

Prevalence of Anti-Thyroid Peroxidase Antibody positivity and its Effect on Pregnancy Outcome in women with Unexplained infertility

Faranak Jalilvand¹, *Shahla Farzipour¹, Firouz Amani², Ghinus Ghamisi¹

1. Department of Obstetrics and Gynecology, School of medicine, Ardabil University of Medical Sciences, Ardabil, Iran.

2. Department of Community Medicine and Biostatistics, School of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran.

ARTICLE INFO	ABSTRACT
<p>Article type: Original Article</p> <hr/> <p>Article History: Received: 27 May 2023 Accepted: 29 Oct 2023</p> <hr/> <p>Key words: Anti-TPO, Euthyroid, Pregnancy outcome.</p>	<p>Introduction: Thyroid disease is the second endocrine disorder that affects women in reproductive age and its autoimmunity can affect the outcome of the pregnancy. The aim of this study was to investigate the prevalence of Anti-TPO positivity and its effect on pregnancy outcomes in women with unexplained infertility.</p> <p>Materials and Methods: In this cross-sectional descriptive study, 93 infertile women who referred to infertility center at Ardabil city during 2020-2021 were recruited for the study. Information such as age, BMI, TSH, prolactin and results of Anti-TPO were completed for all cases and then analyzed by statistical methods in SPSS version 23.</p> <p>Results: The prevalence of anti-TPO positivity was 73.1% (n=68). The mean of BMI, Age, TSH and prolactin were not significantly different in women with Anti-TPO positivity as compared to others. There was no relation between TSH and Anti-TPO results and Also between TSH and results of pregnancy.</p> <p>Conclusion: Our results indicate that anti-TPO screening in pregnancy, may aid in early identification of the women at risk at the future.</p>
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*Corresponding Author:

Department of Obstetrics and Gynecology, School of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran.
E-mail: sh.farzipour2019@gmail.com; sh.farzipour@arums.ac.ir

Introduction

Infertility refers to one year of intercourse without prevention and pregnancy. Fertility for a normal couple is estimated to be 20-25%, as a result, pregnancy will occur in 85%-90% of couples 1 year after marriage and about 10-15% of couples have fertility problems in the first year after marriage. Normal thyroid function is important for maintaining normal reproduction. Thyroid dysfunction is associated with decreased fertility (1). Thyroid disease is the second endocrine disorder that affects women of reproductive age and usually associated with infertility. Autoimmune thyroid disease are associated with unknown infertility and non-implantation. Uncontrolled thyroid diseases (hypothyroid and hyperthyroid) are associated with infertility (2).

The increase of thyroid autoantibodies in barren women has a high prevalence rate. Women with high titer of anti-thyroid antibody have poor function or suffer from autoimmune disease. Research shows that there are reproductive problems in women with high levels of antibodies to prevent the transfer of autoimmune genes to the next generation (3).

Increased thyroid stimulating hormone (TSH) and the presence of anti-thyroid peroxidase (TPO) antibodies during pregnancy are associated with miscarriage, premature birth and adverse perinatal outcomes. Therefore, in infertile women, thyroid supplementation is usually prescribed to maintain TSH levels below 2.5/mIU. However, there is insufficient evidence of the relationship between TSH levels or AntiTPO antibodies and pregnancy outcomes, miscarriage and live birth in infertile women. Thyroid hormones seem to play an important role in implantation and pregnancy. Thyroid dysfunction is reported as hypothyroidism in 4.6% of the general population. Subclinical hypothyroidism (TSH level—above 4.5 mU/L) was observed in 2.3% of pregnant women, and is associated with an increased risk of infertility and perinatal side effects (4).

Thyroid dysfunction is associated with decreased fertility. Ovarian overstimulation leads to an increase in estradiol, which in turn may have an adverse effect on thyroid

hormones and TSH. In the presence of autoimmune thyroid disease, the effect of ovarian overstimulation may be more severe depending on the amount of thyroid abnormalities, autoimmune thyroid disease is present in 5-20% of pregnant women (1). The presence of thyroid autoantibodies may cause cytotoxicity in the growing ovarian follicle and damage to the mature egg, which may reduce its quality and consequently its fertilization and development (5).

The presence of antithyroid antibody (ATA) is frequently encountered in general population and approximately 1/5 of childbearing-age women are positive for the anti-thyroid peroxidase antibody (TPO-Ab) or anti-thyroglobulin antibody (TG-Ab) (6).

Previous studies showed that, there were 10.5% of infertility women who were positive for ATA. It has been shown that the TPO-Ab level was associated with the thyroid-stimulating hormone (TSH) level for example, TPO-Ab positive women had significantly increasing TSH level and also some women with normal TSH level may be found to be positive for TPO-Ab (7-9).

