Iodine adequacy in reproductive age and pregnant women living in the Western region of Saudi Arabia

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Firas Azzeh
Umm Al-Qura University

Bassem Amr Refaat
Umm Al-Qura University

bassem.refaat@yahoo.co.uk

Corresponding Author

ORCiD: https://orcid.org/0000-0003-4267-1016

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Abstract

**Background:** Despite the serious maternal and foetal complications associated with iodine deficiency during pregnancy, surveys related to pregnant women in the Kingdom of Saudi Arabia (KSA) are lacking. This study, therefore, measured urine iodine concentrations (UIC) alongside the potential socioeconomic factors contributing towards iodine inadequacy in reproductive age and pregnant Saudi women from the Western province of KSA.

**Methods:** Spot urine samples were collected from 1222 pregnant and 400 age-matched non-pregnant/non-lactating reproductive age women. The socioeconomic characteristics were obtained through a structured questionnaire. The WHO criteria for iodine sufficiency in non-pregnant (100–199 μg/L) and pregnant (150–249 μg/L) women were applied.

**Results:** The median UIC in the non-pregnant women (101.64 μg/L; IQR: 69.83 – 143.55) was at the lowermost WHO recommended cut-off, whereas the pregnant group were iodine deficient (112.99 μg/L; IQR: 81.01 – 185.57). Moreover, the median UIC was below adequacy across the different trimesters. Multiparity (OR = 3.091; 95%CI: 1.707–5.598) and earning below the minimum wage (2.520; 95%CI: 1.038–6.119) significantly increased the risk of iodine deficiency only in the non-pregnant women. Passive smoking, however, was an independent risk factor for iodine deficiency in the non-pregnant (OR = 1.818; 95%CI: 1.097–3.014) and pregnant (OR = 1.653; 95%CI: 1.043–2.618) groups. The use of non-iodised salt also significantly increased the risk of iodine deficiency in the non-pregnant (OR = 2.052; 95%CI: 1.118–3.766) and pregnant women (OR = 3.813; 95%CI: 1.992–7.297), whereas iodine supplements significantly lowered the risk in both groups (OR = 0.364; 95%CI: 0.172–0.771 and OR = 0.002; 95%CI: 0.001–0.005, respectively). Moreover, BMI correlated independently and significantly with median UIC in the non-pregnant in both study populations.

**Conclusions:** This study is the first to show borderline iodine sufficiency in reproductive age Saudi women from the Western province, whereas mild iodine deficiency was observed in the pregnant population and could represent a serious public health problem. This study also advocates the necessity to establish routine iodine dietary advice services by the health authorities to foster adequate iodine intake in pregnant women to avoid the perilous maternal-foetal health consequences.
of iodine deficiency.

**Background**

Iodine is essential for the synthesis of thyroid hormones, and suboptimal intake of this nutrient at the periconceptual and/or during pregnancy has been linked with maternal goitre and hypothyroidism [1, 2]. Iodine deficiency during pregnancy also significantly increases the risk of delayed neurodevelopment and poor cognitive functions of the offspring [3, 4]. Although many countries have implemented the universal salt iodisation (USI) policy to ensure adequate access to iodine by the general public [5, 6], numerous reports from developed and developing countries have demonstrated high rates of iodine insufficiency among pregnant women [7-11]. Accordingly, many researchers have emphasised the need for alternative means (e.g. iodine supplements) to ensure adequate iodine intake during pregnancy [7-11], and the World Health Organisation (WHO) has recommended increasing iodine intake from 150 to 250 μg/day [12].

About 90% of ingested iodine from diet and/or supplement is excreted by the kidney and, measuring urinary iodine concentration (UIC) in spot samples and estimating 24-hour urine iodine excretion (24-hr UIE) are reliable approaches for assessing iodine status [13-15]. Surveying school-age children (SAC) is also the currently accepted method for evaluating iodine status within a population since they are easy to access and are believed to reflect the nutritional status of their families [16]. However, the most recent report by the Iodine Global Network (IGN) in 2019 has revealed that 29 countries reported iodine deficiency in pregnant women albeit that their SAC populations were sufficient [5]. Hence, it has been proposed that pregnant women should be surveyed independently from SAC to precisely measure their iodine status [7-11]. Additionally, the updated guidelines by the United Nations International Children's Emergency Fund (UNICEF) has also recommended that iodine should be assessed in different subsets of a population, especially those who are vulnerable for deficiency [17].

In the Kingdom of Saudi Arabia (KSA), thyroid disorders are common among the general population at the different ages [18-21] and goitre was frequently reported in Saudi children, particularly among those who were living in high altitude areas of the kingdom [22, 23]. Alissa et al. (2009) followed the
WHO recommended median UIC cut-off values for iodine adequacy, and their results revealed severe deficiency in the enrolled hypothyroid patients as well as healthy participants from the Western region of KSA [24]. Although KSA is currently classified by the IGN (2019) as iodine sufficient based on a national survey of SAC in 2012 [5], other more recent national studies have revealed marked iodine deficiency and high prevalence of goitre in their SAC populations [25, 26]. According to another recent national survey, KSA has also adopted the USI policies since 1995 and most of the locally available salt is adequately iodised (15–40 ppm) [27]. However, salt iodisation is not obligatory in the kingdom, only 70% of the Saudi households were found to consume iodised salt, and the numbers are below the WHO references [27]. Concomitantly, we have previously shown that 26.8% and 4.8% of pregnant Saudi women from the Western region had hypothyroidism and isolated hypothyroxinaemia, respectively [28]. However, currently there is no report on iodine status among reproductive age and pregnant Saudi women.

