(International Print/Online Journal)

SJIF IMPACT FACTOR: 6.829
PUBMED-National Library of Medicine ID-101739732

ISSN (Print): 2209-2870
ISSN (Online): 2209-2862

International Journal of Medical Science and Current Research (IJMSCR)
Available online at: www.ijmscr.com
Volume 9, Issue 2 , Page No: 143-152
March-April 2026

IJMSCR

Clinicopathological Study Of Autoimmune Hypothyroidism And Its Correlation With Thyroid Autoantibodies

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Type of Publication: Original Research Paper
Conflicts of Interest: Nil

Abstract

Purpose: To assess the epidemiological, clinical, and diagnostic aspects of autoimmune hypothyroidism.

Methods: This cross-sectional study was conducted at the Regional Institute of Medical Sciences, Imphal, between April 2023 to March 2025. The sociodemographic data, radiological investigations, ultrasound of the neck, and Fine-needle aspiration cytology (FNAC) were recorded. The study also determined the correlation between thyroid autoantibodies, demographic distribution, and thyroid hormone status.

Results: A total of 176 patients with goiter were included in the study, with 86.40% females. The mean age of patients was 39.6 ± 13.58 years. The majority of patients 60.20% had diffuse goiter and subclinical hypothyroidism (35.80%), followed by overt (33%) hypothyroidism. The anti-TPO levels were raised in 93% of patients. Females had a higher mean anti-TPO antibody level (448.15) compared to males (124.40), P <0.00. The 42.60% patients had diffuse thyroiditis and a Thyroid Imaging Reporting and Data Systems score of 2 (68.20%). The majority of patients (72.10%) showed FNAC findings of lymphocytic thyroiditis, classified as benign. The mean anti-TPO levels were higher in the 19-30 age group and in overt hypothyroidism, while anti-TG levels gradually increased with age and declined gradually after 46 years. Correlation analysis showed a weak negative relationship between age and anti-TPO levels (r = -0.059, P = 0.438. The anti-TPO was significantly higher in overt hypothyroidism than in euthyroid individuals (P = 0.037).

Conclusion: Autoimmune hypothyroidism predominantly affects middle-aged women, with subclinical hypothyroidism being the most common clinical presentation.

Keywords: Hypothyroidism, autoimmune thyroiditis, anti-TG, anti-TPO, fine-needle aspiration cytology

Introduction

Hypothyroidism is a condition wherein the thyroid gland does not synthesize enough thyroid hormone. Body functions are affected due to insufficient thyroid hormones. The factors such as a history of smoking and drinking, aging, pregnancy, geographical area, sex, genetics, ethnicity, and history of smoking and drinking affect the pathogenesis [1].

Hypothyroidism shows various etiologies, such as overt or subclinical. Generally, in subclinical hypothyroidism (SCH), thyroid-stimulating hormone (TSH) levels are higher with normal triiodothyronine (T3) levels and/or thyroxine (T4) levels [2]. In overt hypothyroidism, TSH is high, with low T3 and T4 levels [3].

Initial symptoms often include fatigue, constipation, dry skin, and weight gain. With advancing disease, patients may develop cold intolerance, reduced sweating, peripheral neuropathy, low energy levels, depression, cognitive decline, muscle cramps, joint pain, hair loss, sleep apnea, and menstrual irregularities such as heavy or irregular periods. In some cases, thyroid inflammation results in goiter [4].

Autoimmune thyroiditis (Hashimoto's disease), iodine deficiency, or iatrogenic factors like thyroidectomy are the major causes of hypothyroidism. Women are more affected than men due to higher autoimmune susceptibility [5]. The presence of anti-thyroid peroxidase (anti-TPO) and anti-thyroglobulin (anti-TG) antibodies acts as a key marker in autoimmune hypothyroidism [6]. The presence of these antibodies may also represent a chance of further overt hypothyroidism [7]. Most patients are asymptomatic initially, and later present with painless, diffuse, and symmetrical enlargement of the thyroid [8].

Fine-needle aspiration cytology (FNAC) is widely used for assessing thyroid swellings and diagnosing Hashimoto's thyroiditis because it is minimally invasive, has a strong safety profile, and demonstrates high diagnostic sensitivity for detecting lymphocytic thyroiditis. Along with FNAC, clinical assessment, serological testing for anti-TPO and anti-TG antibodies, profiling of thyroid hormone profiling, and high-resolution ultrasonography is used for clinical evaluation [9].

