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The frequency and pattern of thyroid disorders in pregnant women during the first antenatal visit

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Abstract

Background: Maternal thyroid problems have been attributed to a spectrum of adverse pregnancy outcomes. Considering iodine deficiency in our population, screening for thyroid disorders during the first prenatal visit is important because early detection reduces the risk of complications for both mother and child by proper management.

Objective: To determine the frequency and pattern of dysfunction in pregnant women who appeared to be in good health during their first antenatal visit, regardless of gestational age.

Methods: A cross-sectional analysis was used in this study. A total of 1102 apparently healthy pregnant women were recruited during their first antenatal visit. Women with known thyroid disorders, chronic diseases, e.g., chronic kidney disease (CKD), chronic liver disease (CLD), or a history of taking drugs that interfere with thyroid function were excluded. TSH and FT4 levels were measured and evaluated according to reference intervals for thyroid hormones based on gestational age recommended by the American Thyroid Association (ATA) and according to conventional criteria. The Department of Microbiology and Immunology of Bangabandhu Sheikh Mujib Medical University (BSMMU) investigated lab variables.

Results: The mean age of the participants was 25.7±5.0 years. The most frequent thyroid dysfunction was subclinical hypothyroidism, which was 50.5% in the second trimester, 28.8% in the first trimester, and 18.7% in the third trimester. According to ATA and conventional criteria, dysfunction was detected in 32.8% and 18.9% of participants, respectively. Goiter was present among 39.6% of participants. The odds for thyroid dysfunction in women with goiter were 2.5-fold in comparison to those without goiter (95% CI: 1.93-3.24; $p<0.05$).

Conclusion: Clinically euthyroid pregnant women frequently have laboratory evidence of thyroid disease. So, thyroid function should be assessed in all pregnant women during the initial antenatal visit, regardless of gestational age. *[J Assoc Clin Endocrinol Diabetol Bangladesh,* July 2023;3(2)*: 40-46]*

Keywords: Pregnant women, Antenatal visit, Bangladesh, Thyroid disorder

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Introduction

Bangladesh, with its unique sociodemographic and healthcare landscape, faces distinct challenges in addressing the health needs of its pregnant population. In the context of our iodine deficiency situation, especially in pregnant women, the frequency and pattern of thyroid disorders among them have emerged as a significant area of concern.[1] The first antenatal visit serves as a crucial entry point into the continuum of prenatal care, allowing healthcare providers to assess and manage potential risk factors that may impact the course of pregnancy.

Thyroid diseases are common in reproductive-age women and, therefore, can occur during pregnancy and

postpartum.[2] Untreated, undetected thyroid disease during pregnancy has negative impacts on the health of both the fetus and the mother.[3] Thyroid disorder has detrimental effects that go beyond pregnancy and delivery, disrupting the neurointellectual development of children during early life.[4]

Recent developments in the evaluation of thyroid function have revealed that the assessment of thyroid function tests depends on the different trimesters of pregnancy.[5] Hyperthyroidism is present in 2 out of every 1000 pregnancies. The most frequent cause (85%) of hyperthyroidism is Graves' disease, caused by the activation of the thyroid gland by thyrotropin receptor antibodies (TRAbs). Miscarriage, abruptio placentae, preterm delivery, and pre-eclampsia are significant maternal complications.[6] Approximately 1 to 5% of newborns born to mothers with Graves' illness have hyperthyroidism as a result of the transfer of maternal TRAbs across the placenta. This transfer can happen even if the mother has normal thyroid function and has been treated for Graves' disease in the past.[7] Subclinical hyperthyroidism, characterised by normal levels of T4 and T3 but lower than normal levels of TSH, affects around 1.7% of pregnant women. However, it has no adverse consequences on pregnancy outcomes.[8] Nevertheless, evaluating the thyroid status will improve pregnancy outcomes.[9]

