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Prevalence of Thyroid Dysfunction among Children with Type I Diabetes Mellitus in Al-Ramadi Teaching Hospital for Maternity and Children, Anbar, Iraq

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ABSTRACT

Background: Thyroid dysfunction and type I diabetes mellitus (TIDM) often coexist. Many studies reported a higher prevalence of thyroid diseases among patients with diabetes. However, there is no local relevant study on this subject.
Objectives: To determine the prevalence of thyroid diseases among children with TIDM at Al-Ramadi Teaching Hospital for Maternity and Children.
Materials and methods: A cross-sectional study was conducted at Al-Ramadi Teaching Hospital for Maternity and Children from October 1, 2022, to May 1, 2023. Children aged 2-16 years of both sexes with TIDM who attended the hospital for any complaints were enrolled. All patients were screened for thyroid dysfunction.
Results: Of 190 children with TIDM, 25 (13.2%) had thyroid disorders. Children with thyroid dysfunction had significantly higher rates of parental consanguinity, diabetic ketoacidosis, hospital admissions, and chest infections (P-value < 0.05). Children with thyroid disorders had a significantly higher rate of positive anti-thyroid peroxidase and antithyroglobulin antibodies (P-value < 0.05). Glycated hemoglobin levels were significantly higher in children with thyroid dysfunction than in those with normal thyroid function. Glycated hemoglobin levels were significantly correlated with thyroid-stimulating hormone (P-value < 0.05).
Conclusion: Thyroid dysfunction is a common comorbidity in children with TIDM. Affected patients exhibit a higher rate of diabetic ketoacidosis, hospital admission, and chest infection.
Keywords: Thyroid dysfunction; Type 1 diabetes mellitus; Children; Adolescents.

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INTRODUCTION

Diabetes mellitus (DM) is defined by the World Health Organization (WHO) as a metabolic disorder characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both, leading to impaired metabolism of carbohydrates, fats, and proteins [1]. The development of DM involves various pathogenic mechanisms, including autoimmune destruction of β-cells of the pancreas and abnormalities that lead to insulin resistance [2].

The incidence of both type I and type II diabetes is increasing in pediatrics. However, type I diabetes mellitus (TIDM) remains the most common form diagnosed in pediatric patients, with its prevalence rising by 3-5% annually [3]. TIDM accounts for approximately 2% of all diabetes cases across all age groups, with prevalence rates reaching up to 15% in Northern European countries but remaining below 1% in Pacific populations [4].

A strong link exists between thyroid disease and diabetes. Several studies have reported an increasing frequency of thyroid disorders among children with DM [5]. The literature suggests that genetic factor plays a role in TIDM, making individuals more susceptible to other autoimmune disorders such as thyroid diseases, celiac disease, and adrenal insufficiency. According to previous studies, approximately 24% of TIDM patients develop hypothyroidism, while 27-44% test positive for antithyroid antibodies, indicating underlying autoimmune thyroid disorders [6].

Thyroid dysfunction and diabetes are among the most com-

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mon coexisting endocrine disorders. Several international studies have attempted to estimate the prevalence of thyroid dysfunction in diabetic patients, with reported rates ranging from 6.6% to 13.4% [7, 8]. While the prevalence of thyroid dysfunction in patients with TIDM tend to increase with age, it remains unclear whether the onset or duration of diabetes influences the risk [7]. In adults with TIDM, thyroid dysfunction occurs in 17-30% of cases, with a higher predisposition toward both autoimmune hypothyroidism and hyperthyroidism [9]. This association is linked to the presence of thyroid autoantibodies, such as thyroid peroxidase antibody (TPO Ab) and thyroglobulin antibody (TG Ab) [10].

Despite this well-established association, no relevant local studies have investigated the relationship between TIDM and thyroid dysfunction in Anbar Governorate, Iraq. Therefore, this study aimed to assess the prevalence of thyroid dysfunction among children with TIDM at Al-Ramadi Teaching Hospital for Maternity and Children.

MATERIALS AND METHODS

This cross-sectional study was conducted at Al-Ramadi Teaching Hospital for Maternity and Children, Ramadi City, Anbar, Iraq. The study was carried out over seven months, from October 1, 2022, to May 1, 2023. The study was approved by the Ethical Approval Committee of the University of Anbar (Reference number 159 on September 25th, 2022). Informed consent was obtained from the parents of each child.