Using a combined diagnostic strategy that incorporates the patient's clinical features, laboratory test results, and cytomorphological findings improves overall diagnostic accuracy compared with relying on any one factor alone. This study was carried out to assess the epidemiological, clinical and diagnostic aspects of autoimmune hypothyroidism.

Methods

Study design

This cross-sectional study was conducted at the Regional Institute of Medical Sciences (RIMS), Imphal, between April 2023 to March 2025. The sociodemographic profile, thyroid status, and clinicopathological features of patients with autoimmune hypothyroidism were assessed. The study was conducted in accordance with International Council for Harmonization Good Clinical Practice (ICH-GCP) and the Declaration of Helsinki guidelines. The protocol for the study was approved by the research ethics board, RIMS, Imphal (No: A/206/REB-Comm(SP)/RIMS/2015/1117/148/2023 on 30 September 2023). Written informed consent was obtained from all the patients about the whole treatment process and follow-ups.

Inclusion criteria and exclusion criteria

Patients of either sex aged above 18 years with goiter, presence of anti-TPO or anti-TG antibodies, visiting the medicine or endocrinology OPD, or admitted at medicine, ENT, or surgery ward. Patients with goitrous enlargement who were euthyroid or had subclinical or overt hypothyroidism status were included in the study. Patients with acute thyroiditis, thyroid malignancies, and hyperthyroidism were excluded from the study.

Data collection

The sociodemographic data, detailed clinical history of the patients, general physical examination, and routine hematological data were recorded. All the patients were subjected to investigations like serum thyroid profile (goiter, thyroid function test, serum thyroid-stimulating hormone (TSH), serum total triiodothyronine (T3) and serum total thyroxine (T4)**,** serum free triiodothyronine (T3) and serum free thyroxine (T4)**,** anti- thyroid peroxidase antibody, anti- thyroglobulin antibody, etc.) and radiological investigations, ultrasound of neck, fine needle aspiration cytology.

All patients underwent an ultrasound of the neck to detect the volume of the gland, echotexture, echogenicity, and vascularity.

Patient classification

The patients were graded as per The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC), third edition, 2023**;** I- non-diagnostic, II- benign**,** III - atypia of undetermined significance (AUS)**,** IV- follicular neoplasm (FN) and follicular neoplasm oncocytic follicular neoplasm (FCN)**,** V- Suspicious for Malignancy**,** VI- Malignant.

Sample size calculation

The sample size was calculated according to the formula:

Sample size, $N = 1.96^2PQ/L^2$

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Where, P = Taking the proportion of autoimmune hypothyroidism among patients with hypothyroid status as 66% according to a study by Jayshankar et al [10]

Precision (L) = 7%, Q = 100- P, Alpha = 1.96

Therefore, N = 176

Statistical analysis

The collected data were analyzed using statistical package for the Social Sciences (SPSS) version 21. Descriptive statistics were used to describe categorical variables (frequency and percentages) and continuous variables (mean with standard deviation [SD]). An independent t-test was employed to test the association of mean age with overt and subclinical hypothyroidism. Association between variables was explored using an independent sample t-test and a one-way ANOVA.

Results

Demographic characters

A total of 176 patients with goiter were included in the study, with 86.40% females. The mean age of patients was 39.6 ± 13.58 years. Most of the patients were in the age group of 41-50 years (30.80%). The 72% of patients were residing in urban area and 32.90% of patients were in class I social class, followed by 29.50% in class II. The hypothyroid symptoms, such as fatigue (18.20%), weight gain (15.90%), and cold intolerance (12.50%), along with goiter-related symptoms (neck swelling [100%], local discomfort/pressure sensation [52.80%]), were observed in patients. Goiter was further classified after clinical examination, where 60.20% of patients had diffuse, 20.40% had multinodular goiter (Table 1).

Clinical investigations

The majority of the patients had SCH (35.80%), followed by overt hypothyroidism (33%) and euthyroid (31.30%), and there was no statistical significance in their mean age. The anti-TPO levels were raised in 93% of patients. Females had a higher mean anti-TPO antibody level (448.15) compared to males (124.40), P <0.001. The anti-TG antibody level was normal in (67.60%) of patients.

