

*Short Communication*

# Are pregnant women in New Zealand iodine deficient? A cross-sectional survey

Amy PETTIGREW-PORTER<sup>1</sup>, Sheila SKEAFF<sup>1</sup>, Andrew GRAY<sup>2</sup>, Christine THOMSON<sup>1</sup> and Michael CROXSON<sup>3</sup>

<sup>1</sup>Department of Human Nutrition, University of Otago, Dunedin, <sup>2</sup>Department of Preventive and Social Medicine, University of Otago, Dunedin, and <sup>3</sup>Auckland District Health Board Endocrinology Service, Auckland, New Zealand

Severe iodine deficiency in pregnancy can result in cretinism. There is growing concern that less severe iodine deficiency may also affect fetal growth and development. A handful of prior small New Zealand studies focussed on pregnant women living in Dunedin. This study utilised biochemical, clinical and dietary indices to assess iodine status of 170 women living throughout New Zealand. The median urinary iodine concentration (UIC) of the women was 38 µg/L, well below the 150 µg/L cut-off value that indicates adequate iodine status; 7% of women had goitre. Not surprisingly, iodine intake was also low at 48 µg/day. The majority of women had TSH and FT4 concentrations within pregnant reference ranges, suggesting that despite the low UIC observed in these women, thyroid hormone production appeared unaffected.

**Key words:** goitre, iodine, New Zealand, pregnancy, thyroid hormones.

## Introduction

An adequate supply of iodine is needed for the synthesis of the thyroid hormones, thyroxine (T<sub>4</sub>) and tri-iodothyronine (T<sub>3</sub>), required for normal growth and development, particularly of the brain and central nervous system. The most serious consequence of iodine deficiency in pregnancy is cretinism, characterised by a child born with physical abnormalities and mental retardation. Cretinism occurs in pregnant women with severe iodine deficiency; however, there is an increasing concern that less severe iodine deficiency (ie moderate to mild) in pregnancy may also affect fetal development. Given this, it is important to assess the iodine status of pregnant women, particularly in New Zealand (NZ) and parts of Australia, which have a long history of iodine deficiency.

Urinary iodine concentration (UIC) is the most commonly accepted index of iodine status because approximately 90% of dietary iodine is excreted in the urine. In schoolchildren and non-pregnant adults, including breastfeeding women, a median UIC of 50–100 µg/L, 20–49 and <20 µg/L is indicative of mild, moderate and severe iodine deficiency, respectively.<sup>1</sup> In 2007, the World Health Organization (WHO) suggested that a median UIC between 150 and 249 µg/L be used to indicate adequate iodine status

in pregnant women;<sup>2</sup> however, no cut-off values were suggested for categorising severe, moderate or mild iodine deficiency in pregnancy.

According to this criteria, iodine deficiency has been consistently reported in studies conducted between 1998 and 2009 of pregnant women living in Tasmania,<sup>3</sup> Victoria,<sup>4</sup> New South Wales<sup>5–7</sup> and, recently, the Australian Capital Territory<sup>8</sup> with median UICs ranging from 52 to 104 µg/L. Between 1997 and 2005, a few small studies had been conducted in NZ on convenience samples of pregnant women living in Dunedin finding a median UIC <50 µg/L.<sup>9–11</sup> The aim of this study was to assess the iodine status of a more nationally representative sample of pregnant women living throughout NZ.

## Materials and methods

### Subjects

The survey was a cross-sectional, observational survey of pregnant women living throughout NZ conducted over six weeks between October and November 2005. Thirty clusters were randomly selected using a proportionate to population sampling method from cities or towns with a population >20 000 people. In the North Island, 24 clusters were selected with 13 of these located in Auckland, the largest city in NZ. In the South Island, six clusters were selected. We aimed to measure ten women per cluster, recruited through maternity clinics located in that cluster or by local advertising on the radio or community newspaper, for a projected final sample size of 300 women.

