

Association between Thyroid Autoantibodies and Abnormal Thyroid Function and Structure of Thyroid Gland

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Abstract

Original Research Article

Introduction: Antithyroperoxidase antibody (TPOAb), antithyroid receptor antibody (TRAb) and antithyroglobulin antibody (TgAb) are common thyroid autoantibodies in patients with autoimmune thyroid disease. Studies have demonstrated that the serum presence of thyroid autoantibodies is correlated with the presence of lymphocytic infiltration and the severity of histological thyroiditis. However, one or more of these antibodies are frequently detected in the general population. Abnormalities in thyroid function and structure are common in the population. **Aim of the study:** The aim of this study was to evaluate the association between thyroid autoantibodies and abnormalities in thyroid function and structure. **Methods:** This was a multi-center, cross-section, observational study and was conducted in the Department of Endocrinology of Ibn Sina Medical College Hospital, Dhaka, Bangladesh and Enam Medical College, Savar, Dhaka, Bangladesh during the period from September, 2022 to September, 2023. In our study we included 324 patients with thyroid dysfunction. The patients were selected consecutively attending tertiary care hospitals. The study participants provided demographic and clinical data. Thyroid function, thyroid ultrasonogram and serum concentration of TPOAb, TRAb, and TgAb were measured. **Result:** A total 324 patients were included in this study. Most of the study population were female (79%) and mean age were 37.0±12.4 years. 58.6% belonged to the 21-40 age group. The mean BMI was found 22.0±4.5 kg/m² in positive TRAb and 26.5±5.0 kg/m² in negative TRAb. 229 (70.7%) were hypothyroid and 95 (29.3%) were hyperthyroid patients. Among the study population 211 (65.1%) patients were TPOAb, 112 (34.6%) were TgAb and 80 (24.7%) were TRAb positive. Among the TPOAb positive patients, 78.7% were hypothyroid and 21.3% were hyperthyroid. On the contrary, among the TRAb positive patients, 97.5% were hyperthyroid. Most (158) of the patients have normal ultrasonogram of thyroid. Among them 60.1% were TPOAb positive and only 9.5% were positive for TRAb. 57 patients were shows thyromegaly with homogenous parenchyma, in which 59.6% were positive for TRAb. **Conclusion:** In our study, we found female sex, BMI, thyroid volume, thyroid hypoechogenicity and heteroechogenicity were risk factors for the presence of thyroid autoantibodies. Thyroid autoantibodies were detected in subjects with thyroid dysfunction and in those who were euthyroid. An increased prevalence of thyromegaly with homogenous parenchyma correlated with elevated levels of TRAb. Women with thyroid enlargement, abnormal BMI, thyroid hypoechogenicity and heteroechogenicity would benefit from routine evaluation of thyroid autoantibody status and thyroid function.

Keywords: Thyroid Autoantibodies, TPOAb, TRAb, TgAb, Thyroid gland.

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INTRODUCTION

Antithyroperoxidase antibody (TPOAb) and antithyroglobulin antibody (TgAb) are common thyroid autoantibodies in patients with autoimmune thyroid disease [1]. Studies have demonstrated that the serum presence of thyroid autoantibodies is correlated with the presence of lymphocytic infiltration and the severity of histological thyroiditis [2, 3]. However, one or both of

these two antibodies are frequently detected in the general population [4]. Abnormalities in thyroid function and structure are common in the population [5]. The DanThyr (Danish Investigation of Iodine intake and Thyroid Diseases) cohort, evaluated as part of the Danish iodine supplementation program, consisted of 4649 people from the population. In this cohort abnormal serum TSH was found in 9.2%, goitre in 12.1%, one or more thyroid nodules above 10 mm in diameter by

ultrasonography in 29.7% and autoantibodies against thyroid peroxidase (TPO) or thyroglobulin (Tg) in 18.8% of the participants [6-8]. These results correspond more or less to results derived from other epidemiological studies performed in different areas of the world [5].

Abnormalities of the thyroid function and its structure are commonly seen and many factors like environmental factors such as iodine nutrition, age, sex and smoking habits might influence thyroid function, thyroid autoantibodies and thyroid structure [9-12]. Age and gender composition of the population is also important as the prevalence of thyroid dysfunction, thyroid autoantibodies and goitre increases with age and is more common in females than in males. [13-17] Chronic autoimmune hypothyroidism occurs with or without goitre. In the goitrous form, which is the variant described by Hashimoto, the histology of the thyroid is characterized by massive lymphocytic infiltration with formation of germinal centres [18]. However, the concordance rate in monozygotic twins is below one, suggesting that environmental factors are important. At the time of diagnosis only a minority of patients with autoimmune overt hypothyroidism have goitre, and it has been suggested that chronic atrophic thyroiditis may be a late stage of previous goitrous Hashimoto's disease [19-21]. A cross-sectional survey conducted in populations with no current or prior thyroid disease, showed that the prevalence of serum positivity for TPOAb and TgAb were 13.1% and 13.0%, respectively [4]. The National Health and Nutrition Examination Survey III (NHANES III) study reported that TPOAb and TgAb were present in 11.3% and 10.4%, respectively, of a disease-free population [22]. The prevalence of thyroid autoantibodies varies between populations and is influenced by many factors including as heredity and the environment [5, 23]. Although several cross-sectional surveys have reported the prevalence of thyroid autoantibodies, studies in the south-western region, have rarely explored the prevalence of these thyroid autoantibodies since universal salt iodization began in 1996 [22, 23].

