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Original Research Article

Thyroid dysfunction in children with type 1 diabetes mellitus: prevalence, patterns and clinical associations

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ABSTRACT

Background: To determine the prevalence and pattern of thyroid dysfunction in children with Type 1 diabetes mellitus, identify associated risk factors that predispose diabetic children to develop thyroid abnormalities and evaluate the impact on glycemic control.
Methods: This prospective observational study included 50 children with Type 1 diabetes mellitus attending a tertiary care centre. Clinical characteristics, including age, gender, duration of diabetes, other autoimmune diseases, family history of autoimmunity, along with metabolic parameters like HbA1c and daily insulin requirement, were recorded. Thyroid status was categorised as euthyroid antibody negative, euthyroid antibody positive, subclinical hypothyroidism, overt hypothyroidism and hyperthyroidism. Associations between thyroid status and clinical variables, glycemic parameters were analysed.
Results: Thyroid dysfunction was present in 9 children (18%): subclinical hypothyroidism in 4 (8%), overt hypothyroidism in 4 (8%) and hyperthyroidism in 1 (2%). Among the remaining children, 28 (56%) were euthyroid with negative anti–thyroid peroxidase antibodies, while 13 (26%) were euthyroid with positive antibodies. Thyroid dysfunction was significantly associated with longer duration of diabetes and the coexistence of other autoimmune disorders. Daily insulin requirement differed significantly across thyroid subgroups, whereas glycated haemoglobin levels were comparable between T1DM children with and without thyroid dysfunction.
Conclusions: Thyroid dysfunction is common in children with Type 1 diabetes mellitus, affecting nearly one-fifth of patients, with subclinical hypothyroidism being a frequent abnormality. Longer duration and presence of other autoimmune diseases increase the risk of thyroid dysfunction. Periodic routine thyroid screening in children with Type 1 diabetes mellitus is essential for early detection and optimal metabolic management.

Keywords: Autoimmune diseases, Glycated haemoglobin A, Hyperthyroidism, Hypothyroidism, Thyroiditis, Autoimmune

INTRODUCTION

Type 1 diabetes mellitus (T1DM) is a chronic autoimmune disorder caused by immune-mediated destruction of pancreatic β-cells, resulting in lifelong insulin dependence. Because of its autoimmune nature, T1DM is frequently associated with other autoimmune conditions like thyroid dysfunction, celiac disease, Addison's disease and pernicious anaemia, of which autoimmune thyroid disease (AITD) is the most common. The spectrum of thyroid disorders associated with T1DM includes subclinical hypothyroidism, Hashimoto's thyroiditis and Graves' disease. Early detection of thyroid disease in children with T1DM is clinically important as thyroid abnormalities have a detrimental impact on insulin sensitivity, metabolic control, growth and pubertal development.[1] The coexistence of T1DM and

hypothyroidism supports the presence of polymorphisms in some of the immune response regulatory genes, causing a more severe disease with stronger features of autoimmunity. The reported prevalence of thyroid dysfunction in children with T1DM varies widely in the literature. European studies report thyroid autoimmunity in approximately 15–25% of children with T1DM; Kordonouri et al observed thyroid autoantibodies in 21.6% while Mantovani et al reported AITD in 16.7% of affected children.[2,3]

Indian data, though limited, suggest a relatively higher burden of thyroid autoimmunity in our region. Menon et al reported anti-thyroid peroxidase antibody (TPO) positivity in 54.3% and anti-thyroglobulin antibody positivity in 31.4% of Indian children with T1DM, although overt thyroid dysfunction was present in only 2.9% of the cases.[4] These regional variations highlight the need for population-specific data to guide screening and follow-up strategies in children with T1DM.

Hypothyroidism and metabolic derangement in patients with T1DM form a vicious cycle affecting disease severity, as hypothyroidism has been shown to increase insulin resistance and impair glucose metabolism. On the other hand, metabolic derangement has been shown to depress the hypothalamic pituitary thyroid axis, thus impairing thyroid function.[5] The evidence on the impact of coexisting thyroid disease on insulin dose requirements and Glycated haemoglobin (HbA1c) in children with T1DM is inconsistent across studies.

Mohn et al reported no significant difference in HbA1c or insulin requirement between children with subclinical hypothyroidism and euthyroid controls with T1DM, but noted a higher frequency of hypoglycaemic episodes before diagnosis, which reduced after treatment.[6] On the other hand, Metwalley et al reported poorer glycaemic control, reflected by significantly higher mean HbA1c in children and adolescents with T1DM with coexisting thyroid abnormalities.[7]

Despite a significant burden of thyroid dysfunction reported globally in children with T1DM, data from Central India are lacking. Most existing studies evaluate thyroid involvement in T1DM as a binary outcome; however, data examining associations across distinct thyroid subcategories like euthyroid antibody positive, subclinical hypothyroidism, overt hypothyroidism and hyperthyroidism remain limited.