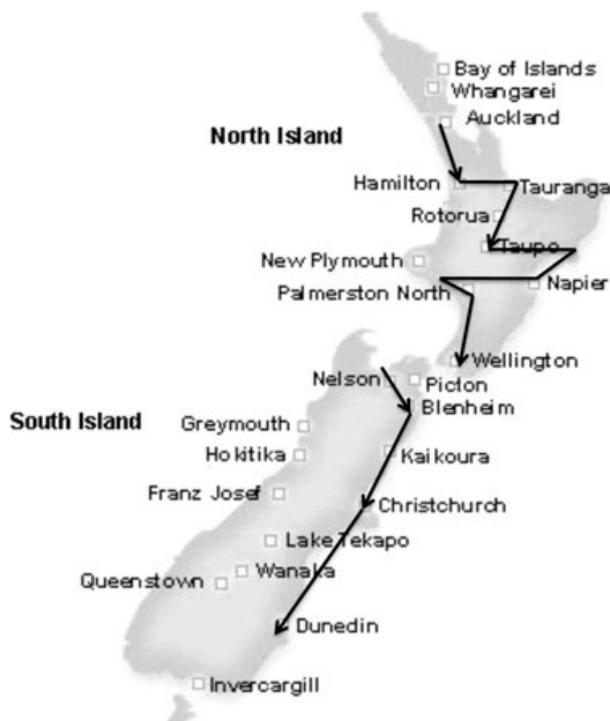
*Correspondence:* Dr Sheila Skeaff, Department of Human Nutrition, University of Otago, PO Box 56, 9054 Dunedin, New Zealand. Email: sheila.skeaff@otago.ac.nz

Received 21 February 2011; accepted 21 April 2011.

Inclusion criteria were healthy, pregnant women expecting a singleton birth, with no known thyroid disease, who were not taking iodine-containing medications or kelp supplements. Ethical approval was obtained from the Multi-Region Ethics Committee. From Auckland to Dunedin (Fig. 1), women were visited in their cluster by the ThyroMobil (Merck, Darmstadt, Germany), a Merck sponsored mobile health van that has been used in field studies assessing iodine status in other countries, including Australia.<sup>12</sup> A spot urine sample, fingerprick blood sample and ultrasound scan of the thyroid gland were obtained from each woman. Participants were asked to complete a questionnaire that collected information about socio-demographic characteristics, obstetric history and consumption of multivitamin/mineral and dietary supplements. The questionnaire also included an iodine-specific semi-quantitative food frequency questionnaire (FFQ) pertaining to the frequency of consumption of the main sources of iodine (ie milk, dairy products, red meat, poultry, fish, seafood, egg and iodised salt) for NZ pregnant women at the time.

### Assessment of iodine status

Participants collected a single spot urine sample between 07:00 and 17:00 h. Urine samples were kept frozen at  $-20^{\circ}\text{C}$  until analysis. UIC was determined using a modification of the method of Pino *et al.*<sup>13</sup> An external reference standard (Serorm; Sero As, Asker, Norway) was analysed with each batch of samples and had a mean iodine concentration of  $147\ \mu\text{g/L}$  (expected range:  $132\text{--}150\ \mu\text{g/L}$ )



**Figure 1** Route and cities throughout New Zealand visited by ThyroMobil (—).

with a coefficient of variation of 9.2% ( $n = 93$ ). Approximately 1 mL of whole blood was obtained from a fingerprick between 09:00 and 17:00 h. Serum was obtained within 60 min of blood collection and frozen at  $-20^{\circ}\text{C}$  until analysis. Serum TSH was measured by immunoradiometric assay (Coat-A-Count TSH IRMA; Diagnostic Products Corporation, Los Angeles, CA, USA) (Manufacturer's reference range for non-pregnant euthyroid adults is  $0.3\text{--}5.0\ \text{mU/L}$ ) and free T4 (FT4) was measured using solid-phase  $^{125}\text{I}$  radioimmunoassay (Coat-A-Count Free T4; Diagnostic Products Corporation) (Manufacturer's reference range for pregnant women in 1st trimester is  $11.6\text{--}28.3\ \text{pmol/L}$  and in 3rd trimester is  $10.3\text{--}27.0\ \text{pmol/L}$ ) in a single batch. All biochemical analyses were conducted (APP) in the Department of Human Nutrition, University of Otago.

