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ORIGINAL ARTICLE

THYROID PEROXIDASE AUTOANTIBODY IN SUBCLINICAL AND OVERT HYPOTHYROIDISM: A HOSPITAL BASED RETROSPECTIVE STUDY

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ABSTRACT

Introduction: *Thyroid peroxidase (TPO) is a key enzyme of thyroid hormone biosynthesis as it catalyzes the iodination and the coupling steps. Subclinical hypothyroidism is the condition of increased Thyroid Stimulating Hormone (TSH) and normal levels of serum free thyroxine (ft4) and free triiodothyronine (ft3) levels. Subclinical hypothyroidism can be progressed to overt hypothyroidism in which ft3 and ft4 levels are decreased along with an increment of TSH levels.*

Materials and Methods: *This was the hospital-based retrospective study conducted on the patients who had undergone thyroid function test measurements along with thyroid peroxidase autoantibody level in serum. The study duration was eight months (January 2022 to August 2022). All the data were entered in Microsoft Excel version 10 and analyzed in SPSS version 22 accordingly.*

Result: *In the study among 424 patients, 73.8% were female and 26.2% were male. Firstly, our study revealed subclinical hypothyroidism was predominant (41.7%), followed by euthyroidism (34.7%) overt hypothyroidism (20.3%), and overt hyperthyroidism (3.3%). Secondly, there was no statistically significant difference in age (P value: 0.26) and gender (0.64) between subclinical and overt hypothyroidism. There was no statistically significant difference in serum anti-TPO antibodies level between subclinical (median 6.25) and overt hypothyroidism (median 6.12) (P value: 0.92) when median and interquartile ranges were compared. Correlation analysis revealed a significant positive correlation of TPO antibodies with TSH (0.27, 0.00) and no significant negative correlation with fT4 (-0.02, 0.46) and fT3 (-0.05, 0.37).*

Conclusion: *The current study revealed the elevation of thyroid peroxidase autoantibodies in both subclinical and overt hypothyroid patients though subclinical hypothyroidism was predominant.*

Keywords: *Autoantibody, Hypothyroidism, Thyroid hormones, Thyroperoxidase.*

INTRODUCTION

Thyroperoxidase (TPO) also known as thyroid peroxidase is a key enzyme of thyroid hormone biosynthesis as it catalyzes two crucial steps which are the iodination of tyrosine residues on thyroglobulin and coupling reactions.[1]

Hypothyroidism is a clinical condition in which the thyroid gland cannot synthesize thyroid hormones to meet the need of peripheral tissues. In primary hypothyroidism, the thyroid gland itself is defective, and in secondary hypothyroidism and tertiary hypothyroidism respectively anterior pituitary and hypothalamus are defective. Decreased thyroidal secretion and serum level cause elevation of thyroid-stimulating hormone.[2]

Subclinical hypothyroidism is a condition of increased Thyroid Stimulating Hormone (TSH) and normal serum

levels of free thyroxine (ft4) and free triiodothyronine (fT3). Moreover, it is considered a mild form of hypothyroidism.[3] In addition, the most common cause of subclinical hypothyroidism is autoimmune thyroiditis with its association of raised anti thyroperoxidase autoantibodies (anti-TPO).[4] TPO antibodies can be present in the serum of euthyroid individuals and they are more prone to develop subclinical hypothyroidism and subsequently, overt hypothyroidism.[5] Overt hypothyroidism is a condition of increased thyroid Stimulating Hormone (TSH) and decreased serum level of free thyroxine (ft4) and free triiodothyronine (fT3). Subclinical hypothyroidism can be progressed to overt hypothyroidism in untreated cases. Some studies also revealed the progression of subclinical hypothyroidism to overt hypothyroidism is more when the titers of anti-thyroperoxidase antibodies are high.[6, 7]

Our study aimed to compare thyroperoxidase autoantibody level and other thyroid function test parameters between subclinical and overt hypothyroidism and to correlate the serum anti-TPO antibody level with fT3, ft4, and TSH levels.

MATERIALS AND METHODS

This study was a Hospital based retrospective study conducted in the Department of Biochemistry of a tertiary care hospital of National Medical College, Birgunj, Nepal. Recorded data of the patients visiting Clinical Laboratory Services was taken. All the patients who had undergone anti-thyroperoxidase autoantibody level and thyroid function tests were enrolled in the study.

The data of four hundred twenty-four (424) patients were retrieved from the software which was available during our study duration (January 2022 to August 2022). The study groups were categorized based on serum levels of fT3, fT4, and TSH levels

- Subclinical hypothyroidism: TSH increased, Normal fT3 and fT4
- Overt hypothyroidism: TSH increased, Decreased fT3 and fT4
- Euthyroidism: Normal TSH, fT3, and fT4
- Overt hyperthyroidism: TSH decreased, increased fT3 and fT4

The biochemical parameters measured in our study were fT3, fT4, TSH, and anti-TPO antibodies. The reference ranges in our laboratory as per the manufacturer of the reagent kit were fT3 (2.5-3.9pg/mL), fT4 (0.61-1.12 ng/dL), TSH (0.34-5.6µIU/mL) and anti-TPO antibody (<25 IU/mL). The principle of laboratory assay was Chemiluminescence Immunoassay (CLIA). A fully automated Immunoassay analyzer (BECKMANN COULTER INC. Access 2, California) was used. The ethical clearance was obtained from the Institutional Review Committee (IRC) of National Medical College, Birgunj, Nepal (Ref no: F-NMC/580/078-079) before starting the research.

