

# Urinary iodine excretion in pregnant women as an index of the impact of a national iodization programme

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## Abstract

**Objective:** To evaluate the extent to which increase in iodine requirement was achieved in pregnant women who attended the antenatal clinic at Harare Central Hospital.

**Design:** Cross sectional.

**Setting:** Samples were collected from pregnant women attending antenatal clinic at Harare Central Hospital, and from lactating mothers and their infants.

**Subjects:** 100 pregnant women attending the antenatal clinic at Harare Central hospital, 80 infants, 80 lactating women and 18 non-pregnant women.

**Main Outcome Measures:** Comparison of urinary iodine excretion levels among pregnant women, lactating mothers and their infants.

**Result:** The results indicated lower urinary iodine excretion levels for the pregnant women and lactating mothers compared to the urinary iodine excretion of the infants and the breast milk iodine content. The urinary iodine excretion level of the non-pregnant control women was median (first and third quartiles): 18.5µg/dl (30.0, 30.2µg/dl). The urinary iodine excretion level of the lactating mothers was median (first and third quartiles): 12.0 mg/dl (7.6, 19.5 mg/dl) compared to the level of the infants, median (first and third quartiles): 26.5 mg/dl (18.8, 11.5 mg/dl). A significant difference was noted between the median urinary iodine excretion levels of the mothers, and the median levels of the infants,  $p = 0.001$ . The mean milk iodine content was  $21.2 \pm 6.8$  mg/dl. There was no correlation between breast milk iodine levels and the urinary iodine excretion levels of the infants, ( $p = 0.96$ ,  $r = 0.006$ ). Positive correlation was found between maternal urinary iodine excretion levels and the urinary iodine excretion levels of the infants,  $p = 0.016$   $r = 0.285$ . Serum FT4, and TSH levels were found to be higher for infants at six weeks after birth, (FT4 =  $20.91 \pm$

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65pmol/L) and median TSH= 2.28 mIU/ml (1.36, 0.86)mIU/ml, compared to levels at 12 weeks *postpartum*: (FT4=17.53 -\*6.4pmol/L) and median TSH=2.02 mIU/ml. (0.84, 1.55)mIU/ml. The differences were not significant.

**Conclusion:** The results indicated a significant reduction in the urinary iodine content of pregnant women, and lactating mothers which did not appear to have any relationship to the urinary iodine excretion levels of infants and iodine content of breast milk. Iodine intake needed to be raised to reflect the recent proposed recommendations.

## Introduction

Iodine requirements are increased during pregnancy, lactation and adequate iodine intake is important for normal brain development of the foetus/infant.<sup>1</sup> Sufficient nutritional iodine supply is important especially during pregnancy, lactation and in the foetus. The reasons for increased iodine requirements are:

- (1) enhanced transfer of iodine and thyroxin from the mother to the foetus as well as
- (2) a higher need of iodine for thyroid hormone synthesis to maintain normal metabolism in the mother, and
- (3) an increased loss of iodide through the kidneys due to an increase in the renal clearance of iodide.

Because of these factors the recommended iodine concentration in the blood during pregnancy is higher than the recent value of 150µg/L recommended for non-pregnant adult.<sup>1</sup> A study found that iodine rapidly crossed the placenta and was actively concentrated in foetal plasma up to five fold with respect to maternal plasma. Following the administration of radioactive iodide, a 20 to 30 fold increase of radioactivity was observed in milk compared to plasma. The capacity in concentrating iodine was mediated by enhanced mammary 5'iodination.<sup>1</sup>

Delange *et al.*<sup>2</sup> studied thyroid function during early infancy in relation to gestational age at birth. The results showed that the mechanism which regulated the production and release of thyroid hormones in premature infants was relatively immature at birth. Therefore, preterm infants have a higher risk of developing transient primary hypothyroidism compared to full term infants. The risk decreased with time.<sup>2</sup> Transient hypothyroidism was observed in infants of less than 30 weeks gestation.<sup>3</sup> In these preterm infants, it was found that free serum thyroxin levels increased slightly on the first *post natal* day and then decreased below cord blood levels. This phenomenon was found to be more pronounced the more premature the infant was, and it took six to eight weeks before serum thyroid hormone levels reached those of term infants of the same *post natal* age.<sup>3</sup>