Hence, this study measured iodine adequacy in non-pregnant, non-lactating reproductive age Saudi women as well as in pregnant Saudi women at the different trimesters. Additionally, the socio-economic characteristics were collected to identify the factors that could contribute to iodine deficiency. A better understanding about iodine status in in the targeted populations could enlighten the health authorities and policymakers regarding the magnitude of iodine deficiency and may possibly support the development of appropriate policies regarding the screening and prevention of iodine inadequacy during pregnancy.

Methods

Study design

This non-randomised cross-sectional study was conducted from March 2017 to May 2019, and ethical approval (AMSEC 21-16-02-2017) was obtained from the Faculty of Applied Medical Sciences Ethics Committee in Umm Al-Qura University. The study populations included 1222 apparently healthy pregnant Saudi women (18-44 years) at the different trimesters and who were recruited from the antenatal care unit in the Medical Centre of Umm Al-Qura University in Makkah city. Another 400 primi- or multiparous non-pregnant, non-lactating, reproductive age Saudi women, and who had no
relevant bad obstetrics history were also recruited from the same centre during the routine vaccination of their children. All the pregnant and non-pregnant participants had no current symptoms/signs or history of thyroid disorders, chronic diseases (e.g. hypertension, diabetes mellitus, etc.), gestational related medical disorders (e.g. pre-eclampsia, gestational diabetes, anaemia, etc.) or autoimmune diseases. According to the 2017 reports issued by the Saudi General Authority for Statistics and Ministry of Health, the total numbers of reproductive age and pregnant Saudi women in the Western region of KSA were 1140185 and 29701, respectively [29, 30]. The Epi Info™ software was used (https://www.cdc.gov/epiinfo/index.html), and the minimal required sample sizes were 384 non-pregnant and 379 pregnant women to achieve a study power of 95%.

A fresh spot urine sample (5 ml) was collected from each woman in a sterile urine container between 9:00 am and 1:00 pm and the samples were stored at -70 °C till transported to the Research Laboratories of the Faculty of Applied Medical Sciences in Umm Al-Qura University for processing. Additionally, the socioeconomic characteristics were obtained through a structured questionnaire that included information related to age (years), pre-pregnancy and/or current weight (Kg) and height (cm) to calculate the body mass index (BMI), parity, type of salt intake, the use of daily iodine-containing supplements, family size, education level, employment status, total monthly income, smoking, residency and gestational age at the time of sample collection from the pregnant population. The question related to the use of iodised salt was categorised as previously reported into non-iodised, iodised and I don't know [31].

**Urine Creatinine concentrations**

Urine creatinine concentrations were measured on Cobas e411 (Roche Diagnostics International Ltd; Risch-Rotkreuz, Switzerland) according to the manufacturer’s protocol. The predicted 24-hour urine creatinine excretion (24-hr Cr; g/day) was calculated by the previously published equation as follow [32]:

\[
\text{Predicted 24-hr Cr for females} = (0.00163 \times [140 - \text{age (years)}]) \times [\text{weight (kg)}^{1.5} \times \text{height (cm)}^{0.5}] \times [1 + 0.18 \times (\text{black} = 1, \text{nonblack} = 0)] \times [1.429 - 0.0198 \times \text{BMI (kg/m}^2)]/1000).
\]
Urine iodine concentrations

1. **Preparation of working solutions**

All the chemicals were analytical grade from Sigma-Aldrich Co. (MO, USA). The required working solutions for measuring urine iodine were prepared as previously described [15]. Briefly, the acid ashing solution was freshly made by adding perchloric acid to nitric acid at the ratio of 4:1. Arsenic trioxide (4.8 g) were dissolved in 500 ml of 0.3 NaOH followed by vigorous stirring at 40 °C for 48 hours to prepare the 0.125 molar arsenious solution as previously described [33]. Subsequently, 10 ml of 96% sulfuric acid followed by 30 g of sodium chloride were carefully added. The ceric ammonium solution was made by dissolving 14 g of tetra-ammonium cerium (IV) sulfate dihydrate in 300 mL deionised water with the subsequent addition of 52 mL of 96% sulfuric acid [15].

2. **Iodine calibrators**

The calibrators were prepared with potassium iodate (KIO₃) that contains 59.3% iodine, and 3.423 g of KIO₃ were dissolved in 1000 ml of deionized water to make a stock solution of 16000 nmol/l that was then stored at 7 °C in the refrigerator in a brown bottle. Seven calibrators were freshly prepared as serial dilutions using deionized water to prepare the following standards: 1600; 800; 400; 200; 100; 50 and 25 nmol/l, which were equivalent to 203; 102; 51; 25; 13; 6 and 3 μg/l of iodine. No zero-standard was added since the concentrations of iodine are logarithmically graded for the standard curve [15].

