Research Article

Utility of thyroid peroxidase autoantibodies as risk marker of thyroid dysfuction in pregnant women

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Abstract

Undiagnosed thyroid diseases in pregnant women can result in miscarriage, preterm birth and gestational hypertension. Autoimmunity has been implicated as one among the causes for thyroid illness in pregnancy. This study intended to define the prevalence of autoimmune thyroid disease by measuring thyroid peroxidase autoantibodies (ATPO) in pregnant women which can aid in predicting the hypothyroidism and early intervention. Pregnant women (n=107) were screened for Thyroid Stimulating Hormone (TSH) and ATPO. This study revealed that the prevalence of thyroid illness in pregnant women by TSH as 14.1% and the prevalence increased to 29.9% on combining TSH with ATPO. The sensitivity and specificity of positive ATPO for the thyroid illness was 26.6% and 81.5% respectively. Hypothyroid subjects had high levels of ATPO which was statistically significant by one-way analysis of variance. Therefore, detection of raised ATPO in pregnant women may be of use in early diagnosis of thyroid illness and help in preventing adverse out comes.

Keywords: Thyroid peroxidase autoantibodies, pregnant women, thyroid stimulating hormone.

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INTRODUCTION

Pregnancy influences thyroid function in multiple ways. Not only does the maternal hypothalamic-pituitary-thyroid (HPT) axis undergo a series of adjustments, the fetus also develops its own HPT axis and the placenta plays an active role in iodide and T4 metabolism. Thus, an integrated three-compartment thyroid model exists during gestation.[1] The fetal and neonatal HPT axis is influenced by thyroid disease in the mother. Also, it has been found that maternal and fetal/neonatal outcomes in pregnancy are adversely affected if thyroid dysfunction is undiagnosed.[2] Therefore, there is a need for early detection of thyroid dysfunction in pregnancy. Autoimmunity has been implicated as one among the causes for thyroid illness in pregnancy and in particular for hypothyroidism. Thyroid peroxidase (TPO), a key enzyme in the synthesis of thyroid hormones is a frequent epitope of auto antibodies called anti-thyroid peroxidase antibodies (ATPO).[3] There are several studies showing the presence of raised ATPO in pregnancy of which one of the studies found the prevalence of raised ATPO in pregnant women as high as 19.6%.[4] But, the role of ATPO in pregnancy for routine screening is yet on debate. Therefore, this study intended to estimate the levels of ATPO in pregnancy and find its utility. Also, there are limited studies on ATPO levels in pregnant women in Indian population and its role in pregnancy as indicator of thyroiditis and hypothyroidism is less studied. This study was also intended to find the relationship between ATPO and Thyroid status by estimating thyroid stimulating hormone (TSH) levels in pregnant women.

METHODOLOGY

This Cross sectional study included the 107 pregnant women attending the out patients department of M S Ramaiah Hospital. Written informed consent was obtained from all the subjects after explaining the nature

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and purpose of the study. This study was carried out after obtaining the approval from the institutional ethics committee. About 5ml of venous blood was collected in *BD Vacutainer*® SST™ *GEL* Tubes and allowed to clot. This is later centrifuged to separate the serum which was stored as aliquots at -20°C and later ATPO and TSH levels were estimated using ELISA kits (*calibiotech, Inc*®, California). Pregnant women with complications like pre-eclampsia, gestational diabetes and existing thyroid dysfunction were excluded from the study. The pregnant women were grouped as euthyroid, hypothyroid and hyperthyroid based on the TSH values; based on ATPO values, pregnant women were grouped as negative, borderline positive and positive (Table 1).

The quantitative parameters serum TSH and ATPO levels are expressed in terms of mean ± standard deviation (SD) and were analyzed by one-way ANOVA. Pearson's product-moment correlation was performed between serum ATPO and TSH values. Fisher's Exact Test was performed to find the significance in distribution for the Count Data in various groups. The p value of <0.05 was considered statistically significant, value <0.01 was considered as highly significant and value >0.05 was considered as not significant.

RESULTS

The prevalence of thyroid illness by ATPO (>75 IU/ml) and TSH was 19.6% and 14.1% (hyperthyroidism: 1.9%, hypothyroidism: 12.2%). respectively. The prevalence increased to 29.9% on using both ATPO and TSH for detecting thyroid illness. This sensitivity and specificity of ATPO for the thyroid illness was 26.6% and 81.5% respectively. Other results are shown in tables 1-3. Table 1 and figure 1 shows the distribution of the pregnant women among the various groups. The distribution was not statistically significant by Fisher's Exact Test. Table 2 shows the mean ± SD of the TSH and ATPO in various groups. There is significant difference between the means of ATPO in TSH based groups and between the means of TSH in ATPO based groups. Table 3 and figure 2 shows the Pearson's correlation between the parameters TSH and ATPO. It is shown that there is highly significant correlation between the parameters.

