The Effect of Maternal Iodine Status on Infant Outcomes in an Iodine-Deficient Indian Population

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Background: An adequate intake of iodine during pregnancy is essential for the synthesis of maternal thyroid hormones needed to support normal fetal development. This study aimed to assess the iodine status of pregnant tribal Indian women and their infants and to determine the impact of maternal iodine status on infant growth and behavior.

Methods: A prospective, observational study was undertaken to assess the iodine status of tribal pregnant Indian women living in Ramtek, northeast of Nagpur, India. Pregnant women were recruited at 13–22 weeks gestation (n=220), visited a second time at 33–37 weeks gestation (n=183), and again visited at 2–4 weeks postpartum with their infants. Sociodemographic, anthropometric, and biochemical data, including household salt, blood, and urine samples were obtained from pregnant women. Urine samples, anthropometric, and neonatal behavioral data were collected from infants.

Results: The median urinary iodine concentration (MUIC) at recruitment (mean gestation=17.5 weeks) of mothers was 106 µg/L, which declined to 71 µg/L at the second visit (mean gestation=34.5 weeks) similar to the postpartum MUIC of 69 µg/L, indicating that these women were iodine deficient. Infant (mean age=2.5 weeks) MUIC was 168 µg/L. Median maternal thyroid stimulating hormone (TSH) and free thyroxine (FT4) concentrations at first and second visits were 1.71 and 1.79 mIU/L and 14.4 and 15.4 pmol/L, respectively; 20.0% of women at first visit had TSH >97.5th percentile and 1.4% had FT4 <2.5th percentile. Salt iodine concentration was a significant predictor of maternal UIC (p<0.001), and postpartum maternal UIC was a significant predictor of infant UIC (p<0.001). For every pmol/L increase in maternal FT4 concentration at first visit, both infant weight-for-age Z-score and length-for-age Z-score increased by 0.05 units. There was no relationship between maternal UIC, FT4, or TSH at first visit and neonatal behavior.

Conclusions: Despite three quarters of the women in this study having access to adequately iodized salt (i.e., >15 ppm), these pregnant tribal Indian women were iodine deficient. Increasing the iodine content of salt deemed adequately iodized and iodine supplementation are two strategies that might improve the iodine status of these pregnant women and, consequently, the growth of their infants.

Introduction

Over the last three decades, significant progress has been achieved in controlling iodine deficiency disorders (IDDs) worldwide through the adoption and promotion of universal salt iodization programs. Despite the capacity for adequate production of iodized salt to meet the demands of a massive population, IDDs continue to be major public health problem in India, affecting millions of children and pregnant women (1). Severe IDD is known to adversely affect both pregnant women and the fetus, resulting in increased miscarriage, neonatal hypothyroidism, increased perinatal and infant mortality, growth retardation, and intellectual impairment (2). Less severe IDD in pregnancy has also been shown to affect psychoneuromotor development in children (3).

Iodine requirements increase sharply during pregnancy because of the increased maternal need for thyroid hormones and the transfer of iodine and thyroid hormones to the fetus.
In the first half of gestation, the mother is the primary source of thyroid hormones for the fetus. Compared with nonpregnant women, the concentration of thyroid-stimulating hormone (TSH) declines in the first trimester of pregnancy, rising later in gestation. In response to the thyroid-stimulating effect of human chorionic gonadotropin, the concentration of free thyroxine (FT\(_4\)) peaks at 10–12 weeks gestation, but then decreases as the pregnancy progresses. The use of trimester-specific reference intervals for the interpretation of thyroid hormone measurements in pregnancy is recommended (5), although factors such as methodology, iodine status, age, and ethnicity need to be considered (6).

