

Association of anti TPO with symptoms of hypothyroidism

¹Virija Dharanikota, Intern, Dr D Y Patil Medical College and Hospital, Pimpri, Pune.

²Manasi Harale, MBBS, MD Medicine, Associate professor, Department of Medicine, Dr. DY Patil Medical College and Hospital, Pimpri, Pune.

Corresponding Author: Manasi Harale, MBBS, MD Medicine, Associate professor, Department of Medicine, Dr. DY Patil Medical College and Hospital, Pimpri, Pune.

How to citation this article: Virija Dharanikota, Manasi Harale, “Association of anti TPO with symptoms of hypothyroidism”, IJMACR- March - 2024, Volume – 7, Issue - 2, P. No. 70 – 75.

Open Access Article: © 2024, Virija Dharanikota, et al. This is an open access journal and article distributed under the terms of the creative common’s attribution license (<http://creativecommons.org/licenses/by/4.0>). Which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Background & Objectives: Subclinical hypothyroidism is TSH more than normal but below 10. The main objective of this study is to study association of Anti-TPO antibodies and symptoms in subclinical hypothyroidism. TPO antibodies attack complexes that are present in thyroid gland. These autoantibodies serve as useful markers for autoimmune thyroid diseases.

Methods: This is co-relation study including 30 ‘subclinical cases’ of hypothyroidism aged above 18 years, who were not on any treatment for thyroid currently or previously. Patients with diabetes mellitus, other autoimmune diseases, overt hypothyroidism were excluded.

Questionnaire regarding symptoms was filled by participants and they were examined for any clinical signs of hypothyroidism.

Results: The patients with both positive and negative Anti TPO antibodies revealed the symptoms and signs

such as fatigue, weight gain, impaired memory, constipation, menstrual changes, depression, hair loss, puffy face, goiter, ankle jerk, dry skin. But the association was much higher with patients with positive anti TPO antibody. Goiter was seen in 26.67% of patients with positive anti TPO antibody levels against 6.67% patients with negative anti TPO antibodies. Delayed ankle jerk was seen in 40% of patients with positive anti TPO antibody levels against none with negative anti TPO antibodies.

Interpretation & Conclusions: This proves that there is a clear relationship between the level of Anti TPO antibody levels and symptoms and signs in patients with subclinical hypothyroidism. This relationship will further be helpful in providing better treatment and improving their quality of life.

Keywords: Anti TPO antibodies, Hypothyroidism, Subclinical hypothyroidism, Thyroid, TSH

Introduction

Hypothyroidism can be detected by TSH, T3, T4 hormone level tests and thyroid antibody tests like anti-thyroid peroxidase antibodies. Thyroid peroxidase (TPO) enzyme is required for the synthesis of thyroid hormones. It regulates the amount of hormone to be released as well as thyrotropin receptor. Any alterations might result in a deranged thyroid profile. In few cases, auto-antibodies may also be formed against TPO. Measuring the levels of circulating antibodies against TPO as well as Thyroglobulin (TG) helps in the detection of auto-immune thyroid diseases easily.

Unnikrishnan et al. mentioned that about 42 million people in India were estimated to be suffering from thyroid diseases. A population study had suggested that the prevalence of Anti-TPO and Anti-TG antibodies was 9.5% and 8.5% respectively. However, it is reasonable to measure only TPO antibodies since antibodies against TG are uncommon. Auto-immune thyroid diseases present clinically either as hyperthyroidism or hypothyroidism due to overproduction of hormone or destruction of the glandular follicles respectively. But laboratory analysis show that >90% Hashimoto's thyroiditis and 40%-70% Grave's disease cases possess autoantibodies irrespective of the functional status of thyroid gland^[1].

TPO antibodies attack the complexes that are present in the thyroid gland. Thus, auto-antibodies serve as useful markers for autoimmune thyroid diseases. As the auto-immune process reduces thyroid function gradually, there is a compensatory phase where normal thyroid hormone levels are maintained by a rise in TSH. Later, TSH levels rise further, and symptoms become apparent presenting as clinical hypothyroidism. In such cases,

there is always a risk of patient's condition progressing to overt hypothyroidism.

In the recent years, it has also been hypothesized that puberty goiter in adolescents and multi-nodular goiter in adults are due to autoimmune thyroiditis. Prevalence of thyroid antibodies is higher in women than in men. As per Whickham survey, the annual risk of developing hypothyroidism in Anti-TPO antibodies positive women with normal thyrotropin levels was 2.1%. Prevalence in high TSH group was 18.6% versus 3% in low TSH group.

