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Assessment of Iodine Deficiency in Pregnant Women and Neonates in the Capital Territory of Pakistan

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ABSTRACT

One of the major nutritional problems in Pakistan is the deficiency of iodine in different groups of population, e.g., pregnant women and neonates. The neonates and their expectant mothers have been significant target groups of the population to be studied for the deficiency of iodine. The objective of the present research work was to evaluate the status of iodine deficiency in neonates and their mothers in Islamabad, Pakistan. A hospital based study was carried out on two hundred sixty one pregnant women and one hundred twenty five neonates of these women, to find out iodine level among these samples. Fifty healthy and non pregnant women were used as control in the maternity and gynecological unit of the hospitals of Islamabad. The status of iodine of the pregnant and non-pregnant women was assessed by catalytic reduction method. Thyroid function was assessed by determining the concentration of TSH in the cord blood of neonates using radioimmunoassay technique, in the environmental laboratory of the Chemical and Materials Engineering Department at Pakistan Institute of Engineering and Applied Sciences (PIEAS) Islamabad. Ninety-four percent pregnant women and ninety-eight percent non-pregnant women exhibited urinary iodine concentration (UIC) between 20 µg/L to 99 µg/L respectively. It indicates that there was severe to mild iodine deficiency in population of study area. The median values of urinary iodine concentrations in the pregnant women and control group were 30.37 µg/L and 19.08 µg/L respectively. Statistically it was found that there was a significant ($p<0.05$) difference between the levels of urinary iodine concentration of non-pregnant and pregnant women. It was also found that there was a non-significant ($p>0.05$) difference in the concentration of urinary iodide between the pregnant women of different age groups. An overall 57.14% neonates exhibited TSH levels >5 mIU/L. From these results, it is concluded that the pregnant women had moderate iodine deficiency while their neonates had severe iodine deficiency. Keeping in view these results it is suggested that the practice of iodized salt utilization could be continued, and it is recommended that the screening of neonates or TSH levels should be compulsory in the iodine deficient areas.

1 Introduction

Iodine is an integral part of thyroid hormones tri-iodothyronine (T3) and tetra-iodothyronine (T4) [1]. Thyroid hormones are important for life as they are involved in the regulation of important biochemical reactions such as synthesis of proteins and different activities of enzymes in the development of brain, heart, muscle, kidney and pituitary [2]. The amount of iodine present in the human body is 15 to 20 mg out of which 70 to 80 % is situated in the thyroid gland [3]. The thyroid absorbs iodine in the quantity that is needed for sufficient thyroid hormone synthesis [4].

Diet and water are the main sources of iodine, which is primarily absorbed as inorganic anions (iodide) via gastrointestinal tract. The iodine concentration in water is normally taken as an indicator of the iodine intake. Generally, equilibrium is established between ingested iodine (such as sodium or potassium iodide) and urinary iodide excretion [5, 6]. Previous day's intake of iodine can be best estimated by determining the urinary iodide concentration because 90% of absorbed iodide is excreted in urine [7]. Thus, the iodine status in a population can be assessed by measuring the concentration of iodide in urine [8, 9].

Because of increased metabolic needs and other physiological changes within the women having pregnancy, they are at high risk of deficiency of iodine [9]. During pregnancy excretion of iodine in urine and transfer of iodine and thyroid hormones to the fetus increases. This results in an increased demand of iodine intake. Deficiency of iodine in pregnancy period also affects the neonatal thyroid function [10, 11]. For non-pregnant adults a recommended daily intake of iodine is 150 µg per day [12, 13]. For pregnant women a recommended intake of iodine should be 200 µg per day [9].

Similar studies conducted in Lahore, have shown that 63 (24.8%) pregnant women were moderately iodine deficient (UI < 50 µg /L). Whereas, about 80 (31.5%)

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pregnant women had some visible goiter and some 87 (34.2%) were using iodized salt [14]. Keeping in view this prevailing condition of decreasing iodine in population, the current research work was carried out to identify the variations in excretion of iodide in urine samples in pregnant women and their comparison with control values and to determine the thyroid stimulating hormone (TSH) levels in neonates at the time of birth.