Hypothyroidism is a frequently observed disorder during pregnancy, unlike hyperthyroidism.[10] The prevalence of subclinical hypothyroidism, characterised by elevated levels of thyroid-stimulating hormone (TSH) and normal or slightly low levels of thyroxine (T4), is at least 2.5%. These women do not exhibit any clinical signs and are typically asymptomatic.[11] It is essential to mention that endemic iodine deficiency is the prevailing cause of hypothyroidism observed in pregnant women globally.[12] Only a small proportion, around 2.74% of women, have overt hypothyroidism.[13] In recent years, it has been clear that untreated maternal hypothyroidism and subclinical hypothyroidism during pregnancy are linked to negative consequences for both the fetus and the mother.[14,15] However, these consequences can be changed by administering sufficient levothyroxine therapy.[16] The cited incidents included miscarriages, pregnancy-related anaemia, preeclampsia, maternal high blood pressure, placental abruption, and postpartum haemorrhage in untreated mothers. In addition, infants born to women with hypothyroidism could have premature delivery, a low weight at birth, and neonatal respiratory distress.[17] Elevated maternal TSH levels, even within the conventional normal range for non-pregnant individuals, can lead to a greater probability of experiencing miscarriages, as well as complications in the fetus and newborn and preterm delivery.[18,19] Even more important than the above is the fact that gestational mother hypothyroidism harms the brain development of the fetus. The growing nerve cells in the fetus need thyroxine to develop and function properly.[20] Both iodine deficiency and autoimmune thyroid illness have been demonstrated to cause a decrease in the levels of maternal thyroxine in the bloodstream. In both retrospective and prospective studies, a decreased concentration of thyroxine in mothers' blood, either because of a lack of iodine or autoimmune thyroid disease, has been linked to lower IQ in babies and young kids.[2,21]

So, understanding the frequency and patterns of thyroid disorders among Bangladeshi pregnant women at this early stage is essential for tailoring effective interventions and ensuring optimal outcomes for both mother and child. This also helps to acknowledge the need for targeted research and healthcare strategies that align with the country's unique healthcare challenges and socio-cultural conditions.

Methods

Study design and participants: This cross-sectional observational study was conducted among healthy pregnant women (clinically euthyroid and no history of systemic illness that interferes with thyroid function tests) aged 18 years and above during their first antenatal visit. After obtaining their informed consent, 1,102 pregnant women were recruited from January 2016 to December 2020 from the Department of Obstetrics and Gynecology and the Department of Endocrinology of Bangabandhu Sheikh Mujib Medical University (BSMMU). Pregnant women with a known thyroid disorder, chronic systemic disease (e.g., CKD, CLD, etc.), or taking any drug that interferes with thyroid function test (e.g., Carbamazepine, Phenytoin, Lithium, Glucocorticoids, etc.) or not willing to give consent were excluded. Data were collected in a predesigned structured questionnaire.

Analysis of FT4, TSH: Serum FT4, TSH analysed by chemiluminescent immunoassay method (ADVIA. Centaur SIEMENS, Germany) in the Department of Microbiology and Immunology, BSMMU. The functional sensitivity of the TSH and FT4 assay were 0.010- 150 mIU/l and 0.10-12.0 ng/dl respectively. The intra-assay coefficients of variation (CV) for serum TSH

Table-I: Functional subgroups of thyroid dysfunction in pregnancy according to ATA and conventional criteria

Functional subgroups	ATA criteria	Conventional criteria
Hypothyroidism	TSH >2.50 mIU/L and FT4 < 0.8 ng/dl or TSH ≥10.0 irrespective of FT4 level	TSH >4.0 mIU/L and FT4 <0.8 ng/dl
Sub-clinical hypothyroidism	TSH between 2.5-10.0 mIU/L with normal FT4	TSH between 4.0-10.0 mIU/L with normal FT4
Hyperthyroidism	TSH <0.10 mIU/L and FT4 >1.8 ng/dl	TSH <0.4 m IU/L and elevated FT4 >1.8 ng/dl
Sub-clinical hyperthyroidism	TSH <0.10 mIU/L with normal FT4	Suppressed serum TSH <0.4 mIU/L with normal FT4
Euthyroid	TSH between 0.10-2.50 mIU/L with normal FT4	TSH between 0.4-4.0 mIU/L with normal FT4

ATA: American Thyroid Association; Normal FT4: 0.8 to 1.8 ng/dl

and FT4 were 1.2% and 1.9%, respectively. The inter-assay CV for serum TSH and FT4 at lower and higher levels was 2.3-2.6% and 2.5-2.7%, respectively.