3. **Laboratory procedures for measuring urine iodine concentrations**

The spot urine samples were processed in 96-well clear polystyrene flat-bottomed microplates (Thermo Fisher Scientific, CA, USA) and on a fully automated ELISA machine (Human Diagnostics, Wiesbaden, Germany) to measure the UIC according to the principles of the Sandell-Kolthoff method [15]. Low (13 μg/l), intermediate (102 μg/l) and high (203 μg/l) iodine calibrators were also processed five times to measure the assay performances. The intra-assay coefficient of variation was 5.7%, 4.3% and 4.1% for the low, intermediate and high calibrators, respectively. Additionally, the inter-assay precision was 10% for the low, 7% for the intermediate and 4.5% for the high calibrators.
The 24-hr UIE was calculated according to the previously published equation as follow [14]: Spot urine [Iodine/Creatinine (μg/g)] × predicted 24-hour Cr (g/day). The amount of 24-hr UIE were classified according to the WHO reference values for iodine adequacy as follow: deficiency (< 100 and < 150 μg/day), sufficiency (100-199 and 150-249 μg/day) and excess (≥ 200 and ≥ 250 μg/day) for non-pregnant and pregnant women, respectively [13].

Statistical analysis

Statistical analysis was done with SPSS software version 25 (New York, USA), and P < 0.05 was considered statistically significant. The Kolmogorov-Smirnov test for normality and Levene test for homogeneity were performed for continuous data that were expressed either as mean ± standard deviation (SD) or median with the interquartile range (IQR) depending on data normality. Ordinal and discontinuous data were shown as numbers and percentages, and cross-tabulation followed by Chi square ($\chi^2$) test were applied for frequency analysis. Based on data normality, one-way ANOVA or Kruskal-Wallis were used to compare between more than two groups followed by either Tukey’s HSD or Games-Howell post-hoc tests according to variance equality. Multinomial regression analysis was also performed to identify the socioeconomic predictors of iodine status in each of the study populations.

Results

The socioeconomic characteristics of the study groups

The mean ± SD of age and BMI in the non-pregnant population were 29.1 ± 7.3 years and 24.03 ± 5.4 kg/m², respectively. The majority of participants were primiparous (n = 228; 57%) and their families comprised ≤ four members (n = 236; 59%). Nineteen (4.7%) women were illiterate, whereas 34 (8.5%) had primary education, 125 (31.2%) had secondary education, and the remaining 222 subjects (55.5%) had a university degree. However, unemployment was predominant within the group (n = 311; 77.8%). While 14% (n = 56) reported that their monthly income was below the Saudi national minimum wage (3000 SAR), 37.3% (= 159) were receiving between 3001 and 5000 SAR, 33.5% (n = 134) were gaining between 5001 and below 10000 SAR and 15.3% (n = 61) were earning ≥ 10,000 SAR. Active and passive smoking were also reported by 5.8% (n = 23) and 34.2% (n = 137),
respectively. Moreover, 292 women (73%) were using iodised salt and the remainders either were using of non-iodised salt (n = 84; 21%) or chose ‘I don’t know’ (n = 24; 6%). Finally, 46 women (11.5%) were using daily iodine supplements (150 μg/day).

On the other hand, the mean of age was 28.7 ± 5.7 years and the mean of pre-conceptional BMI was 25.7 ± 4.7 kg/m² in the pregnant group (n = 1222). Multigravidity (n = 956; 78.2%), having more than four family members (n = 786; 64.3%), being a university graduate (n = 694; 56.8%), unemployment (n = 956; 78.2%) and earning a monthly income between 3001 and 5000 SAR (n = 642; 52.5%) were common among the pregnant population. Furthermore, the majority was neither active (n = 1158; 94.8%) nor passive (n = 792; 64.8%) smokers. Meanwhile 71.5% (n = 874) were using iodised salt, 21.8% (n = 266) were utilising non-iodised salt and 6.7% (n = 82) answered by ‘I don’t know’. Additionally, only 338 (27.7%) pregnant women reported using iodine supplements (220 μg/day). The sub-analysis also showed that 364 (22.4%), 352 (21.7%) and 506 (31.2%) women were in the first, second and third trimesters, respectively. Furthermore, the distribution of age, BMI, family size, educational levels, monthly income, active smoking, the use of iodised salt and consumption of iodine supplements were significantly different between the three trimesters (Table 1).

**Urine iodine concentrations and associated factors with iodine inadequacy**

**A. Non-pregnant population**

The median spot urine iodine and creatinine concentrations together with the I/Cr ratio in the non-pregnant population were 75.3 μg/L (IQR: 51.6 - 106.2), 0.73 g/L (IQR: 0.62 - 0.85) and 102.86 μg/g (IQR: 67.6 - 153.2), respectively. Additionally, the estimated 24-hr urine Cr excretion in the non-pregnant women was 1.1 g/L (IQR: 0.97 - 1.32), whereas the 24-hr UIE (101.64 μg/L; IQR: 69.83 - 143.55) was at the lowest WHO recommended limit for adequate iodine intake for reproductive age women (100 - 199 μg/L).