Autoimmune thyroid disorders (AITDs) are a diverse group of organ-specific autoimmune diseases, the most common of which include Hashimoto's thyroiditis and Graves' disease [24]. Several predisposing genetic loci including CTLA4, HLA, and IL2RA have been identified and certain environmental factors like radioiodine treatment, iodine deficiency, and cigarette smoking have been implicated in pathogenesis of AITDs [25, 26]. Although AITDs occur in only 1% of population, subclinical and focal thyroiditis and circulating antithyroid antibodies may be found in 15% of euthyroid subjects [27]. Anti-thyroid peroxidase (TPO) antibodies arise against a transmembrane protein of thyrocytes involved in thyroid hormone synthesis. Anti-thyroglobulin (TG) antibodies are against thyroglobulin, a thyroid hormone precursor AntiTPO

antibodies (formerly known as anti-thyroid microsomal antibodies) and anti-TG antibodies are considered diagnostic of AITDs because these are present in over 90% cases of Hashimoto's thyroiditis and over 80% cases of Graves' disease [24]. Anti-TPO and anti-TG antibodies are related to levels of thyroid stimulating hormone (TSH) and both alone or in combination have been used to predict development of hypo-/hyperthyroidism. It has been determined in different studies that altered levels of anti-thyroid antibodies and TSH in euthyroid subjects have been associated with development of hypothyroidism in future [28, 29]. Since anti-thyroid antibodies have been detected in healthy individuals especially females [30], follow-up thyroid profile testing in anti-thyroid antibody positive individuals is very important for making timely diagnosis. The use of biomarkers to predict susceptibility and outcome in thyroid autoimmunity has steadily increased over time. Thyroid genetic susceptibility testing along with thyroid autoantibodies is highly predictive of later thyroid autoimmunity and thyroid dysfunction [31]. However, prevalence of anti-thyroid antibodies among general population is unknown. And so is its relation with thyroid profile (TSH, T4, and T3). Determining association of anti-thyroid antibodies with thyroid profile testing could identify such group of patients who have deranged thyroid profile and subsequently also need screening for thyroid autoantibodies to rule out underlying autoimmune process. Therefore, this cross-sectional survey investigated the prevalence of serum thyroid autoantibodies and evaluated the association between their presence and abnormalities in thyroid function and structure in Bangladeshi population.

Objective of the study

The main objective of the study was to evaluate the association between thyroid autoantibodies and abnormalities in thyroid function and structure.

METHODOLOGY & MATERIALS

This was a multi-center, cross-section, observational study and was conducted in the Department of Endocrinology of Ibn Sina Medical College Hospital, Dhaka, Bangladesh and Enam Medical College, Dhaka, Bangladesh during the period from September, 2022 to September, 2023. In our study we included 324 patients with thyroid dysfunction. The patients were selected consecutively attending tertiary care hospitals. The study participants provided demographic and clinical data. Thyroid function, thyroid ultrasonogram and serum concentration of TPOAb, TRAb, and TgAb were measured.

These are the following criteria to be eligible for the enrollment as our study participants: a) Patients aged 18 to 60 years; b) Patients diagnosed with thyroid dysfunction; c) who were willing to participate were included in the study And a) Patients with uncontrolled

DM, b) Patients with pregnancy & postpartum within 1 year; c) Patients taking any drugs for the condition; d) Patients taking antiepileptic drugs (e.g. phenytoin, carbamazepine); e) Patients with any history acute illness (e.g., renal or pancreatic diseases, ischemic heart disease etc.) were excluded from our study.

The patients were divided into three groups, based on thyroid function: euthyroid (both FT4 and TSH levels were within normal limits and without antithyroid or thyroxine treatment for more than 12 months), hypothyroid (low FT4 with elevated TSH with or without thyroxine replacement therapy), subclinical hypothyroid (normal FT4 with elevated TSH) enrolled into the hypothyroid group, hyperthyroid (elevated thyroid hormone levels in the face of suppressed TSH or euthyroid under antithyroid treatment), and subclinical hyperthyroid (normal FT4 with low TSH level) enrolled into the hyperthyroid group. The same classification was used to define thyroid functional status up to the end of the study (at reevaluation). We maintained medication for hypothyroid patients and discontinued antithyroid drugs for hyperthyroid patients when they achieved a euthyroid status in the follow-up period [32].

Laboratory Measurements

Thyroid function and thyroid autoantibodies were measured using Roche chemiluminescence immunoassay kits (thyroid-stimulating hormone [TSH]: kit no. 11731459122; free triiodothyronine [FT3]: kit no. 03051986190; free thyroxine [FT4]: kit no. 11731297122; TgAb: kit no. 04738578190; TPOAb: kit no. 11820818122) and a Roche cobas 6000 (e601 module) analyser (Roche, Mannheim, Germany). The intra- and interassay coefficients of variation were all 6.25 mIU/l, then only the FT4 level was measured. The normal reference ranges of FT3, FT4 and TSH were 3.1–6.8 pmol/l, 12.0–22.0 pmol/l and 0.71–6.25 mIU/l, respectively. The normal negative references for TPOAb and TgAb were 34 IU/ml and 115 IU/ml, respectively. The minimum detectable concentrations were 0.005 mIU/l for TSH, 0.400 pmol/l for FT3, 0.300 pmol/l for FT4, 5 IU/ml for TPOAb and 10 IU/ml for TgAb. The reference range of TSH was based on a thyroid epidemiological survey of 10 cities in China and has been demonstrated to be suitable for Chinese populations [33].

