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Correlation of offspring thyroid function and maternal iodine status in iodine deficient-coastal area

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ABSTRACT

Thyroid hormone is vital for children's growth and metabolism, relying on sufficient iodine levels for synthesis. Maternal intake determines iodine supply to fetuses and children under two years old. This study aimed to correlate offspring thyroid function with maternal iodine status in coastal areas. A cohort study was conducted, involving pregnant coastal residents. Maternal urinary iodine levels were measured via the ammonium persulfate method, while offspring thyroid stimulating hormones (TSHs) and free thyroxine hormone (fT4) levels were assessed using electro-chemiluminescence immunoassay (ECLIA). Iodine intake was determined through a semiquantitative food frequency questionnaire (FFQ). The correlation between offspring thyroid function and maternal iodine status was analyzed using Pearson's correlation test. Differences in TSHs and fT4 levels among iodine status groups were examined using the One way-ANOVA test. Maternal iodine status was insufficient with a median urinary iodine of 125 µg/L, resulting in a 60.8% prevalence of iodine insufficiency. Iodine intake (62.20±43.45 µg/day) fell short of recommended levels (RDA). Offspring TSH was 2.29±1.07 µIU/mL, fT4 was 1.26±0.14 ng/dL. TSH and fT4 concentrations showed no significant inter-group differences (p=0.852, p=0.075). Offspring thyroid function did not correlate with maternal iodine status (TSHs: p=0.314; fT4: p=0.258). Offspring thyroid function did not correlate to maternal iodine status in a population of iodine-insufficient and mercury-contaminated coastal areas.

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1. INTRODUCTION

Iodine is an important micronutrient for maintaining the body's normal metabolism, as an essential substance in synthesis of thyroid hormones, namely triiodothyronine and thyroxine hormone [1]. During pregnancy, the need for iodine increases to meet the needs of the maternal metabolism as a consequence of physiological changes including an increase in the rate of nutrient excretion due to an increase in glomerular

filtration rate [2], as well as to meet the needs of the fetus's thyroid hormone (<20 weeks of gestation) and for fetal neurodevelopment [3]. For this reason, pregnancy is a period that is vulnerable to iodine deficiency [4]. Iodine deficiency during pregnancy will result in physiological and metabolic changes known as iodine deficiency disorders (IDD) [5]. IDD imposes several risks in pregnancy including abortion, fetal death, neurodevelopmental, and language disorders.

The incidence of iodine deficiency in the population of pregnant women remains high worldwide, namely 53%. This incidence is higher in areas with insufficiency status [6]. Iodine status is determined by the intake of foods derived from marine sources. WHO recommends an iodine intake of 250 µg/day during pregnancy [5]. This intake is used to maintain normal iodine status, which is between 150-240 mcg/L. Data on the incidence of iodine deficiency in pregnant women in Indonesia's coastal areas was not found, even data on iodine status was not available.

Iodine is crucial for thyroid hormone production in infants, influenced by maternal iodine intake. Babies under 20 weeks gestational age cannot produce thyroid hormone independently. Studies suggest iodine supplements for pregnant women in iodine-deficient areas can boost thyroid hormone levels [7]. The period from intrauterine life to age two is critical for growth and development, with nutrition playing a key role. Hypothyroidism in pregnant women can increase the risk of hypothyroidism in the fetus. Hypothyroidism in children under five can impact their development [8]. In addition, thyroid hormone synthesis is also influenced by interactions between iodine and various factors including environmental contaminants such as mercury and perchlorate [9]. There were no data on the impact of prenatal mercury exposure on thyroid function in children.

The purpose of this study was to examine the correlation between thyroid function of the offspring and maternal iodine status of population living in the mercury-contaminated coastal areas. This study's significance lies in its pursuit of uncovering the potential correlation between offspring thyroid function and maternal iodine status within the context of mercury-contaminated coastal areas. By shedding light on this relationship, the study endeavors to contribute to the broader understanding of the impacts of environmental factors on human health, specifically in the context of maternal and child well-being.

