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Short Communication

Unexpected high frequency of anti-thyroid peroxidase (anti-TPO) antibodies in Golestan province, Iran

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Abstract

Background: Anti-TPO antibodies are one of the characteristic factors in autoimmune thyroiditis (AIT). Previous studies reported a high prevalence of anti-TPO antibodies (Abs) in Iran. We have therefore assessed the prevalence of anti-TPO Abs in Gorgan, Iran.

Methods: This cross-sectional study, conducted from 2015 to 2018 in Gorgan city, Northeast of Iran. The Participants included women with Poly cystic ovary syndrome (PCOs), celiac patients, men with hepatitis C infection, and age and sex-matched controls. ELISA method was used for the analysis of laboratory tests.

Results: The number of enrolled subjects in PCOs, celiac disease, and Hepatitis C infection groups were 76, 67, and 60, respectively. Anti-TPO Abs positivity was significantly higher in patients with PCOS than in the control group (18.4% vs. 0.00%; p = 0.000). There were no significant differences in the frequency of anti-TPO Abs positive cases between CD patients and the controls (26.9% vs. 21.1% p =0.413). The incidence of anti-TPO Abs positivity was significantly higher in the control group (10% vs. 25%; P = 0.031).

Conclusion: Very high level of anti-TPO Abs was observed in both patients and healthy population in Golestan province. Considering this rate and its association with autoimmune disorders, it is suggested to prioritize screening programs for related disease in this area.

Keywords: Anti-thyroid Peroxidase (anti-TPO), Autoimmune thyroiditis (AIT), Celiac disease, Hepatitis C infection, Iran

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The thyroid gland is the most common site of autoimmune diseases (1). Autoimmune thyroiditis (AIT) is characterized by anti-Thyroid peroxidase (anti-TPO) and anti-Thyroglobulin (anti-Tg) autoantibodies (2). The prevalence of thyroid dysfunction in a different population depends on geographic/environmental factors, sex, age, ethnicity, etc (3,4). Previous studies in Iran reported a high prevalence of anti-TPO antibodies (Abs) either in patients with specific disorders or in the general population (5–8). We have therefore assessed the prevalence of anti-TPO Abs in women with polycystic ovarian syndrome (PCOS), male with hepatitis C and celiac patients (CD) compared to the control group.

Methods

This cross-sectional study, conducted from 2015 to 2018 in Gorgan city, Northeast of Iran. The Participants included 1) Women with confirmed PCOs with diagnostic criteria such as oligoovulation, anovulation, clinical or biochemical hyperandrogenism, and polycystic ovaries at ultrasonography (9).

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The control group included healthy age and sex-matched women who visited gynecology clinics for other gynecological concerns except for POCS and AIT; 2) Celiac patients diagnosed with positive serological tests for tissue transglutaminase (TTG) antibodies, followed by an intestinal biopsy (10). The control group included healthy age and sex-matched patients who visited gastroenterology clinics for other concerns except for CD, AIT, and no IgA deficiency; 3) Men recently diagnosed with hepatitis C using a rapid HCV antibody test and PCR method (11). The control group included healthy age and sex-matched men who visited gastroenterology clinics for other concerns except HCV, AIT, with no history of being in prison, addiction to IV drugs, and positive HBsAg. Anti-TPO Abs was checked with an ELISA method in the same laboratory.

The local ethical committee of the Golestan University of Medical Sciences approved the protocol (IR.GOUMS.REC.1398.164).

Results

The PCOs patients consisted of 76 women with a mean age of 26.62±5.58 years. In the control group, there were 66 females. PCOS was diagnosed based on oligoovulation in 61 patients (85.9%), polycystic ovaries at ultrasonography in 48 (67.7%), clinical or biochemical hyperandrogenism in 26 (36.6%), and anovulation in 22 (31%). Anti-TPO Abs positivity was significantly higher in patients with PCOS than in the control group (p = 0.000) (table 1). In the CD patients, there were 18 males and 49 females with a mean age of 38.65±11.48 years. The control group consisted of 28 males and 57 females. There were no significant differences in the frequency of anti-TPO Abs positive cases between CD patients and the control (p =0.413) (table 1). Hepatitis C patients consisted of 60 men with a mean age of 41.17±8.033 years. In the control group, there were 60 men. The incidence of anti-TPO Abs positivity was significantly higher in the control group (P = 0.031) (table 1).

