Iodine Nutrition Status in Clinically Euthyroid Pregnant Women in Different Trimester Attending in Tertiary Care Hospital

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Iodine deficiency disorders (IDD) are global public health problem. All groups of people are affected by it, but growing children and pregnant women are most vulnerable. This study was aimed to determine the urinary iodine status of clinically euthyroid pregnant women during different trimesters of pregnancy. This cross sectional observational study comprised of 114 pregnant women in different trimesters and 38 healthy controls. Each trimester included 38 subjects. The urinary iodine content was estimated in spot urine sample using the method of Dunn et al. with the modification of Sandell & Kolthoff (wet digestion method). Most of the pregnant women belonged to occupation as house wife (68.4%) whereas most of the controls were service holder (94.7%). Cent percent studied subjects were taking packet salt. Median value of urinary iodine in pregnant women was 40.65 μg/L compared to 37.30 μg/L in control group. Mean (±SEM) urinary iodine was not statistically different between pregnant and non-pregnant women (50.07±4.65 vs. 54.87±8.80; p = 0.615). Considering the WHO recommended cut-off value (<150 μg/L), cent percent of pregnant women in 1st and 3rd trimesters and about 90% in 2nd trimester were deficient for iodine nutrition. Even when cut-off value considered at 100 μg/L, again cent percent of 1st trimester women whereas around 80-85% of 2nd and 3rd trimester women found deficient for iodine nutrition. Among all the subjects more than 60% were moderately (<50 μg/L) deficient while about 25% were severely (<20 μg/L) deficient for iodine nutrition. 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). UI level did not correlate with nor seemed predictable by any of variables as: age of mother, socioeconomic status, gravida, gestational weeks or presence of goiter. This study demonstrated that UIC during pregnancy as well as in non-pregnant women is markedly lower than those previously reported in our country. Further studies are needed to elucidate the cause and find out ways to correct the problem.

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Introduction

Iodine deficiency disorders (IDD) are major global public health problem. According to the latest estimate, almost 2 billion people worldwide have inadequate iodine intake, of which 313 million are in the south-east Asia. Bangladesh is one of the countries most affected by iodine deficiency disorders. The alleviation of soil by numerous rivers, together with heavy rainfall and annual flooding constantly washes iodine from the soil and makes the country extremely vulnerable to iodine deficiency.[1] Severe iodine deficiency, even mild-to moderate iodine deficiency in pregnancy has adverse effects on obstetric and neonatal outcomes due to inadequate thyroid hormone production. Although fetal thyroid starts functioning from 12 weeks onwards, depends entirely upon the availability of iodine transferred from maternal circulation. Thyroid hormone plays an essential role in neuronal migration, myelination, and synaptic transmission and plasticity. Animal models have demonstrated that even mild and transient maternal hypothyroxinemia during pregnancy can disrupt neuronal migration in the fetus, resulting in ectopic neurons in different cortical layers including the subcortical white matter and hippocampus.[2] Therefore, iodine deficiency is associated with adverse effects on the fetus including congenital anomalies, decreased intelligence, and neurological cretinism (which includes spasticity, deaf mutism, mental deficiency, and squint). Severe iodine deficiency is also linked to intellectual development in early childhood in the absence of overt mental retardation.[3,4] A 2005 meta-analysis of Chinese studies comparing intelligence quotient (IQ) of children living in naturally iodine-sufficient areas to children living in severely iodine deficient areas found that the IQ of iodine-sufficient children, on average, was 12.45 points higher.[5] In spite of universal iodination program from 1993, urinary iodine is still low. The results of survey conducted by UNICEF and ICCIDD in Bangladesh during 1993 (70.2%), 1999 (45.6%) and 2005 (38.6%) show iodine deficiency that presented still alarming picture of iodine deficiency in the country especially in pregnancy. 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 comprised of 114 pregnant women (38 from each trimester) recruited on referral basis from the antenatal clinic/outpatient department of Obstetrics & Gynecology as well as from the department of Endocrinology of BSMMU from March, 2013 to March, 2014 and control group comprised of 38 apparently healthy non-pregnant and non-lactating women included in the present study with inclusion and exclusion criteria. Characteristics of study subjects are shown in table-I. Written informed consent was taken from patient / husband after complete explanation of the utility of this study. All patients were interviewed by structured questionnaire. 5 ml spot urine sample was collected from each patient and control subjects in screw capped plastic bottles, preserved in eppendrofs in duplicates under -20^{o} C before analysis of iodine in department of Designated Reference Institute for Chemical Measurements (DRiCM) of Bangladesh Council of Scientific and Industrial Research (BCSIR), Dhaka. The urinary iodine content was estimated using the wet digestion method of Dunn et al (1993) with the modification of Sandell and Kolthoff (1937). Data from the study was analyzed using computer based SPSS Program (version 13.0 for Windows supplied by SPSS lnc.

