Advanced Medical Journal, Vol.10, No.4, P.205-211,2025 https://doi.org/10.56056/amj.2025.416

Thyroid Dysfunction and Anti Thyroid Autoantibodies among Type I Diabetes Mellitus Patients

Farznda Mustafa Salih Zebari* Halgurd Fathulla Ahmed**

Abstract

Background and objectives: Studies have shown a strong association between Type I diabetes and autoimmune thyroid diseases, particularly autoimmune thyroiditis, with higher rates of thyroid autoantibodies in diabetic patients. Our aim is to study the prevalence of undiagnosed thyroid dysfunction and positive thyroid autoantibodies in Type I diabetes patients.

Methods: This was an observational analytic cross-sectional study conducted at Layla Qasim Diabetes Center in Erbil City, Kurdistan Region-Iraq. A total of 86 type I diabetes patients were enrolled during the period between November 2022 and August 2023. We conducted various laboratory tests for all study participants, including thyroid-stimulating hormone, triiodothyronine, thyroxine, fasting blood glucose, glycated hemoglobin, anti-thyroid peroxidase, and Thyroid Stimulating Hormone receptor antibodies.

Results: Among the participant patients 8.1% of them had hypothyroidism, and 10.5% had subclinical hypothyroidism and 9.3% of patients had thyroid-stimulating-hormone antibodies, 15.1% had Thyroid Peroxidase antibodies, and 3.5% had both of them. Among patients with hypothyroidism, higher proportion (85.7%) had positive Thyroid Peroxidase antibodies followed by those with subclinical hypothyroidism (55.6%), while in patients with normal thyroid function positive Thyroid Peroxidase antibodies were found in only 2.9% with highly significance difference (p-value <0.001).

Conclusion: Higher rates of autoimmune thyroid diseases and positive thyroid antibodies have been reported in patients with type I diabetes mellitus.

Keywords: Autoimmune thyroid disease, Type I diabetes mellitus, Thyroid Peroxidase antibodies

*M.B.Ch.B, F.K.B.M.S Internal Medicine, Corresponding author, Email: farzndaz@gmail.com,
**M.B.Ch.B, F.I.B.M.S, Professor of Internal Medicine. Director of training Kurdistan Higher Council for Medical Specialties.Email: halgurd.ahmed@khcms.edu.krd

Introduction

Both of autoimmune thyroid disease (AITD) and Type I diabetes mellitus (T1DM) are autoimmune conditions that often coexist or appear together in individuals. In fact, there is strong evidence regarding the consistent high rates of thyroid autoantibodies among type I diabetic patients who are diagnosed at childhood or adulthood period. These autoantibodies can be considered as significant markers and predictors of autoimmune thyroid disease.[1,2] It has been well-established that the commonest endocrine disorder diagnosed in patients with T1DM is the thyroid disorders.[3] Furthermore, there's evidence supporting the shared pathogenesis and genetic predisposition between autoimmune thyroid disease and T1DM. Both type 1 diabetes mellitus and autoimmune thyroid diseases have a significant genetic component in their development.[3] In clinical practice, these two endocrine disorders represent among the most frequent endocrine disorders encountered. They are considered major metabolic and endocrine disorders that significantly impact an individual's health and wellbeing. As they are common endocrine disorders, thyroid dysfunction and TIDM, can indeed affect different populations and present at various ages, although there can be some overlap.[4] With regards to the pathogenesis of TIDM, it primarily involves autoimmune processes that lead to damage of the insulin producing cells, Beta cells, of the pancreas. However, the etiology of autoimmune disorders is multifactorial, in TIDM, genetic risk factors have shown to be strongly associated, so as for the pathogenesis of autoimmune thyroid diseases and other similar diseases, these factors are also of large impact.[5] Interestingly, certain variations in the human leukocytes antigens (HLA) have shown to be also associated with the autoimmune thyroid disorders and this characteristic shared with that of type I DM. With strong evidence, it had been suggested that the risk of both TIDM and AITD can be attributed to the specific genetic changes in the HLA region.[6-8] Therefore, the HLA considered as significant factor that link these two autoimmune diseases (TIDM and AITD), moreover, within the HLA, specific genes like HAL-DQA and HLA-DQB contribute to some disorders in the immune system that affect the thyroid gland leading to a different of thyroid dysfunction.[9] It had been widely postulated that AITD is associated with two types of thyroid auto-antibodies, these are specific autoantibodies including anti-TPO antibodies and TSH receptors antibodies (TRAb).[10,11] However, as a diagnostic biomarker, anti-TPO is widely used in many institutions for detection of AITD. From other point of view, Anti-TPO antibody also used in screening for thyroid antibodies in patients with TIDM as early predictor and diagnostic test in these patients. It is worth mentioned that metabolic function can be significantly affected by thyroid dysfunction which potentially affect the glycemic control in diabetic patients. Hence, regular reliable screening for thyroid autoantibodies is so important and crucial in patients with TIDM for early detection and timely treatment of thyroid diseases in this population of patients. The purpose of this cross-sectional study was to determine the prevalence of thyroid dysfunction that had not been diagnosed before, as well as the prevalence of anti-thyroid autoantibodies, such as anti-TPO antibodies and thyroid-stimulating hormone-receptor (TRAb) autoantibodies, in type 1 diabetic patients.