Table 1. Anti-thyroid Peroxidase (anti-TPO) positive rate and median in polycystic ovarian syndrome (PCOS), Celiac disease (CD), and hepatitis C infection, and control groups

	PCOs			CD			Hepatitis C infection		
	Case (N:76)	Control (N:66)	P-value	Case (N:67)	Control (N:85)	P-value	Case (N:60)	Control (N:60)	P-value
Positive Anti-TPO, N (%)	14 (18.4%)	0 (0%)	0.000	18 (26.9%)	18 (21.2%)	0.413	6 (10%)	15 (25%)	0.031
Anti-TPO median (IU/ml)	5.4200	3.2400	-	16.3000	19.8000	-	11.4500	17.4000	-

Discussion

Results showed a higher rate of anti-TPO antibodies in PCOS patients than in controls. Other studies also claimed a significant relationship between PCOS and Autoimmune thyroiditis disease (AITD). studies in the Slovak Republic (18.75% vs. 7.35% P=0.045) (12), Turkey (37.9% vs. 11.1% p <0.001) (13) and Isfahan, Iran, (30.6% vs. 27.8% P = 0.730) reported a higher prevalence of anti-TPO Abs in PCOS women compared to the control group (14). Although the mechanisms of this association are not clear but probable justifications were offered. Evidences showed excess in estrogens secretion in women leads to higher prevalence of systemic autoimmune disorders (15). The expression of interleukin-6 increases due to over-secretion of estrogens; this process reduces the level of progesterone and its inhibitory effect on immune system in patients with PCOS (16). The result of the immune system over-stimulation could be the inappropriate production of autoantibodies (17,18).

The prevalence of anti-TPO Abs in CD patients was not significantly different from controls in our study. Whereas other studies reported a significant correlation between CD and thyroid autoimmunity. An Italian study in 2001, showed a high prevalence of anti-TPO *Abs* in CD patients compared to the control group (16.2% vs. 3.8% p<0.0005) (19). In another study by Baharvand et al. in 2020, rate of positive anti-TPO *Abs* was 4-fold higher in cases than in controls (1.7% vs. 0.4% p=0.03) (20).

The positive anti-TPO Abs level was found in 10% of hepatitis C patients (before interferon therapy). However, controls showed a higher rate of anti-TPO *Abs*. Previous

studies reported contradictory findings. Some researchers including Acay et al. (21) and Hasan Mohammed et al. (22) did not find an association between hepatitis C infection and anti-TPO positive *Abs*. Whereas other studies like studies in Pakistan (23) and China (24) reported that patients with chronic hepatitis C have a high-risk of AITD.

A notable result in this study was the high level of anti-TPO Abs in both case and control groups. Other studies from other parts of the world like a screening studies in Spain (weman:9.4%;men:2.4%) (25), a study in berlin (3.4%) (26), an African screening study(0%) (27), and A cross-sectional study in Malaysia (12.2%) (28), reported a significantly lower prevalence of anti-TPO Abs in the gener

al population than ours. This high prevalence of anti-TPO *Abs* in the general population was seen in previous studies in Iran. A studies in Shiraz (22.7%) (29) and Tehran (25.2%) (30) demonstrate a significantly high level of anti-TPO *Abs* in the control group also a population-based cohort study in Isfahan reported a considerable rate of thyroid dysfunction (23.4%) (7).

A high level of Anti TPO Abs has been thought to arise from a complex combination of genetic, environmental, and endogenous factors (31). In our region, this high level of anti-TPO *Abs* could be due to racial and regional differences (32), and iodine consumption (33). Golestan province composes of different ethnicities (32), so this may play a role in these results. Some studies demonstrated an association between genetic variations of TPO gene and anti-TPO Abs level. A study in Iran (2017) demonstrate A2173C polymorphism of TPO gene increases the rate of anti-TPO Abs level (P=0.035) (34) also another study in India found other TPO gene polymorphisms (Thr725Pro and Asp666Asp) associated with hypothyroidism (p = 0.01) (35). Therefore, due to the association of TPO gene variations with racial differences, evaluation of TPO gene polymorphisms in our region could shed more light on this issue.

Another reason for the higher rate of anti-TPO Abs in our region could be the iodine sufficient area by consumption of iodine salt (36,37). Iodine sufficiency is related to the increase of thyroid autoimmunity in iodine-sufficient areas (26). Some studies have mentioned excess iodine ingestion as a predisposing factor for thyroid dysfunctions. Studies from areas with high dietary iodine intake in Africa (38) and Japan (39) reported an increase in anti-TPO Abs. Therefore, iodine consumption is better to be done under close control of the health care system and nutritional habits of people such as consumption of salt (38,39).

In conclusion, we found a significant relationship between PCOS and a high level of anti-TPO Abs, but there was not in CD and hepatitis C. In addition, a high level of anti-TPO Abs was seen in the general population. Considering the high prevalence of anti-TPO Abs in this area, and the fact that it could be a strong predictive marker for future thyroid autoimmunity, it may be suggested that the Golestan health system take screening program more seriously. Further studies need to be conducted in order to identify etiologies and underlying reasons of this data in Golestan province.

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Authors' contribution: Study concept and design: BK, MM, TA; Acquisition of data: HH, FH, FA, MM; Analysis and interpretation of data: HH, FH. ; Drafting of the manuscript: HH.FH, MM; Critical revision of the manuscript for important intellectual content: FA, SB; Statistical analysis: HH, FH; Administrative, technical, and material support: BK, TA, SB; Study supervision: HH, FH and FA

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