Original Article

Iodine status in pregnancy and household salt iodine content in rural Bangladesh

Abu Ahmed Shamim*, Parul Christian†, Kerry J. Schulze†, Hasmat Ali*, Alamgir Kabir*, Mahbubur Rashid*, Alain Labrique†, Qauzi Salamatullah‡ and Keith P. West Jr†

*The Jivita Maternal and Child Research Project, Godown Road, Gaibandha-5700, Gaibandha, Bangladesh, †Center for Human Nutrition, Department of International Health, Johns Hopkins Bloomberg School of Public Health, 615 N. Wolfe St, Baltimore, Maryland 21205, USA, and ‡Institute of Nutrition and Food Science, Dhaka University, Dhaka-1000, Bangladesh

Abstract

Adequate maternal iodine intake is essential during pregnancy for the development of the foetus. To assess the extent of iodine insufficiency and its association with household iodized salt in rural Bangladesh, we measured urinary iodine and household salt iodine content among pregnant women in early (≤ 16 weeks, $n = 1376$) and late (≥ 32 weeks, $n = 1114$) pregnancy. Salt (~ 20 g) and a spot urine sample (~ 10 mL) were collected from women participating in a randomized, placebo-controlled trial of vitamin A or beta-carotene supplementation in rural northwestern Bangladesh during home visits in early and late pregnancy. Salt iodine was analyzed by iodometric titration, and urinary iodine by the Ohashi method. Almost all salt samples had some detectable iodine, but over 75% contained < 15 ppm. Median (interquartile range) urinary iodine concentrations were 66 (34–133) and 55 (28–110) $\mu\text{g L}^{-1}$ in early and late pregnancy, respectively; urinary iodine $< 150 \mu\text{g L}^{-1}$ was found in $\sim 80\%$ of women at both times in pregnancy. Although the risk of iodine insufficiency declined with increasing iodine content of household salt (P for trend < 0.05), median urinary iodine did not reach $150 \mu\text{g L}^{-1}$ until iodine in household salt was at least 32 ppm and 51 ppm during early and late pregnancy, respectively. Despite a national policy on universal salt iodization, salt iodine content remains insufficient to maintain adequate maternal iodine status throughout pregnancy in rural northern Bangladesh. Alternative measures like direct iodine supplementation during pregnancy could be considered to assure adequate iodine status during this high-risk period of life.

Keywords: salt iodine, urinary iodine, pregnancy, Bangladesh.

Correspondence: Parul Christian, Center for Human Nutrition, Department of International Health, Johns Hopkins Bloomberg School of Public Health, 615 N. Wolfe Street, Rm E2541, Baltimore, MD 21209, USA. E-mail: pchristi@jhsph.edu

Introduction

Maternal iodine deficiency has long been recognized to increase the risk of miscarriage and stillbirth, and is associated with severe mental retardation and developmental delays in the offspring of affected mothers (Dunn & Delange 2001). Mild or subclinical maternal hypothyroidism during pregnancy may lead to impaired mental development in the offspring (Haddow *et al.* 1999), and the severity of maternal

hypothyroidism is inversely correlated with the intelligence quotient of the offspring (Klein *et al.* 2001).

The foetus is dependent on maternal thyroxine for normal brain development because the fetal thyroid gland development and hormone production are relatively delayed during gestation (Becker *et al.* 2006). The production and transfer of thyroxine (T₄) and iodide to the foetus requires that women consume an additional 50–100 μg of iodine during pregnancy in order to maintain euthyroidism (Delange 2004).

Recommendations for daily iodine intake during pregnancy range from 200 μg (WHO *et al.* 2001) to 220 μg (Food and Nutrition Board 2000), and a World Health Organization (WHO) Technical Consultation proposed to increase it to 250 μg (Andersson *et al.* 2007; WHO *et al.* 2007). Furthermore, new guidelines for the assessment of iodine status using urinary iodine (UI) excretion have been advocated for pregnant women; population median UI values 150–249 $\mu\text{g L}^{-1}$ indicate adequacy among pregnant women, compared with median iodine $<100 \mu\text{g L}^{-1}$ used an indication of iodine deficiency in the non-pregnant/non-lactating population (Andersson *et al.* 2007; WHO *et al.* 2007). Universal salt iodization has been the primary means of maintaining iodine status in many populations, with the iodine content of salt in households recommended to contain between 20 and 40 ppm iodine, depending on the typical utilization of salt, as well as availability of other sources of iodine in the food supply (WHO *et al.* 2007). Adequate iodized salt in over 90% of households is indicative of the elimination of iodine deficiency (WHO *et al.* 2007).

The Government of Bangladesh has set its criteria for adequate salt iodization levels at 45–50 ppm at the site of production, ≥ 20 ppm at retail sites and ≥ 15 ppm in households (Bangladesh Gazette 1989, 1994). That these recommendations differ somewhat from those of WHO, reinforces that adequate levels of salt iodization depend on local factors and need to be evaluated and verified. Recommendations in Bangladesh were made based on surveys conducted since the 1960s that have revealed a high prevalence of iodine deficiency. Goiter prevalence ranged from

nearly 30% in 1962–1964 (Nutrition Survey of East Pakistan 1966) to 10.5% in 1981–1982 (IPHN 1983) to nearly 50% in 1993 (Dhaka University *et al.* 1993). The Government of Bangladesh responded and salt iodizing plants were installed in all of the 265 salt factories in the country between 1993–1995 (IPHN *et al.* 1999). As a result, the proportion of individuals with urinary iodine $<100 \mu\text{g L}^{-1}$ dropped to 38.6% among women in 2004–2005 compared with 70% in 1993; the median UI for the same population increased to 140 $\mu\text{g L}^{-1}$ from 28–57 $\mu\text{g L}^{-1}$ (for different geological regions of the country) during the same period (Dhaka University *et al.* 1993, 2007; Yusuf *et al.* 2008). However, an evaluation of the universal salt iodization effort in 2004–2005 found that only 4% of salt samples at the production site contained adequate iodine as per local law (45–50 ppm); 50.3% of samples collected from the rural retailer's shop sold adequately iodized salt (≥ 20 ppm) and less than half of the rural households (45.2%) used salt with at least 15 ppm iodine (Dhaka University *et al.* 2007). Thus, although improvements have been made over the last decade, iodine deficiency still remains a major problem in Bangladesh.

