Maternal Iodine Status and Thyroid Volume during Pregnancy: Correlation with Neonatal Iodine Intake


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ABSTRACT

Differences in pregnancy-associated alterations in thyroid volume and urinary iodine (UI) excretion have been attributed to geographical variations in dietary iodine intake. In this study, ultrasound-measured thyroid volume and UI excretion were assessed during the 3 trimesters of pregnancy, at delivery, and at 6 weeks postpartum. Urine specimens also were obtained from mothers and both breast- and formula-feeding infants at 3 days after delivery. Thyroid volume showed a significant increase (maximum 47.0%), compared with nonpregnant control values over the 3 trimesters of pregnancy, which occurred as early as the first trimester and was paralleled by increased UI excretion, followed in turn by a precipitous fall at delivery. UI excretion in breast-feeding neonates (100 ± 6.8 µg/L) was significantly higher than in their mothers (78 ± 5.6 µg/L; p < 0.01) but was significantly lower (43 ± 3.5 µg/L) in formula-fed infants. The results suggest that in an area of moderate dietary iodine intake, UI loss during pregnancy may result in maternal thyroid enlargement. The ability of the breast to transport iodine compensates for this loss in breast-fed infants, but this protection may be lost in formula feeding.

Dietary Iodine requirements have been the subject of considerable recent attention (1–3). There is consensus on the need to take action to eliminate iodine deficiency in those countries where endemic goiter, or even cretinism, is prevalent (4, 5). However, in regions where dietary iodine intake is borderline (50–100 µg/day), it may be necessary to focus on increasing dietary iodine supply during pregnancy, the fetal state, and the first years of life (3). The Food and Nutrition Board of the National Academy of Sciences (6) has recommended a minimum daily iodine intake between 40–70 µg for infants and children, whereas a European report has suggested 90 µg/day (7). Although such figures can be readily achieved in North America (8–9), dietary supplements would be required in many parts of the world (10).

Increased renal loss of iodine has been suggested as the cause of thyroid enlargement during pregnancy, the so-called pregnancy goiter (11). Ultrasound-measured increases in thyroid volume during pregnancy have been reported (12–15) from areas where daily dietary iodine intake was low (~50 µg), but no change or a decrease was reported in urinary iodine (UI) excretion (13, 15–16). In contrast, areas replete in iodine showed either no difference or only a slight increase in goiter prevalence or ultrasound-measured thyroid volume between pregnant and nonpregnant women (17–20). The objective of the present study was to elucidate more fully the relationship between thyroid volume and UI excretion in pregnancy groups in Ireland, an area of moderate dietary iodine intake (median UI 82 µg) (21–22) and to study UI excretion in neonates of breast- and formula-feeding mothers.

Materials and Methods

Subjects

Thyroid volume was measured by ultrasound in 115 women during each pregnancy trimester (T): T1, n = 41; T2, n = 29; T3, n = 45. These women (Group A) were selected opportunistically, in that each trimester’s study group comprised different individuals. An additional group of 108 women had urine sampled 3 days after delivery; 64 of these were breast feeding and 44 were formula feeding. A further 84 patients were studied during the late puerperium (approximately 40 days postpartum). Nonpregnant control values for ultrasound-determined thyroid volume were obtained from 95 premenopausal control females. Urine specimens from 1063 premenopausal women attending a Breast Clinic over a 1-yr period served as controls for UI excretion studies. Group B consisted of 38 women from whom casual urine samples were collected sequentially during the 3 trimesters of pregnancy and at approximately 6 weeks postpartum. Of those 38 subjects, 20 had thyroid ultrasound scans during each trimester of pregnancy and at 6 weeks postpartum. Ages and parity of study subjects are shown in Table 1. All pregnant women studied were delivered of live-born, normally formed, singleton infants and received no iodine-containing supplements during their pregnancy. All were clinically and biochemically euthyroid throughout gestation.