The regression analysis showed that having > 4 family members (2.4-fold), earning below the national minimal wage (2.5-fold), passive smoking (1.8-fold) and using non-iodised salt (2-fold) significantly increased the risk of iodine deficiency in the non-pregnant population (Table 2). Contrariwise, primiparity (3-fold) and the consumption of iodine supplements (2.7-fold) significantly
decreased the risk of iodine deficiency. Furthermore, low educational level (illiterate; 10-fold and primary education; 4-fold) was the only independent factor that increased the risk of iodine excess, whereas BMI was independently and significantly correlated with median UIC in the non-pregnant women (Table 2).

**B. Pregnant population**

The spot urine concentrations in the pregnant group were 83.69 μg/L (IQR: 60 – 137.46) for UIC, 0.83 g/L (IQR: 0.71 – 0.97) for creatinine and 102.47 μg/g (IQR: 74.88 – 151.09) for I/Cr ratio. The estimated 24-hr urine Cr median was 1.12 g/L (IQR: 0.97 – 1.32), whereas the 24-hr UIE median (112.99 μg/L; QR: 81.01 – 185.57) was less than the WHO recommended minimal limit for adequate iodine intake during pregnancy (150 – 249 μg/L).

While the first trimester median spot UIC was significantly lower than the third trimester (P = 0.02), the concentrations of both groups were comparable to the second trimester (Figure 1A). Furthermore, the spot urine creatinine concentrations were similar in the first and second trimesters, and both groups were significantly lower than the third trimester levels (Figure 1B). However, no significant difference was detected in the I/Cr ratio between the three trimesters (Figure 1C). Although the estimated 24-hr urine creatinine was also significantly lower in the first and second trimesters compared with the third trimester (Figure 1D), the 24-hr UIE was only significantly different between the first and third trimesters (Figure 1E; P = 0.004). Nevertheless, the 24-hr UIE levels in each of the three trimesters were below the WHO advocated minimum for adequate iodine during pregnancy (Figure 1E).

While the use of non-iodised salt (> 3.5-fold) and passive smoking (1.6-fold) were independent factors associated with increased risk of iodine insufficiency during pregnancy, taking iodine supplements strongly and significantly associated with reduced odds (500-fold) of iodine inadequacy (Table 3). Alternatively, none of the socioeconomic factors increased the risk of excess iodine during pregnancy, whereas the use of non-iodised salt (6-folds) and 2nd trimester (2.4-fold) were significantly associated decreased risk of excess iodine. Significant independent associations were also detected between the BMI and median UIC in the pregnant population (Table 3).
Discussion
The available reports regarding iodine status in the Saudi population are scarce, their results are controversial, and none investigated iodine adequacy among vulnerable groups, including pregnant women. To the best of our knowledge, this study is the first to measure iodine adequacy in reproductive age and pregnant Saudi women. The data showed that the majority of non-pregnant women (73%) were using iodised salt, 2.8% were using iodine supplements, and the median UIC was at the lowest WHO recommended limit for iodine adequacy in reproductive age women [13]. In contrast, the pregnant group median UIC was below the WHO minimal level for iodine sufficiency despite that iodised salt and/or daily iodine supplements were used by 71.5% and 27.6% of the participants, respectively. Our findings infer that the reproductive age Saudi women were marginally iodine sufficient, while the pregnant population had mild deficiency that could denote a public health burden [25-28].

The IGN report (2019) has classified the general Saudi public as iodine sufficient based on the outcomes of a 2012 national SAC survey [5, 16]. Others also showed an enhancement of SAC iodine status after the execution of USI in the Southwestern of KSA, a previously classified severe iodine deficient region [34]. Contrariwise, a research group has disclosed severe iodine deficiency (median UIC 17 μg/L) in 3046 SAC from the same region, and 24% of the children had goitre [25]. Moderate iodine deficiency (median UIC 84 μg/L) has also been reported in 1887 SAC from Makkah province, and 7.4% of the participants were goitrous [26]. Another national survey has shown that 69% of local salt samples were adequately iodised (15 - 40 ppm). Nevertheless, only 70% of the Saudi households were using iodised salt, which did not reach the USI target of ≥ 90% coverage [27]. The present study is aligned with the prior national studies proclaiming iodine adequacy in the general Saudi population since the non-pregnant women were iodine sufficient [5, 16, 34]. However, the levels were at the lowest margin of adequacy, thus providing additional sustenance for the prior demands to ban non-iodised salt in order to enhance iodine intake in KSA [27].

On the other hand, mild iodine deficiency was detected in our pregnant population across the different trimesters. The daily iodine requirements increase immensely during pregnancy to supply
the demands of growing foetus as well as to compensate the physiological increase in iodine renal excretion [28]. An explanation for the observed iodine deficiency in our study could be related to inappropriate nutrition during pregnancy as many studies have indicated that most of Saudi pregnant women were malnourished, and their consumption of essential nutrients were below the recommended daily requirements [35-38]. Saudi women from the Western region also had significantly low micronutrients intake, thus their offspring had a higher risk of developing birth defects [39-41]. Our findings agree with the earlier studies since the use of iodine supplements was only confirmed by a minority (27.6%) of the enrolled pregnant population. Accordingly, this study reinforces the many calls for improving awareness regarding the importance of iodine intake from dietary and supplement sources during pregnancy [42-45]. Moreover, iodine insufficiency during pregnancy could precipitate maternal thyroid disorders alongside poor foetal neurodevelopment [1-4]. We have previously reported that 26.8% and 4.8% of 500 pregnant Saudi women from the Western region had hypothyroidism and isolated hypothyroxinaemia, respectively [28]. However, little is currently known in KSA about the links between iodine intake and thyroid diseases during pregnancy. Hence, more studies to measure the associations between iodine status and thyroid hormones in pregnant Saudi women are still needed.