Given the significance of ensuring iodine adequacy for pregnant women, we sought to investigate iodine status in a subsample of pregnant women participating in a large community-based trial in Bangladesh, where women were followed from the time of pregnancy ascertainment to 3 months post-partum. We measured household salt iodine content and UI among women in early and late pregnancy to explore whether the current levels of salt iodization are suffi-

Key messages

- Iodine insufficiency is common among women during pregnancy in Bangladesh, despite the adoption of universal salt iodization since 1989.
- Because iodized salt remains a substantial source of dietary iodine in Bangladesh, greater emphasis needs to be placed on monitoring salt iodine at all levels (production, retail and household) to ensure that more households use adequately iodized salt.
- Although relatively few households are achieving even the minimum goal of at least 15 ppm iodine in household salt, 20–40 ppm is a more appropriate goal in this environment.
- Iodine adequacy during pregnancy is unlikely to be achieved unless the iodine level in household salt reaches at least 30 ppm, although even this salt iodine content may not optimize iodine status during late pregnancy.
- Greater attention should be paid to monitoring the iodine status of women during pregnancy; direct iodine supplementation should be considered in settings where salt is not adequately iodized.

cient to support adequate iodine status, i.e. median UI excretion values of 150–249 $\mu\text{g L}^{-1}$ during pregnancy (Andersson *et al.* 2007; WHO *et al.* 2007). We also explored characteristics of the pregnant women and their households that were associated with consumption of salt containing iodine sufficient to maintain iodine adequacy.

Materials and methods

Study design and subjects

Data were collected in the context of a large, double masked, cluster-randomized, placebo-controlled trial being implemented in rural northwest Bangladesh from 2001–2007 to examine the impact of vitamin A and beta-carotene supplementation on pregnancy-related mortality (West *et al.* 2006). The study encompassed a total area of approximately 450 km², from which all consenting women of reproductive age, married and living with their husbands, were screened every 5 weeks for their menstrual status, and amenstrual women were offered a urine-based pregnancy test to ascertain pregnancy. Women were invited to enroll when pregnancies were confirmed, and women were randomized-based on sector of residence, provided with weekly supplements and followed through 3 months post-partum.

All women who resided within a ~22 km² geographic area of the trial, accessible by main roads, were invited to participate in a 'substudy' that involved more intensive assessment of nutritional and health status, including home-based collections of biospecimens and anthropometric measures conducted in early pregnancy (before initiation of the study intervention), late pregnancy, and at 3 months post partum. In total, 2118 women (~3% of women in the main trial) consented to participate in the substudy. Household salt and urine were collected as part of these home visits in early and late pregnancy. Among women participating in the substudy, inclusion criteria for the study reported here were (1) availability of salt and urine samples collected on or before 16 wk of gestation during the early pregnancy interview, or (2) availability of salt and urine samples collected beyond 31 weeks of gestation during the late pregnancy interview.

Ethical approval for this study was granted by the Committees on Human Research, Johns Hopkins University, USA and Bangladesh Medical Research Council, Dhaka, Bangladesh. The randomized trial (i.e. JiVitA) has also been registered at www.clinicaltrials.gov (identifier NCT00198822).

Data collection

Data on demographics, reproductive history, and socioeconomic status were collected as part of the main trial. Trained female interviewers conducted home-based interviews of each participant using structured questionnaires to collect information about characteristics including age, parity, level of schooling completed by the women and their husbands, primary occupation of the women, ownership of assets like radio and TV. At early and late pregnancy trained interviewers also asked to the women about the frequency of intake of 28 food items during the week prior to the interview. The intake of these foods were summarized under 7 food-groups and the proportion of women consuming these foods at least three times during the week preceding the interview was calculated. The date of the last menstrual period (LMP), obtained during the pregnancy surveillance rounds, was used to calculate gestational age at the time of subsequent home visits in early pregnancy and late pregnancy. Home-based anthropometry i.e. weight, mid upper arm circumference (MUAC), skinfold thickness (subscapular, SSF; and triceps, TSF) was measured by a team of trained anthropometrists in the substudy participants at early and late pregnancy, at the time salt and urine samples were collected. Height was measured only at the early pregnancy visit, and early pregnancy BMI was calculated.

Collection of salt and urine sample and analysis

Two heaping spoonfuls (>20 g) of salt were collected using a disposable spoon and were preserved in double polyethylene bags. The subject provided urine in a disposable plastic cup, and ~10 mL of urine was transferred to duplicate dry screw-cap plastic bottles. Urine and salt samples were transported to the laboratory within 6 h of collection, using a cool-bag lined

with ice-packs for urine. Urine samples were preserved at -20°C and salt samples at room temperature until processing for urine and salt iodine content at the Institute of Nutrition and Food Science, Dhaka University. The salt samples were analyzed using iodometric titration method (De Maeyer *et al.* 1979; WHO *et al.* 2001) and UI was analyzed using the microplate method described by Ohashi and colleagues (Ohashi *et al.* 2000).

Statistical analysis

Data on iodine status in early and late pregnancy were treated as two distinct cross-sectional datasets, despite the fact that women may have contributed to both time points, to maximize our sample size at both time points and to allow us to look generally at the risk of iodine deficiency by stage of pregnancy.