Patients and methods

This was an observational analytic cross-sectional study conducted at Layla Qasim diabetes center in Erbil city, Kurdistan region-Iraq. The data were collected between November 2022 and August 2023. Eighty-six diabetic patients participated in the study.

https://doi.org/10.56056/amj.2025.416


The study proposal has been approved by the research ethics committee of the Kurdistan Higher Council of Medical Specialties. An informed verbal consent was taken from each participant. Participants aged 3.5 years and above with type 1 diabetes mellitus were recruited; those with severe diabetic complications, pregnant patients, patients with acute or chronic systemic illnesses were excluded from the study. Each patient was interviewed and informed consent was taken. Patients with type 1 diabetes who were already on insulin injections diagnosed using the American Diabetes Association (ADA) diagnostic criteria.[12] In the present study, according to study protocol, we conducted necessary investigations for all study participants. These included thyroids stimulating hormone (TSH), triiodothyronine (FT3), thyroxine (FT4), fasting blood glucose (FBG), glycated hemoglobin (HbA1c), Anti-Thyroid Peroxidase antibodies (anti-TPO) and TSH receptor antibodies (anti-TRAb). For purpose of this study, standard reference ranges of thyroid function tests were used; for TSH: 0.270 – 4.20 mIU/ml, for FT3: 3.10 – 6.80 pmol/L and for FT4: 12 - 22pmol/L.Case definition was in accordance with clinical guidelines; a case was defined to have subclinical hypothyroidism when the level of TSH was higher than the normal reference range and the FT4 was at normal levels. Overt hypothyroidism case was defined when he/she had TSH levels of higher than the normal reference range while FT4 is lower than its normal reference range. A case was defined to have sub-clinical hyperthyroidism when the TSH levels are lower than its normal reference range while both FT3 and FT4 within their normal reference levels. Overt hyperthyroidism was defined when the patient had TSH levels of lower-than-normal reference range and the levels of FT4 and or FT3 were higher than the normal reference range.[13] HbA1c and Fasting blood glucose levels were measured only to diagnose or confirm the diagnosis and not in relation to the study. Data of participant patients were checked for errors or inconsistency then entered, managed and analyzed using the statistical package for social sciences (SPSS) software for windows version 26, According to the type of variables, data were summarized as frequencies and simple percentages for nominal (qualitative) variables and as a mean, standard deviation (SD), median and range for scale (quantitative) variables. Statistical tests were applied accordingly; when the p-value < 0.05, the difference or association was considered significant. Fisher's exact test used to compare qualitative variables.

Results

Eighty-six diabetic patients participated in the study, their mean age (SD) was 16.2 (7.9) years, the median was 14.5 years and the age range was 3.5-44 years. More than half (52.3%) were females. The majority (83.7%0 had normal free T3 values, and 90.7% had normal free T4 values. Fifteen patients (17.4%) had high TSH values. Other details are presented in Table (1). It is evident in Figure (1) that 8.1% of patients had hypothyroidism, and 10.5% had subclinical hypothyroidism Figure (1). None of the patients had clinical or subclinical hyperthyroidism.

https://doi.org/10.56056/amj.2025.416

Table (1): Basic characteristics of patients.

	No.	(%)	Mean (SD)	Median	Range
Age (years)		16.2 (7.9)		14.5	(3.5-44)
< 10	18	(20.9)			
10-19	44	(51.2)			
20-29	18	(20.9)			
≥ 30	6	(7.0)			
Sex					
Female	45	(52.3)			
Male	41	(47.7)			
FT3		4.5 (1.2)		5	(1.5-8)
< 3.1	10	(11.6)			
3.1-6.8	72	(83.7)			
> 6.8	4	(4.7)			
FT4			14.9 (3.4)	15	(2.4-31)
< 12	8	(9.3)			
12-22	78	(90.7)			
TSH		3.5 (4.3)		2	(0.5-31)
0.27-4.2	71	(82.6)			
> 4.2	15	(17.4)			
Total	86	(100.0)			