The data were expressed in Mean & Standard Deviation, Median & Interquartile range (IQR) based on the nature of the data. An Independent t-test was applied for the comparison of serum fT3 and fT4 levels. Mann Whitney U test was applied to compare serum TSH and anti-TPO antibody levels as the data was skewed. Pearson's correlation for parametric and Spearman's rho for non-parametric data was used considering P≤0.05 as statistically significant at a 95% confidence interval.

RESULTS

Our study revealed the distribution of thyroid status, anti-TPO antibody level, and correlation with TFT parameters among 424 participants, out of which 74% were female and 26% were male subjects. The serum anti-TPO antibody level of more than 25IU/mL was considered TPO positive. In the current study, 42.2% of female patients were TPO positive and 36% of males were TPO positive as depicted in figure 1.

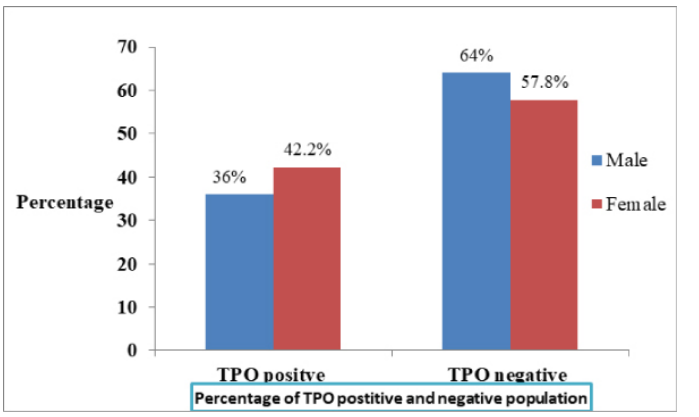

Figure 1: Gender-wise distribution of study population based on TPO positivity (n=424)

Out of 424 participants, subclinical hypothyroidism was

predominant 177 (41.74 %), followed by euthyroidism 147 (34.66%), then overt hypothyroidism 86 (20.28%) and overt hyperthyroidism 14(3.30%) as depicted in figure 2.

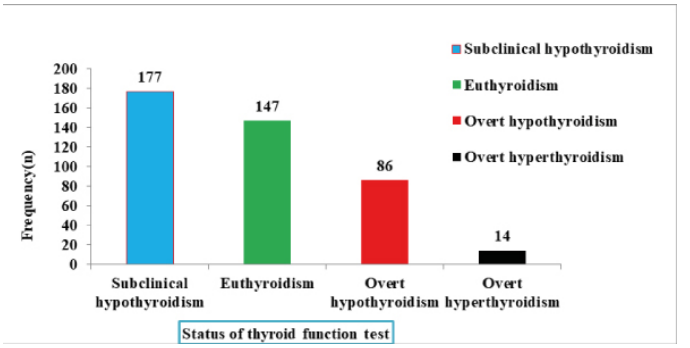

Figure 2: Distribution of population based on thyroid function status (n=424)

Table 1 illustrates the comparison of variables between subclinical and overt hypothyroidism. There was no significant difference in age (P value: 0.26) and gender (P value: 0.64) between the groups. Free triiodothyronine (Ft3) and free thyroxine (Ft4) levels were significantly higher in subclinical hypothyroidism (P value: 0.01). Thyroid-stimulating hormone (TSH) level was significantly higher in overt hypothyroidism (P value: 0.01) when the median, first, and third quartiles were compared. In contrast, the anti-TPO antibody level was not significantly different between the groups (P value: 0.92). The median anti-TPO antibodies for subclinical and overt hypothyroidism were respectively 6.25 and 6.12.

Table 1: Comparison of variables between subclinical and overt hypothyroidism (n=424)

S.N.	Variables	Subclinical hypothyroidism (n=177)	Overt hypothyroidism (n=86)	P value*
1	Age (years)	34.34±14.73	32.19±14.23	0.26
2	Gender (F/M)	132/45	67/19	0.64
3	fT_3(pg/mL)	2.9844±0.64863	1.9181±0.84	0.01*
4	fT_4(ng/dL)	0.92±0.44	0.43±0.26	0.01*
5	TSH (µIU/mL)	6.91[3.68, 12.85][*1]	7.11[3.69,12.94][*1]	0.01*
6	Anti-TPO antibody (IU/mL)	6.25[1.32, 268.72][*1]	6.12[1.30, 264.90][*1]	0.92

*Values are Median [first quartile, third quartile].

The study population was divided into two categories that are anti TPO positive and negative. Cross tabulation was done with thyroid function test status. On comparing the row percentage, a significant difference was observed (P value: 0.01).

