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A STUDY ON ASSOCIATION BETWEEN ANTI-THYROID ANTIBODIES (ANTI TPO/TG) IN NEWLY DETECTED HYPOTHYROID PATIENTS.

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Abstract

Background: Hypothyroidism is one of the most common endocrine disorders in India. The most common cause for hypothyroidism is Iodine deficiency. Second most frequent cause is the autoimmune thyroid disease characterized by elevated TPO antibodies and Thyroglobulin (TG) antibodies;However, these autoantibodies are commonly present in the general population as well. Hence, this study is to make a comparison in Anti TPO and Anti TG antibodies in hypothyroid patients in a healthcare set up, which may help in the prognosis and early treatment of the disease.
Methods:30 newly detected hypothyroidism patients aged between 18 years to 65 years were randomly selected. A detailed medical history was obtained, and general physical, systemic examination was carried out with prior consent. All the necessary investigations were done, and the results were statistically analyzed.
Results: Anti TPO antibody was positive in 30% of the subjects i.e. autoimmune hypothyroidism was prevalent in 30% of the subjects. Anti TG antibody was found in only 10% of the subjects.
Conclusion: Overall association between thyroid antibody and hypothyroidism was assessed. Anti TPO antibody has strong association with autoimmune hypothyroidism compared to anti TG antibody.

Keywords: Anti TPO antibody, Hypothyroidism, Anti TG antibody, Autoimmune thyroid disease

INTRODUCTION

Hypothyroidism is one of the most common endocrine disorders in India. A study done in 2013 concluded that hypothyroidism is prevalent in 11% of population[1]. The most common cause for hypothyroidism is Iodine deficiency. Second most frequent cause is the autoimmune thyroid disease characterized by elevated anti thyroid peroxidase antibody (anti TPO).

Clinically we come across Subclinical Hypothyroidism which refers to biochemical evidence of thyroid hormone deficiency (TSH- 6 to 15 mU/L, normal T3, T4 and low-normal fT4) in patients who have few or no apparent clinical features of hypothyroidism[2].

The thyroid gland requires TPO and TG(Thyroglobulin) for efficient synthesis of T_4 and T_3[3].Anti-TPO autoantibodies are very important to diagnose autoimmune thyroid diseases and estimating its clinical course.

Hashimoto's and Grave's diseases are the commonly seen autoimmune thyroid disorders. 80% of Grave's patients have high levels of TPO antibodies. About 4% of subclinical hypothyroid patients with positive TPO antibodies develop clinical hypothyroidism. TPO antibodies fix the complement resulting in the formation of a complex of membrane and complement, and these complexes are present in autoimmune thyroid disease patients[4].

Antibodies to TPO are detectable in 50% to 90% of patients with grave's disease, indicative of the associated thyroiditis that is evident histologically as a heterogenous lymphocytic infiltration. High antibody titers are found in 90% of patients with chronic Hashimoto's thyroiditis. In patients with subclinical hypothyroidism, the presence of TPO antibodies is associated with an increased risk of developing overt hypothyroidism. Both thyroglobulin & TPO antibodies are found in almost 100% of such patients, but TPO Ab are more specific since they have higher affinity and exist in higher concentrations.[3]

TPO is a key enzyme in the synthesis of thyroid hormone. TPO is involved in the organification and coupling reactions, for the synthesis of thyroid hormone. TPO is a major antigen corresponding to thyroid microsomal autoantibodies. Thyroid autoimmunity is a major cause for hypothyroidism. The diagnostic hallmark of the Autoimmune thyroid disorder (AITD) is circulating antibodies, mainly TPO antibodies and Thyroglobulin (TG) antibodies which are elevated in hypothyroidism. However, these autoantibodies are commonly present in the general population as well. Hence, this study is to make a comparison in Anti TPO and Anti TG antibodies in hypothyroid patients in healthcare set up, which may help in the prognosis and early treatment of the disease.[3]

OBJECTIVES:

1. To determine anti TPO anti TG antibody positivity
2. To assess the significance of anti TPO anti TG antibody in newly detected hypothyroid patients in comparison to various parameters

MATERIALS AND METHODS

Source of data:

Newly detected hypothyroid patients (outpatients and in-patients) at Dr. B.R. Ambedkar Medical College and Hospital Bangalore.

