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ORIGINAL ARTICLE

Urinary iodine concentrations of pregnant women in rural Bangladesh: A longitudinal study

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Iodine is an essential dietary element required for normal fetal growth and development. We aimed to explore intraindividual and interindividual variations in iodine intake in pregnant women and whether non-dietary factors might influence the intake. Iodine intake was assessed in 271 women, residing in Matlab, rural Bangladesh, by measuring their urinary iodine concentration (UIC) at gestational week (GW) 8, 14, 19, and 30 with inductively coupled plasma mass spectrometry. The women's UIC increased significantly during pregnancy (median 241 (GW8) and 300 μg/l (GW30)). About 6% of the women had insufficient iodine intake (UIC $<$ 150 μg/l) and 10% had excessive iodine intake (UIC $\geq$ 500 μg/l) at all of their four sampling occasions. The women's UIC were dependent on their education, socio-economic status, and BMI, as well as the season of sampling and iodine concentrations in drinking water. Supplementation with a multi-micronutrient capsule, including 150 μg potassium iodine, increased the UIC in women with the lowest UIC (10th percentile) at GW30 but decreased the UIC in women with the highest UIC (90th percentile) at GW30. In conclusion, median UIC throughout pregnancy indicated adequate intake of iodine among pregnant women in Matlab, but, notably, consistently insufficient and excessive intake was also prevalent.

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Keywords: urinary iodine; pregnancy; deficiency; excessive intake; iodine supplementation

INTRODUCTION

Iodine is an essential component of thyroid hormones, which in turn, are required for normal growth and development.[1] The global iodine status has improved markedly during the past decade,[2,3] but still it has been estimated that 1.88 billion people of the global population have insufficient iodine intake.[2] The diet is considered as the main source of iodine. A large part of the absorbed dietary iodine is eventually excreted in urine, primarily as iodide, and therefore the urinary iodine concentration (UIC) is considered a valid biomarker of recent iodine intake.[1,4] In fact, the World Health Organization (WHO) has recommended that the median UIC is to be used as a key indicator of a population's iodine status.[1] Currently, the median UIC is mainly monitored in school-aged children (6–12 years of age) as they are easy to assess via school-based surveys, and the optimal UIC for them is considered to range between 100 μg/l and 199 μg/l.

Pregnancy is associated with an increased iodine requirement; mainly because of (1) increased thyroxin (T4) synthesis to maintain an euthyroidal state and to enable transfer of thyroid hormone to the fetus, primarily during the first trimester; before functioning of the fetal thyroid gland; (2) iodine transfer to the fetus' own thyroid gland during later gestation; and (3) increased renal clearance, resulting in loss of iodine in urine.[5] Therefore, to ensure adequate iodine status during pregnancy, a higher reference range for the median UIC has been established for pregnant women (150 μg/l to 249 μg/l).[6] Iodine deficiency during pregnancy has been associated with increased risk of spontaneous abortion, stillbirth, perinatal mortality, and foremost impaired neurodevelopment in the offspring.[7,8] Thus, pregnant women are considered as a high-risk population group. Despite this, only a limited number of countries have completed national or large sub-national surveys of UIC in pregnant women.[2]

The latest national survey in Bangladesh, conducted in 2004–2005, reported a median UIC of 158 μg/l among pregnant women.[9] Recently, a study on pregnant women in rural northwestern Bangladesh reported even lower median UIC of 66 μg/l and 55 μg/l in early and late pregnancy, respectively.[10] This clearly emphasizes the need for continuous national monitoring of iodine intake among pregnant women. The aim of the present study was to explore intraindividual and interindividual differences in iodine intake of pregnant women, residing in Matlab, a rural area about 50 km southeast of Dhaka in Bangladesh and to assess non-dietary factors that may influence the women's iodine intake (e.g. demographic characteristics, season, iodine supplementation, and iodine in drinking water).

MATERIALS AND METHODS

Study Area, Design and Participants

The present study of iodine status during pregnancy is part of our ongoing studies concerning the impact of various environmental factors on early life development,[11] which, in turn, are nested into a randomized population-based food and micronutrient supplementation trial (Maternal and Infant Nutrition Interventions, Matlab; MINIMat) during pregnancy. The MINIMat trial was conducted in Matlab, a rural sub-district located about 50 km southeast of Dhaka, Bangladesh.[12,13] In Matlab, there is a well-established health and demographic surveillance system (HDSS)

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with community health research workers who perform monthly visits to every household. This enabled an early detection of pregnancy, on average at gestational week (GW) 8.