Methods

Thyroid volume was measured by ultrasound (23). Thyroid volumes greater than 18.0 mL were termed enlarged (24). UI excretion was measured in random urine samples using a manual method based on a modification of Barker’s dry-ash technique (25). Results were expressed both as microgram of iodine per gram creatinine (µg/g) or directly as microgram of iodine per liter of urine (µg/L).
Statistics

Results were analyzed using Student’s t, Wilcoxon’s rank sum, Bartlett’s, or chi² tests.

Results

Thyroid volumes

Fig. 1 shows that the mean thyroid volume of 13.9 ± 0.8 mL, observed as early as T1, was already significantly greater than the nonpregnant control value (11.3 ± 0.5 mL; P < 0.05) and reached a maximum of 16.0 ± 0.7 mL, a 47% increase (P < 0.01) in T3 and continued to be significantly elevated into the late puerperium. As shown in Fig. 1, an identical pattern was observed in the 20 sequentially studied subjects in Group B, with mean values being almost superimposable on those obtained in Group A. Mean values in all trimesters were, as in Group A, significantly different from nonpregnant control values (Wilcoxon’s test, P < 0.05 and P < 0.01). The number of enlarged thyroids increased from the nonpregnant control value of 6.3%, through 19.5% in T1, to reach a plateau of 31.0 and 32.0% in T1 and T2, which was maintained, even up to 40 days postpartum. Pregnant subjects with enlarged thyroid volumes were more likely to be multiparous than those with normal volumes (P < 0.05). When results were analyzed from the 84 subjects studied during the late puerperium, 57 had normal vol (<18.0 mL) and 27 had enlarged thyroids. Nulliparity and multiparity were equally represented in both groups.

UI excretion

Median values for UI excretion (µg/L) in pregnancy and the puerperium (Early, +3 days; Late, +40 days). Group A, different subjects at each study interval; group B, same subjects studied sequentially. The distribution (% prevalence) of UI values within the 3 trimesters (T1-T3) is shown in the accompanying histograms.

Table 1. Age and parity of study groups

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Age (years) Mean ± se</th>
<th>Range (Median)</th>
<th>Parity Range (Median)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pregnant</td>
<td>115</td>
<td>28.0 ± 0.8</td>
<td>16–44 (27)</td>
<td>0–6 (1)</td>
</tr>
<tr>
<td>Delivery</td>
<td>108</td>
<td>28.6 ± 0.9</td>
<td>18–45 (28)</td>
<td>1–6 (1.5)</td>
</tr>
<tr>
<td>Breast-feeding</td>
<td>64</td>
<td>29.5 ± 0.6</td>
<td>19–43 (30)</td>
<td>0–6 (2)</td>
</tr>
<tr>
<td>Formula feeding</td>
<td>44</td>
<td>28.6 ± 0.8</td>
<td>18–38 (30)</td>
<td>0–8 (2)</td>
</tr>
<tr>
<td>Postpartum (~40 days)</td>
<td>84</td>
<td>28.3 ± 0.6</td>
<td>18–45 (28)</td>
<td>1–6 (1.5)</td>
</tr>
<tr>
<td>Group B</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary iodine</td>
<td>38</td>
<td>27.5 ± 1.0</td>
<td>16–39 (27)</td>
<td>0–5 (1.5)</td>
</tr>
<tr>
<td>Thyroid volume</td>
<td>20</td>
<td>26.4 ± 1.0</td>
<td>18–31 (27)</td>
<td>0–3 (1.5)</td>
</tr>
<tr>
<td>Nonpregnant controls</td>
<td>95</td>
<td>28.0 ± 0.8</td>
<td>18–44 (31)</td>
<td></td>
</tr>
</tbody>
</table>

Group A, different subjects selected opportunistically; group B, same subjects studied sequentially.
Maters were normally distributed, and the pattern of excretion was similar when results were expressed as μg/L urine and as μg iodine/g creatinine.