The predominantly vegetarian diets of Indian pregnant women, which contain little dairy or seafood, mean that in areas of India where the iodine content of soil is low this additional iodine must come from iodized salt or iodine-containing supplements. Thus, it is not surprising that IDD has been reported in rural Indian pregnant women in these areas (7,8). However, there is little information on the iodine status of tribal Indian pregnant women as tribal areas are typically more deprived than rural parts of India. In an earlier study of nonpregnant women of reproductive age, we found the existence of concurrent multiple micronutrient deficiencies such as iron, zinc, and vitamin B\(_{12}\) along with pockets of IDD in tribal areas near Nagpur, a city located in central India (9). The present study was designed to further investigate the extent of iodine deficiency in pregnant women and its impact on infant outcomes such as anthropometry and neurobehavioral development. The specific objectives were (i) to assess the iodine status and factors associated with indicators of maternal iodine status of tribal Indian pregnant women, (ii) to assess the iodine status and factors associated with an indicator of infant iodine status, and (iii) to explore the relationship between maternal indicators of iodine status and infant growth and behavior.

Materials and Methods

**Study design and subjects**

This was an observational, longitudinal study conducted from February to December 2008 of pregnant Indian women. Women were visited three times: at recruitment (13–22 weeks gestation), at ~35 weeks gestation, and ~3 weeks after birth. Questionnaires and anthropometric measurements were administered to women on all three visits, but urine and blood samples were only obtained at recruitment (i.e., first visit) and ~35 weeks gestation (second visit). The following data were collected from infants: anthropometric measurements, a urine sample, and an assessment of neonatal behavior.

The women were from three tribal primary health centers (PHC) of Ramtek, a rural region of central India located outside the city of Nagpur, Maharashtra State, India. These women lived in villages designated as “tribal,” because they belonged to the Gond tribe, which has a distinct culture and language (10). Over the last 20 years, the people of the Gond tribe have been displaced from their indigenous villages and relocated to villages in Ramtek. A PHC is typically the first point of contact with a qualified medical practitioner for rural and tribal Indian people. The number of villages and inhabitants covered by the respective tribal PHCs in Ramtek Block for this study were as follows: Hiwra Bazaar (45 villages with 23,141 inhabitants), Karwahi (32 villages with 20,569 inhabitants), and Bhandarbodi (30 villages with 18,927 inhabitants).

**Sample size**

Based on a predicted prevalence of 30% (9), a sample size of 170 women was required to estimate the prevalence of iodine deficiency in pregnant women with a 95% confidence interval width of ±10%. Assuming 85% of those approached would meet inclusion criteria, and 10% would be lost to follow-up, 225 women were needed at baseline.

**Participant recruitment**

A list of all pregnant women at 13–22 weeks gestation who were willing to participate in the study was obtained from each of the three PHCs as well as subcenters and Integrated Child Development Centers to ensure that no pregnant woman was missed. The inclusion criteria for participation were healthy pregnant women aged between 18 and 30 years. The exclusion criteria were women with self-reported HIV/AIDS, tuberculosis, fever lasting longer than 2 weeks, and thyroid disease and women who planned to move out of the location for delivery. The study was explained to the participants and their families and written and verbal consent was obtained. Ethical approval was obtained from the Ethics Committee of the Health and Family Welfare Training Center, Nagpur, India.

**Socioeconomic, health status, and obstetric questionnaire**

Trained Indian research assistants administered pretested questionnaires to elicit information on the socioeconomic and health status of each participant. Sociodemographic variables included maternal age, years of education, annual household income, family size, vegetarian, and marital status. Health variables included information on illnesses, breastfeeding at the time of recruitment (it was not uncommon for women to be still breastfeeding a child from a previous pregnancy), date of the start of the last menstrual cycle, parity, and anticipated place of delivery. A trained medical doctor performed a clinical examination, which included an assessment of goiter. Women who were diagnosed with goiter were referred to a medical practitioner. For six participants it was necessary to adjust for errors in self-reported last menstrual period to match a biologically possible time frame for length of pregnancy (11). Gestation week was adjusted by 1 month backward for participants with unadjusted pregnancy duration ≥44 but <46 weeks (n=2) and by 2 months backward for those who had an unadjusted pregnancy gestation ≥46 weeks (n=4).

