https://doi.org/10.29309/TPMJ/2022.29.09.6959

The Professional Medical Journal
www.theprofesional.com
2022, Volume, 29 Issue, 09

ORIGINAL ARTICLE

Gender effect on anti TPO antibodies and hypothyroidism in patients presenting to a teaching hospital, Bahawalpur, Pakistan.

Sara Khan[1], Ayesha Siddiqa[2], Maryam Rafiq[3], Nudrat Fayyaz[4], Muhammad Ammad Asghar[5], Rizwan Hafeez[6]

Article Citation: Khan S, Siddiqa A, Rafiq M, Fayyaz N, Asghar MA, Hafeez R. Gender effect on anti TPO antibodies and hypothyroidism in patients presenting to a teaching hospital, Bahawalpur, Pakistan. Professional Med J 2022; 29(9):1379-1383. https://doi.org/10.29309/TPMJ/2022.29.09.6959

ABSTRACT… Objective: To know the gender difference in the autoimmune profile that is anti TPO antibodies and thyroid profile in patients with hypothyroidism and in euthyroid controls. **Study Design:** Case Control study. **Settings:** Medical Out Door Department of Bahawal Victoria Hospital, Bahawalpur. **Period:** 01/09/2018 to 31/08/2019. **Material & Methods:** Case control study that was conducted after taking ethical approval from hospital ethical committee. After taking informed consent data was entered on a predesigned questionnaire and 5 ml of venous blood was taken for thyroid profile and anti TPO antibodies. Study population was selected by nonprobability sampling. A total 128 patients in which 69 in the hypothyroid group A and 69 in euthyroid control group were added. **Results:** Most of the anti TPO positive hypothyroid participants were females but TSH value was more in males. All euthyroid anti TPO participants were females. Female hypothyroid patients were young compared to males. **Conclusion:** Autoimmune thyroid disorders are more common in females, autoimmunity appears before biochemical failure of thyroid.

Kew words: Anti TPO Antibodies, Autoimmune Thyroid Disorders, Euthyroid, Hypothyroidism.

INTRODUCTION

Autoimmunity includes a number of disorders and effect many organs. It can be due to cytotoxic T cells and autoantibodies. Data from studies from North America, New Zealand, Asia, Middle East and South America showed that most frequent being Graves's disease, hashimoto thyroiditis and autoimmune thyroiditis among thyroid disorders. It was also observed that there is a gender difference in the prevalence of autoimmune diseases and being more common in females.[1] Several genetic loci of autoimmune thyroid diseases have been identified and include CTLA4, HLA and IL2RA and many environmental factors are also implicated such as radioactive iodine therapy, iodine deficiency and smoking.[2]

The frequency of autoimmune thyroid disease is 0.1% of the population, but it can be as high as 15% in the form of subclinical focal thyroiditis and euthyroid population with positive antithyroid antibodies.[2] thyroid peroxidase enzyme involved in the hormone synthesis. A study from India showed the prevalence of anti TPO antibodies to be 9.5% and antiTG antibodies in 8.5% people. It is often sufficient to measure anti TPO antibodies because anti TG antibodies is rare. Studies have shown around 90% of hashimoto thyroiditid and 40-70% Garves's disease cases have positive autoantibodies.[3]

Autoimmune thyroid disorders are 5 to 10 fold more frequent in females than males.[4] One study showed that the frequency autoantibodies was 23% in females and 10% in males and the difference is statistically significant with P value of <0.01.[5] Though less frequent in males, there are certain factors which may have adverse outcome with respect to male gender. Like advancing age and male gender are associated

1. FCPS, Assistant Professor Chemical Pathology, CMH Institute of Medical Sciences Bahawalpur.
2. FCPS, Assistant Professor Chemical Pathology, PIMS Islamabad.
3. FCPS, Assistant Professor Chemical Pathology, Sahiwal Medical College, Sahiwal.
4. FCPS, Associate Professor Chemical Pathology, Multan Medical and Dental College. Multan.
5. FCPS, Senior Registrar Medicine, Sahiwal Teaching Hospital, Sahiwal.
6. FCPS, Assistant Professor Medicine, Shahida Islam Medical College Lodhran.