Additionally, this study further supports the notion that SAC median UIC could be an imprecise approach for estimating iodine status in pregnant women [7-11]. In consolidation, The IGN has revealed that 29 countries reported iodine deficiency in pregnant women, whereas their SAC populations were sufficient [46]. The most recent UNICEF guidelines have likewise stated that measuring UIC in SAC may conceal suboptimal iodine intake in subsets of vulnerable groups, including pregnant women [17]. Studies from Austria [7], Denmark [9], China [11] and the United States [47] have also demonstrated marked iodine insufficiency among pregnant women despite using iodised salt and/or iodine supplements. Taken together, our study and the prior reports advocate that the health authorities in each country should consider measuring iodine intake in pregnant women independently from SAC to accurately evaluate iodine adequacy in this vulnerable group [7-11]. Educational programs should also be developed to increase the awareness of pregnant women, or
those who are planning for conception, about the significance of iodine for them as well as for their offspring wellbeing [48, 49].

Iodine adequacy in reproductive age and pregnant women could be influenced by numerous factors [50]. Herein, the risk of iodine deficiency in the non-pregnant population increased with multiparity, which agrees with studies from the United States [51], Denmark [52], Germany [53] and Italy [54]. A possible construal for the associations between parity and iodine intake could be illustrated by the findings of Ratondi et al. who have proclaimed a cumulative, non-reversible goitrogenic effect for each pregnancy, which may require increasing iodine supply for preventing thyroid abnormalities [55]. Additionally, earning below the Saudi minimal wage also increased the odds of inadequate iodine in our non-pregnant women. Likewise, a linkage between poverty and iodine inadequacy has been reported by several community studies, which could be due poor adherence of low-income populations to appropriate micronutrients and iodised salt intake [56, 57]. Numerous population-based studies have also demonstrated the negative impact of smoking on thyroid functions and iodine adequacy in reproductive age and pregnant women [50, 52, 53, 58, 59]. In agreement, our data showed that passive, but not active, smoking was an independent factor that significantly increased the risk of iodine inadequacy in both the non-pregnant and pregnant groups. Accordingly, the present study strengthens the numerous requests to employ the necessary policies for smoking cessation as well as to encourage pregnant women to avoid staying in rooms where others have smoked [60].

Our results also revealed 2-fold and 3-fold higher risks of iodine insufficiency for consuming non-iodised salt by the reproductive age and pregnant women, respectively. The WHO and UNICEF have adopted the USI policy since 1994 to ensure that the general public adequately consume sufficient iodine [61]. Although the salt iodisation is implemented in KSA, the household consumption of iodised salt (70%) was found to be lower than the USI target of 90% usage by the general population to avoid deficiency [27]. More recently, the WHO has also recommended salt reduction to 5 gram/day for adults, including reproductive age and pregnant women, to reduce the likelihood of developing cardiovascular diseases [6]. Suggested plans to simultaneously maintain iodine adequacy with
decreasing salt intake include fortifying salt with higher amounts of iodine [6]. Alternatively, Australia and New Zealand have adopted a different strategy by fortifying bread to ensure the delivery of adequate iodine, and several studies have reported that the median UIC in adults, including pregnant women, met the WHO recommendations post-fortification [62, 63]. Therefore, the reported inadequate use of iodised salt in KSA alongside the advised reduction of salt intake accentuate the importance of developing other vehicle(s) for delivering iodine, thus decreasing the incidence of iodine deficiency disorders [62, 63]. Furthermore, reproductive age (150 µg/day) and pregnant (250 µg/day) women could temporarily benefit from using daily iodine supplements till developing a solid and effective national salt/bread iodisation program [27, 62, 63].

The present study also showed a weak positive association between BMI and UIC, which correlates with previous reports from Bangladesh and Romania [64, 65]. A possible explanation could be that pregnant and non-pregnant women with high BMI were consuming higher foods rich in iodine than lean individuals. Additionally, pregnant women often change their dietary habits and eat more fish and milk, the richest sources of iodine, and the tendency for consuming these foods is higher in obese than lean women [66]. On the contrary, several other studies either have reported negative association between BMI and UIC [9, 67] or have shown no correlation between body weight and iodine intake [8, 42]. These discrepancies between the studies could be linked to differences in eating habits and dietary patterns between the different populations as well as between cities of each country [68, 69].

The present study has several limitations. Although the number of participants is larger compared with several other reports on pregnant women [7-9], our participants were enrolled from a single site, and other cities from the same region were not included. Additionally, we did not measure the dietary habits and intake alongside the thyroid function parameters to investigate their correlations with iodine status. However, this is a phase 1 study and we will conduct further research to measure the interactions between nutritional habits, iodine intake and thyroid functions in pregnant women.