Substantial amounts of T4 need to be transferred from mother to foetus during gestation.<sup>3</sup> A reduction in maternal T4 levels therefore, in early pregnancy as a result of iodine deficiency might lead to neurological damage.<sup>4</sup> In areas with sufficient iodine intake, the thyroid adjusted easily to maintaining stable-free thyroid hormone levels. In areas with severe iodine

deficiency, goitre as well as hypothyroidism was observed in mother and newborn as a result of the inability of the thyroid gland to adjust to changes associated with pregnancy.<sup>3</sup>

A minimal amount of iodine had to be present in the milk ingested by infants for thyroid hormone synthesis. The median iodine level in breast milk was set at a reference value of 70µg/L.<sup>5</sup> Other studies reported mean values between 78 to 146 µg/L, and a lower mean milk iodine value of 47 µg/L was also reported.<sup>1</sup> Maternal breast milk iodine, cow's milk and infant formula were reported as the major sources of iodine in the early life of infants.<sup>5</sup> The level of iodine in the mother's diet affected that in the breast milk. Insufficient iodine intake due to low iodine concentration in breast milk or infant formula might lead to iodine deficiency disorders in some children.<sup>5</sup> Maternal milk iodine level was found to decrease significantly six months after delivery compared with that at one month.<sup>6</sup> No correlation was found between milk iodine and maternal urinary iodine excretion by the study.<sup>6</sup> Recently a higher proposed recommendation for breast milk iodine content was set at 150 to 180µg/L,<sup>1</sup> for urinary iodine excretion in pregnancy at 250 to 300µg/L, in lactating mothers at 225 to 350µg/L and the level in the neonate set at 180 to 225µg/L.<sup>1</sup>

Pregnant, lactating women and neonates are the main targets of the effects of iodine deficiency, because the reduction in thyroid hormone levels can result in irreversible brain damage and retarded psychomotor development. Therefore, a salt iodization programme in a population should pay special attention to these groups.<sup>1</sup> Iodine deficiency was endemic in Zimbabwe with goitre prevalence reaching as high as 70 % in some areas. In 1993 the Government of Zimbabwe introduced the universal iodization of salt programme.<sup>7</sup> For this reason the level of iodine especially in pregnant and lactating women needs to be monitored to ensure it is at its optimum. The aim of this study was to evaluate the extent to which the increase in iodine requirement was met in pregnant women who attended the antenatal clinic at Harare Central Hospital. The criteria used were:

- 1) Urinary iodine excretion,
- 2) breast milk iodine content,
- 3) biochemical indices for thyroid function; thyrotropin, thyroxin (TSH, FT4).

## Material and Methods

### Study Population.

The subjects were selected from women eight to nine

months pregnant who were attending the ante-natal clinic. Their average age was 25.8 years. The women were consecutively recruited. Each selected pregnant woman had her hospital card tagged.

After delivery the lactating women who were apparently healthy and were prepared to feed their infants exclusively on breast milk for three months were selected. Two groups of infants were studied: the first group were those infants delivered at full term with a gestational age of 39 weeks and above, and the second group were those infants delivered at preterm with a gestational age less than 30 weeks, and birth weight < 2.5 kg. The inclusion criteria were that delivery took place at Harare Central Hospital and that the infant was born healthy. None of the women were found to be goitrous. Mothers with systemic illness or with sick babies were excluded from the study. Ten percent of the pregnant women refused to take part in the study, and 20% of the women dropped out of the study after delivery. Another 30% dropped out after six weeks *post partum*. Exclusive breastfeeding in this study implied that the infant was fed only on breast milk and nothing else, not even water for a period of three months.

All data and samples were collected at the Harare Central Hospital antenatal clinic. Blood and urine samples were taken from the pregnant women and they were advised to visit the clinic at six weeks and 12 weeks after delivery.

Blood, urine and breast milk specimens were taken on each visit. Verbal consent was sought from the participants. This research was approved by Medical Research Council and by Harare Central Hospital ethical committee.

To estimate iodine status, five to 10 ml samples of blood and urine were collected during the last week of pregnancy, and at six and 12 weeks after delivery. The breast milk of the mothers was sampled simultaneously with blood and urine of their newborns at six weeks and 12 weeks after delivery. Breast milk samples were collected by manually expressing the milk into dark glass bottles, and 2ml aliquots were stored in brown polypropylene screw cap tubes at -20°C and then -80°C until analyzed.

There were samples from 100 pregnant women attending the antenatal clinic at Harare Central Hospital, 80 infants, 80 lactating women and 18 non-pregnant women were also sampled.