**Anthropometry**

Maternal weight was taken using a digital scale (Seca Robusta 813; Seca Corporation) and height using a portable stadiometer designed and built by the University of Otago (12). Weight gain during pregnancy was calculated as difference in maternal weight between the weights at the first visit and the second visit. Nude infant weight was measured to the nearest 5 g with a digital infant scale (Seca 374; Seca Corporation) and recumbent length was measured using a pediatric length board (O’Leary; Ellard Instrumentation Ltd).
accurate to within ±0.1 cm. Weight-for-age, length-for-age, and weight-for-height Z-scores were determined using the CDC growth charts (13). All anthropometric measurements were taken by one trained research assistant.

**Biochemical assessment**

Experienced phlebotomists collected morning fasting venous blood samples, which were processed and sera stored at −20°C until analysis. Maternal blood samples were analyzed for serum TSH and FT4 by radioimmunoassay (Coat-A-Count IRMA; Diagnostics Products Corporation) at Molecular Diagnostics. Bio-Rad quality control reference standards (Bio-Rad) were used as an external standard. The reference range for TSH in euthyroid adults was 0.3–5 mIU/L. The mean (SD) for TSH concentration of the low, medium, and high external standards were 0.68 (0.2) mIU/L (expected range: 0.45–0.84 mIU/L), 6.5 (1.4) mIU/L (expected range: 4.2–6.9 mIU/L), and 38.8 (5.8) mIU/L (expected range: 30.0–52.0 mIU/L), with coefficients of variation (CVs) of 10.7%, 7.9%, and 5.6%, respectively (n = 6). The reference range for FT4 in euthyroid adults was 10.3–25.7 pmol/L. The mean (SD) for FT4 concentrations of the low, medium, and high external standards were 9.2 (0.2) pmol/L (expected range: 8.3–11.3 pmol/L), 19.7 (1.7) pmol/L (expected range: 16.9–22.9 pmol/L), and 35.5 (11.0) pmol/L (expected range: 26.0–37.1 pmol/L), with CVs of 2.7%, 8.6%, and 29.7%, respectively (n = 6).

Casual morning urine samples were collected into clean plastic containers and stored at −20°C until analysis. Urinary iodine concentration (UIC) was determined by Molecular Diagnostics, using the microplate method (13). The mean (SD) UIC concentrations of the low, medium, and high external standards (Centre for Disease Control, Atlanta) were 37.8 (3.1) μg/L (expected range: 28.0–45.0 μg/L), 114.8 (7.1) μg/L (expected range: 100.0–125.0 μg/L), and 284.5 (14.6) μg/L (expected range: 250.0–310.0 μg/L), with CVs of 8.2%, 6.2%, and 5.1%, respectively (n = 6). A median urinary iodine concentration (MUIC) of <150 μg/L for pregnant women and <100 μg/L for postpartum women and infants was used to define IDD (2).

Salt samples were collected from households at the time of first and second visits in sealed plastic bags and analyzed by iodometric titration at the State Nutrition Bureau, Nagpur (14). A salt iodine concentration of >15 ppm was considered as adequately iodized salt in India (15).

**Neonatal behavioral assessment**

The Neonatal Behavioral Assessment Scale (NBAS) was used to assess the impact of maternal iodine status on neonatal development (16). The NBAS was administered and scored by a single senior pediatrician for all infants, who followed standardized procedures for scoring as described by Brazelton and Nugent (16). Scores were reduced to seven clusters as follows: habituation, orientation, motor performance, range of states, state of regulation, autonomic stability, and abnormal reflexes, as per the data reduction scheme described elsewhere (16, 17).

**Statistical analysis**

Descriptive statistics were used to summarize baseline characteristics of the participants. Random coefficient models were used for maternal UIC and FT4, with gestation week used as a continuous predictor to account for differences in the timing of the visits (between 13 and 22 weeks gestation for the first visit and between 33 and 37 weeks for the second visit). Random participant and gestation week effects were included in these models. Exponential spatial covariance patterns were investigated to see whether they improved model fit as measured by the Akaike Information criterion. Denominator degrees of freedom were estimated using the Kenward-Rogers approach. Fractional polynomial transformations were applied to continuous predictor variables to test for and when appropriate model nonlinear associations. The interactions between categorical predictors and duration of gestation were investigated in the final model for each outcome and included where p < 0.05. Variables with p < 0.20 in univariate analyses were included in multivariate models. Linear regression was used for all other outcomes. Outcome variables were log transformed where this improved normality and/or homoscedasticity of residuals.

