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COMPARISON OF RAISED LEVEL OF ANTI-THYROID PEROXIDASE ANTIBODY IN PATIENTS OF HYPOTHYROIDISM AND EUTHYROIDS

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Abstract:

Objective: *To compare the frequency of raised level of anti-thyroid peroxidase antibody in patients of hypothyroidism and euthyroids.*

Material and methods: *This case/control study was conducted at Department of Medicine, DG Khan Hospital, DG Khan from March 2019 to September 2019 over the period of 6 months. Frequency of raised level of anti-thyroid peroxidase antibody in patients of hypothyroidism and euthyroids was compared.*

Results: *In present study, mean age of the cases was 32.42±10.09 years and mean age of controls is 32.45±10.12 years. Raised Anti-Thyroid Peroxidase Antibodies were found in 20 (28.99%) cases and in 5 (7.25%) controls. After applying chi-square test, statistically significant (P = 0.00) difference of Raised Anti-Thyroid Peroxidase Antibodies between cases and controls was detected.*

Conclusion: *Results of present study showed higher rate of Raised Anti-Thyroid Peroxidase Antibodies in cases as compared to controls. Raised Anti-Thyroid Peroxidase Antibodies significantly associated with age and female gender.*

Keywords: *Hypothyroidism, Euthyroids, Anti-thyroid peroxidase antibody*

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INTRODUCTION:

Hypothyroidism is characterized by abnormally low serum T_4 and T_3 levels and high TSH level. The defect that makes a person liable to development of autoimmune thyroid disease is still unknown. There is a precise tissue defect in suppressor T-cell function in the suggested methods, an idiotype/anti-idiotype reaction and a biologically programmed antigen.[1]The existence of anti-thyroid peroxidase (anti-TPO) antibodies and the occurrence of autoimmune hypothyroidism are well-documented relations.[2] according to A survey by Amritha Institute, Cochin, that 9.5% subjects (Out of 19.6% of individuals suffering from thyroid function abnormalities) had anti-TPO antibodies.[3] The reported prevalence of subclinical hypothyroidism in male and female population is 3% and 8% respectively. Risk of development of clinical hypothyroidism is 4% annually if sub-clinical hypothyroidism is related to positive TPO antibodies. [4] According to a research conducted in Muzaffarabad, there are no age-related positive anti-thyroid peroxidase antibodies, but they were found to be linked with high levels of thyroid-stimulating hormone.[5]

For effectiveness of treatment and diagnosis of autoimmune thyroid disease an important factor is anti-TPO antibodies. According to a research in 2007, 11 to 74.5% and 56% of the cultured thyroid cells can be harmed by the antibody-dependent cell cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC) methods of anti-TPO antibodies.[6] The monocytes, via their FcγRI, are important effector cells in antibody-dependent cell cytotoxicity (ADCC) mediated by anti-TPO antibodies and may contribute with T cells to the destruction of thyroid gland in autoimmune thyroid disease.[7] The clinical diagnosis of autoimmune thyroid disease is usually confirmed by the detection of various antibodies in the patient's blood sample.[8]

A study conducted by Elmugadam AA et al[9] showed that anti-thyroid peroxidase antibody of thyroid disease patients and control group was positive in 21.2% and 5% respectively.

The existence of thyroid peroxidase antibodies may indicate future thyroid diseases, we have planned this study to see raised anti-thyroid peroxidase antibody in cases of hypothyroidism and in euthyroids so that some practical recommendations could be made for preemptive prevention of developing hypothyroidism by early detection of anti-thyroid peroxidase antibody and subsequent early management by immunosuppressive drugs.

OPERATIONAL DEFINITIONS:

Hypothyroidism

- Patients of hypothyroidism was diagnosed by measuring FT3 and FT4 below the lower limit of normal range (normal range of FT3: 3.2-8.0 pmol/L and normal range of FT4: 10.3-34.7 pmol/L) and TSH above the higher limit of normal range (normal range of TSH: 0.4-4.2 mIU/L).

Euthyroids

- Euthyroids was labeled when the person has no signs and symptoms and FT3, FT4 and TSH was within normal range (normal range of FT3: 3.2-8.0 pmol/L, normal range of FT4: 10.3-34.7 pmol/L and normal range of TSH: 0.4-4.2 mIU/L).

Raised anti-thyroid peroxidase antibody

- These are autoantibodies targeted against thyroid peroxidase (TPO) enzyme and serum value ≥10 IU/ml was labeled as raised anti-thyroid peroxidase antibody and <10 was labeled as normal.