Children and adolescents who were previously diagnosed with TIDM were included in the study. The diagnostic criteria for TIDM and diabetic ketoacidosis (DKA) depend on the International Society for Pediatric and Adolescent Diabetes (ISPAD). Eligible participants were aged 2-16 years of both sexes and had attended the hospital for any complaints. While those younger than 2 years or older than 16 years, taking medications which affect thyroid function or size (e.g. phenytoin, carbamazepine, aspirin, amiodarone, or thyroxine preparations), experiencing acute illness at the time of thyroid function testing, those with a history of thyroid surgery, those who used iodine therapy for hyperthyroidism, those who had thyroidectomy, and those who declined to participate were excluded from the current study.

The data was recorded from each patient through direct interview with the parents of children regarding the following: Age, sex, consanguinity, type and family history of autoimmune disease, environmental factors during early life, chronic diseases, first presentation for DKA and hyperglycemia, hospital admission, duration of diabetes, and diabetes treatment. The weight and height were calculated to estimate the (BMI) body mass index [BMI = weight (Kg)/square of height (m^2)].

A total of 8 ml of blood was drawn from each patient and distributed into two test tubes, one of them (gel tube) used for measuring anti-thyroid peroxidase (TPO) antibody, anti-thyroglobin (TG) antibody, thyroid-stimulating hormone (TSH), and thyroxine (T4) levels. While, The EDTA tube is used to measure the glycated haemoglobin (HbA1c) level. Serum TPO and TG antibodies were analyzed using Vidas (Serial No. vn05930, Italy) through an enzyme-linked immunosorbent assay (ELISA). The reference ranges (in agreement with the ranges suggested by the manufacturer) are 2.4-1000.0 IU/mL for TPO antibody, 6.4-800.0 IU/mL for TG antibody, 0.5-4.1 mU/mL for TSH, and 5-14 μg/mL for T4. Hypothyroidism is defined as an elevation of TSH and low T4, subclinical hypothyroidism is the elevation of TSH and normal T4, hyperthyroidism is low TSH and elevated T4, and subclinical hyperthyroidism is low TSH and normal T4 [11]. HbA1c was measured using the ion-exchange resin fast-separation with Mindray Bs230 (China) as an indicator of glycemic control. HbA1c levels were categorized as: Poor control of diabetes occurs when HbA1c is more than 10, fair control when HbA1c = 8-9.9, and good control when HbA1c = 6-7.9.

Data was analyzed using the statistical package for social sciences (SPSS) version 26 (IBM Corporation, Armonk, New York, USA). Descriptive statistics were used to summarize numerical variables, which were presented as mean, standard deviation, and standard error. Categorical variables were reported as frequencies and percentages. Pearson's correlation coefficient (r) was calculated to evaluate the strength and direction of the linear relationship between numerical variables. A Chi-square test was used to compare the categorical variables. A P-value less than 0.05 was considered a statistically significant difference.

RESULTS

The mean age of the participants was 7.84 ± 3.64 years, with an age range of 2-16 years. The highest proportion of cases (37.4%) was observed in the 5-8 years age group (71 children), while the lowest proportion (14.6%) was in the 13-16 years age group (28 children). There were 101 (53.2%) females, with a male-to-female ratio of 1:1.13. The majority of children (n = 173, 91.1%) had a normal weight. Parental consanguinity was reported in 27 children (14.2%). A family history of autoimmune disorders in first-degree relatives was noted in 27 children (14.2%). Of them, 24 (12.6%) had a family history of TIDM, and 3 (1.6%) had a family history of vitiligo. Additionally, 9 patients (4.7%) had a previous diagnosis of celiac disease, while one patient (0.6%) had a history of eczema. The initial clinical presentation of the disease was DKA in 110 children (57.9%). Hospitalization was required for 127 (66.8%), and 60 children (31.6%) experienced infections such as chest infections (n = 16, 8.4%). Among 190 patients with TIDM, 25 were diagnosed with thyroid dysfunction, resulting in a prevalence of 13.2%. Of these, 21 patients (84%) had overt hypothyroidism, while 4 patients (16%) had subclinical hypothyroidism. An analysis of thyroid status about demographic and clinical characteristics revealed that thyroid dysfunction was significantly (P-value < 0.05) associated with parental consanguinity, first clinical manifestation, hospital admission, and history of infections. Specifically, children with thyroid dysfunction had higher rates of parental consanguinity (29.6%, P = 0.006), DKA (18.3%, P = 0.014), hospital admissions (17.3%, P-value = 0.016), and chest infections (31.3%, P-value = 0.025). Conversely, other factors, including age, sex, BMI, family history of autoimmune disease, and past medical history, were not significantly associated with thyroid dysfunction (P-value > 0.05) as presented in Table 1.