2. METHOD

2.1. Study design, subjects recruitment, and ethical considerations

This observational cohort study, conducted from November 2021 to June 2022, involved 165 pregnant women from mercury-contaminated coastal villages in Sekotong. Ethical guidelines (registration number 286/UN18.F7/ETIK/2021) were followed. Maternal data collection focused on those in the second trimester without serious complications or underlying thyroid issues. For children, data collection occurred in January 2023 under ethical recommendation 302/UN18.F7/ETIK/2022. Parental consent was obtained for child participation, and sample size was calculated for the correlation study as (1).

$$\text{Sample size} = N = [(Z\alpha+Z\beta)/C]2 + 3 = 47 \text{ (Confident interval of 95\%, } \beta = 80\%) \quad (1)$$

Of the 165s of pregnant women who were in their second and third trimesters of pregnancy were enrolled in the study, 67 of them approved their offspring to participate.

2.2. Sample collection and analysis

2.2.1. Iodine intake

Data ascertaining iodine intake was collected via interviews utilizing the food frequency questionnaire (FFQ), which captured the consumption of iodine-containing foods within the preceding three months. The assessment of iodine intake involved analyzing each meal documented in the FFQ with the aid of nutrisurvey software. Through this process, a comprehensive understanding of participants' iodine consumption patterns over the specified timeframe was established.

2.2.2. Urinary iodine

Pregnant women's spot-urine samples were collected in sterile containers and stored at -20 °C. The assessment was conducted at the Indonesian Ministry of Health's Center for Iodine Deficiency Disorders using the ammonium persulfate digestion method. Each test tube containing urine, standard solution, and control was treated with 1 ml ammonium persulfate and heated at 80-100 °C for 1 hour. After cooling, arsenic acid solution was added and incubated for 20 minutes. Subsequently, ceric ammonium solution was introduced, mixed, and the absorbance was read in a spectrophotometer at 420 nm exactly 30 minutes after its addition.

2.3. Thyroid function test

2.3.1. Thyroid stimulating hormone test

Blood samples were taken from children's blood veins in sterile tubes, which were then centrifuged to separate serum and cells. Thyroid-stimulating hormone (TSH) analysis was performed using electro-chemiluminescence immunoassay (ECLIA). This involved creating a sandwich complex with TSH-specific antibodies and ruthenium-labeled antibodies, followed by incubation and the addition of streptavidin-coated microparticles. The resulting complex was measured for chemiluminescent emission using a photomultiplier. The minimum detectable TSH concentration was 0.005 µIU/mL.

2.3.2. Free thyroxine hormone (FT4)

Children's fT4 levels were measured using the ECLIA method, employing the competitive principle. In the first step, 15 µL of serum and ruthenium-labeled T4-specific antibody were incubated. The second step involved the addition of biotin and streptavidin-coated microparticles to the solution, forming a complex bound to the solid phase through biotin-streptavidin interaction. The resulting solution was aspirated into a measuring cell, where microparticles were magnetically trapped at the electrode surface. Unbound substances were removed, and voltage induced chemiluminescent emission was detected by a photomultiplier in the Cobas E-411 device at Prodia Laboratory. The minimum detectable concentration for fT4 is 0.3 pmol/L (0.02 ng/dL).

2.4. Data analysis

The Kolmogorov-Smirnov test, with necessary transformations, was used for the data normality test. The correlation between maternal iodine status and offspring's thyroid function was assessed using Pearson's correlation test. Mothers were categorized into insufficiency, adequate, and excessive groups based on urine iodine excretion values, and iodine intake was compared among these groups using the one-way ANOVA test. The mean values of TSH and fT4 were also compared among groups with the one-way ANOVA test. Statistical significance was set at $p<0.05$, and the analysis was conducted using SPSS software version 23.0.