The presence of ATA in Euthyroid women may lead to some fertility problems, including increased miscarriage rates and infertility. Recently, researchers believe that in women with positive ATA and even in women with Euthyroid results

The prevalence of autoimmune thyroid disease (TAI) in infertile women, especially in women with endometriosis and polycystic ovary syndrome, is significantly higher compared to women of the same age (10). It has also been shown that controlled ovarian hyperstimulation (COH) in the preparation of ART has a significant effect on thyroid function, especially in women with TAI. Levothyroxine should be prescribed to women with thyroid dysfunction before or in the early stages of pregnancy (11).

Habibzadeh et al. (2017), in a research, investigated the prevalence of TPO-Ab positive cases in euthyroid individuals with unexplained infertility in patients referred to an infertility center. In this study, 75 euthyroid patients with unexplained infertility using easy sampling were selected as the case group and 150 euthyroid women with no history of infertility and a successful

pregnancy were selected as the control group. The amount of TPO-Ab in the serum of the participants in the study was measured and analyzed by the Liazon method. These researchers concluded that the level of Anti-TPO antibody in Euthyroid women with unexplained infertility is higher than in the control group (12). Considering the importance of thyroid diseases in fertility and few documented studies on the relationship between TPO-Ab and unjustified infertility, in order to identify one of the effective factors in infertility and programing intervention to resolve this factor, the purpose of this study is to investigate the prevalence of positive anti-TPO cases and pregnancy outcome in patients referred to the infertility treatment center of Ardabil University of Medical Sciences.

Materials and Methods

This cross-sectional descriptive study was conducted on 93 infertile women with an abnormal thyroid test with the criteria of entering the infertility center of Ardabil University of Medical Sciences in 2019-2019 and registered by code IR.ARUMS.REC. 1399. 110. After registering the study in the Ethics Committee of Ardabil University of Medical Sciences and also registering it in the Iranian Clinical Trials Registration Center, informed consent was obtained from eligible mothers to participate in the study. Age information, Anti-TPO test result and TSH level of women were registered in a checklist and women were followed up until the end of pregnancy and pregnancy result was recorded. Women with at least one year of infertility after marriage, without proven thyroid diseases, age between 18 to 43, non using immune suppressive drugs and corticosteroids such as levothyroxine, methimazole and propylthiouracil currently and in the last 3 months, not having other endocrinopathies and chronic heart, respiratory, liver and kidney diseases, without a history of thyroid, ovary and uterus surgery were entered in the study. Women with chronic disease and high BMI, with thyroid diseases, uses of immunosuppressive drugs and corticosteroids, endocrine diseases, patients with other autoimmune diseases, or positive

anticardiolipin antibody, antinuclear antibody, lupus anticoagulant factor or positive rheumatoid factor and genetic thrombophilia were excluded from the study.

After collecting the information and coding, the data were analyzed using SPSSv 23 software and descriptive statistics methods in the form of tables and graphs and statistical and analytical indicators using the t-test and chi-square tests.

Results

The average age of women was 32.53 ± 6.79 (within the age range of 19-48) and the average BMI was 24.66 ± 4.01 . The average prolactin level was 111.441 ± 167.64 (in the range of 3.50-855) and the average TSH level was 5.75 ± 8.31 mIU/L (in the range of 0.02-73.44). The average level of Anti-TPO was 194.27 IU/ml (in the range of 0.08-1000), 25 cases (26.9%) were in the normal range and 68 cases (73.1%) were positive (Chart 1). Patients with abnormal anti-TPO antibody test results were treated. In 37 (39.8%) infertility cycles were not performed. Among the cases that had an infertility cycle, the infertility treatment was ISCI in 40 cases (43%), IUI in 14 cases (15.1%), and egg donation in 2 cases (2.2%), and the result of pregnancy was in 11 cases (11.8%) was reported positive (Figure 1).

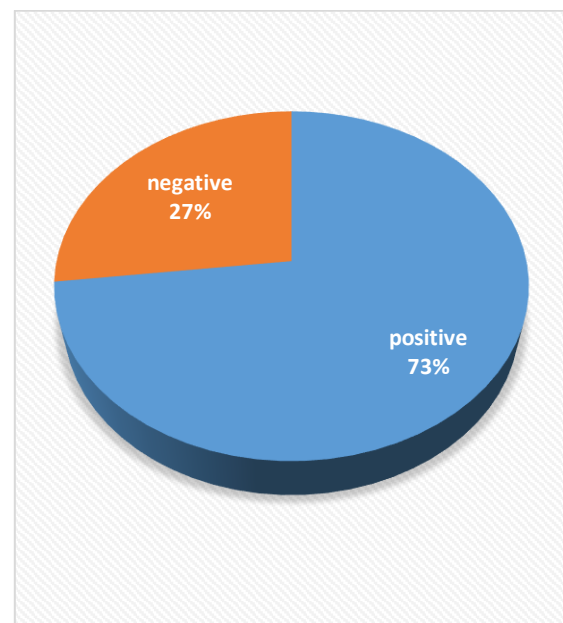


Fig. 1: Frequency distribution of women by anti-TPO results

Based on the independent t-test, there was no statistically significant difference between the average values of TSH, BMI, prolactin and age in the two groups with anti-TPO above normal (positive) and normal.