Thyroid volume (TV) was measured with a Siemens Sonoline Prima Ultrasound Imaging System (Siemens, Munich, Germany) equipped with a 7.5 MHz transducer. Women were lying in the supine position with the neck fully extended. The volume (mL) of each lobe was calculated using the formula: width (cm)  $\times$  height (cm)  $\times$  length (cm)  $\times$  0.479. TV was calculated as the sum of both lobes and did not include the isthmus. A single, trained ultrasonographer conducted all scans.

### Statistical analysis

Statistical analyses were performed using STATA 9.1 (Stata Corporation, College Station, TX, USA). Data were checked for normality, and where the residuals from the models were skewed, log transformation was employed. Multivariate regression analysis was used to identify factors associated with UIC and TV. Variables included in the model were age, region (upper and lower North Island, South Island), parity, weeks gestation, dietary iodine intake, use of iodised salt at the table and in cooking and use of iodine-containing supplements, and for TV, the concentration of FT4 and TSH was also included. Results were considered significant at  $P < 0.05$ .

## Results

### Subjects

Recruitment of subjects in Auckland was poor with only 22 of the projected 130 women (ie ten women from 13 clusters) taking part in the study. For the remaining clusters, 148 of the projected 160 women participated (ie 87%) resulting in a final sample size of 170 women; 120 women were recruited through maternity clinics and 50 women by advertising. The demographic and obstetric characteristics of the participants are shown in Table 1. The mean (SD) age of the women was 31.9 (five) years.

### Iodine status

The median UIC was  $38\ \mu\text{g/L}$ , well below the  $150\text{--}249\ \mu\text{g/L}$  range indicative of adequate iodine status in pregnancy<sup>2</sup>

(Table 2); only two women had a UIC >150 µg/L. Multivariate regression analysis showed that the consumption of iodine-containing supplements was significantly associated with UIC ( $P = 0.008$ ); women taking an iodine-containing supplement (ie multivitamin/mineral tablet) had a MUIC of 48 µg/L compared with 35 µg/L in women who were not taking an iodine-containing supplement. The median TV was 10.5 mL (Table 2), and 7% of pregnant women had goitre, defined as a TV >18 mL.<sup>14</sup> None of the variables tested were significantly associated with TV. The median

TSH and FT4 concentration was 1.3 mU/L and 14.2 pmol/L, respectively. None of the women had a TSH >4.0 mU/L, while using more stringent criteria specific to pregnancy (ie 2.3, 3.1, and 3.5 mU/L in the 1st, 2nd and 3rd trimester, respectively<sup>15</sup>) 2.6% of women ( $n = 4$ ) had TSH concentrations indicating subclinical hypothyroidism. Using kit-specific reference ranges for pregnant women, only women in the 3rd trimester (ie 15%;  $n = 10$ ) had a low FT4 concentration (ie <10.3 pmol/L). However, caution should be exercised in the interpretation of FT4 in pregnancy as immunoassays have been shown to overestimate the number of women with low FT4, particularly in the 2nd and 3rd trimester.<sup>16</sup>

The estimated mean (SD) daily iodine intake was 48 (23) µg I/day (Table 2), well below the Recommended Daily Intake of 220 µg I/day for pregnant women.<sup>17</sup> More than half of women ate fish regularly, with 38% consuming fish once a week and 30% consuming fish 2–4 times a week; however, 77% of women never consumed other types of seafood such as oysters or mussels. Although iodised salt was used at the table and in cooking by 60% and 73% of participants, respectively, only 26% and 25% reported using iodised salt at least once per day. An iodine-containing vitamin/mineral or dietary supplement was consumed by 23% of women, and these supplements provided between 50 and 300 µg I/day.