3. RESULTS AND DISCUSSION

3.1. Results

This research involved 148 pregnant women who had their antenatal care at integrated healthcare services in the Sekotong subdistrict. The 64 subjects agreed to participate in the collection and assessment of their child's thyroid function. The general features of the subjects are shown in Table 1.

Table 1. Characteristics of the subjects

Characteristic	Value (mother, n=148; children, n=64)
Maternal age (year), mean±SD	25.8±6.2
Gestational period (month), mean±SD	6.94±1.6
Distribution based on trimester of pregnancy period (n)	
First trimester, n (%)	0
Second trimester, n (%)	35.8
Third trimester, n (%)	64.2
Age of the children (month), mean±SD	10.75±2.30
Sex of the children	
Males, n (%)	56.25
Females, n (%)	43.75
Iodine intake (µg/day), mean±SD	62.20±43.45
Urine iodine excretion/UIE (µg/L)	
Mean±SD	146.95±95.27
Median	125.00
Minimum	38.00
Maximum	538.00
TSHs (uIU/mL)	
Mean±SD	2.29±1.07
Minimum	0.48
Maximum	5.31
fT4 (ng/dL)	
Mean±SD	1.26±0.14
Minimum	0.92
Maximum	1.62

Table 1 demonstrated that the pregnancies were predominantly in the third trimester (64.2%), and the children were predominantly male (56.25%) with the mean age being 10.75 months. Maternal iodine intake was 62.20±43.45 µg/day, and UIE was 146.95±95.27 µg/L. The children's mean TSHs was 2.29±1.07 µIU/mL and FT4 was 1.26±0.14 ng/dL. Furthermore, maternal iodine status based on iodine intake and UIE are presented in Table 2.

Table 2. Maternal iodine status

Iodine status	Value
Group of age's iodine intake (µg/day) n=148:	
16–18-year-old, n=17	58.61
19–29-year-old, n=87	67.00
30–49-year-old, n=44	54.11
UIE classification	
Insufficiency (<150 µg/L), n=%	60.8
Adequate (150-249 µg/L), n=%	26.4
Above requirement (249-499 µg/L), n=%	12.2
Excessive (≥500 µg/L), n=%	0.7

Table 2 revealed that the highest iodine intake was in the 19-29 age group, and the lowest intake was in the group of 30-49 years old women. The iodine status of pregnant women was predominantly in insufficient condition (60.8%). Of all insufficient group, 9.5% was severely deficient (<50 µg/L). There is a positive correlation between the group of age and iodine intake (p=0.002). Otherwise, UIE did not correlate with age (p=0.632). The feature of maternal iodine intake is illustrated in Figure 1.