Its relationship with disease duration, glycemic control and insulin requirement in children is not well defined, particularly in resource-limited settings. The present study was undertaken to determine the prevalence of thyroid dysfunction in children and adolescents with T1DM in this region, identify associated risk factors that predispose diabetic children to develop thyroid abnormalities and evaluate the impact of different subcategories of thyroid problems on glycemic control.

METHODS

This prospective observational study was conducted over a period of eighteen months from June 2024 to November 2025 in the Paediatric Endocrinology clinic of a tertiary care centre in Central India after obtaining approval from the Institutional Ethics Committee.

Patients were enrolled consecutively at routine OPD visits. Clinical details were recorded at enrolment and relevant biochemical investigations were obtained either from existing records or advised and documented at subsequent follow-up visits.

Children less than 14 years of age diagnosed with T1DM and being treated at our centre during the study period were included after obtaining written informed consent from parents or legal guardians. Exclusion criteria were children with incomplete clinical or biochemical data, diabetes other than Type 1 (including Type 2 diabetes, monogenic, cystic fibrosis-related and drug-induced diabetes) and the presence of other coexisting chronic systemic illnesses known to affect metabolic control or thyroid function, such as sickle cell disease, thalassemia or malignancy.

Demographic and clinical details, including age, sex, age at diagnosis of T1DM, history of diabetic ketoacidosis (DKA) at presentation, duration of diabetes, family history of autoimmune diseases, presence of other autoimmune disorders and insulin dose (units/kg/day) were recorded using a structured case record form (CRF).

Anthropometry and detailed clinical examination were performed as part of routine care. Biochemical data included thyroid function tests (TFT–fT3, fT4, TSH) and anti-Thyroid Peroxidase Antibody (TPO), which were performed using the Siemens ADVIA Centaur XPT automated immunoassay system. Thyroid-stimulating hormone (TSH) was measured using a third-generation two-site sandwich chemiluminescent immunoassay employing capture and tracer monoclonal antibodies, while serum fT3, fT4 and anti-TPO antibodies were estimated using competitive chemiluminescent immunoassays. HbA1c at diagnosis of T1DM and latest HbA1c, defined as the most recent HbA1c measurement available within the preceding 3 months, were measured using ion exchange chromatography. All assays were performed with appropriate internal quality control measures at the study centre.

Thyroid status was categorised as euthyroid antibody negative, euthyroid antibody positive, subclinical hypothyroidism (elevated TSH with normal fT4), overt hypothyroidism (elevated TSH with decreased fT4) or hyperthyroidism (suppressed TSH with normal or increased fT4) and was also dichotomized as thyroid dysfunction absent (normal TFT irrespective of TPO status) or present (abnormal TFT) for specific analyses. All children received routine diabetes care, including

insulin dose titration, dietary counselling and diabetes education as per unit protocol. Children diagnosed with hypothyroidism or hyperthyroidism were initiated on levothyroxine or carbimazole, respectively, at age and weight-appropriate doses.

The sample size was calculated using the formula for prevalence estimation in observational studies, $n=Z^2P(1-p)/d^2$, where Z corresponds to the standard normal deviate at 95% confidence level (1.96), p is the expected prevalence (15%) and d is the absolute precision (10%).[8,9] The minimum required sample size was 48. All eligible patients presenting during the study period were consecutively enrolled, which were 51 in number; one patient was excluded due to incomplete data, resulting in a final sample size of 50.

Statistical analysis

Data were entered into a Microsoft Excel spreadsheet and subsequently analysed using Statistical Package for the Social Services (SPSS) for Windows, version 26.0 (IBM Corp., Armonk, New York, USA) software. Continuous variables were assessed for normality using the Shapiro-Wilk test and expressed as median with interquartile range (IQR). Distribution of continuous variables across categories was illustrated using box and whisker plots. Categorical variables were expressed as frequencies and percentages. Associations between categorical variables were analysed using the Chi-square test or Fischer's exact test, where applicable. A p value of <0.05 was considered statistically significant.

RESULTS

Fifty children (60% boys) with T1DM were included in the final analysis. The median age was 10.4 years (IQR, 5.4 years) and the median duration of diabetes was 2 years (IQR, 1 year). Thyroid dysfunction was present in 9 (18%) of the 50 children studied, out of which subclinical hypothyroidism and overt hypothyroidism were present in 4 each (8%), while 1 child was hyperthyroid (2%). Among the remaining 41 children (82%), 28 (56%) were euthyroid with negative anti-TPO antibodies and 13 (26%) were euthyroid with positive anti-TPO antibody status (Table 1).