In India very few studies had been conducted to find out the relation of antiTPO antibodies with thyroid dysfunction. Hence, present study was carried out to analyze the relation of Anti-TPO antibodies with symptoms of hypothyroidism.

Hamid Nawaz Tipu et al. reported that Anti-thyroid antibodies (specifically Anti-TPO antibodies) are more often present when TSH is deranged. The individuals with deranged thyroid profile (specifically TSH) should also be screened for anti-thyroid antibodies to rule out underlying autoimmune phenomenon. This importance of screening is compounded by the fact that anti-thyroid antibodies may be positive in a significant percentage of elderly people.^[2]

Philip R Orlander et al. Reported that Primary hypothyroidism is virtually the only disease that is characterized by sustained rises in TSH levels. Assays for Anti-thyroid peroxidase (anti-TPO) and antithyroglobulin (anti-Tg) antibodies may be helpful in determining the etiology of hypothyroidism or in predicting future hypothyroidism.^[3]

Aziz Muzafar Jafaar1 et al. reported that the majority of hypothyroidism were having positive both antithyroid peroxidase and antithyroglobulin antibodies and these

antibodies were significantly higher in patients when comparing with control group (healthy individual).^[4]

Eleonore Fröhlich et al. reported that increased levels of anti-thyroid antibodies usually accompany Autoimmune thyroid diseases, and their detection may support its diagnosis.^[5]

Vikas Kumar Srivastava et al. concluded from their study that Subclinical hypothyroidism is more common in females, there is high prevalence of TPO antibody in Subclinical hypothyroidism patients that means autoimmune etiology, dyslipidemia is significant if TPO positivity is there and females with Subclinical hypothyroidism are more prone to develop dyslipidemia, especially with TPO positivity as compared to male.^[6]

Ashwini Manish Jantikar reported that anti-TPO antibodies were commonly associated with hypothyroid dysfunction. It was noted more among females of reproductive age group.^[7]

Materials and Methods

This co-relation study was conducted at tertiary care hospital in Pune during September-November 2021. Ethical approval was obtained from the Institutional Ethics Committee. Informed consent from all the patients under study was obtained.

The subjects of the study included 30 (thirty) 'subclinical cases' of hypothyroidism aged above 18 years, who were not on any treatment for thyroid currently or previously. Patients with diabetes mellitus were excluded from study. Patients with other autoimmune diseases were also excluded from study. Patients with overt hypothyroidism were also excluded from the study.

On detection of patients, a detailed history of the patients was taken to assess if they fulfilled the inclusion and exclusion criteria. A systematic clinical examination was

carried out to rule out any comorbidity, including systemic illnesses and deficiency disorders. The patient's reports were checked for recent thyroid profile. After the completion of the aforementioned, random blood samples were collected in separate vacutainers and sent to the Central Clinical Laboratory, for the Anti Thyroid Peroxidase antibodies, Lipid profile and Thyroid function tests if not done recently.

Depending on the level of Anti-TPO antibodies, the patients were divided into group A and group B. There were 15 patients in each group. In group A all the patients with Anti TPO antibodies positive (Anti- TPO antibody value greater than 5 IU/ml) were included and in group B all the patients with Anti TPO antibodies negative (Anti- TPO antibody value less than 5 IU/ml) were included. Later the patients were asked to fill out a questionnaire.

All the data obtained on examination of patients and from laboratory reports were meticulously entered in Microsoft Excel and analyzed using percentages and other appropriate functions wherever necessary for Statistical Analysis. The findings of both groups were then compared using Epi info software.

Results

A thorough screening of the patients, 30 (thirty) patients of subclinical hypothyroidism with TSH between 5-10 μ IU/ml with Anti-TPO positive and negative were included in the study, out of which 15 had positive Anti TPO antibody levels and the other 15 patients had negative Anti TPO antibody levels.

There were total 27 females and 3 males with mean age of 38.4 years. Mean age for females was 38.4 whereas for males it was 40.4. There were 9 patients each in age groups of 20-30 and 31-40. There were 8 patients in age

group of 41-50. There were 2 patients each in the age groups of 51-60 and 61-70.