2. Subjects and Methods

2.1 Subjects

The target population was consisted of two hundred sixty one pregnant women admitted in the ward of obstetrics at the Poly Clinic Hospital, Islamabad and Pakistan Atomic Energy Commission General Hospital, Islamabad. There were also one hundred twenty five neonates, which were born to these pregnant women. The size of the sample was limited to the pregnant women having gestation period as > 36 weeks with the reproductive age cluster of 15 to 45 years, during one calendar year. Fifty healthy, but non-pregnant women of the same age group accompanied with the patients or as visitors from Islamabad served as controls. The average age of pregnant women and non-pregnant women were 26 ± 4.88 and 29.56 ± 7.54 year, respectively. Control population was completely randomized regarding the occupation, age and lodging place.

2.2 Exclusion Criteria

Pregnant women and controls with the history of thyroid consumption of thyroid affecting medication (medicines having iodine preparations), consumption of iodized salt or having any acute or chronic ailment at the time of checkup were excluded.

2.3 Inclusion Criteria

Pregnant women who were healthy (not having acute or chronic ailment), with more than 36 weeks of pregnancy and having no history of thyroid consumption drugs and iodized salt consumption were included in the study as subjects. The samples were collected from controls on the basis of same inclusion criteria.

2.4 Sample Collection

Urine samples (5-10 ml) were collected from non-pregnant and pregnant women in plastic bottles and frozen at 4°C. Urinary iodine concentration (UIC) was analyzed in samples by the catalytic kinetic process. Process was established on the principle of the Sandell-Kolthoff reaction [15].

For neonatal serum TSH assay, cord blood samples were collected just after delivery. Four milliliter cord blood was taken in a disposable syringe by ligating the cord from the placental side and coagulated the cord blood at room temperature. The blood serum was separated using low-speed centrifuge (2000 × gravity) at room temperature for 5 minutes and stored at –20°C till analysis.

TSH was analyzed by a highly sensitive technique called as immunoradiometric assay (IRMA) which employed antibody coated tubes. There was a reaction between TSH present in the sample of the neonate and a monoclonal mouse antibody attached to the tube and I-125 radiolabelled polyclonal antibody. The collected data was statistically analyzed by using one-way analysis of variance, in Mini-tab v11 and Chi-square analysis was also performed.

3. Results

3.1 Urinary Iodine Assay Evaluation by Using Different Parameters

For iodine concentrations between 0 and 200 μg/L, the absorbance on a log scale was linear. The correlation coefficient for linearity was greater than 0.999, having six calibrators. For each assay, separate calibration curve was made. A standardized calibration curve is presented in Fig. 1. The urinary iodine assay was evaluated by different parameters given in Table 1.

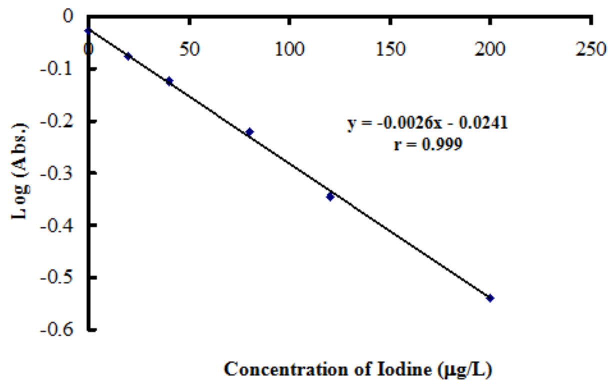

Fig. 1: Standardized calibration curve for urinary iodine assay.

Table 1: Iodine detection limit for urinary iodine assay.

Exp. No.	Mean Abs.	SD	2*SD	Mean (Abs-2*SD)	Log (Mean Abs-2*SD)	Conc. (μg/L)	Detection Limit (μg/L)
1	0.9390	0.017088	0.034176	0.904824	-0.04344	2.0	
2	0.0971	0.005	0.011	0.961000	-0.01720	1.0	1.88
3	0.9150	0.006364	0.012728	0.902272	-0.04466	2.64	

Exp. = Experiment; Abs. = Absorption; SD = Standard Deviation; Conc. = Concentration

3.1.1 Limit of detection

The limit of detection of urinary iodine assay, based on three analyses, from the zero calibrator was 1.88 μg/L (range, 1.0-2.64 μg/L) (Table 1).