#### Laboratory Analysis.

The iodine status of the mothers and infants was assessed using urinary iodine excretion level and breast milk iodine content. Thyroid function was also determined. For the analysis, iodine in urine and breast milk was measured by using the modification of Sandell-Kolthoff<sup>10</sup> reaction. For the evaluation of thyroid function, TSH and free thyroxin were measured. The blood samples were collected by venipuncture, centrifuged at 3 000rpm for 10 minutes and the serum was separated. Serum in 2ml and 1ml (or less for

newborns) aliquots was stored in test tubes at -20°C until analyzed. TSH was measured by solid phase immunoradiometric<sup>10</sup> assay based on monoclonal and polyclonal anti-TSH antibodies. <sup>125</sup>I labelled anti-TSH polyclonal antibodies in liquid phase and monoclonal anti-TSH antibodies immobilized to the wall of a polystyrene tube. Free thyroxin was measured by a solid phase radioimmunoassay, where <sup>125</sup>I-labelled T4 analogue competes with free T4 in the patient sample for sites on T4-specific antibody.<sup>11</sup>

#### Statistical Analysis.

Results expressed as means ( $\pm$  SD) and medians, with first and third quartiles values were calculated for all variables. Group comparisons were made using paired T-test and Box and Whiskers plot. An F-test was used to test the significance, and Spearman's rank-order correlation was used to test relations among the variables.<sup>10</sup>

We used urinary iodine excretion as an indicator for IDD therefore, the following cut-off points were used as recommended by WHO/ICCIDD: severe <2 $\mu$ g/dl, moderate 2.0 to 4.9 $\mu$ g/dl, mild 5.0 to 9.9 $\mu$ g/dl, and >10 $\mu$ g/dl is normal.<sup>11</sup> The concentration of iodine in breast milk was taken to be 6.4 to 17.8 $\mu$ g/dl. The cut-off point for sub-optimal breast milk iodine concentration was considered to be <6.4  $\mu$ g/dl.<sup>1</sup> The reference values for FT4 is for euthyroid 16.73 pmol/L, pregnant women 19.3 pmol/L, and for hyperthyroidism 48.9 pmol/L. Detection level was at 0.13 pmol/L. For TSH, the reference normal range was 0.3-5mIU/mL<sup>12</sup> with detection level at 0.03 mIU/mL, hyperthyroid <0.15mIU/mL and hypothyroid >5.5mIU/mL.

## Results

The iodine excretion levels in casual urine samples in all the groups is shown in Figure 1 and Table 1. The urinary iodine excretion of the non pregnant women was median (first and third quartiles): 18.5 (30.0, 30.2). The mothers had lower urinary iodine excretion levels, median (first and third quartiles): 12.0 mg/dl (7.6, 19.5)mg/dl compared to the infants, median (first and third quartiles): 28.9 mg/dl (18.8, 11.5) mg/dl,  $p=0.001$ . Positive correlation was found between maternal urinary iodine excretion levels and the urinary iodine excretion levels of the infants,  $p=0.016$ ,  $r=0.285$ .

Figure I: Box and Whisker plot showing the concentration of iodine in the urine of pregnant women, lactating mothers, and infants, and in the lactating mothers' breast milk. Boundaries of the boxes represent the first and third quartile, the whiskers represent ranges of value and the centre lines across the boxes represent the median. The numbers above the whiskers are the outliers.

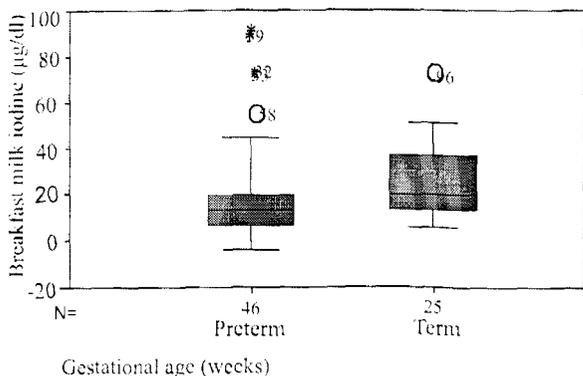
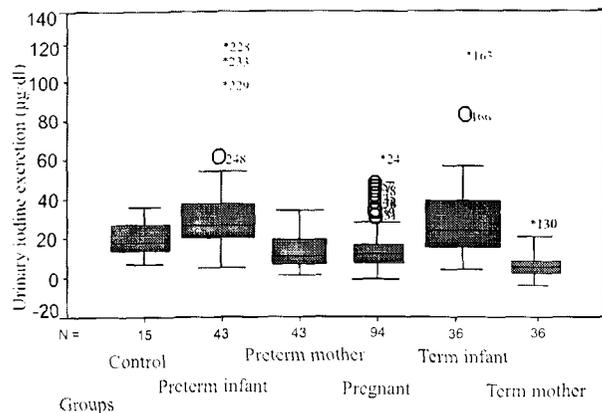


Table I: Urinary iodine excretion ( $\mu\text{g/dl}$ ) concentration in all subjects.