Data on demographic and socioeconomic status and reproductive history were expressed categorically. Dietary data was summarized as the number (%) of women who consumed specific food groups more than three times during a 1-week period based on self-reported data collected using a food frequency questionnaire designed to capture intake of local foods.

Salt iodine content was expressed as median (interquartile range) and by category according to ranges of content in ppm. UI was expressed as median and as the percent of individuals whose UI fell within predetermined categories: $<50\text{ }\mu\text{g L}^{-1}$, $50\text{--}99.9\text{ }\mu\text{g L}^{-1}$, $100\text{--}149.9\text{ }\mu\text{g L}^{-1}$, $150\text{--}249.9\text{ }\mu\text{g L}^{-1}$, $250\text{--}499.9\text{ }\mu\text{g L}^{-1}$ and $\geq 500\text{ }\mu\text{g L}^{-1}$. Although median UI $\geq 150\text{ }\mu\text{g L}^{-1}$ indicates iodine sufficiency (Andersson *et al.* 2007; WHO *et al.* 2007) the three categories for median UI below this have previously been used to explore iodine deficiency during pregnancy (Schulze *et al.* 2003).

Median UI, geometric mean of UI and its difference were examined by categories of salt iodine content, in early and late pregnancy with $15\text{--}19.9\text{ ppm}$ being the reference category, based on previous studies conducted in Bangladesh, which considered salt with at least 15 ppm of iodine to be adequate (Dhaka University *et al.* 2007; Yusuf *et al.* 2008). To estimate the difference in UI by salt iodine content, we used linear regression analysis where the log of UI

was included as a dependent variable, and categories of salt iodine as the independent indicator variable. We used a stepwise procedure to adjust for confounding in a multivariate model using the Akaike Information Criterion. Because UI was log-transformed, the exponentiated coefficients are to be interpreted as the ratio of the expected geometric mean of the UI for each salt iodine category vs. the reference, generally expressed as 'percent change'.

The exposure (salt iodine) and outcome (UI concentration) data were also examined by using locally weighted polynomial regression (Cleveland 1979) to examine the salt iodine content required to support a median UI concentration above $150\text{ }\mu\text{g L}^{-1}$. Based on the results of the previous analyses, social and demographic factors associated with having iodized salt $\geq 30\text{ ppm}$ were examined using logistic regression analysis. The odds ratios were adjusted for potential confounders identified from univariate analysis ($P < 0.2$ using χ^2 test).

Because maternal supplementation with vitamin A or β -carotene vs. placebo had no effect on UI ($P = 0.53$ for early and $P = 0.67$ for late pregnancy, Kruskal–Wallis test), subjects from all three groups were combined in all analyses. Although we collected information on other supplement use during pregnancy, we found no evidence that women took supplements containing iodine. Only 13% and 19% of women reported using iron-folic acid during early and late pregnancy, respectively. All analyses were conducted using R, version 2.9.1 (R Development Core Team 2009), which is an open source statistical software, and associations were considered significant at $P < 0.05$.

Results

Data from 1376 women were available from the early pregnancy visit and 1114 women from the late pregnancy visit. Out of 2118 women enrolled in the substudy, 193 (12%) were considered ineligible for the early pregnancy analysis because they were enrolled too late in pregnancy or the date of the LMP was not available, and 46 (4%) women were considered ineligible for the late pregnancy analysis because data collection occurred prior to the third trimester cut-off of 32-week gestation or LMP date

were not available. Additionally, for 549 (25.9%) women in early and 177 (13.2%) in late pregnancy, data on salt or UI were missing. From the early to late pregnancy, the loss to follow-up included pregnancy outcomes (both foetal loss and live births) that occurred prior to the scheduled visit ($n=600$), refusals ($n=96$), women not met ($n=89$) and one maternal death. Among the participants, $n=824$ women contributed data at both early pregnancy and late pregnancy visits. There was a moderate but statistically significant correlation between both urinary ($r=0.17$, $P<0.0001$) and household salt ($r=0.19$, $P<0.0001$) iodine content within individuals between time points.

A variety of sociodemographic and anthropometric indicators are detailed in Table 1. At baseline, 85% of the participating women were younger than 30 years, and about half of them were nulliparous. Over one-third of them had no formal schooling, but ~40% of them earned some type of income, including income from home-based economic activities. Only ~20% and ~10% of households owned radio and television, respectively.

The women were visited at a mean [standard deviation (SD)] gestational age of 9.9 weeks (2.7) during early pregnancy, and 32.5 weeks (1.6) during late pregnancy. The nutritional status of the participants was poor, with a mean (SD) weight of 42.4 kg (5.9) and 47.6 kg (5.8) during early and late pregnancy, respectively. The quality of their diet was also poor, as food groups such as meat, fish, egg, milk and milk products, leafy vegetables, other vegetables and fruits were consumed more than three times during the previous week of interview by fewer than 30% of women; fish was consumed more than three times per week by 40–45% of women.

Almost all household salt contained detectable iodine, but it was below the currently recommended levels of 15–19.9 ppm in 79% of households (Table 2). Median values for UI in early ($65.9 \mu\text{g L}^{-1}$) and late ($55.3 \mu\text{g L}^{-1}$) pregnancy were far below the established cut-off of $<150 \mu\text{g L}^{-1}$. UI was below this cut-off in approximately 80% of women, and even when a more conservative cut-off of $<100 \mu\text{g L}^{-1}$ was used, ~70% of women were below this at both times in pregnancy (Table 2).

Median UI content increased in relation to the category of salt iodine content (P for trend <0.001 ; Table 3). However, adequate pregnancy-associated UI excretion was achieved in early pregnancy in households with salt iodine content within the range of 20–29.9 ppm, while in late pregnancy only women from households with over 40 ppm salt achieved median UI excretion levels $\geq 150 \mu\text{g L}^{-1}$. More specifically, based on the associations of urinary vs. salt iodine content, UI $\geq 150 \mu\text{g L}^{-1}$ was achieved only when salt iodine content was at least 32 ppm in early pregnancy and 51 ppm in late pregnancy, respectively (Fig. 1). Finally, the geometric mean of UI increased in a linear manner (P for trend <0.001) as the women consumed salt with increasing iodine content of household salt (Table 3).