Diagnostic criteria for thyroid disease Clinical hypothyroidism was diagnosed when the serum TSH concentration was >6.25 mIU/l and the serum FT4 was 6.25 mIU/l and the serum FT4 was within the normal range. Clinical hyperthyroidism was diagnosed when the serum TSH concentration was 22.0 pmol/l and/or the FT3 concentration was >6.8 pmol/l. Subclinical hyperthyroidism was diagnosed when the serum TSH concentration was Thyroid autoantibodies were regarded as positive when the TPOAb level was >34 IU/ml and/or

the TgAb level was >115 IU/ml. Goitre was defined as a thyroid volume >14.4 ml for women and >18.8 ml for men. This definition was derived from the mean (\pm 2 SD) thyroid volume in 250 subjects with no personal or family history of thyroid disease, with no thyroid autoantibodies, and with an undetected goitre or nodules using B-mode ultrasonography [34].

Statistical Analysis

All data were recorded systematically in preformed data collection form and quantitative data was expressed as mean and standard deviation and qualitative data was expressed as frequency distribution and percentage. Statistical analysis was performed using SPSS 21 (Statistical Package for Social Sciences) for windows 10. Probability value <0.05 was considered as level of significance. The study was approved by Ethical Review Committee of Ibn Sina Medical College Hospital, Dhaka, Bangladesh.

RESULT

A total 324 patients aged >18 years who fulfilled the inclusion criteria were included in this study. Among the study population 79% (total 256) were female and rest (21%; 68 in number) were male. The mean age of our study population were 37.0 \pm 12.4 years, in which 190 (58.6%) patients belonged to the age 21-40 years. The mean BMI was 25.4 \pm 5.3 kg/m². The demographic characteristics of the study participants are presented in Table -1.

Table 1: Demographic characteristics of the study populations (n=324)

| Demographic characteristics | Frequency | Percentage |
|-----------------------------|-----------|------------|
| Age (years) | | |
| ≤20 | 20 | 6.2 |
| 21-40 | 190 | 58.6 |
| 41-60 | 101 | 31.2 |
| >60 | 13 | 4.0 |
| Mean \pm SD | 37.0 | \pm 12.4 |
| Sex | | |
| Male | 68 | 21.0 |
| Female | 256 | 79.0 |
| BMI (kg/m ²) | | |
| <18.5 | 26 | 8.0 |
| 18.5-24.9 | 133 | 41.0 |
| 25.0-29.9 | 101 | 31.2 |
| ≥30.0 | 64 | 19.8 |
| Mean \pm SD | 25.4 | \pm 5.3 |

Table 1 shows that 190(58.6%) patients belonged to age 21-40 years with mean age was 37.0 \pm 12.4 years, 256(79.0%) were female and mean BMI was 25.4 \pm 5.3 kg/m².

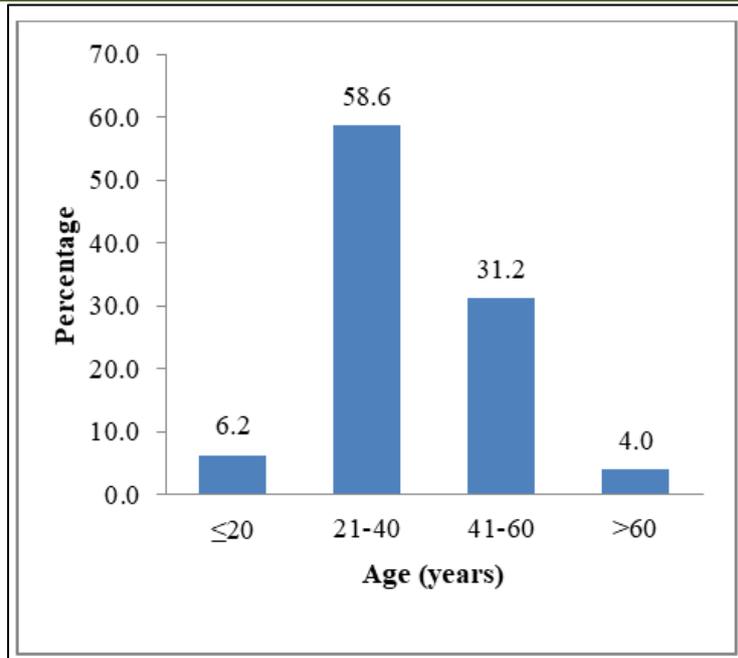


Figure 1: Bar diagram showing age distribution of the study populations (n=324)

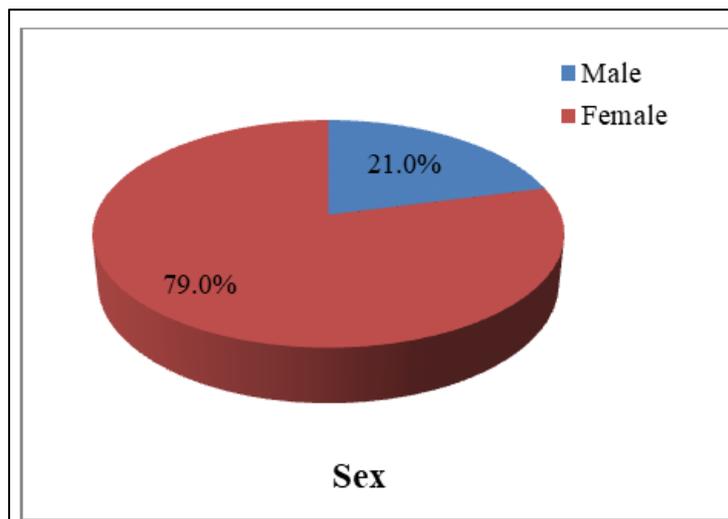


Figure 2: Pie chart showing sex distribution of the study populations (n=324)

Among the study population (n- 324) 229 (70.7%) were found hypothyroid and 95 (29.3%) were found hyperthyroid (Table-2).

