

IODINE DEFICIENCY DISORDER AMONG PREGNANT WOMEN IN A TERTIARY CARE HOSPITAL OF KOLKATA, INDIA

Indranil Chakraborty¹, Piyeanku Mazumdar¹, Partha Sarathi Chakraborty²,
Gopaldev Chattopadhyay³ and Kaushik Bhowmick¹

¹Department of Biochemistry, ²Department of Gynecology and Obstetrics, Medical College Kolkata, Kolkata, West Bengal; ³Bureau of Applied Economics and Statistics, Burdwan, West Bengal, India

Abstract. The present unicentric, hospital based, non-interventional, cross-sectional study was undertaken to assess the iodine status of pregnant women attending the antenatal clinic at a medical college in Kolkata, India, during the different trimesters of pregnancy and to compare their iodine status with those of age-matched non-pregnant control women. Assessment of the iodine status was based on urinary iodine excretion (UIE). Serum levels of free triiodothyronine (fT_3), free thyroxine (fT_4) and thyroid stimulating hormone (TSH) were assayed as an indirect measure of iodine status. A statistical comparison between the median values for UIE, TSH, fT_4 and fT_3 in pregnant women and non-pregnant controls revealed a significant difference between the median values for UIE ($p < 0.0047$), TSH ($p < 0.00001$) and fT_4 ($p < 0.001$). UIE and fT_4 were significantly lower and TSH was significantly higher in pregnant women than in non-pregnant controls. However, no significant difference in median values for fT_3 concentration between the groups was seen ($p = 0.4$). Only 4 cases out of 200 pregnant women had an UIE of less than the lower cut-off value for UIE recommended by the WHO corresponding to optimal iodine intake. The results indicate most pregnant subjects attending the antenatal clinic at Medical College Kolkata, India, a tertiary care institution, did not suffer from significant iodine depletion. This may be ascribed to increased awareness of this condition and the accessibility of iodized salt among the study population.

Key words: urinary iodine excretion, iodine deficiency disorder, India

INTRODUCTION

Iodine is a non-metallic element found in the human body in trace amounts and is principally responsible for synthesis of

thyroid hormones. A deficiency of this element produces a constellation of signs and symptoms collectively termed iodine deficiency disorder (IDD). IDD is characterized by mental retardation, hypothyroidism, goiter, and various other growth and developmental abnormalities (Mahesh *et al*, 1990). All groups are affected by it, but growing children and pregnant women are most vulnerable (Kapil, 1998; Kurtoglu *et al*, 2004a,b).

Correspondence: Dr Indranil Chakraborty,
Block: A/2, Flat No: 7, Uttaraman Housing Estate,
102, BT Road, Kolkata 700035, West Bengal,
India.
Tel: 0091-33-25319059
E-mail: drindranilchakraborty@rediffmail.com

IDD is a significant public health problem and is the most common cause of brain damage throughout the world (WHO/UNICEF/ICCIDD, 1992). According to the WHO, IDD afflicts about 740 million people worldwide, of which nearly 50 million suffer from some degree of brain damage. Several studies conducted around the world have shown pregnant women to be particularly vulnerable to IDD (Kibirige *et al*, 2004; Kurtoglu *et al*, 2004a,b). This has been attributed to an increased metabolic demand and other physiological adaptations in a pregnant subject (Ardawi *et al*, 2002; Neale and Burrow, 2004). A compromised iodine status during pregnancy has been found to affect the thyroid function of neonates as well (WHO/UNICEF, 1994; Dunn, 1998).

In India, IDD is present in the irrigated plains as well as the hilly regions of the sub-himalayas (Dunn, 1998). A urinary iodine excretion (UIE) of less than 10 µg/dl was found in 22.9% and 9.5% of pregnant women in the states of Delhi and Himachal Pradesh, respectively (Kapil *et al*, 1999, 2003). In Uttaranchal, a median UIE of 9.5 µg/dl was found in adolescents and pregnant women, indicating a high prevalence of IDD in this population (Pathak *et al*, 2003). In West Bengal, a study of prevalence of IDD among school children in different blocks of Bardhaman District reveal the reference population was in a transitional phase of iodine repletion with poor utilization of iodized salt (Sen *et al*, 2005).