Predictors with relevance to maternal UIC and FT4 included in the analysis were maternal age, parity (no child, one child, vs. ≥2 children), salt iodine concentration, maternal education (≤8 vs. >8 years), annual household income, location (Hiwra Baazar, Karwahi vs. Bhandarbodi), breastfeeding at first visit (breastfeeding vs. nonbreastfeeding), family size (≤5 vs. >5 members), and duration of gestation. Predictors of infant UIC included were postpartum maternal UIC, use of iodine containing antiseptics during delivery (did not use, used, vs. did not know), infant age, and all predictors that were related to maternal UIC shown above excluding family size and duration of gestation. Infant sex and prematurity were included in the multivariate infant UIC model. Predictors of infant anthropometric variables were maternal UIC, TSH, and FT4 concentration at first visit and all predictors that were related to maternal UIC excluding family size and duration of gestation. Stata (versions 9.1.2 and 11.0; Stata Corporation, 2009, Stata Statistical Software: Release 11, StataCorp LP, College Station, TX) and SAS (version 9.1.3; SAS Institute, Inc.) for Windows were used for all analyses. All significance tests were two-sided at the 0.05 level.

**Results**

A total of 228 pregnant women were recruited, there were 5 dropouts, and 3 women were excluded (positive diagnosis of HIV [n = 1], and twins [n = 2]); thus, baseline data (i.e., first visit) are reported for 220 women. Urine and blood samples were obtained at the second visit from 183 women (women moved out of the study area to have their baby [n = 26], dropouts [n = 5], spontaneous abortion [n = 4], medical termination of pregnancy [n = 3]) and data were obtained at the postpartum visit from 180 infants (stillbirth [n = 2] and infant death [n = 1]). The baseline sociodemographic, anthropometric, and obstetric characteristics of the mothers and infant characteristics are shown in Table 1. The mean (SD) unadjusted gestational age of women at first visit was 17.5 (2.1) weeks and at the second visit was 34.5 (0.5) weeks, whereas the mean infant age at the postpartum visit was 2.5 (0.4) weeks. Seven participants used iodine supplements at both visits. Despite being pregnant, nearly 18% of the women were breastfeeding at the time of first visit. Weight gained from the first to the second visit
Infant characteristics at postpartum visit

- 24.6 (4–48), 28.6 (3–49), and 29.6 (3–63) ppm, respectively.

- In Hiwra Bazaar, and Bhandarbodi was 25.5 (4–61), 22.2 (4–53), and 22.3 (3.1); range of state 17.1 (2.0); regulation of state 19.3 (4.3); further analysis.

Mean (range) iodine concentration for every 1 year increase in maternal age and every 1 week increase in gestation, UIC fell by 5% (95% CI: 1%, 8%), and for every 1 kg increase in maternal age, UIC decreased by 12% (95% CI: 1%, 8%).

Discussion

To date this is the first longitudinal study that has investigated the iodine status of pregnant Indian women and their infants using a variety of indices, including UIC and thyroid.
hormones. Despite concerted attempts by the government to improve the iodine status of the Indian population through strategies such as the universal iodization of salt and nutrition education programs, the women in this study were iodine deficient. The MUIC of women at the first and second visits was 106 and 71 µg/L, respectively, below the 150 µg/L cutoff, indicating iodine deficiency (2); UIC decreased by 2% for every week of gestation. IDD in pregnant Indian rural women was observed recently in two cross-sectional studies from the Indian state of Rajasthan, which reported an MUIC of 127 µg/L in pregnant women at any stage of gestation and 118 µg/L in pregnant women of >28 weeks of gestation (7,8).

The low MUIC of women in our study suggests that their intake of iodized salt was insufficient to meet the iodine requirements of pregnancy. The MUIC of women at the first and second visits was 106 and 71 µg/L, respectively, below the 150 µg/L cutoff, indicating iodine deficiency (2); UIC decreased by 2% for every week of gestation. IDD in pregnant Indian rural women was observed recently in two cross-sectional studies from the Indian state of Rajasthan, which reported an MUIC of 127 µg/L in pregnant women at any stage of gestation and 118 µg/L in pregnant women of >28 weeks of gestation (7,8).