While examining the association of thyroid dysfunction with demographic and clinical variables, no significant association was observed with age group (p=0.406) or gender (p=0.652).

Duration of diabetes was found to be significantly associated with thyroid dysfunction (p=0.049), with a higher prevalence observed in children with longer disease duration. The presence of other autoimmune diseases was strongly associated with thyroid dysfunction (p<0.001), while family history of autoimmune diseases did not show a significant association with thyroid dysfunction in our cohort (p=0.297) (Table 2).

Thyroid status was not found to be significantly associated with the presence of DKA at diagnosis of T1DM (p=0.525), HbA1c at diagnosis (p=0.858) or latest HbA1c (p=0.422) (Table 3). On the other hand, a significant association was observed between thyroid dysfunction and daily insulin requirement (p=0.015) (Table IV). The distribution of insulin requirement and HbA1c levels according to thyroid status is illustrated in Figure 1 and 2.

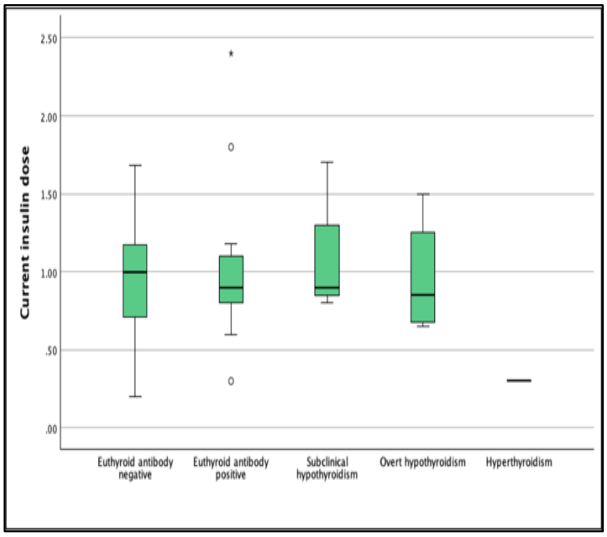

Figure 1: Distribution of current insulin dose according to thyroid status.

Box represents the interquartile range with the median shown as a horizontal line. Whiskers indicate the minimum and maximum values excluding outliers. Circles denote outliers and asterisks denote extreme values.

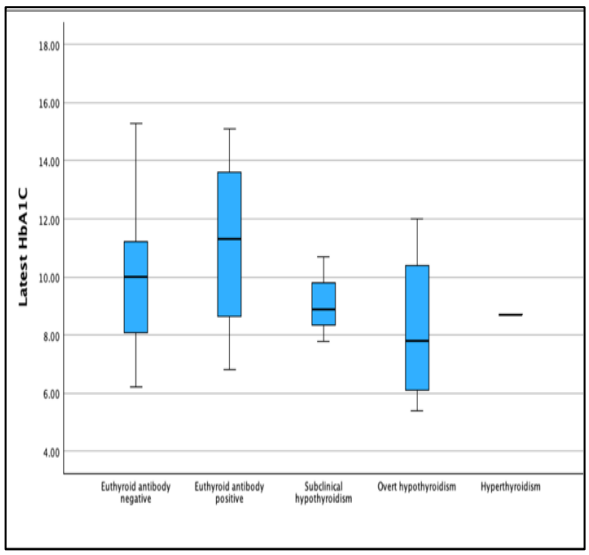

Figure 2: Distribution of latest glycated haemoglobin levels according to thyroid status.

Box represents the interquartile range with the median shown as a horizontal line. Whiskers indicate the minimum and maximum values excluding outliers.

Table 1: Pattern of thyroid function and thyroid autoimmunity in children with Type 1 diabetes mellitus (n=50).

		Number of patients (n=50)	(%)
Pattern of thyroid dysfunction	Euthyroid antibody negative	28	56.0
	Euthyroid antibody positive	13	26.0
	Subclinical hypothyroidism	4	8.0
	Overt hypothyroidism	4	8.0
	Hyperthyroidism	1	2.0
Thyroid dysfunction	Present	9	18.0
	Absent	41	82.0

Table 2: Association of thyroid dysfunction with demographic and clinical characteristics.

