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Autoimmune thyroid disease in women with ages between 35 to 45 years based on Azar cohort data

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Abstract

Introduction: Autoimmune thyroid diseases are common findings in women of childbearing age that could affect fertility rate, pregnancy outcome and complications after pregnancy. These diseases also correlated with other autoimmune diseases.
Objectives: In this study, we aim to evaluate the autoimmune thyroid disease in women aged 35 to 45 years based on Azar cohort study data.
Patients and Methods: In this cross-sectional analytical study, 507 women 35-45 years old without previous thyroid disease from Azar cohort study were evaluated. Demographic findings, data related to previous pregnancies, abortion, miscarriage, infertility and gestational diabetes were recorded for all patients. Blood samples were taken from all patients to measure TSH and anti-thyroid peroxidase (anti-TPO) levels. Anti-TPO levels ≥40 IU/mL were considered positive.
Results: In the studied women, miscarriage occurred in 5.3%, abortion in 27.6% and infertility in 7.3%. Gestational diabetes was reported in 3.9%. The positive anti-TPO prevalence was 21.5%. Patients with positive anti-TPO compared to those with negative anti-TPO had significantly higher cases of hypothyroidism ($P<0.001$). There was no difference between patients with and without positive anti-TPO regarding miscarriage (5% versus 6.4%), abortion (27.4% versus 28.4%), infertility (7.5% versus 6.4%) and gestational diabetes (7.9% versus 3.6%) ($P>0.05$). There was no correlation between age and anti-TPO levels.
Conclusion: The prevalence of thyroid antibodies in our study population is higher than previous studies. Anti-TPO positivity has no significant effect on pregnancy outcome in this population. Further studies are necessary to define the exact effect of anti-TPO on pregnancy outcomes.

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Introduction

Autoimmune thyroid diseases including Graves' disease and Hashimoto's thyroiditis affect almost five percent of the general population (1). There are multiple risk factors for autoimmune thyroid disease including familial history of autoimmune thyroid disease, older age, iodine deficiency and European ethnicity (2).

Studies have reported that thyroid autoimmunity defined as positive thyroglobulin or anti-thyroid peroxidase (anti-TPO) antibodies, can lead to miscarriage or recurrent abortion (3), preterm labor (4), infertility (2-4), and fetal neurodevelopmental disorders (2). In addition, the increase in anti-TPO positivity can lead to postpartum depression (5), intrauterine growth retardation, higher prenatal mortality (6) and postpartum thyroiditis (7).

Previous studies have indicated that the prevalence of thyroid autoimmunity in women in childbearing ages increases with age with higher prevalence in women 40-49 years old (16.4-18%) (2,8).

Objectives

In this study, we aimed to evaluate the autoimmune thyroid disease in women with aged 35 to 45 years based on Azar cohort study data.

Patients and Methods

Study design

In this cross-sectional analytical study, 507 women between 35-45 years old without known thyroid diseases from Azar cohort study were included. All patients with history of receiving thyroid treatments or with known thyroid diseases as well as those with history of infertility were excluded. Patients were then referred to a laboratory for the anti-TPO antibody test. For those with positive anti-thyroglobulin test, TSH levels were also checked. Other information were obtained from Azar cohort data. The demographic findings as well as marital status, number of pregnancies and outcome, familial history of thyroid disease, previous gestational diabetes mellitus, history of other autoimmune diseases

Key point

Autoimmune thyroid diseases are common findings in women of childbearing age that could affect fertility rate. This cross-sectional analytical study, 507 women 35-45 years old without previous thyroid disease from Azar Cohort study were evaluated. Blood samples were taken from all patients to measure TSH and anti-TPO levels. Anti-thyroid peroxidase (anti-TPO) ≥40 IU/ml were considered positive. There was no difference between patient with and without positive anti-TPO regarding miscarriage (5% versus 6.4%), abortion (27.4% versus 28.4%), infertility (7.5% versus 6.4%) and gestational diabetes (7.9% versus 3.6%; p>0.05). There was no correlation between age and anti-TPO levels.

including vitiligo and diabetes mellitus were recorded in a checklist.

Statistical analysis

All data were analyzed using the SPSS software 20 (Statistical Package for the Social Sciences, SPSS Inc., Chicago, IL, U.S.A.). Results were presented as mean and standard deviation (SD) or frequency and percentage. Thyroid autoimmune disease incidence was presented with Odds ratio and CI 95%. Binary logistic regression was used to define the correlation between anti-TPO levels and intrauterine fetal deaths (IUFDs), abortion and infertility. Pearson's correlation was used to show the relations between patients' age and anti-TPO levels. *P* values of <0.05 were considered significant.

Results

In this study, 507 women between 35 and 45 years old with mean age of 39.66 ± 2.94 years were included. Patients were single in 21 cases (4.1%), 10 (2%) were pregnant during the study period and 37 (7.3%) had no previous pregnancies. Abortion and IUFD were reported in 140 (27.6%) and 27 (5.3%) of participants. There was no history of postpartum thyroiditis, preterm labor or infants with neurologic complications.