Table 2: Thyroid function of the study populations (n=324)

| Thyroid function | Frequency | Percentage |
|------------------|-----------|------------|
| Hypothyroidism | 229 | 70.7 |
| Hyperthyroidism | 95 | 29.3 |

Table 2 shows that 229(70.7%) patients were found in hypothyroidism and 95(29.3%) in hyperthyroidism.

112 (34.6%) patients were positive for TgAb, 211 (65.1%) patients positive for TPOAb and 80 (24.7%) was positive for TRAb. Female subjects were

significantly more likely to be positive for all the thyroid auto antibodies than male subjects (Table-6). The mean BMI was found 22.0 ± 4.5 kg/m² in positive TRAb patients and 26.5 ± 5.0 kg/m² in negative TRAb patients, which were statistically significant ($P = < 0.05$) but other variables like age did not show any statistically significant relationship ($P = > 0.05$).

Table 3: Thyroid autoantibody of the study populations (n=324)

| Thyroid autoantibody | Frequency | Percentage |
|----------------------|-----------|------------|
| TgAb | | |
| Positive | 112 | 34.6 |
| Negative | 212 | 65.4 |
| TPOAb | | |
| Positive | 211 | 65.1 |
| Negative | 113 | 34.9 |
| TRAb | | |
| Positive | 80 | 24.7 |
| Negative | 244 | 75.3 |

Table 3 shows that 112(34.6%) patients had positive TgAb, 211(65.1%) had positive TPOAb and 80(24.7%) had positive TRAb.

211 patients were positive for TPOAb, among them 166 (78.7%) in hypothyroid group and 45 (21.3%) were in the hyperthyroid group which were statistically

significant ($P=0.001$). It was also evident that 80 patients were positive for TRAb, in which 2 (2.5%) were hypothyroid and 78 (97.5%) were hyperthyroid which was also statistically significant ($P=0.001$). But TgAb did not show any significant association with hypothyroid or hyperthyroidism patients ($P=0.325$).

Table 4: Association between thyroid function with thyroid autoantibody (n=324)

| Thyroid autoantibody | Hypothyroidism | | Hyperthyroidism | p value |
|----------------------|----------------|------------|-----------------|---------|
| | n | n (%) | n (%) | |
| TgAb | | | | |
| Positive | 112 | 83 (74.1) | 29 (25.9) | 0.325 |
| Negative | 212 | 146 (68.9) | 66 (31.1) | |
| TPOAb | | | | |
| Positive | 211 | 166 (78.7) | 45 (21.3) | 0.001 |
| Negative | 113 | 63 (55.8) | 50 (44.2) | |
| TRAb | | | | |
| Positive | 80 | 2 (2.5) | 78 (97.5) | 0.001 |
| Negative | 244 | 227 (93.0) | 17 (7.0) | |

P value reached from chi square test

Table 4 shows that 211 patients had positive TPOAb among them 166(78.7%) in hypothyroidism and 45(21.3%) in hyperthyroidism group. Eighty patients had positive TRAb among them 2(2.5%) in hypothyroidism and 78(97.5%) in hyperthyroidism group.

The number of subjects having normal ultrasonogram (USG) of thyroid, thyromegaly with homogenous parenchyma, thyromegaly with heterogeneous parenchyma, nodular goitre and multinodular goitre were 158, 57, 43, 41 and 25 respectively.

158 patients were found normal USG, among them 44(27.8%) were positive for TgAb. 95 (60.1%) was positive for TPOAb and 15 (9.5%) was positive for TRAb which indicate that there is a significant negative association between TRAb and normal thyroid structure (P value 0.001). Total 57 patients were shown thyromegaly with homogenous parenchyma, among them 21 (36.8%), 33 (57.9%) and 34 (59.6%) were positive for TgAb, TPOAb and TRAb respectively, in

which TRAb shows a positive association with thyromegaly with homogenous parenchyma which is statistically significant (P value 0.001). Other structural abnormality like multinodular goitre, thyromegaly with heterogeneous parenchyma did not show any significant association with thyroid autoantibodies (Table 5).

Table 5 shows that 158 patients were found normal USG among them 44(27.8%) in positive TgAb and 114(72.2%) in negative TgAb group. Forty-three patients were found thyromegaly with heterogeneous parenchyma among them 36(83.7%) in positive TPOAb and 7(16.3%) in negative TPOAb group. Forty-one patients were found nodular goiter among them 16(39.0%) in positive TRAb and 25(61.0%) in negative TRAb group. Fifty-seven patients were found thyromegaly with homogeneous parenchyma among them 34(59.6%) in positive TRAb and 23(40.4%) in negative TRAb group. One hundred fifty-eight patients were found normal USG among them 15(9.5%) in positive TRAb and 143(90.5%) in negative TRAb group.