Method of collection of data:

30 newly detected hypothyroidism patients aged between 18 years to 65 years were randomly selected. A detailed medical history was obtained, and general physical, systemic examination was carried out with prior consent. Study details were explained to them in local language. All the necessary investigations were done, and the results were statistically analyzed.

Inclusion criteria:

- Patients aged 18 to 65 years.
- Patients who signed informed consent
- Non pregnant women

Exclusion criteria:

- Pre-diagnosed thyroid dysfunction or autoimmune thyroid disorder.
- Patients on steroids or other immunomodulator drugs.
- Patients who have undergone previous thyroid surgery.
- Patients who have undergone neck irradiation or iodine therapy.
- Diabetes Mellitus.
- Pregnancy
- Menopause.
- Patients on previous lithium or amiodarone medication.

Investigations:

- CBC and ESR
- Lipid profile.
- Thyroid profile (T3,T4,TSH).
- Anti-Tg Ab assay.
- Anti TPO Ab assay.
- FNAC (if needed).

Statistical methods:

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at a 5 % level of significance. The following assumptions on data are made, Assumptions: 1.Dependent variables should be normally distributed, 2. Samples drawn from the population should be random, Cases of the samples should be independent

The Chi-square/ Fisher Exact test has been used to find the significance of study parameters on a categorical scale between two or more groups.

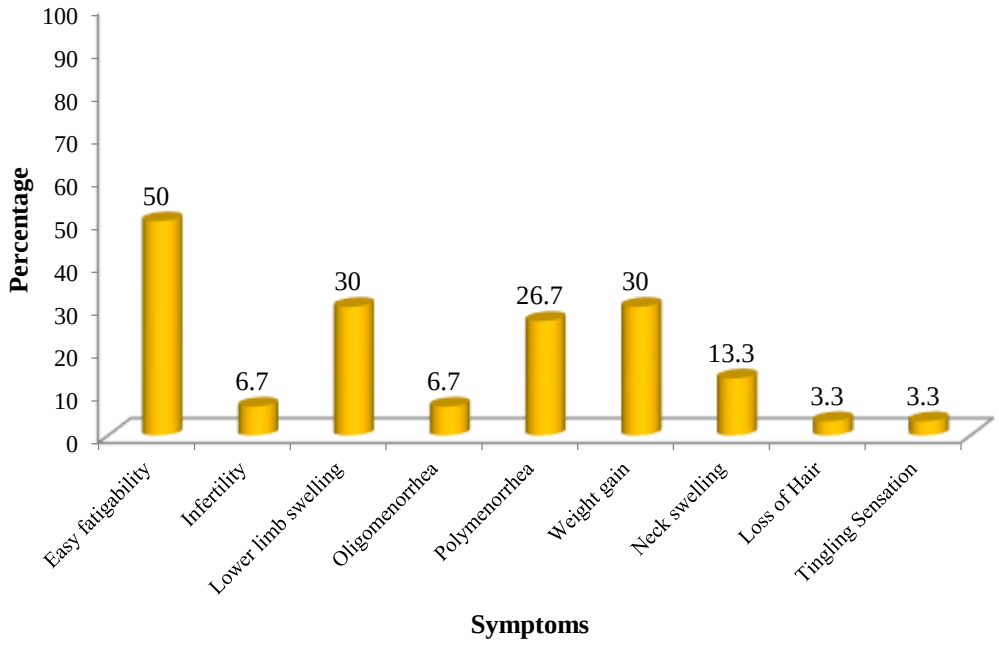
Statistical software:

The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, Medcalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc

RESULTS AND ANALYSIS

In this study of 30 subjects, the majority were females 26 (86.7%) and males were only 4(13.3%). Most of the subjects in our study were in the age group of 21-30 years with mean age being 36years.