Maternal and neonatal UI excretion

The mean UI level in mothers measured at 3 days after delivery (74.0 ± 5.7 μg/L, median 73 μg) was not significantly different from that of 68.5 ± 4.6 μg (median 56 μg) in their infants. However, this finding was shown to be deceptive when results were divided on the basis of those who were breast- or formula feeding. The iodine content of the four formulas being fed to neonates was 100–150 μg/L. The mean maternal UI of 76.5 ± 5.6 μ/L in breast-feeding mothers was significantly lower than that of 100 ± 6.8 μg/L (<0.001) in their infants, whereas the mean UI excretion value of 43 ± 3.5 μ/L in bottle-fed infants was significantly lower than that of 100 ± 6.8 μ/L in the breast-feeding group (P < 0.01). In addition, the proportion of low (<50 μg/L) individual UI values (62.5% in bottle feeders) was 10 times greater than that of 6.25% in the breast-feeding groups (P < 0.01).

Discussion

The finding of an increase in thyroid volume during the 3 trimesters of pregnancy is consistent with previous reports from areas of low dietary iodine intake (~50 μg/day) (12–13, 15). However, identification of a significant increase in UI excretion observed in both the random and sequential groups, respectively, occurring as early as the first trimester and being maintained throughout the 3 trimesters, is at variance with earlier reports that have shown that UI excretion either declined (15) or was unchanged (13, 16), compared with nonpregnant controls. The increase in UI observed in our study throughout pregnancy is consistent with the thesis of Crooks and his colleagues (11) that renal clearance of iodine is increased during gestation and remains enhanced until delivery (26). These workers reported a consequent fall in serum inorganic iodine during pregnancy, although this was not confirmed in a recent study (27) that failed to document a fall in serum nonprotein-bound iodine during pregnancy. The hypothesis that increased renal loss of iodine contributed to thyroid enlargement is supported by some (14–15, 27), but not all (16), reports that women receiving iodide or a mixture of iodide and T₄ showed no gestational increase in thyroid volume.

The greatly increased UI excretion observed in this study during pregnancy would suggest that in the absence of increased dietary iodine intake, subjects would be in negative iodine balance, as previously reported in 77 out of 129 daily iodine intake balances (28). These workers suggested the existence of an iodostat set according to the usual dietary iodine intake of the population. Iodine loss may therefore reflect not only daily dietary intake but also initial thyroid iodine content, which could explain the difference in UI excretion in this, compared with previous studies (12, 13–15). Crude calculations, based on median iodine excretion values recorded in the 38 patients studied sequentially in this study, would suggest a diminution in thyroidal iodine stores of approximately 40% over a 280-day gestation period, which is comparable with that previously reported (28). Although iodine loss in the course of successive pregnancies is consistent with our finding that thyroid enlargement was more frequently observed in multiparous women, parity did not seem to be related to the persistence of enlargement in the late puerperium. Could this enlargement contribute in susceptible individuals to what later becomes the female preponderance of thyroid disease, and if so, will the effect, as previously postulated (29), be confined to areas of marginal dietary iodine intake? The acute fall (45.0%) in the median UI to values indistinguishable from those in nonpregnant controls, observed by us 3 days after delivery, suggests a direct effect of pregnancy on UI excretion. This precipitous fall has not, as far as we are aware, been previously recorded, although others (15, 30) have noted a decline in UI excretion from booking to delivery. The cause of the acute fall in UI is unknown, but it may reflect rapid normalization of renal clearance or, perhaps, even placental loss.

The lower UI values in infants on formula feed suggests that iodine content, despite being comparable with breast milk iodine concentrations in iodine-replete areas (7), is inadequate (31) or is presented in a form that does not permit satisfactory neonatal absorption.

Our results once again pose the question as to the desirability of increasing dietary iodine intake during pregnancy (3, 7). Only comparative studies of neonatal iodine and thyroid status in populations of differing dietary intake, combined with long-term assessment of women showing persistent thyroid enlargement postpartum, will resolve this uncertainty.

Acknowledgments

We thank the Health Research Board and The National Maternity Hospital Research College for financial assistance; the Master and staff of The National Maternity Hospital and Professor N. J. O’Higgins of the Breast Clinic, St. Vincent’s Hospital, Dublin, for their cooperation during the course of the study.

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