All women in the MINIMat trial were randomized to both food and micronutrient supplementation during pregnancy; two food groups and three micronutrient supplementation groups, resulting in a total of six different supplementation groups.[12] The food supplementation (608 kcal of energy and 18 g of vegetable protein) was provided 6 days per week throughout pregnancy and the two different groups were defined as either early invitation (in connection with detection of pregnancy, around GW9) or usual care invitation (around GW20). The micronutrient supplementation was initiated at GW14 and taken daily throughout pregnancy and the three different groups consisted of 60 mg iron and 400 μg folic acid (Fe60Fol; usual care), 30 mg iron and 400 μg folic acid (Fe30Fol), or a multiple micronutrient supplementation capsule containing 15 micronutrients (MMS), including 150 μg iodine (potassium iodine).[14]

In total, the MINIMat trial recruited 4436 pregnant women from November 2001 through October 2003.[12] During one calendar year, from January through December 2002, 2119 women were recruited to the MINIMat trial. From these 2119 women, we randomly selected 500 women for assessing their UIC at GW8, GW14, GW19, and GW30, and whether the UIC were associated with the women's demographic characteristics. In total, 392 out of the 500 randomly selected women were followed until delivery, and out of them 271 women provided enough urine to enable measurements of UIC at all four sampling occasions (Figure 1). To assess whether the food and micronutrient supplementation ingested during pregnancy had influenced the women's UIC, we used the urinary concentrations measured at GW14 (baseline of the micronutrient supplementation) and GW30, which resulted in a final sample of 307 women (Figure 1). Finally, to explore whether drinking water contributed to the women's UIC, we measured iodine in 100 water samples collected from tube-wells used during pregnancy throughout Matlab.

The study was approved by the ethics committee both at the International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b) and at Karolinska Institutet, Sweden. Consent was obtained from all women, and they were free to refrain from any part of the study at any time.

Sample Collection and Measurements of Iodine

We measured UIC, considered to be a valid biomarker for assessment of iodine intake on population basis.[1] Urine was collected as spot samples, and the collection procedure has been described in detail elsewhere.[15] In short, urine collection at GW8 was performed at home, whereas the collection of urine at GW14, 19, and 30 was performed during the antenatal visits at the health-care facilities. Urine was collected in plastic urine collection cups, transferred to 24-ml plastic bottles, and thereafter frozen at −70 °C. Collection of water samples was performed in a parallel study assessing the concentration of arsenic in all functioning tube-wells in the Matlab area in 2002–2003.[16] Water was sampled in acidified 24-ml plastic bottles after approximately 30 strokes on the pump, minimizing contamination from the pump, and then frozen at −20 °C.

Concentrations of iodine in urine and water were measured with inductively coupled plasma mass spectrometry (ICP-MS; Agilent 7700x; Agilent Technologies, Tokyo, Japan) equipped with an octopole reaction system. The ICP-MS was operated in standard mode (no gas) and iodine^{127} was monitored with iridium^{193} as internal standard. The concentration of the internal standard was 200 μg/l, and it was added on-line at a flow rate of 0.04 ml/min. Carrier gas flow was 0.80 l/min and dilution gas flow 0.30 l/min. The sample uptake flow rate was 0.4 ml/min. Standard solutions of iodine and iridium were prepared daily in 0.1% ammonium hydroxide solution (NH_4OH; 25% suprapur, Merck, Darmstadt, Germany) from 1000 mg/l stock solutions (CPI international, Amsterdam, The Netherlands, and Inorganic Venture, VA, USA, respectively). The concentrations of the external calibration standards ranged from 0.1 μg/l to 200 μg/l. Samples were initially diluted 1:10 with 0.1% NH_4OH, and if needed, the dilution was thereafter increased. The limit of detection (LOD), calculated by multiplying the SD of the blanks with three, was <0.5 μg/l, and no samples contained an iodine concentration $<$LOD. Commercial control materials were included in each analytical run as quality control (Seronorm Trace Elements Urine Blank, REF 201305, LOT OK4636 and Seronorm Trace Elements Urine, REF 201205, LOT NO2525; SERO AS, Billingstad, Norway), and the obtained concentrations (mean ± SD) of iodine were 130 ± 10 μg/l ($n = 142$; recommended value 139 ± 8 μg/l) and 281 ± 23 μg/l ($n = 174$; recommended value 282 ± 18 μg/l), respectively.

