

A Study of Plasma Anti-Thyroperoxidase Antibodies and Anti-Thyroglobulin Antibodies in patients with Hypothyroidism

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ABSTRACT

Aim: To determine the plasma anti-thyroperoxidase antibodies (Anti-TPO) and anti-thyroglobulin antibodies (ATG) in hypothyroid patients

Methods: This study was carried out at Arif Clinical Laboratory and Diagnostic center, Lahore. Samples were collected from 750 patients diagnosed with hypothyroidism. The blood samples were analyzed for the levels of anti-thyroperoxidase antibodies (n=450) and anti-thyroglobulin (n=300) antibodies. Depending upon the serum levels of these antibodies, the obtained titers were categorized as normal, mildly elevated, moderately elevated and highly elevated. Duration of study was around 08 months, extending from November 2021 to May 2022.

Results: Among the total 750 patients with hypothyroidism, 450 were estimated for Anti-TPO antibodies, whereas, 400 patients were analyzed ATG antibodies. Anti-TPO antibodies were normal in 191 patients (42.44%) and high levels were observed in 259 patients (57.55%), indicating a greater role of these antibodies in the causation of hypothyroidism. In contrast, among the 300 patients analyzed for ATG antibodies, 213 patients had normal levels (71%), while 87 has high plasma levels of these antibodies (29%)

Practical Implications: Current study provides an insight into the more frequent incidence of Anti-TPO antibodies, thus indicating its more crucial role in causing hypothyroidism in the given population. Therefore, estimation of these autoantibodies earlier in the disease can serve as better indicators of the severity and response to treatment, compared with Anti-TGB antibodies, which are present less frequently in patients with hypothyroidism

Conclusion: Anti-TPO antibodies were found to be high in 57.55% patients (n=450) with hypothyroidism, indicating its greater role in the causation of hypothyroidism, whereas, ATG were high in only 29% patients (n=300). The results stress the need to evaluate all patients of hypothyroidism with plasma antibody levels for early diagnosis and a prompt management plan.

Keywords: anti-thyroglobulin, anti-thyroperoxidase, hypothyroidism, Thyroxine, Triiodothyronine

INTRODUCTION

Thyroid gland is one of the most important gland, playing a major role in growth, metabolism and other body functions¹. Thyroid hormones have a pivotal role in the mental and physical development especially in fetal and postnatal life.

Main hormone produced by thyroid include Thyroxine (T4) and its deiodination in local tissues results in the production of biologically active thyroid hormone, triiodothyronine (T3)². The secretion of thyroid hormones is largely under the control of TSH, Thyroid stimulating hormone which is produced by pituitary gland, and that in turn is controlled by TRH, Thyroid releasing hormone, produced from hypothalamus^{2,3}. Thyroid hormones produce their effect by interacting with thyroid hormones receptors (TRs) which belong to a super-family of receptors, similar to sex hormone receptors and vitamin D receptors².

Hypothyroidism is associated with hallmark clinical features like increased sleep, constipation, weight gain and neuro-cognitive decline. Specific oro-facial features include macroglossia, altered tooth morphology, poor periodontal health and delayed wound healing³.

Thyroid peroxidase (TPO) is an enzyme in thyroid tissue catalyzing the synthesis of thyroid hormone via iodination. Anti-TPO-antibodies are primarily produced by the infiltrating thyroid lymphocytes, and the titer of these antibodies clearly reflects the extent of lymphocytic infiltration within the thyroid gland. It is a well known fact that Anti-TPO and ATG antibodies are closely related with impaired thyroid function, but it is still controversial which antibody exerts its profound impact on which indicator of thyroid function⁴.

Hypothyroidism is a chronic condition characterized by underactive thyroid gland, resulting in decreased formation of T3 and T4⁵. This condition manifests as weight gain, tiredness, cold

intolerance, constipation and decreased heart rate.¹ A cross-sectional study carried out in Saudi Arabia in 2019, also supported innumerable metabolic effects of thyroid hormones. Consequently, deficiency of thyroid hormones is associated with metabolic effects like impaired glucose tolerance, thus predisposing not only to higher glucose levels but also to increased cholesterol levels, insulin levels and insulin resistance, thus necessitating the need of its prompt diagnosis and subsequent management⁶.

Hypothyroidism has a spectrum of clinical manifestations, and apart from generalized signs and symptoms, there are characteristic oro-facial abnormalities, such as retained deciduous teeth or delayed tooth eruption. Early diagnosis and detection of plasma antibodies against thyroid tissue can help prevent associated complications

In addition to infective causes of hypothyroidism, it can also result from autoimmune inflammation. Finding the underlying cause is crucial, as it overwhelmingly changes the management plan⁷. Not much data is available regarding the incidence of plasma antibodies and exploration of plasma levels of anti-thyroperoxidase antibodies (Anti-TPO) and anti-thyroglobulin antibodies (ATG antibodies), in patients with hypothyroidism. Few recent reviews have described these circulating thyroid antibodies (Anti-TPO & ATG) to be low or even absent⁸.