MATERIAL AND METHODS:

This case/control study was conducted at Department of Medicine, DG Khan Hospital, DG Khan from March 2019 to September 2019 over the period of 6 months. Total 69 patients of hypothyroidism (as per operational definition) having age 18-60 years either male or female were selected. Age and sex matched euthyroids (FT3, FT4 and TSH within normal range) as described in operational definition was served as controls

Patients taking medicine for thyroid disease, patients with hyperthyroidism, thyroiditis or thyroid malignancy, patients having other medical illness like renal diseases, cardiac diseases, hepatic diseases, pulmonary diseases or any neoplastic disease, patients having autoimmune diseases or on immunosuppressive therapy and pregnant patients were excluded from the study.

This study was approved from hospital ethical committee and written informed consent was taken from every patient. Patients were recruited from medical OPD. Patients presenting with hypothyroidism (FT3 and FT4 below the lower limit of normal range and TSH above the higher limit of normal range) were served as cases and placed in group-A. Age and sex-matched euthyroids (FT3, FT4 and TSH within normal range) were served as control group and placed in group-B. Both in group-A and group-B, 5 ml blood was withdrawn from the vein of elbow or the back of hand. Blood was immediately collected and transferred to red-top or gel tubes. Samples were allowed to clot for one hour before centrifugation. Test serum was clear and non-hemolysed. Serum was analyzed through fully automated chemistry analyzer using enhanced chemiluminecence method to detect serum FT3, FT4 and TSH. Anti-thyroid peroxidase antibodies were measured by ELISA (Bio Rad Kallestad). A

proforma was used to collect the pertinent information from every patient.

Data was analyzed by using SPSS version 20. Numerical data was presented as mean and SD and categorical data was presented as frequencies and percentages. Chi-square test was applied to detect difference of raised anti-thyroid peroxidase antibodies between the cases and controls. P-value ≤0.05 was taken as significant.

RESULTS:

In present study, mean age of the cases was 32.42±10.09 years and mean age of controls is 32.45±10.12 years. Raised Anti-Thyroid Peroxidase Antibodies were found in 20 (28.99%) cases and in 5 (7.25%) controls. After applying chi-square test, statistically significant (P = 0.00) difference of Raised Anti-Thyroid Peroxidase Antibodies between cases and controls was detected. (Table 1) Age distribution of the selected patients was done and two groups were formed, age group 18-30 years and age group 31-60 years. In age group 18-30 years, total 37 (53.62%) were cases and 41 (59.42%) controls. Raised Anti-Thyroid Peroxidase Antibodies was noted in 9 (24.32%) cases and in 2 (4.88%) controls. Difference of Raised Anti-Thyroid Peroxidase Antibodies between the cases and controls was statistically significant with p value 0.02.

In age group 31-60 years, out of 32 (46.38%) cases, Raised Anti-Thyroid Peroxidase Antibodies were found in 11 (34.38%) cases while among the 28 (40.58%) controls Raised Anti-Thyroid Peroxidase Antibodies were detected in 3 (10.71%) controls. Significantly higher rate of Raised Anti-Thyroid Peroxidase Antibodies was noted in cases as compared to controls with p value 0.03 (Table 2) Total 13 (18.84) cases were male and 11 (15.94) controls were male. Total 4 (30.77) male cases were found with Raised Anti-Thyroid Peroxidase Antibodies and no control found with Raised Anti-Thyroid Peroxidase Antibodies. Difference was not statistically significant (P 0.09) between male cases and male controls. In 56 (81.16) female cases, Anti-Thyroid Peroxidase Antibodies were found raised in 16 (28.57) female cases. Out of 58 (84.06) female controls, Anti-Thyroid Peroxidase Antibodies were found raised in 5 (8.62) female controls. Difference was statistically significant with p value 0.00. (Table 3)

TABLE No. 1: Comparison of raised anti-thyroid peroxidase antibodies in both groups

Group	Raised Anti-Thyroid Peroxidase Antibodies		Total	P value
	Yes (%)	No (%)		
Cases (Hypothyroidism)	20 (28.99)	49 (71.01)	69	0.00
Controls (Euthyroid)	5 (7.25)	64 (92.75)	69	

TABLE No. 2: Comparison of raised Anti-Thyroid Peroxidase Antibodies between both groups for age