The mean level of total cholesterol of all patients was 156.84, where normal level is considered as less than 200mg/dl. In group A the levels ranged from 109 to 235mg/dl with the mean being 152.41. Whereas in group B the levels of cholesterol ranged from 111 to 226 mg/dl with the mean being 161.30. Only 5 patients had elevated total cholesterol level than normal.

Evaluation of the Anti-TPO antibodies level of both groups revealed that the mean level was 218.8 with level ranging from 0 to 1000 IU/ml. Group A had a mean of 488.61 where the level ranged from 25.72 to 1000. Group B ranged from 0 to 4.9 IU/ml with a mean of 0.95.

The evaluation of the questionnaire revealed the following about the symptoms from each group.

GROUP-A (Anti TPO antibodies positive) -

1. Fatigue: 86.67% (13 out of 15 patients) of the patients from this group had this symptom.
2. Weight gain: 53.33% (8 out of 15 patients) of the patients had this symptom.
3. Impaired memory: 40% (6 out of 15 patients) of the patients had this symptom.
4. Constipation: 53.33% (8 out of 15 patients) of the patients had this symptom.
5. Menstrual changes: 46.67% (7 out of 15 patients) of the patients had this symptom.
6. Depression: 46.67% (7 out of 15 patients) of the patients had this symptom.
7. Hair loss: 80% (12 out of 15 patients) of the patients had this symptom.
8. Puffy face: 26.67% (4 out of 15 patients) of the patients had this symptom.

GROUP- B (Anti TPO antibodies negative) –

1. Fatigue: 66.67% (10 out of 15 patients) of the patients had this symptom.
2. Weight gain: 33.33% (5 out of 15 patients) of the patients had this symptom.
3. Impaired memory: 13.33% (2 out of 15 patients) of the patients had this symptom.
4. Constipation: 33.33% (5 out of 15 patients) of the patients had this symptom.
5. Menstrual changes: 20% (3 out of 15 patients) of the patients had this symptom.
6. Depression: 33.33% (5 out of 15 patients) of the patients had this symptom.
7. Hair loss: 46.67% (7 out of 15 patients) of the patients had this symptom.
8. Puffy face: 13.33% (2 out of 15 patients) of the patients had this symptom.

On evaluation of the questionnaire the following has been revealed about the signs from each group:

GROUP-A (Anti TPO antibodies positive) -

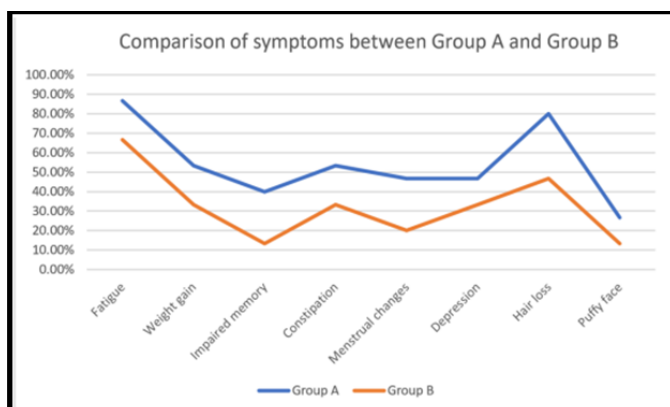
1. Goiter: 26.67% (4 out of 15 patients) of the patients have had this sign.
2. Ankle jerk: Normal ankle jerk is seen in 53.33% (8 out of 15) patients. Delayed ankle jerk is seen in 40% (6 out of 15) of patients. Absent ankle jerk is seen in 6.67% (1 out of 15) of patients.
3. Dry skin: 73.33% (11 out of 15 patients) of the patients have had this sign.

GROUP- B (Anti TPO antibodies negative) -

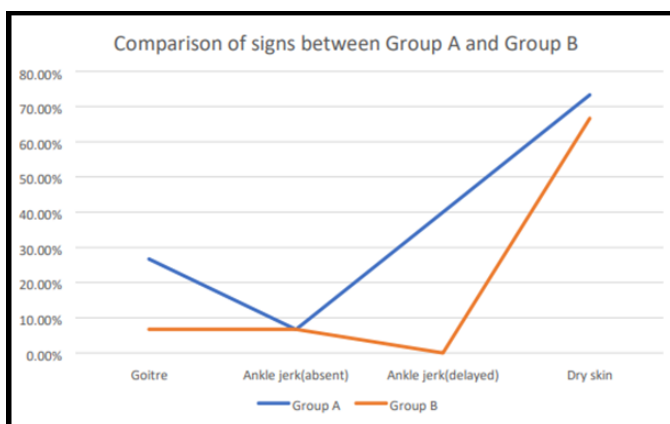
1. Goiter: 6.67% (1 out of 15 patients) of the patients have had this sign.
2. Ankle jerk: Normal ankle jerk is seen in 93.33% (14 of 15) patients. Delayed ankle jerk is seen in none of patients.

