ORIGINAL RESEARCH PAPER

Volume-7 | Issue-12 | December-2018 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

SIGNIFICANCE OF ANTI-THYROPEROXIDASE ANTIBODY ESTIMATION IN PATIENTS WITH HYPOTHYROIDISM

Biochemistry

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ABSTRACT

Introduction: Hypothyroidism is a common endocrine disorder characterized by decreased levels of thyroid hormones. Anti-thyroperoxidase antibody is produced in autoimmune thyroiditis which inhibits the synthesis of thyroid hormones.

Aims & Objectives: The study was planned to explore the significance of anti-TPO antibody in hypothyroid patients.

Materials and Methods: 150 newly diagnosed patients, age 20-60 years were enrolled for the study. Patients were divided on the basis of anti-TPO levels as anti-TPO positive(n=87) anti-TPO negative (n=63).Thyroid hormones viz. serum triiodothyronine (T3), thyroxine (T4), free T3 (FT3), free T4 (FT4) and thyroid stimulating hormone (TSH) levels were compared between the two groups.

Results: Mean serum TSH level was significantly higher in anti-TPO positive group. Mean serum T3 & T4 levels were comparable (P= NS) among the two groups whereas FT3 (P= 0.014) and FT4 (P= 0.003) were significantly lower in the anti-TPO positive group.

Conclusion: Serum FT3 & FT4 represent the biologically active proportion of thyroid hormones. The present study suggests that lower FT3 & FT4 levels can better correlate with anti-TPO activity in patients of hypothyroidism.

KEYWORDS

hypothyroidism, anti-TPO antibody, Free T3, Free T4, thyroperoxidase

INTRODUCTION

Hypothyroidism is one of the most common endocrine dysfunction resulting from the deficiency of thyroid hormones or their impaired activity. Decrease in concentration of triiodothyronine (T3) and thyroxine (T4) concentration leads to hyper secretion of pituitary TSH [1, 2]. Hypothyroidism produces subtle changes such as lower metabolic rate and clinical manifestation like overweight, fatigue, cold intolerance, feeling of tiredness, hypertension, depression, hoarseness of voice, puffiness of face, edema, high cholesterol, constipation etc. When thyroid hormone deficiency becomes very severe such subjects may eventually develop cardiomegaly, ischemic heart disease, pericardial effusion, drowsiness, myxoedema and coma etc [3,4].

Thyroperoxidase is a key enzyme in the synthesis of thyroid hormone. Patients with high titer of anti thyroperoxidase (anti-TPO) antibodies are more likely to progress to hypothyroidism[5]. Estimation of anti-TPO antibody level is important in diagnosing autoimmune thyroid diseases and judging treatment efficacy[6]. Anti-TPO antibodies are cytotoxic in vitro as detected by antibody dependent cell cytotoxicity tests, [7] thus are likely to be involved in the development of hypothyroidism. [8]

Although, serum T3 and T4 levels are commonly assessed to monitor thyroid function, the unbound component of these hormones i.e. free T3 (FT3) and free T4 (FT4) is said to be the biologically active form. FT4 acts as an indicator of thyroid production and is used to confirm the diagnosis suggested by TSH. FT3 can be produced by the thyroid gland, in preference over T4 (e.g. in cases of iodine deficiency). However, FT3 is an indicator of peripheral deiodination of T4. The present study was planned to evaluate the significance of anti-TPO antibody in patients with hypothyroidism.

METHODOLOGY

The study was conducted in Department of Biochemistry in association with Department of General Medicine and Endocrinology of Mahatma Gandhi Medical College & Hospital, Jaipur after seeking approval from the Institutional Ethics Committee. Total 150 subjects, age between 20 – 60 years, biochemically confirmed for hypothyroidism were enrolled for the study. Patients with other comorbid conditions and pregnant and lactating females were excluded from the study. Blood samples following an overnight fast were collected by standard aseptic techniques and analysed for serum T3, T4, FT3, FT4, TSH by chemiluminescence using Vitros ECI and Serum anti-TPO by ELISA using Immunoshop Chorus.

The enrolled hypothyroid patients were grouped on the basis of anti-TPO levels(anti-TPO negative <31.5 IU/ml, anti-TPO positive >31.5 IU/ml). All results obtained were presented as mean ± SD and subjected to statistical evaluation by applying students' t-test. A P-value of ≤0.05 was considered as statistically significant.