Figure 1: Graph showing the distribution of symptoms of subjects studied.



In this study group, the common SYMPTOMS presented with was easy fatigability 15 (50%), followed by lower limb swelling 9 (30%), weight gain 9 (30%) and polymenorrhea 8

(26.7%)**(Figure 1)**. This study had 4 patients (13.3%) who did not have any symptoms and they were considered to have subclinical hypothyroid.

Table 1: Signs distribution of subjects studied.

Signs	No. of patients(n=30)	%
Normal	7	23.3
Pallor	14	46.7
Goiter	8	26.7
Loss of hair	5	16.7
Dry skin	5	16.7
Hoarseness of voice	5	16.7
Non pitting Edema	11	36.7
Delayed DTR relaxation	5	16.7

The common sign that patient had was pallor 14 (46%), next most common sign was bilateral non pitting oedema 11 (36.7%)**(Table 1)**.23.3% of the study subjects did not have any signs.
In our study majority 20 (66.7%) were obese i.e. BMI between 25-35 kg/m^2, whereas 9 (30%) were overweight i.e. BMI between 23-24.9 kg/m^2 and only 1(3.3%) subject had normal BMI i.e. between 18.5-22.9 kg/m^2. The mean BMI recorded was 27.18 kg/m^2.

Table 2: Table showing the distribution of Lipid profile of subjects studied.

Fasting Lipid	No. of patients	%
Normal	19	63.3
Dyslipidemia	11	36.7
Total	30	100.0

In this study, only 11(36.7%) subjects had dyslipidemia and majority of the subjects 19(63.3%) lipid profile was within normal limits**(Table 2)**.

Table 3: Hemogram distribution of subjects studied.

Hemogram	No. of patients(n=30)	%
Normal	15	50.0
Anemia	15	50.0
● Dimorphic Anemia	3	10.0
● Microcytic hypochromic anemia	3	10.0
● Macrocytic normochromic anemia	1	3.3
● Normocytic normochromic anemia	8	26.7

15(50%) subjects had normal haemogram whereas 15(50%) had Anaemia. Among the subjects who had anaemia major type of anaemia present was Normocytic normochromic anaemia i.e. 8(26.7%) subjects, followed by Microcytic hypochromic and dimorphic anaemia in 3(10%) subjects each. Only 1(3.3%) subject had Macrocytic normochromic anaemia**(Table 3)**.
In this study FNAC wad one on 8(26%) subjects, among the subjects whom FNAC was done majority 4 (13.3%) individuals had Lymphocytic infiltration of thyroid gland suggestive of

Hashimoto's thyroiditis, 3(10%) subjects had colloid goiter and 1subject(3.3%) had Colloid goiter with mild lymphocytic infiltration, suggestive of Hashimoto's thyroiditis**(Table 4)**.

Table 4: FNAC findings distribution of subjects studied.

FNAC	No. of patients(n=30)	%
Not done	22	73.3
Colloid goiter	3	10.0
Lymphocytic infiltration s/o Hashimoto's thyroiditis.	4	13.3
Colloid goiter with mild lymphocytic infiltration? Hashimoto's thyroiditis	1	3.3

On Antibody study, 9(30%) subjects had positive Anti TPO antibody suggestive of auto immune etiology whereas 21(70%) subjects Anti TPO antibody was negative. On Anti TG antibody analysis only 3(10%) subjects had positive anti TG antibody whereas 27(90%) subjects anti TG antibody was negative**(Table 5)**.

Table 5: Anti TPO and TG antibody distribution of subjects studied.