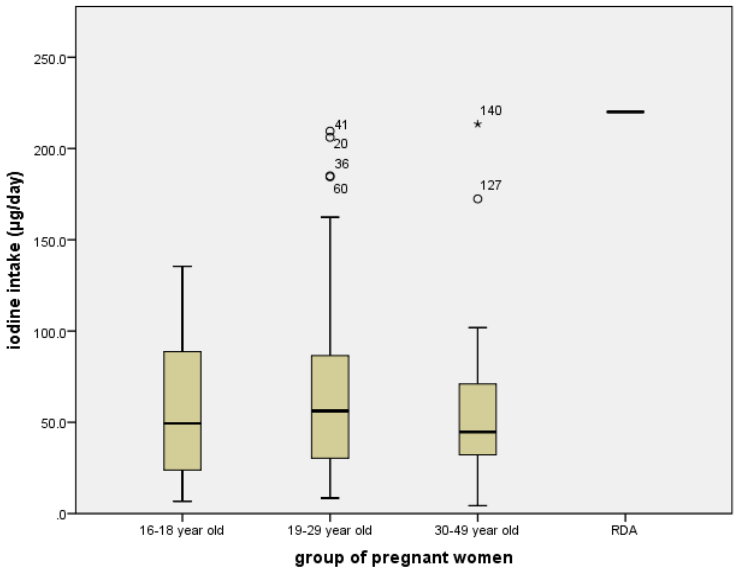


Figure 1. Dietary iodine intake of pregnant women

Figure 1 depicts that none of all subject groups acquired recommended daily allowance (RDA) (220 µg/day). Iodine intake by the population was significantly different from that suggested by the RDA (p=.000). However, there was no substantial difference in intake among groups (p=0.260). Table 3 describes that the highest iodine intake was in the insufficient group (67.58±45.59 µg/day) and the lowest intake was by the adequate group (51.13±38.70 µg/day). However, the intake among groups was not different significantly. Comparison of offspring's TSH value and FT4 value between the insufficiency group and other groups is presented in Figure 2.

In Figure 3, specifically in Figure 3(a) it can be seen that the highest TSHs value was the offspring of mother with insufficient iodine status (2.34±1.10 µIU/mL), however there were no differences significantly among groups (p=0.852). Meanwhile, in Figure 3(b) the highest fT4 value was in the insufficient group (1.28±0.15 ng/dL). Meanwhile, the lowest value was in the excessive group (1.17±0.13 ng/dL). However, the values among group were not significantly different in which p=0.075.

Table 3. Iodine intake and iodine status

Iodine status	Iodine intake (µg/day)	p-value
Insufficient	67.58±45.59	
Adequate	51.13±38.70	0.136
Excessive	59.46±39.45	

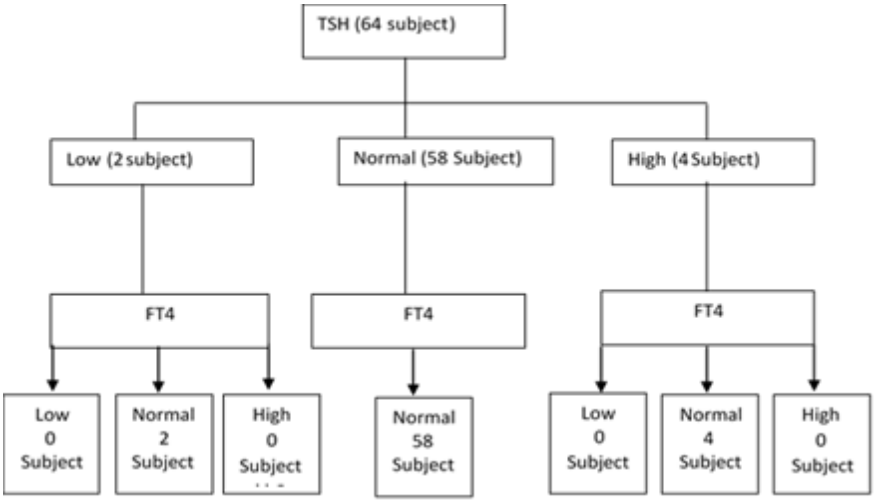
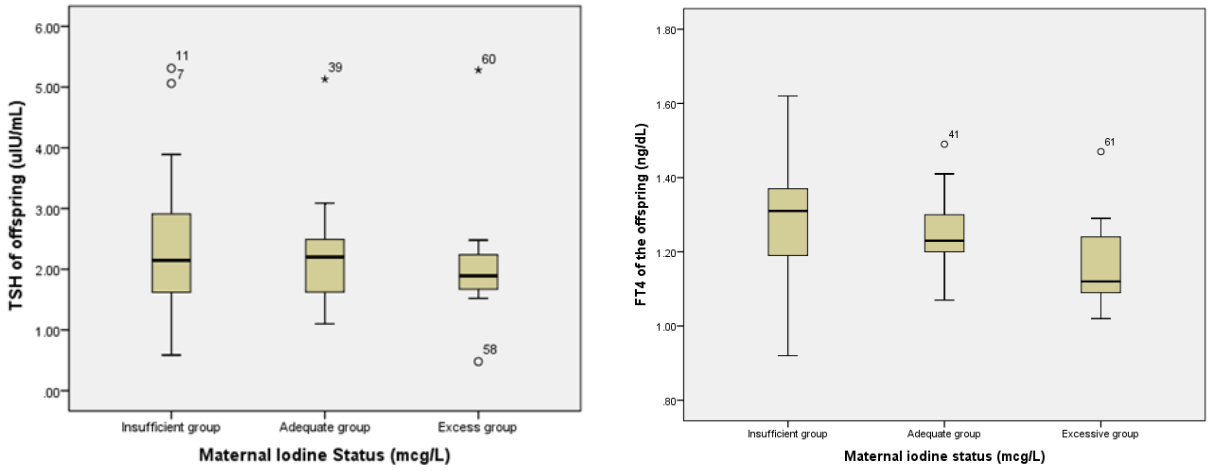