Groups	Number of Subjects	Median	First quartile	Third quartile
Preterm infant	43	25.60	34.80	11.50
Preterm mother	43	13.00	7.80	19.50
Term infant	36	27.10	18.80	35.60
Term mother	36	9.30	7.60	21.60
Pregnant	94	11.55	22.50	4.30
Control	15	18.50	30.00	30.20

GROUPS	Mean difference $\pm$ std. error	p value	Comment
Pregnant vs Term mother	3.4 $\pm$ 2.9	0.244	Not significant (NS)
Pregnant vs Preterm mother	0.3 $\pm$ 2.8	0.903	NS
Pregnant vs Term infant	-17.0 $\pm$ 2.9	0.000**	Significant (S)
Pregnant vs Preterm infant	-18.4 $\pm$ 2.8	0.000**	S
Pregnant vs Control	-6.4 $\pm$ 4.2	0.128	NS
Term mother vs preterm mother	-3.1 $\pm$ 3.4	0.362	NS
Term mother vs Term infant	-20.4 $\pm$ 3.5	0.000**	S
Term mother vs Preterm infant	-21.9 $\pm$ 3.4	0.000**	S
Term mother vs Control	-9.8 $\pm$ 4.6	0.034*	S
Preterm mother vs Term infant	-17.3 $\pm$ 3.4	0.000**	S
Preterm mother vs Preterm infant	-18.8 $\pm$ 3.2	0.000	S
Preterm mother vs Control	-6.7 $\pm$ 4.5	0.137	NS
Term infant vs Preterm infant	-1.4 $\pm$ 3.4	0.676	NS
Term infant vs Control	10.6 $\pm$ 4.6	0.022	S
Preterm infant vs Control	12.1 $\pm$ 4.5	0.000**	S

\*\*p = 0.001.

\*p < 0.05.

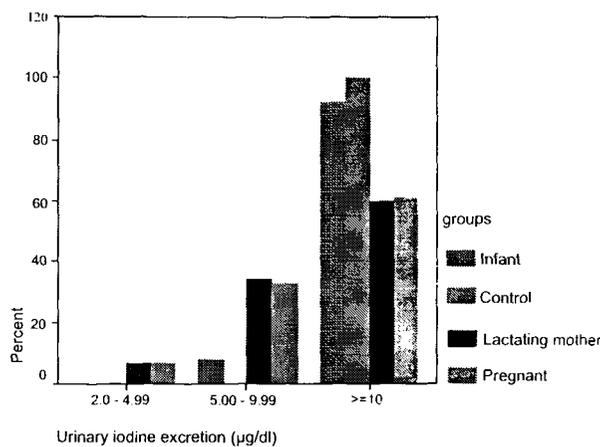
NS = Not significantly different.

S = Significant.

The median urinary iodine concentration for full term infants was median (first, second quartiles): median 27.1  $\mu\text{g/dl}$  (18.7, 35.6)  $\mu\text{g/dl}$ , whereas that of the mother who gave birth at term was median 9.30  $\mu\text{g/dl}$  (7.6, 21.6)  $\mu\text{g/dl}$ . For the preterm infants the median urinary iodine level was: median (first, third quartiles): median 25.6  $\mu\text{g/dl}$  (34.8, 11.5)  $\mu\text{g/dl}$  and median 13.0  $\mu\text{g/dl}$  (7.8, 19.5)  $\mu\text{g/dl}$  for the preterm mother. There was significant difference between the median urinary excretion of the infants and those of the mothers,  $p = 0.001$ . There was no significant difference between mothers who delivered at term and at preterm or between infants who were delivered at term and those who delivered at preterm. (Table I). Over 90% of infants had urinary iodine excretion level  $\geq 10 \mu\text{g/dl}$ . About 60% of lactating mothers and 60% of pregnant women had urinary iodine excretion values  $\geq 10 \mu\text{g/dl}$ .

