Assessment of Thyroid Function in Early Pregnancy

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ABSTRACT

Objectives: **Thyroid disorders are commonly observed in pregnancy. Thyroid hormones play an important role in embryogenesis and fetal development. The fetus is completely dependent on the mother for thyroid hormone in first trimester. About 10% of all pregnant women can be affected by thyroid disorders during pregnancy. Thyroid function abnormalities in pregnancy are a challenge for the concerned physicians. The objective of this study was to assess the maternal thyroid function in first trimester of pregnancy.**

Patients and Methods: **A descriptive cross sectional study was carried out at the Combined Military Hospital (CMH), Dhaka over a period of one year from January 2013 to December 2013 to see the serum FT3, FT4, TSH, thyroid antibodies level and common thyroid disorders in pregnancy. A total of 138 pregnant women in their first trimester (up to 12 weeks) of pregnancy with an age range of 18-35 years were enrolled in this study. Pregnant women with known thyroid disorder and on treatment and pregnancy more than three months were excluded. Measurement of serum FT3, FT4, TSH, antiTPO-Ab and antiTG-Ab were done in each patient at the time of enrolment. Ultrasonography of each patient was done for confirmation of pregnancy and correlation of gestational age.**

Results: **Among 138 pregnant women, subclinical hypothyroidism was detected in 10 (7.2%) patients and subclinical hyperthyroidism was detected in 3 (2.2%) patients. Mean difference of the investigation findings were not statistically significant among primi and multi gravida. TPO-Ab and TG-Ab difference were statistically significant between two age groups.**

Conclusion: **Subclinical thyroid disorders are fairly high among pregnant women. Correct diagnosis in early pregnancy and prompt treatment will bring an excellent prognosis for both mother and offspring.**

Key words: **Early pregnancy, thyroid hormones, thyroid auto-immunity**

INTRODUCTION

Thyroid disorders are observed more frequently in women of child bearing age, and pregnancy is often complicated by these disorders (1). Pregnancy is a stress test for the thyroid, resulting in hypothyroidism in women with limited thyroidal reserve or iodine deficiency, and postpartum thyroiditis in women with underlying Hashimoto's disease who were euthyroid prior to conception (2). Thyroid hormones play an important role in embryogenesis and fetal development during pregnancy (3). The fetus is completely dependent on the mother for thyroid hormone in first trimester of pregnancy. The thyroid disorders that can affect pregnancy includes clinical and subclinical hyperthyroidism, clinical and subclinical hypothyroidism and thyroid autoimmunity (2).

The American Association of Clinical Endocrinologists (AACE) recommended thyroid function screening in all women during the first trimester of pregnancy (4).

Abalovich et al., revealed the prevalence of subclinical hypothyroidism is 3–5% (5). Klein et al reported that hypothyroidism is common in pregnancy with an estimated prevalence of 2-3% and 0.3-0.5% for subclinical and overt hypothyroidism respectively (6). Subclinical hypothyroidism is the commonest form of hypothyroidism in pregnancy and is usually due to progressive thyroid destruction due to autoimmune thyroid disease. Several studies, mostly retrospective, have shown an association between overt hypothyroidism and adverse fetal and obstetric outcomes (7). Maternal complications such as miscarriages, anemia in pregnancy, pre-eclampsia, abruptio placenta and postpartum hemorrhage can occur in pregnant women with overt and subclinical hypothyroidism. Also, the offspring of these mothers can have complications such as premature birth, low birth weight, impaired neurological development and increased neonatal respiratory distress (8).

In pregnancy, levothyroxine is the treatment of choice for hypothyroidism. It is recommended that TSH levels are maintained below 2.5 mIU/L in the first trimester of pregnancy and below 3 mIU/L in later pregnancy (5). Hyperthyroidism occurs in about 0.1-0.4% of all pregnancies. Most cases are due to Graves' disease, although less common causes like toxic nodules and thyroiditis may be seen (9). Hyperthyroidism due to Graves' disease may worsen in the first trimester of pregnancy, remit in later pregnancy, and subsequently relapse in the postpartum. Uncontrolled hyperthyroidism in pregnancy is associated with an increased risk of severe pre-eclampsia and up to a four fold increased risk of low birth weight deliveries. Some of these unfavorable outcomes are more marked in women who are diagnosed for the first time in pregnancy. Uncontrolled and inadequately treated maternal hyperthyroidism may also result in fetal and neonatal hyperthyroidism (10). Methimazole and propylthiouracil (PTU) are effective in preventing pregnancy complications by hyperthyroidism (11).

Thyroid autoimmunity has an incidence of 8–14% among women of fertile age (12). The presence of thyroid autoantibodies in euthyroid women is associated with a significant risk for unexplained subfertility (13). Pregnant women with thyroid autoimmunity have an increased risk of miscarriage, preterm birth and maternal postpartum thyroiditis (13, 14). Autoimmune thyroid disease shows impairment of thyroid function during gestation and seems to suffer from higher rate of obstetrical complications. As there is alteration of thyroid function in pregnancy it is necessary to diagnose this alteration and to monitor thyroid function during pregnancy (15).