3.1.2 % Recovery

Recovery of iodine added in urine samples at various concentrations was 70-104% (Fig. 2) and the average percentage recovery was 129%.

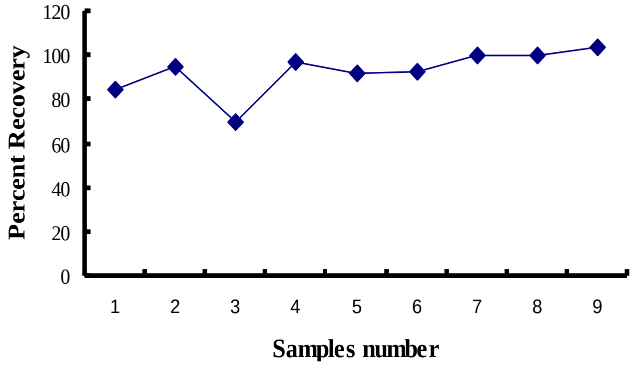

Fig. 2: Percent recovery of urinary iodide assay of nine urine samples (each closed square indicates one urine sample).

3.1.3 Precision

At different urinary iodide concentrations, the intra assay coefficient of variation was 1.91-3.57% (Fig. 3) and the inter assay coefficient of variation was 1.18-2.40% (Fig. 4). The working detection limit, i.e., the lowest concentration measured with an inter assay CV greater than 5% was as 34 μg/L.

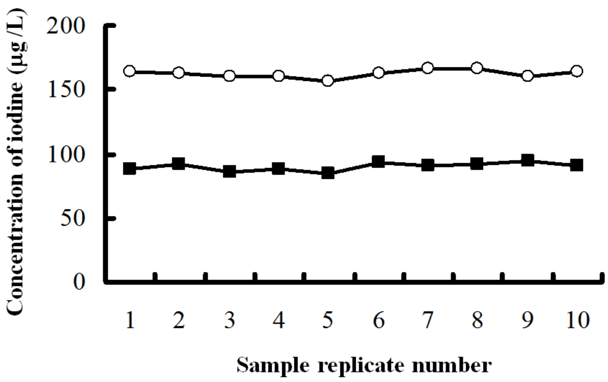

Fig. 3: Intra assay precision of two urine samples.

3.1.4 Consistency of quality control urine specimens

The mean value of QC specimens of the assay was 306 μg/L, which is close to the given value of QC range (*i.e.*, 304 μg/L). The %CV was 6.07% (less than 10%) (Fig. 5).

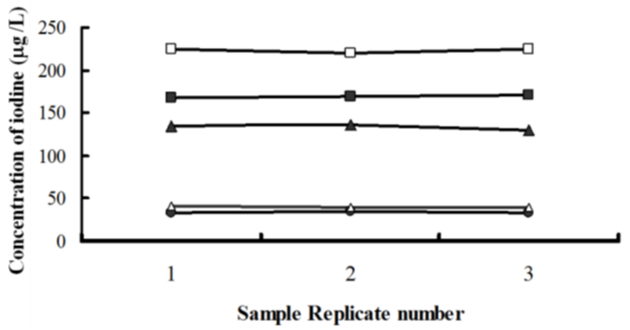

Fig. 4: Inter assay precision of five urine samples.

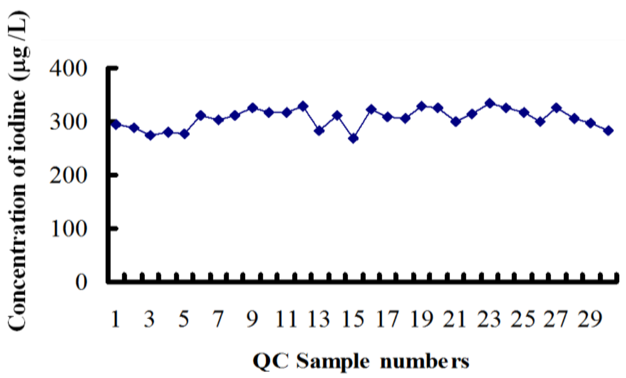

Fig. 5: Iodine level of quality control samples (each closed square indicates one urine sample) in different urinary iodine assays.