The operational definition for thyroid dysfunction in pregnancy: Thyroid dysfunction was considered based on the cut-off value set by the American Thyroid Association (ATA) for pregnant women in addition to conventional criteria.[22] Thus, functional status is shown in Table-I.

Statistical Analysis: Statistical analysis was done using IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp. Descriptive statistics were carried out. Frequencies and percentages are presented for categorical variables. Continuous variables were presented as mean±SD. Functional status and association of goiter, categories of function in context to trimester were analysed by Chi-square test, and kappa statistics examined discordance of functional status between ATA and conventional criteria. Pearson's correlation test analysed correlations among variables. A p-value ≤0.05 was considered to be statistically significant.

Ethical aspects: Informed consent was obtained from each of the participants. The Institutional Review Board of BSMMU approved the study (BSMMU/2016/2755).

Results

The mean age of the participants was 25.7±5.0 years. Most women were housewives (78.1%), 10.9% were service holders, 4.6% were students, and 3.3% were medical professionals. Regarding parity, nulliparous were 35.3%, primiparous were 25.2%, and multiparous were 39.4%. About one-half (54.5%) of the participants were in the first trimester, 10.1% were in the second trimester, and 35.4% were in the third trimester (Table II).

Table-II: Characteristics of the studied subjects

Characters	Values
Number (n)	1102
Age (mean ± SD, year)	25.7±5.0
Profession	
Housewife	861 (78.1)
Service	120 (10.9)
Student	51 (4.6)
Medical professional	36 (3.3)
Others	34 (2.1)
Gestational age	
1st trimester	601 (54.5)
2nd trimester	111 (10.1)
3rd trimester	390 (35.4)
Gravida	
Primi	431 (39.1)
Multi	671 (60.9)
Parity	
Nulliparous	389 (35.3)
Primiparous	278 (25.2)
Multiparous	435 (39.4)
Presence of goiter	
Present	436 (39.6)
Absent	666 (60.4)

Within parentheses are percentages over column total

The most frequent thyroid dysfunction was subclinical hypothyroidism, which was 50.5% in the second trimester, 28.8 % in the first trimester, and 19.2 % in the third trimester (Table III). Most of the women with thyroid dysfunctions were in the 18-25 year age group (56.4%), followed by the 26-30 year age group (28.3%). In addition, 14.2% and 1.1% of women with thyroid dysfunction were in the 31-35 years and above 36 years age group, respectively. (Table IV). There was no association between parity and thyroid functional status

Table-III: Thyroid dysfunction according to trimester

Trimester	Subclinical Hypothyroid n (%)	Hypothyroid n (%)	Subclinical Hyperthyroid n (%)	Hyperthyroid n (%)	Euthyroid n (%)
1st Trimester (n=601)	173 (28.8)	17 (2.8)	15 (2.5)	14 (2.3)	382 (63.6)
2nd Trimester (n=111)	56 (50.5)	0 (0)	0 (0)	0 (0)	55 (50.0)
3rd Trimester (n=390)	75 (19.2)	9 (2.3)	1 (0.3)	0 (0)	307 (78.7)

Within parentheses are percentages over the row total

Table-IV: Thyroid dysfunction according to age

Age in years	Subclinical Hypothyroid n (%)	Hypothyroid n (%)	Subclinical Hyperthyroid n (%)	Hyperthyroid n (%)	Total dysfunction n (%)
18-25	176 (57.9)	8 (30.8)	12 (75.0)	7 (50.0)	203 (56.4)
26-30	88 (28.9)	8 (30.8)	4 (25.0)	2 (14.3)	102 (28.3)
31-35	37 (12.2)	10 (38.4)	0 (0)	4 (28.6)	51 (14.2)
36-40	3 (1.0)	0 (0)	0 (0)	1 (7.1)	4 (1.1)
Total	**304**	**26**	**16**	**14**	**360**

Within parentheses are percentages over the column total

(p=0.066), but trimester and thyroid function were significantly associated (p<0.001) (Table V).