Among the women who had a positive pregnancy result, 54.5% had anti-TPO above normal (positive) and the rest were normal, and there was no significant difference between pregnancy results with normal and high anti-TPO levels (Table 1).

Table 1. Compare quantitative variables by Anti-TPO results

Variables	Anti-TPO	n	Mean	Std. Deviation	p-value
BMI	normal	25	26.39	4.14	0.69
	positive	68	26.76	3.99	
Age	normal	25	30.56	6.3	0.09
	positive	68	33.25	6.87	
Prolactin	normal	25	154.682	237.75	0.13
	positive	68	95.5	131.86	
TSH	normal	25	4.01	3.52	0.22
	positive	68	6.39	9.44	

Discussion

Thyroid disorders are common during pregnancy and can affect the outcome. High anti-thyroid antibodies play an important role in infertility related to thyroid autoimmunity in women (13). Many researches have been conducted on the effect of thyroid disorders in pregnant women and have evaluated the positivity of anti-thyroid antibodies in the sample population. The positivity rate of anti-thyroid antibody is different in studies and depends on the sample size as well as geographical factors of the studied group (14). In this study, which was conducted on infertile women referred to infertility treatment center, there was no correlation between pre-pregnancy TSH levels and pregnancy outcomes, as well as between AntiTPO antibody levels and pregnancy outcomes. The results of this study showed that the high level of AntiTPO antibody before pregnancy is not a risk factor for poor pregnancy outcome. The results of this research suggest that identifying and treating women with high AntiTPO antibody levels before pregnancy can be effective in improving pregnancy outcomes (4). The findings of this research that there is no relationship between the increase in AntiTPO antibody levels before pregnancy in infertile and pregnant women are different from a number of studies that found a relationship (14-15). The lack of correlation between the level of AntiTPO antibody

before pregnancy and the rate of pregnancy was consistent with recent studies conducted in the population of infertile women (16-17). The results of the present study were different from the results of a number of studies based on higher TSH and AntiTPO antibody values that were evaluated during pregnancy and resulted in abortion. Therefore, screening time for TSH level and AntiTPO antibody is important in case of suspicious values before pregnancy. However, the value of screening in pregnancy is still controversial and unproven. In addition, there may be conflicting results between research results and causes of abortion (14,18). In a research, the relationship between AntiTPO antibody and pregnancy was investigated and it was concluded that in women with high AntiTPO antibody, due to thyroid function defects, problems do not occur before pregnancy and appear with complications in the early stages of pregnancy (5,19). In a research, it was found that there was a significant relationship between Anti-TPO antibody and the rate of miscarriage and low birth rate (20). Also, in a research, it was found that the presence of Anti-TPO antibody reduces the potential of fertilization and egg, and as a result, the implantation of the embryo (5), while in the present study, no correlation between Anti-TPO and pregnancy rate was observed. The findings of another study also showed similar rates of pregnancy, abortion and delivery and did not confirm the

negative effect of TSH level above 2.5 milliunits/liter on the rate of pregnancy and live birth (21).

Presence of thyroid autoimmunity does not interfere with normal embryo implantation, but the risk of early miscarriage is substantially raised. Autoimmune thyroid disease is present in around 4% of young females, and up to 15% are at risk because they are thyroid antibody-positive (22). In order to prepare for assisted reproductive techniques, increasing circulating estrogen levels can severely disrupt thyroid function. Systematic screening for thyroid disorders in women with female infertility to diagnose autoimmune thyroid disease should be done before starting assisted reproductive techniques, which is not consistent with our study (23).

Several studies with conflicting results regarding the timing of thyroid tests and completion of the course. Follow up has been done. Comparing the results of a systematic review study showed that high AntiTPO antibody has no effect on the fertility rate, but increases the abortion rate, which is in line with the present study (24). Zhong's study shows that patients with high anti-thyroid antibody compared to people with normal anti-thyroid antibody have a lower conception rate, implantation rate and pregnancy rate and a higher risk of miscarriage following IVF-ET (10). In our study, most of the patients referred to the infertility center were from the entire Ardabil province for treatment, and it is possible that the prevalence of anti-TPO positivity in the current study does not reflect the entire population of the province or the country.

Conclusion

The results of present study showed that most of women with thyroid disorders in this study had Anti-TPO positivity. Larger studies with bigger sample size and population subsets from different geographical regions of country are needed to establish the relationship between result of Anti-TPO and adverse pregnancy outcomes. Also, our results indicate that anti-TPO screening in pregnancy, may aid in early identification of the women at risk and

promotion of pregnancy results at the future. Also by treating hypothyroidism and hyperthyroidism before starting infertility treating, we can improve the results of pregnancy techniques.

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