3.2 Concentration of Urinary Iodine in Pregnant Women vs Non-Pregnant Women

The urinary iodine concentrations (UIC) of the subjects were measured by using catalytic reduction method. The median iodide concentration in pregnant women was 30.37 μg/L showing range 2 to 386 μg/L, whereas in non pregnant women its concentration was 19.08 μg/L showing range 2 to 104 μg/L (Table 2).

In our investigation, normal UIC was calculated only in 6%, mild iodine deficiency in 17%, moderate deficiency in 50% and severe iodine deficiency in 27% of pregnant women. It was observed that only 2% of the control population had normal urine iodine concentration. The iodine deficiency levels were mild in 14%, moderate in 32% and severe in 52% non-pregnant women (Fig. 6). World Health Organization and International Council for the Control of Iodine Deficiency Disorders (WHO/ICCIDD) approved epidemiological criteria for assessing iodine status, which is presented in Table 3.

Fifty percent of the pregnant women had UIC between 20-49 μg/L (Table 4), almost 77% of women having pregnancy had a urinary iodide concentration less than 50 μg/L. This depicts that these women had moderate iodine deficiency (Table 3). Almost 84% of control population had a UIC <50μg/L (Table. 4).

Table 2: Median urinary iodine concentration of pregnant and non-pregnant women.

Observations	Pregnant women(N=261)	Control population(N=50)
Median urinary iodine concentration (UIC) in μg/L	30.37	19.08

3.3 *Variation in Urinary Iodine Concentration among Pregnant and Control Population of Different Age Groups*

Different age groups were formed of pregnant and non-pregnant populations. It was found that statistically no difference in UIC in these age groups within pregnant (Fig. 7) as well as within non-pregnant (control) (Fig. 8) women exists.

3.4 *Neonatal Cord Blood TSH Level at Birth*

In our study, cord blood TSH levels of one hundred twenty five neonates were assessed. Thyroid stimulating hormone (TSH) values ranged from 2.675-19.2 mlU/L, having a mean value as 3 mlU/L and a median of 5.502 mlU/L. An overall 57.14% neonates had TSH concentration >5mlU/L (Fig. 9).

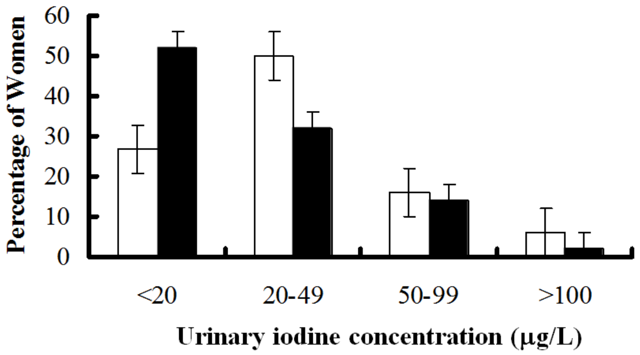

Fig. 6: Comparison of urinary iodide concentration among pregnant (open, non-filled bars) and non-pregnant (closed, filled bars) women, grouped according to different UIC.

4. Discussion

4.1 *Urinary Iodine Assay Evaluation by Using Different Parameters*

The Sandell-Kolthoff reaction has been used generally as a simple and sensitive method for the assessment of iodine in urine. Ohashi et al. [16] performed ammonium per sulfate digestion in the oven instead of heating block and then Sandell-Kolthoff reaction was performed. In contrast to our results, the limit of detection of their assay was 0.11μmol/L (ranges 0.07-1.4μmol/L), the intra assay variation was 1.7-2.0% while the inter assay variation was 4.4-4.5%. The recovery of iodine added in urine samples at various concentrations was 89-109% and the absorbance found on a log scale was linear for iodine concentration between 0 and 3.15 μmol/L.