Given that our analysis demonstrated that salt iodine content of at least 30 ppm was required to maintain median concentrations of UI $\geq 150 \mu\text{g L}^{-1}$ during pregnancy, we examined sociodemographic factors related to the presence of salt iodized at this level in households (Table 4). Women aged between 20 and 29 years were most likely to consume adequately iodized salt both during early and late pregnancy. Early pregnancy body mass index was associated with consumption of adequately iodized salt, an association that was, however, not maintained during late pregnancy. The proportion of women consuming adequately iodized salt increased in a dose-response manner, both at early and late pregnancy as the women had more education, although the association was not statistically significant. The odds of consuming adequately iodized salt increased in a dose-response manner in relation to their husband's level of education, significantly so among women with husbands educated beyond secondary school. Women living in households with electricity were more likely to consume adequately iodized salt both at early and late pregnancy. Other measures of socioeconomic status, as assessed by household ownership of goods, land and livestock, were not consistently related to having adequate salt iodine content. However, women whose household own cattle were significantly less likely to consume adequately iodized salt during early pregnancy.

Table 1. Characteristics of the subjects at early (≤ 16 weeks of gestation) and at late pregnancy (≥ 32 weeks of gestation) who contributed urine and salt samples*

	Early pregnancy ($n = 1376$) [†]	Late pregnancy ($n = 1114$) [‡]
	<i>n</i> (%)	
Age (years)		
<20	581 (42.3)	519 (46.6)
20–29	586 (42.6)	495 (44.5)
≥ 30	207 (15.1)	99 (8.9)
Parity		
0	625 (45.5)	570 (51.2)
1	306 (22.3)	287 (25.8)
≥ 2	444 (32.3)	256 (23.0)
Education		
No formal schooling	514 (37.4)	372 (33.4)
Primary	328 (23.9)	264 (23.7)
Secondary or more	533 (38.8)	477 (42.9)
Husband's education		
No formal schooling	621 (47.8)	476 (45.4)
Primary	251 (19.3)	195 (18.6)
Secondary or more	428 (32.9)	377 (36.0)
Employment	601 (43.7)	442 (39.7)
Radio ownership	271 (19.7)	235 (21.1)
TV ownership	146 (10.6)	119 (10.7)
Cattle ownership	604 (43.9)	488 (43.9)
Bi-cycle ownership	508 (36.9)	418 (37.6)
Crop-land ownership	595 (44.6)	490 (45.3)
Electricity connection	205 (14.9)	156 (14.0)
Weekly frequency of food intake [§]		
Any meat	82 (6.0)	77 (7.7)
Any fish	588 (42.7)	449 (45.2)
Egg	166 (12.5)	119 (12.6)
Milk and milk products	356 (25.9)	283 (28.5)
Dark green leafy vegetables	181 (13.6)	106 (11.3)
Other vegetables	232 (16.9)	159 (16.0)
Fruit	352 (25.6)	201 (20.2)
	Mean $\pm$ SD	Mean $\pm$ SD
Gestational age (w)	9.9 $\pm$ 2.7	32.5 $\pm$ 1.6
Weight (kg)	42.4 $\pm$ 5.9	47.6 $\pm$ 5.8
Height (cm)	149.3 $\pm$ 5.2	149.3 $\pm$ 5.3
BMI (kg m^{-2}) [¶]	19.0 $\pm$ 2.2	21.3 $\pm$ 2.1
MUAC (cm)	23.0 $\pm$ 2.2	22.7 $\pm$ 1.9
Triceps skinfold (mm)	11.0 $\pm$ 4.1	10.8 $\pm$ 3.7
Subscapular skinfold (mm)	13.5 $\pm$ 5.1	14.1 $\pm$ 4.7

*Data on women's age, parity, education, husband education, employment, ownership of assets and electricity connection were collected in early pregnancy. Data on weekly frequency of food consumption and women's anthropometric (except height taken only in early pregnancy) were collected in both early and late pregnancy. [†]Missing data for age ($n = 2$), parity ($n = 1$), education ($n = 1$), husband's education ($n = 76$), cattle ownership ($n = 1$), cropland ownership ($n = 43$), egg ($n = 44$), DGLV ($n = 41$), weight ($n = 9$), height ($n = 1$), body mass index (BMI, $n = 9$), MUAC ($n = 1$), SSF ($n = 1$), TSF ($n = 1$). [‡]Missing data for age ($n = 1$), parity ($n = 1$), education ($n = 1$), husband's education ($n = 66$), occupation ($n = 1$), radio ownership ($n = 1$), TV ownership ($n = 1$), cattle ownership ($n = 2$), bicycle ownership ($n = 1$), crop-land ownership ($n = 32$), electricity ownership ($n = 1$), meat ($n = 120$), fish ($n = 120$), egg ($n = 172$), milk ($n = 120$), DGLV ($n = 120$), other vegetables ($n = 120$), fruits ($n = 120$), weight ($n = 17$), MUAC ($n = 1$), TSF ($n = 1$) and SSF ($n = 1$). [§]Women who consumed each food group more than three times in the past week. [¶]BMI was calculated using height measured at early pregnancy. DGLV, dark green leafy vegetables; MUAC, mid-upper arm circumference; TSF, triceps skinfold thickness; SSF, substance skinfold thickness.

