ANTI-THYROID PEROXIDASE ANTIBODY PREVALENCE IN REPRODUCTIVE AGE GROUP FEMALES- A STUDY FROM CENTRAL KERALA, INDIA

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ABSTRACT

BACKGROUND
Assessment of serum TSH and anti-TPO antibody titre will play an important role in the early detection of hypothyroidism and autoimmune thyroid disorders, thus helping in the initiation of appropriate treatment. Anti-TPO antibody-positive subjects can also be evaluated for other autoimmune disorders. The present study was proposed to assess the prevalence of anti-TPO antibodies in asymptomatic women of reproductive age.

MATERIALS AND METHODS
The study consisted of 200 asymptomatic females in reproductive age group from a tertiary care center in Central Kerala. TSH and anti-TPO were measured using chemiluminescence immunoassay system for all the participants.

RESULTS
A total of 23.5% participants in the study were anti-TPO positive. TSH had a statistically significant correlation with anti-TPO in anti-TPO positive group (r=0.306; p=0.0362). About 10 participants (21.28%) in this group had high TSH values suggestive of hypothyroidism. Maximum number of anti-TPO positive participants were found in 45-49 years age group, but the mean value was highest in 35-44 years age group. These two groups also had high TSH levels. Levels of anti-TPO are associated with TSH values indicating a negative impact on thyroid function. It can lead to hypothyroidism or subclinical hypothyroidism, which in turn affect fertility, pregnancy and other reproductive outcomes.

CONCLUSION
The study shows the need for screening for anti-TPO antibodies in all women of reproductive age group to estimate the risk of infertility among them.

KEYWORDS
Anti-TPO antibodies, Thyroid Autoimmunity, Anti-thyroid Antibodies.

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BACKGROUND

Autoimmunity is one of the most frequent cause of thyroid dysfunction in women of reproductive age. About 5-15% of euthyroid women and up to 2% of euthyroid men have thyroid antibodies and these individuals are at increased risk of developing thyroid dysfunction.[1] Prevalence of thyroid antibodies like antithyroid peroxidase antibodies (anti-TPO) was related to low rate of fertilisation, implantation and pregnancy.[2] Autoimmune thyroiditis is considered to be one of the aetiological factors for hypothyroidism in a population[3] and this condition was found to be significantly linked with infertility.[4] Thyroid autoimmunity was found to be highly prevalent in women with polycystic ovary syndrome cementing the importance of screening for anti-TPO antibodies in women.[5]

To our knowledge, studies on anti-TPO antibody titre in young asymptomatic females in central region of Kerala are negligent. Assessment of serum TSH and anti-TPO antibody titre will play an important role in the early detection of hypothyroidism and autoimmune thyroid disorders and also in the initiation of appropriate treatment for prevention of complications. Anti-TPO antibody-positive subjects can also be evaluated for other autoimmune disorders. The present study was proposed to assess the prevalence of anti-TPO antibodies in asymptomatic women of reproductive age.

MATERIALS AND METHODS

The cross-sectional study consisted of 200 asymptomatic females in reproductive age group, all of whom were either students or staff of a tertiary healthcare centre. The study was conducted from September 2015 to August 2016. Potential participants were excluded if they were-

- Pregnant.
- Had already diagnosed thyroid disease.
- Currently receiving thyroid medications.
- Not willing to participate in the study.

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The participants were grouped into four based on age. Medical and family histories of the patients were collected using a semi-structured questionnaire. TSH and anti-TPO were measured using chemiluminescence immunoassay system- Roche Cobas E411. Appropriate calibrators were used for validating the test.

For analyses, the reference value taken was <35 IU/mL for anti-TPO antibodies and 0.34-4.25 μIU/mL for serum TSH. Exploratory analysis was done using EPI Info version 1. TSH and anti-TPO levels were analysed using multivariate linear regression models after log transformation due to skewness of their distribution in their original scale. Mean ± SD was used for other parameters. Age-wise prevalence of TSH and anti-TPO was compared using Chi-square test. Hypothyroidism state of the participants was analysed on the basis of TSH level alone due to economic constraints.

RESULTS

In this cross-sectional study, 200 participants from the department were evaluated for the presence of anti-thyroid peroxidase antibody. The mean age (mean ± SD) of the participating women were 32.92 ± 11.82 years. More than half of the participants (65.5%) were staff of the department, while the rest were students. About 17% of the participants had a family history of thyroid disorders. Most of them had a regular menstrual cycle and only 7% reported irregularities in periods. Infertility rate was also low in the group with only 3.5% diagnosed as having the condition. About 3% of the women in the study had a history of preterm delivery. Mean values of the different biochemical parameters of the participants are given in Table 1.

Parameter	Mean
Fasting blood sugar (mg/dL)	90.57
Total cholesterol (mg/dL)	198.17
Triglycerides (mg/dL)	105.15
HDL (mg/dL)	58.38
LDL (mg/dL)	118.88
TSH (μ IU/mL)	2.51
Anti-TPO (IU/mL)	68.12

Table 1. Mean Values of the Different Biochemical Parameters of the Participants

TSH and anti-TPO antibodies had a statistically significant correlation (r=0.192, p=0.006)*. But, the antibodies were not significantly correlated with BMI.