Correspondence Address:
Dr. Sara Khan
Department of Chemical Pathology
CMH Institute of Medical Sciences Bahawalpur.
sarakhan105@gmail.com

Article received on: 01/01/2022
Accepted for publication: 30/05/2022

with more severe ophthalmopathy, more severe biochemical derangement in Graves's disease. It is also reported that males less likely to go into remission after treatment with thalidomide and radioactive iodine treatment compared to females. It is also observed with thyroid disorder have more severe biochemical hyperthyroidism and goiter size and family history positive rate.[4]

So the aim of the study was to know the gender difference in the autoimmune profile that is anti TPO antibodies and thyroid profile in patients with hypothyroidism and in euthyroid controls. It is important to know these in local population as local studies are lacking. Also physician can be made aware of the fact that many euthyroid patients with positive thyroid antibodies will progress to hypothyroidism, so these patients should have a close follow so that complications because of thyroid derangement can be prevented.

MATERIAL & METHODS

This was a case control study that was conducted in the medical out door department of Bahawal Victoria Hospital, Bahawalpur between 01/09/2018 to 31/08/2019 after taking ethical approval from hospital ethical committee with IRB No Pub1276/18. After taking informed consent data was entered on a predesigned questionnaire and 5 ml of venous blood was taken for thyroid profile and anti TPO antibodies. Study population was selected by nonprobability sampling. Age sex matched euthyroid controls were selected. Hypothyroid patients between age group 18 to 60 years were included in the study. A total 128 patients in which 69 in the hypothyroid group A and 69 in euthyroid control group were added. The sample was analyzed by using fully automated analyzer by enhanced chemiluminecence method to analyze T3, T4 and TSH. Anti TPO antibodies were assessed by enzyme linked immunosorbent assay.

All data was entered in the predesigned questionnaire. The normal values for FT3 (3.2 -8.0 pmol/L) FT4 (10.3-34.7 pmol/L) and TSH (0.4-4.2 mIU/L) were set according to the kit. The FT3 and FT4 should be lower than lower normal limit and TSH should be above the upper normal limit.

Data Analysis

Data was entered and analyzed by using SPSS 20. Numerical variables were presented by mean and standard deviation while categorical data was measured by frequency and percentages. Chi square test was used to measure the significance and P value ≤ 0.05 was taken as significant.

RESULTS

In this case control study a total of 128 participants were included in the study in which 69 were hypothyroid and 69 age and sex matched controls. The mean age of the group A was 32.42±10.09 and in group B it was 32.45±10.12. The age distribution of the study group is shown in the Table-I below.

Age (In years)	(n= 69)	(n=69)
	No. of Patients (%)	No. of Patients (%)
18-30	37 (53.62%)	41 (59.42%)
31-60	32 (46.38%)	28 (40.58%)
Total	69 (100%)	69 (100%)
Mean+SD	32.42+10.09	32.45+10.12

Table-I. Age distribution (n=138)

When compared, the male and females with hypothyroidism with respect to age groups. It was observed that most of the females were from age group 18-30 years while in males highest number were from 30-60 years age group. The mean TSH value for females in hypothyroid group was 15.12±5.2 and in males it was 21.2±4. So mean TSH was high in males but it was not statistically significant with p value of 0.67.

Most of the participants were females with female to male ratio of 4.30:1 in group A and 5.27:1 in group B. The gender distribution is shown in the table below (Table-II).

Gender	Group-A (n=69)	Group-B (n=69)	
	No. of Patients (%)	No. of Patients	%
Male	13 (18.84%)	Male	13 (18.84%)
Female	56 (81.16%)	Female	56 (81.16%)
Total	69 (100%)	Total	69 (100%)

Table-II. Gender distribution (n=138)

The raised anti TPO antibodies were more in the female and the difference was statistically significant with p value of 0.000 which is highly significant.

Stratification for raised anti-thyroid peroxidase antibodies in both groups with regards to gender was done and found that out of 20 cases in Group-A 20% (n=4) were male and 80% (n=16) were females while out of 5 cases of Group-B 100% (n=5) were females, p value was calculated as 0.000 which shows a significant difference in age groups.

The stratification of raised anti TPO antibodies with respect to age group was done and following results were obtained as shown in the Table-III.