Mean TSH levels were 3.46±3.36 mLU/L (range 0.25-38.20 mLU/L) and anti-TPO levels was 46.88 ± 17.50 IU/mL (range 0.9-1041 IU/mL). Positive anti-TPO (≥40) were seen in 109 women (21.5%) with CI 95% [17.91-25.09]. According to reference classifications, 13 (2.6%) were hyperthyroid (TSH <0.5 mLU/L), 372 (73.4%) were euthyroid and 122 (21.4%) were hypothyroid (TSH >4.5). Three patients (0.6%) were hyperthyroid (TSH<0.3 mLU/L), 443 individuals (78.4%) were euthyroid since 31 persons (12%) were hypothyroid (TSH >6.1 mLU/L).

Mean TSH levels in women with positive and negative anti-TPO were 5.39 ± 0.55 IU/mL and 2.93 ± 0.09 IU/mL) respectively which was significantly higher in anti-TPO positive cases ($P < 0.001$). Women with positive anti-TPO compared to negative anti-TPO had significantly higher cases of hypothyroidism according to reference and laboratory classifications ($P < 0.001$; Figures 1 and 2).

Pregnancy outcomes between women with positive and negative anti-TPO are demonstrated in Table 1. There was no significant difference between groups.

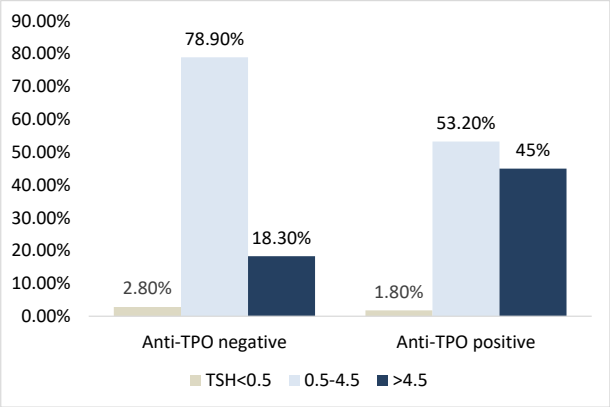

Figure 1. Comparison of frequency of hypothyroidism according to reference (a) and laboratory classification (b) in women with and without positive anti-TPO.

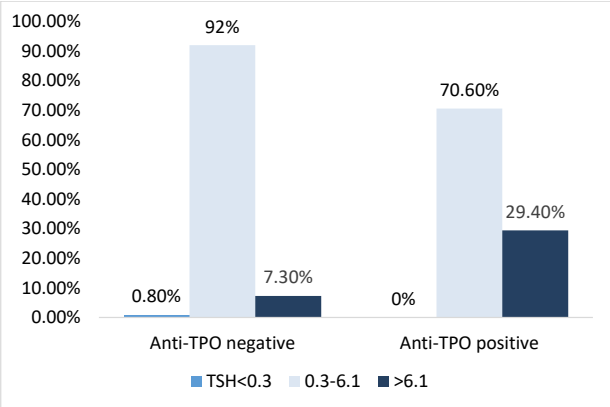

Figure 2. Comparison of frequency of hypothyroidism according to reference (a) and laboratory classification (b) in women with and without positive anti-TPO.

We found no significant correlation between age and anti-TPO level (r = -0.032, $P = 0.47$).

Using binary logistic regression and excluding age and TSH levels as confounding factors, the correlation between anti-TPO level and infertility, abortion and IUFD were evaluated, which showed no significant correlations (Table 2).

Discussion

Previous studies have shown that autoimmune diseases, especially thyroid autoimmune diseases, are more common in women than men (9). However, there is no complete information on the prevalence of thyroid autoantibodies in non-pregnant women. In the literature, most of the studies conducted have examined the frequency and role of autoantibodies in pregnant women and pregnancy consequences.

In the present study, we investigated the prevalence of thyroid autoimmune diseases in women aged 35 to 45

Table 1. Pregnancy outcome between women with positive and negative anti-TPO

	Positive anti-TPO	Negative anti-TPO	*P* value
IUFD	7 (6.4%)	20 (5%)	0.56
Abortion	31 (28.4%)	109 (27.4%)	0.82
Infertility	7 (6.4%)	30 (7.5%)	0.69
Gestation DM	7 (7.9%)	13 (3.6%)	0.07

Table 2. Correlations between anti-TPO and infertility, abortion and IUFD

Variable	Odds ratio	95% Confidence interval		*P* value
		Lower limit	Upper limit	
Infertility	0.853	0.349	2.083	0.72
Abortion	1.097	0.666	1.808	0.71
IUFD	0.643	0.256	1.615	0.34

years in the Azeri population of Shabestar region from Azar cohort study. The results of the present study showed that the frequency of positive anti-TPO in the general population was 21.5%, which is higher than the values reported in previous studies.