Table 2. Iodine status of the pregnant women by household salt iodine content and urinary iodine excretion

	Early pregnancy <i>n</i> = 1376	Late pregnancy <i>n</i> = 1114
Salt iodine, median (IQR), ppm	6.2 (4.0, 12.4)	6.3 (4.0, 13.8)
Salt iodine, ppm	<i>n</i> (%)	<i>n</i> (%)
<5.0	507 (36.8)	417 (37.4)
5–9.9	453 (32.9)	321 (28.8)
10–14.9	130 (9.4)	119 (10.7)
15–19.9	75 (5.5)	65 (5.8)
20–29.9	102 (7.4)	87 (7.8)
30–39.9	57 (4.1)	55 (4.9)
≥40.0	52 (3.8)	50 (4.5)
Urinary iodine median (IQR), µg L ⁻¹	65.9 (33.6, 133.1)	55.3 (28.1, 109.6)
Urinary iodine, µg L ⁻¹	<i>n</i> (%)	<i>n</i> (%)
<50.0	537 (39.0)	517 (46.4)
50.0–99.9	376 (27.3)	284 (25.5)
100.0–149.9	172 (12.5)	123 (11.0)
150.0–249.9	138 (10.0)	90 (8.1)
250.0–499.9	118 (8.6)	89 (8.0)
≥500.0	35 (2.5)	11 (1.0)

IQR, interquartile range.

Discussion

This study examined the relationship between household salt iodine content and iodine status early in gestation and in the third trimester among pregnant women of rural Bangladesh, a country with known iodine insufficiency but with a government-mandated and functioning salt iodization programme. This study demonstrates that current levels of household salt iodine content in this area of Bangladesh do not meet government recommendations of at least 15 ppm. More importantly, however, even household salt iodine levels currently considered adequate are insufficient to protect pregnant women, and thus, their foetuses, from iodine insufficiency during pregnancy. Household salt iodine content of at least 30 ppm would be required to ensure iodine adequacy during early pregnancy, with even greater demand for iodine apparent in late pregnancy.

Although this study was not designed to be regionally representative, the high rates of participation among eligible women from this locale suggest

Table 3. Association between iodine content in salt and urinary iodine during early and late pregnancy

Salt Iodine (ppm)	Urinary Iodine		
	Median (IQR)	Unadjusted ratio of geometric mean (95% CI)	Adjusted ratio of geometric mean (95% CI)*
Early pregnancy			
<5.0	47.6 (26.3, 84.3)	0.4 (0.4, 0.6)	0.4 (0.4, 0.6)
5–9.9	60.9 (31.8, 100.0)	0.5 (0.4, 0.7)	0.5 (0.4, 0.7)
10–14.9	91.0 (45.9, 151.6)	0.8 (0.6, 1.0)	0.7 (0.5, 0.9)
15–19.9	116.6 (55.0, 238.1)	1.0	1.0
20–29.9	161.4 (71.8, 286.4)	1.3 (1.0, 1.7)	1.3 (1.0, 1.8)
30–39.9	157.4 (104.8, 335.8)	1.6 (1.1, 2.1)	1.5 (1.1, 2.1)
≥40.0	278.0 (132.1, 519.9)	2.0 (1.5, 2.8)	2.0 (1.4, 2.8)
<i>P</i> for trend	<0.001	<0.001	<0.001
Late pregnancy			
<5.0	41.1 (21.3, 66.7)	0.5 (0.4, 0.6)	0.4 (0.3, 0.6)
5–9.9	49.4 (27.4, 92.8)	0.6 (0.4, 0.7)	0.5 (0.4, 0.7)
10–14.9	61.0 (27.6, 106.9)	0.6 (0.5, 0.9)	0.6 (0.5, 0.9)
15–19.9	88.2 (59.8, 141.0)	1.0	1.0
20–29.9	109.3 (54.0, 194.0)	1.0 (0.8, 1.4)	1.0 (0.7, 1.4)
30–39.9	126.8 (55.6, 232.6)	1.3 (0.9, 1.8)	1.3 (0.9, 1.8)
≥40.0	203.4 (97.7, 346.3)	2.1 (1.5, 3.0)	2.0 (1.3, 3.0)
<i>P</i> for trend	<0.001	<0.001	<0.001

*Adjusted in early pregnancy for subscapular skinfold thickness, ownership of cropland, fish and leafy vegetables intake, and in late pregnancy for subscapular skinfold thickness, education and, fish, egg, leafy vegetables, other vegetables and fruits intake. CI, confidence interval; IQR, interquartile range.

Fig. 1. Association between urinary iodine ($\mu\text{g L}^{-1}$) and iodine content in salt (ppm) by locally weighted polynomial regression.

that our results likely reflect the current situation among rural families in this area of northwestern Bangladesh. At the early pregnancy visit, over 75% of the salt collected in households contained <15 ppm of iodine, with over 65% of households having <15 ppm during the late pregnancy visit. This situation is worse than that reported in a recent nationwide survey showing that ~45% of the salt samples collected from rural households contained at least 15 ppm of iodine (Dhaka University *et al.* 2007). Ideally, over 90% of households should have appropriately iodized salt (WHO *et al.* 2007). Increased monitoring at the level of production, distribution and households would help to ensure that iodized salt is being consumed, and that mandated levels of iodine are being maintained over time. Because locally available spot testing kits only confirm the presence of iodine and cannot discern concentration, they are limited in their utility; thus, higher quality semi-quantitative kits might be an important tool in this regard. Moreover, ensuring proper packaging may help to retain iodine in salt from production to household use.

