

ORIGINAL RESEARCH

Correlation Analysis of Anaemia with TSH Level and Anti-TPO Expression in Anti-TPO Positive Hypothyroid Patients

Bhawna Sandhir¹, Sumeet Chadha², Gagan Sandhir³, Rajesh Kashyap⁴, Suraj Bisht⁵, Neeraj Joshi⁶, Jagdeep Singh⁷

^{1,5}Postgraduate Resident, ⁴Professor, ⁶Senior Resident, Department of Medicine, Maharishi Markandeshwar Medical College, Kumarhatti, Solan, Himachal Pradesh, India

²Associate Professor, Department of Community Medicine, Maharishi Markandeshwar Medical College, Kumarhatti, Solan, Himachal Pradesh, India

³Postgraduate Resident, Department of Radiodiagnosis, Srinivas Institute of Medical Sciences and Research Centre, Mukka, Mangalore, Karnataka, India

⁷Emergency Medical Officer, Maharishi Markandeshwar Medical College, Kumarhatti, Solan, Himachal Pradesh, India

Correspondence:

Dr. Neeraj Joshi

Senior Resident, Department of Medicine, Maharishi Markandeshwar Medical College, Kumarhatti, Solan, Himachal Pradesh, India

Email: joshineeraj941@gmail.com

ABSTRACT

Introduction: Elevated anti-thyroid peroxidase (Anti-TPO) antibodies and thyroid stimulating hormone (TSH) levels in hypothyroidism have been linked to the alter the vitamin B12 metabolic pathway thereby imparting the anemia. Thyroid peroxidase is an important enzyme responsible during organification of iodide for synthesis of thyroid hormone. Antibodies to TPO are formed as a part of autoimmune response of body causing autoimmune thyroiditis in patients. Antibodies to thyroid peroxidase (TPO) are clinically useful markers of thyroid autoimmunity

Objectives: Present study aims to correlate the thyroid stimulating hormone and anti-thyroid peroxidase expression in Anti-TPO positive patients with the anemia.

Methods: 60 patients who were anti-TPO positive and hypothyroid were recruited in present study. TSH level, anti-TPO antibodies level and haemogram was analysed among all patients.

Results: There was a positive correlation between the haemoglobin and TSH level ($r=0.09580$). There was a negative correlation between the Haemoglobin and Anti-TPO expression ($r=-0.2086$).

Conclusion: Present study revealed a correlation of anemia with TSH level and Anti-TPO expression which have the diagnostic value. Anti-TPO positive hypothyroid patients have risk of developing anaemia.

Keywords: Anemia, TSH, Anti-TPO, Thyroid.

INTRODUCTION

Thyroid peroxidase is an important enzyme responsible during organification of iodide for synthesis of thyroid hormone. Antibodies to TPO are formed as a part of autoimmune response of body causing autoimmune thyroiditis in patients. Antibodies to thyroid peroxidase (TPO) are clinically useful markers of thyroid autoimmunity, but any other pathogenic effect is only restricted to a secondary role for amplifying already ongoing

autoimmune response. Abnormal laboratory findings in hypothyroid patients include anemia, except when accompanied by iron deficiency, the anemia and other abnormalities which gradually resolve with thyroxine replacement.¹ TPO antibodies have also been related to an increased risk of anaemia in hypothyroidism. TSH levels beyond a certain threshold were linked to more severe anaemia.²

Anti-TPO and anti-TG antibodies are linked to thyroid stimulating hormone (TSH) levels and have been used to predict the development of hypothyroidism and hyperthyroidism alone and in combination. Anti-thyroid antibodies and TSH levels in euthyroid people have been linked to the development of hypothyroidism in the future, according to several research.^{3,4} Anti-thyroid antibodies, in fact, are implicated in the aetiology of autoimmune thyroiditis via complement-dependent cytotoxicity; hence, their manifestation may occur several years before overt thyroid illness or abnormal thyroid function tests.⁵ Because anti-thyroid antibodies have been found in healthy people, particularly women, follow-up thyroid profile testing in anti-thyroid antibody positive people is critical for prompt diagnosis.⁶

