

Prevalence of maternal dietary iodine insufficiency in the north east of England: implications for the fetus

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Background: Maternal subclinical hypothyroidism is a cause of poor neurodevelopment outcome in the offspring. Although iodine deficiency is the most common cause of hypothyroidism world wide, there are no screening programmes for it in the United Kingdom where the population is assumed to be iodine replete.

Objective: To determine the prevalence of reduced iodine intake by measuring urinary iodide concentrations in pregnant and non-pregnant women from the north east of England.

Methods: Urinary iodide excretion (UIE) rate was estimated using inductively coupled mass spectrometry in 227 women at 15 weeks gestation and in 227 non-pregnant age matched controls. A reduced intake of iodine is indicated by a concentration in urine of less than 50 µg/l or less than 0.05 µg iodine/mmol creatinine.

Results: Eight (3.5%) pregnant women and 13 (5.7%) controls had a reduced iodine/creatinine ratio. These values were higher when UIE was expressed as iodine concentration: 16 (7%) and 20 (8.8%) respectively. Ninety (40%) of the pregnant women had a UIE of 0.05–0.10, which is consistent with borderline deficiency.

Conclusion: In this study, 3.5% of pregnant women had evidence of iodine deficiency, and 40% may be borderline deficient. Larger scale studies are required to estimate the true prevalence of iodine deficiency in the United Kingdom.

Thyroid hormone production depends on an adequate supply of iodine. Thyroid hormones are critical for both antenatal and postnatal brain development. Thyroxine regulates neurogenesis, neuronal migration, and neuronal differentiation in definitive regions of the brain during specific developmental windows.^{1–4}

During the first trimester of pregnancy the fetal supply of thyroxine is largely maternal in origin, and, when there is no fetal thyroid hormone synthesis, as for example in thyroid agenesis, the fetus is dependent on maternal thyroxine throughout pregnancy.

If the mother has either overt or subclinical hypothyroidism due to autoimmune disease, then the fetus may be susceptible to reduced thyroid hormone supply. A similar situation could arise with iodine deficiency sufficient to cause maternal hypothyroxinaemia or frank hypothyroidism. Recently maternal subclinical hypothyroidism has been linked with less favourable neurodevelopmental outcome in children assessed at 7 years of age.⁵ As a result, screening for the condition during pregnancy has been advocated.⁶ Dietary iodine deficiency, the most common worldwide thyroid disorder, has been treated with iodine supplementation in countries known to be iodine deficient.^{7–8} The prevalence of iodine deficiency has been examined in various European countries, but no studies have been published in the United Kingdom. Countries in which iodine deficiency is recognised have introduced national programmes of iodine supplementation. Where such a programme does not exist because iodine sufficiency is assumed, this may put pregnant women and their fetuses at risk.^{9–10} Monitoring of the prevalence of iodine deficiency is imperative based on the recent publications from other countries.^{9–12}

In the iodine deficient state, iodine intake by the thyroid gland increases and there is concomitant decrease in urinary iodide excretion (UIE). There is increased trapping of iodide which results in the accumulation within the gland of

ingested exogenous iodide and a more efficient reuse of iodide directly released by the thyroid or generated by the degradation of thyroid hormones. To be adequate, the daily intake of iodine in the diet must at least equal the daily amount of hormonal iodine degraded in the peripheral tissues and not recovered by the thyroid.¹³ WHO recommends a urinary iodine concentration of 100–200 µg/day.¹⁴ As UIE does not exceed the dietary intake, it can be used as a screening test for iodine deficiency.

In addition to the fetal demands, there is increased UIE during pregnancy. Thus during pregnancy, the daily UIE should be greater and the corresponding intake greater than that of the non-pregnant normal adult recommended by WHO.

The aim of this pilot study was to establish the prevalence of reduced iodine intake according to WHO specifications during pregnancy by determining UIE at 15 weeks gestation.

PATIENTS AND METHODS

The study was conducted at the James Cook University Hospital, Middlesbrough, in the north east of England between March 2000 and March 2001 after approval by the South Tees ethics committee.

Written consent was obtained from pregnant women attending the antenatal clinic at 15 weeks gestation and non-pregnant age matched controls. The controls were either friends of the pregnant women or identified by the midwives from the same district. A 20 ml sample of early morning urine was collected from each of the pregnant women and non-pregnant controls. All women with known thyroid disease or other systemic illness were excluded from the study.