	Anti TPO (%)	Anti TG
Negative	21(70%)	27 (90%)
Positive	9 (30%)	3 (10%)
Total	30 (100%)	30 (100%)

In our study Anti TPO antibody positivity was more common in subjects who belong to the lower age group of 21-30 years, i.e. in 7(77.8%) subjects with the mean age of 28.22years. There was statistically significant association between lower age with Anti TPO antibody positivity with P value of 0.008 suggesting the younger age group is more prone to have autoimmune thyroiditis.Anti TG antibody was present most commonly in the age group of 21-30years i.e. in 2(66.7%) subjects. The mean age of anti TG antibody positivity was 29years.
There was no significant statistical association between particular age group with anti TG antibody positivity.

Table 6:Age distribution of subjects studied according to Anti TPO and TG antibody.

Age in years	Anti TPOPositive	Anti TGPositive
21-30	7(77.8%)	2(66.7%)
31-40	2(22.2%)	1(33.3%)
41-50	0(0%)	0(0%)
51-60	0(0%)	0(0%)
Total	9(100%)	3(100%)

Anti TPO positivity with P=0.008** Mean ± SD: 28.22±5.35 age group 21-30 years
Anti TG positivity with P=0.781 Mean ± SD: 29±6.68

All the subjects who had positive Anti TPO antibody were females i.e. 9(100%), whereas none of the male subjects had positive Anti TPO antibody suggesting autoimmune thyroid disease is more common in females. Anti TG antibody positive were females i.e. 3(100%) subjects.

Table 7: BMI (kg/m^2) distribution according to Anti TPO/TG antibody.

BMI (kg/m^2)	Anti-TPOPositive (N=9/30)	Anti-TG Positive (N=3/30)
18.5-22.9	1(11.1%)	0(0%)
23-24.9	5(55.6%)	1(33.3%)
25-35	3(33.3%)	2(66.7%)
Total	9(100%)	3(100%)

Anti TPO positivity with P=0.027* Lower BMI
Anti TG positivity P=1.000, Not significant, Fisher Exact

Lower BMI is significantly associated with Anti TPO positivity with P=0.027*. In the present study, among the subjects with positive Anti TPO antibody most subjects 5(55.6%) belong to overweight category i.e. BMI of 23-24.9 Kg/m^2 suggesting auto immune thyroid disease is more common in subjects with low BMI(P value 0.0027) rather than in Obese individuals. Anti TG antibody positivity was seen more commonly in the 25-35 Kg/m^2 BMI group in 2(66.7%) subjects. There was no statistically significant association between BMI and anti TG antibodies**(Table 7).**

Table 8: Association of Lipid profile with Anti TPO/TG antibody

Lipid profile	Anti TPO antibody Positive	Anti TG antibody Positive
Normal	8(88.9%)	3(100.0%)
Dyslipidemia	1(11.1%)	0
Total	9(100%)	3(100%)

P=0.057+, not Significant, Chi-Square test and P=0.279, Not Significant, Fisher Exacttest

In our study, among 9 subjects with positive Anti TPO antibody only 1(11.1%) had dyslipidemia whereas 8(88.9%) subjects had normal lipid profile and there was no statistically significant association between dyslipidemia and anti TPO antibody positivity. 3(100%) who were anti TG antibody positive had normal lipid profile, whereas none of the subjects with positive anti TG antibody had dyslipidemia**(Table 8)**.

Among 9 subjects with positive anti TPO antibody the most common FNAC finding was Lymphocytic infiltration of the gland suggestive of Hashimoto's thyroiditisin 4(44.4%) subjects, followed by Colloid goiter with mild lymphocytic infiltration? Hashimoto's thyroiditis in 1(11.1%) subject. There was statistically significant association between positive anti TPO antibody and Lymphocytic infiltration of gland with P value of 0.005 which is positively suggestive of role of Anti TPO antibody in autoimmune etiology of hypothyroidism (Hashimoto's thyroiditis)**(Table 9).**