Table 5: Association between USG structure with thyroid autoantibody (n=324)

| Thyroid autoantibody | USG | | | | |
|----------------------|----------------------------|-----------------------|---|---|--------------|
| | Multinodular goiter (n=25) | Nodular goiter (n=41) | Thyromegaly with in heterogeneous parenchyma (n=43) | Thyromegaly with in homogeneous parenchyma (n=57) | Normal (158) |
| | n (%) | n (%) | n (%) | n (%) | n (%) |
| TgAb | | | | | |
| Positive | 12 (48.0) | 15 (36.6) | 20 (46.5) | 21 (36.8) | 44 (27.8) |
| Negative | 13 (52.0) | 26 (63.4) | 23 (53.5) | 36 (63.2) | 114 (72.2) |
| p value | 0.142 | 0.771 | 0.077 | 0.691 | 0.013 |
| TPOAb | | | | | |
| Positive | 15 (60.0) | 32 (78.0) | 36 (83.7) | 33 (57.9) | 95 (60.1) |
| Negative | 10 (40.0) | 9 (22.0) | 7 (16.3) | 24 (42.1) | 63 (39.9) |
| p value | 0.576 | 0.063 | 0.006 | 0.207 | 0.066 |
| TRAb | | | | | |
| Positive | 8 (32.0) | 16 (39.0) | 7 (16.3) | 34 (59.6) | 15 (9.5) |
| Negative | 17 (68.0) | 25 (61.0) | 36 (83.7) | 23 (40.4) | 143 (90.5) |
| p value | 0.378 | 0.023 | 0.170 | 0.001 | 0.001 |

P value reached from chi square test

Table 6: Association between demographic characteristics with thyroid autoantibody (n=324)

| Thyroid autoantibody | n | Age (years) Mean±SD | p value | Sex | | p value | BMI (kg/m ²) Mean±SD | p value |
|----------------------|-----|------------------------|--------------------|---------------|-----------------|--------------------|-------------------------------------|--------------------|
| | | | | Male n (%) | Female n (%) | | | |
| TgAb | | | | | | | | |
| Positive | 112 | 36.5±11.1 | ^a 0.612 | 22 (19.6) | 90 (80.4) | ^b 0.666 | 26.6±5.6 | ^a 0.003 |
| Negative | 212 | 37.2±13.0 | | 46 (21.7) | 166 (78.3) | | 24.8±5.0 | |
| TPOAb | | | | | | | | |
| Positive | 211 | 36.3±11.8 | ^a 0.171 | 38 (18.0) | 173 (82.0) | ^b 0.072 | 25.7±5.4 | ^a 0.204 |
| Negative | 113 | 38.2±13.3 | | 30 (26.5) | 83 (73.5) | | 24.9±5.0 | |
| TRAb | | | | | | | | |
| Positive | 80 | 36.9±12.6 | ^a 0.989 | 22 (27.5) | 58 (72.5) | ^b 0.099 | 22.0±4.5 | ^a 0.001 |
| Negative | 244 | 37.0±12.3 | | 46 (18.9) | 198 (81.1) | | 26.5±5.0 | |

^aP value reached from unpaired t-test^bP value reached from chi square test

Table 6 shows that mean BMI was found 26.6±5.6 kg/m² in positive TgAb and 24.8±5.0 kg/m² in negative TgAb. The mean BMI was found 22.0±4.5

kg/m² in positive TRAb and 26.5±5.0 kg/m² in negative TRAb.

Table 7: Association between USG structure with thyroid function (n=324)

| Thyroid function | USG | | | | |
|------------------|----------------------------|-----------------------|---|---|--------------|
| | Multinodular goiter (n=25) | Nodular goiter (n=41) | Thyromegaly with in heterogeneous parenchyma (n=43) | Thyromegaly with in homogeneous parenchyma (n=57) | Normal (158) |
| | n (%) | n (%) | n (%) | n (%) | n (%) |
| Hypothyroidism | 14 (56.0) | 25 (61.0) | 34 (79.1) | 20 (35.1) | 136 (86.1) |
| Hyperthyroidism | 11 (44.0) | 16 (39.0) | 9 (20.9) | 37 (64.9) | 22 (13.9) |
| p value | 0.093 | 0.144 | 0.194 | 0.001 | 0.001 |

P value reached from chi square test

Table 7 shows that 57 patients were found thyromegaly with in homogeneous parenchyma among them 20(35.1%) in hypothyroidism and 37(64.9%) in hyperthyroidism group. One hundred fifty-eight patients were found normal USG among them among them

136(86.1%) in hypothyroidism and 22(13.9%) in hyperthyroidism group.

A total 158 patients have normal thyroid structure (normal USG). Among them 136 (86.1%) were

hypothyroidism patients and 22 (13.9%) were hyperthyroidism patients which shows strong association between hypothyroidism and normal thyroid structure (P value 0.001). Another strong association was found between hyperthyroidism and thyromegaly with homogenous parenchyma (P value 0.001). It was shown that 37 (64.9%) hyperthyroid patients have thyromegaly with homogenous parenchyma, whereas 20 (35.1%) hypothyroid patients have thyromegaly with homogenous parenchyma. Other thyroid structural abnormality did not show any statistically significant association between hyper or hypothyroidism (P value 0.194, 0.144, 0.093 for thyromegaly with heterogenous parenchyma, nodular goitre and multinodular goitre respectively).

DISCUSSION

It was found that most of the study population (79%) were female, that means, thyroid disorders are more prevalent in female which was consistent with many other studies. In our study, thyroid auto antibodies were also significantly more prevalent in female than male, which were consistent with previous research [4, 5, 35].

The occurrence of antithyroid antibodies varies between population, which may be result of differences in genetic and environmental factors including infections, iodine supply, stress, smoking, and use of numerous medications [5, 10, 12, 23]. However it should also be noted that methods of antibody determination and their sensitivity differ between laboratories [45]. Thus the direct comparison of the prevalence of antithyroid antibodies may be difficult. Nevertheless, in a Danish population based study of iodine sufficient subjects, TPOAb was found in 12% and TgAb in 14% of women aged 25-30 years [4]. Similar result were obtained in an American epidemiological study performed more than two decades ago that showed the occurrence of TPOAb in 10.4% of women without thyroid disease aged 20-29 years and 12.6% of those aged 30-39 years, and TgAb in 8.5% and 13% respectively [46].