PATIENTS AND METHODS

This cross sectional study was performed at Obstetrics and Gynecology outpatient department (OPD) of Combined Military Hospital (CMH) Dhaka. A total of 138 pregnant women during their first trimester were selected who visited the outpatient department (OPD) irrespective of reason for their visit. The study was approved by the institutional appropriate ethical committee of the National Institute of Nuclear Medicine and Allied Sciences, BSMMU campus, Dhaka. Permission was taken from Obstetrics and Gynecology Department, CMH. Informed consents were taken from the patients. All relevant data were collected in a preformed data collection sheet. Pregnant women with known thyroid disorder or other medical illness were excluded. All the patient were evaluated by the detailed history and clinical examination during enrolment. Measurement of serum FT3, FT4, TSH, antiTPO-Ab and anti TG-Ab were done in each patient. The cut off value for serum FT3 is 2.8-7.1 pmol/L, serum FT4 is 11.6-24.6 pmol/L (16),TSH level in first trimester is 0.1-2.5 mIU/L (2). The reference intervals for TPO-Ab (>40 IU/ml) and TG-Ab (>125 IU/ml) were considered as positive result taken from the manufacturers literature (17). Ultrasonography of each patient was done for confirmation of pregnancy and correlation of gestational age. The collected data were compiled and analyzed using computer based software MS Excel and SPSS (Statistical Package for Social Science) version 19 for windows by appropriate statistical methods. Continuous data were presented as mean and standard deviation (SD). Unpaired t-test was done for continuous data. In each analysis level of significance was 0.05 and p value <0.05 was considered significance.

RESULTS

The study sample comprised of 138 women with mean age being 25.51 ± 3.95 years (range 18 to 35 years). Of these, 81.2% patients were multi-gravida and 18.8% patients were primi-gravida. Regarding hormonal status among study population, it was observed that majority had normal serum FT3 (99.3%), FT4 (99.3%) and TSH (90.6%) level. One patient had high serum FT3 level. One patient had low serum FT4. In this study high serum TSH was found in 10 (7.2%) patients and low serum TSH was found in 3 (2.2%) patients.

Among three patient with low TSH, serum FT3 and FT4 were normal in all. So they were diagnosed of having subclinical hyperthyroidism (Table 1).

Table 1: Status of serum FT3 and FT4 in women with low TSH (n=3)

	Low	Normal	High	
Serum FT_3 (pmol/L)	0	3	0	3 Subclinical hyperthyroid
Serum FT_4 (pmol/L)	0	3	0	

Regarding thyroid hormone status in women with high TSH, serum FT3 and FT4 were found within normal limit in all 10 patients. Therefore, these 10 patients were diagnosed as having subclinical hypothyroidism (Table 2).

Table 2: Status of serum FT3 and FT4 in women with high TSH (n=10)

	Low	Normal	High	
Serum FT_3	0	10	0	10 Subclinical hypothyroid
Serum FT_4	0	10	0	

In this study, 14 (10.1%) had both high level of TPO-Ab and TG-Ab, two women had only high TPO-Ab and one woman had only high TG-Ab. Therefore, TPO-Ab was high in 16 (11.6%) women and TG-Ab was high in 15 (10.9%) women. A total of 17 (12.31%) women had thyroid autoimmunity 95% CI being 6.8-17.8.

Table 3: Distribution of antithyroid antibodies among study population (n=138)

Antibody	Number of patients	Percentage (%)	95% CI
TPO-Ab	16	11.6	(6.3 - 16.9)
TG-Ab	15	10.9	(5.7 - 16.1)
Both TPO-Ab & TG-Ab	14	10.1	(5.1 - 15.1)
Total	**17**	**12.31**	**(6.8 - 17.8)**

CI= Confidence interval

It was observed that one primi-gravida and two multi-gravida had subclinical hyperthyroidism, two primi-gravida and eight multi-gravida had subclinical hypothyroidism and four primi-gravida and 13 multi-gravida had thyroid autoimmunity. There was no statistically significant difference (p>0.05) between primi-gravida and multi-gravida in terms of subclinical hyperthyroidism, subclinical hypothyroidism and thyroid autoimmunity (Table 4).

Table 4: Comparison of thyroid disorders between primi-gravida and multi-gravida (n=138)

	Primi-gravid (n=26)	Multi-gravid (n=112)	Total (n=138)	*P* value
Subclinical hyperthyroid	1	2	3	0.468^{ns}
Subclinical hypothyroid	2	8	10	0.596^{ns}
Thyroid autoimmunity	4	13	17	0.402^{ns}

ns= not significant

P value reached from Chi-square (χ^2) test

Table 5 shows comparison of different study variables in different age groups. There was no statistically significant difference (P>0.05) between the two age groups in term of serum FT3, FT4, and TSH. The mean TPO-Ab was 14.27 ± 17.86 IU/ml in 18-26 years and 57.54 ± 101.64 IU/ml in 27-35 years. The mean TG-Ab was 55.58 ± 53.43 IU/ml in 18-26 years and 130.13 ± 214.43 IU/ml in 27-35 years. The mean TPO-Ab and TG-Ab difference were statistically significant (p<0.05) between two age groups.