## Discussion

The results of this survey indicate that pregnant NZ women were iodine deficient. Although there are no criteria to define the severity of iodine deficiency in pregnancy, it is believed that lower UICs indicate a greater degree of deficiency, thus the median UIC of 38 µg/L found in this sample of NZ women suggests a significant degree of iodine deficiency. Despite this low UIC, the majority of women had TSH and FT4 concentrations within pregnant reference ranges.

**Table 1** Characteristics of participating pregnant New Zealand women

Characteristic	<i>n</i> †	%
Trimester of pregnancy		
First	12	7
Second	83	50
Third	72	43
Parity		
Nulliparous	84	50
Multiparous	83	50
Ethnicity		
NZ European and Other	157	92
Maori	9	5
Pacific Island	3	2
Total household income in NZ\$		
<\$20 000	7	5
\$20 000–\$50 000	30	21
>\$50 000	105	72
Highest level of education		
Secondary	31	21
Tertiary	79	53
Postgraduate	40	27

†Not all subjects answered all questions.

**Table 2** Indices of iodine status for participating pregnant New Zealand women

	<i>n</i>	Trimester			Overall
		First	Second	Third	
Urinary iodine concentration (µg/L)					
Median (25th, 75th percentile)	170	41 (22, 62)	39 (23, 58)	37 (25, 56)	38 (24, 56)
Mean (95% confidence interval)†	170	36 (27, 48)	35 (31, 41)	35 (29, 42)	35 (31, 40)
Thyroid volume (mL)					
Median (25th, 75th percentile)	170	10.4 (8.0, 12.9)	10.7 (9.0, 13.2)	10.2 (8.8, 13.4)	10.5 (8.9, 13.3)
Mean (95% confidence interval)†	170	10.4 (8.8, 12.0)	11.1 (10.3, 12.0)	12.0 (10.9, 13.2)	11.4 (10.7, 12.2)
Serum TSH (mU/L)					
Median (25th, 75th percentile)	154	1.1 (0.8, 1.7)	1.4 (0.8, 1.8)	1.3 (1.0, 2.0)	1.3 (0.9, 1.8)
Mean (95% confidence interval)†	154	1.2 (1.0, 1.5)	1.2 (1.1, 1.4)	1.3 (1.2, 1.5)	1.3 (1.2, 1.4)
Serum free T4 (pmol/L)					
Median (25th, 75th percentile)	154	19.3 (16.7, 23.2)	15.4 (12.9, 18.0)	14.2 (12.9, 16.7)	14.2 (12.9, 18.0)
Mean (95% confidence interval)†‡	154	18.0 (15.4, 16.7) <sup>a</sup>	15.4 (15.4, 16.7) <sup>b</sup>	14.2 (12.9, 15.4) <sup>c</sup>	15.4 (14.2, 15.4)
Iodine intake (µg/day)					
Mean (standard deviation)	168	52 (32)	49 (24)	46 (20)	48 (23)

†Adjusted for age, parity, region, iodine intake, use of iodine containing supplement, and use of iodised salt.

‡Values across row with different superscripts significantly different at  $P < 0.05$ .

Elevated TSH was found in 2.6% of women in this study; the prevalence of subclinical hypothyroidism in iodine-sufficient pregnant populations is 2–3%.<sup>15</sup> The discrepancy between UIC and thyroid hormone concentrations raises questions about the assessment of iodine deficiency in pregnancy. There are two possible explanations. Firstly, the mother, by decreasing the excretion of iodine in the urine and increasing TV (7% of women in this study had goitre), is conserving iodine to ensure adequate amounts of thyroid hormones are produced for the fetus. Secondly, UIC may not be a good index of iodine status in pregnant women in countries such as NZ. The UICs found in Australian and NZ women, including this study, are among some of the lowest reported in the developed world, yet infants born in these countries appear healthy and meet developmental milestones. Further studies are needed to investigate the iodine status of mothers in NZ and Australia and to critically examine the consequences of iodine deficiency in pregnancy on the child.