It was evident that thyroid disorders were significantly higher in younger age group (mean age 37 ± 12.4 years). Mean BMI 25.4 ± 5.3 kg/m² suggest that most of the recipient with thyroid disorders were obese. It can be explained by maximum patients were hypothyroid (70.7%) in this study. In the present study, BMI has a negative relationship with TRAb but not with TgAb or TPOAb. The prevalence of positive thyroid autoantibodies was increased in obese children, particularly in those with elevated TSH [36]. Obese patients had a higher frequency of antithyroid antibodies than control patients [36]. The prevalence of TPOAb positivity was greater in the obese group in a cross sectional study [37]. Though our study did not coincide with this study. Future studies are needed to understand,

how obesity might enhance the risk of thyroid auto immunity.

The prevalence of TPOAb was as high as 65.1%. Among the positive TPOAb most of the patients were hypothyroid (78.7%) and only (21.3%) were hyperthyroid. Significant differences were observed in the prevalence of positive TPOAb between hypothyroid and hyperthyroid patients. The previous studies shows that thyroid autoantibodies were involved in thyroid dysfunction [36-38]. Anti TPOAb may be implicated in the pathogenesis of autoimmune thyroid disorders by (1) activating the complement cascade and inducing complement mediated tissue damage to thyroid cells [39] and (2) inducing antibody dependent cell mediated cytotoxicity, with TPO antibody titers correlating with the severity of lymphocyte infiltration, regardless of the presence or absence of hypothyroid [42]. In a 5 years follow-up study of 3018 patients, Li Y *et al.*, [39] found that a high iodine intake by subjects who were TPOAb and TgAb positive at the baseline was a more common risk factors for developing hypothyroid status among this group than among seronegative patients. The mechanisms behind this phenomenon may be that thyroglobulin combined with a high iodine intake enhance the antigenicity of thyroglobulin and promotes lymphocyte proliferation [8]. TSH exerts its activity by binding to the extracellular domain of TSH receptor located in the basolateral membrane of thyroid follicular cells [43]. TSH receptor stimulating or blocking antibodies (TRAb), which may interfere with normal receptor function, influence the action of TSH. They are considered to induce hyper or hypothyroid states, depending on their activity [44]. On the other hand 97.5% hyperthyroid patient was positive for TRAb in our study.

A study undertaken in people with elevated TSH demonstrated that there was a strong association between thyroid autoantibodies and an enlarged thyroid [39]. In hypothyroid patients, a high level of auto antibodies (TPOAb and /or TgAb) was significantly associated with thyroid enlargement. Patients with thyroid enlargement had the highest value of both TPOAb and TgAb [40]. In another study, antibody positive subjects had large thyroid volume than control subjects [41]. But in our study TRAb shows a positive association with thyromegaly with homogenous parenchyma. It was also evident that there was a significant negative association between TRAb and normal thyroid structures. Other structural abnormality did not show any significant association with thyroid autoantibodies.

On the other hand, 86.1% hypothyroid patients have normal thyroid structure in our study which shows strong association between hypothyroidism and normal thyroid structure.

Limitations

The current study had the numbers of limitations. First, the study did not include subjects < 18 years of age. Secondly the study was cross sectionals and hence did not investigate individual changes over time. After evaluating once, we did not follow-up those patients for a long periods and have not known other possible interference that may happen in the long term.

CONCLUSION

In conclusion, female sex, abnormal BMI, thyroid volume, thyroid hypoechogenicity and heteroechogenicity were risk factors for the presence of thyroid autoantibodies. Thyroid autoantibodies were detected in subjects with thyroid dysfunction and in those who were euthyroid. An increased prevalence of thyromegaly with homogenous parenchyma correlated with elevated levels of TRAb. Women with thyroid enlargement, abnormal BMI, thyroid hypoechogenicity and heteroechogenicity would benefit from routine evaluation of thyroid autoantibody status and thyroid function.