The ultrasonography neck findings revealed 42.60% patients had diffuse thyroiditis, 29% with multinodular goiter. The majority of patients had a Thyroid Imaging Reporting and Data Systems (TIRADS) score of 2 (68.20%) followed by a score of 3 (23.30%). The majority of patients (72.10%) showed FNAC findings of lymphocytic thyroiditis, classified as benign (TBSRTC-II) while 23.80% had features of lymphocytic thyroiditis with colloid goiter (Table 2).

Thyroid antibody profile according to age and thyroid type

The mean anti-TPO levels peaked in the 19-30 age group and declined for subsequent age groups, while anti-TG levels gradually increased with age and declined gradually after 46 years. Overall, anti-TPO levels were consistently higher than anti-TG across all age groups (Figure 1). There was a negative correlation between age and anti-TPO (r = -0.059).

Mean anti-TPO antibody levels were highest in patients with overt hypothyroidism, followed by SCH and euthyroid individuals. The anti-TG levels were consistently lower than the anti-TPO levels across all thyroid status groups (Figure 2).

The mean anti-TPO levels in overt hypothyroidism were 504.21, followed by 376.11 in SCH and 331.31(334.39) in euthyroid. The comparison between mean anti-TPO antibody levels in euthyroid and overt hypothyroidism reveals a significant difference (P = 0.037), indicating that anti-TPO levels increase in overt hypothyroidism compared to those with euthyroid status (Table 3).

Discussion

The mean age of patients in this study was 39.6 ± 13.58 years, with the highest proportion of cases observed in the 41–50 years age group (30.80%). Other studies also reported an age group between 25-55 years with thyroid disorder [11-13]. The major patients included in the study were female (87%), similar to other reported studies with females (55%-93%) [11, 13-15]. The 72% of patients were from urban areas, as noted in another study where 87% patients were from urban areas [16]. Among the patients included in the current study, 32.90% of patients were in class I social class, followed by 29.50% in class II. Varying results were seen in another study with patients with euthyroid (10%,18%) and hypothyroidism (1%, 32%) in Class I and Class II, respectively [13].

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The current study recorded fatigue, weight gain, and cold intolerance as prevalent hypothyroidism symptoms, which are common in a parallel study [16-18]. Goiter-related symptoms occurred where 60.20% of patients had diffuse goiter. Studies by Thomas et al., Chandanwale et al. also reported the maximum patients (68-73%) with diffuse goiter [19-20].

The majority of the patients had SCH (35.80%), followed by overt hypothyroidism (33%) and euthyroid (31.30%). Multiple studies reported different types of hypothyroidism in patients; SCH (6-18 %) [11, 16, 17], overt hypothyroidism (2-6) [11, 21], euthyroid (69.4%) [19].

The anti-TPO levels were raised in 93% of patients. Other studies also reported higher anti-TPO levels in patients [67%- 100%] [19, 21, 22]. Whereas the anti-TG antibody level was normal in the majority of patients, as reported in the study by Thomas et al. [19]. Females had a higher mean anti-TPO antibody level compared to males. In general, other studies also reported females with higher antibodies [11, 23, 24].

The ultrasonography neck findings revealed 42.60% patients had diffuse thyroiditis, 29% with multinodular goiter. A study by Aghoury et al., 68.8% had a solitary thyroid nodule and 31.2% had multinodular goiter [23]. Another study reported 50% of patients with diffuse, 32.20% patients with multinodular goiter [22].

In this study TIRADS score of 2 was found in the maximum patients, followed by a score of 3. Similar results were seen in other study [22, 26]. The majority of patients showed FNAC findings of lymphocytic thyroiditis, classified as benign (TBSRTC-II). In another study by Chandanwale et al., noted 79% patients with lymphocytic infiltration. And Anila et al. reported lymphocytic thyroiditis with 91.6% under category II [20, 27]. There was a negative correlation between age and anti-TPO (r = -0.059) and no significant association was seen; similar results were seen in another study [11].

Strengths and limitation of study

The major strengths of this study include its comprehensive, multi-dimensional diagnostic approach that integrates clinical, biochemical, serological, radiological, and cytopathological parameters, providing a holistic understanding of autoimmune hypothyroidism. Additionally, the use of robust correlation analysis to link thyroid functional status with anti-TPO antibody levels and cytological features offers deeper understanding of disease progression and improves the study's clinical relevance compared to prior research that examined limited diagnostic parameters.