Absent ankle jerk is seen in 6.67% (1 out of 15) of patients.

3. Dry skin: 66.67% (10 out of 15 patients) of the patients have had this sign.



Graph 1



Graph 2

Discussion

Thyroid peroxidase (TPO) is an enzyme involved in thyroid hormone synthesis, catalyzing the oxidation of iodide on tyrosine residues in thyroglobulin for the synthesis of triiodothyronine and thyroxine (tetraiodothyronine). TPO is a membrane associated hemoglycoprotein expressed only in thyrocytes and is one of the most important thyroid gland antigens.

Disorders of the thyroid gland are frequently caused by autoimmune mechanisms with the production of autoantibodies. Anti-TPO antibodies activate complement and are thought to be significantly involved

in thyroid dysfunction and the pathogenesis of hypothyroidism.

The determination of TPO antibody levels is the most sensitive test for detecting autoimmune thyroid disease (e.g., Hashimoto thyroiditis, idiopathic myxedema, and Graves' disease) and detectable concentrations of anti-TPO antibodies are observed in most patients with these disorders. The highest TPO antibody levels are observed in patients suffering from Hashimoto thyroiditis. In this disease, the prevalence of TPO antibodies is about 90% of cases, confirming the autoimmune origin of the disease. These autoantibodies also frequently occur (60%-80%) in the course of Graves' disease.

In patients with subclinical hypothyroidism, the presence of TPO antibodies is associated with an increased risk of developing overt hypothyroidism. Many clinical endocrinologists use the TPO antibody test as a diagnostic tool in deciding whether to treat a patient with subclinical hypothyroidism. Since there are very few studies that are similar to this topic, it was difficult to compare it.

All the symptoms were seen in both the groups, but they were comparatively higher in those with Anti TPO antibodies positive. Delayed ankle jerk was the only sign that was seen in those with Anti TPO antibodies positive only.

Further such studies are required on larger scale so that we treat hypothyroidism early and give cases with subclinical hypothyroidism a better quality of life.

References

1. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3169866/> Unnikrishnan AG, Menon UV. Thyroid disorders in India: An epidemiological perspective. Indian J Endocrinol Metab. 2011 Jul;15(Suppl

- 2):S78-81. doi: 10.4103/2230-8210.83329. PMID: 21966658; PMCID: PMC3169866.
2. <https://www.hindawi.com/journals/jtr/2018/9610497> /Hamid Nawaz Tipu, Dawood Ahmed, Muhammad Mukarram Bashir, Naveed Asif, "Significance of Testing Anti-Thyroid Autoantibodies in Patients with Deranged Thyroid Profile", *Journal of Thyroid Research*, vol. 2018, Article ID 9610497, 5 pages, 2018. <https://doi.org/10.1155/2018/9610497>
 3. <https://emedicine.medscape.com/article/122393-workup>.
 4. <https://jmscr.igmpublication.org/home/index.php/archive/93-volume-4-issue-08-august-2016/995-anti-thyroid-peroxidase-and-anti-thyroglobulin-antibodies-in-patients-with-hypothyroidism>
 5. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5422478/#S5title>Fröhlich E, Wahl R. Thyroid Autoimmunity: Role of Anti-thyroid Antibodies in Thyroid and Extra-Thyroidal Diseases. *Front Immunol.* 2017 May 9;8:521. doi: 10.3389/fimmu.2017.00521. PMID: 28536577; PMCID: PMC5422478.
 6. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5629902/> Srivastava VK, Singh H. Association of thyroid peroxidase antibody and dyslipidemia in subclinical hypothyroidism. *J Family Med Prim Care.* 2017 Jan-Mar;6(1):63-68. doi: 10.4103/2249-4863.214958. PMID: 29026751; PMCID: PMC5629902.
 7. <https://www.ijcbr.in/html-article/11624>