Group	Raised Anti-Thyroid Peroxidase Antibodies		Total	P value
	Yes (%)	No (%)		
Age group 18-30 years				
Cases	9 (24.32)	28 (75.68)	37 (53.62)	0.02
Controls	2 (4.88)	39 (95.12)	41 (59.42)	
Age group 31-60 years				
Cases	11 (34.38)	21 (65.63)	32 (46.38)	0.03
Controls	3 (10.71)	25 (89.86)	28 (40.58)	

TABLE No. 3: Comparison of raised Anti-Thyroid Peroxidase Antibodies between both groups for gender

Group	Raised Anti-Thyroid Peroxidase Antibodies		Total	P value
	Yes (%)	No (%)		
Male patients				
Cases	4 (30.77)	9 (69.23)	13 (18.84)	0.09
Controls	0	11 (100)	11 (15.94)	
Female patients				
Cases	16 (28.57)	40 (71.43)	56 (81.16)	0.00
Controls	5 (8.62)	53 (91.38)	58 (84.06)	

DISCUSSION:

For primary care environments, physicians need to be aware of a potentially high-risk demographic to be detected and monitored more closely. Patients with high normal TSH or strong anti-TPOAbs may be at higher risk over time to develop hypothyroidism.[10]

In this research, we hypothesized that the expression of thyroid peroxidase antibodies could serve as an indicator of possible thyroid disease, but we intended this analysis to see elevated anti-thyroid peroxidase antibodies in patients with hypothyroidism and euthyroidism so that some realistic suggestions could be made to prevent the development of hypothyroidism by early detection of anti-thyroid peroxidase antibody and subsequent early management by immunosuppressive drugs.

In present study, mean age of the cases was 32.42±10.09 years and mean age of controls is 32.45±10.12 years. Raised Anti-Thyroid Peroxidase Antibodies were found in 20 (28.99%) cases and in 5 (7.25%) controls. After applying chi-square test, statistically significant (P = 0.00) difference of Raised Anti-Thyroid Peroxidase Antibodies between cases and controls was detected. (Table 1) Age distribution of the selected patients was done and two groups were formed, age group 18-30 years and age group 31-60 years. In age group 18-30 years, total 37 (53.62%) were cases and 41 (59.42%) controls. Raised Anti-Thyroid Peroxidase Antibodies was noted in 9 (24.32%) cases and in 2 (4.88%) controls. Difference of Raised Anti-Thyroid Peroxidase Antibodies between the cases and controls was statistically significant with p value 0.02.

In age group 31-60 years, out of 32 (46.38%) cases, Raised Anti-Thyroid Peroxidase Antibodies were found in 11 (34.38%) cases while among the 28 (40.58%) controls Raised Anti-Thyroid Peroxidase Antibodies were detected in 3 (10.71%) controls. Significantly higher rate of Raised Anti-Thyroid Peroxidase Antibodies was noted in cases as compared to controls with p value 0.03

Our findings are in agreement with a study conducted by Elmugadam AA et al[9] showed that anti-thyroid peroxidase antibody of thyroid disease patients and control group was positive in 21.2% and 5% respectively. Whickham and Busselton reported that probability of development of hypothyroidism by increasing serum levels of TSH and in presence of TPOAbs, this probability is further increased. [11-12]

The pathophysiological mechanism behind the TPOAbs prevalence and possible thyroid disorder relationship is complicated and not fully understood.[13] Not only is thyroid peroxidase (TPO) recognized as the main enzyme in thyroid hormone synthesis, but it also functions as a major autoantigen.[14] Therefore, it was hypothesized that TPOAbs should not be regarded as one group because their pathogenic ability could be affected based on the epitope of TPO to which they are attached.[15] TPOAbs are typical of autoimmune thyroid disease.[16] Both in hypothyroidism (thyroiditis of Hashimoto) and (hyperthyroidism of Graves). A combination of genetic susceptibility and environmental factors is believed to be the cause of Hashimoto's thyroiditis. The antibodies are primarily formed in the thyroid gland by a lymphocytic infiltrate.[17] The degree of this lymphocytic infiltration is substantially associated with the titer of microsomal antibodies.[18] The involvement of TPOAbs can therefore be seen as an indicator of increased risk of future thyroid loss in tandem with the observed higher prevalence of positive TPOAbs with - TSG levels, even in euthyroidism.

CONCLUSION:

Results of present study showed higher rate of Raised Anti-Thyroid Peroxidase Antibodies in cases as compared to controls. Raised Anti-Thyroid Peroxidase Antibodies significantly associated with age and female gender.

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