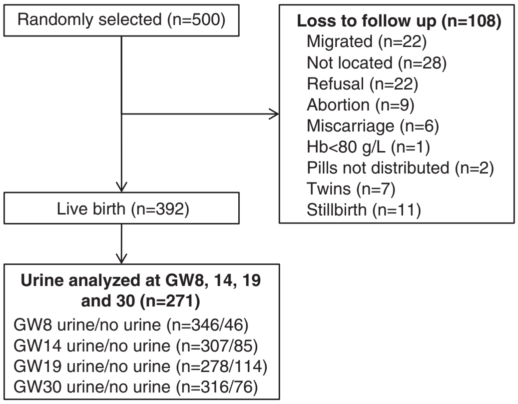

Figure 1. Flow chart of study participation.

All spot urine sample concentrations were adjusted for the specific gravity (SG) in order to compensate for the variation in dilution (UIC × (mean SG − 1/individual SG − 1)).[17] The SG was measured with a digital refractometer (EUROMEX RD712 Clinical Refractometer, Holland). The overall mean SG throughout pregnancy (GW8, GW14, GW19, and GW30) was 1.010 g/ml.

Demographic Factors

Data on maternal and family characteristics (age, weight in early pregnancy (on average GW8), height, parity, education, socio-economic status, and use of tobacco/betel) were obtained within the MINIMat trial as well as from the HDSS database maintained by icddr,b. Socio-economic status was estimated through a wealth index, based mainly on several household assets.[18] Tobacco smoking and betel/tobacco-chewing habits during pregnancy were categorized as never or ever. The season of urine sampling was categorized into premonsoon (January–May), monsoon (June–September), and postmonsoon (October–December).

Statistical Analyses

The statistical analyses were performed with STATISTICA for Windows version 9.1 (StatSoft, USA) and STATA (version 11, Statacorp, TX, USA). All tests were two-sided, and a *P*-value <0.05 was considered as statistically significant. Depending on the type of data, bivariate analyses between UIC and potential influential factors were evaluated with Spearman correlation coefficient, Kendall Tau, or analysis of variance. Mann–Whitney's *U*-test was used to test differences in the distribution of continuous variables between two independent groups.

For assessing the women's iodine intake during pregnancy on a population basis, we used the criteria developed by WHO,[1] where a median UIC <150 μg/l is considered to reflect insufficient intake, 150–249 μg/l—adequate intake, 250–499 μg/l—more than adequate, and ≥ 500 μg/l—excessive intake.

To explore whether the micronutrient supplementation (Fe60Fol (usual care), Fe30Fol, or MMS (including 150 μg potassium iodine)) ingested during pregnancy had any impact on the women's UIC at GW30, we estimated the mean UIC with linear regression and the 10th, 50th, and 90th percentiles of the UIC at GW30 with quantile regression. The exposure variable of interest was micronutrient supplement (0 = Fe60Fol (usual care), 1 = Fe30Fol, 2 = MMS). We considered the following potential confounders: the women's UIC at GW14 (baseline; categorized into quartiles), age (numeric variable), BMI at GW8 (numeric variable), socio-economic status (numeric, normalized variable), and food supplementation ingested during pregnancy (usual start = 0, early start = 1).

RESULTS

The mean age of the 392 pregnant women followed from enrollment at GW8 to delivery was 27 years (range 14–44 years; Figure 1). The mean BMI of the women at GW8 was 20 kg/m^2 and about 30% of the women were classified as undernourished (BMI <18.5 kg/m^2). One-third of the women had no formal education, and among those who had formal education the mean level of education was 7 years (range 2–14 years). Seventy-two percent of the women were multiparous (range 1–7 children). None of the women smoked tobacco during pregnancy, but 42% of the women chewed betel/tobacco. The UIC at GW 8, 14, 19, and 30 was measured in 271 out of 392 women (Figure 1). The women who had their UIC measured at four occasions did not differ from the women who did not have their UIC measured at all four occasions with regard to age, level of formal education, socio-economic status, or BMI (GW8), but they were more likely to be multiparous than primiparous ($P = 0.013$).