In our study, among 3 anti TG antibody positive subjects, FNAC was done for 2 subjects. The most common FNAC finding present was Lymphocytic infiltration of the gland suggestive of Hashimoto's thyroiditis in 2(66.7%) subjects. There was significant statistical association (P value 0.039) between anti TG antibody positivity with Lymphocytic infiltration of the thyroid gland, proving the anti TG antibody role in autoimmune hypothyroidism**(Table 10).**

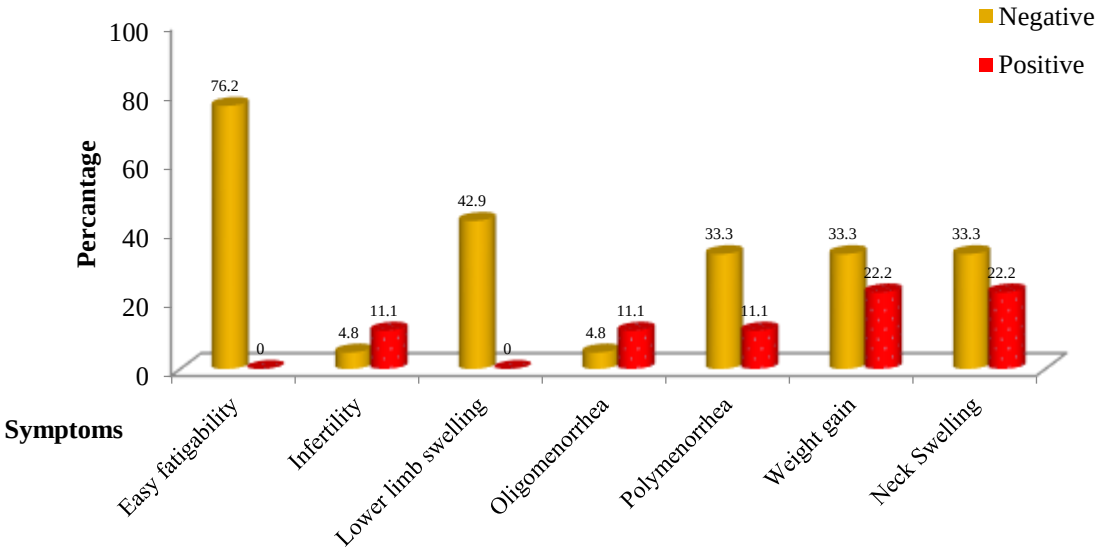
Table 9: Association of FNAC findings with Anti TPO Antibody.

FNAC	Anti TPO		Total(n=30)	P value
	Negative (n=21)	Positive (n=9)		
Colloid goiter	3(14.3%)	0	3(10.0%)	0.534
Lymphocytic infiltration s/o Hashimoto's thyroiditis	0	4(44.4%)	4(13.3%)	0.005**
Colloid goiter with mild lymphocytic infiltration? Hashimoto's thyroiditis	0	1(11.1%)	1(3.3%)	0.300

Table 10: Association of FNAC findings with Anti TG antibody.