Figure 2. Distribution of thyroid function among offsprings



(a) (b)

Figure 3. *Thyroid function test of infant* (a) TSHs value of offspring among maternal iodine status; and (b) fT4 value of offspring among maternal iodine status

3.1.1. Classification of thyroid function test

Figure 2 indicates that two of 64 children with TSH values were lower than the reference value (0.7-5.97 µIU/mL) and all of the children have normal fT4 values (reference value: 0.48-2.34 ng/dL for <1 year-old children; 0.85-1.75 ng/dL for >1-year-old children). Table 4 presents the Pearson's correlation test demonstrates that offspring thyroid function did not correlate to the iodine status of the mother (TSHs, p=0.314; fT4, p=0.258)

Table 4. Correlation of maternal iodine status and their offspring thyroid function

Thyroid function of offspring	Maternal iodine status			p
	Insufficient group	Adequate group	Excessive group	
TSHs (µIU/mL)	2.34±1.10	2.29±0.99	2.12±1.17	0.314
fT4 (ng/dL)	1.28±0.15	1.26±0.11	1.17±0.13	0.258

3.2. Discussion

Pregnancy vulnerability to iodine deficiency makes it a key indicator of iodine intake adequacy. In the research area, pregnant women demonstrated insufficient iodine status (median urine iodine: 125 µg/L), aligning with findings in Zhejiang's coastal pregnant population [10]. The same result was also found by Wang in the following year in Zhejiang [11]. Lou *et al*. also found that iodine status was affected by geography. Pregnant women who live in the coastal areas of Zhejiang had lower UIE than those who live in inland [12]. This research found a higher percentage of insufficient population compared to pregnant women who lived in the deficient area Ponorogo in West Java, Indonesia, namely 59.5% [13]. Patriota added that the prevalence of iodine insufficiency was 53% for women of childbearing age population [6]. Also, this research prevalence was higher than the prevalence found by other studies in pregnant women population in Brazil [14], Kolkata [15], India [16], as well as coastal areas of China (9) [17]. Whereas, the prevalence of iodine deficiency worldwide in insufficiency areas was higher (86%) than the prevalence of insufficiency in this research areas [6]. Pregnant women with high-risk pregnancy based on age were 25.1%, this was a higher percentage than found by Supadmi [13]. Additionally, this finding was also different from previous studies that the older age of the maternal, the higher risk of having an insufficient intake of iodine [14], [18].

The location is the coastal area affected with contamination of mercury and flooding annually. Flooding influences the availability of iodine in soil and foodstuff [19]. Subjects living in areas that produce iodine-rich food such as fish should have sufficient iodine intake [20]. However, iodine intake is not enough if it is only from fish. Other study showed that the decrease in fish consumption by pregnant women is due to several obstacles [21]. This study observed that there was no difference in iodine intake between insufficient and adequate groups, well this is contrary to the previous research [22], [23]. The limitation of this research was not measure the iodine content in salt, but suggested that iodized salt is crucial for meeting iodine needs, especially for certain groups like pregnant women.

Rajput *et al*. and Kusrini *et al*. studied pregnant women who did not consume iodine-containing vitamins and minerals and they found that UIE decreased with increasing gestational age [16], [24]. Further research is needed to link mercury contamination levels, iodine status, and salt consumption. Mercury not only restricted iodine intake from fish but also antagonist to iodine storage in colloid and interferes with deiodination of thyroid hormone [25]. A study has verified that mercury affects the homeostasis of thyroid function [25].