Urine samples were stored frozen at –70°C and transported frozen to the trace element laboratory in Southampton. Samples were analysed in batches of 20 samples at a time. Analysis was by inductively coupled mass spectrometry. This

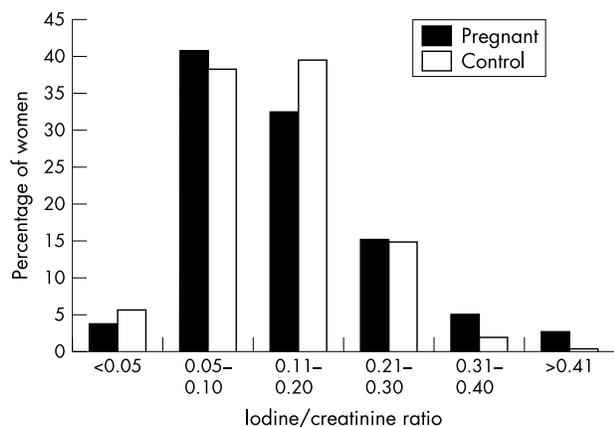


Figure 1 Distribution of iodine/creatinine ratio. A ratio of 0.05 shows iodine deficiency, and 0.05–0.10 is borderline.

technique involves producing an aerosol from a diluted sample solution, transporting this aerosol using argon gas into high temperature argon gas plasma, and measuring the ions produced with a high vacuum mass spectrometer. In this context the plasma is an ionised gas not the physiological plasma. The high temperature, about 8000°C ionises the iodine (and almost all other elements) in the same sample aerosol, and the ions are introduced into a quadruple mass spectrometer where they are measured. The detection limit for iodine is less than 1 µg/l, so that simple dilutions of urine samples can be used for analysis.

UIE was expressed as both iodine concentration in µg/l and µg iodine/mmol creatinine. An iodine concentration of less than 50 µg/l or an iodine/creatinine ratio of less than 0.05 indicates reduced intake.

Screening for congenital hypothyroid was carried out as described by the National Neonatal Hypothyroidism Screening Laboratory, Durham, on the fifth postnatal day using a solid phase, two site fluoroimmuno-metric immuno-assay (Perkin-Elmer; DELFIA). The results of congenital hypothyroid screening are reported as either negative, thyroid stimulating hormone (TSH) less than 10 µg/l, borderline TSH 11–45 µg/l, or TSH greater than 45 µg/l as positive. All children with either borderline or positive results are investigated.

Analysis

The women studied were white or Asian. We sought differences in UIE between the pregnant women and non-pregnant controls and between white and Asian women. We also subdivided women into three age groups: under 20,

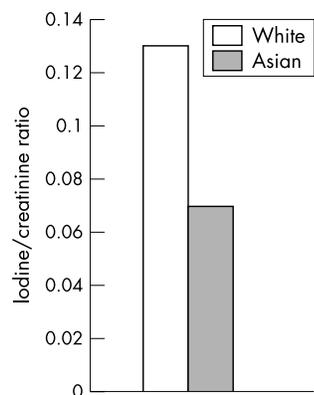


Figure 2 Iodine/creatinine ratio for Asian and white women.

group A; 20–29, group B; 30 and above, group C. We also determined whether or not babies from this cohort had been referred with a positive congenital hypothyroidism screen test during the study period.

A *t* test or χ^2 test was used to analyse data between the groups, with *p* < 0.05 taken as significant. Fisher’s exact test was used to analyse the small numbers in the group of women less than 20 years of age and the Asian women.

RESULTS

A total of 227 pregnant women and 227 age matched non-pregnant controls were recruited. The mean age was 28.3 years (range 15.9–39.2) and 28.5 years (15.3–39.9) respectively. Figure 1 shows the distribution of UIE in pregnant and non-pregnant women. The distribution of the iodine/creatinine ratio was skewed. Logarithmic transformed data showed a normal distribution. Eight of the pregnant women (3.5%) and 13 of the non-pregnant controls (5.7%) had an iodine/creatinine ratio below 0.05, indicating low iodine intake. The pregnant women had a mean iodine/creatinine ratio of 0.14 with median iodine of 0.11. The corresponding values for non-pregnant women were 0.13 and 0.11. Sixteen of the pregnant women (7%) and 20 of the non-pregnant controls (8.8%) had iodine concentrations below 50 µg/l. Ninety (40%) of the pregnant women showed UIE (50–100 µg/l) consistent with borderline deficiency. There was no significant difference between the pregnant and non-pregnant women. Figure 2 shows the difference between the ethnic groups.

When pregnant women were classified according to ethnicity, 11 women of Asian origin had a mean (SD) iodine/creatinine ratio of 0.07 (0.01). This was significantly (*p* < 0.05) lower than that of the 216 white women: 0.13 (0.01). Figures 3 and 4 show the UIE expressed as a concentration and iodine/creatinine ratio respectively. When the iodine/creatinine ratio of pregnant women in age groups A, B, and C were compared, a lower ratio was found in the teenage women, but the difference did not reach statistical significance (table 1).

Congenital hypothyroid screening

The 227 pregnancies resulted in 218 live births. No baby was referred with a capillary TSH greater than 10 µ/l. Seven pregnancies resulted in births before 36 completed weeks of gestation. Two pregnancies were miscarried.