Iodine requirements are exacerbated by the demands of pregnancy. Newly established recommendations state that pregnant women should consume 250 μg of iodine daily, and that the corresponding population median UI excretion among pregnant women should be 150–249.9 $\mu\text{g L}^{-1}$ after considering the metabolic needs of iodine to support thyroid status of the mother and developmental needs of the foetus (Andersson *et al.* 2007). Median UI was considerably lower than this in early pregnancy (66 $\mu\text{g L}^{-1}$) and further compromised in late pregnancy (55 $\mu\text{g L}^{-1}$), when demands for iodine are increased. To achieve intakes of 250 μg iodine from salt containing 15 ppm of iodine, it would be necessary to consume ~17 g day⁻¹, which is more than the assumed average daily salt consumption for adults of 10 g that is used to estimate levels for fortification (WHO *et al.* 2001). Considering that median salt iodine content was only ~6 ppm in households in Bangladesh, salt intake would have to be unreasonably high to achieve adequate intakes during pregnancy. Although we did not collect information about salt consumption of the participating women, it is

Table 4. Factors associated with consumption of adequate iodized salt (≥ 30 ppm) in early and late pregnancy

Characteristics	Early pregnancy		Late pregnancy	
	<i>n</i> (%) [*]	Adj. OR (95% CI) [†]	<i>n</i> (%) [*]	Adj. OR (95% CI) [‡]
Age (years)				
<20	39 (6.7)	1	35 (6.7)	1
20–29	55 (9.4)	1.7 (1.1, 2.8)	61 (12.3)	2.4 (1.4, 4.0)
≥ 30	15 (7.2)	1.6 (0.7, 3.2)	9 (9.1)	1.7 (0.7, 4.0)
BMI [§]				
<18.5	29 (4.7)	1	6 (9.0)	1
18.5–22.9	69 (10.3)	2.4 (1.5, 4.0)	71 (8.8)	1.0 (0.4, 3.0)
≥ 23.0	11 (14.9)	2.6 (1.1, 6.0)	25 (11.7)	0.8 (0.3, 2.7)
Education				
No education	35 (6.8)	1	21 (5.6)	1
Primary	25 (7.6)	1.1 (0.6, 2.0)	24 (9.1)	1.4 (0.7, 2.8)
Secondary or more	49 (9.2)	1.1 (0.6, 2.1)	60 (12.6)	1.1 (0.5, 2.2)
Husband's education				
No education	32 (5.2)	1	22 (4.6)	1
Primary	23 (9.2)	2.1 (1.2, 3.9)	15 (7.7)	1.7 (0.8, 3.5)
Secondary or more	46 (10.7)	2.4 (1.3, 4.5)	60 (15.9)	2.8 (1.5, 5.5)
Electricity connection				
No	76 (6.5)	1	74 (7.7)	1
Yes	33 (16.1)	2.5 (1.4, 4.4)	31 (19.9)	2.0 (1.1, 3.6)
TV ownership				
Not owned	93 (7.6)	1	82 (8.2)	1
Owned	16 (11.0)	0.7 (0.3, 1.3)	23 (19.3)	1.1 (0.5, 2.1)
Radio ownership				
Not owned	86 (7.8)	1	71 (8.1)	1
Owned	23 (8.5)	1.0 (0.6, 1.7)	34 (14.5)	1.6 (1.0, 2.7)
Cropland ownership				
Not owned	65 (8.8)	1	43 (7.3)	1
Owned	42 (7.1)	0.7 (0.4, 1.1)	58 (11.8)	1.3 (0.8, 2.3)
Bicycle ownership				
Not owned	71 (8.2)	1	51 (7.3)	1
Owned	38 (7.5)	0.9 (0.5, 1.5)	54 (12.9)	1.5 (0.9, 2.5)
Cattle ownership				
Not owned	75 (9.7)	1	58 (9.3)	1
Owned	34 (5.6)	0.6 (0.3, 0.9)	46 (9.4)	0.5 (0.3, 0.9)

^{*}No of women (%) consuming sufficiently iodized salt (≥ 30 ppm). [†]Adjusted for all variables except parity and employment which were not associated with salt iodine (χ^2 test, $P \geq 0.2$) at any of the two time points. [‡]Late pregnancy BMI was adjusted for gestational age. BMI, body mass index; CI, confidence interval; OR, odds ratio.

unlikely that salt consumption was reduced during pregnancy.

Based on the results for median UI, pregnant women in this area of northern Bangladesh are considerably more iodine deficient than national data would suggest. Based on the national survey data, median gestational UI was $142 \mu\text{g L}^{-1}$, with 41% of surveyed women having a UI level below $100 \mu\text{g L}^{-1}$ (Dhaka University *et al.* 2007; Yusuf *et al.* 2008). However, pregnant women made up only 3% ($n = 56$) of the total sample in that survey, leaving the represen-

tativeness of the findings uncertain. Given our sample size enrolled under normal community conditions, the data reported here are likely to give a better picture of the extent of iodine deficiency during pregnancy.

Although most national surveys target iodine status of school-age children, and therefore provided limited information about iodine status during pregnancy, a growing number of recent studies from the region have focused specifically on the iodine status of pregnant women. These studies have typically demonstrated compromised iodine status among

women throughout South Asia, including some areas of India (Pathak *et al.* 2003; Ategbo *et al.* 2008; Singh *et al.* 2008), Thailand (Gowachirapant *et al.* 2009; Jaruratanasirikul *et al.* 2009), Nepal (Schulze *et al.* 2003) and Hong Kong (Kung 2007). This can occur even when iodine levels, in salt or other food sources, are seemingly sufficient to ensure adequate status (median UI excretion $>100 \mu\text{g L}^{-1}$) of children from the same households (Burgess *et al.* 2007; Ategbo *et al.* 2008; Gowachirapant *et al.* 2009).

This study and others have demonstrated a direct association between UI during pregnancy and the adequacy of available iodized salt at the community (Schulze *et al.* 2003) or household (Ategbo *et al.* 2008) level. Our results in Bangladesh suggest that median pregnancy UI concentrations can be maintained at $\geq 150 \mu\text{g L}^{-1}$ only when household salt iodine content is at least 30 ppm, consistent with the findings of others (Ategbo *et al.* 2008). Ategbo *et al.* (2008) also found that greater iodine intakes were required to achieve enhanced UI excretion in pregnant women vs. children; with the $15\text{--}20 \mu\text{g L}^{-1}$ increase in UI per 10 ppm increase in salt iodine content among pregnant women being half of that observed in children. This difference in iodine utilization by physiological status is consistent with the dramatically different slopes of the associations between salt iodine content and UI output observed in our data between early and late pregnancy, and suggests that late pregnancy is a time of higher demand for iodine than during early pregnancy. Thus, maintaining iodine adequacy among pregnant women is likely to become more difficult as pregnancy advances.