Table 1: Shows the distribution of the study population (N=107) among the various groups

Groups		Groups based on ATPO			
		Negative (< 50 IU/ml) N= 86 (80.4%)	Borderline Positive (50 – 75 IU/ml) N=3 (2.8%)	Positive (> 75 IU/ml) N=18 (16.8%)	p value*
Groups based On TSH	Euthyroid (0.4 – 4.2 µIU/ ml) N=92 (86.0%)	75 (70.1%)	2 (1.9%)	15 (14.0%)	0.41
	Hypothyroid (< 0.4 µIU/ ml) N=13 (12.1%)	9 (8.4%)	1 (0.9%)	3 (2.8%)	
	Hyperthyroid (> 4.2 µIU/ ml) N=2 (1.9%)	2 (1.9%)	0 (0.0%)	0 (0.0%)	

Figures in parenthesis show the percentage w.r.t total study population; *Fisher's Exact Test for Count Data

Table 2: Shows the Mean and SD of serum ATPO and TSH values in various groups

Groups	ATPO values (Mean ± SD)	P value*	TSH values (Mean ± SD)	P value*
Euthyroid	42.6 ± 68.0		2.1 ±0.9	
Hypothyroid	129.6 ± 217.5	0.01	7.2 ± 3.3	<0.01
Hyperthyroid	15.6 ± 3.9		0.3 ± 0.1	
Negative	17.4 ± 11.1		2.4 ± 1.9	
Borderline	57.2 ± 5.5	<0.01	5.0 ± 5.0	0.02
Positive	220.4 ± 163.4		3.6 ± 2.5	

*one-way ANOVA

Table 3: Shows Pearson's product-moment correlation between serum ATPO and TSH values

	ATPO	
TSH	r value	p value
	0.39	<0.01

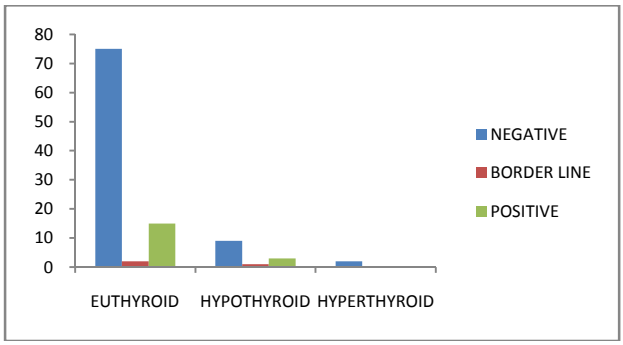

Figure 1: Distribution of raised ATPO pregnant women in the euthyroid, hypothyroid and hyperthyroid groups

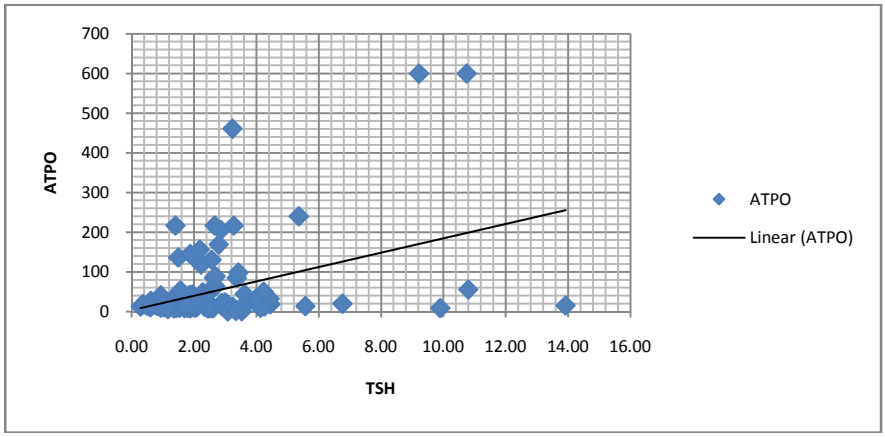

Figure 2: Shows correlation between serum ATPO and TSH values in pregnant women

DISCUSSION

Maternal and fetal/neonatal outcomes in pregnancy are adversely affected by thyroid dysfunction. The complications include miscarriage, preterm birth and gestational hypertension.[5] Therefore, the American Association of Clinical Endocrinologists, the American Thyroid Association, and the Endocrine Society recommend routine screening for TSH during pregnancy.[6] Autoimmunity is cause for thyroiditis and later for hypothyroidism in general population and also in pregnancy. ATPO measurements indicate the presence and severity of autoimmunity against thyroid gland protein namely thyroid peroxidase. Therefore, this study intended to find the utility of estimating ATPO levels as a screening tool in pregnant women. Nambiar V *et al*, in their study on Asian-Indian pregnant women showed the prevalence of hypothyroidism as 4.8% and ATPO as 12.4%.[7] This study also yielded similar results. The frequency of the pregnant women with high titers of ATPO is greater than the frequency of pregnant women with high/low TSH levels. Also, from table 1 it can be noted that as high as 15% euthyroid individuals had high titers of ATPO. Thus, emphasizing the importance of screening for raised ATPO in pregnant women. The sensitivity and specificity of ATPO for the thyroid illness was 26.6% and 81.5% respectively i.e. it has high negative predictive value. Hence it may be used along with the TSH rather than independently. Association of autoimmunity and hypothyroidism has been shown by several studies.[8] One-way ANOVA for the comparison of means between the groups showed that hypothyroidism group was associated with high ATPO values and ATPO positive group was associated with high TSH values. Further, it is shown that there is highly significant correlation between the ATPO and TSH. Thus, this study emphasizes the use of ATPO with TSH in pregnant women. The major limitation for this study is its small sample size.

CONCLUSION

This study emphasizes the utilization of ATPO for screening along with the TSH to identify pregnant women who are at risk to develop hypothyroidism and help in early intervention to prevent complications.

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