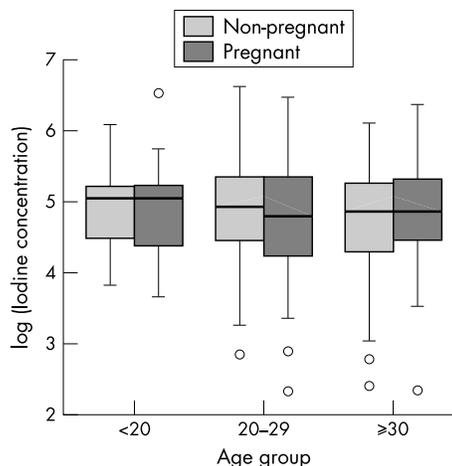


Figure 3 Box plots of log (urinary iodine concentration).

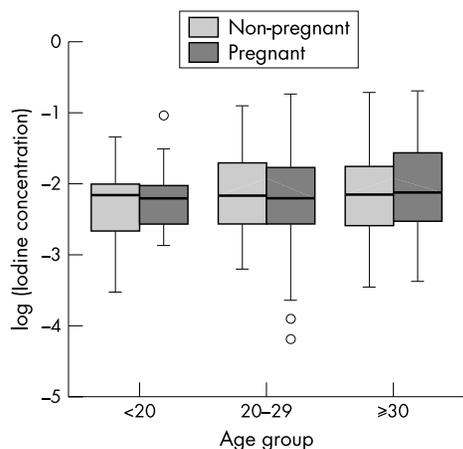


Figure 4 Box plots of log (urinary iodine/creatinine ratio).

DISCUSSION

This pilot study shows that 3.5% of the pregnant women had reduced iodine/creatinine ratio and 7% had a reduced UIE consistent with reduced iodine intake.^{15, 16} Women of Asian origin had a lower mean UIE than white women (0.07 v 0.13). A combination of reduced iodine intake and the effect of phytates and different eating habits on iodine absorption may explain the results in Asian women, but the numbers are too small to allow a firm conclusion to be drawn. Iodine in the red meat commonly consumed in Asian communities is not properly absorbed.

The measurement of UIE in morning voiding samples has been validated in epidemiological studies as an index of iodine sufficiency.¹⁷ Our results show a skewed distribution, suggesting that the 40% of the women studied have a borderline intake of iodine with an excretion of less than 100 µg/l.

The only identifiable role of iodine is the synthesis of thyroid hormones, and its deficiency leads to inadequate thyroid hormone production.¹⁸ Our results show a 3.5% prevalence of dietary iodine insufficiency in the north east of England, a part of the country where the population is thought to be iodine replete. This may contribute to maternal hypothyroxinaemia and possibly subclinical hypothyroidism. Iodine deficiency is a cause of preventable mental handicap³ and is 150 times more common world wide than congenital hypothyroidism,^{4, 19} yet few countries screen for it, at least during pregnancy.

Iodine intake before conception and during early pregnancy eliminates the problem.^{9, 20, 21} Our data support the view that mild to moderate iodine deficiency may be a problem in the United Kingdom even though iodine sufficiency is taken for granted.

The importance of maternal iodine sufficiency is underlined by the work of Haddow and colleagues,⁵ who have shown that subclinical hypothyroidism has subtle effects on fetal neurodevelopment. Our data suggesting that some pregnant women in our region of England may be iodine deficient has important implications for fetal health.

Subjects with moderate iodine deficiency do not show clear signs of substrate deficiency for thyroid hormone synthesis.²²

Reduced iodine intake leads to chronically enhanced thyroid stimulation associated mainly with relative hypothyroxinaemia and goitre. This results from the pituitary-thyroid feedback mechanism. The serum concentration of thyroid binding globulin is normal unless there is decreased synthesis because of protein malnutrition. In clinical practice, several

Table 1 Urinary iodide excretion expressed as µg iodine/mmol creatinine in 227 pregnant and non-pregnant women according to age

Age (years)	Pregnant women	Non-pregnant women
15–19 (n = 24)	0.12 (0.06)	0.11 (0.08)
20–29 (n = 104)	0.13 (0.08)	0.14 (0.08)
30–40 (n = 99)	0.16 (0.1)	0.14 (0.08)
Total (n = 227)	0.14 (0.08)	0.13 (0.06)

Values are mean (SD).

biochemical parameters have been advocated including relative hypothyroxinaemia, preferential triiodothyronine secretion, changes in serum TSH (which usually remains within the reference range), and changes in secretion of thyroid binding globulin (which tends to be increased during pregnancy).²³

The results of our study and that of Haddow *et al*⁵ raise a number of questions. Firstly, do we need to screen for iodine deficiency and should we consider the reintroduction of iodised salt or iodine tablets especially for pregnant women? Secondly, do we need to screen for subclinical maternal hypothyroidism? UIE can be used to screen for iodine deficiency, but measurement of venous free thyroxine and TSH would be needed to screen for hypothyroidism.

In conclusion, this study has shown that the prevalence of reduced iodine intake in pregnant women is 3.5%, and 40% may have incipient or borderline iodine deficiency. A collaborative study is required to examine the prevalence of low UIE in the United Kingdom. Given the importance of periconceptual health, there may be a case for examining the iodine status of school leavers.

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