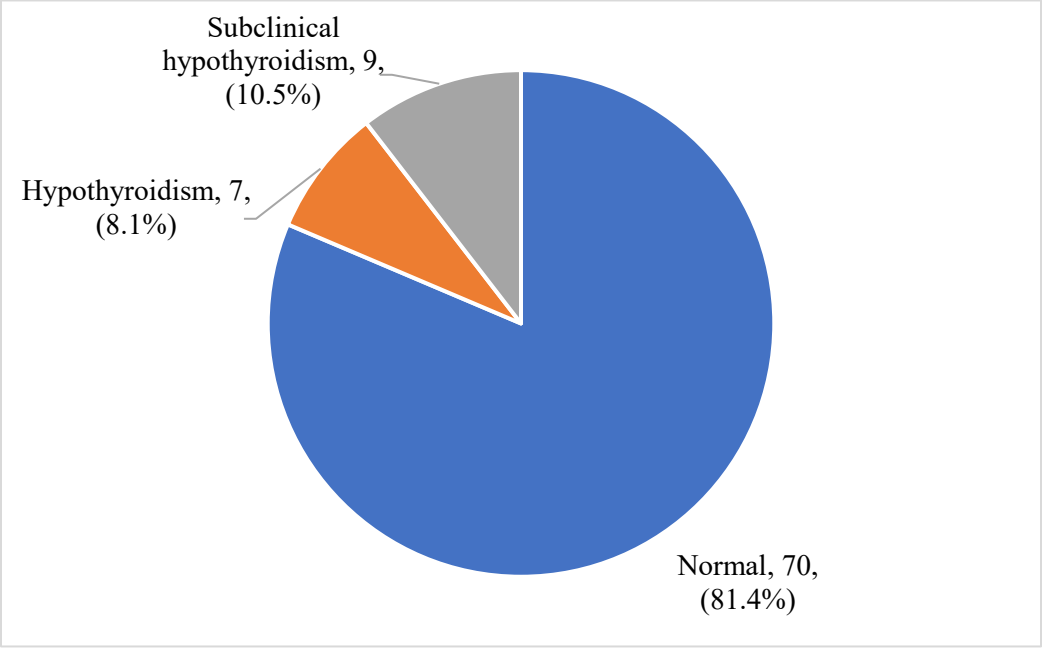

Figure (1): Prevalence of hypothyroidism among diabetic patients.

Figure (2) shows that 9.3% of patients had anti TSH antibodies, 15.1% had anti TPO antibodies, and 3.5% had both of them, Figure (2).

https://doi.org/10.56056/amj.2025.416

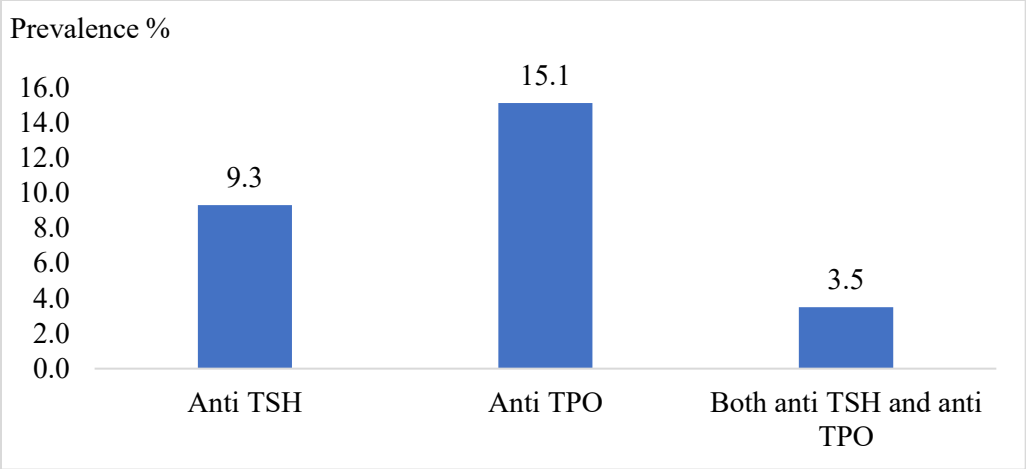

Figure (2): Prevalence of positive anti TSH and anti TPO among the diabetic patients.

No significant association was detected between the diagnosis (based on thyroid hormones level) and the presence of anti TSHR antibodies (p = 0.158). The prevalence rates of anti TPO antibodies were high among patients with overt hypothyroidism (85.7%) and subclinical hypothyroidism (55.6%), compared with 2.9% among patients with normal thyroid function (p < 0.001), as presented in Table (2).

