopausal women in Kismantoro Sub-district were more diverse, the income as merchants or employees was still below the regional minimum wage (IDR 1,665,000) or equivalent with 106.5 USD.

3.2. Nutrients intake dan goiter

The intake of energy and macronutrients were also described to determine the adequacy of nutrient intake in general. Table 2 shows the intake of energy, protein, carbohydrates, and fat in menopausal women included in the low category (55.4%; 41.4%; 64.8%; and 49.2%) respectively. These results indicated that the intake of energy and macronutrients in general were insufficient.

Table 2. Characteristics of respondents based on nutrients intake category, goitrogens, and goiter

Characteristics	n	%	Characteristics	n	%
Energy (%RDA)			Fat (%RDA)		
Low (<80%)	170	55.4	Low (<80%)	151	49.2
Moderate (80-110%)	105	34.2	Moderate (80-110%)	107	34.9
High (>110%)	32	10.4	High (>110%)	49	16.0
Protein (%RDA)			Iodine (%RDA)		
Low (<80%)	127	41.4	Insufficient (< 77%)	219	71.3
Moderate (80-110%)	100	32.6	Sufficient (≥77%)	88	28.7
High (>110%)	80	26.1	Goitrogens (score)		
Carbohydrate (%RDA)			Rare (<median)	96	31.3
Low (<80%)	199	64.8	Frequent (≥median)	211	68.7
Moderate (80-110%)	86	28.0	Goiter Status		
High (>110%)	22	7.2	Yes	32	10.4
			No	275	89.6

In particular, in this area of iodine deficiency, 71.3% of menopausal women had insufficient iodine intake. Most of the respondents consumed food sources of iodine in a rare frequency, which was 1-2 times/week, 1-2 times/month or even never consumed high sources of iodine food. The types of foods containing iodine that were commonly consumed were dried salted fish, anchovies, salted milkfish, shrimp paste, *ebi* (small prawn), and *rese* (small *ebi*). Meanwhile, sources of iodine from marine fish, shrimp and

other seafood were very rare or never even consumed. Contrary to the frequency of iodine intake, the frequency of goitrogens intake in postmenopausal women was in frequent category (68.7%), which was 3-6 times/week or 1-2 times/week. The most commonly consumed sources of goitrogens were cassava, cassava leaves, cabbage, cauliflower, spinach, young *gudhe* (pigeon pea) and mustard greens. Table 2 also shows the prevalence of goiter in menopausal women in Kismantoro Sub-district of 10.4%.

3.3. Differences in nutrients intake and goiter among menopausal women

Table 3 presents data on the mean and standard deviation of age and nutrient intake in menopausal women. This study found the average age of 307 menopausal women was 50.00±10.41 years. The ANOVA test found that there was a significant age difference in the three groups ($p<0.001$). The average intake of energy and nutrients almost all lower in the postmenopausal group, except for the average RDA percentage of energy and fat intake which higher in the postmenopausal group. Energy intake with an average of 1431.02±272.08 kcal with a decreasing value in the three groups, with the lowest average in the postmenopausal group, and the Kruskall-Wallis test proved to be significantly different ($p=0.006$). Likewise, the percentage RDA of protein and carbohydrates, decreased significantly in the postmenopausal group ($p<0.001$) respectively. The average protein intake of 53.00 g took up 14.82% of total energy. The average intake of carbohydrates and fats were 209.93 g and 42.14 g, respectively, amounting to 58.68% and 26.50% of the total energy.

The average of iodine intake (μg/d) was 100.01±30.69 and the percentage RDA of iodine was 72.24±25.06 which decreased in the postmenopausal group but did not differ significantly with the values of $p=0.188$ and $p=0.857$, respectively. This study found a very low percentage of the minimum RDA for iodine intake, which was 29.09%. While a fairly high average goitrogens score of 171.73, higher than the median value of 160.00 based on the recommendation of Indonesian Ministry of Health for analysis in population. There was no difference in goitrogens intake between premenopausal, perimenopausal and postmenopausal women ($p=0.084$). The Chi-square test showed that there was no difference in the prevalence of goiter between the three groups ($p=0.227$), but there was a tendency of increases in the prevalence of goiter in premenopausal, perimenopausal women and the highest prevalence was in the postmenopausal group (40.6%).