4.2 *Concentration of Urinary Iodide of Pregnant and Non-Pregnant Women*

International Council for the Control of Iodine Deficiency Disorders (ICCIDD) had recommended that the median concentration of iodine for ideal nutrition of iodine during pregnancy should have the range in between 150-230 μg/L per day [17]. According to the standard criteria suggested by the WHO, the UNICEF and the ICCIDD [13] which was used to assess the iodine nutrition, was the urinary iodine concentration of pregnant and non-pregnant women, with a median of 30.37 μg/L and 19.08 μg/L, respectively. Different research workers have earlier testified comparable results of low iodine in pregnant women in different groups of the population [18-22].

We found that only 6% of pregnant and 2% of non-pregnant women had normal urine iodine concentration (>100μg/L) (Table 4). Our findings are supported by the observations made by Travers et al. [23], this study was conducted in the Central Coast area of New South Wales, who found that 12% of pregnant women had urinary iodide concentration of 150 μg/L. In contrast, Mezosi et al. [24] observed different levels of iodine deficiency within the pregnant women population. They found normal urinary iodide concentration in 42.9% of women; the iodine deficiency concentrations were mild, moderate and severe in 25.6%, 15.9% and 15.6% of pregnant women, respectively.

International Council for the Control of Iodine Deficiency Disorders and World Health Organization (ICCIDD /WHO) approved indicators for assessing iodine status, which are presented in Table 3. These strategies

Table 3: Epidemiological criteria* for assessing severity of iodine deficiency based on median urinary iodine concentration (UIC) and whole-blood thyroid stimulating hormone (TSH) levels.

Indicator	Target	Severe	Moderate	Mild	Normal
Median UIC (μg/L)	Women	<20	20-49	50-99	≥100
TSH >5 mlU/L	Neonates	≥40.0%	20.0-39.9%	3.0-19.9%	<3.0%

*World Health Organization and the International Council for the Control of Iodine Deficiency Disorders [8, 9].

Table 4: Distribution of urinary iodine concentration (UIC) among the pregnant women and the control population.

	Urinary iodine concentration range (µg/L)			
Observations	<20	20-49	50-99	≥100
Pregnant women (N=261)	71(27)	131(50)	43(17)	16(6)
Non pregnant controls group (N=50)	26(52)	16(32)	7(14)	1(2)

*(Values in parentheses are percentages)

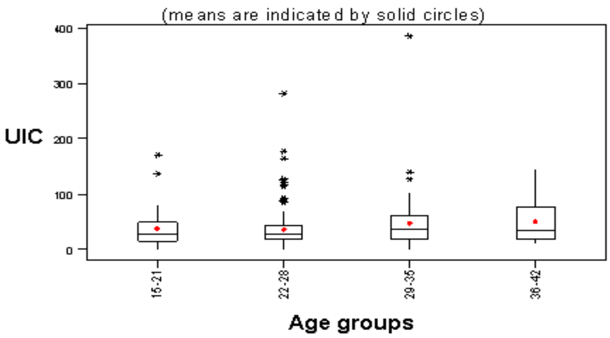

Fig. 7: Distribution of UIC in different age groups of pregnant women.

Fig. 8: Distribution of UIC in different age groups of non-pregnant (control) women.

endorsed that no more than 20 percent urinary iodide samples in a population should have an iodine concentration less than 50 µg/L [8]. In this study, almost 77% of pregnant women and 84% of control population had a UIC <50 µg/L. These results suggest that the population is at a risk of iodine deficiency as per WHO criteria. Chakraborty et al. [25] directed that the pregnant population group was iodine depleted. Travers et al. [23] stated that the median concentration of iodine for pregnant group was 85 µg/L, showing a mild deficiency of iodine. They further indicated that nearly 17 % of pregnant women had a UIC less than 50 µg/L; contrary to this, Dunn [26] reported that 6.7% pregnant women had the concentration of iodine in the range from moderate to severe deficiency.

Iodine is a crucial nutrient of thyroid hormone, which play vital role in metabolism, normal growth and development [27]. One of the reasons of iodine deficiency is insufficient intake of iodine in diet, which may result in less thyroid hormone production, which may affect different organs, body systems and results in adverse effects on health, commonly known as IDD (Iodine deficiency disorders) [28].