This study found that pregnant women had low iodine intake compared to recommended levels by WHO (p=0.000). This deficiency may impact the future thyroid function of both the mother and her children, highlighting the importance of adequate iodine intake for pregnant women. Inadequate iodine intake is the most common cause of hypothyroidism [26]. Fetus is dependent to the maternal thyroid supplied before 20 weeks of the gestation and fetus initiates to synthesis the thyroid hormone since 30 weeks of gestation period. In fact, at all stages of pregnancy, adequate iodine is required. Maternal iodine status did not affect TSHs (p=0.314). This result was relevant to that found by Censi *et al*. [26]. The result of this study also showed that the maternal iodine status did not correlate with the offspring thyroid function. However, Dei-Tutu *et al.* revealed results that contradicted the result of this study [27].

Farha *et al.* found in an iodine-deficient population, there is a strong correlation between maternal iodine status and infant thyroid hormone [28]. Although maternal iodine status did not correlate with their offspring's thyroid function, the concern from this result was two (3.12%) of the children had low TSH concentrations with normal fT4 reflecting subclinical hyperthyroidism [29]. However, 6.25% (n=4), had TSH concentration >5 mIU/mL indicating the potencial for the development of subclinical hypothyroidism [29] with the adverse impact on their neurodevelopment and growth, especially growth in children aged 1-12 years. For children under two years old, their normal thyroid function depends on their mother's iodine status, and independent on their iodine status [30]. The lactating mammary glands are capable to concentrate iodine due to increased sodium-iodine symporter, even when the supply of iodine from breast milk is lacking [4].

Additionally, this research discovered valuable information about iodine insufficiency in polluted coastal regions and the potential negative impact of maternal iodine deficiency on children's thyroid function. However, the study has some limitations, such as the lack of certain endemic foods in the software's food database and the absence of data on iodine-containing supplements or iodized salt intake. Furthermore, the study did not examine the connection between thyroid function and heavy metal exposure in relation to genetic expression and iodine deficiency.

4. CONCLUSION

Based on the research findings, it can be concluded that maternal iodine status did not correlate with offspring thyroid function. Some children have potency to develop thyroid hormone disorder and its impact. The prevalence of iodine deficiency in pregnant women who lived in contaminant coastal areas was 60.8%. The implication of this research is iodine fortification or supplementation for pregnant women is important in

the future. Further research is needed to explore the health determinants of iodine deficiency in coastal area and further impact of deficiency state and pollutants on child development.

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REFERENCES

[1] J. Köhrle, "Selenium, iodine and iron–essential trace elements for thyroid hormone synthesis and metabolism," *International Journal of Molecular Sciences*, vol. 24, no. 4. pp. 3393–3411, 2023. doi: 10.3390/ijms24043393.

[2] K. Rahayu and A. Rahmawati, "Literature review: pregnant women nutrition during a pandemic," *Pharmacology, Medical Reports, Orthopedic, And Illness Details (COMORBID)*, vol. 1, no. 3, pp. 1–14, 2022.

[3] Y. Chen, W. Chen, and W. Zhang, "Reply to: iodine nutrition and thyroid function in pregnant women exposed to different iodine sources," *Biological Trace Element Research*, vol. 193, no. 2. pp. 52–59, 2020. doi: 10.1007/s12011-019-01724-4.

[4] P. M. Farias *et al.*, "Minerals in pregnancy and their impact on child growth and development," *Molecules*, vol. 25, no. 23. pp. 5630–5652, 2020. doi: 10.3390/molecules25235630.

[5] W. H. Organization, "Urinary iodine concentrations for determining iodine status in populations," *Urinary iodine concentrations for determining iodine status in populations*, pp. 1–5, 2013.