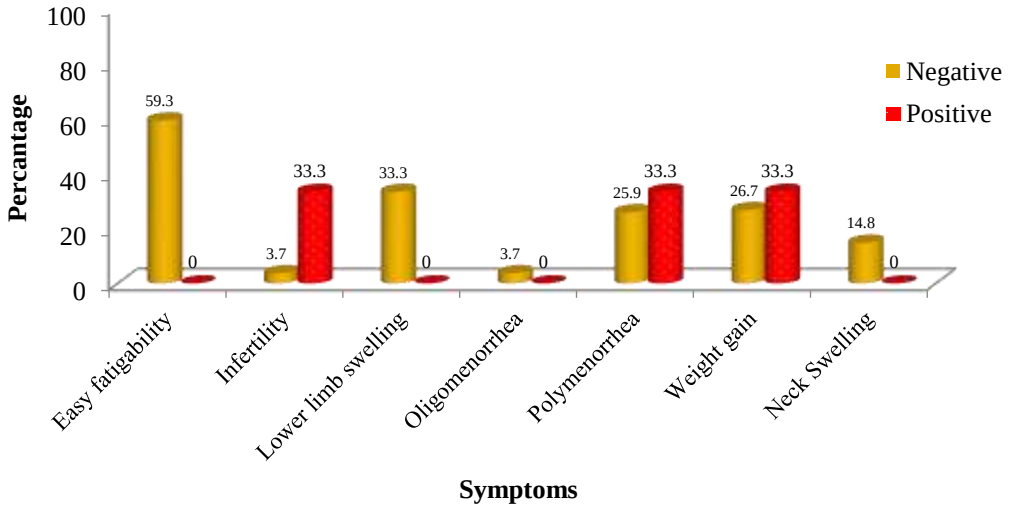
FNAC	Anti TG		Total(n=30)	P value
	Negative (n=27)	Positive (n=3)		
Colloid goiter	3(11.1%)	0(0%)	3(10%)	1.000
Lymphocytic infiltration s/o Hashimoto's thyroiditis	2(7.4%)	2(66.7%)	4(13.3%)	0.039*
Colloid goiter with mild lymphocytic infiltration? Hashimoto's thyroiditis	1(3.7%)	0(0%)	1(3.3%)	1.000

Figure 2: Graph showing the distribution of various symptoms according to Anti TPO Antibody



In our study among 9 subjects who had positive Anti TPO antibodies, 4 (44.4%) subjects were asymptomatic at presentation i.e. subclinical hypothyroid. Whereas 5(55.5%) subjects had symptoms at the time of presentation, most common symptoms were weight gain and neck swelling in 2(22.2%) subjects each**(Figure 2)**.Also, in our study the presence of symptoms was negatively associated with anti TPO with P value 0.005, in other words anti TPO antibody positivity was present more commonly in subjects with Subclinical hypothyroidism.

Figure3: Graph showing the distribution of various Symptoms according to Anti TG Antibody.



Among 3 anti TG antibody positive subjects, 1(33.3%) subject was asymptomatic i.e. subclinical hypothyroid. whereas 2(66.7%) subjects had symptoms, the presenting symptoms were infertility, polymenorrhea and weight gain in each, i.e. 1 (33.3%)**(Figure 3)**.There was no statistically significant association between presence or absence of symptoms with anti TG antibody positivity.

DISCUSSION

The present study showed that highest incidence of subjects suffering from hypothyroidism was in the age group of 21 – 30 years i.e. 11(36.7%) with a mean age of 36.3 years. Rubina Mansoor[5] et.al. in their study on 139 subjects with hypothyroidism noted that the maximum number of subjects were in the age group of 16-40 years.

The incidence of hypothyroidism was higher among females than in males, females being 86.7% of total subjects. The Female to male ratio in our study was 6.5:1. Amit Saxena[6] et.al. found female to male hypothyroidism ratio similar to our study.

In our study among the total 30 subjects, 26(87%) subjects had symptoms at presentation whereas 4(13%) subjects did not have any symptoms at the time of presentation i.e. 13% were Subclinical hypothyroid. Study by Abhyudhay Verma[7] et.al. on 625 hypothyroid subjects concluded that subclinical hypothyroidism was present in 12% of the subjects which is comparable to our study.Kawther T, El-Shafie[8] et.al. in their study noted easy fatigability as the most common symptom in 25% of subjects.

In our study,23.3% of the subjects did not have any of the signs of hypothyroidism whereas 77.7% of the subjects had signs of hypothyroidism. Ali Jabbari[9] et.al. in their descriptive cross-sectional study in Iran had pallor in 60% of the subjects and lower limb oedema in 80% of the subjects. B. Zoofishan, A. Kabir[10] et.al. in their case control study on 400 subjects from Pakistan found 24%had neck swelling,14% had hoarseness of voice which was comparable to our study.