Anti-thyroglobulin antibody (ATG) has been considered as a conventional marker for autoimmunity against thyroid gland, although it is less useful than Anti-TPO antibodies for predicting thyroid dysfunction. Plasma levels of ATG primarily depends upon degree of exposure to specific antigens⁹.

Current study aims to find strong clues about the etiology of hypothyroidism related to auto-antibodies production. Primary objective of the study is to determine the plasma levels of Anti-TPO and ATG antibodies in patients diagnosed with hypothyroidism. More studies are, however, required to elucidate other associated causative factors implicated in the etiology and pathogenesis of hypothyroidism.

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METHODOLOGY

In this study, we analyzed the blood samples of 750 diagnosed patients of hypothyroidism, who presented in the medical laboratory for the evaluation of plasma thyroid hormones and related profiles. All these patients were already diagnosed on the basis of plasma T3, T4 and TSH estimation. After informed consent, the venous blood samples were drawn from ante-cubital vein. The samples were kept 20–25°C temperature for 2-3 hours, centrifuged at 3000 r/min for 15 minutes for separation of the serum. Finally, stored at -20°C, and then sequentially analyzed for the presence of Anti-TPO and ATG antibodies. The antibodies were measured through solid phase electro-chemiluminescence immunoassay “ECLIA” (COBAS, Roche Diagnostics GmbH, Germany). The obtained titers were then further categorized as being normal, mildly elevated, moderately high elevated and very highly elevated, thus providing an insight of their role in development of hypothyroidism in the given population

RESULTS

Results show 57.55% of hypothyroid patients had high plasma levels of Anti-TPO antibodies (Table 2, Fig. 1), in contrast, ATG antibodies were found to be high in 29% patients (Table 4, Fig. 2). A total of 750 patients diagnosed with hypothyroidism were selected for this study. Among these patients, plasma Anti-TPO levels were estimated in 450 patients, whereas ATG estimation was done in the other 300 patients group. In 450 patients, 162 were males, whereas, 288 were females. Mean age of male patients in this group was 42 (±3) years, while mean age of female patients was 37.5 (±3) years. Following observations were made; 191 patients (42.44%) had normal plasma Anti-TPO antibodies levels, 82 patients (40.44%) had mildly elevated levels, whereas, 68 patients had moderately high (15.11%) and 109 had very high plasma Anti-TPO antibodies (24.22%). Over all, Anti-TPO antibodies were high in 259 patients (57.55%)

In the other group of 300 patients, following findings were observed; 213 patients had normal plasma ATG-antibodies (71%), while 59 had mildly elevated ATG-antibodies (19.66%), 17 patients had moderately high (5.66%), while only 11 patients had very high plasma ATG-antibodies (3.66%).

Overall, among 750 patients with hypothyroidism, 404 patients had normal plasma levels of auto-antibodies (53.86%). The auto-antibodies were found to be high in 346 patients (46.13%)

Table 1: Plasma anti-TPO levels (n=450)

Plasma Anti-TPO levels	n	% age
Normal levels (< 5.61 IU/ml)	191	42.44
Mildly elevated up to 100 IU/ml	82	18.22
Moderately elevated (101-500 IU/ml)	68	15.11
Very high (above 500 IU/ml)	109	24.22

Table-2: Over all plasma anti-TPO levels (n=450)

Normal plasma levels	High plasma levels
191(42.44%)	259(57.55%)

Fig. 1: Plasma anti-TPO antibodies levels

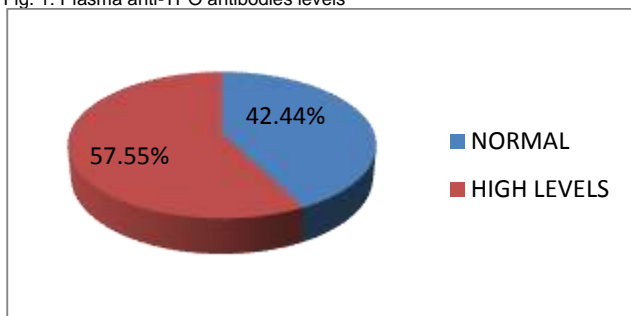


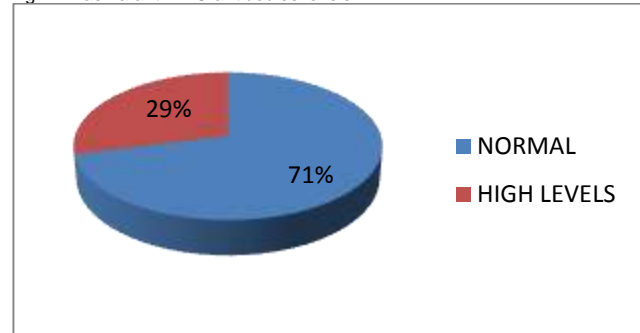
Table 3: Plasma ATG-antibodies level (n=300)