Conclusions
This is the first study to demonstrated borderline iodine sufficiency among reproductive age women
from the Western region of Saudi Arabia, whereas the pregnant women were deficient, despite the use of iodised salt. Similar to other countries, this study highlighted the need to survey iodine intake in pregnant women regularly and independently from schoolchildren. Although the use of iodine supplements was associated with a significant decreased risk of deficiency among the targeted populations, less than 30% of pregnant women reported using supplements rich in iodine. Hence, our findings advocate the necessity to develop/implement effective national programs in the different regions of KSA to overcome any potential complications arising from suboptimal iodine intake during pregnancy. Suggested actions include developing educational and awareness campaigns regarding the importance of iodine, and to encourage adequate nutritional schemes based on diets rich in iodine (e.g. fish, milk, iodised salt intake and iodine fortified foods). However, further studies are mandatory to assess the factual magnitude as well as the potential complications of iodine deficiency during pregnancy in the kingdom.

Declarations

**Ethics and Consent to Participate**

Ethical approval was obtained the Faculty of Applied Medical Sciences Ethics Committee (AMSEC 21-16-02-2017). Informed written consent was also obtained from all participants included in the study.

**Consent for publication**

Not applicable.

**Competing of Interest**

The authors declare no conflict of interest.

**Availability of data and materials**

All data generated or analysed during this study are included in this published article [and its supplementary information files].

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**Authors’ contributions**
Conceptualization: FA & BR; methodology: FA & BR; formal analysis: FA & BR; investigation: FA & BR; funding acquisition: BR & FA; resources and project administration: BR; data curation: FA; writing—original and revised draft: FA & BR; supervision: FA. Both authors have read and approved the manuscript.

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Abbreviations

24-hr Cr 24-hour urine creatinine excretion
24-hr UIE Estimated 24-hour urine iodine excretion
BMI Body mass index
KSA Kingdom of Saudi Arabia
I/Cr Iodine/creatinine ratio
IGN Iodine Global Network
IQR Interquartile range
KIO₃ Potassium iodate
SAC School-age children
SAR Saudi Riyal
SD Standard deviation
UIC Urine iodine concentration
USI Universal salt iodisation
WHO World Health Organisation

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Tables
Table 1: The socioeconomic characteristics of the pregnant participants (n = 1222).
| Parameter                        | Pregnant group (n = 1222)                                                                 |
|---------------------------------|---------------------------------------------------------------------------------------------|
|                                 | First trimester (n = 364; 29.8%) | Second trimester (n = 352; 28.8%) | Third trimester (n = 506; 41.4%) |
| **Mean ± SD of Age (year)**     | 28.6 ± 6.2 | 27.9 ± 5.5 | 29.2 ± 5.1 |
| **Age groups**                  |                                                      |                                                      |                                                      |
| 18- <25                         | 132 (10.8%) | 134 (10.9%) | 118 (9.6%) |
| 25- <35                         | 160 (13.1%) | 172 (14.1%) | 296 (2.2%) |
| >35                             | 72 (5.9%)   | 46 (3.8%)   | 92 (7.4%)  |
| **Mean ± SD of Weight (kg)**    | 66.4 ± 13.6 | 65.9 ± 13.5 | 69.1 ± 13.0 |
| **Mean ± SD of Height (cm)**    | 160.8 ± 7.9 | 160.9 ± 7.0 | 163.3 ± 7.0 |
| **Mean ± SD of BMI (kg/m²)**    | 25.8 ± 5.5  | 25.4 ± 4.6  | 25.8 ± 4.2  |
| **BMI Classes**                 |                                                      |                                                      |                                                      |
| Underweight                     | 12 (1%)     | 18 (1.5%)   | 24 (2%)    |
| Normal                          | 164 (13.4%) | 156 (12.8%) | 186 (14%)  |
| Overweight                      | 124 (10.2%) | 136 (11.1%) | 230 (18%)  |
| Obese                           | 64 (5.2%)   | 42 (3.4%)   | 66 (5%)    |
| **Parity**                      |                                                      |                                                      |                                                      |
| Primiparous                     | 72 (5.9%)   | 90 (7.4%)   | 104 (8%)   |
| Multiparous                     | 292 (23.9%) | 262 (21.4%) | 402 (32%)  |
| **Family Size**                 |                                                      |                                                      |                                                      |
| ≤ 4 members                     | 240 (19.7%) | 248 (20.3%) | 298 (24%)  |
| > 4 members                     | 124 (10.1%) | 104 (8.5%)  | 208 (17%)  |
| **Total income (SR)**           |                                                      |                                                      |                                                      |
| < 3000                          | 78 (6.4%)   | 64 (5.2%)   | 123 (1%)   |
| 3001-5,000                      | 196 (16%)   | 196 (16%)   | 250 (2%)   |
| 5,001-10,000                    | 76 (6.2%)   | 68 (5.6%)   | 114 (9%)   |
| > 10,001                        | 14 (1.2%)   | 24 (2%)     | 19 (1.5%)  |
| **Education Level**             |                                                      |                                                      |                                                      |
| Illiterate                      | 16 (1.3%)   | 20 (1.6%)   | 40 (3.2%)  |
| 1^ Education                    | 32 (2.6%)   | 26 (2.1%)   | 52 (4%)    |
| 2^ Education                    | 76 (6.2%)   | 94 (7.7%)   | 172 (13.6%)|
| University                      | 240 (19.7%) | 212 (17.4%) | 242 (19.3%)|
| **Employment**                  |                                                      |                                                      |                                                      |
| Yes                             | 92 (7.5%)   | 74 (6.1%)   | 100 (8.1%) |
| No                              | 272 (22.3%) | 278 (22.7%) | 406 (31.8%)|
| **Residency**                   |                                                      |                                                      |                                                      |
| Urban                           | 356 (29.1%) | 342 (28%)   | 494 (4%)   |
| Rural                           | 8 (0.7%)    | 10 (0.8%)   | 12 (1%)    |
| **Active smoking**              |                                                      |                                                      |                                                      |
| Yes                             | 8 (0.7%)    | 19 (1.6%)   | 37 (2.8%)  |
| No                              | 356 (29.1%) | 333 (27.2%) | 469 (37.3%)|
| **Passive smoking**             |                                                      |                                                      |                                                      |
| Yes                             | 128 (10.5%) | 112 (9.1%)  | 190 (1.5%) |
| No                              | 236 (19.3%) | 240 (19.7%) | 316 (2.5%) |
| **Salt Intake**                 |                                                      |                                                      |                                                      |
| Don’t know                      | 28 (2.3%)   | 12 (1%)     | 42 (3.3%)  |
| Non-iodised                     | 84 (6.9%)   | 82 (6.7%)   | 100 (8%)   |
| Iodised                         | 252 (20.6%) | 258 (21.1%) | 364 (2.9%) |
| **Iodine supplement**           |                                                      |                                                      |                                                      |
| Yes                             | 80 (6.6%)   | 106 (8.7%)  | 152 (1.2%) |
| No                              | 284 (23.2%) | 246 (20.1%) | 354 (2.9%) |