In about half (54.4%) of the thyroid dysfunction group, goiter was present. The odds for thyroid dysfunction in women with goiter were 2.5 times in comparison to those with the absence of goiter (95% CI: 1.93-3.24; p <0.001) (Table VI).

According to ATA criteria, 32.8% were detected to have dysfunction, whereas 18.9 according to conventional criteria (Table VII). The ATA criteria categorised 26 individuals as having hypothyroidism but applying the conventional criteria, 6 of them classified as sub-clinical hypothyroidism. Similarly, the ATA method classified 304 persons in the sub-clinical hypothyroidism group,

Table-V: Association between obstetric characteristics and thyroid function status

Obstetric Characteristics	Thyroid Function		p-value
	Dysfunction (n=360)	Euthyroid (n=742)	
Parity			
Nullipara	157 (43.6)	325 (43.8)	
Primipara	131 (36.4)	307 (41.4)	0.066
Multipara	72 (20.0)	110 (14.8)	
Trimester			
1st Trimester	221 (61.4)	380 (51.2)	
2nd Trimester	56 (15.6)	55 (7.4)	<0.001
3rd Trimester	83 (23.0)	307 (41.4)	

Within parentheses are percentages over the column total

Table-VI: Thyroid dysfunction among subjects with or without gaiter

	Thyroid Function		Odds ratio (95% CI)	p-value
	Dysfunction	Normal		
Goiter Present	196 (54.4%)	240 (32.3%)	2.50 (1.93-3.24)	<0.001
Goiter Absent	164 (45.6%)	502 (67.7%)		
Total	**360**	**742**		

p-value obtained from the chi-square test

Table-VII: Thyroid function of studied subjects: ATA vs conventional criteria (N=1102)

Functional status	ATA Frequency (%)	Conventional Frequency (%)
Euthyroid	742 (67.3)	894 (81.1)
Thyroid Dysfunction	360 (32.8)	208 (18.9)
Subclinical Hypothyroid	304 (27.6)	120 (10.9)
Hypothyroid	26 (2.4)	20 (1.8)
Subclinical yperthyroid	16 (1.5)	54 (4.9)
Hyperthyroid	14 (1.3)	14 (1.3)

but 190 of them were classified as euthyroid by the conventional method. So, there was a 62.5% mismatch. Further, the ATA method classified 742 individuals in the euthyroid group, but the conventional method classified 38 of them as having sub-clinical hyperthyroidism. There is no mismatch between the classification of subclinical hyperthyroidism and overt hyperthyroidism in the two criteria. Overall,

Table-VIII: Concordance among functional status based on ATA and conventional cut-offs for TSH in studied pregnant subjects

ATA	Hypothyroidism	Sub-clinical hypothyroidism	Euthyroid	Sub-clinical Hyperthyroid	Hyperthyroidism	Total
Conventional						
Hypothyroidism	**20 (1.8%)**	0	0	0	0	20
Sub-clinical hypothyroidism	6	114 (10.3%)	0	0	0	120
Euthyroid	0	190	704 (63.9%)	0	0	894
Sub-clinical hyperthyroidism	0	0	38	16 (1.5%)	0	54
Hyperthyroidism	0	0	0	0	14 (1.3%)	14
Total	**26**	**304**	**742**	**16**	**14**	**1102**

Within parentheses are percentages over grand total

conventional cutoffs missed 21.2% (234/1102) cases. The kappa statistic was 0.497, representing a moderate agreement (p<0.001) (Table VIII).

Discussion

In this study, according to ATA criteria, subclinical hypothyroidism was most frequently observed in the second trimester (50.5%). The frequency was low in the first trimester (28.78%) and further in the third trimester (19.23%). The observed prevalence rates across trimesters could be attributed to physiological variations in thyroid function during pregnancy. The increased demand for thyroid hormones, particularly in the first and second trimesters, might increase frequency during these periods.[22] Bangladesh is particularly an iodine-deficient area, with reduced dietary iodine consumption, which may contribute to this higher frequency of SCH. Anwar et al. also reported the iodine nutritional status among pregnant women, considering WHO suggested cut-off value median urinary iodine (<150mg/L); all pregnant women in the first and third trimesters and around 90% in the second trimester were deficient in iodine nutrition, indicates that practically all pregnant women lack sufficient iodine in their diet.[1,23] Similar studies conducted among pregnant women in the first trimester in Bangladesh by Farhana et al. and Jahangir et al. found the frequency of subclinical hypothyroidism at 21.5% and 11.33%, respectively.[24,25] These disparities may be related to differences in sample size. Another study by Murshed et al. found that the frequencies of SCH were 28%, 51%, and 41% among the first, second, and third trimesters, respectively.[26] The findings of these studies are consistent with our results.