Table 3. Differences in mean age, intake of energy, protein, carbohydrates, fat, iodine and goitrogens based on menopausal status

Variables	Pre-menopause mean (SD)	Peri-menopause mean (SD)	Post-menopause mean (SD)	Total mean (SD)	p
Age (year)	36.13 (4.01)	48.41 (4.03)	61.82 (5.12)	50.01 (10.41)	<0.001[a]
Energy (kcal)	1514.19 (261.64)	1413.08 (260.64)	1399.27 (285.84)	1431.02 (272.08)	0.006[b]
Protein (g)	64.45 (23.51)	50.79 (16.52)	48.24 (14.50)	53.00 (18.74)	<0.001[b]
Carbohydrate (g)	214.12 (50.78)	209.36 (40.59)	207.84 (44.13)	209.93 (44.07)	0.059[b]
Fat (g)	44.43 (9.43)	41.37 (9.24)	41.65 (9.38)	42.14 (9.38)	0.060[b]
Iodine (μg)	102.43 (35.47)	102.34 (33.63)	95.06 (20.97)	100.01 (30.69)	0.188[b]
Energy (%RDA)	74.78 (14.57)	76.17 (21.11)	90.29 (24.86)	80.41 (22.22)	<0.001[b]
Protein (%RDA)	115.78 (45.57)	91.12 (36.23)	90.32 (30.82)	96.32 (38.25)	<0.001[b]
Carbohydrate (%RDA)	66.56 (15.60)	71.84 (20.76)	87.30 (25.36)	75.65 (22.89)	<0.001[b]
Fat (%RDA)	78.61 (19.59)	79.60 (23.87)	94.80 (28.39)	84.28 (25.57)	<0.001[b]
Iodine (%RDA)	73.55 (28.03)	72.72 (26.26)	70.67 (21.02)	72.24 (25.06)	0.857[b]
Goitrogens	176.69 (53.27)	177.14 (49.93)	160.77 (41.23)	171.73 (48.54)	0.084[b]
Goiter status	n (%)	n (%)	n (%)	n (%)	
Yes	9 (28.1)	10 (31.3)	13 (40.6)	32 (100)	0.227[c]
No	58 (21.5)	130 (47.3)	86 (31.3)	275 (100)	

[a]One way ANOVA; [b]Kruskall-Wallis; [c]Chi-square

This study found that the average of energy intake of 1,431.02 kcal which lower than the minimum energy requirement according to the RDA for the 30-80 year age group, which is 1,550-2,150 kcal [23]. The average energy intake was lower compared to the average energy in postmenopausal women from the results of previous research which was 1,506.9 kcal [48]. The average protein intake in this study was 14.82% of total energy as the recommendation from the Indonesian Ministry of Health which is 10-15% of total energy. Meanwhile, the average carbohydrate intake was 58.68% of total energy, slightly lower than the recommendation which was 60-65% of total energy. Meanwhile, the average fat intake was 26.50% of total energy, slightly higher than the set limit, which was 20-25% of total energy [23].

Energy and macronutrients intake such as protein, carbohydrates and fat are very important to verify along with iodine intake, because iodine is needed in producing thyroid hormone by the thyroid gland which functions as a regulator of energy metabolism processes to maintain the basal metabolic rate (BMR) and

energy expenditure [49]–[51]. Iodine also plays a role in protein, carbohydrate and fat metabolism [49], [50], [52] as well as in metabolic syndrome [53], [54]. The function of thyroid hormone in energy and nutrient metabolism through the mechanism of thyroid hormone stimulates BMR by increasing the production of adenosine triphosphate (ATP) for metabolic processes and by generating and maintaining an ion gradient. In the ATP production process, thyroid hormone stimulates the metabolic cycle in the form of catabolism and anabolism of fat, glucose, and protein [49]. This study also found a decrease in nutrient intake in the postmenopausal group compared to the premenopausal group, which was significantly different especially in energy intake, protein intake, and the percentage of RDA for energy, protein, carbohydrates and fat. This difference is because physiologically postmenopausal women experience decreased nutritional needs and some of them had less nutrient intake [55], [56].