REFERENCES

1. Bjoro, T., Holmen, J., Kruger, O., Midthjell, K., Hunstad, K., Schreiner, T., ... & Brochmann, H. (2000). Prevalence of thyroid disease, thyroid dysfunction and thyroid peroxidase antibodies in a large, unselected population. The Health Study of Nord-Trondelag (HUNT). *European journal of endocrinology*, 143(5), 639-647.
2. Lindberg, B., Svensson, J., Ericsson, U. B., Nilsson, P., Svenonius, E., & Ivarsson, S. A. (2001). Comparison of some different methods for analysis of thyroid autoantibodies: importance of thyroglobulin autoantibodies. *Thyroid*, 11(3), 265-269.
3. Arai, T., Kurashima, C., Utsuyama, M., Sawabe, M., & Ito, H. (2000). Measurement of Anti-Thyroglobulin and Anti-Thyroid Peroxidase Antibodies Using Highly Sensitive Radioimmunoassay An Effective Method for Detecting Asymptomatic Focal Lymphocytic Thyroiditis in the Elderly. *Endocrine journal*, 47(5), 575-582.
4. Pedersen, I. B., Knudsen, N., Jørgensen, T., Perrild, H., Ovesen, L., & Laurberg, P. (2003). Thyroid peroxidase and thyroglobulin autoantibodies in a large survey of populations with mild and moderate iodine deficiency. *Clinical Endocrinology*, 58(1), 36-42.
5. Heiberg Brix, T., Skov Hansen, P., Ohm Kyvik, K., & Hegedüs, L. (2004). Aggregation of thyroid autoantibodies in first-degree relatives of patients with autoimmune thyroid disease is mainly due to genes: a twin study. *Clinical endocrinology*, 60(3), 329-334.
6. Davidson, A., & Diamond, B. (2001) Autoimmune diseases. *New England Journal of Medicine*, 345, 340–350.
7. Safran, M., Paul, T. L., Roti, E., & Braverman, L. E. (1987) Environmental factors affecting autoimmune thyroid disease. *Endocrinology and Metabolism Clinics of North America*, 16, 327–342.
8. Laurberg, P., Bülow Pedersen, I., Knudsen, N., Ovesen, L., & Andersen, S. (2001) Environmental iodine intake affects the type of nonmalignant thyroid disease. *Thyroid*, 11, 457–469.
9. Bülow Pedersen, I., Laurberg, P., Knudsen, N., Jørgensen, T., Perrild, H., Ovesen, L., & Rasmussen, L. B. (2005). A population study of the association between thyroid autoantibodies in serum and abnormalities in thyroid function and structure. *Clinical Endocrinology*, 62(6), 713-720.
10. Laurberg, P., Cerqueira, C., Ovesen, L., Rasmussen, L. B., Perrild, H., Andersen, S., ... & Carlé, A. (2010). Iodine intake as a determinant of thyroid disorders in populations. *Best practice & research Clinical endocrinology & metabolism*, 24(1), 13-27.
11. Loviselli, A., Velluzzi, F., Mossa, P., Cambosu, M. A., Secci, G., Atzeni, F., ... & Mariotti, S. (2001). The Sardinian Autoimmunity Study: 3. Studies on circulating antithyroid antibodies in Sardinian schoolchildren: relationship to goiter prevalence and thyroid function. *Thyroid*, 11(9), 849-857.
12. Szabolcs, I., Bernard, W., & Horster, F. A. (1995). Thyroid autoantibodies in hospitalized chronic geriatric patients: prevalence, effects of age, nonthyroidal clinical state, and thyroid function. *Journal of the American Geriatrics Society*, 43(6), 670-673.
13. Tunbridge, W. M., Evered, D. C., Hall, R., Appleton, D., Brewis, M., Clark, F., Grimley Evans, J., Young, E., Bird, T., & Smith, R. A. (1977). The spectrum of thyroid disease in a community: the Wickham survey. *Clinical Endocrinology*, 7, 481-493.
14. Loviselli, A., Velluzzi, F., Mossa, P., Cambosu, M. A., Secci, G., Atzeni, F., Taberlet, A., Balestrieri, A., Martino, E., Grasso, L., Songini, M., Bottazzo, G. F., Mariotti, S., & Sardinian Schoolchildren Study Group. (2001). The Sardinian Autoimmunity Study: 3. Studies on circulating antithyroid antibodies in Sardinian schoolchildren: relationship to goiter prevalence and thyroid function. *Thyroid*, 11, 849-857.
15. Okamura, K. E. N., Nakashima, T., Ueda, K., Inoue, K., Omae, T., & Fujishima, M. (1987). Thyroid disorders in the general population of Hisayama Japan, with special reference to prevalence and sex differences. *International journal of epidemiology*, 16(4), 545-549.
16. Brochmann, H., Bjøoro, T., Gaarder, P. I., Hanson, F., & Frey, H. M. (1988). Prevalence of thyroid dysfunction in elderly subjects. *European Journal of Endocrinology*, 117(1), 7-12.