Table 2: The socioeconomic risk factors associated with insufficient and excess iodine intake among
the non-pregnant participants (n = 400) by multinomial regression analysis.

| Risk factors       | Insufficiency (< 100 μg/L) | Excess (≥ 200 μg/L) |
|--------------------|-----------------------------|---------------------|
|                    | Odds ratio (95%CI)          | P Value             | Odds ratio (95%CI) |
| Age (years)        | 1.017 (0.983-1.052)         | NS                  | 0.978 (0.919-1.041) |
| BMI (Kg/m²)        | 1.004 (0.959-1.051)         | NS                  | 1.084 (1.010-1.163) |
| Parity             |                             |                     |                    |
| Primiparous        | Ref.                        | P < 0.0001          | Ref.               |
| Multiparous        | 3.091 (1.707-5.598)         |                     | 0.607 (0.214-1.724) |
| Family Size        |                             |                     |                    |
| ≤ 4 members        | Ref.                        | NS                  | Ref.               |
| > 4 members        | 2.390 (1.390-4.112)         | NS                  | 2.102 (0.843-5.242) |
| Total income (SR)  |                             |                     |                    |
| < 3000             | 2.520 (1.038-6.119)         | P = 0.04            | 1.452 (0.333-6.338) |
| 3001-5,000         | 1.465 (0.740-2.902)         | NS                  | 0.755 (0.219-2.595) |
| 5,001-10,000       | 1.552 (0.769-3.012)         | NS                  | 0.707 (0.203-2.458) |
| > 10,001           | Ref.                        |                     | Ref.               |
| Education Level    |                             |                     |                    |
| Illiterate         | 1.387 (0.355-5.416)         | NS                  | 9.884 (2.028-48.163) |
| Primary Education  | 0.549 (0.224-1.344)         | NS                  | 4.212 (1.218-14.570) |
| Secondary Education| 1.087 (0.639-1.848)         | NS                  | 1.774 (0.662-4.956) |
| University         | Ref.                        |                     | Ref.               |
| Employment         |                             |                     |                    |
| Yes                | 1.009 (0.546-1.867)         | NS                  | 0.769 (0.273-2.165) |
| No                 | Ref.                        |                     | Ref.               |
| Active smoking     |                             |                     |                    |
| Yes                | 1.226 (0.394-3.815)         | NS                  | 0.699 (0.069-7.043) |
| No                 | Ref.                        |                     | Ref.               |
| Passive smoking    |                             |                     |                    |
| Yes                | 1.818 (1.097-3.014)         | P = 0.02            | 1.309 (0.549-3.125) |
| No                 | Ref.                        |                     | Ref.               |
| Salt Intake        |                             |                     |                    |
| Iodized            | Ref.                        |                     | Ref.               |
| Non-iodized        | 2.052 (1.118-3.766)         | P = 0.02            | 1.247 (0.420-3.700) |
| Don't know         | 0.449 (0.161-1.251)         | NS                  | 0.753 (0.167-3.398) |
| Iodine supplement  |                             |                     |                    |
| Yes                | 0.364 (0.172-0.771)         | P < 0.01            | 1.367 (0.479-3.900) |
| No                 | Ref.                        |                     | Ref.               |