Iodine intake in this study was measured using the SQ-FFQ method, taking into account the frequency of intake and the amount according to household size which was converted into weight (μg/day). Iodine intake in this study also considered iodine intake from salt. The calculation of the average salt consumption is 5 g/day [57], with an average iodine content in salt in Indonesia ranging from 18.0-23.0 ppm [58], while also taking into account the decrease in the iodine content due to storage and cooking process by an average of 51.1% with assumption of the absorbed iodine was 48.9% [59]. Thus, the intake of iodine from salt ranging from 44.01-56.24 μg/day. A previous review by Zimmermann and Andersson [60], states that the average iodine from salt is 40.0 μg/day, which is still very far from the individual needs per day according to the RDA. The average intake of iodine in this study (100.01 μg/day), was lower than the RDA standard of iodine requirement in adult women, which was 150 μg/day. This result was lower than the study of Brough *et al*. [61] who estimated an iodine intake of 138 μg/day based on the excretion of iodine in the urine. This result is also lower than the iodine intake of women in the US ranging from 190-210 μg/day [18].

Most menopausal women were rarely consumed foods high in iodine, apart from being seen from the intake below the requirement, it is also seen from the frequency of consuming infrequently (1-2 times/week), very rarely (1-2 times/month) and even in the results of interviews using SQ-FFQ for the last 3 months, there were respondents who had never consumed food sources of iodine from the sea such as fresh shrimp, fresh sea fish and seaweed. Whereas the iodine content in seafood is very high, ranging from 40-150 μg/100 g [18] and 24.5-101.13 μg/100 g [62], especially in shrimp, marine fish and shellfish. The category of iodine intake based on the percentage of RDA, with a cut off point of 77%, showed that 71.3% of menopausal women have insufficient iodine intake, with the average of 72.24%. The results of this study were lower than the results of the previous study which found 91% of middle-aged women had low intake (<150 μg/day) [63]. However, it was higher than other previous research that found the average intake of iodine in 5 types of food ingredients (dried seaweed, seaweed snacks, kelp soup, shellfish and kelp) in the rare category is 58.80% [64].

This study also found the highest percentage of insufficient iodine intake in the perimenopausal group (44.7%) compared to the premenopausal and postmenopausal groups, however, there was no significant difference in the category of iodine intake in the three groups. This study did not find differences in iodine intake in the premenopausal, perimenopausal and postmenopausal women groups, both in terms of intake in terms μg of weight or in the percentage of RDA. This was because the three groups of menopausal women lived in the same calcareous mountain area. The research in southwest Ethiopia stated that in a geographical area that lacked iodine, the availability of food ingredients and eating habits would not be much different for the population, including consuming relatively low iodine sources and high intake of goitrogens [65].

Goitrogens intake in this study focused on foods that contain high thiocyanate. Based on the results of the SQ-FFQ in menopausal women, the average of goitrogens score was 171.73±48.54. The goitrogens score in this study was obtained based on scores in the frequency group. Frequency ≥3 times/day is given a score of 50; 1-2 times/day scored 20; 3-6 times/week scored 15; 1-2 times/week scored 10; 1-2 times/month given a score of 5; and if the menopausal women have never consumed it is given a score of 0. The highest goitrogens intake scores were in perimenopausal women (177.14), premenopausal (176.69), and postmenopausal (160.77), however, there was no proven differences in the three groups. This goitrogens intake was no different because the type of food and the frequency and amount consumed were relatively homogeneous in each group, because they came from areas with the same calcareous mountainous geographical conditions.