2003, Mapinfo Corp. NY, USA). Results are presented as means (±SD), and median unless mentioned otherwise. Iodine nutrition status was assessed by using cut-offs and status expressed in frequencies. Iodine levels in various trimesters were compared by ANOVA or Student's t- test with Bonferroni adjustment. Between control and pregnant mothers, iodine level was compared by unpaired Student's t- test. Frequencies of iodine deficiency were compared between control group and pregnant mothers by Chi-square test. Relationships of iodine level with gestational age, age of mothers etc were analyzed by Pearson's linear correlation. After dicotamazing the iodine level by cut-off value, multiple regression was done to see impact of various factors on iodine status. All statistical tests was considered statistically significant whenever $P \leq 0.05$. Prior to the commencement of this study, the research protocol was approved by Institutional Review Board (IRB) of BSMMU, Dhaka.

Results

The present study compared 114 pregnant women of different trimesters and 38 age matched non-pregnant subjects for iodine nutrition status.

Characteristics of the studied subjects

As showed in table-I mean (±SD) age of the pregnant women was 26±4.7 years compared to 26±3.7 years in non-pregnant women (p = 0.935). Most of the pregnant women belonged to occupation as house wife (68.4%) whereas most of the controls were service holder (94.7%) (p < 0.001). About 50% of subjects in both groups were of average socioeconomic status whereas about 30% of pregnant women were of good status and 30% of non-pregnant were of poor status (p = 0.190). There was no statistical difference of parity between two groups of subjects (p = 0.188) nor there any difference for presence of goiter (pregnant vs. non-pregnant: 32.5% vs. 31.6%, p = 0.545).

Table I: Characteristics of the studied subjects

Variables		Pregnant	Non-pregnant	p
N=152		114	38	
Age (Mean±SD)		26±4.7	26±3.7	0.935
Occupation	House wife	78(68.4)	0	<0.001
	Service	26(22.8)	36(94.7)	
	Student	10(8.8)	2(5.3)	
Socioeconomic status	Good	34(29.8)	7(18.4)	
	Average	58(50.9)	19(50.0)	0.19
	Poor	22(19.3)	12(31.6)	
Gestational age (Mean±SD, wks)		20.5±9.8	-	
Gravida	1st gravida	43(37.7)	-	
	2nd gravida	49(43.0)		
	3rd gravida	22(19.3)		
Parity	0 parity	53(46.5)	23(60.5)	
	1st parity	49(43.0)	10(26.3)	0.188
	2nd parity	12(10.5)	5(13.2)	
Presence of goiter		37(32.5)	12(31.6)	0.545

Within parenthesis are percentages over column total

Mean and median of urinary iodine

Table-II displayed the iodine level of the study subjects. Median value of urinary iodine in pregnant women was 40.65 µg/L in comparison to 37.30 µg/L in controls. Mean (±SEM) urinary iodine was not statistically difference between pregnant and non-pregnant women (pregnant vs. non-pregnant 50.07±4.65 vs. 54.87±8.80; p = 0.615).

Table II: Iodine nutrition status in pregnant and non-pregnant women

Subjects	Urinary iodine (µg/L)	
	Mean±SEM	Median
Pregnant women	50.07±4.65	40.65
Non-pregnant women	54.87±8.80	37.3
p	0.615	

Table III displayed the mean (±SEM) and median values of urinary iodine in different trimesters of pregnant women, the lowest urinary level was found in 1st trimester (37.82 ± 4.30) in comparison to 2nd (62.77 ± 11.31) and 3rd (49.63 ± 6.43) trimester (p = 0.090). However, median value in 2nd and 3rd trimester was similar (41.24 vs. 41.67) though it was far lower for 1st trimester (35.09). Mean value of urinary iodine in 1st trimester was significantly (p = 0.029) lower than that of 2nd trimester as well as that of 3rd trimester though not significant (p = 0.296).