The lowest BMI recorded was 22.8 kg/m^2 and the highest being 32.74 kg/m^2. The mean BMI was 27.18 kg/m^2.Majority of the subjects, i.e. 66.7% in the present study were obese with BMI in the range of 25-35 kg/m^2. Study by Abhyudhay Verma[7] et.al. in their retrospective study on 625 subjects concluded that Obesity was present in 46% 0f subjects, in most of the other study by Irfan M. Khurram[11] et al obesity was present in 40-60% of the subjects. Our study had a higher incidence of obesity contrary to other studies.Studies also found that BMI is directly proportional to TSH i.e. higher the BMI more the TSH value. The association between TSH and BMI could be due to TSH directly stimulating preadipocyte differentiation and resulting in adipogenesis.

In the present study dyslipidemia was present in 11(36.7%), whereas the majority i.e. 19(63.3%) had normal lipid profile. Amit Saxena[14] et al. in their prospective study on 180 hypothyroid subjects found dyslipidemia was found in 83 (46.11%) cases which is very high compared to our study.

Most common lipid profile abnormality present in our study was elevated total cholesterol, triglycerides and LDL cholesterol, low HDL cholesterol and normal VLDL which is similar to almost all the study. Which is an independent risk factor for cardiovascular mortality.

In the present study 50% of the subjects had hematological abnormalities in the form of Anemia.In study by Antonijevic N[12] et.al. anemia was prevalent in 60% of the subjects which is comparable to our study.

Study by Chanchal Das [13] et al in their study on sixty adult nonpregnant untreated primary hypothyroid patients with anemia concluded that Normocytic normochromic anemia was present in 31 patients (51.6%) followed by microcytic anemia in 26 patients (43.3%). Six patients (10%) had megaloblastic anemia with vitamin B12 deficiency which is similar to the findings in our study.

Direct or indirect stimulation of erythroid colony by thyroid hormones, inhibition of the same in its absence, reduction in oxygen distribution to tissues, and diminution in erythropoietin level in the absence of thyroid hormone causes normocytic normochromic anemia.

In our study among the total of 30 subjects, 9(30%) had positive anti TPO antibodies suggesting a probability of autoimmune etiology for hypothyroidism in them.Dr. AG Unnikrishnan[15]et al.concluded in their study in 2013 that approximately one-fourth (25%) of the study population had anti-thyroid peroxidase antibodies [TPO] positivity which is comparable to our study.Araujo J[16] et.al. in their study on 214 subjects concluded that anti- TPO was positive in 54 subjects with a prevalence of 25.2% which is comparable to our study.30 hypothyroid subjects prevalence of Anti

TG antibody was found in only 3(10%) of the subjects. Leqakis I[24] et.al. in their study on 909 subjects found that anti TG antibody was prevalent in 15.4% of the subjects which is comparable to our study

Anti TPO antibody positivity was found more commonly in subjects who belong to lower age groups i.e. in 21-30 years i.e. 7(77.8%) subjects with a mean age of 28.22 years. Also there was statistically significant association between lower age with Anti TPO antibody positivity with a P value of 0.008. Positive anti TG antibody was present most commonly in the age group of 21-30years i.e. in 2(66.7%) subjects with mean age of 29years, there was no significant statistical association between the particular age group with anti TG antibody positivity. Sarwat Fatima[17] et.al. in their prospective study on 44 subjects concluded that most of the cases who presented with autoimmune thyroiditis were young and belonged to the age group of 21-30 years and were predominantly females and very few cases were seen in >50years of age, which is similar to our study.

In the present study all the subjects who had positive Anti TPO and TG antibody were females i.e. 9(100%) and 3(100%) of the subjects, whereas none of the male subjects had thyroid antibody positive, suggesting autoimmune thyroid disease is more common in female gender than in males.

Neelam sood[18] et.al. in their study on 175 subjects concluded that the commonest age group of autoimmune thyroid disease was 21–30 years with male: female ratio being 1:10. Anti-TPO and TSH were elevated in 96.16%.