The results of the total score of all food ingredients in each respondent were added up, and categorized based on the median; Rare (score <160.00) and Frequent (score ≥160.00). It was found that the majority of menopausal women with frequent intake of goitrogens was 68.7%. Referring to these sources of thiocyanate precursors, the intake of the most and most frequently consumed goitrogens in Kismantoro Sub-district could be divided into 3 types: first, goitrogens from the cyanoglucoside group (cassava, sweet potato,

cassava leaves, spinach, bamboo shoots, and chayote); second, goitrogens from the glucosinolate group (cabbage, cauliflower, Chinese cabbage, mustard greens, and water spinach); third, goitrogens from the flavonoids group (tempeh, tofu, vegetable *koro* (jack beans), winged bean, young *gudhe* (pigeon pea) vegetables, chickpeas, and long beans). The hydrogen cyanide (HCN) content in various goitrogenic food that were most often consumed in Indonesia, including cassava, cassava leaves, cabbage, bamboo shoots, water spinach, spinach, tofu, and tempeh. The highest HCN content in various goitrogenic food is cassava, previous research found that HCN content ranged from 29.35-66.00 mg/kg [66]. The safe limit for HCN content in food was set by FAO and WHO, especially in sweet cassava it should be <50 mg/kg, for cassava flour it should be <10 mg/kg and for bitter cassava 50 mg/kg [67].

Various reviews regarding the consumption of glycosinolate and cyanoglucoside goitrogens as precursors of thiocyanates and isothiocyanates and flavonoids continuously and frequently will trigger thyroid function disorders [68]. Thiocyanates will affect thyroid function disorders through the mechanism of inhibiting iodide uptake by the thyroid gland, while the flavonoids group has large effects on thyroid hormones and the hypothalamic-pituitary axis. For example, the compounds genistein and daidzein from soybeans inhibit the activity of thyroperoxidase (TPO) which catalyzes the iodination and biosynthesis of thyroid hormones [69], [70]. Its influence increase in areas that are geographically experiencing iodine deficiency, both in soil, water and food produced in the region [27].

Goitrogens intake in high amounts and with frequent frequency can cause enlargement of the thyroid gland, through the mechanism of decreasing circulating thyroid hormone in the blood and increasing TSH release which induces hypertrophy and hyperplastic thyroid gland [27]. Enlargement of the thyroid gland or better known as goiter, is an indicator of endemicity in areas of iodine deficiency. Based on the total goiter rate (TGR), an area is categorized as non-endemic (0-4.9%); mild endemic (5-19.9%); moderate (20-29.9%) and severe (≥30%) [22]. This study found that the prevalence of goiter in menopausal women in Kismantoro Sub-district was 10.4%, although this result was categorized as mild endemic, it has become a public health problem because it exceeds the maximum limit set by WHO of 5%. The prevalence of goiter was lower compared to the results of previous studies in women of childbearing age by 43% [71], and 13% [72].

There was no difference in the prevalence of goiters between groups of premenopausal, perimenopausal and postmenopausal women. Although there was no statistical difference, there was a tendency for the goiter prevalence to increase with menopausal status, namely premenopausal (28.1%), perimenopausal (31.3%), and postmenopausal women (40.6%). The trend of increasing the percentage of goiters in the postmenopausal women group is in line with the results of the previous study which found the goiter rate in postmenopausal and elderly women reached 50% and continued to increase with age [4]. Goiter is also a typical sign of thyroid disorders, both hypothyroidism and hyperthyroidism, which can have a long-term impact on women's nutritional status, such as waist-to-hip ratio [73].

4. CONCLUSION

The community's macronutrient and iodine intake was still low, while the goitrogens consumption was in frequent category. This study found the prevalence of goiter in the mild endemic category. The results of the research need to be followed up through efforts to improve diet in this calcareous mountainous region so the women in this area does not continue in more severe impact of iodine deficiency disorder. Follow-up recommendations for solving the problem of low iodine intake, high goitrogenic food, and high cases of goiter in women of menopausal age in the Kismantoro area can be done through community empowerment. The programs including: providing education about preventing the effect of iodine deficiency, high iodine food fortification, and ongoing iodine deficiency disorders (IDD) surveillance.

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