Considering the maternal age, the current study found that thyroid dysfunction was more commonly observed in younger pregnant women, and dysfunction gradually decreased with the advancement of age. Dieguez et al. found no association between TSH, FT4 and mother age.[27] After evaluating 5223 pregnant women, Potlukova et al. concluded that advancement of maternal age is not associated with thyroid disorders.[28] Another study by Korevaar et al. found that advanced maternal age was associated with an increased risk of gestational thyroid dysfunction. This association may be related to changes in immune regulation and hormonal fluctuations that occur with the advancement of age.[29] Nevertheless, it is not possible to conclude from this study that the increasing gestational age is a significant predictor of thyroid dysfunction because we did not measure TSH in all three trimesters in the same patients.

This study examines the relationship between obstetric factors and the condition of thyroid function. The findings indicate no association between parity and thyroid function status (p = 0.066). Still, trimesters have a significant association with thyroid function (p=<0.001). However, in another study at BSMMU, Fatema et al. found a substantial association with parity but no association with trimester.[30] This disparity may be due to different sample sizes and the cross-sectional nature of both studies.

In our study, about 54.4% (219/650) of mothers had associated goiter. The association between thyroid dysfunction and goiter is statistically significant. This may be a part of the pregnancy-related enlargement of the thyroid gland, which happens commonly to most pregnant ladies.[30,31]

The present study evaluated thyroid function under the ATA criteria. It was found that stringent criteria of ATA encompass 32.8% of women as dysfunctional, whereas 18.9% by conventional criteria. Concordance and discordance of the frequencies of thyroid dysfunction between the two criteria were also studied here, which showed that functional subgroups between these two reference categories were significantly different. Out of 304 subclinical hypothyroid women, as detected by ATA, 190 subjects were detected as euthyroid by

conventional criteria, and out of 26 hypothyroid, 6 women were considered as subclinical hypothyroidism by conventional criteria. 21.2% of women with thyroid dysfunction, mostly with subclinical hypothyroidism, could have been misclassified if we used a non-pregnant reference value.

A study in Australia investigated 2159 pregnant women during the 9th to 13th weeks of pregnancy. The findings revealed that using the conventional laboratory reference range for pregnant women would lead to inappropriate classification of thyroid status in more than 20% of the cases.[32] In a study by Wang et al., it was found that using reference intervals for non-pregnant women on pregnant women leads to misclassification of thyroid status in 6.1-31.0% of cases among the 1744 pregnant women evaluated.[33] These studies support similar findings in pregnant women of this study.

The strengths of this study include large sample sizes, pregnant women of different trimesters, and residents of various areas of Bangladesh. Thyroid peroxidase (TPO) antibodies, urine iodine levels, and thyroid gland ultrasonography were not assessed. Although this study has several limitations, it does highlight the urgent need for extensive research to ascertain the efficaciousness of thyroid disorders in Bangladesh during the various trimesters of pregnancy.

Conclusion

This study noticed thyroid disorders are common in asymptomatic pregnant women at their initial antenatal assessment. So, regardless of gestational age, all pregnant women should have a thyroid function test at their initial antenatal checkup. The ATA reference values for thyroid function tests for each gestational age should be considered to avoid missing diagnoses of thyroid disorders.

Conflict of interest

The authors have no conflicts of interest to disclose.

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Disclosure

The authors have no multiplicity of interest to disclose.

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Data Availability

Any inquiries regarding supporting data availability of this study should be directed to the corresponding author and are available from the corresponding author on reasonable request.

Ethical Approval and Consent to Participate

This study was approved by the Institutional Review Board (IRB) of BSMMU, Reg no. BSMMU/2016/2755. Informed written consent was obtained from each of the participants included in the study.

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