Anti-TPO Positive Prevalence

A total of 47 women (23.5%) in the study group were anti-TPO positive with a mean age (mean ± SD) of 34.55 ± 12.09 years. More than 25% of these women in the anti-TPO positive group had a family history of thyroid dysfunction. The mean values of parameters in this group are given in Table 2.

Parameters	Mean
BMI (kg/m^2)	22.7
Fasting blood sugar (mg/dL)	91.43
Total cholesterol (mg/dL)	200.64
Triglycerides (mg/dL)	125.04
HDL (mg/dL)	55.23
LDL (mg/dL)	115.57
TSH (μ IU/mL)	3.57
Anti-TPO (IU/mL)	249.8

Table 2. Mean Values of Different Parameters in Anti-TPO +ve Participants

Correlation between the different parameters in the group is given in Table 3. TSH had a statistically significant correlation with anti-TPO in anti-TPO positive group (r=0.306; p=0.0362). BMI and FBS were not significantly associated with these antibodies. About 10 participants (21.28%) in this group had high TSH values suggestive of hypothyroidism.

	Anti-TPO	
	R	p
TSH	0.306	0.0362*
BMI	0.262	0.076
FBS	0.064	0.183

Table 3. Correlation between Different Parameters and Anti-TPO in Anti-TPO Positive Group

The anti-TPO positive group was further categorised on the basis of family history of thyroid dysfunction. The mean TSH value was 2.30 μ IU/mL, while that of anti-TPO was high (196.33 IU/mL) in participants with a family history of thyroid disorders. The correlation shown between parameters like BMI and FBS with anti-TPO in this group (anti-TPO positive with family history) was not statistically significant (FBS- r=0.036, p=0.909; BMI- r=0.172, p=0.593). There was a statistically significant correlation between TSH and anti-TPO when the participant had a family history of thyroid disorders (r=0.630, p=0.028*).

Age-Specific Prevalence

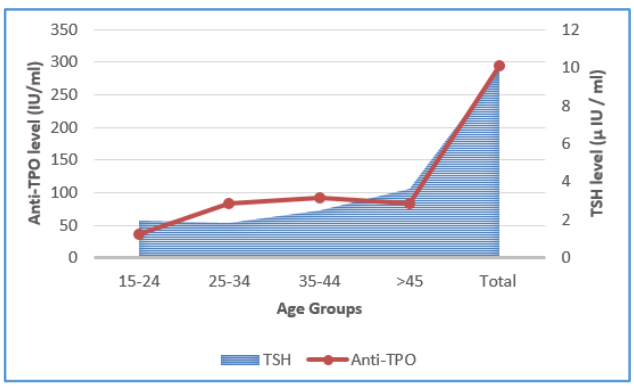
The study subjects were divided into different age groups- 15-24, 25-34, 35-44 and 45-49 years. The mean ± SD values for different parameters are given in Table 4.

	15-24 yrs.	25-34 yrs.	35-44 yrs.	Above 45 yrs.
Mean age (years)	19.32 ± 1.41	29.52 ± 2.21	39.27 ± 2.77	47.6 ± 1.46
Mean body weight (kg)	46.56 ± 6.62	57.45 ± 5.99	61.87 ± 9.33	58.93 ± 6.90
Mean BMI (kg/m^2)	19.61 ± 2.44	23.61 ± 3.04	25.16 ± 3.50	24.67 ± 2.49
Family history (no:)	11	7	6	10
FBS (mg/dL)	77.72 ± 10.88	88.17 ± 8.40	95.22 ± 18.17	105.11 ± 20.64
TSH (μ IU/mL)	1.95 ± 2.15	1.82 ± 1.10	2.52 ± 2.02	3.63 ± 7.20

Anti-TPO (IU/mL)	35.41 ± 62.29	84.03 ± 173.05	91.22 ± 181.38	83.93 ± 144.36
Anti-TPO +ve (no:)	15	5	11	16

Table 4. Mean Values (Mean ± SD) of Different Parameters in Different Age Groups. (Family History and Anti-TPO +ve are Represented as Numbers)

Maximum number of anti-TPO positive participants were found in above 45 years group, but the mean value was highest in 35-44 years group. These two groups also had high TSH levels. Chi-square test between TSH and anti-TPO in the different age groups did not reveal a statistically significant association between the groups ($\chi 2=0.989$, $p<0.005$). The levels of anti-TPO antibodies and TSH in relation to age distribution is given in below figure.



Rate of Anti-TPO Antibodies and TSH in Relation to Age Distribution

Prevalence of Hypothyroidism

A total of 18 participants (9%) had TSH value higher than the normal range suggesting presence of hypothyroidism. Mean age (mean ± SD) of this group was 38.89 ± 10.59 years. Mean TSH value in the group was 9.69 ± 11.37 µ IU/mL. Ten participants (55.55%) in this group had high anti-TPO levels (mean ± SD=192.68 ± 244.28 IU/mL). But, a statistically significant association was lacking between TSH and anti-TPO in this group ($r=0.014$, $p=0.954$). There was no significant association between TSH and BMI in this group with clinical hypothyroidism.