Table III: Iodine nutrition status in different trimester of pregnancy

Trimester	Urinary iodine (µg/L)	
	Mean±SEM	Median
1st trimester	37.82±4.30	35.09
2nd trimester	62.77±11.31	41.24
3rd trimester	49.63±6.43	41.67
p	0.090	

by one-way ANOVA and using LSD at 0.05
1st trimester vs. 2rd trimester: p = 0.029
1st trimester vs. 3rd trimester: p=0.296

Iodine nutrition status under various cut-offs

Table IV depicted the frequency for iodine nutrition status under different cut-off values for the pregnant women in different trimesters. Considering the WHO recommended cut-off value (<150 µg/L) cent percent of pregnant women in 1st and 3rd trimesters and about 90% in 2nd trimester were deficient for iodine nutrition, indicating virtually all pregnant women deficient for iodine nutrition. If cut-off value considered at 100 µg/L, again cent percent of 1st trimester women whereas around 80-85% of 2nd and 3rd trimester women were found deficient for iodine nutrition. Among all the subjects more than 60% were moderately (<50 µg/L) deficient while about 25% were severely (<20 µg/L) deficient for iodine nutrition.

Table IV: 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 (WHO)
1st trimester (n=38)	11(28.5)	29(76.3)	38(100)	38(100)
2nd trimester (n=38)	9(23.7)	20(52.6)	31(81.6)	35(92.1)
3rd trimester (n=38)	8(21.1)	25(65.8)	33(86.8)	38(100)
Total (N=114)	28(24.6)	74(64.9)	102(89.5)	111(97.4)
p	0.718	0.095	0.026	0.046

Within parenthesis are percentages over row total; by χ^2 test

Iodine nutrition in contrast to presence of goiter

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 (p = 0.224) nor in the non-goitrous group (p = 0.171). Likewise there was no statistical difference for UI between goitrous and non-goitrous within each trimester and non-pregnant women (p = NS for all compared groups).

Table V: Iodine nutrition and goiter status

Subjects	Goitrous	Non-goitrous	p
Urinary iodine concentration, Mean (µg/L, ±SEM)			
1st trimester (n=20,18)	42.34±6.37	32.79±5.65	0.274
2nd trimester (n=9,29)	46.86±14.82	67.70±14.19	0.444
3rd trimester (n=8,30)	37.17±5.19	52.95±7.96	0.324
Non-pregnant (n=12,26)	72.12±19.65	46.89±8.93	0.185
p	0.224	0.171	

Analysis by ANOVA using LSD at 95% level 1st trimester vs. 2nd trimester: p=0.031 for non-goitrous

Correlations and regression

UI level did not correlate with any of variables of: age of mother, socioeconomic status, gravida, gestational weeks or presence of goiter. Similarly, when dichotomized on the basis of cut-off value at 100 μg/L, iodine nutrition status was not found to be related age of mother, socioeconomic status, gravida, gestational weeks and goiter.

Table VI: Correlations between different variables under study (Pearson or Spearman)

Variables	r	P
Iodine vs. Age	-0.088	0.280
Iodine vs. Gestational wks	0.107	0.257
Iodine vs. Socioeconomic status	0.043	0.599
Iodine vs. Gravida	0.010	0.917
Iodine vs. Goiter	0.012	0.885

Table VII: Multiple régressions analysis of different variables

Variables	β	T	p
Constant		0.569	0.571
Age	-0.022	-0.203	0.839
Socioeconomic status	0.033	0.332	0.740
Gravida	0.031	0.294	0.769
Gestational wks	-0.058	-0.573	0.568
Goiter	-0.138	-1.317	0.191

Discussion

This study represents evaluation of iodine nutrition status in clinically euthyroid pregnant women at their 1st, 2nd and 3rd trimester of pregnancy and compared with age-matched non-pregnant women. This is a tertiary hospital based study and not representing the community as a whole. Therefore observation may not represent the iodine nutrition status in pregnant and non-pregnant women of the whole community. It was found that almost cent percent of the 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 of age of mother, socioeconomic status, gravida, gestational weeks or presence of goiter.

Adequate supply of iodine is essential to maintain the normal thyroid function. It is especially important particularly during pregnancy where the iodine requirement is increased due to enhanced renal clearance of iodine, transfer of iodine from mother to fetus as well as greater need of iodine to make more thyroid hormones to support the increased metabolic demand in pregnancy. Therefore it is not unlikely for pregnant ladies to develop relative iodine deficiency during pregnancy unless specific dietary care is taken in this regard.[6] Bangladesh is a country with known iodine insufficiency but with a government-mandated and functioning salt iodization program. Iodine requirements are exacerbated by the demands of pregnancy. Newly established recommendations state that pregnant women should consume 250μg of iodine daily, and the corresponding population median UI excretion among pregnant women should be 150-249.9μ g/L after considering the metabolic needs of iodine to support thyroid status of the mother and developmental needs of foetus.[7] In our study, median UI was considerably lower both in pregnant women (40.65μg/L) and in non-pregnant women (37.30μg/L). Mean (±SEM) urinary iodine was not statistically difference 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 (37.82±4.30) in comparison to 2nd (62.77±11.31) and 3rd (49.63±6.43) trimester (p=0.090). However, median value in 2nd and 3rd trimester was similar (41.24 vs. 41.67) though it was far lower for 1st trimester (35.09). Mean value of urinary iodine in 1st trimester was lower than that of 2nd trimester

as well as that of 3rd trimester. 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 data, median gestational UI was 142µg/L, with 41% of surveyed women having a UI level below 100 µg/L.[8]