TABLE 1: Comparison of Thyroid hormone levels of the study groups on basis of Anti-TPO levels

Groups	Anti-TPO negative n = 63	Anti-TPO positive n = 87	t-value	P-value
S.T3 (ng/ml)	0.79 ± 0.33	0.83 ± 0.80	-0.374	NS
S.T4 (µg/dl)	4.20 ± 1.96	4.05 ± 2.01	0.456	NS
S.TSH (µIU/ml)	30.85 ± 29.39	57.15 ± 31.33	-5.207	0.000
S. FT3 (pg/mL)	2.90 ± 1.14	2.45 ± 1.06	2.486	0.014
S.FT4(ng/dl)	0.94 ± 0.53	0.70 ± 0.41	3.058	0.003

TABLE 2: Comparison of Male and Female of the study groups on basis of Anti-TPO levels

Groups	Anti-TPO (-ve)		Anti-TPO (+ve)	
	n	%	n	%
Male	23	36.50	35	40.20
Female	40	63.50	52	59.80

RESULTS:

The enrolled patients were grouped on the basis of anti-TPO levels as anti-TPO negative (n= 63) and anti-TPO positive (n= 87). On applying t-test (Table 1), serum T3 and T4 levels were found to be similar in both groups and the variation was non-significant. However, serum TSH levels were observed to be statistically higher in the anti-TPO positive group (P=0.000). In other words, patients with a raised anti TPO concentration exhibited higher TSH levels. Further, FT3 (P=0.014) and FT4 (P=0.003) levels were observed to be lower in the anti-TPO positive group. This means that the serum FT3 and FT4 levels were decreased with higher concentration of anti-TPO antibody levels. On comparison of anti-TPO levels on the basis of sex, among the male hypothyroid patients, 40.2% were reported to have anti-TPO positive levels whereas among the female patients a higher percentage i.e. 59.8% patients were reported anti TPO positive (Table 2).

DISCUSSION

Thyroperoxidase (TPO) is an enzyme which catalyses the oxidation of iodide ion on tyrosine residues in thyroglobulin for the synthesis of T3 and T4. TPO is a membrane-associated hemoglycoprotein expressed only in thyrocytes and is one of the most important thyroid gland antigens.[9] Anti-thyroid peroxidase (anti-TPO) antibodies are specific for the autoantigenTPO, a 105kDa glycoprotein that catalyses iodine oxidation and thyroglobulin tyrosyl iodination reactions in the thyroid gland [10]. In patients with subclinical hypothyroidism, the presence of TPO antibodies is associated with an increased risk of developing

overt hypothyroidism [11]. The prevalence of positive thyroid auto antibodies increases with age, with the highest frequency observed in women aged 40–60 years [12].

In a previous study, **Jeena Jacob et al., 2013** reported that the prevalence of anti-TPO antibody noted in patients with hypothyroidism was 80% and 50% respectively[13]. **Mohanty et al., 2008** reported that among the 38 frank hypothyroid patients, 76% had raised anti-TPO levels [14].

TPO positive patients are more prone to develop thyroid dysfunction. Thyroperoxidase being responsible for iodination of tyrosine moieties is essential for active thyroid hormone T4 and T3 synthesis. When inhibited by anti TPO, the active T4, T3 synthesis decreases, resulting in low T4, T3 level and there is a compensatory increase in TSH level, which with increased anti TPO titer and duration leads to deterioration of thyroid function from sub clinical dysfunction to fully manifested clinical hypothyroidism[15].

Ganesan Subramanyam et al., 2012 demonstrated that there was increased level of anti TPO antibody and increased level of TSH and low T4 and T3 level indicating hypothyroidism [15]. In another study significant correlation between TSH or T4 concentration and elevated anti-TPO antibody was demonstrated by **Ghoraishianet al., 2006**[16] . **Bjoro et al., 2000** in their study have found that the positive anti-TPO levels correlated significantly with thyroid dysfunction and the prevalence of elevated TSH was nearly tenfold higher in both females and males with positive anti-TPO when compared to anti-TPO negative subjects [17]. In the present study, serum TSH levels were almost twice as high in the anti-TPO positive subjects as compared to anti-TPO negative hypothyroid patients.

In primary hypothyroidism, TSH values are expected to be high, indicating a lack of responsiveness of the thyroid gland to TSH stimulation. Generally in such cases, (FT3) and reverse T3 will also be low or low normal [18]. Thyroiditis can also present a laboratory picture of primary hypothyroidism. In addition to low FT4, low FT3 and elevated TSH, anti-thyroglobulin or anti-thyroid peroxidase may be elevated, blocking the production and release of thyroid hormone. **Hong Li et al., 2014** have observed that correlation between FT3 and FT4 were statically significant (P=<0.01) in patients with hypothyroidism[19] .

The study suggests that FT3 & FT4 levels are better in predicting the activity of thyroid hormones in the blood, and directly correlate with anti-TPO levels. So estimation of FT3 & FT4 levels can be helpful in diagnosing autoimmune thyroiditis.