Scarce information regarding iodine status among pregnant women in West Bengal exists in contemporary literature. These pregnant women attending the antenatal clinics are an important target group for IDD surveillance due to their high vulnerability, and their representation of the community (Kapil, 2004). In view of these facts, the present study was

conducted with an objective of assessing the iodine status of pregnant women attending an antenatal clinic at a medical college in Kolkata, India, during different trimesters of pregnancy and to compare their iodine status with those of age-matched non-pregnant control women. The three most important indicators recommended by the WHO for IDD surveillance are goiter prevalence, urinary iodine excretion and thyroid function tests (WHO/UNICEF/ICCIDD, 1992). In the present study, assessment of the iodine status was based on median UIE, serum free triiodothyronine (fT₃), free thyroxine (fT₄) and thyroid stimulating hormone (TSH).

MATERIALS AND METHODS

The present unicentric, hospital based, non-interventional, cross-sectional study was undertaken by the Department of Biochemistry in collaboration with the Department of Gynecology and Obstetrics, the Medical College of Kolkata, West Bengal, India during May 2007-April 2008. Cases were selected from pregnant women aged 15 to 45 years attending the Antenatal clinic of the Department of Gynecology and Obstetrics at the Medical College and Hospital of Kolkata. The controls were selected from apparently healthy non-pregnant women aged 15 to 45 years. Written informed consent was obtained from all participants prior to the study. The study was approved by the institutional ethics committee of the Medical College of Kolkata, West Bengal.

All preexisting cases of hypothyroidism and hyperthyroidism were excluded from the study, as were cases with acute or chronic infection, history of ingestion of certain drugs (*eg*, steroids, and iodine containing dyes). One hundred pregnant women during their first trimester, 50

Table 1
Comparison of median values for UIE, TSH, fT₄ and fT₃ between pregnant women and non-pregnant controls.

Parameters	Median value		p-value
	Cases (n=200)	Controls (n=100)	
UIE (µg/dl)	14.28	18.88	p < 0.0047
TSH (mIU/ml)	3.40	2.66	p < 0.00001
fT ₄ (ng/ml)	1.21	1.58	p < 0.001
fT ₃ (pg/ml)	3.00	3.02	p = 0.4

pregnant women during their second trimester and 50 pregnant women during their third trimester were selected as cases. One hundred non-pregnant women were selected as controls.

Spot urine samples from all subjects included in the study were collected in the morning during their visit at the antenatal clinic. The urine samples were collected in screw capped plastic bottles with toluene as a preservative and were refrigerated at 4°C. Simultaneously, venous blood samples were also collected from these subjects. UIE was assayed using the method of Dunn *et al* (1993) with the modification of Sandell and Kolthoff (1937) involving colorimetric estimation of the rate of discoloration of ceric ammonium sulphate as an inverse measure of organic iodine present. The TSH was assayed using ELISA (ELISCAN TSH, Ranbaxy India). fT₄ was assayed as using ELISA (ELISCAN fT₄, Ranbaxy India). The fT₃ was assayed using an ELISA (ELISCAN fT₃, Ranbaxy India). The data obtained was subjected to statistical analysis.

RESULTS

A statistical comparison between the median values the UIE, TSH, fT₄ and fT₃ in the pregnant women and in the non-

pregnant controls is shown in Table 1. There were significant differences in median values for UIE (p < 0.0047), TSH (p < 0.00001) and fT₄ (p < 0.001) between these two groups. However, the difference in the median value for fT₃ concentration was not significant between the groups (p = 0.4). The median values for UIE, TSH, fT₄ and fT₃ during different trimesters of pregnancy are shown in Table 2. A statistical comparison of the median values for UIE, TSH, fT₄ and fT₃ in pregnant women among the different trimesters of pregnancy is shown in Table 2.