The women's median UIC increased significantly during pregnancy ($P < 0.001$), and the concentrations varied widely at each gestational week (Table 1). The highest individual UIC of 11,694 μg/l was observed at GW19; however, this woman had a much lower UIC, both before and after GW19 (GW14: 129 and GW30: 156 μg/l, respectively). In early pregnancy (GW8 and 14), 30–31% of the women had a UIC <150 μg/l, and later in pregnancy this percentage had decreased by 8–6% (Table 1). In contrast, the percentage of women with a UIC ≥ 500 μg/l increased by 7% from GW8 to 30. Notably, we found that 15 women (6%) maintained a UIC <150 μg/l at all four sampling occasions, and 26 women (10%) maintained a UIC ≥ 500 μg/l.

We explored whether the women's UIC were associated with any demographic characteristics (Table 2) and found that the women's UIC from GW8 to 30 were positively associated with their level of formal education (P for all <0.0073) and the family's socio-economic status ($P < 0.034$; Table 2). Similarly, the women's UIC from GW14 to 30 were positively associated with the women's weight ($P < 0.046$) and BMI ($P < 0.0062$) in early pregnancy. We observed no associations with age, parity, or betel/tobacco-chewing habits during pregnancy. Additionally, we tested whether the women's UIC at GW8 was associated with the season of sampling, and indeed, there was an overall difference ($P = 0.037$). The concentration was lower during the monsoon season (median 175 μg/l; $n = 104$) compared with the premonsoon (median: 265 μg/l; $n = 109$; $P = 0.059$) and postmonsoon season (median: 279 μg/l; $n = 58$; $P = 0.16$).

Table 1. Urinary iodine concentrations at four different gestational weeks of 271 Bangladeshi women.

Variables	*Gestational weeks (weeks; mean ± SD)*			
	8.3 ± 2.2	*14.4 ± 1.7*	*19.8 ± 1.9*	*30.7 ± 1.9*
Urinary iodine (μg/l)[a]				
Median	241	268	296	300
25–75th percentiles	118–484	129–540	152–569	148–592
10–90th percentiles	62–836	74–826	89–948	83–1062
Total range	1.6–2459	13–2021	27–11,694	34–3323
n (%) <50 μg/l[b]	16 (6%)	14 (5%)	5 (2%)	5 (2%)
n (%) <150 μg/l[b]	85 (31%)	80 (30%)	63 (23%)	68 (25%)
n (%) >500 μg/l[b]	59 (22%)	76 (28%)	81 (30%)	79 (29%)

[a] Adjusted for the mean specific gravity during pregnancy (1.010 g/ml).
[b] World Health Organization's criteria for assessing iodine status on population basis: children and non-pregnant women moderate iodine deficiency <50 μg/l; for pregnant women insufficient intake <150 μg/l and excessive intake ≥ 500 μg/l.

We performed multiple linear regression analyses (Model 1; Table 3), to assesses whether the micronutrient supplementation (Fe60Fol (usual care), Fe30Fol, or MMS (including 150 μg potassium iodine)) ingested during pregnancy had any impact on the women's UIC at GW30. We found that women who ingested either MMS or Fe30Fol had similar mean UIC at GW30 as those who ingested Fe60Fol ($P = 0.77$ and 0.60, respectively; Table 3). Further adjustment for other covariates did not change any estimates of the effect markedly (Model 2; Table 3). We also performed quantile regression to explore if the micronutrient supplementations had different impact on women who had either low (10th percentile), medium (50th percentile), or high (90th percentile) UIC at GW30 (Table 3). In women with low UIC, the MMS supplementation increased their UIC by 49 μg/l compared with women who only ingested Fe60Fol ($P = 0.016$). On the contrary, in women with high UIC, the MMS supplementation lowered their UIC by 247 μg/l compared with women who only ingested Fe60Fol ($P = 0.030$).