Plasma ATG- antibodies level	n	% age
Normal levels (< 5.61 IU/ml)	213	71
Mildly elevated up to 100 IU/ml	59	19.66
Moderately elevated(101-500 IU/ml)	17	5.66
Very high (above 500 IU/ml)	11	3.66

Table 4: Overall plasma ATG- antibodies level (n=300)

Normal plasma levels	High plasma levels
213(71%)	87(29%)

Fig. 2: Plasma anti-TPO antibodies levels



DISCUSSION

The number of patients diagnosed with hypothyroidism, reporting in medical laboratories for the estimation of Anti-TPO and ATG antibodies, has dramatically increased in the last few years. Scarce data is, however, available regarding the incidence of high plasma levels of these antibodies in hypothyroid patients.

A study carried out in Japan in 2019, evaluated the titers of Anti-TPO and ATG antibodies and it revealed significantly higher levels of both in hypothyroid patients, who eventually improved after treatment¹⁰. Anti-TPO and ATG antibodies, both are considered polyclonal antibodies, requiring prolonged duration of exposure to antigen. While the antigen for anti-TPO is intracellular and is accessed after destruction of thyroid tissue, antigen for ATG is intra-follicular which can be accessed with or without tissue destruction. However, if remain untreated, both these antibodies can lead to some extra-thyroidal pathologies like encephalopathy and increased risk of breast carcinoma¹¹.

In the same lines, a study carried out in 2019 in India led to the finding that anti-TPO antibodies are more common and more suggestive of an autoimmune thyroid disorder compared with ATG antibodies, being positive in almost 90-95% thyroid diseases¹¹. ATG antibodies are the first antibody to be detected in autoimmune thyroid disorders, in 1956. Serial measurements of these antibodies have their own significance in assessing prognosis of thyroid cancers post- operatively¹². ATG antibodies usually do not lead to progressive destruction of thyroid tissue, this is mainly attributed to the variety of its epitopes, which are considerably widely distributed, which subsequently decreases the cross-linking¹³.

Another study conducted by Yan et al, in China in 2015 identified the prevalence of thyroid antibodies to be as high as 83.3% in patients with clinical hypothyroidism. Additionally, this study also confirmed that the concentration of both Anti-TPO and ATG antibodies were significantly higher, than titer of either one of these when they are singly present in blood. This might be owing to increased reactivity of immune system against thyroid antigens when both these antibodies are present¹⁴.

A recent study conducted in Egypt in 2019 stated hypothyroidism to be second most common endocrine abnormality after diabetes mellitus and autoimmune thyroiditis, to be the most common cause of hypothyroidism. This results from direct or indirect effect of antibodies¹⁰. Anti-thyroid antibodies, although are a sensitive marker of autoimmune thyroid disease, still they are detectable in 5-27% of general population¹⁵.

Based on the findings and available literature, it can be deduced that thyroid antibodies, are valuable markers of autoimmunity and probably play a major role in the causation of hypothyroidism.

CONCLUSION

The obtained data shows that among a total number of 750 hypothyroid patients, 346 patients (46.13%) had high plasma levels of these antibodies, whereas 404 patients (53.86%) showed normal plasma antibody levels. Anti-TPO antibodies were high in 259 patients (57.55%), whereas, ATG antibodies were high in 59 patients (19.66%). ATG-antibodies were found to be normal in 213 patients, which accounts for 71% of these patients. High plasma levels of these antibodies were found in only 87 patients (29%), which is in clear contrast to the pattern of Anti-TPO antibodies in hypothyroid patients which were high in 57.55% cases.

Ethical issues: There were no ethical issues related to this article

Author's contributions: **US:** Processing of blood samples, measurement of plasma antibody levels, results compilation, final conclusion, **SS:** Obtaining blood samples from selected population, article write-up, Discussion, **QM:** Obtaining blood samples, article write-up, tables, diagrams, **AY:** Article write-up, follow up of patients, assisting in sample processing and estimation of antibodies

Conflict of interest: Nil

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