

Original Article

Distribution of thyroid peroxidase positivity and its effects on thyroid function in normal pregnant women during 1st trimester in Dhaka city.

Ohida Sultana^a, Nasim Jahan^b, Nayma Sultana^c, Farzana Mahmuda^d, Tazdik G Chowdhury^e

- a. Assistant Professor Kumudini Women's Medical College, Mirzapur.
- b. Professor & Head, Department of Physiology, SSMC
- c. Associated Professor, SSMC
- d. Assistant Professor Kumudini Women's Medical College, Mirzapur.
- e. Assistant Professor & Head, Department of Paediatric Dentistry, Update Dental College & Hospital, Dhaka.

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ABSTRACT

Objective: To measure the distribution of TPO-Ab positivity and to observe the effect of thyroid peroxidase positivity on thyroid function during first trimester in normal pregnancy. **Method:** A cross sectional among 120 subjects were taken in this study and divided into control and study groups. Control group (Group A) consisted of 60 healthy non pregnant women age ranged between 20 to 35 years. Study group (Group B) consisted of 60 normal pregnant women of same age range. Group B was further subdivided into group B₁ and group B₂ according to the level of TPO-Ab. Group B₁ consisted of TPO-Ab positive pregnant women and group B₂ consisted of TPO- Ab negative pregnant women. Control group was selected from personal contacts and study group from Out Patient Department (OPD) of Obstetrics and Gynecology of Sir Salimullah Medical College and Mitford Hospital. For assessment of thyroid function, serum free thyroxine (FT₄), thyroid stimulating hormone (TSH) were measured. Serum FT₄, TSH were measured by Enzyme link immunosorbant (ELISA) method. Again, serum TPO-Ab of total study population and hCG of all the pregnant women were measured. Serum TPO-Ab by Micro particle Enzyme Immunoassay (MEIA) method and hCG was estimated by ELISA. Statistical analysis was done by SPSS version 17. **Results:** In this study, serum FT₄ and was significantly (P<0.001) higher and TSH level was significantly (P<0.001) lower in normal pregnant women during 1st trimester in comparison to those of non pregnant women. Again, 18% of pregnant women showed TPO-Ab positivity. However, serum FT₄ level was significantly (P<0.001) lower whereas, TSH level was significantly (p<0.001) higher in TPO-Ab positive pregnant women in comparison to those of TPO-Ab negative pregnant women. **Conclusion:** TPO-Ab positivity increases during 1st trimester of normal pregnancy which decreases the hyper functional state of thyroid hormones. So, thyroid screening should be done routinely during pregnancy.

*Address of Correspondence:

Ohida Sultana,

MBBS, M.phil(Physiology)

Assistant Professor Kumudini Women's Medical College, Mirzapur. Bangladesh.

Phone: +88-01818068886.

INTRODUCTION

During pregnancy various physiological and biochemical changes take place to meet the metabolic demand of the developing fetus¹. Among the hormonal changes, thyroid

hormone change is a remarkable one. The production, circulation and disposal of thyroid hormones are all altered during pregnancy². Thyroid hormone is a calorogenic hormone which increases metabolic activities of almost all cells of the body and is essential for proper development of central nervous system³. First trimester of pregnancy which is up to 12 weeks of gestation is the most important period as organogenesis of fetus takes place at this stage. During 1st trimester, the fetus completely depends on transplacental passage of maternal thyroxine, as fetal thyroid gland is non functional during this period⁴. So, normal thyroid function of mother during 1st trimester is very important for fetal development⁵.

Due to structural similarity with TSH and its high concentration, human chorionic gonadotropin (hCG) causes a transient increase in FT₄ level and decrease in TSH level during this period⁶. But, during pregnancy thyroid hypofunction may occur due to presence of thyroid peroxidase antibody (TPO-Ab)⁷.

Thyroid peroxidase enzyme is a key enzyme in the formation of thyroid hormone, a major autoantigen in autoimmune thyroid disease. Thyroid peroxidase antibody (TPO-Ab) titer of 12 IU/ml or more is regarded as positive⁸. Pregnant women have a higher chance to develop thyroid autoantibodies specially thyroid peroxidase antibodies (TPO-Ab) in first trimester. Usually, TPO-Ab positivity causes decrease in FT₄ level and increase in TSH level⁹. This altered thyroid function causes higher incidence of obstetrical complication¹⁰ and negative pregnancy outcome such as miscarriage, prematurity, maternal post partum thyroiditis and post partum depression¹¹.

The rate of thyroid peroxidase antibody positivity is different in different countries. The rate of thyroid peroxidase antibody positivity is 11.2% among Pakistani pregnant women¹², 11.7% in Italy¹³, (12-26) % in Netherlands¹⁴.