The women's UIC at GW8 was positively associated with iodine in drinking water ($r_s = 0.33$; $P = 0.004$; $n = 76$). The median iodine concentration in drinking water, collected from 100 tube-wells in the study area, was 65 μg/l (10th–90th percentile 11–243 μg/l; range 3.5–438 μg/l). Depth of the tube-well was available for 75 out of the 100 sampled tube-wells, and the average depth was 140 m (range 40–330 m). We found that the concentrations of iodine in drinking water were positively associated with tube-well depth ($r_s = 0.55$; $P < 0.001$), and after further examination, we found that the higher iodine concentrations were more frequent in tube-wells deeper than the average depth of ≥ 140 (median 144 μg/l; $n = 37$) compared with those with a depth of <140 m (median: 30 μg/l; $n = 38$; $P < 0.001$; Figure 2).

DISCUSSION

The present study shows that the iodine intake of pregnant women in Matlab, in rural Bangladesh, was adequate or even more than

Table 2. Spearman's rank correlation coefficients (*P*-value) of associations between the women's urinary iodine concentrations at different gestational weeks and demographic characteristics.

Variables	*Urinary iodine (μg/l)*[a]			
	GW8	*GW14*	*GW19*	*GW30*
Maternal age (years)	0.061 (0.32)	0.059 (0.33)	0.021 (0.73)	0.040 (0.52)
Maternal height (cm)	0.011 (0.85)	0.0050 (0.93)	0.015 (0.80)	− 0.093 (0.13)
Maternal weight (GW8; kg)	0.084 (0.17)	0.18 (0.0036)	0.15 (0.016)	0.12 (0.046)
BMI in early pregnancy (GW8; kg/m^2)	0.099 (0.10)	0.21 (<0.001)	0.17 (0.0062)	0.19 (0.0015)
Parity (no. of children)	− 0.059 (0.33)	− 0.032 (0.60)	− 0.053 (0.39)	− 0.0058 (0.92)
Socio-economic status	0.19 (0.0014)	0.17 (0.0042)	0.17 (0.0062)	0.13 (0.034)
Formal education (years)[b]	0.14 (<0.001)	0.15 (<0.001)	0.11 (0.0073)	0.12 (0.0035)
Betel chewing (yes/no)[c]	(0.59)	(0.30)	(0.61)	(0.95)

[a] Adjusted to the average specific gravity during pregnancy (1.010 g/ml).
[b] Assessed by Kendal Tau.
[c] Assessed by Mann–Whitney *U*-test.

Table 3. Estimated effects of the different micronutrient supplementations (Fe60Fol, Fe30Fol, and MMS) ingested during pregnancy on the mean, as well as the 10th, 50th, and 90th percentile of urinary iodine at GW30 using linear regression analyses and quantile regression analyses, respectively.

Variable	*Model 1*		*Model 2*	
	B (95% CI)	*P*-value	*B (95% CI)*	*P*-value
Linear regression, mean				
Fe60Fol (reference group)	—		—	
Fe30Fol	−16 (−120 to 89)	0.77	−14 (−119 to 89)	0.78
MMS	−28 (−133 to 76)	0.60	−38 (−143 to 68)	0.49
Quantile regression, 10th percentile				
Fe60Fol (reference group)	—		—	
Fe30Fol	6.6 (−31 to 44)	0.73	0.77 (−35 to 36)	0.97
MMS	43 (8.6 to 77)	0.014	49 (9.2 to 89)	0.016
Quantile regression, 50th percentile				
Fe60Fol (reference group)	—		—	
Fe30Fol	−8.1 (−67 to 51)	0.79	−0.70 (−71 to 70)	0.99
MMS	6.2 (−63 to 76)	0.86	9.4 (−66 to 84)	0.81
Quantile regression, 90th percentile				
Fe60Fol (reference group)	—		—	
Fe30Fol	−203 (−443 to 36)	0.096	−132 (−419 to 156)	0.37
MMS	−310 (−465 to −155)	<0.001	−247 (−471 to −23)	0.030

Model 1 is adjusted for the women's urinary iodine concentration at GW14 (baseline; categorized into quartiles). Model 2 is adjusted for the women's urinary iodine concentration at GW14 (baseline; categorized into quartiles), age, socio-economic status, BMI at GW8, and food supplementation ingested during pregnancy (usual start = 0, early start = 1).