The low MUIC of women in our study suggests that their intake of iodized salt was insufficient to meet the iodine requirements of pregnancy. Salt with an iodine content >15 ppm is considered adequately iodized in India. In Switzerland an increase in the iodine content of salt from 15 to 20 ppm was necessary to improve the iodine status of pregnant Swiss women (18). Increasing the iodine content of salt deemed adequately iodized might also offset the loss of iodine caused by cooking (19), as in this area of India most foods are prepared in the home and eaten cooked. The higher infant and maternal MUIC seen in Bhandarbodi compared with the other two study areas could be ascribed to the higher iodine content of salt combined with a greater percentage of women who consumed adequately iodized salt (i.e., >15 ppm) in this location. Despite the higher MUIC in women from Bhandarbodi, 54% had UIC <150 µg/L at the second visit, suggesting that other factors need to be considered when addressing iodine deficiency in pregnant women. A recent report examining the coverage of iodized salt in eight Indian states identified socioeconomic status, awareness of iodine deficiency, consumer motivation, retailers, and wholesalers as key factors affecting the use of iodized salt (20). Changes in the diet specific to pregnancy also need to be considered; for example, women still receive advice to limit salt consumption in pregnancy to reduce swelling in their ankles and feet. Given the growing concern worldwide that pregnant women are not consuming enough iodine, these factors should be considered when addressing iodine status in pregnant women from both developing and developed countries.

Given the low and declining UIC observed in these women over the course of pregnancy, it was not surprising that elevated TSH concentrations were found in 20% of women at

<table>
<thead>
<tr>
<th>Variable</th>
<th>n</th>
<th>At first visit</th>
<th></th>
<th>At second visit</th>
<th></th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum TSH (mIU/mL)</td>
<td>220</td>
<td>1.71 (1.24, 2.34)</td>
<td></td>
<td>183</td>
<td>1.79 (1.37, 2.39)</td>
<td>0.004</td>
</tr>
<tr>
<td>Serum FT4 (pmol/L)</td>
<td>220</td>
<td>14.4 (12.6, 16.3)</td>
<td></td>
<td>183</td>
<td>15.4 (13.7, 17.3)</td>
<td>0.034</td>
</tr>
<tr>
<td>Urinary iodine (µg/L)</td>
<td>220</td>
<td>106 (52, 191)</td>
<td></td>
<td>183</td>
<td>71 (42, 151)</td>
<td>0.006</td>
</tr>
<tr>
<td>Salt iodine (ppm)</td>
<td>220</td>
<td>24.7 (14.0)</td>
<td></td>
<td>190</td>
<td>27.7 (13.8)</td>
<td>0.015</td>
</tr>
</tbody>
</table>

aAs determined by paired t-test of log-transformed data.
bMedian (25th, 75th, percentiles); TSH, thyroid-stimulating hormone; FT4, free thyroxine.
cMean (SD).

Table 3. Predictors of Maternal Urinary Iodine Concentration and Free Thyroxine Concentration of Pregnant Tribal Women from Ramtek, Nagpur, India, as Determined by Multivariate Linear Regression

| Predictors                           | UIIC    | FT4     |  |
|--------------------------------------|---------|---------|  |
| Predictors                           | Ratio (CI) | P     | Ratio (CI) | P     |
| Maternal age (years)                 |          |        |          |        |
| >8 years                             | 0.95 (0.92, 0.99) | 0.006 | 0.99 (0.98, 0.99) | 0.040 |
| <8 years                             | 0.79 (0.67, 0.94) | 0.007 | 1.00 (0.99, 1.00) | 0.052 |
| Duration of gestation (weeks)        |          |        |          |        |
| >44 weeks to <46 weeks               | 1.00     |        | 1.00     |        |
| ≤44 weeks                            | 0.63 (0.52, 0.77) | <0.001 | 1.00 (0.99, 1.00) | 0.052 |
| Location                             |          |        |          |        |
| Bhandarbodi                          | 1.00     |        | 1.00     |        |
| Hiwra Bazaar                         | 0.63 (0.52, 0.77) | <0.001 | 1.00 (0.99, 1.00) | 0.052 |
| Karwahi                              | 0.58 (0.47, 0.71) | <0.001 | 1.00 (0.99, 1.00) | 0.052 |