None of the subject characteristics were consistently associated with the presence of adequately iodized salt in the household early or late in pregnancy, although there was some suggestion of a link with socioeconomic status. Women with more education or married to more educated men, and women from households with electricity or televisions, tended to consume adequately iodized salt. Other factors not considered were the type and brand of salt purchased, although previous studies have shown that salt sold in higher priced packaging retains greater iodine content (Dhaka University *et al.* 2007). Thus, better

understanding of factors that influence the availability and cost of salt in the markets, as well as household factors related to the purchase of iodized salt, may provide greater insights into how the purchase of higher quality salts can be encouraged. Consideration should also be given to raising the targeted iodine content in salt to 20–40 ppm, within the range currently recommended by WHO (WHO *et al.* 2007). Our data also point to the need for greater monitoring of iodine status among pregnant women, and also suggest that supplements may be necessary if increasing salt iodine content substantially is unattainable. Current recommendations are for pregnant and lactating women to receive a daily oral dose of iodine as potassium iodide so that the total iodine intake meets the recommended nutrient intake of $250 \mu\text{g day}^{-1}$, either alone or in combination with other micronutrients, or as a single annual oral dose of 400 mg of iodine in oil (Andersson *et al.* 2007).

Limitations of our study included unavailability of any metric to assess the quality of the UI assay, although the procedure was performed in the national reference laboratory for iodine assays. Additionally, we used a standard 7-day food frequency questionnaire to measure food intake, which while it has previously been shown to be a valid method for vitamin A rich foods, may be limited for assessing iodine intake. Another shortcoming was that we did not collect urine in the post-partum period.

The consequences of the mild-moderate iodine deficiency in this population have not yet been described. It is likely that maternal and infant thyroid status is affected by the extent of iodine deficiency observed here, supporting the concern that iodine deficiency remains a cause of mental retardation in Bangladesh (Durkin *et al.* 2000). Future studies will allow us to examine the consequences of iodine deficiency during pregnancy to the offspring of women in this population.

Our findings are among a growing number that demonstrate that women may be at risk of iodine deficiency during pregnancy despite the presence of functioning salt iodization programmes. Efforts should be refocused to ensure that this population group has access to this important nutrient during this critical life stage.

Acknowledgements

We especially thank the JiVitA Senior and Field Management Team, and members of the Center for Human Nutrition Data Management team Allan Massie, Lee Shu-Fune Wu, Maithilee Mitra and Andre Hackman, and Professor M Mohiduzzaman and Ms Cadi Parvin Banu, Institute of Nutrition and Food Science, Dhaka University.

Source of funding

This study was conducted by the Center for Human Nutrition, Department of International Health, Bloomberg School of Public Health, Johns Hopkins University, under Global Research Activity cooperative agreement GHS-A-00-03-00019-00 between Johns Hopkins University and the Office of Health and Nutrition; the US Agency for International Development, Washington, DC; with additional support from Bill and Melinda Gates Foundation Seattle, WA, Grant No. 614 Global Control of Micronutrient Deficiency. Additional support was provided by Sight and Life, Basel, Switzerland, the Sight and Life Research Institute at the Johns Hopkins University, Baltimore, MD, Nutrilite Health Institute, Nutrilite Division, Access Business Group, LLC, Buena Park, CA, the Canadian International Development Agency, and the National Integrated Population and Health Programme of the Ministry of Health and Family Welfare of the government of the People's Republic of Bangladesh.

Conflicts of interest

The authors declare that they have no conflicts of interest.

References

- Andersson M., de Benoist B., Delange F. & Zupan J. (2007) Prevention and control of iodine deficiency in pregnant and lactating women and in children less than 2-years-old: conclusions and recommendations of the Technical Consultation. *Public Health Nutrition* **10**, 1606–1611.
- Ategbro E.A., Sankar R., Schultink W., Haar F. & Pandav C.S. (2008) An assessment of progress towards universal salt iodization in Rajasthan, India, using iodine nutrition indicators in school-aged children and pregnant women from the same households. *Asia Pacific Journal of Clinical Nutrition* **17**, 56–62.
- Bangladesh Gazette (1989) *Iodine Deficiency Disease Prevention Act*. Government of the Peoples Republic of Bangladesh: Bangladesh.
- Bangladesh Gazette (1994) *Iodine Deficiency Disease Prevention regulation*. pp. 5261–5270. Government of the Peoples Republic of Bangladesh: Bangladesh.
- Becker D.V., Braverman L.E., Delange F., Dunn J.T., Franklyn J.A., Hollowell J.G. *et al.* (2006) Iodine supplementation for pregnancy and lactation—United States and Canada: recommendations of the American Thyroid Association. *Thyroid* **16**, 949–951.
- Burgess J.R., Seal J.A., Stilwell G.M., Reynolds P.J., Taylor E.R. & Parameswaran V. (2007) A case for universal salt iodisation to correct iodine deficiency in pregnancy: another salutary lesson from Tasmania. *Medicine Journal of Australian*. **186**, 574–576.
- Cleveland W.S. (1979) Robust locally weighted regression and smoothing scatterplots. *Journal of the American Statistical Association* **74**, 829–836.
- De Maeyer E.M., Lowenstein F.W. & Thilly C.H. (1979) *The Control of Endemic Goiter*. World Health Organization: Geneva.
- Delange F. (2004) Optimal iodine nutrition during pregnancy, lactation and the neonatal period. *International Journal of Endocrinology and Metabolism* **2**, 1–12.
- Dhaka University, IPHN, BSCIC, ICCIDD & UNICEF (1993) *Report of the National Iodine Deficiency Disorder Survey in Bangladesh-1993*. Dhaka University, Institute of Public Health Nutrition, Bangladesh Small and Cottage Industries Corporation, International Council for Control of Iodine Deficiency Disorder, and United Nations Children Fund: Dhaka.
- Dhaka University, BSCIC, IPHN, UNICEF & ICCIDD (2007) *National Survey on Iodine Deficiency Disorders and Universal Salt Iodization in Bangladesh 2004–05*. Dhaka University, BSCIC IPHN, UNICEF and ICCIDD: Dhaka.
- Dunn J.T. & Delange F. (2001) Damaged reproduction: the most important consequence of iodine deficiency. *Journal of Clinical Endocrinology and Metabolism* **86**, 2360–2363.
- Durkin M.S., Khan N.Z., Davidson L.L., Huq S., Munir S., Rasul E. *et al.* (2000) Prenatal and postnatal risk factors for mental retardation among children in Bangladesh. *American Journal of Epidemiology* **152**, 1024–1033.
- Food and Nutrition Board, Institute of Medicine (2000) *Dietary Reference Intakes for Vitamin A, Vitamin K,*

- Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium and Zinc. A Report of the Panel on Micronutrients Subcommittee on Upper Reference Levels of Nutrients and of Interpretation and Uses of Dietary Reference.* National Academy Press: Washington, DC.
- Gowachirapant S., Winichagoon P., Wyss L., Tong B., Baumgartner J., Melse-Boonstra A. *et al.* (2009) Urinary iodine concentrations indicate iodine deficiency in pregnant Thai women but iodine sufficiency in their school-aged children. *Journal of Nutrition* **139**, 1169–1172.
- Haddow J.E., Palomaki G.E., Allan W.C., Williams J.R., Knight G.J., Gagnon J. *et al.* (1999) Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. *The New England Journal of Medicine* **341**, 549–555.
- IPHN (1983) *Report of National Goiter Prevalence Study of Bangladesh 1981–82*. Institute of Public Health Nutrition, Ministry of Health and Population Control: Dhaka.
- IPHN, BSCIC, ICCIDD & UNICEF (1999) *Iodine Deficiency Disorder Survey in Bangladesh-1999*. Institute of Public Health Nutrition, Bangladesh Small and Cottage Industries Corporation, International Council for Control of Iodine Deficiency Disorder, & UNICEF: Dhaka.
- Jaruratanasirikul S., Sangsupawanich P., Koranantakul O., Chanvitan P., Ruaengrairatanaroj P., Sriplung H. *et al.* (2009) Maternal iodine status and neonatal thyroid-stimulating hormone concentration: a community survey in Songkhla, southern Thailand. *Public Health Nutrition* **12**, 2279–2284.
- Klein R.Z., Sargent J.D., Larsen P.R., Waisbren S.E., Haddow J.E. & Mitchell M.L. (2001) Relation of severity of maternal hypothyroidism to cognitive development of offspring. *Journal of Medical Screening* **8**, 18–20.
- Kung A.W.C. (2007) Iodine nutrition of pregnant and lactating women in Hong Kong, where intake is of borderline sufficiency. *Public Health Nutrition* **10**, 1600–1601.
- Nutrition Survey of East Pakistan (1966) 1962–64. Dhaka, U.S. Department of Health, Education and Welfare and University of Dhaka.
- Ohashi T., Tamaki M., Pandav C.S., Karmakar M.G. & Irie M. (2000) Simple micropalate method for determination of urinary iodine. *Clinical Chemistry* **46**, 529–536.
- Pathak P., Singh P., Kapil U. & Raghuvanshi R.S. (2003) Prevalence of iron, vitamin A, and iodine deficiencies amongst adolescent pregnant mothers. *Indian Journal of Pediatrics* **70**, 299–301.
- R Development Core Team (2009) *R: A Language and Environment for Statistical Computing*. R Foundation for Statistical Computing: Vienna, Austria. ISBN: 3-900051-07-0. Available at: <http://www.R-project.org>
- Schulze K.J., West K.P., Jr, Gautschi L.A., Dreyfuss M.L., LeClerq S.C., Dahal B.R. *et al.* (2003) Seasonality in urinary and household salt iodine content among pregnant and lactating women of the plains of Nepal. *European Journal of Clinical Nutrition* **57**, 969–976.
- Singh M.B., Fotedar R. & Lakshminarayana J. (2008) Micronutrient deficiency status among women of desert areas of western Rajasthan, India. *Public Health Nutrition* **12**, 624–629.
- West K.P. Jr, Christian P., Klemm R., Labrique A., Rashid M., Shamim A.A. *et al.* (2006) The JiVitA Bangladesh Project: research to improve nutrition and health among mothers and infants in rural south Asia. *Sight and Life Newsletter* [1], 10–14. Basel, Sight and Life.
- WHO, UNICEF & ICCIDD (2001) *Assessment of Iodine Deficiency Disorders and Monitoring Their Elimination. A Guide for Program Managers*, 2nd edn, World Health Organization: Geneva.
- WHO, UNICEF & ICCIDD (2007) *Assessment of Iodine Deficiency Disorders and Monitoring Their Elimination. A Guide for Program Managers*, 3rd edn, World Health Organization: Geneva.
- Yusuf H.K., Rahman A.M., Chowdhury F.P., Mohiduzzaman M., Banu C.P., Sattar M.A. *et al.* (2008) Iodine deficiency disorders in Bangladesh, 2004–05: ten years of iodized salt intervention brings remarkable achievement in lowering goitre and iodine deficiency among children and women. *Asia Pacific Journal of Clinical Nutrition* **17**, 620–628.