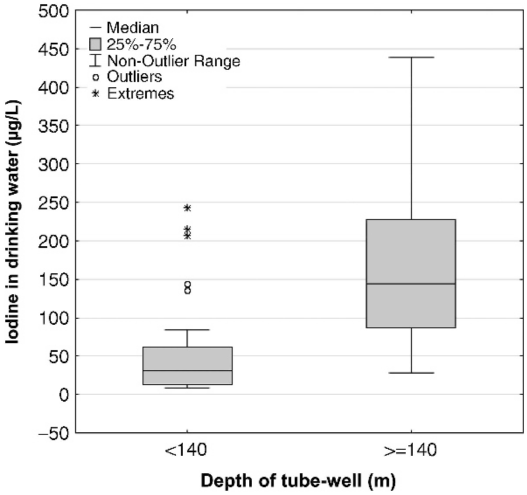

Figure 2. Concentrations of iodine in drinking water by depth of the tube-well (<140 m and ≥ 140 m).

adequate, according to the WHO criteria (median UIC between 150–249 μg/l and 250–499 μg/l, respectively).[1] Notably, 6% of the pregnant women had consistently insufficient iodine intake throughout the whole pregnancy period (UIC $<150\,\mu$g/l), whereas 10% of the women had the opposite pattern with excessive intake throughout pregnancy (UIC $\geq 500\,\mu$g/l). The women's UIC increased with increasing level of education, socio-economic status, BMI, and iodine concentrations in drinking water, and the concentrations varied by season of sampling. Compared with the usual care (Fe60Fol), supplementation with a multiple micronutrient capsule, including iodine, had a normalizing effect, increasing the concentrations among the women with the lowest UIC (10th percentile) at GW30 and decreasing the concentrations among the women with the highest UIC (90th percentile) at GW30.

The latest national survey in Bangladesh, conducted between September 2004 to March 2005, about 2 years after the present urine samples were collected showed that pregnant women in rural areas had much lower median UIC (142 μg/l) than our median UIC of 241 μg/l at GW8.[9] In the survey, the prevalence of iodine deficiency among pregnant women in rural areas was about 41% ($<100\,\mu$g/l) compared with 12–20% in the present study, depending on gestational week. Even with a cutoff of 150 μg/l, <31% of the women in Matlab had UIC below this level. The survey provided no detailed information about excess iodine intake (UIC $\geq 500\,\mu$g/l); only that it was detected in 10% of all women and that it was more pronounced in urban than in rural areas. However, no distinction was made between non-pregnant and pregnant women. Still, we can conclude that the prevalence of excessive iodine intake was higher among pregnant women in Matlab (about 22–30%). A more recent study conducted in a rural area of northwestern Bangladesh showed that about 80% of the pregnant women had UIC $<150\,\mu$g/l in both early and late pregnancy.[10] This indicates that there may be marked geographical differences within Bangladesh concerning iodine intake and that there is still a need to monitor iodine intake to avoid both low as well as excessive intake.

Iodine deficiency, particularly during early pregnancy, has been associated with impaired neurodevelopment.[7,8,19] On the other hand, excessive iodine intake during pregnancy has also been associated with adverse effects in the mother and her offspring.[20,21] In a Chinese study, the risk of subclinical hypothyroidism was higher in pregnant women with more than adequate iodine intake (UIC $>250\,\mu$g/l *vs* $<250\,\mu$g/l; OR = 6.20; 95% CI: 6.6–264; $P<0.001$).[21] Subclinical hypothyroidism has been associated with placental abruption and pre-term delivery.[22] In a Japanese study, it was shown that an estimated daily iodine intake of 820 to 3180 μg during pregnancy could result in hyperthyrotropinemia in the infant, which in some cases appeared to be permanent.[20] Whether the consistently low or excessive iodine intake in some of the pregnant women in Matlab is related to any adverse pregnancy outcomes or adverse effects in their offspring remains to be elucidated.