Despite being on appropriate thyroxine dosages, hypothyroid individuals frequently have paraesthesia, numbness, weakness, and impaired memory.⁷ Vitamin B12 deficiency becomes more common as people become older. It is caused by malabsorption as a result of hypothyroidism-related pernicious anaemia.⁸ Folic acid deficiency is also one of the causes of macrocytic anemia due to intestinal malabsorption caused by hypothyroidism.⁹ Vitamin B12 deficiency anaemia is more common in patients with autoimmune thyroid diseases. Of note is that aplastic anemia may develop in autoimmune thyroid diseases. It is caused by T-Lymphocyte hyperactivation which induces apoptosis of haematopoietic cells by excessive secretion of Th1 lymphokines, such as interleukin 2 and interferon gamma.¹⁰ MMMC&H is a tertiary care hospital located in mid Himalayan range of Himachal Pradesh and prevalence of hypothyroidism was found to be 55.79% in 2015.¹¹

The present study was conducted to analyze the correlation of anemia in anti-thyroid peroxidase antibody positive hypothyroid patients. Serum T3, T4, TSH was investigated among patients having complaints suggestive of hypothyroid, previously diagnosed cases of hypothyroidism. An attempt to correlate the severity of TSH values with anemia profile among these patients was also made. Level of anti-TPO antibodies was also be correlated with anemia profile among these patients.

MATERIALS AND METHODS

PATIENTS RECRUITMENT

Present study was conducted for a period of one year with 60 patients over that period which included evaluation of all the new patients diagnosed with hypothyroidism and those with old subclinical/ overt hypothyroidism presenting to outpatient department of institute. Patients with newly diagnosed or past history of hypothyroidism not controlled on drugs and exhibiting anti- thyroid peroxidase antibody positivity were include in the study. Patients with other comorbidities, Coagulation disorders, other endocrine disorders like, patients taking drugs affecting thyroid function like propylthiouracil, neomercazole, amiodarone and iodine, patients taking drugs affecting haematopoietic system like immunomodulators etc, patients on radioactive iodine and whose partial thyroidectomy were done were excluded from the study.

ANALYSIS OF SERUM SAMPLES

Serum T3, Serum T4 done by ADVIA Centaur XP immunoassay system with help of Chemiluminescence immunoassay (CLIA) method. Serum TSH was done by ADVIA Centaur XP immunoassay with help of CLIA method. Anti TPO antibodies was done by ADVIA Centaur XP immunoassay with help of CLIA method.

There was a negative correlation between the Haemoglobin and Anti-TPO level with Pearson correlation (r)= -0.2086 (P value: 0.1067) (Figure 3).