Age (in years)	Group-A (n=20) No. of Patients (%)	Group-B (n=5) No. of Patients (%)
18-30	9 (45%)	2 (40%)
31-60	11 (55%)	3 (60%)
Total	20 (100%)	5 (100%)

Table-III. Stratification for raised anti-thyroid peroxidase antibodies in both groups with regards to age. (n=25)
P value: 0.000

DISCUSSION

Thyroid gland has two major components that are thyroglobulin and thyroid peroxidase; these are involved in the production of thyroid hormones. Antibodies against these may indicate the initial phase of autoimmune thyroiditis. Antibodies against TPO may result in the destruction of thyroid gland resulting in hypothyroidism. There is high genetic influence on thyroid autoimmunity. According to studies genetic influence on anti TPO for male 61% and 72% for females.[6] This difference of susceptibility between two gender is due difference of the immune system. Male have more immune suppression compared to females that is linked to male sexual activity. This more immune reactivity puts females more vulnerable to autoimmune diseases.[7] In the current study, it was also observed that autoimmune thyroid disorders are more common in females in both hypothyroid and euthyroid groups.

Male to female ratio of current study population was 4.42:1, similar results were reported by a study conducted in Norway, where it was 4.9:1.[8] Though hypothyroidism more common in females but studies have shown that incidence in women decrease with increasing age especially after 60 years of age.[8] In present study majority of females were young compared to males with hypothyroidism and anti TPO antibodies.

In current study 7.25% participants from euthyroid group were anti TPO positive. It is also pertinent to note that all these were females. Studies have shown that subclinical hypothyroidism is more common in females.[9] So it is important to know that research has shown that people with circulating anti TPO antibodies with normal thyroid profile will progress to overt thyroid failure in future. Follow up of such patient will result in decreasing the morbidity related to undiagnosed thyroid disorders.[5,10,11] These studies have shown that baseline TSH can also predict the progression to overt thyroid failure. Antibody positive with TSH less than 2.5 mU/L, the risk of development of hypothyroidism 1% and 0.2% per year for subclinical and overt hypothyroidism respectively. For those with TSH between 2.5-4.0 mU/L with positive antibodies have 4% and 1% per year risk of development of subclinical and overt hypothyroidism. As it can be seen that rate of progression from euthyroid to hypothyroid is quite high. So this should be kept in mind that patients with high suspicion of thyroid disorder the diagnostic rate can be raised by evaluating the antibody status and correlating it with TSH level.[5,11,12]

In the present study lower age at diagnosis was observed in females compared to males. Similar findings were reported by Manji et al.[4] One study from Pakistan had shown that male patients have high mean TSH (36.83mIU/L) and lower mean TSH in females(17.63mIU/L) in patients with hypothyroidism.[14] In current study it was also observed that male patients have high mean TSH which is in agreement with this study.

It can be concluded from the above discussion that there is female preponderance in autoimmune

thyroid disorders like other autoimmune diseases. But it can be seen that autoimmune hypothyroidism occur relatively early in females than males and this is especially prominent after 60 years of age. Males have high mean TSH in contrast to the females. A number of euthyroid patients with positive anti TPO antibodies will progress to thyroid failure and its predictive value to diagnose progression can be increased by combining TSH value and anti TPO antibodies. So physician can be guided about its relevance especially in patients with nonspecific thyroid symptoms. This will help in early diagnosis of hypothyroidism and complications associated with hypothyroidism can be avoided. Single center study with small sample size and tertiary care hospital study are limitations of the study that limit results generalization.

CONCLUSION

It can be concluded from the above discussion that there is female preponderance in autoimmune thyroid disorders like other autoimmune diseases. But it can be seen that autoimmune hypothyroidism occur relatively early in females than males and this is especially prominent after 60 years of age. Males have high mean TSH in contrast to the females.

REFERENCES

1. Fröhlich E, Wahl R. **Thyroid autoimmunity: Role of anti-thyroid antibodies in thyroid and extra-thyroidal diseases.** Frontiers in immunology. 2017; 8:521.

2. Tipu HN, Ahmed D, Bashir MM, Asif N. **Significance of testing anti-thyroid autoantibodies in patients with deranged thyroid profile.** Journal of thyroid research. 2018 Apr 11;2018.

