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Abstract:

Background: Iodine deficiency disorders (IDD) are common nutritional problem globally. All groups of people are affected by it, but the pregnant women and their neonates are most vulnerable. **Objectives:** This study was carried out to see the iodine status of pregnant women using median urinary iodine concentration (MUI) as a measure of outcome. **Methods:** This cross sectional observational study assessed the MUI in casual urine samples from 225 pregnant women (75 pregnants from each trimester) and 75 non-pregnant healthy controls. The urinary iodine content was estimated in urine sample using the method of Dunn et al. with the modification of Sandell & Kolthoff (wet digestion method). **Results:** Median value of urinary iodine in pregnant women was 48.21Ug/L compared to $52.27\boxtimes g/L$ in control group. Mean (\pm SEM) urinary iodine was 51.61 ± 3.41 in pregnant and 61.43 ± 5.54 in non-pregnant women (p=NS). Lowest urinary level was found in 1st trimester (47.42 ± 4.60) in comparison to 2nd (57.89 ± 7.60) and 3rd (49.51 ± 5.08) trimester (p=0.090). Considering the WHO recommended cut-off value ($<150\boxtimes g/L$), more than 90% of pregnant women in all trimesters were deficient for iodine nutrition. There was no statistical difference for urinary iodine (UI) either in the goitrous groups (p=0.224) or in the non-goitrous groups (p=0.171). UI level did not correlate nor seemed predictable by any of variables as: age of mother, socioeconomic status, gravida, gestational weeks or presence of goiter. **Conclusions:** This study demonstrated that the pregnant as well as non-pregnant women are markedly iodine deficient. Further studies in national level are needed to establish the status and to elucidate the cause and find out ways to correct the problem.

Key words: iodine, pregnancy, gestation.

Introduction:

Iodine is an essential micronutrient required for thyroid hormone synthesis. Its role in fetal and early childhood brain development is emphasized by studies showing iodine deficiency in pregnancy associated with stunted growth and neuromotor, intellectual, behavioral, and cognitive impairment, as well as, cretinism in severe cases.^{1,2} The outcome indicators of iodine nutrition in a community include the goiter rate and median urinary

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iodine (MUI) in school children (age 6-12 years), serum TSH in neonates, and thyroglobulin in the general population. The key indicator of population iodine nutrition recommended by the World Health Organization (WHO) and the International Council for Control of Iodine Deficiency Disorders (ICCIDD) is the determination of median urinary iodine concentration in a representative sample of school-aged children.³ The majority of dietary iodine (>90%) is excreted in the urine. Urine iodine excretion (UIE) is largely a passive process dependent on glomerular filtration rate (GFR).⁴ The UIE in a non-pregnant individual on a stable diet represents a

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dynamic equilibrium between dietary intake, thyroidal iodine extraction, the total body thyroid hormone pool, and GFR. During normal pregnancy, GFR increases within the first month following conception, peaking by the end of the first trimester by approximately 40-50% above pre-pregnant levels.5 Hence, pregnancy can be expected to result in increased renal iodine loss. Increased ioduria during early pregnancy, resulting from increased GFR is likely to be the explanation for the potential overestimation of iodine nutrition in pregnancy, using UIE. This has the capacity to conceal the degree of iodine deficiency, which only becomes fully evident in these subjects in the later stages of pregnancy. Epidemiological criteria based on the WHO, UNICEF and ICCIDDs guidelines for assessing iodine nutrition recommend the median or range in urinary iodine excretion for pregnant women.⁶ Wet digestion method of urinary iodine measurement has been unanimously accepted as a method of urinary iodine measurement in population studies.⁶ The reference ranges recommended in children would not be adequate for optimum iodine nutrition in pregnancy. Taking these physiological changes into consideration, the WHO and the American Thyroid Association have recommended higher pregnancy-specific urinary iodine ranges^{6,7} (Table-I).