		Thyroid dysfunction		Total	P value
		Present	Absent		
Age group (in years)	0-5	0	6	6	0.406
	5-10	5	16	21	
	>10	4	19	23	
Gender	Male	6	24	30	0.652
	Female	3	17	20	
Duration of diabetes (in years)	0-2	4	18	22	0.049*
	2-4	0	16	16	
	4-6	3	4	7	
	6-8	2	2	4	
	>z8	0	1	1	
Other autoimmune diseases	Yes	6	4	10	<0.001*
	No	3	37	40	
Family history of autoimmune diseases	Yes	2	4	6	0.297
	No	7	37	44	

*p<0.05 considered statistically significant.

Table 3: Association of thyroid dysfunction pattern with glycemic control.

		Pattern of thyroid dysfunction					Total	P value
		Euthyroid antibody negative	Euthyroid antibody positive	Subclinical hypothyroidism	Overt hypothyroidism	Hyperthyroidism		
HbA1c at diagnosis	6-8	1	1	0	0	0	2	0.858
	8-10	5	2	1	1	0	9	
	10-12	6	3	0	1	0	10	
	12-14	5	1	1	0	1	8	
	>14	9	4	0	2	0	15	
	Missing	2	2	2	0	0	6	
Latest HbA1c	<6	0	0	0	1	0	1	0.422
	6-8	5	3	1	1	0	10	
	8-10	7	1	1	1	1	11	
	10-12	8	2	1	0	0	11	
	12-14	2	2	0	1	0	5	
	>14	3	3	0	0	0	6	
	Missing	3	2	1	0	0	6	

p<0.05 considered statistically significant

Table 4: Association of thyroid dysfunction pattern with insulin requirement.

Current insulin dose (U/kg/day)	Pattern of thyroid dysfunction					Total	P value
	Euthyroid antibody negative	Euthyroid antibody positive	Subclinical hypothyroidism	Overt hypothyroidism	Hyperthyroidism		
<0.5	1	1	0	0	1	3	0.015*
0.5 to 0.75	12	1	0	3	0	16	
0.75 to 1	4	5	3	0	0	12	

Continued.

Current insulin dose (U/kg/day)	Pattern of thyroid dysfunction					Total	P value
	Euthyroid antibody negative	Euthyroid antibody positive	Subclinical hypothyroidism	Overt hypothyroidism	Hyperthyroidism		
1 to 1.25	8	4	0	0	0	12	
1.25 to 1.5	2	0	0	0	0	2	
1.5 to 1.75	1	0	1	1	0	3	
1.75 to 2	0	1	0	0	0	1	
>2	0	1	0	0	0	1	
Total	28	13	4	4	1	50	

*p<0.05 considered statistically significant.

DISCUSSION

Thyroid dysfunction was observed in 18% of patients with T1DM, out of which subclinical and overt hypothyroidism were present in 8% each and hyperthyroidism was present in 2%. This prevalence is comparable to previously reported rates of thyroid dysfunction ranging from 7% to 40% across different populations.[2,3] The wide variation in prevalence reported in literature has been attributed to differences in ethnicity, iodine status, age at diagnosis, duration of diabetes and screening protocols.[10]

Thyroid autoimmunity, as inferred from positive Anti-TPO was present in 45.8% of T1DM patients in cohort. Mantovani et al reported thyroid autoimmunity in 16.7%.[3] In contrast, Menon et al reported a higher prevalence of thyroid autoantibody positivity (54.3%) in Indian children with T1DM, possibly reflecting genetic predisposition and increased autoimmune clustering in the Indian population.[4] This emphasises the importance of routine thyroid screening in children with T1DM, not only to detect overt abnormalities but also to identify early autoimmune thyroid involvement that may have long-term implications for disease severity and progression. In the present study, age and gender were not significantly associated with thyroid dysfunction. While several studies have reported a female predominance of AITD, others have failed to demonstrate a significant gender difference in paediatric T1DM cohorts.[3,4] This suggests that the autoimmune milieu associated with T1DM may attenuate the gender related differences usually seen in the general population.[11]

Duration of diabetes showed a significant association with thyroid dysfunction, with a higher prevalence observed in children with longer disease duration. Mantovani et al demonstrated a significantly increased risk of thyroid autoimmunity after nine years of diabetes duration, with similar findings also being reported in other longitudinal paediatric studies, supporting the role of cumulative autoimmune exposure over time.[3,12] The presence of other autoimmune disorders like celiac disease, vitiligo, autoimmune hepatitis, hypoparathyroidism and immune thrombocytopenic purpura in our cohort was significantly associated with thyroid dysfunction in children with T1DM. This finding reinforces the concept of shared genetic susceptibility and immune dysregulation underlying autoimmune polyglandular syndromes.[13] Previous studies have also shown that children with T1DM and coexisting autoimmune conditions are at a significantly higher risk of developing thyroid dysfunction.[11] Family history of autoimmune diseases did not show a statistically significant association in our cohort. This may be due to the complex polygenic inheritance and variable penetrance of autoimmune disorders.[14]