Table (2): Prevalence of Anti TSH and anti TPO by diagnosis.

	Normal	Hypothyroidism	Subclinical hypothyroidism	Total	
	No. (%)	No. (%)	No. (%)	No. (%)	P*
Anti TSH					
Negative	64 (91.4)	5 (71.4)	9 (100.0)	78 (90.7)	
Positive	6 (8.6)	2 (28.6)	0 (0.0)	8 (9.3)	0.158
Anti TPO					
Negative	68 (97.1)	1 (14.3)	4 (44.4)	73 (84.9)	
Positive	2 (2.9)	6 (85.7)	5 (55.6)	13 (15.1)	< 0.001
Total	70 (100.0)	7 (100.0)	9 (100.0)	86 (100.0)	

*By Fisher's exact test.

Discussion

Type I diabetic patients have shown to be at high risk to have other autoimmune disorders, like Autoimmune thyroid disease AITD which is considered as one of the most common coexisting autoimmune diseases in these patients. In this study a total of 86 type I diabetes patients were enrolled, among them we found that 16 patients had thyroid dysfunction in a rate of 18.6% which is a high rate compared to the general population. Furthermore, the distribution of this thyroid dysfunction revealed that 8.1% with overt hypothyroidism and 10.5% subclinical hypothyroidism. In a previous large study included 7097 children and adolescent with type I DM reported that a prevalence rate of 9.5%.[14] Sajid et al. reported in 2019 a rate of 11.1% for both clinical and subclinical hypothyroidism.[5] In this study, we didn't find any significant difference in the prevalence of thyroid dysfunction between both genders. According to the presence of thyroid dysfunction, this result is in agreement with that observed in a study by Elmenshawi et al. In this study 15.1% of patients had anti TPO

https://doi.org/10.56056/amj.2025.416

antibodies. [15] Also, in a study conducted by Orzan et al. it's mentioned that the thyroid autoimmunity is present among (T1DM). Among the participants, 18% were positive for thyroid antibody (anti-TPO).[16] The prevalence rates of anti TPO antibodies were high among patients with overt hypothyroidism (85.7%) and subclinical hypothyroidism (55.6%), compared with 2.9% among patients with normal thyroid function ($p < 0.001$) in our study, conversely, our findings are inconsistent with that reported by Franzese et al. who showed a prevalence of 16%.[17] In the current study 9.3% of patients had anti TSH receptor antibodies, however, the association between the presence of anti-TSH receptor antibodies and thyroid dysfunction was statistically insignificant, ($P>0.05$). In a study conducted by Unnikrishnan et al., the prevalence of positive TRAb alone was 18%, which is higher than our findings.[18] From other point of view, we did not report hyperthyroidism among our studied group. The absence of hyperthyroidism in the study might be due to various reasons, one of which could indeed be the relatively small number of subjects involved. Other reason may be due to the fact that some patients may not showed immediate symptoms of thyroid dysfunction despite they have anti-thyroid antibodies.[19] Hence, the clinical guidelines recommended assessment of thyroid function in children with TIDM. These guidelines included the American Diabetes Association and International Association of pediatric and Adolescent Diabetes.[20] Our study has two limitations; firstly, it is a single center study and the second is the small sample size, however, further studies are recommended that involve multiple centers and larger sample size to get more precise conclusions and findings.

Limitations

We regret to say that anti-thyroglobulin antibody, an important antibody in thyroid diseases, was not available at our center. Therefore, we could not test patients for anti-thyroglobulin antibody.

Conclusions

The available data consistently demonstrate a frequent occurrence of autoimmune thyroid disease among individuals diagnosed with Type I Diabetes Mellitus TIDM. Therefore, screening for thyroid dysfunctions and diseases among these patients is highly recommended with implementation of anti-TPO antibody testing for all patients with TIDM at the time of diagnosis and further regular periodical testing during follow-up of these patients to get timely management of these disorders.

Recommendation

We recommend routine screening for thyroid dysfunction and related conditions in patients with T1DM. Additionally, we advise that anti-TPO testing be conducted for all T1DM patients at the time of diagnosis, followed by regular testing during subsequent follow-ups.

Conflicts of interest

There are no conflicts of interest.