In spite of global universal iodination program from 1993, urinary iodine is still low in Bangladeshi population. The results of survey conducted by UNICEF and ICCIDD in Bangladesh during 1993 (70.2%), 1999 (45.6%) and 2005 (38.6%) showed iodine deficiency that presented still alarming picture of iodine deficiency in the country especially during pregnancy.6 This study was conducted to know the iodine nutrition status of clinically euthyroid pregnant women in all trimesters of pregnancy as well as healthy adult women, so that we can ensure adequate iodine nutrition in pregnancy to overcome adverse maternal as well as fetal outcome.

Methods:

This cross sectional observational study was conducted in the department of Endocrinology and department of Obstetrics & Gynaecology of Bangabandhu Sheikh Mujib Medical University (BSMMU), from October 2012 to March 2014, after due approval from Institutional Review Board to evaluate iodine nutrition status at different trimesters of pregnancy and to compare their iodine status with that of non-pregnant women. 75 consecutive women (age group of 20 to 35 years) of each trimester of pregnancy (total 225) attending the antenatal clinic were recruited after informed voluntary consent. 75 non-pregnant, non-lactating, age-matched, adult female attendants accompanying patients in the clinic were recruited as controls. Pregnant women with known thyroid abnormalities, with chronic systemic disease (eg. bleeding diathesis, CKD, CLD etc) or history of taking any drug that interfere thyroid function test (e.g. Phenytoin, Lithium, Glucocorticoids etc.) were excluded from the study. Informed written consents were obtained from all subjects. A single morning sample of urine was collected from each participant in a screw capped plastic bottle and stored at -20°C in the laboratory till analysis. Urinary iodine content was estimated by the wet digestion method based on the Sandell-Koltoff reaction.8 The median urinary iodine concentration was defined as a concentration of iodine in a spot urine sample and the results were expressed as micrograms per liter (μ g/l). Data were analyzed using SPSS (version 22.0). P value ≤0.05 was considered significant.

Results:

Two hundred twenty five (n=225) pregnant women of different trimesters and 75 non-pregnant control women were the subjects of study. The mean (\pm SD) age of the pregnant women was 25.53 \pm 4.55 years compared to 25.95 \pm 4.09 years in non-pregnant women. Most of the pregnant women belonged to occupation as house wife (71.11%) whereas controls as service holders (65.34%). Around 50% of subjects in both groups were of average socioeconomic status whereas about 37.8% of pregnant

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women were of good socioeconomic status. Goiter was present in higher frequency in pregnant (34.2%) than non-pregnant women (25.3%). [Table- II].

Table-III displayed the iodine level of the study subjects. Median value of urinary iodine in pregnant women was $48.21 \boxtimes g/L$ in comparison to $52.27 \boxtimes g/L$ in controls. Mean (\pm SEM) urinary iodine was not statistically difference between pregnant and non-pregnant women (pregnant vs. non-pregnant 51.61 ± 3.41 vs. 61.43 ± 5.54 , p=NS). Median urinary iodine concentration was found to be $48.21 \boxtimes g/L$ in pregnant women compared to $52.27 \boxtimes g/L$ in non-pregnant women whereas mean values were 51.61 ± 3.41 and $61.43\pm5.54 \boxtimes g/L$ respectively (p=0.412), all of which were far below the recommended level.

Table-1V displayed the mean (\pm SEM) and median values of urinary iodine in different trimesters of pregnant women, the lowest mean urinary iodine level was found in 1st trimester (47.42 \pm 4.60) in comparison to 2nd (57.89 \pm 7.60) and 3rd (49.51 \pm 5.08) trimester (p=0.029). However, median value in 2nd and 3rd trimester was similar (40.90 vs. 40.11), though it was slightly lower in 1st trimester (35.37).

Table-V depicted the frequency for iodine nutrition status under different cut-off values for the pregnant women in different trimesters. Considering WHO recommended cut-off value (<150 \exists g/L), more than 90% percent of pregnant women in all trimesters were deficient for iodine nutrition, indicating virtually all pregnant women deficient for iodine nutrition. Considering cut-off value at 100 \exists g/L as for non-pregnant, 80-85% of women were found deficient for iodine nutrition. Among all the subjects, more than 60% were moderately (<50 \exists g/L) deficient while about 20% were severely (<20 \exists g/L) deficient for iodine nutrition.