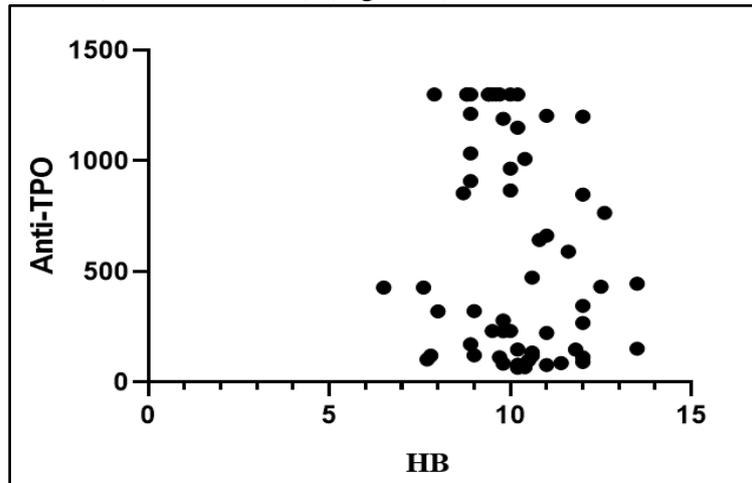


Figure 3: Correlation between HB and Anti-TPO

DISCUSSION

In the research by Kulkarni and Jadhav, the mean serum TSH levels in patients were 45.49 mIU/ml and 3.81 mIU/ml in controls. The blood TSH levels in hypothyroid individuals were substantially greater than in controls.¹² These results were similar to those of Mehmet et al study. According to Mehmet et al research, the mean serum TSH levels in the hypothyroid and control groups were 43.1 and 1.7 mIU/mL, respectively, and the hypothyroid group serum TSH levels were higher than the control group (9). The mean blood TSH values in the hypothyroid and control groups of Dorgalaleh et al study was 4.97 and 2.6 mIU/ml, respectively.¹³ In our study TSH levels and haemoglobin levels in patients had a positive correlation. Such findings were also obtained in research by Dorgaleleh in which MCH, MCHC, RDW, Hb and HCT done in hypothyroid and hyperthyroid vs control group had statistically significant difference between two groups of patients (P-value <0.05).¹³

TPO antibodies were found to be positive in 63.33 percent of hypothyroid patients and 10% of controls in research done by Kulkarni and Jadhav, and the incidence of hypothyroid cases was greater than the controls.⁸ The results were similar to those found by Mehmet et al and Das et al in their studies. In a study by Mehmet et al., TPO antibody positivity was observed in 100 percent of hypothyroid people and 22.5 percent of controls.⁹ TPO antibody was positive in 58.3 percent of patients in the research by Das et al.¹⁴

According to Akhter et al., a significant difference in thyroid hormone status in iron deficient individuals might be attributable to interrupted activities of iron-dependent enzymes like TPO, which alter thyroid hormone metabolism in general.¹⁵ In a similar study, Hess et al. discovered that thyroid peroxidase activity is drastically reduced in iron-deficient rats.¹⁶ They also emphasized the significance of iron in the transfer of thyroid hormone into cells, and how a shortage of iron causes thyroid hormone to pool, resulting in metabolic hypothyroidism. External thyroxine consumption increases erythropoiesis overall by raising erythropoietin levels, resulting in greater iron needs and the presentation of iron deficiency anaemia, according to Christ-Crain et al.¹⁷ When comparing clinical and subclinical hypothyroidism patients to controls, Endogan et al. discovered a comparable rise in the prevalence of microcytic hypochromic anaemia.¹⁸ The increasing level of rT3 is negatively connected with changes in plasma ferritin content, according to Eftekhari et al. They also confirm the relationship between iron deficiency status and rT3.¹⁹

Other research has found an inverse relationship between Hb and thyroid hormone levels. Bremmer et al. discovered a strong link between free T3 and haemoglobin, as well as an

inverse relationship between TSH and serum iron and transferrin saturation.²⁰ Bivolarska et al. discovered a substantial correlation between T4 and Hb levels.²¹ Some research, such as those conducted by Yavuz et al., have revealed no relationship between thyroid hormone and iron deficiency.²²

CONCLUSION

Our research attempted to demonstrate a link between Anemia and changed thyroid profile in patients with thyroid diseases, which will aid medical professionals in assessing haematocrit parameters in patients with thyroid problems. Present study revealed a correlation of anemia with TSH level and Anti-TPO expression which have the diagnostic value. Haemogram profile should be conducted in patients having thyroid disorders especially those with Anti-TPO positivity.