aValues adjusted for breast feeding at first visit and parity (n=400).
bValues adjusted for maternal UIC and number of family members (n=403).
cRatio of geometric means (95% confidence interval) from mixed model analysis with log-transformed data.
dGestation week adjusted by 1 month backward for participants with >44 weeks to <46 weeks and by 2 months for >46 weeks gestation estimated based on their self-reported last menstrual period (n=6).

UIC, urinary iodine concentration.
Iodine-containing antiseptics

Table 4. Predictors Associated with Urinary Iodine Concentration of Infants of Ramtek, Nagpur, India, as Determined by Multivariate Linear Regression

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Ratio (CI)&lt;sup&gt;a,b&lt;/sup&gt;</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postpartum maternal UIC (µg/L)</td>
<td>1.00 (1.00, 1.01)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Location</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bhandarbodi</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Hiwra Bazaar</td>
<td>0.73 (0.54, 0.99)</td>
<td>0.047</td>
</tr>
<tr>
<td>Karwahi</td>
<td>0.64 (0.45, 0.89)</td>
<td>0.011</td>
</tr>
<tr>
<td>Iodine-containing antiseptics at birth</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Did not use</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Used</td>
<td>1.35 (0.96, 1.89)</td>
<td>0.084</td>
</tr>
<tr>
<td>Don’t know</td>
<td>1.13 (0.85, 1.52)</td>
<td>0.398</td>
</tr>
</tbody>
</table>

<sup>a</sup>Values adjusted for prematurity and infant sex (n = 163).
<sup>b</sup>Ratio of geometric means (95% confidence interval).

first visit; 19.5% had subclinical hypothyroidism and 0.5% had overt hypothyroidism. In other studies of pregnant women, the prevalence of subclinical hypothyroidism was 2%-3% (21). An FT4 concentration < 2.5th percentile was found in 1.4% of women at first visit and 1.1% at second visit. The number of women with palpable goiter increased from three women at first visit to nine women at the second visit. It is possible that as pregnancy advances, the thyroid strives to conserve iodine by decreasing urinary output and increasing thyroid volume to produce adequate amounts of maternal T4 for normal fetal development. It was of interest to note that increasing maternal age was associated with a small decrease in both maternal UIC and FT4; the implications of this association are unknown.

Our results showed that maternal FT4 at first visit was a significant predictor of infant length-for-age and weight-for-age Z-scores. There are few studies investigating the role of iodine deficiency or thyroid hormone concentrations in pregnancy on anthropometric birth outcomes. Das et al. (22) in a study of pregnant Nigerian women and their term infants found that mothers of low birth weight infants (i.e., birth weight < 2.5 kg) had a significantly lower maternal and cord serum FT4 index, T4, and triiodothyronine concentration than mothers of normal birth weight babies in both iodine-deficient (n = 46) and iodine-sufficient (n = 26) areas; however, the difference in maternal thyroid parameters between the two groups of infants was more pronounced in pregnant women from iodine-deficient areas. Another longitudinal study of 538 mother-infant pairs from Spain reported that women with a third trimester UIC of 100–149 µg/L had a 5% lower risk for small-for-gestational age newborns than women who had a UIC < 50 µg/L (23). Together, our data and results of these published studies suggest that iodine status and consequently thyroid hormone concentrations in the first half of gestation can influence infant growth. Another factor that influenced anthropometric outcomes of infants was the mother still breastfeeding a previous child while pregnant, a common occurrence in this part of India. The combined energy and nutrient requirements of breastfeeding one child while pregnant with another may explain why pregnant women who were not breastfeeding when recruited had heavier and longer infants at 3 weeks after birth.