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 Asia, Europe, Australia and other parts of World including Bangladesh. Those studies showed that iodine deficiency (UIE< 100µg/L) was 68.9%, 43.1% on 1993, 1999 and the prevalence of iodine deficiency was 33.8% in children and 38.6% in women and 35.6% in pregnant women in National survey of Bangladesh.[9] Shamim et al.[10] found that median UI concentrations were 66 and 55 µg/L in early and late pregnancy, respectively. UI concentrations <150 µg/L was found in about 80% of women at both times of pregnancy.

Ara et al.[11] found the median UIC of adolescent girls and pregnant women were 135µg/L and 133µg/L respectively. Among adolescent girls, 37% had UIC <100 µg/L and among pregnant women, 56% had UIC <150 µg/L. In India, Nina et al.[12] found the total goiter rate was 45%. The urinary iodine excretion pattern revealed mild iodine deficiency. 55% of women had <50 µg/L and 13.2% <20 µg/L. Chakraborty et al.[13] found Median UIE (µg/L) 142.80 and 188.80 in pregnant and non-pregnant women respectively. Median values of 1st, 2nd and 3rd trimester were 137.50 µg/L, 135.00 µg/L and 160.00 µg/L respectively. In Pakistan, Elahi et al.[14] found median value of UIE was 67 µg/L whereas frequencies for UIE <100 µg/L, 50-99 µg/L and <50 µg/L were 79.5%, 68.8% and 24.8% of pregnant women respectively. However, our results show much lower values for mean and median UI in pregnant mothers in all trimesters. Among all pregnant women 31.5% had slightly visible goiter. The difference in UIE between goitrous and non-goitrous pregnant women was not significant. In Nepal, Agrawal et al.[15] found that 28.88% pregnant women had UIE<150µg/L and frequency for <100 µg/L was 22.9%. In Thailand, Gowachirapant et al.[16] found that the median UI in pregnant women was 108 µg/L and 69.2% of pregnant women had a value <150 µg/L. The median value in 1st, 2nd and 3rd trimesters was 102µg/L, 122 µg/L and 106µg/L respectively and with no difference for UI among the trimesters. The maternal age and parity were not predictors of UI nor was socioeconomic level of the family. Appropos with this, present study also found no predictable capability of age of mothers, socioeconomic status, gravida, gestational weeks or presence of goiter over the deficiency of iodine nutrition. In Europe, Alvarer-Pedrerol et al.[17] found the median UIC was 95 µg/L and 104 µg/L during 1st and 3rd trimester respectively. Hiernimus et al.[18] found that median UIE was 64 µg/L. Frequency of iodine deficiency was 85.8% (100-150 µg/L) among pregnant women. Peris-Roig et al.[19] found the median UIC 100 µg/L and 66% had UIC below the recommended level. Mian et al.[20] found that median UIC was 83 µg/L whereas <50 µg/L and >150 µg/L were 33%, 27% respectively. In Australia, Stilwell et al.[21] found the overall median UIC during pregnancy was 75 µg/L. Stratification by gestation showed that median UIC was elevated in early pregnancy and subsequently declined with advancing gestation.

The increased renal clearance of iodine above the UI-threshold results in increased iodine loss. This threshold is masked at higher iodine intakes but in iodine deficiency lead to negative iodine balance and thyroid depletion.

This loss is compensated by increased thyroid volume to allow for more iodine storage. The existence of this compensatory mechanism to offset increased iodine loss is an adaptation to ensure the retention of extra iodine during gestation. Thus increased thyroid volume (goiter) during pregnancy indirectly indicates iodine deficiency. About 32 percent of both pregnant and non-pregnant women of this study subjects had slightly visible goiter. 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 any of variables of: age of mother, socioeconomic status, gravida, gestational weeks or presence of goiter. Similarly, when dichotomized on the basis of cut-off value at 100μg/L, iodine nutrition status was not found to be related to age of mother, socioeconomic status, gravida, gestational weeks or goiter.

Conclusion

Salt iodization is currently running under nation policy in Bangladesh. We observed iodine nutrition status deficient during various trimester of pregnancy. Therefore we conclude that studies at mass scale is needed to elucidate the cause and to find the ways of correction of the problem.

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