The study is limited by a relatively small sample size and its cross-sectional design, which restrict generalizability and precludes assessment of disease progression and long-term outcomes. Exclusion of atrophic Hashimoto's thyroiditis and Hashitoxicosis limits representation of the full clinical spectrum of autoimmune hypothyroidism. Additionally, population-specific variations in antibody profiles could not be explored due to the absence of genetic and environmental data.

Conclusion

This study concludes that autoimmune hypothyroidism predominantly affects middle-aged women, with subclinical hypothyroidism being the most common clinical presentation. A comprehensive diagnostic approach is essential for early detection, risk stratification, and appropriate management, while emphasizing the need for longitudinal and genetic studies to better understand disease progression and pathogenesis.

Statements and Declarations

Funding: No funding was received to assist with the preparation of this manuscript.

Competing Interests: The authors have no competing interests to declare that are relevant to the content of this article.

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Figure 1: Mean anti-TPO antibody and anti-TG antibody according to age groups

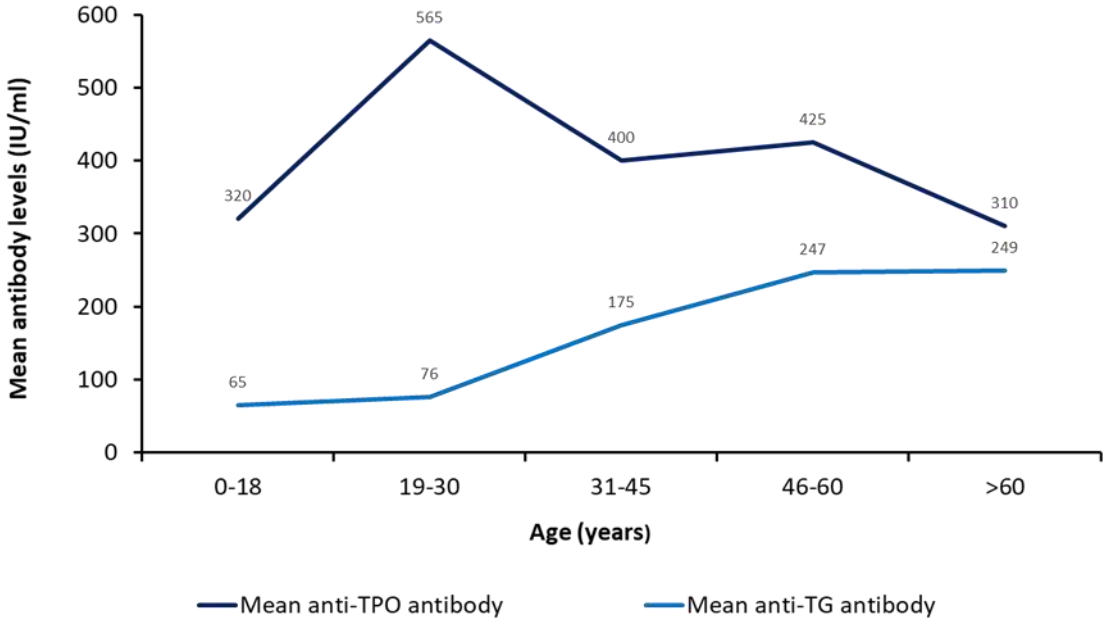

Figure 2: Mean anti-TPO and anti- TG levels according to thyroid status

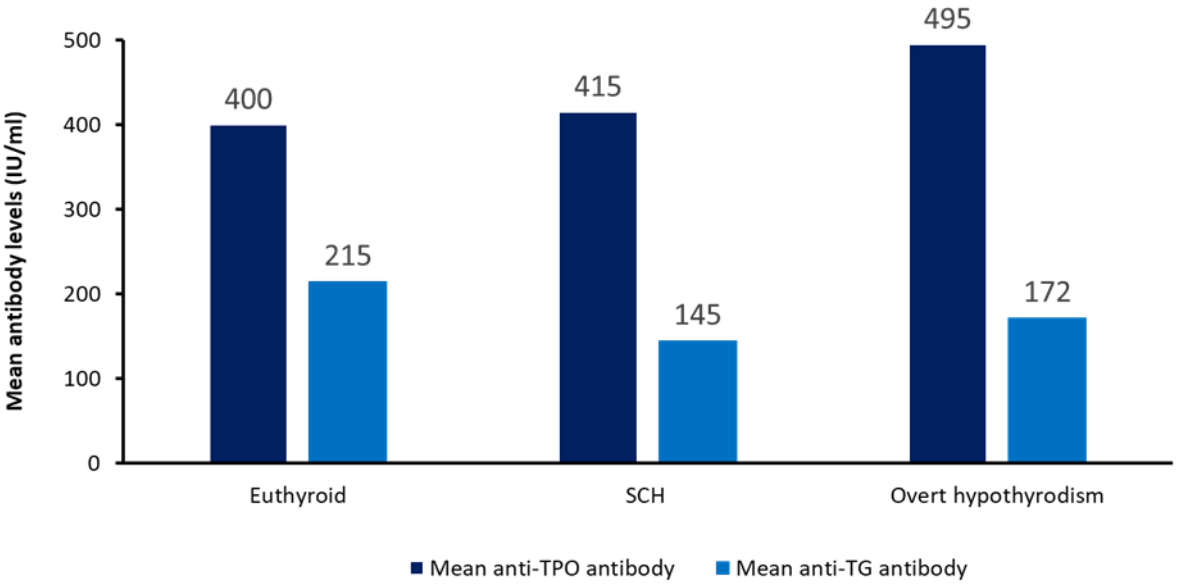

Table 1: Demographic characteristics

Parameters	Number of patients (N=176)

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Sex	
Male	24 (13.60)
Female	152 (86.40)
Age [years]	
18-30	47 (26.70)
31-40	34 (19.31)
41-50	54 (30.70)
51-60	31 (17.61)
61-70	10 (5.70)
Area of residence	
Urban	127 (72)
Rural	49 (28)
Social class	
Class I	58 (32.90)
Class II	52 (29.50)
Class III	37 (21.15)
Class IV	18 (10.20)
Class V	11 (6.25)
Clinical symptoms	
Fatigue / Easy fatigability	32 (18.20)