References

1. Karagüzel G, Şimşek S, Değer O, Ökten A. Screening of diabetes, thyroid, and celiac diseases-related autoantibodies in a sample of Turkish children with type 1 diabetes and their siblings. Diabetes Res Clin Pract. 2008;80(2):238-243.
2. Libman IM, Sun K, Foley TP, Becker DJ. Thyroid autoimmunity in children with features of both type 1 and type 2 diabetes. Pediatr Diabetes. 2008;9(4pt1):266-271.
3. Chatzigeorgiou A, Harokopos V, Mylona-Karagianni C, Tsouvalas E, Aidinis V, Kamper E. The pattern of inflammatory/anti-inflammatory cytokines and chemokines in type 1 diabetic patients over time. Ann Med. 2010 1;42(6):426-438.
4. Hage M, Zantout MS, Azar ST. Thyroid disorders and diabetes mellitus. J Thyroid Res. 2011;2011: 439463.

https://doi.org/10.56056/amj.2025.416

5. Sajid N, Riaz M, Fawwad A, Basit A. Thyroid dysfunction in subjects with type 1 diabetes at a tertiary care unit of Karachi, Pakistan. Clin Epidemiol Glob Health. 2019 1;7(3):435-438.
6. Tomer Y, Dolan LM, Kahaly G, Divers J, D'Agostino Jr RB, Imperatore G, et al. Genome wide identification of new genes and pathways in patients with both autoimmune thyroiditis and type 1 diabetes. J Autoimmun. 2015 1; 60:32-9.
7. Kahles H, Fain PR, Baker P, Eisenbarth G, Badenhoop K. Genetics of autoimmune thyroiditis in type 1 diabetes reveals a novel association with DPB1* 0201: data from the Type 1 Diabetes Genetics Consortium. Diabetes care. 2015 1;38(Suppl_2): S21-8.
8. Li CW, Osman R, Menconi F, Concepcion ES, Tomer Y. Flexible peptide recognition by HLA-DR triggers specific autoimmune T-cell responses in autoimmune thyroiditis and diabetes. J Autoimmun. 2017 1; 76:1-9.
9. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes care. 2014 1;37(Suppl_1): S81-90.
10. Hughes JW, Bao YK, Salam M, Joshi P, Kilpatrick CR, Juneja K, et al is quoted. Late-onset T1DM and older age predict risk of additional autoimmune disease. Diabetes Care. 2019 1;42(1):32-38.
11. Rydzewska M, Jaromin M, Pasierowska IE, Stożek K, Bossowski A. Role of the T and B lymphocytes in pathogenesis of autoimmune thyroid diseases. Thyroid res. 2018; 11:2
12. American Diabetes Association Professional Practice Committee, American Diabetes Association Professional Practice Committee: 2. Classification and diagnosis of diabetes: Standards of Medical Care in Diabetes—2022. Diabetes care. 2022 1;45 (Supplement_1): S17-38.
13. Surks MI, Chopra IJ, Mariash CN, Nicoloff JT, Solomon DH. American Thyroid Association guidelines for use of laboratory tests in thyroid disorders. JAMA.1990 16;263(11):1529-1532.
14. Reddy PA, Suresh V, Rajagopal G, Harinarayan CV, Raj N, Sachan A. Prevalence of thyroid autoimmunity in type 1 diabetes mellitus: thyroid autoimmunity in type 1 diabetes. Thyroid Res Pract. 2011: 1;8(3):7-11.
15. Elmenshawi I, Alotaibi S, Alazmi A, Alazmi A, Alruwaili F, Alazmi N, et al is quoted. Prevalence of thyroid dysfunction in diabetic patients. J Diabetes Metab Disord Control. 2017; 4:55-56.
16. Orzan A, Novac C, Mihaiela MI, Tirgoviste CI, Balgradean M. Type 1 diabetes and thyroid autoimmunity in children. Maedica. 2016 ;11(4):308.
17. Franzese A, Buono P, Mascolo M, Leo AL, Valerio G. Thyroid autoimmunity starting during the course of type 1 diabetes denotes a subgroup of children with more severe diabetes. Diabetes care. 2000 1;23(8):1201-.
18. Unnikrishnan AG, Kumaravel V, Nair V, Rao A, Jayakumar RV, Kumar H, et al. TSH receptor antibodies in subjects with type 1 diabetes mellitus. Ann N Y Acad Sci. 2006:1079:220-5. doi: 10.1196/annals.1375.034/
19. Kakleas K, Soldatou A, Karachaliou F, Karavanaki K. Associated autoimmune diseases in children and adolescents with type 1 diabetes mellitus. Autoimmun Rev. 2015;14(9):781-97. doi: 10.1016/j.autrev.2015.05.002/
20. American Diabetes Association. Standards of medical care in diabetes—2014. Diabetes care. 2014 1;37(Supplement_1): S14-80.