REFERENCES

1. Harrison T, AS F. Harrison's principles of internal medicine. New York: McGrawHill Medical, 2008. 7. Simon DA, Dix FP, McCollum CN. Management of venous leg ulcers. *BMJ*. 2004;328(1358):62.
2. Anand R, Mishra AK, Mahdi AA, Verma SP, Gupta KK. A study of prevalence and pattern of anemia in primary hypothyroidism. *International Journal of Medical Science and Public Health*. 2018;7(2):153-60.
3. 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.
4. Roos A, Links TP, Gans RO, Wolffenbuttel BH, Bakker SJ. Thyroid peroxidase antibodies, levels of thyroid stimulating hormone and development of hypothyroidism in euthyroid subjects. *European Journal of Internal Medicine*. 2010;21(6):555-9.
5. Hutfless S, Matos P, Talor MV, Caturegli P, Rose NR. Significance of prediagnostic thyroid antibodies in women with autoimmune thyroid disease. *The Journal of Clinical Endocrinology & Metabolism*. 2011;96(9):E1466-E71.
6. 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;2018:9610497.
7. Jabbar A, Yawar A, Waseem S, Islam N, Ul Haque N, Zuberi L, et al. Vitamin B12 deficiency common in primary hypothyroidism. *Journal of the Pakistan Medical Association*. 2008;58(5):258.
8. Kulkarni VK, Jadhav DU. A study of anemia in primary hypothyroidism. *Int J Adv Med*. 2017;4:383-9.
9. Mehmet E, Aybike K, Ganidagli S, Mustafa K. Characteristics of anemia in subclinical and overt hypothyroid patients. *Endocrine journal*. 2012;59(3):213-20.
10. Szczepanek-Parulska E, Hernik A, Ruchała M. Anemia in thyroid diseases. *Pol Arch Intern Med*. 2017;127(5):352-60.
11. Shashi A, Sharma N. Prevalence and clinical aspects of thyroid disorders in himachal pradesh, India. *Int J Basic Appl Med Sci*. 2015;5(1):86-94.
12. Das K, Mukherjee M, Sarkar T, Dash R, Rastogi G. Erythropoiesis and erythropoietin in hypo- and hyperthyroidism. *The Journal of Clinical Endocrinology & Metabolism*. 1975;40(2):211-20.
13. Dorgalaleh A, Mahmoodi M, Varmaghani B. Effect of thyroid dysfunctions on blood cell count and red blood cell indice. *Iranian journal of pediatric hematology and oncology*. 2013;3(2):73.

14. Das C, Sahana PK, Sengupta N, Giri D, Roy M, Mukhopadhyay P. Etiology of anemia in primary hypothyroid subjects in a tertiary care center in Eastern India. *Indian journal of endocrinology and metabolism*. 2012;16(Suppl 2):S361.
15. Akhter S, Nahar Z, Parvin S, Alam A, Sharmin S, Arslan M. Thyroid status in patients with low serum ferritin level. *Bangladesh Journal of Medical Biochemistry*. 2012;5(1):5-11.
16. Hess SY, Zimmermann MB, Arnold M, Langhans W, Hurrell RF. Iron deficiency anemia reduces thyroid peroxidase activity in rats. *The Journal of nutrition*. 2002;132(7):1951-5.
17. Christ-Crain M, Meier C, Huber P, Zulewski H, Staub J-J, Muller B. Effect of restoration of euthyroidism on peripheral blood cells and erythropoietin in women with subclinical hypothyroidism. *Hormones-Athens*. 2003;2:237-42.
18. Erdogan M, Kösenli A, Ganidagli S, Kulaksizoglu M. Erratum: Characteristics of anemia in subclinical and overt hypothyroid patients [*Endocrine Journal* Vol. 59 (3): 213-220, 2012]. *Endocrine Journal*. 2013;60(4):541.
19. Eftekhari MH, Keshavarz SA, Jalali M, Elguero E, Eshraghian MR, Simondon KB. The relationship between iron status and thyroid hormone concentration in iron-deficient adolescent Iranian girls. *Asia Pacific journal of clinical nutrition*. 2006;15(1):50.
20. Bremner AP, Feddema P, Joske DJ, Leedman PJ, O'Leary PC, Olynyk JK, et al. Significant association between thyroid hormones and erythrocyte indices in euthyroid subjects. *Clinical endocrinology*. 2012;76(2):304-11.
21. Bivolarska A, Gatseva P, Maneva A. Association between thyroid and iron status of pregnant women in Southern Bulgaria. *Journal of Endocrinology and Diabetes Mellitus*. 2013;1(1).
22. Yavuz Ö, Yavuz T, Kahraman C, Yeşildal N, Bundak R. The relationship between iron status and thyroid hormones in adolescents living in an iodine deficient area. *Journal of Pediatric Endocrinology and Metabolism*. 2004;17(10):1443-50.