Mean (\pm SEM) value of UI was compared among trimesters and non-pregnant women in light of the presence or absence of goiter. As shown in Table VI, there was no statistical difference for UI among the trimesters, neither in the goitrous group (p=0.224) nor in the non-goitrous group (p=0.171). There was no statistical difference for

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UI between goitrous and non-goitrous within each trimester and non-pregnant women (p=NS for all compared groups).

| Table-I | | | |
|--|--|--|--|
| WHO and American Thyroid Association recommended | | | |
| urinary iodine in pregnancy ⁶ . | | | |

| Median urinary iodine (µg/L) | Iodine intake |
|------------------------------|--------------------|
| <150 | Insufficient |
| 150-249 | Adequate |
| 250-499 | Above requirements |
| >500 | Excess |

Table-II Characteristics of pregnant women

| | Variables | Pregnant | Non- pregnant |
|--------------------|-------------|------------|------------------|
| N=300 | 225 | 75 | |
| Age (Mean±SD) | 25.53±4.55 | 25.95±4.09 | |
| Occupation | House wife | 160(71.11) | 18(24.0) |
| | Service | 55(24.44) | 49(16.3) |
| | Student | 10(4.44) | 8(10.67) |
| Socioeconomic | | | |
| status | Good | 85(37.8) | 23(30.7) |
| | Average | 108(48.0) | 38(50.7) |
| | Poor | 32(14.2) | 14(18.7) |
| Gravida | lst gravida | 83(36.9) | |
| | 2nd gravida | 91(40.4) | |
| | 3rd gravida | 51(22.7) | |
| Presence of goiter | 77(34.2) | 19(25.3) | |

(Within parenthesis are percentages over column total)

Table-III

Iodine nutrition status in pregnant and non-pregnant women

| Subjects | Urinary iodir | ie (µg/L) |
|------------------|---------------|-----------|
| <u></u> | Mean±SEM | Median |
| Pregnant women | 51.61±3.41 | 48.21 |
| Non-pregnant wor | men61.43±5.5 | 452.27 |

| Р | 0.412 | æ | | |
|--|-------|---|--|--|
| Table-IV | | | | |
| Iodine nutrition status in different trimesters of | | | | |
| pregnancy | | | | |
| - | | | | |

| Trimester | Urinary iodine (µg/L) | | |
|---------------|-----------------------|--------|--|
| | Mean±SEM | Median | |
| 1st trimester | 47.42±4.60 | 35.37 | |
| 2nd trimester | 57.89±7.60 | 40.90 | |
| 3rd trimester | 49.51±5.08 | 40.11 | |
| р | 0.090 | | |

by one-way ANOVA and using LSD at 0.05 1st trimester vs. 2rd trimester: p = 0.0291st trimester vs. 3rd trimester: p=0.296

Table -V

Iodine nutrition status under various cut-off values in different trimester of pregnancy

| Trimester | Urinary iodine (μg/L) <20μg/L<50 μg/L <100 μg/L<150 μg/L | | |
|-------------------------|---|-----------|--|
| | | | |
| 44 | | (WHO ref) | |
| 1st trimester (n=75) | 18(24.0) 53(70.7) 66(88.0) | 73(97.3) | |
| 2nd trimester (n=75) | 18(24.0) 46(61.3) 62(82.7) | 70(93.3) | |
| 3rd trimester (n=75) | 16(21.3) 51(68.0) 68(90.7) | 74(98.7) | |
| Total (N=225) | 52(23.1) 150(66.7) 196(87.1) | 217(96.4) | |

 Table -VI

 Iodine nutrition and goiter status in pregnant women

| Subjects | Goitrous Urinary iodin Mean (µg/L, = | Non-goitrous e concentration, ±SEM) | р |
|----------------------------|--|---|-------|
| 1st trimester (n=36,39) | 45.17±5.57 | 49.51±7.26 | p>0.5 |
| 2nd trimester (n=17,58) | 39.36±8.55 | 63.32±9.42 | p>0.5 |
| 3rd trimester (n=24,51) | 51.70±11.25 | 48.49±5.37 | p>0.5 |
| Non-pregnant | 72.25±12.5 | 57.76±6.09 | p>0.5 |