Table 2: Cross-tabulation of TPO positivity with thyroid status (n=424)

S.N.	Group	Anti TPO positive	Anti TPO negative	P value*
1	Subclinical hypothyroidism	108 (61%)	69 (39%)	0.01*
2	Euthyroidism	5 (4.3%)	142 (96.6%)	
3	Overt hypothyroidism	51 (59.3%)	35 (40.7%)	
4	Overt hyperthyroidism	8(57.1%)	6(42.9%)	

In subclinical hypothyroidism, TPO-positive cases were 61% which is the maximum among all groups. Similarly, in overt hypothyroidism, TPO-positive cases were 59.3%. In the population with normal thyroid status that is euthyroidism; the least individuals were TPO positive which is 4.3% as shown in table 2.

Table 3: Comparison of different age groups between TPO positive and negative populations (n=424)

S.N.	Categories of age (Years)	TPO +ve population	TPO -ve population	Total population	P value*
1	1-20	26(42.6%)	35(57.4%)	61 (100%)	0.01
2	21-40	101(46.5%)	116 (53.5%)	217 (100%)	
3	41-60	36(28.8%)	89(71.2%)	125(100%)	
4	>60	9(42.9%)	12(57.1%)	21 (100%)	

Table 3 illustrates the cross-tabulation of different categories of age and thyroperoxidase positive and negative populations. The majority of TPO positive population was between 21 to 40 years contributing 46.5% of that group. On the other hand, the least number of patients were observed in the age group 41- 60 years contributing 28.8% population of that group.

Correlation analysis revealed a significant positive correlation of anti-TPO antibody with TSH levels (P value: 0.00). However, a negative correlation was seen with Ft3and Ft4 which was not statistically significant as illustrated in table no.4.

Table 4: Correlation of anti-TPO antibody with thyroid function test parameters (n =424)

S.No.	Parameters	r value	P value
1	fT3	-0.05	0.37
2	fT4	-0.02	0.46
3	TSH	0.27	0.00

DISCUSSION

First of all, the current study revealed the comparison of thyroid function test parameters (fT3, ft4 and TSH) along with anti-thyroid peroxidase levels between subclinical and overt hypothyroidism. Secondly, the majority of TPO-positive populations were found in subclinical hypothyroidism. Our results support the findings of Mohanty S et al.[4] and Abdulateef DS et al.[8] They revealed the higher prevalence of anti-TPO antibodies in subclinical hypothyroidism. Similar to our study, Shimizu Y et al. revealed TPO positivity in subclinical hypothyroidism.[9]

The current study revealed the predominance of subclinical hypothyroidism followed by euthyroidism then overt hypothyroidism and overt hyperthyroidism. However, we didn't get any subclinical hyperthyroid population. A study conducted in Copenhagen, Denmark by Carle A et al revealed a 95% prevalence of measurable anti-TPO antibodies in overt hypothyroid patients; this is higher than our study.[10] In addition, we revealed that anti-TPO antibodies may be increased not only in subclinical hypothyroidism but also in overt hypothyroidism. Robert CG and Ladenson PW reported that most patients develop hypothyroidisms which is autoimmune in origin.[11]

The correlation analysis revealed a significant positive correlation between serum anti-thyroperoxidase autoantibody and serum thyroid stimulating hormone (TSH). However, the a negative correlation between fT3 and fT4 levels. In agreement with our study, Al-Rabia MW revealed a significant positive correlation of anti-TPO antibodies with serum TSH levels.[12] Similar types of findings were observed in the study by Dhakal S et al in a cross-sectional study conducted at Pokhara, Nepal.[14]

Our study revealed the TPO-positive population was predominant in female patients contributing to 42.2% of the female participants. Moreover, TPO positive population was predominant in the age group 21 to 40 years old followed by those below 20 years old. Al-Rabia MW revealed similar results.[12] Swain et al. reported that autoimmune disease is most commonly found in 30 to 50 years old.[13] A study conducted in the Western part of Nepal by Dhakal S et al also revealed a higher prevalence of anti-TPO antibody positivity in females in comparison to male patients. In their study, 74.07% were female participants who had anti-TPO antibody positive.[14]

Our study also revealed that the anti-TPO antibody-positive population is predominant in subclinical hypothyroidism (61%). Subclinical hypothyroidism is mostly due to autoimmune thyroiditis associated with raised anti-TPO antibodies.[4] In contrast, an anti-TPO positive population was also detected in the euthyroid group contributing to 4.3% of the euthyroid population. Meier C et al. reported the presence of these antibodies in euthyroid subjects and these subjects are more prone to develop subclinical hypothyroidism.[5]

CONCLUSION

The thyroperoxidase autoantibody level in serum can be elevated in both subclinical and overt hypothyroidism. Subclinical hypothyroidism was the most common thyroid disorder among the participants. The serum anti-TPO antibody should be monitored in hypothyroid patients to rule out autoimmune cases of hypothyroidism due to inadequate iodination and coupling steps of thyroid hormone biosynthesis.

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