Ref = Reference category
NS = Non-significant

Table 3: The socioeconomic risk factors associated with insufficient and excess iodine intake among the pregnant participants (n = 1222) by multinomial regression analysis.
### Risk factors

| Risk factors                  | Insufficiency (< 150 μg/L) | Excess (≥ 250 μg/L) |
|-------------------------------|-----------------------------|---------------------|
|                               | Odds ratio (95%CI)          | P Value             | Odds ratio (95%CI)          |
| Age (years)                   | 1.007 (0.968-1.048)         | NS                  | 0.979 (0.924-1.036)         |
| BMI (Kg/m²)                   | 0.951 (0.913-0.991)         | P = 0.01            | 1.090 (1.013-1.173)         |
| Pregnancy groups              |                             |                     |                               |
| 1st Trimester                 | 1.384 (0.858-2.231)         | NS                  | 0.957 (0.481-1.902)         |
| 2nd Trimester                 | 1.092 (0.682-1.747)         | NS                  | 0.407 (0.175-0.947)         |
| 3rd Trimester                 | Ref.                         |                     | Ref.                         |
| Parity                        |                             |                     |                               |
| Primiparous                   | 1.384 (0.858-2.231)         | NS                  | 0.957 (0.481-1.902)         |
| Multiparous                   | 1.092 (0.682-1.747)         | NS                  | 0.407 (0.175-0.947)         |
| Family Size                   |                             |                     |                               |
| ≤ 4 members                   | 0.951 (0.913-0.991)         | P = 0.01            | 1.090 (1.013-1.173)         |
| > 4 members                   | 0.951 (0.913-0.991)         | P = 0.01            | 1.090 (1.013-1.173)         |
| Education Level               |                             |                     |                               |
| Illiterate                    | 0.953 (0.372-2.440)         | NS                  | 1.607 (0.596-4.335)         |
| Primary Education             | 1.487 (0.709-3.117)         | NS                  | 1.096 (0.322-3.735)         |
| Secondary Education           | 0.778 (0.490-1.234)         | NS                  | 1.305 (0.605-2.813)         |
| University                    | Ref.                         |                     | Ref.                         |
| Employment                    |                             |                     |                               |
| Yes                           | 1.182 (0.716-1.950)         | NS                  | 1.082 (0.440-2.659)         |
| No                            | 1.182 (0.716-1.950)         | NS                  | 1.082 (0.440-2.659)         |
| Active smoking                |                             |                     |                               |
| Yes                           | 0.951 (0.507-1.464)         | NS                  | 1.637 (0.606-4.421)         |
| No                            | 0.951 (0.507-1.464)         | NS                  | 1.637 (0.606-4.421)         |
| Passive smoking               |                             |                     |                               |
| Yes                           | 1.996 (0.648-6.144)         | NS                  | 0.445 (0.056-3.525)         |
| No                            | 1.996 (0.648-6.144)         | NS                  | 0.445 (0.056-3.525)         |
| Salt Intake                   |                             |                     |                               |
| Iodized                       | 3.813 (1.992-7.297)         | P < 0.001           | 0.157 (0.036-0.685)         |
| Non-iodized                   | 3.444 (1.287-9.214)         | P = 0.01            | 1.505 (0.551-4.117)         |
| Don’t know                    | Ref.                         |                     | Ref.                         |
| Iodine supplement             |                             |                     |                               |
| Yes                           | 0.002 (0.001-0.005)         | P < 0.0001          | 0.936 (0.478-1.835)         |
| No                            | 0.002 (0.001-0.005)         | P < 0.0001          | 0.936 (0.478-1.835)         |

**Ref = Reference category**

**NS = Non-significant**

### Figures

**Median spot UIC in the pregnant group according to trimesters**

![Median spot UIC in the pregnant group according to trimesters](image-url)
C) Median spot urine creatinine ratio in the pregnant group by trimesters

B) Median spot urine creatinine in the pregnant group by trimesters
Figure 1

The median of (A) spot urine iodine concentrations, (B) spot urine creatinine concentrations, (C) urine spot iodine/creatinine ratio, (D) estimated 24-hour urine creatinine excretion and
(E) estimated 24-hour urine iodine excretion in each trimester of pregnancy. (a = P < 0.05 compared with the 1st trimester and b = P < 0.05 compared with 2nd trimester by one-way ANOVA and green rectangle = the recommended WHO intervals for iodine adequacy in pregnant women).
The median of (A) spot urine iodine concentrations, (B) spot urine creatinine concentrations, (C) urine spot iodine/creatinine ratio. (D) estimated 24-hour urine creatinine excretion and (E) estimated 24-hour urine iodine excretion in the non-pregnant (n = 400) and the pregnant (n = 1222) study populations. (* = P < 0.05 compared with the non-pregnant women by Mann-Whitney U test; green square = the recommended WHO intervals for iodine adequacy in the non-pregnant and pregnant women).
The median of (A) spot urine iodine concentrations, (B) spot urine creatinine concentrations, (C) urine spot iodine/creatinine ratio, (D) estimated 24-hour urine creatinine excretion and (E) estimated 24-hour urine iodine excretion in each trimester of pregnancy as well as in the non-pregnant women. (a = P < 0.05 compared with the non-pregnant women; b = P < 0.05 compared with 1st trimester; c = P < 0.05 compared with 2nd trimester by one-way ANOVA; green square = the recommended WHO intervals for iodine adequacy in non-pregnant
women and green rectangle = the recommended WHO intervals for iodine adequacy in pregnant women).

Supplementary Files
This is a list of supplementary files associated with this preprint. Click to download.
Iodine Study RAW DATA_BR.xlsx