3. Jantikar AM. **A study on relationship between thyroid peroxidase antibodies (Anti-TPO antibodies) and thyroid dysfunction patients.** International Journal of Clinical Biochemistry and Research 2020; 7(2):238–242.

4. Manji N, Carr-Smith JD, Boelaert K, Allahabadia A, Armitage M, Chatterjee VK, Lazarus JH, Pearce SH, Vaidya B, Gough SC, Franklyn JA. **Influences of age, gender, smoking, and family history on autoimmune thyroid disease phenotype.** The Journal of Clinical Endocrinology & Metabolism. 2006; 91(12):4873-80.

5. Shinkov A, Borissova AM, Vlahov J, Dakovska L, Blajeva E. **Male gender differences in the thyroid ultrasound features, thyroid peroxidase antibodies and thyroid hormone levels: A large population-based study.** Journal of endocrinological investigation. 2014; 37(3):269-76.

6. Matana A, Popović M, Boutin T, Torlak V, Brdar D, Gunjača I, Kolčić I, Perica VB, Punda A, Polašek O, Hayward C. **Genome-wide meta-analysis identifies novel gender specific loci associated with thyroid antibodies level in Croatians.** Genomics. 2019; 111(4):737-43.

7. Ngo ST, Steyn FJ, McCombe PA. **Gender differences in autoimmune disease.** Frontiers in neuroendocrinology. 2014; 35(3):347-69.

8. Bjoro T, Holmen J, Krüger O, Midthjell K, Hunstad K, Schreiner T, Sandnes L, Brochmann H. **Prevalence of thyroid disease, thyroid dysfunction and thyroid peroxidase antibodies in a large, unselected population.** The Health Study of Nord-Trondelag (HUNT). European journal of endocrinology. 2000; 143(5):639-47.

9. Díez JJ, Iglesias P. **Spontaneous subclinical hypothyroidism in patients older than 55 years: An analysis of natural course and risk factors for the development of overt thyroid failure.** The Journal of Clinical Endocrinology & Metabolism. 2004; 89(10):4890-7.

10. Deokar PG, Nagdeote AN, Lanje MJ, Basutkar DG. **Prevalence of thyroid disorders in a tertiary care center.** International Journal of Current Research and Review. 2016; 8(9):26.

11. Siriwardhane T, Krishna K, Ranganathan V, Jayaraman V, Wang T, Bei K, Ashman S, Rajasekaran K, Rajasekaran JJ, Krishnamurthy H. **Significance of anti-TPO as an early predictive marker in thyroid disease.** Autoimmune diseases. 2019 Oct;2019.

12. Unnikrishnan AG, Kalra S, Sahay RK, Bantwal G, John M, Tewari N. **Prevalence of hypothyroidism in adults: An epidemiological study in eight cities of India.** Indian journal of endocrinology and metabolism. 2013; 17(4):647.

13. Walsh JP, Bremner AP, Feddema P, Leedman PJ, Brown SJ, O'Leary P. **Thyrotropin and thyroid antibodies as predictors of hypothyroidism: A 13-year, longitudinal study of a community-based cohort using current immunoassay techniques.** The Journal of Clinical Endocrinology & Metabolism. 2010; 95(3):1095-104.

14. Naz N, Rizvi S, Sadiq Z. **Assessment of thyroid hormone levels and thyroid disorders: A case study from Gujranwala, Pakistan.** Pakistan journal of pharmaceutical sciences. 2017 Jul 1;30(4).

AUTHORSHIP AND CONTRIBUTION DECLARATION

No.	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Sara Khan	Study design, data collection, writing the manuscript, formulation of tables reviewed and approved.	Sara Khan
2	Ayesha Siddiqa	Statistical analysis, result interpretation, manuscript writing and revising it critically for important intellectual content.	Ayesha Saddiqua
3	Maryam Rafiq	Statistical analysis, interpretation of results Reviewed and approved the manuscript.	Maryam Rafiq
4	Nudrat Fayyaz	Data collection, Writing the manuscript, formulation of tables reviewed and approval.	Nudrat
5	M. Ammad Asghar	Result interpretation, manuscript writing and revising it critically for important intellectual content.	M Ammad
6	Rizwan Hafeez	Manuscript writing and revising it critically for important intellectual content.	Rizwan Hafeez