Because the glomerular filtration rate increases during pregnancy, we adjusted the UIC for the average SG during pregnancy, to minimize the variation caused by dilution of urine as well as increased urine volume. Previous studies have mainly related the UIC to urinary creatinine.[23–25] This was not possible in the present study, as the urinary creatinine excretion is very low in the present population, due to undernourishment and low protein intake.[17] Thus correcting for urinary creatinine would have overestimated the iodine intake. We found that the SG-adjusted median UIC increased as pregnancy progressed. In contrast, the opposite pattern was observed exploring the crude median UIC (GW8: 248 μg/l; GW14: 180 μg/l; GW19: 196 μg/l; and GW30: 204 μg/l). Our results are in accordance with observations in studies conducted in Belgium and Japan where the median UIC:creatinine ratio was lower than the crude median UIC during the first trimester, whereas the opposite pattern was observed in the third trimester.[23,25] These findings confirm that the increased glomerular filtration during pregnancy has a large impact on the UIC. However, to note, a Swiss study found that both the UIC:creatinine ratio and the crude UIC decreased from the first to the third trimester.[24] Therefore, it can be speculated that these dissimilarities in the pattern of UI excretion during pregnancy are not only dependent on the glomerular filtration rate but also on the initial iodine status of the women (deficient/moderate/sufficient), ethnic dietary habits, and supplement use, as well as differences in study design and sample size.

Iodized salt has been the main instrument in the combat against iodine deficiency in Bangladesh since 1989.[9] Unfortunately, we did not have any information concerning the iodine content in the salt utilized in each household. However, as the women's UIC increased with increasing level of education, socio-economic status, and BMI, known determinants for the usage of iodized salt in other regions of Bangladesh,[26] iodized salt is most likely the main source of iodine intake. These findings also show that women who are poor and undernourished, and thus already have an increased risk of adverse pregnancy outcomes and poor growth and development of their offspring after delivery,[27,28] are indeed also those with the highest risk of insufficient iodine intake.

Surprisingly, the supplementation with 150 μg iodine among approximately 30% of the women appeared to have marginal impact on the women's UIC when assessing the mean concentration at GW30. However, when assessing women with either low (10th percentile) or high (90th percentile) UIC, we found that the supplementation had different effects; positive in women with low concentrations and inverse in women with high concentrations when comparing with those who received the usual care (Fe60Fol). The reasons for why the supplementation did not affect some women's UIC or why it even had a negative impact on the UIC in women with high iodine intake are unknown. Supplementation with a daily dose of 150 μg iodine during pregnancy is in accordance with the recommendations by the American Thyroid Association,[29] but it is lower than the total recommended daily intake of 250 μg by WHO.[1] Moreover, several other trials have shown that iodine supplementation with doses varying from 50 μg/day to 230 μg/day significantly increased the UIC, despite the fact that not all individuals were considered to be iodine deficient.[30,31] Thus, more studies are needed to confirm and to further explore the present findings.

Interestingly, we found that drinking water, especially that from deeper tube-wells ($\geq$140 m), also contained rather high iodine concentrations (10–90th percentile 42–332 μg/l). Assuming a daily intake of 3–4 l of water, a women consuming drinking water with the concentrations of the 90th percentile would ingest about 996–1328 μg of iodine via drinking water only. Indeed, the increasing UIC with increasing iodine concentrations in drinking water in the present study confirm that water may actually contribute to the daily iodine intake. In accordance, a Chinese study also found a positive association between concentrations of iodine in urine and drinking water.[32] They also observed that the iodine concentrations in drinking water correlated with indicators of thyroid size, however, it should be noted that the water concentrations were higher (median 552 μg/l) than in the present study (median 144 μg/l).

The main strengths of this study are that the UIC was measured at four different occasions throughout pregnancy and that all measurements of iodine were performed with ICP-MS a highly accurate, precise, high-throughput method. The main limitations were the lack of information concerning iodine concentrations in edible salt utilized by each household and that we had no markers of the women's thyroid function. It would also have been informative to have a control group of non-pregnant women residing in the same area for comparison.

In conclusion, pregnant women in Matlab, in rural Bangladesh, have generally, adequate or even more than adequate iodine intake during pregnancy. However, it should be noted that both low and excessive iodine intake also occurred in some women throughout the whole pregnancy period. Supplementation with a multiple micronutrient capsule, including iodine, appeared to increase the UIC of women with the lowest iodine intake. Demographic factors that have previously been associated with the use of iodine salt, as well as season of sampling and iodine concentrations in drinking water, influenced the women's UIC. Further studies are needed to clarify the potential impact the women's consistently low or excessive iodine intake may have had on the health of their developing offspring.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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