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(n=19,56) **Discussion :**

In our study, it was found that virtually all studied subjects were iodine deficient especially when considered on the basis of WHO recommended cut-off for pregnancy and not predictable by any of the factors as age of mother, socioeconomic status, gravida, gestational weeks or presence of goiter. Iodine requirements are exacerbated by the demands of pregnancy. Newly established recommendations state that pregnant women should consume 250 g of iodine daily, and the corresponding population median UI excretion among pregnant women should be 150-249.9 g/L after considering the metabolic needs of iodine to support thyroid status of the mother and developmental needs of foetus.9 In our study, median UI was considerably lower both in pregnant women (48.21\2/L) and in non-pregnant women (52.27^[]g/L). Mean (±SEM) urinary iodine was not statistically different between pregnant and non-pregnant. However, the mean (±SEM) and median values of urinary iodine in different trimesters of pregnant women, the lowest urinary iodine level was found in 1st trimester (47.42±4.60) in comparison to 2nd (57.89±7.60) and 3^{rd} (49.51±5.08) trimester (p=0.090). On the other hand, median value in 2nd and 3rd trimester was similar (40.90 vs. 40.11) though it was far lower for 1st trimester (35.37). Based on the results for median UI, pregnant women in all trimesters were found much deficient for iodine than that shown in national data. On national survey, median gestational UI was 142\g/L, with 41% of surveyed women having a UI level below 100 \vee g/L.10

Although most national surveys target iodine status of school-age children, and therefore provided limited information about iodine status during pregnancy, a number of recent studies have focused specifically on the iodine status of pregnant women. These studies have typically demonstrated compromised iodine status among pregnant women throughout South Asia11, Europe11, Australia12 and other parts of World including Bangladesh. In National survey of Bangladesh showed that iodine deficiency (UIE< $100\mu g/L$) was 68.9%, 43.1% on 1993, 1999 respectively and the prevalence of iodine deficiency was 33.8% in children and 38.6% in women and 35.6% in pregnant women.10 Shamim et al. (2012) found that

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median UI concentrations were 66 and 55 μ g/L in early and late pregnancy, respectively. UI concentrations <150 μ g/L was found in about 80% of women at both stages of pregnancy.

In India, Nina et al. (1993) found the total goiter rate was 45%. The urinary iodine excretion pattern revealed mild iodine deficiency. 55% of women had <50 μ g/L and 13.2% had <20 μ g/L. In Pakistan, Elahi et al.15 found median value of UIE was 67 μ g/L whereas frequencies for UIE <100 μ g/L, 50-99 μ g/L and <50 μ g/L were 79.5%, 68.8% and 24.8% of pregnant women respectively. In Nepal, Agrawal et al.16 found that 28.88% pregnant women had UIE<150 μ g/L and frequency for <100 μ g/L was 22.9%. However, our results showed much lower values for mean and median UI in pregnant mothers in all trimesters. Among all pregnant women, 34.2% had slightly visible goiter. The difference in UIE between goitrous and non-goitrous pregnant women was not significant.

About 34 percent of pregnant and 25 percent non-pregnant women of this study subjects had slightly visible goiter. Reasons for this high prevalence of goiter might be due to most of the women were born before the iodized salt became widely available in Bangladesh and in pregnancy the thyroid gland become slightly enlarged. Mean±SEM value of UI was compared among trimesters and non-pregnant women in light of presence or absence of goiter. There was no statistical difference for UI among the trimesters, neither in the goitrous group nor in the non-goitrous group in the present study. Likewise, there was no statistical difference for UI between goitrous and non-goitrous within each trimester and non-pregnant women.

This study also revealed that UI level did not correlate with age of mother, socioeconomic status, gravida, gestational weeks or presence of goiter. Similarly, when dichotomized on the basis of cut-off value at 100\vee g/L, iodine nutrition status was not found to be related to age of mother, socioeconomic status, gravida, gestational weeks

or goiter. Conclusions:

This small hospital-based study of pregnant women observed iodine nutrition status deficient during various trimesters of pregnancy. Therefore, we conclude that studies at mass scale are needed to elucidate the cause and to find the ways of correction of the problem.

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