Table 5: Comparison of different study variables in different age groups(n=138)

Investigation findings	18-26 years (n = 73)				27-35 years (n = 65)				P value
	Mean ± SD		Min,	max	Mean ± SD		Min,	max	
S. FT_3 (pmol/l)	5.2	±0.69	3.9	,8	5.28	=0.57	4	,6.4	0.462^{ns}
S. FT_4 (pmol/l)	15.39	±2.66	10.2	,24	15.85	=2.43	11.8	,22	0.292^{ns}
S. TSH (µIU/ml)	1.62	±1.47	0.03	,13	1.55	=1.1	0.06	,4.66	0.754^{ns}
TPO-Ab (IU/ml)	14.27	±17.86	5	,95	57.54	=101.64	5	,523	0.001^{s}
TG-AB (IU/ml)	55.58	±53.43	10	,428	130.13	=214.43	12.5	,1210.5	0.047^{s}

s= significant, ns= not significant

P value reached from unpaired t-test

Different study variables were compared between primi-gravida and multi-gravida and the mean differences were not statistically significant (p>0.05) between the two groups (Table 6).

Table 6: Comparison of different study variables in primi-gravida and multi-gravida (n=138)

Study Variables	Primi-gravida (n=26)			Multi-gravida (n=112)			*P* value
	Mean ± SD	Min,	max	Mean ± SD	Min,	max	
S. FT_3 (p mol/L)	5.28 ± 0.85	4	,8	5.22 ± 0.59	3.9 ,	6.4	0.670^{ns}
S. FT_4 (p mol/L)	15.58 ± 2.65	11,	20.8	15.56 ± 2.57	10.2,	24	0.971^{ns}
S. TSH (μIU/ml)	1.91 ± 2.44	0.09,	13	1.52 ± 0.92	0.03,	4.66	0.182^{ns}
TPO-Ab (IU/ml)	15.35 ± 22.63	5,	95	34.11 ± 73.18	5,	523	0.199^{ns}
TG-Ab (IU/ml)	58.85 ± 40.75	12.5,	203	89.43 ± 156.15	10,	1210.5	0.324^{ns}

ns= not significant

P value reached from unpaired t-test

DISCUSSION

Thyroid disorders among the pregnant women are a challenge for the physicians. Thyroid disorders are quite common in pregnancy. Present study was undertaken to determined serum FT3, FT4, TSH, TPO-Ab and TG-Ab levels in pregnant women of first trimester. This study also tried to identify common thyroid disorders among pregnant women. In this present study, 137 women had normal FT3 and FT4, only one had low serum FT4 (10.2 p mol/L) and one had high serum FT3 (8 pmol/L). But both of them had normal serum TSH. Serum TSH was found within normal level in 125 (90.6%) with 95% CI 85.74-95.46. Low TSH was found in three (2.2%) and high TSH was found in 10 (7.2%) women All three women with low TSH had normal FT3 and FT4 suggesting subclinical hyperthyroidism Similarly all 10 women with high TSH had normal FT3 and FT4 suggesting subclinical hypothyroidism. In this study no patient had overt hypothyroidism and overt hyperthyroidism. The mean FT3, FT4 and TSH level of this study have similarity with some other study (18, 19).The present study showed high TSH level indicating subclinical hypothyroidism in 7.2% cases which is supported in a study (6.3%) conducted by Quinn et al. (20). Nahar at al. found it much higher (30%) in comparison to this study (15). In their study they found both subclinical and overt hypothyroidism where in present study there was no overt hypothyroidism. Casey et al. did a population based study and found the high TSH level in 3.4% (21). Shan et al. and Springer et al. also found high TSH level of 4.68% and 4.48% respectively (19, 22).

Low TSH level indicating subclinical hyperthyroidism was fount 2.2% women in this study have similarity in studies done by other authors (23, 24). The result showed 11.6% women with high TPO-Ab, 10.9% with high TG-Ab, and 10.1% with both high TPO-Ab and TG-Ab level. Srticker et al. observed similar findings in his study (25). Study conducted by Nahar et al. showed positive TPO-Ab in 21.5% which was higher than present study (15). No statistical significance found between primi-gravida and multi-gravida in terms of subclinical hypothyroidism, subclinical hyperthyroidism and thyroid autoimmunity in this study. Comparison of mean level of serum FT3, FT4 and TSH between two age groups (18-26 years and 27-35 years) did not show any significant difference. Mean level of TPO-Ab and TG-Ab were higher in the elder age group and found statistically significant.

CONCLUSION

Proper maternal thyroid function during pregnancy is important for both the mother and the developing child. Detection of thyroid disorder during pregnancy helps to identify women at future risk of thyroid diseases. Systemic screening for thyroid disorders in early pregnancy may be useful even when it does not represent immediate clinical manifestations. Routine screening at the first antenatal visit, preferably in the first trimester will be the most conservative policy for both the mother and the fetus. The present study showed that subclinical thyroid disorders are fairly high among women in first trimester of pregnancy. Mean difference of the investigation findings were not statistically significant among primi and multi gravida though thyroid autoimmunity was more in elder age group.

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