The mean milk iodine content was  $21.2 \pm 6.8 \text{ mg/dl}$ . There was no correlation between breast milk iodine levels and urinary iodine levels of the infants, ( $p = 0.962$ ,  $r = 0.006$ ). The iodine content of breast milk sampled at 6 weeks ( $23.45 \pm 17.64$ )  $\mu\text{g/dl}$  and the iodine content of the milk sampled at 12 weeks ( $14.90 \pm 8.69$ )  $\mu\text{g/dl}$  showed a significant difference,  $p = 0.05$ . Over ninety percent of infants were fed breast milk with an iodine content within the normal range recommended by the WHO/ICCIDD.<sup>8</sup>

Figure II: Percent distribution of urinary iodine concentration in the different groups.



Serum FT4, and TSH levels were found to be higher for infants at six weeks after birth. (FT4 =  $20.91 \pm 5.65 \text{ pmol/L}$ ) and median TSH = 2.28 mIU/ml, (1.36, 0.86) mIU/ml, compared to levels at 12 weeks *post partum*: (FT4 =  $17.53 \pm 6.4 \text{ pmol/L}$ ) and median TSH = 2.02 mIU/ml, (0.84, 1.55) mIU/ml, (Table II) but the differences were not significant. The serum TSH levels of infants were generally higher than maternal levels. Serum FT4, and TSH levels were found to be higher for infants at six weeks after birth, Table II.

Table II: Summary of thyrotropin and free thyroxin concentrations in all the subjects.

Groups	Thyrotropin mIU/ml (median)	First quartiles	Third quartiles	Thyroxin pmol/L (mean±SD)
Infant (12 weeks)	2.03	0.84	1.55	17.53±6.41
Infant (6 weeks)	2.27	1.36	0.86	20.91±5.65
Mother (12 weeks)	1.00	0.99	3.06	12.44±0.74
Mother (6 weeks)	1.15	4.66	1.15	16.90±6.22
Pregnant	1.75	0.96	3.48	15.96±4.80
Control	1.30	3.46	1.04	19.31±4.38

## Discussion

The major finding of this study is the high urinary iodine excretion by the infants compared to the low excretion by the pregnant and lactating women. These results confirmed those of Vermiglio, *et al.*<sup>6</sup> which showed a significant reduction in urinary iodine content of pregnant and lactating women. The high urinary iodine excretion by the infants was probably due to the enhanced renal clearance and transfer of iodine from the mother to the foetus.<sup>1</sup> It had been estimated that the transfer of iodide from mother to foetus is 50 to 75ug/day.<sup>15</sup> The above factors and the increased need of thyroxin to maintain the normal metabolism in the lactating mother might be responsible for the low level of iodide in pregnancy and lactation.<sup>16</sup> However, the increased iodine was not associated with an alteration in thyroid function as expected.<sup>9</sup> It was also reported that urinary iodine excretion decreased with increasing age.<sup>7</sup> We found a similar trend in our study.

The lack of significant difference in thyroid hormones and in urinary iodine levels between term and preterm infants might be due to the fact that the measurements were taken at six to 12 weeks *postpartum* when the levels had been equalised in the infants of the same post natal age.<sup>3</sup> The milk iodine levels did not correlate with that of the infant urinary iodine levels as published by Vermiglio,<sup>6</sup> *et al.* We found the mean milk iodine level of 21.3 ±µg/dl was above the median milk iodine levels of 9.4µg/dl reported by Delange, *et al.* for women in Brussels. It was also above the reference value set by the European society for paediatric gastroenterology and nutrition,<sup>14</sup> but agreed with the proposed recommended level.<sup>1</sup> The differences could be due to the relative iodine intake by the lactating women. However, this did not reflect on the level of the thyroid hormones as reported by Paravicini, *et al.*<sup>9</sup>

In iodine sufficient region, over 95 percent of newborns have TSH levels less than 5mIU/ml as determined by TSH-IRMA<sup>10</sup>. We observed similar findings. We did not observe hypothyroidism or hyperthyroidism in any of the subjects.

## Conclusion

The results indicated a significant reduction in the urinary iodine content of pregnant women and lactating mothers but not in the urine of the infants and in the milk iodine content. The present data showed that maternal

thyroid function and urinary iodine excretion levels in pregnancy, and in newborn infants, were normal. However, the median urinary iodine excretion levels of the infants were higher than the maternal levels. The proposed recommendation set the levels almost similar.

The results therefore indicate that iodine deficiency is present in the population studied. The urinary iodine concentration in the lactating women was low and needs to be monitored. There must be constant monitoring of pregnant women to ensure that the iodization programme is yielding the benefits envisaged.

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