17. Szabolcs, I., Bernard, W., & Horster, F. A. (1995). Thyroid autoantibodies in hospitalized chronic geriatric patients: prevalence, effects of age, nonthyroidal clinical state, and thyroid function. *Journal of the American Geriatrics Society*, 43(6), 670-673.
18. Livolsi, V. A. (1994). The pathology of autoimmune thyroid disease: a review. *Thyroid*, 4, 333-339.
19. Nobuyuki, A., & De Groot, L. J. (2004). Hashimoto's thyroiditis. Available at <http://www.thyroidmanager.org/thyroidbook.ht-m>.
20. Weetman, A. P., & McGregor, A. M. (1994). Autoimmune thyroid disease: further developments in our understanding. *Endocrine Reviews*, 15, 788-830.
21. Laurberg, P., Bülow Pedersen, I., Pedersen, K. M., & Vestergaard, H. (1999). Low incidence rate of overt hypothyroidism compared with hyperthyroidism in an area with moderately low iodine intake. *Thyroid*, 9, 33-38.
22. Hollowell, J. G., Staehling, N. W., Flanders, W. D., Hannon, W. H., Gunter, E. W., Spencer, C. A., & Braverman, L. E. (2002). Serum TSH, T4, and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III). *The Journal of Clinical Endocrinology & Metabolism*, 87(2), 489-499.
23. Prummel, M. F., Strieder, T., & Wiersinga, W. M. (2004). The environment and autoimmune thyroid diseases. *European Journal of Endocrinology*, 150(5), 605-618.
24. Stathatos, N., & Daniels, G. H. (2012). Autoimmune thyroid disease. *Current Opinion in Rheumatology*, 24(1), 70-75.
25. Antonelli, A., Ferrari, S. M., Corrado, A., Di Domenicantonio, A., & Fallahi, P. (2015). Autoimmune thyroid disorders. *Autoimmunity reviews*, 14(2), 174-180.
26. Iddah, M. A., & Macharia, B. N. (2013). Autoimmune thyroid disorders. *International Scholarly Research Notices*, 2013.
27. Aruna, N., & Pushpa, N. (2015). Pregnancy outcome in euthyroid women with anti thyroid peroxidase antibodies. *Te Journal of Obstetrics and Gynecology of India*.
28. Walsh, J. P., Bremner, A. P., Feddema, P., Leedman, P. J., Brown, S. J., & O'Leary, P. (2010). 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*, 95(3), 1095-1104.
29. Roos, A., Links, T. P., Gans, R. O., Wolffenbuttel, B. H., & Bakker, S. J. (2010). Thyroid peroxidase antibodies, levels of thyroid stimulating hormone and development of hypothyroidism in euthyroid subjects. *European Journal of Internal Medicine*, 21(6), 555-559.
30. McLeod, D. S., & Cooper, D. S. (2012). The incidence and prevalence of thyroid autoimmunity. *Endocrine*, 42, 252-265.
31. Rose, N. R. (2007). Prediction and prevention of autoimmune disease: a personal perspective. *Annals of the New York Academy of Sciences*, 1109(1), 117-128.
32. Chou, K. M., Huang, B. Y., Chen, C. H., Lin, J. D., Chiu, S. Y. H., & Lee, C. C. (2015). Correlation and presentation of thyroid functional status with thyroid autoantibodies in long-term follow-up of autoimmune thyroiditis: A study of 116 cases. *Journal of the Formosan Medical Association*, 114(11), 1039-1046.
33. Liu, Y., Huang, H., Zeng, J., & Sun, C. (2013). Thyroid volume, goiter prevalence, and selenium levels in an iodine-sufficient area: a cross-sectional study. *BMC Public Health*, 13(1), 1-7.
34. Teng, W., Shan, Z., Teng, X., Guan, H., Li, Y., Teng, D., ... & Li, C. (2006). Effect of iodine intake on thyroid diseases in China. *New England Journal of Medicine*, 354(26), 2783-2793.
35. Li, Y., Teng, D., Shan, Z., Teng, X., Guan, H., Yu, X., ... & Teng, W. (2008). Antithyroperoxidase and antithyroglobulin antibodies in a five-year follow-up survey of populations with different iodine intakes. *The Journal of Clinical Endocrinology & Metabolism*, 93(5), 1751-1757.
36. Kasagi, K., Kousaka, T., Higuchi, K., Iida, Y., Misaki, T., Alam, M. S., ... & Konishi, J. (1996). Clinical significance of measurements of antithyroid antibodies in the diagnosis of Hashimoto's thyroiditis: comparison with histological findings. *Thyroid*, 6(5), 445-450.
37. Fade, J. V., Franklyn, J. A., Cross, K. W., Jones, S. C., & Sheppard, M. (1991). Prevalence and follow-up of abnormal thyrotrophin (TSH) concentrations in the elderly in the United Kingdom. *Clinical endocrinology*, 34(1), 77-84.
38. Hoogendoorn, E. H., Hermus, A. R., De VegT, F., Ross, H. A., Verbeek, A. L., Kiemeny, L. A., ... & den Heijer, M. (2006). Thyroid function and prevalence of anti-thyroperoxidase antibodies in a population with borderline sufficient iodine intake: influences of age and sex. *Clinical chemistry*, 52(1), 104-111.
39. Bülow Pedersen, I., Laurberg, P., Knudsen, N., Jørgensen, T., Perrild, H., Ovesen, L., & Rasmussen, L. B. (2005). A population study of the association between thyroid autoantibodies in serum and abnormalities in thyroid function and structure. *Clinical Endocrinology*, 62(6), 713-720.
40. Stichel, H., l'Allemand, D., & Grüters, A. (2000). Thyroid function and obesity in children and adolescents. *Hormone Research in Paediatrics*, 54(1), 14-19.
41. Acar, T., Özbek, S. S., Erdogan, M., Özgen, A. G., & Demirel, S. O. (2013). US findings in euthyroid patients with positive antithyroid autoantibody tests compared to normal and hypothyroid

- cases. *Diagnostic and Interventional Radiology*, 19(4), 265-270.
42. Akamizu, T., Kohn, L. D., Hiratani, H., Saijo, M., Tahara, K., & Nakao, K. (2000). Hashimoto's thyroiditis with heterogeneous antithyrotropin receptor antibodies: unique epitopes may contribute to the regulation of thyroid function by the antibodies. *The Journal of Clinical Endocrinology & Metabolism*, 85(6), 2116-2121.
43. Rapa, A., Monzani, A., Moia, S., Vivenza, D., Bellone, S., Petri, A., ... & Bona, G. (2009). Subclinical hypothyroidism in children and adolescents: a wide range of clinical, biochemical, and genetic factors involved. *The Journal of Clinical Endocrinology & Metabolism*, 94(7), 2414-2420.
44. Rapoport, B., & McLachlan, S. M. (2001). Thyroid autoimmunity, *J Clin Invest*, 108, 1253-1259.
45. Aghini-Lombardi, F., Antonangeli, L., Martino, E., Vitti, P., Maccherini, D., Leoli, F., ... & Pinchera, A. (1999). The spectrum of thyroid disorders in an iodine-deficient community: the Pescopagano survey. *The Journal of Clinical Endocrinology & Metabolism*, 84(2), 561-566. doi: 10.1210/jc.84.2.561
46. Serum, T. S. H. (2002). T (4), and thyroid antibodies in the United States population (1988 to 1994): national health and nutrition examination survey (NHANES III) Hollowell JG, Staehling NW, Flanders WD, Hannon WH, Gunter EW, Spencer CA, Braverman LE. *J Clin Endocrinol Metab*, 87(2), 489-499. doi:10.1210/jcem.87.2.8182