Weight gain	28 (15.90)
Cold intolerance	22 (12.50)
Constipation	18 (10.20)
Dry/coarse skin	17 (9.70)
Voice change / Hoarseness	15 (8.50)
Menstrual irregularities (females)	14 (8.00)
Puffy face / Facial swelling	12 (6.80)
Depression / Cognitive slowing	5 (2.80)
Goiter-Related Symptoms	
Neck swelling	176 (100)

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Local discomfort/pressure sensation	93 (52.80)
Dysphagia	47 (26.70)
Foreign body sensation in the throat	10 (5.60)
Type of goiter	
Diffuse	106 (60.22)
Solitary Nodule	36 (20.45)
Multinodular Goiter	34 (19.31)
Data represented as n (%), unless otherwise specified.	

Table 2: Distribution of patients based on clinical investigations

Parameter	**No of patients (N=176)**
Thyroid Status	
SCH	63 (35.80)
Overt hypothyroidism	58 (33)
Euthyroid	55 (31.25)
Anti-TPO antibody	
Normal	165 (93)
Increased	11 (6)
anti-TPO antibody level based on gender (IU/ml) mean (SD)	
Male	124.41 (85.61)
Female	448.15 (375.61)
Anti-TG antibody	
Normal	119 (67.60)
Increased	57 (32.40)
USG neck finding	
Diffuse	75 (42.6)
Multinodular goiter	51 (29)
Solitary nodule	42 (23.90)
Diffuse with micronodular pattern	8 (4.50)

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TIRADS	
2	120 (68.20)
3	41 (23.30)
4	15 (8.50)
FNAC finding	
Lymphocytic thyroiditis (Benign-II)	127 (72.10)
Lymphocytic Thyroiditis with colloid goiter (Benign-II)	42 (23.80)
Papillary carcinoma with lymphocytic thyroiditis (Malignant IV)	7 (4)
Data represented as n (%), unless otherwise specified. SCH, subclinical hypothyroidism	

Table 3: Comparison of thyroid status with anti-TPO antibodies

Thyroid status	Mean (SD)	P value		
		Euthyroid vs SCH	Euthyroid vs Overt hypothyroidism	SCH vs Overt hypothyroidism
Euthyroid	331.31 (334.39)	1.000	0.037	0.164
SCH	376.11(392.81)			
Overt hypothyroidism	504.21(353.18)			

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