4.3 Comparison of Urinary Iodine Concentration of Pregnant and Control Population

Comparison of UIC of pregnant and control population was made in this study. A statistically significant difference was observed between the UIC of two groups (non-pregnant and pregnant) (X^2 = 8.96; df = 1; p< 0.05). The iodine deficiency was significantly higher in pregnant women compared to normal non pregnant women. In contrast to our findings, Chakraborty et al. [25] reported that there was no significant difference between the UIC of two groups and the status of iodine within the pregnant group remained nearly the same as in the non-pregnant group in rural hospital of west Bengal.

In the present study, although variation in UIC among pregnant women was found, no statistical significant difference (p > 0.05) was observed between the concentrations of iodine of pregnant women in different age groups (Fig. 7). Likewise, there was a statistically non-significant difference (p>0.05) between UIC levels in non-pregnant women of different age groups (Fig. 8).

4.4 Neonatal Cord Blood TSH Level at Birth

International Council for the Control of Iodine Deficiency Disorders and World Health Organization (ICCIDD / WHO) approved epidemiological criteria for assessing iodine status, which are presented in Table 3. Previously it has been reported that, not more than 3 percent of neonates should have blood TSH concentration greater than 5 mlU/L [8]; however, present results show that 57.14% neonates had TSH values >5mlU/L (Fig. 9), whereas in the study of Travers et al. [23] 18 newborns (2.2%) were found with TSH values >5mlU/L. On the other hand, Chakraborty et al. [25] found that 2.9% neonates had cord blood TSH values >5mlU/L.

Study conducted in Lahore by Elahi et al. [14], have shown that approximately 79.5% of pregnant women were found to have iodine deficiency, out of that about 24.8% were moderately iodine deficient, which can potentially let the mothers and neonates to develop thyroid disorders.

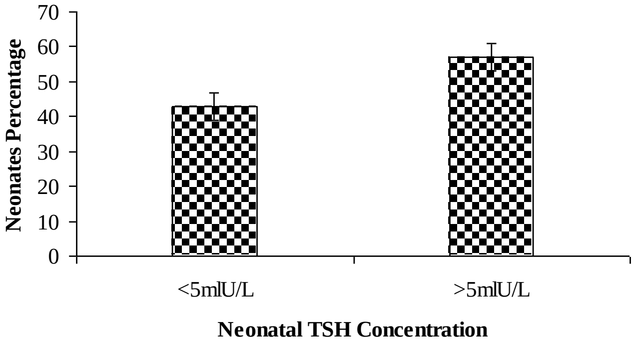

Fig. 9: TSH level in the neonatal cord blood.

Due to the prevailing condition of iodine deficiency in Pakistan, especially in pregnant women and its effects on neonates there is dare need of revising practices for the diagnosis, evaluation and treatment of thyroid during pregnancy. Higher rate of miscarriage, premature delivery, and low intelligent quotient (IQ) of baby is also associated with hypothyroidism [29]. This requires the screening of all cases of pregnancies for iodine deficiency at 1st trimester of pregnancy with subsequent treatment [30].

Kazi et al., [31] investigated about level of iodine, selenium and iron in samples of pregnant women and their neonates in Pakistan. They had found significantly low levels of these elements in serum and urine samples of these subjects. They had also highlighted the effect of iodine deficiency on pregnant women and their neonates. Thus, they had suggested that a simple elemental analysis of urine samples of pregnant women could reveal iodine deficiency and it can simply be treated by supplements, which may prevent pregnancy complications. Mil et al. [32] also investigated about the severe effects of iodine deficiency on children by evaluating the high association of low iodine concentration in urine during early pregnancy and impaired executive functioning in children. Keeping in view the results of present study and high association of low iodine level during pregnancy on neonatal development, it can be inferred that there is a dire need to conduct further such studies, even at more advanced level and to conduct a campaign for the awareness of peoples to increase use of iodine and include iodine rich items in their food, especially during pregnancy.

5. Conclusions

From these findings, it is concluded that pregnant women have moderate iodine deficiency while their neonates have severe iodine deficiency. Keeping in view these results it is suggested that the practice of iodized salt utilization should continue and it is recommended that the screening of neonates by determining the levels of TSH should be compulsory in the iodine deficient areas.

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