Because previous studies found an association between FT4 concentrations in pregnancy and psychomotor development (24,25), another birth outcome explored in this study was the neonatal behavioral profile using the NBAS. Kooistra et al. (26) found that maternal hypothyroxinemia (i.e., FT4 < 10th percentile) at 12 weeks gestation but not at 24 or 32 weeks gestation was a predictor of the orientation cluster score in newborns. In our study, there was no relationship between NBAS cluster scores in term infants and indicators of maternal iodine status, including maternal UIC, TSH, or FT4 concentration. The differences between our study and that of Kooistra et al. could be attributed to several factors that influence fetal development including higher maternal FT4 concentrations in our pregnant women at first visit (i.e., 15.1 vs. 11.4 pmol/L), differences in gestational age at the time of blood sample collection (~17.5 vs. 12 weeks gestation), lower maternal age (i.e., mean age 23 vs. 32 years), and better lifestyle habits (i.e., no participants consumed alcohol or smoked) during pregnancy.

This study has a number of limitations. There was considerable range in the gestational age of women recruited at the first visit, and although weeks of gestation was included as a continuous variable in statistical modeling, the effect of thyroid hormones produced by the fetus on development cannot be ascertained. Another limitation was the use of self-reported last menstrual date to assess gestational age; unfortunately, ultrasound equipment in this deprived region of India was not available. Likewise, we did not have the resources to

Table 5. Maternal Predictors Associated with Infant Anthropometric Z-Scores as Determined by Multivariate Linear Regression

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Weight-for-age Z-scores&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Length-for-age Z-scores&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β (CI&lt;sup&gt;a&lt;/sup&gt;)</td>
<td>P</td>
</tr>
<tr>
<td>Breast feeding at first visit</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breastfeeding</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Not breastfeeding</td>
<td>0.49 (0.19, 0.78)</td>
<td>0.001</td>
</tr>
<tr>
<td>FT4 at first visit (pmol/L)</td>
<td>0.05 (0.02, 0.08)</td>
<td>0.002</td>
</tr>
<tr>
<td>Parity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 2 children</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>One child</td>
<td>−0.09 (−0.39, 0.20)</td>
<td>0.525</td>
</tr>
<tr>
<td>No child</td>
<td>−0.44 (−0.74, −0.13)</td>
<td>0.005</td>
</tr>
</tbody>
</table>

<sup>a</sup>Values adjusted for maternal UIC, weight gain, and prematurity (n = 162).
<sup>b</sup>β, beta coefficient (95% confidence interval).
assess thyroid antibodies in these women. The usefulness of FT₄ in pregnancy has been questioned (6,21), because current assays do not directly measure FT₄ and binding proteins can interfere with the assay (27), and thus caution should be exercised in the interpretation of the results presented here. This study focused on iodine deficiency; however, other micronutrient deficiencies such as iron and vitamin B₁₂ deficiency are prevalent in pregnant Indian women and could also affect infant growth and development. Finally, the tribal women assessed in this study were well integrated into rural society and are not likely to be representative of women from other tribes of India.

Despite these limitations, this is the first study to show that pregnant tribal women of central India were iodine deficient; >20% of women had elevated TSH. Although three quarters of the women had access to iodized salt >15 ppm, they were not consuming enough salt to ensure they had adequate iodine status. Increasing the iodine content of salt deemed adequately iodized and iodine supplementation are two strategies that could improve iodine status in pregnant women in this region of central India. A recent study conducted in pregnant Spanish women living in an area with a history of iodine deficiency also recommended iodine supplements regardless of whether the women used iodized salt (28). Improving iodine status in pregnant women from central India will help to ensure optimal thyroid hormone concentrations during pregnancy, which may improve infant growth and development.

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Disclosure Statement

K.C.M. conducted the research and, along with S.A.S., analyzed the data and prepared the manuscript. S.A.S., E.L.F., and C.D.T. designed and supervised the study, secured funding, and assisted in the interpretation of the data. A.R.G. provided statistical advice and conducted the advanced statistical analysis. S.Z., A.S., and P.K.D. helped with obtaining ethical approval and liaised with district health professionals in Nagpur. C.S.P. supported the research as Regional Director of ICCIDD (South-east Asia). All authors commented on the final draft of the manuscript. None of the authors had a conflict of interest.

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