So, TPO-Ab screening test can be an important routine diagnostic tool in early pregnancy which can help to identify women at risk for poor fetal outcome and post partum depression. But, little work is known on this regard in our country as well as in abroad. So, this study has been under taken which can provide a guideline to the obstetrician to take necessary step in euthyroid pregnant women with TPO-Ab positivity.

METHODS:

This cross sectional study was carried out in the Department of Physiology, Sir Salimullah Medical College and Mitford Hospital, Dhaka from January 2011 to

December 2011. A total number of 120 euthyroid female subject's age ranged 20

To 35 years were included in this study.

Among them sixty (60) were non-pregnant women (Group A) and another sixty (60) were primi gravid women (Group B) with gestational age between 9 to 12 weeks. This group was again subdivided in to group B₁ and B₂ according to the level of thyroid peroxidase antibody (TPO-Ab). Group B₁ Consisted of thyroid peroxidase antibody (TPO-Ab) positive pregnant women (TPO-Ab \geq 12IU/ml) and Group B₂ Consisted of thyroid peroxidase antibody (TPO-Ab) negative pregnant women (TPO Ab<12IU/ml). All the pregnant women were selected from Out Patient Department (OPD) of Obstetrics and Gynecology, Sir Salimullah Medical College and Mitford hospital and non-pregnant women were from personal contact by simple purposive sampling. All the subjects were belonged to middle socio-economic status. Any subject suffering from systemic disease, endocrine abnormalities, user of drug that can affect thyroid function, smoking, alcoholism were excluded from the study. After selection of the subject the purpose, risks and benefits of the study was explained to each of the subject with a cordial attitude and only positive respondents were recruited as research participants. A written informed consents was taken from each participant. Detailed family and medical history were taken. Thorough physical examinations were done and all the informations were recorded in a prefixed questionnaire. Blood was collected for estimation of serum FT₄, TSH, TPO-Ab, hCG levels. Serum FT₄, TSH and hCG were measured by Enzyme Link Immuno sorbent Assay (ELISA) in the laboratory of Department of Physiology, Sir Salimullah Medical college (SSMC). Again, serum TPO-Ab was measured by Micro particle Enzyme Immunoassay (MEIA) in the Department of Biochemistry, Bangabandhu Sheikh Mujib Medical University (BSMMU). The statistical analysis was done by using Statistical Package of Social Science (SPSS) for windows version - 17.

Result

In this study, the mean (\pm SD) serum TSH level was significantly ($P<0.001$) lower whereas, serum FT₄ ($P<0.001$) level was significantly higher in group B in comparison to those of group A

Table I: Serum free thyroxine (FT₄), thyroid stimulating hormone (TSH) level in both groups (n=120)

Groups	n	FT ₄ (μ mol/L)	TSH (μ ml/ml)
A	60	11.193 \pm 2.057 (9.119-20.219)	2.69 \pm 1.32 (0.563-5.731)
B	60	17.197 \pm 5.675 (6.095-25.852)	1.58 \pm 1.11 (0.507-5.592)

Statistical analysis

Groups	FT ₄ (p value)	TSH (p value)
A vs B	0.000***	0.000***

Data are expressed as Mean \pm SD. For statistical analysis, unpaired student's 't' test was performed for comparison between the groups. Figure in parentheses indicate ranges.

Group A: Apparently healthy non pregnant women (Control).

Group B: Normal pregnant women during 1st trimester (study).

*** = Significant at $p < 0.001$

n = total number of subjects

The number of thyroid peroxidase antibody (TPO-Ab) positive pregnant women was 11 (18%) whereas, thyroid peroxidase antibody negative pregnant women was 49 (82%). Table II

Table II: Distribution of pregnant women during 1st trimester by the level of thyroid peroxidase antibody (TPO-Ab) (n=60).

Groups	TPO-Ab (IU/ml)	No	%
B ₁	14.15 \pm 1.49 (12.0-16.6)	11	18
B ₂	4.78 \pm 2.25 (2.1-10)	49	82

Group B₁: Thyroid peroxidase antibody (TPO-Ab) positive (TPO-Ab \geq 12 IU/ml)

Group B₂: Thyroid peroxidase antibody (TPO-Ab) negative (TPO-Ab $<$ 12 IU/ml)

n = total number of normal pregnant women during 1st trimester.

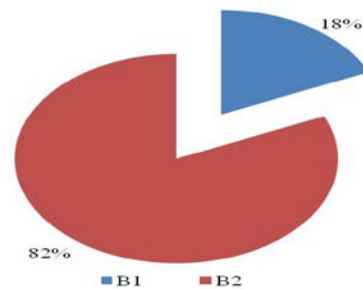


Figure 1: Distribution of pregnant women during 1st trimester by the level of thyroid peroxidase antibody (TPO-Ab) (n=60).

The mean (\pm SD) serum TSH and TPO-Ab levels were significantly ($p < 0.001$) higher, whereas, serum FT₄ level was significantly ($p < 0.001$) lower in group B₁ in comparison to those of group B₂. In contrast, serum hCG level was slightly higher in group B₁ in comparison to that of group B₂ but the difference was not statistically significant (Table III).