### Acknowledgements

The study was funded by a University of Otago Research Grant and Dominion Salt. Amy Pettigrew-Porter was a recipient of the Neige Todhunter Award, which funds postgraduate study for dietitians. We thank Philippe Prouff for selecting centres and ultrasonographer Stephanie Sharp for conducting the thyroid scans. We would like to acknowledge the support of ICCIDD and Asia Pacific Regional Co-ordinator Professor Creswell Eastman for use of the ThyroMobil.

### References

- 1 WHO, UNICEF, ICCIDD. *Assessment of Iodine Deficiency Disorders and Monitoring Their Elimination: A Guide for Programme Managers*, 3rd edn. Geneva: World Health Organization, 2007.
- 2 WHO, UNICEF. *Reaching Optimal Iodine Nutrition in Pregnant and Lactating Women and Young Children*. Geneva, Switzerland: World Health Organization, 2007.
- 3 Burgess JR, Seal JA, Stilwell GM *et al.* A case for universal salt iodisation to correct iodine deficiency in pregnancy: another salutary lesson from Tasmania. *Med J Aus* 2007; **186**: 574–576.
- 4 Hamrosi MA, Wallace EM, Riley MD. Iodine status in pregnant women living in Melbourne differs by ethnic group. *Asia Pac J Clin Nutr* 2005; **14**: 27–31.
- 5 Li M, Ma G, Boyages SC, Eastman CJ. Re-emergence of iodine deficiency in Australia. *Asia Pac J Clin Nutr* 2001; **10**: 200–203.
- 6 Gunton JE, Hams G, Fiegert M, McElduff A. Iodine deficiency in ambulatory participants at a Sydney teaching hospital: is Australia truly iodine replete? *Med J Aus* 1999; **171**: 467–470.
- 7 Travers CA, Guttikonda K, Norton CA *et al.* Iodine status in pregnant women and their newborns: are our babies at risk of iodine deficiency? *Med J Aus* 2006; **184**: 617–620.
- 8 Nguyen B, Baker D, Southcott E *et al.* Iodine deficiency in pregnant women in the ACT. *Aust NZ J Obstet Gynaecol* 2010; **50**: 539–542.
- 9 Thomson CD, Packer MA, Butler JA *et al.* Urinary selenium and iodine during pregnancy and lactation. *J Trace Elem Med Biol* 2001; **14**: 210–217.
- 10 Skeaff SA. The iodine status of vulnerable groups in New Zealand (PhD Dissertation). Dunedin: Department of Human Nutrition, University of Otago, 2004.
- 11 Mulrine HM, Skeaff SA, Ferguson EL *et al.* Breast-milk iodine concentration declines over the first 6 mo postpartum in iodine-deficient women. *Am J Clin Nutr* 2010; **92**: 849–856.
- 12 Li M, Eastman CJ, Waite KV *et al.* Are Australian children iodine deficient? Results of the Australian National Iodine Nutrition Study. *Med J Aus* 2006; **184**: 165–169.
- 13 Pino S, Fang SL, Braverman L. Ammonium persulfate: a safe alternative oxidizing reagent for measuring urinary iodine. *Clin Chem* 1996; **42**: 239–243.
- 14 Gutekunst R, Martin-Teichert H. Requirement for goiter surveys and the determination of thyroid size. In: Delange F, Dunn JT, Glinoeer D, eds. *Iodine Deficiency in Europe: A Continuing Concern*. New York: Plenum Press, 1993; 109–115.
- 15 Abalovich M, Amino N, Barbour LA *et al.* Management of thyroid dysfunction during pregnancy and postpartum: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2007; **92**: S1–S47.
- 16 Lee RH, Spencer CA, Mestman JH, *et al.* Free T4 immunoassays are flawed during pregnancy. *Am J Obstet Gynecol* 2009; **200**: 260.e1–260.e6.
- 17 Nutrient Reference Values for Australia and New Zealand including Recommended Dietary Intakes. Canberra and New Zealand: Commonwealth Department of Healthland Ageing, Ministry of Health, National Health and Medical Research Council, Commonwealth of Australia and New Zealand Government, 2006.