DISCUSSION

Thyroid function abnormalities like hypothyroidism and hyperthyroidism are common in Kerala and the values are higher when compared to reports from other parts of the world.[3,6,7,8] Autoimmune-related thyroid dysfunctions caused by antibodies are one of the most common cause of thyroid diseases.[9] In general population, 8-27% are reported to have anti-TPO antibodies and a high titre of these antibodies is present in 89.9% of patients with autoimmune thyroid disorders.[10,11] Present study show 23.5% of the participants to be anti-TPO positive with a mean ± SD value of 68.12 ± 137.62 IU/mL. It is known that most of the autoimmune diseases and their pathologies remain hidden for several years before their clinical manifestation. Anti-TPO antibodies in the serum are considered as a valuable indicator of autoimmune thyroid disease as they precede the development of disease phenotype.[9,12] Thus, the presence of these antibodies in an asymptomatic individual, especially in females in reproductive age group should not be neglected. The prevalence of antibodies though lesser than that reported in a pilot study points towards a real increase in autoimmune thyroid disease in the population and should be further evaluated with well-designed prospective studies.[13]

TSH values were not significantly different in anti-TPO positive and anti-TPO negative groups, although studies have reported occurrence of thyroid insufficiency in women with autoimmune antibodies.[14] Some values of anti-TPO antibodies in our study were very high in the range of >600 IU/mL, multiple times higher than the acceptable upper limit. This maybe a reflection of an active autoimmune process going on in the thyroid gland with the implication of future thyroid dysfunction. It is possible that thyroid autoimmunity is present in the form of asymptomatic, subclinical hypothyroidism in many patients as reported by Lata et al.[15] Nested case-control study conducted by Hutfless et al showed that these antibodies had increasing prevalence before the clinical diagnosis of the disease.[12]

Earlier studies had reported increasing levels of anti-TPO antibodies and serum TSH levels with advancing age.[16,17,18] This increase in TSH with age might be due to increased presence of anti-TPO antibodies in the participants. The present study did show an increased prevalence in the age group above 45 years. But, this cannot be directly related to the prevalence of diseases as the study focused on indices and not on prevalence of autoimmune thyroid diseases. When anti-TPO positive group was excluded, no age-dependent change was noticed in our study. Data from this study can be used as a reference for future investigations and also for comparisons with other cohorts who have a high risk of thyroid dysfunction and autoimmunity.

Positive family history of thyroid dysfunction is associated with elevated anti-TPO antibodies.[19] In the present study, 34% of the participants with a family history of thyroid disorders had elevated anti-TPO antibodies. Further, majority of the patients with hypothyroidism (55.56%) had elevated amount of anti-TPO antibodies, although a statistically significant relation could not be established between TSH and anti-TPO antibodies. Many studies do show a significant positive correlation between anti-TPO antibodies and TSH.[3,19] But, the increased risk of developing thyroid dysfunctions with increased levels of anti-TPO antibodies is more or less well established. This is a single-centre study and has not included other antibodies involved in thyroid autoimmunity. A higher sample size and a long-term follow up study are warranted to give a better picture of the effect of autoimmunity in the overall health and quality of life.

Matalon et al[20] found that anti-TPO antibodies, even when not associated with overt thyroid dysfunction, cause poor reproductive outcomes. Autoimmunity due to these antibodies is one of the important factors in infertility and

anti-TPO antibody positive women are found to have spontaneous miscarriages, recurrent abortion, lower fertilisation, implantation and pregnancy rate.[2,15,21] The changes in fertility and maintenance of pregnancy maybe channelled by triggering the immune system or by increasing the risk of subclinical hypothyroidism, which later progresses to clinically overt hypothyroidism.[22,23] This may explain why the mean value of TSH is skewed to the higher side of normal range in anti-TPO positive women in our study. As 64% of the participants are not married or are yet to plan for a child, this evaluation and study are significant. With autoimmunity and thyroid dysfunction related to negative reproductive outcomes, early diagnosis is warranted to prevent infertility and other pregnancy-related issues. Preclinical identification of this disease is now possible using antibody testing. Anti-TPO as an indicator of increased risk of thyroid diseases, thus gains importance, particularly in females of reproductive age group. More studies are required to explore the predictive value and clinical management options for women with elevated anti-TPO antibodies to improve the pregnancy outcomes and overall health.

CONCLUSION

The present study shows that about one in four women in the reproductive age have higher levels of anti-TPO antibodies. Most of these women are euthyroid and asymptomatic. Levels of anti-TPO are associated with TSH values indicating a negative impact on thyroid function. It can lead to thyroid dysfunction, which in turn affect fertility, pregnancy and other reproductive outcomes. Early diagnosis and treatment of the autoimmunity will help to improve the reproductive outcomes in women in reproductive age group. More than half of the participants in our study (64%) are not married or are yet to plan for a child making this study and evaluation very relevant. This study can be a reference for future prospective studies and comparisons particularly in people with an elevated risk of thyroid autoimmunity and other autoimmune disorders.

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