Table III: Serum free thyroxine (FT₄), thyroid stimulating hormone (TSH), thyroid peroxidase antibody (TPO-Ab) and human chorionic gonadotropin (hCG) hormone levels in study groups (Group B₁ and B₂) (n=60).

Groups	n	FT ₄ (pmol/L)	TSH (μIU/ml)	TPO-Ab (IU/ml)	hCG (mIU/L)
B ₁	11	8.86 ±3.76 (6.095-19.55)	3.45 1±1.07 (2.076-5.592)	14.15±1.49 (12.0-16.6)	69522 ±32439 (32053-114806)
B ₂	49	19.07 ±4.14 (9.473-25.852)	1.16±0.55 (0.505 2.378)	4.78±2.25 (2.1-10)	63204 ±34302 (22327-181481)

Statistical analysis

Groups	FT ₄ (p value)	TSH (p value)	TPO-Ab (p value)	hCG (p value)
B ₁ vsB ₂	0.000***	0.000***	0.000***	0.580 ^{ns}

Data are expressed as Mean ± SD. For statistical analysis, unpaired student's 't' test was performed for comparison between the groups. Figure in parentheses indicate ranges.

Group B: Normal pregnant women during 1st trimester (study).

Group B₁: Thyroid peroxidase antibody (TPO-Ab) positive (TPO-Ab ≥ 12 IU/ml)

Group B₂: Thyroid peroxidase antibody (TPO-Ab) negative (TPO-Ab < 12 IU/ml)

*** = Significant at p < 0.001.

NS = non significant.

n = total number of normal pregnant women during 1st trimester.

DISCUSSION

The present study, serum free thyroxine (FT₄) level was significantly (p < 0.001) higher and TSH level was significantly (p < 0.001) lower in normal pregnant women during 1st trimester in comparison to those of non pregnant women. These findings are in consistent with the findings of some researchers.^{15,16}

On the contrary, some other researchers had shown a lower level of serum FT₄¹⁷ and higher level of serum TSH¹⁸ in normal pregnant women during 1st trimester in comparison to non pregnant women.

18% of normal pregnant women during 1st trimester had TPO-Ab positivity in this study whereas, this finding was different in other countries¹⁹.

Serum free thyroxine (FT₄) level was significantly (p < 0.001) lower and TSH level was significantly (p < 0.001) higher in TPO-Ab positive pregnant women during 1st trimester in comparison to those of TPO-Ab negative pregnant women. Similar findings were also observed by some researchers.²⁰

Again, serum hCG was slightly higher in TPO-Ab positive pregnant women in comparison to

that of TPO-Ab negative women but the difference was not statistically significant.

There are some postulated mechanisms suggested by various researchers of different countries which may imply the underlying causes regarding the changes in the present study. It has been suggested that, thyrotropic effect by higher concentration of serum hCG seems to be responsible for higher thyroid hormone concentration during 1st trimester²¹

Increased fetal demand and increased placental transfer of thyroid hormone during pregnancy specially in 1st trimester may also be responsible for the higher level of FT₄ indirectly by negative feedback mechanism²².

Growing fetus release enough antigen to stimulate the maternal immune system which subsequently produce thyroid per oxidase antibodies and exerts inverse effect on maternal thyroid hormone synthesis²³. Antibody against thyroid peroxidase enzyme (TPO-Ab) blocks each steps of thyroid hormone synthesis and causes a decrease in serum free thyroxine (FT₄) and increase in serum TSH levels in TPO-Ab positive women in comparison to those of TPO-Ab negative women during 1st trimester²⁴.

In the present study, mild hyper functional state of thyroid was observed in normal pregnant women during 1st trimester as evidenced by higher level of serum FT₄ and lower level of serum TSH in comparison to those of non pregnant women. This higher FT₄ level is most likely due to higher concentration of serum hCG during first trimester. The positive correlation of FT₄ with hCG is in favour of this suggestion. Again, lower TSH level is the result of negative feedback effect of FT₄ on TSH secretion.

Moreover, thyroid peroxidase antibody positivity was present in 18% of pregnant women which indicates the raised autoimmune reaction during pregnancy. Although, serum hCG level was higher, serum FT₄ remained lower and TSH remained higher in TPO-Ab positive pregnant women in comparison to those of TPO-Ab negative pregnant women in this study may be due to competitive inhibition of hCG by higher level of TSH.

CONCLUSION:

The result of the study concludes that thyroid hyper functional state usually observed during 1st trimester in normal pregnancy, which may be due to 'thyrotrophic' effect of higher concentration of hCG during this period. This hyperfunctional state of thyroid gland can decrease in TPO-Ab positive pregnant women, which may cause pregnancy complications. So further study is required to observe the relationship of pregnancy related complication with TPO-Ab positivity.

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