CONCLUSION

Findings of the present study suggest that anti TPO activity is better reflected by serum FT_3& FT_4 levels as compared to total T_3& T_4 levels. Since FT3 and FT4 are the biologically active component of total thyroid hormones, estimation of these hormones becomes diagnostically more significant. The study, therefore, recommends inclusion of serum FT_3 & FT_4 in routine screening of hypothyroid patients. Further, correlation of serum FT3 and FT4levels with serum anti TPO levels can be helpful in identifying patients with autoimmune thyroiditis. Early detection of antibody levels can help in proper and timely patient treatment.

REFERENCES

1. Taylor PK. Thyroid disease: Hypothyroidism and Goitre. Medicine Uptake. 1993; 1:357-366.
2. Galesanu C, Linsic N, Teslaru R, Apostu L, Zbranca E. Lipid profile in a group of hypothyroid patients v/s treated hypothyroid patients. Rev. Med ChirSoc Med. 2004;108(3):554-560.
3. Rizos CV, Elisaf MS, Liberopoulos EN. Effects of thyroid dysfunction on lipid profile. Open Cardiovasc Med J. 2011;5:76-84.
4. Mansourian AR. The state of serum lipid profiles in subclinical hypothyroidism: A review of literature. Pak J Biol Sci. 2010;13(11): 556-562.
5. Tunbridge WMG, Evered DC, Hall R, Appleton D, Brewis M, Clark F et al., The spectrum of thyroid disease in a Community: the Whickham survey. ClinEndocrinol (Oxf). 1977;7:481-493.
6. Guo J, Jaume JC, Rapoport B, McLachlan SM. Recombinant thyroid peroxidase-specific Fab converted to immunoglobulin G (IgG) molecules: evidence for thyroid cell damage by IgG1, but not IgG4, autoantibodies. J ClinEndocrinolMetab. 1997;82(3):925-931.
7. Raspe E, Costagliola S, Ruf J, Mariotti S, Dumont JE, Ludgate M. Identification of the thyroid Na+/I− cotransporter as a potential autoantigen in thyroid autoimmune disease. Eur J Endocrinol. 1995; 132(4):399-405.
8. Chiovato LU, Bassi PA, Santini FE, Mammoli CL, Lapi PA, Carayon PI, et al. Antibodies producing complement-mediated thyroid cytotoxicity in patients with atrophic or goitrous autoimmune thyroiditis. J ClinEndocrinolMetab. 1993;77(6):1700-1705.
9. Feldt-Rasmussen U. Analytical and clinical performance goals for testing autoantibodies to thyroperoxidase, thyroglobulin, and thyrotropin receptor. Clin Chem. 1996;42:160-163.
10. Taurog A. Molecular evolution of thyroid peroxidase. Biochimie. 1999;81(5):557-562
11. Gharib H, Tuttle RM, Baskin HJ, Fish LH, Singer PA, McDermott MT. Subclinical thyroid dysfunction: a joint statement on management from the American Association of Clinical Endocrinologists, the American Thyroid Association, and the Endocrine Society. J Clin Endocrinol Metab. 2005;90(1):581-585.
12. Hollowell JG, Staehling NW, Flanders WD, Hannon WH, Gunter EW, Spencer CA, et al. Serum TSH, T(4), and thyroid antibodies in the United States population. National Health and Nutrition Examination Survey (NHANES III). 2002;87(2):489-499.
13. Jeena EJ, Malathi M, Sudeep K. A hospital-based study of anti-TPO titer in patients with thyroid disease. Muller J Med Sci Res. 2013;4(2):74.
14. Mohanty S, Amruthlal W, Reddy GC, Kusumanjali G, KanagasabapathyAS, Rao P. Diagnostic strategies for subclinical hypothyroidism. Indian J Clin Biochem. 2008;23(3):279-282.
15. Subramanyam G, Pushparaj JL. Prevalence of Anti-TPO antibody in Type-1 diabetes and thyroid dysfunction in TPO antibody positive diabetics. J Evol Med Dent Sci. 2012;1(5):668-676.
16. Ghoraishian SM, Moghaddam SH, Afkhami-Ardekani M. Relationship between anti-thyroid peroxidase antibody and thyroid function test. Iran J Immunol. 2006;3:146-149.
17. Bjoro T, Holmen J, Krüger O, Midthjell K, Hunstad K, Schreiner T, et al. Prevalence of thyroid disease, thyroid dysfunction and thyroid peroxidase antibodies in a large, unselected population. The Health Study of Nord-Trondelag (HUNT). Eur J Endocrinol. 2000;143(5): 639-644.
18. Genova Diagnostics. Comprehensive Thyroid Assessment, College of American Pathologists. 31722-31801.
19. Li H, Yuan X, Liu L, Zhou J, Li C, Yang P et al. Clinical Evaluation of Various Thyroid Hormones on thyroid function. International J Endocrinol. 2014;618572.