In the present study among 9 subjects who had positive Anti TPO antibodies, 4 (44.4%) individuals were asymptomatic at presentation i.e., subclinical hypothyroid. Whereas 5(55.5%) subjects had symptoms at the time of presentation, most common symptoms was weight gain in 2(22.2%), goiter was seen in only 2(22.2%) and among 3 anti TG antibody positive subjects 1(33.3%) was asymptomatic i.e. subclinical hypothyroid. whereas 2(66.7%) subjects had symptoms.

Also, in the present study presence of symptoms was negatively associated with anti TPO with P value 0.005, in other words anti TPO was positive more commonly in subjects with Subclinical hypothyroidism and there was no significant statistical association between presence or absence of symptoms with anti TG antibody positivity.

Study by Ambika Gopalakrishnan[19] et.al. found that about 53% of subjects with subclinical hypothyroidism were positive for anti-TPO antibodies and most of them presented with diffuse goiter, which is similar to the present study.

In the present study, among the subjects with positive Anti TPO antibody most subjects i.e. 66.7% belong to BMI of < 24.9 kg/m^2 suggesting auto immune thyroid disease is more common in subjects with lower BMI rather than in Obese individuals and lower BMI was significantly associated with anti TPO antibody with P value 0.027. Also, anti TG antibody positivity was seen more commonly in 25-35 kg/m^2 BMI group i.e. in 66.7%, there was no significant statistical association between BMI with anti TG antibody.

Mario Rotondi[20] et.al. in their comparative study on healthy normo-weight subjects, normo-weight patients with Subclinical hypothyroidism and with the obese patients with Subclinical hypothyroid patients showed following results. The rate of positivity for circulating thyroid antibody in the 56 hypothyroid normal-weight patient was 66.1%, when compared with the significantly lower figure(32.1%) found in the 28 hypothyroid obese patients(hypothyroid patients with morbid obesity showed an unexpectedly low rate of positive tests for thyroid antibody),which is similar to the findings of present study.

Study by Manorama Swain[21] et.al. Concluded that Anti-TPO autoantibodies are found in over 90% of patients with autoimmune hypothyroidism and Thyroglobulin autoantibodies are found in less than 60% of patients with lymphocytic thyroiditis.
Mandakini M Patel[22] et.al. in their study on 194 goiter subjects concluded that 28.57% were having thyroiditis in FNAC which is of much lesser proportion compared to our study, whereas 24.4% had colloid goiter which is comparable to our study.

Study by Manorama Swain[23] et.al. Concluded that Anti-TPO autoantibodies are found in over 90% of patients with autoimmune hypothyroidism and Thyroglobulin autoantibodies are found in less than 60% of patients with lymphocytic thyroiditis.

In the present study, among 9 subjects with positive anti TPO antibody, FNAC was done for 5 subjects, all of them i.e. 5(100%) subjects had lymphocytic infiltration of the thyroid gland on FNAC suggesting Hashimoto's thyroiditis. And among 5 subjects in whom FNAC was showing lymphocytic infiltration only 2(40%) subjects had positive anti TG antibody. Suggesting Anti TPO antibody is more sensitive test in detecting autoimmune thyroiditis when compared to anti TG antibody.Also there was statistically significant association between positive anti TPO antibody and Lymphocytic infiltration of gland with P value of 0.005. Whereas anti TG antibody was not significantly associated with lymphocytic infiltration

CONCLUSION

Overall association between thyroid antibody and hypothyroidism was assessed. Anti TPO antibodieshas a strong association with autoimmune hypothyroidism when compared to anti TG antibodies.Anti TPO antibodies are more specific and sensitive in assessing autoimmune hypothyroidism.Hypothyroid subjects, especially subclinical hypothyroid subjects should undergo routine antibody assay. Subclinical hypothyroid subjects who are positive antibody, thyroid profile should be monitored regularly because they are more prone to develop overt hypothyroidism.A larger study is required for further correlation.

Competing interest: The authors declare that they have no competing interests.

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