Table 3 shows the 2.5 and 97.5 percentile values for median UIE in pregnant women and non-pregnant controls which were used as the upper and lower cut off limits of these parameters among the reference population.

DISCUSSION

Iodine status is known to be directly related to intake. The recommended daily allowance of iodine during pregnancy is 200-220 µg/day. The major role in excretion of iodine is played by the kidneys. Eighty to 90% of iodine is excreted in the urine and the rest is utilized for thyroid hormone synthesis. Urinary iodine has been shown to be a reliable indicator of

Table 2

Median values of UIE, TSH, fT_4 , fT_3 of pregnant women during different trimesters of pregnancy and significance of difference of median between different trimesters.

Parameters	Median value 1 st trimester (<i>n</i> = 100)	Median value 2 nd trimester (<i>n</i> = 50)	Median value 3 rd trimester (<i>n</i> = 50)	<i>p</i> -value for comparison between 1 st and 2 nd trimesters	<i>p</i> -value for comparison between 2 nd and 3 rd trimesters
UIE ($\mu\text{g/dl}$)	13.75	13.50	16.00	> 0.05	< 0.05
TSH (mIU/ml)	4.94	2.82	1.72	< 0.05	< 0.05
fT_4 (ng/ml)	1.10	1.42	1.12	< 0.05	< 0.05
fT_3 (pg/ml)	3.61	3.10	2.8	< 0.05	< 0.05

Table 3

2.5 and 97.5 percentile value of median UIE in pregnant women and non-pregnant control.

Cases (<i>n</i> =200)		Controls (<i>n</i> =100)	
2.5 percentile value for median UIE ($\mu\text{g/dl}$)	97.5 percentile value for median UIE ($\mu\text{g/dl}$)	2.5 percentile value for median UIE ($\mu\text{g/dl}$)	97.5 percentile value for median UIE ($\mu\text{g/dl}$)
10.2 ^a	17.7	15.0	22.5

^a 4 cases out of 200 had an UIE of <10 $\mu\text{g/dl}$.

iodine status. Determination of urinary iodine is easy and non-invasive. Thyroid status also serves as an indirect measure of iodine status.

Table 1 depicts the comparative median values for TSH, fT_4 , fT_3 and UIE between pregnant subjects and non-pregnant women in the control group with their levels of significance. On statistical analysis, a significant difference was observed for the median values for TSH ($p < 0.00001$) and fT_4 ($p < 0.001$). No significant difference in the median value of fT_3 ($p = 0.4$) between the two groups. The requirement for increased T_4 secretion increases iodine requirements during pregnancy. This need is compounded by the higher glomerular

filtration rate during gestation which enhances renal iodide clearance, leading to higher fractional urinary excretion of circulating iodide. Maternal iodine intake must be increased to supply the requirements of the fetal thyroid during the second and third trimesters. If this requirement is not met, serum T_4 falls and TSH rises. This series of events is well-documented in areas with endemic iodine deficiency or borderline iodine supply, such as Brussels (Glinioer, 1997). In that city, 70% of pregnant women were followed carefully throughout pregnancy; 20% had an increase in thyroid volume during gestation due to increased TSH (Glinioer *et al*, 1992). This contrasted with the lack of goi-

ter during pregnancy in studies in North America (Nelson *et al*, 1987). After delivery, changes in thyroid function gradually return to normal and serum TBG values reach normal levels 6 to 8 weeks postpartum.