There are limited and conflicting data evaluating the course and metabolic control of T1DM in the presence of thyroid disease. The interaction between thyroid dysfunction and glycemic control in children with T1DM is complex. Hypothyroidism alters glucose homeostasis primarily by reducing hepatic gluconeogenesis and insulin clearance, thereby predisposing affected children to hypoglycaemia. In addition, children with coexisting AITD may harbour polymorphisms in immune-regulatory genes reflecting a stronger autoimmune predisposition that may contribute to greater metabolic instability. Consequently, the overall impact of hypothyroidism on glycemic control in children with T1DM remains heterogeneous and incompletely understood.[15]

DKA, as the initial presentation of T1DM, was not significantly associated with thyroid dysfunction in the present study. Shuhoub et al in his study on 212 children reported an increased risk of DKA as the presenting feature of T1DM in children with concomitant hypothyroidism, while Fernandez et al showed comparable DKA risk between patients with and without coexisting thyroid abnormalities.[16,17] This supports the notion that autoimmune thyroid involvement frequently occurs later in the disease course and may not play a major role during the initial presentation of T1DM. Early diagnosis of T1DM and prompt insulin therapy also negates the risk of DKA at presentation.

A key observation in this study was that the insulin dose showed a statistically significant association with thyroid status. However, despite statistical significance, it may not translate into meaningful clinical differences due to the small number of patients in certain thyroid subcategories. Authors did not find a significant association between HbA1c levels at T1DM diagnosis, as well as the latest HbA1c levels, with thyroid dysfunction, probably reflecting the minimal impact of treated thyroid disease on glycemic control. Mohn et al in a retrospective

assessment of 280 children, also did not observe a significant effect of hypothyroidism on HbA1c in children with T1DM.[6] However, Narasimhegowda et al found that children with abnormal thyroid function had higher mean HbA1c and higher daily insulin requirement.[8]

The findings of this study underscore the importance of routine thyroid screening in children and adolescents with T1DM at diagnosis and periodically during follow-up, as these patients can develop thyroid autoimmunity before, simultaneously with or after the development of islet beta cell autoimmunity, which has also been uniformly recommended by various international guidelines.[1,18] The strengths of the study include the assessment of thyroid autoimmunity and function with systematic correlation of different thyroid dysfunction categories with clinical variables and glycemic parameters.

However, limitations include its observational design, lack of correlation with thyroid antibody titres and absence of long-term follow-up to assess disease progression. Finally, the sample size, while adequate for estimating prevalence, may have been insufficient to detect subtle associations between thyroid dysfunction and selected variables. Larger longitudinal studies are required to determine the optimal frequency of screening and treatment thresholds in paediatric T1DM.

Thyroid dysfunction is a common comorbidity in children and adolescents with T1DM, occurring in approximately one-fifth of the affected children. Subclinical hypothyroidism is a frequently occurring abnormality, highlighting the importance of biochemical screening even in asymptomatic patients. Longer duration of diabetes and the presence of other autoimmune diseases were significant risk factors for thyroid dysfunction, whereas age, gender and family history of autoimmune diseases showed no significant association.

An association between thyroid dysfunction and insulin requirement was observed, but this warrants further evaluation in larger cohorts. HbA1c, which is also influenced by treatment adherence and dietary control in addition to metabolic factors, was not found to be associated with thyroid status. These findings emphasise the need for routine and periodic thyroid function screening in paediatric patients with T1DM. Assessment of thyroid autoantibodies, where feasible, will aid in identifying children at higher risk of progression to overt thyroid dysfunction.

CONCLUSION

Thyroid dysfunction is a common comorbidity in children and adolescents with T1DM, occurring in approximately one-fifth of the affected children. Subclinical hypothyroidism is a frequently occurring abnormality highlighting the importance of biochemical screening even in asymptomatic patients. Longer duration of diabetes and the presence of other autoimmune diseases were significant risk factors for thyroid dysfunction, whereas age, gender and family history of autoimmune diseases showed no significant association. An association between thyroid dysfunction and insulin requirement was observed but this warrants further evaluation in larger cohorts. HbA1c, which is also influenced by treatment adherence and dietary control in addition to metabolic factors, was not found to be associated with thyroid status. These findings emphasize the need for routine and periodic thyroid function screening in pediatric patients with T1DM. Assessment of thyroid autoantibodies, where feasible, will aid in identifying children at higher risk of progression to overt thyroid dysfunction.

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