[6] E. S. O. Patriota, I. C. C. Lima, E. A. F. Nilson, S. C. C. Franceschini, V. S. S. Gonçalves, and N. Pizato, "Prevalence of insufficient iodine intake in pregnancy worldwide: a systematic review and meta-analysis," *European Journal of Clinical Nutrition*, vol. 76, no. 5, pp. 703–715, 2022, doi: 10.1038/s41430-021-01006-0.

[7] S. Shenhav *et al.*, "Can mild-to-moderate iodine deficiency during pregnancy alter thyroid function? lessons from a mother–newborn cohort," *Nutrients*, vol. 14, no. 24, pp. 5336–5352, 2022, doi: 10.3390/nu14245336.

[8] A. M. Monaghan *et al.*, "Associations between maternal urinary iodine assessment, dietary iodine intakes and neurodevelopmental outcomes in the child: a systematic review," *Thyroid Research*, vol. 14, no. 1. pp. 1–13, 2021. doi: 10.1186/s13044-021-00105-1.

[9] G. Lisco, A. De Tullio, V. A. Giagulli, G. De Pergola, and V. Triggiani, "Interference on iodine uptake and human thyroid function by perchlorate-contaminated water and food," *Nutrients*, vol. 12, no. 6. 2020. doi: 10.3390/nu12061669.

[10] G. Mao *et al.*, "Iodine deficiency in pregnant women after the adoption of the new provincial standard for salt iodization in Zhejiang Province, China," *BMC Pregnancy and Childbirth*, vol. 18, no. 1, pp. 1–8, 2018, doi: 10.1186/s12884-018-1952-5.

[11] X. Wang *et al.*, "Poor iodine knowledge, coastal region, and non-iodized salt consumption linked to low urinary iodine excretion in zhejiang pregnant women," *Nutrients*, vol. 11, no. 2, pp. 413–425, 2019, doi: 10.3390/nu11020413.

[12] X. Lou *et al.*, "Geographical influences on the iodine status in pregnant women, neonates, and school-age children in China," *Nutrition Journal*, vol. 19, no. 1, pp. 1–7, 2020, doi: 10.1186/s12937-020-0525-4.

[13] S. Supadmi and I. Kusrini, "High risk profile of pregnancy in iodine deficiency areas," *5th Universitas Ahmad Dahlan Public Health Conference, Yogyakarta, Indonesia*, 3-4 July 2019, vol.24. pp. 37-42. doi: 10.2991/ahsr.k.200311.008.

[14] D. A. Saraiva *et al.*, "Iodine status of pregnant women from a coastal Brazilian state after the reduction in recommended iodine concentration in table salt according to governmental requirements," *Nutrition*, vol. 53, pp. 109–114, 2018, doi: 10.1016/j.nut.2018.02.001.

[15] A. Majumder, A. Jaiswal, and S. Chatterjee, "Prevalence of iodine deficiency among pregnant and lactating women: Experience in Kolkata," *Indian Journal of Endocrinology and Metabolism*, vol. 18, no. 4, p. 486, 2014, doi: 10.4103/2230-8210.137491.

[16] R. Rajput, L. Yadav, S. Nanda, and R. Yadav, "Trimester specific nutritional status of iodine among euthyroid pregnant women," *Journal of Thyroid Disorders & Therapy*, vol. 06, no. 1, pp. 1–4, 2017, doi: 10.4172/2167-7948.1000208.

[17] S. Zou *et al.*, "Iodine nutrition and the prevalence of thyroid disease after salt iodization: A cross-sectional survey in shanghai, a coastal area in China," *PLoS ONE*, vol. 7, no. 7, pp. 1–9, 2012, doi: 10.1371/journal.pone.0040718.

[18] L. Liu, J. Liu, D. Wang, H. Shen, and Q. Jia, "Effect of urinary iodine concentration in pregnant and lactating women, and in their infants residing in areas with excessive iodine in drinking water in Shanxi Province, China," *Biological Trace Element Research*, vol. 193, no. 2, pp. 326–333, 2020, doi: 10.1007/s12011-019-01716-4.