These changes may be attributed to the physiological relationship between thyroxine-binding globulin (TBG) and serum concentrations of thyroid hormones. Fernandez-Ulnoa (2003) described the increased TBG level during pregnancy may lead to augmented binding of T_4 and T_3 . This, results in decreased fT_4 and fT_3 , thereby decreasing the negative-feedback mechanism and results in an increased serum TSH concentration (Fernandez-Ulnoa, 2003). Table 2 outlines the changes in thyroid status and UIE during the different trimesters of pregnancy. An initial increase in TSH and a decrease in fT_4 may have resulted from a transient increase in TBG and a consequently lower fT_4 , as documented by Fernandez-Ulnoa (2003). This initial response altered gradually to attain final equilibrium conditions during later stages of pregnancy was observed during the present study. In the present study, no significant difference ($p = 0.4$) was observed between median fT_3 values in cases (pregnant women: 3.00 pg/ml) and controls (non-pregnant women: 3.02 pg/ml), suggesting the signal to increase TSH must be derived from a decrease in the T_3 generated intracellularly from T_4 in the pituitary, the hypothalamus, or both (Riesco *et al*, 1997).

Urinary iodine values in varying populations have not been found to be normally distributed. Inter-individual variation of UIE is predominantly due to several factors, such as geographical area, fluid intake, and daily iodine intake. Thus, the median rather than mean UIE for a reference population has been accepted as the

norm for a population (WHO/UNICEF/ICCIDD, 1992). This parameter was used in the present study for statistical analysis. The median values for UIE in pregnant and non-pregnant women were 14.28 $\mu\text{g}/\text{dl}$ and 18.88 $\mu\text{g}/\text{dl}$, respectively, which were significantly different ($p < 0.05$). In spite of this significant difference, the median value for UIE in the reference population was significantly greater than the lower cut-off value for UIE recommended by the WHO (Gloner, 1998). Optimal iodine nutrition corroborates with a UIE between 10 $\mu\text{g}/\text{dl}$ and 19.9 $\mu\text{g}/\text{dl}$. The 2.5 percentile and 97.5 percentile for median UIE in pregnant women and non-pregnant controls was calculated (Table 3). In the present study a median UIE of 14.28 $\mu\text{g}/\text{dl}$ was obtained. However, 4 out of 200 pregnant women had a UIE of less than the lower cut-off limit of the WHO lower reference value of 10 $\mu\text{g}/\text{dl}$, suggesting they were suffering from mild iodine deficiency. Studies by Kapil *et al* (1997, 2003) 22.9% and 9.5% of pregnant women in Delhi and Himachal Pradesh, respectively, had a UIE of $<10 \mu\text{g}/\text{ml}$. A study in Uttarnchal (Pathak *et al*, 2003) found a median UIE of 9.5 $\mu\text{g}/\text{ml}$ in adolescent pregnant women indicating a high prevalence of IDD.

A study by Chakraborty *et al* (2006) concerning IDD among pregnant women attending a rural hospital in West Bengal determined UIE in this population; 74% of pregnant women had a UIE of $\geq 14.4 \mu\text{g}/\text{ml}$, and were consequently not suffering from IDD. The present study was intended as a second phase of the above study, where a stratification of the study group was made on the basis iodine status during the different pregnancy trimesters.

Pregnancy is associated with an increased demand for iodine, reflected by the lower median UIE level in pregnant women than the non-pregnant women. The

median fT_4 level in pregnant women was lower than that in non-pregnant women, presumably arising from an increase in TBG during pregnancy, associated with its augmented binding to T_4 . The results have helped confirm the iodine status of women during pregnancy is directly related to intake and increased demand due to pregnancy. The median values for UIE, fT_4 and TSH in pregnant subjects were significantly different from non-pregnant controls. However, the median FT_3 levels in the two groups were not significantly different. The median UIE in the pregnant subjects was within the reference range recommended by WHO, suggesting the population surveyed did not suffer from significant iodine depletion. This may be ascribed to an increased awareness of this condition among the study population, predominantly of urban origin. Efforts need to be sustained in this area to maintain this level of heightened awareness.

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