Previous studies have shown that the frequency of thyroid autoantibodies in women under 30 years old is 9.2 to 11.9%, and varies between 14.5 and 18 percent between the ages of 30 and 50 (2,8). Yan et al observed that the positive anti-TPO is present in 11.5% of the general population, which is significantly higher in women than in men (14.5% versus 7.6%) (10). However, some studies have shown that the frequency of positive autoantibodies in the general population can be as high as 20% (1).

The prevalence of anti-TPO antibodies varies between five and 14% in pregnant women (8).

There is a contradictory relationship between age and autoantibodies level. Aminorroaya et al, study suggested that autoantibodies increase with age; however, others have not reported such relationship (11). The results of some studies showed autoantibodies increase with age; however, others have not reported such relationship (12). Similarly, in the present study, no association was found between age and anti-TPO level and positive cases. In contrast to the above study, a large study conducted by Hollowell et al (12) in the United States showed that anti-TPO level increases with age. This discrepancy could be due to racial and geographical differences, as well as the exclusion of women over the age of 45 from the present study.

A review article of studies on the frequency of anti-TPO and thyroid disorders in different countries has yielded that women have a higher risk of developing autoimmune thyroid disease. There are many geographical and racial differences in the frequency of thyroid antibodies. Hashimoto's thyroiditis is the main clinical disease of this category, which becomes more common with older age. Thyroid antibodies are very common and their frequency increases with age and their highest incidence are in the range of 44-55 years and the frequency of positive thyroid antibodies has increased over time (13). Positive autoantibodies to thyroid antibodies, especially anti-TPO, may be associated with hyperthyroidism or hypothyroidism or progress to hypothyroidism over time (1). In the present study, it was observed that people with positive anti-TPO had significantly higher TSH levels and higher rate of hypothyroidism. Many of the previous studies have used the presence or absence of anti-thyroid antibodies, age and gender of the study population to predict the progression of euthyroidism to overt or subclinical hypothyroidism and hyperthyroidism (14). However, few long-term studies, including a 13-year follow-up study in Australia (15) and a 20-year follow-up study in the UK (16), showed increased levels of thyroid antibodies, including anti-TPO and anti-thyroglobulin. They are associated with an increased risk of hypothyroidism and elevated TSH levels (15,16). The presence of anti-TPO may be related to the severity of thyroid lymphocytic infiltration regardless of the presence or absence of hypothyroidism (17). In women of childbearing age, and especially in pregnant women, there has been an association between maternal and fetal outcomes during and after childbirth with thyroid antibodies. However, the available results are contradictory (18). There is a significant positive relationship between the number of pregnancies and the development of autoimmune thyroiditis (19). Additionally, elevated anti-TPO levels are an important risk factor for miscarriage (4).

In the present study, only abortion, stillbirth, infertility and gestational diabetes were present in the study population. Among them, no significant relationship between positive anti-TPO and abortion, stillbirth and infertility was seen.

Similarly, Yehuda and colleagues observed that there was no relationship between anti-TPO levels and the presence and number of pregnancies. Two large cohort studies reported similar results. Bulow Pedersen et al (20), found no association between serum levels of thyroid antibodies and a history of pregnancy.

In contrast to the present study, Boufas et al (21), observed that the presence of positive anti-TPO levels was associated with infertility rates. These findings were also detected by Colicchia et al (22). A meta-analysis evaluating 12 case studies and 19 cohort studies found, a strong association between thyroid autoimmunity and abortion rates (23).

In the present study, the incidence of gestational diabetes in the positive anti-TPO group was also higher; however, the observed difference was not significant. In a previous study evaluating euthyroid women with positive and negative anti-TPO also reported a slight increase in the risk of gestational diabetes (24). The exact mechanism by which thyroid antibodies have effect on pregnancy outcomes was not detected yet. However, Crawford and Steiner suggested that women with positive thyroid antibodies should be fully evaluated and have regular care

during pregnancy to prevent unwanted complications (25).

Conclusion

The prevalence of thyroid antibodies in our study population is higher than previous studies. Anti-TPO positivity has no significant effect on pregnancy outcome in this population. Further studies are necessary to define the exact effect of anti-TPO on pregnancy outcomes.

Limitations of the study

Our sample size was relatively low as we excluded some patients because of missing hospital records

Authors' contribution

VS and FGh were the principal investigators of the study. AM and VS were included in preparing the concept and design. NA and FN revisited the manuscript and critically evaluated the intellectual contents. All authors participated in preparing the final draft of the manuscript, revised the manuscript and critically evaluated the intellectual contents. All authors have read and approved the content of the manuscript and confirmed the accuracy or integrity of any part of the work.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

The ethics committee of Tabriz University of Medical Sciences (Ethical code# IR.TBZMED.REC.1397.872) approved the study protocol and all participants gave written informed consent. This study was conducted as part of the internal medicine residency dissertation of Fatemeh Ghorbani at this university. Additionally, ethical issues (including plagiarism, data fabrication, double publication) were completely observed by the authors.

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