[19] M. Zimmermann and P. R. Trumbo, "Iodine," *Advances in Nutrition*, vol. 4, no. 2, pp. 262–264, 2013.

[20] A. A. Madar, E. Heen, L. A. Hopstock, M. H. Carlsen, and H. E. Meyer, "Iodine intake in Norwegian women and men: The population-based tromsø study 2015-2016," *Nutrients*, vol. 12, no. 11, pp. 3246–3259, 2020, doi: 10.3390/nu12113246.

[21] M. Bouga, M. E. J. Lean, and E. Combet, "Iodine and pregnancy—a qualitative study focusing on dietary guidance and information," *Nutrients*, vol. 10, no. 4, pp. 408–427, 2018, doi: 10.3390/nu10040408.

[22] T. Gebreegziabher, T. Woltamo, D. G. Thomas, T. S. Kennedy, and B. J. Stoecker, "Iodine supplementation of lactating women and assessment of infant visual information processing and maternal and infant thyroid function: A randomized trial," *PLoS ONE*, vol. 14, no. 10, pp. 1–17, 2019, doi: 10.1371/journal.pone.0223348.

[23] V. L. Clifton *et al.*, "The impact of iodine supplementation and bread fortification on urinary iodine concentrations in a mildly iodine deficient population of pregnant women in South Australia," *Nutrition Journal*, vol. 12, no. 1, pp. 1–5, 2013, doi: 10.1186/1475-2891-12-32.

[24] I. Kusrini, J. Farebrother, and D. K. Mulyantoro, "Adequately iodized salt is an important strategy to prevent iodine insufficiency in pregnant women living in Central Java, Indonesia," *PLoS ONE*, vol. 15, no. 11 November, pp. 1–13, 2020, doi: 10.1371/journal.pone.0242575.

[25] R. Pamphlett, P. A. Doble, and D. P. Bishop, "Mercury in the human thyroid gland: Potential implications for thyroid cancer, autoimmune thyroiditis, and hypothyroidism," *PLoS ONE*, vol. 16, no. 2 February, pp. 1–16, 2021, doi: 10.1371/journal.pone.0246748.

[26] S. Censi *et al.*, "The effects of iodine supplementation in pregnancy on iodine status, thyroglobulin levels and thyroid function parameters: Results from a randomized controlled clinical trial in a mild-to-moderate iodine deficiency area," *Nutrients*, vol. 11, no. 11, pp. 2639–2642, 2019, doi: 10.3390/nu11112639.
[27] S. A. Dei-Tutu *et al.*, "Correlating maternal iodine status with neonatal thyroid function in two hospital populations in Ghana: A multicenter cross-sectional pilot study," *BMC Pediatrics*, vol. 20, no. 1, pp. 1–9, 2020, doi: 10.1186/s12887-020-1932-6.
[28] S. Syeda Farha and A. Urooj, "Urinary iodine concentration as an indicator of iodine status and its correlation with the thyroid hormones and hemoglobin levels in first trimester pregnant women-An Exploratory Study," *Current Research in Nutrition and Food Science*, vol. 9, no. 3, pp. 791–799, 2021, doi: 10.12944/CRNFSJ.9.3.07.
[29] S. B. Soh and T. C. Aw, "Laboratory testing in thyroid conditions - Pitfalls and clinical utility," *Annals of Laboratory Medicine*, vol. 39, no. 1. pp. 3–14, 2018. doi: 10.3343/alm.2019.39.1.3.
[30] N. Pal, S. K. Samanta, A. Chakraborty, N. K. Chandra, and A. K. Chandra, "Interrelationship between iodine nutritional status of lactating mothers and their absolutely breast-fed infants in coastal districts of Gangetic West Bengal in India," *European Journal of Pediatrics*, vol. 177, no. 1, pp. 39–45, 2018, doi: 10.1007/s00431-017-3025-6.

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