Out of 190 children, 20 (10.5%) tested positive for anti-TPO antibodies. There was a statistically significant association between thyroid dysfunctions and anti-thyroid antibodies, with 95% of children with thyroid disorders testing positive for anti-TPO antibodies (P-value = 0.001). Regarding anti-TG antibodies, 30 children (15.8%) had positive results. The prevalence of thyroid dysfunctions was significantly higher among children with positive anti-Tg antibodies (60%, P-value = 0.001) as shown in Table 2.

Table 1. Distribution of the 190 patients with TIDM according to baseline characteristics and thyroid status*.

Patients characteristics	Thyroid status		Total, n = 190	P-value
	Dysfunction, n = 25	Normal function, n = 165		
Age (Years)				
2–4	5 (10.6%)	42 (89.4%)	47 (24.7%)	0.843
5–8	9 (12.7%)	62 (87.3%)	71 (37.4%)	
9–12	6 (13.6%)	38 (86.4%)	44 (23.2%)	
13–16	5 (17.9%)	23 (82.1%)	28 (14.7%)	
Sex				
Male	9 (10.1%)	80 (89.9%)	89 (46.8%)	0.242
Female	16 (15.8%)	85 (84.2%)	101 (53.2%)	
BMI Percentile				
Normal (5–84th)	21 (12.1%)	152 (87.9%)	173 (91.1%)	0.184
Overweight (85–94th)	4 (23.5%)	13 (76.5%)	17 (8.9%)	
Consanguinity				
Yes	8 (29.6%)	19 (70.4%)	27 (14.2%)	0.006*
No	17 (10.4%)	146 (89.6%)	163 (85.8%)	
Family History of Autoimmune Disease				
Yes	5 (18.5%)	22 (81.5%)	27 (14.2%)	0.374
No	20 (12.3%)	143 (87.7%)	163 (85.8%)	
Past Medical History				
Yes	3 (30%)	7 (70%)	10 (5.3%)	0.106
No	22 (12.2%)	158 (87.8%)	180 (94.7%)	
First Clinical Manifestation				
DKA	20 (18.3%)	89 (81.7%)	109 (57.4%)	0.014*
Hyperglycemia	5 (6.2%)	76 (93.8%)	81 (42.6%)	
Hospitalization				
Yes	22 (17.3%)	105 (82.7%)	127 (66.8%)	0.016*
No	3 (4.8%)	60 (95.2%)	63 (33.2%)	
Infections				
No	12 (9.2%)	118 (90.8%)	130 (68.4%)	0.025*
Chest Infection	5 (31.3%)	11 (68.7%)	16 (8.4%)	
UTI	8 (18.2%)	36 (81.8%)	44 (23.2%)	

* Significant difference between percentages using the Pearson Chi-square test at the 0.05 level. TIDM: Type I diabetes mellitus, DKA: Diabetic ketoacidosis; UTI: Urinary tract infection.

Table 2. Distribution of the 190 patients according to thyroid status and anti-thyroid antibody results*.

Anti-thyroid Antibodies	Thyroid status		Total, n = 190	P-value
	Dysfunction, n = 25	Normal function, n = 165		
Anti-TPO antibodies				
Positive	19 (95.0%)	1 (5.0%)	20 (10.5%)	0.001*
Negative	6 (3.5%)	164 (96.5%)	170 (89.5%)	
Anti-Tg antibodies				
Positive	18 (60.0%)	12 (40.0%)	30 (15.8%)	0.001*
Negative	7 (4.4%)	153 (95.6%)	160 (84.2%)	

* Significant difference between percentages using the Pearson Chi-square test at the 0.05 level. Anti-TPO antibodies: Thyroid peroxidase autoantibodies; Anti-Tg antibodies: Thyroglobulin autoantibodies.

There was a significantly (P-value = 0.001) higher mean HbA1c level in children with thyroid dysfunction than in those with normal thyroid function (Table 3).

In the Pearson correlation analysis, HbA1c levels showed a significant positive correlation with TSH (r = 0.409, P-value = 0.001). However, there was no significant relationship between HbA1c levels and T4 levels (P-value > 0.05) as shown in Table 4.

DISCUSSION

TIDM accounts for approximately 5-10% of all DM cases and results from an autoimmune attack on pancreatic beta cells [12]. Patients with TIDM have an increased risk of developing other autoimmune disorders, including Hashimoto's thyroiditis and Graves' disease [13]. Autoimmune thyroid disorders (AITD) are closely associated with TIDM, affecting 17-30% of individuals with the condition, increasing their susceptibility to both hypothyroidism and hyperthyroidism [14].

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Table 3. Comparison of HbA1c levels according to thyroid status of the study group*.

HbA1c (%)	Thyroid status		P-value
	Dysfunction Mean ± SD	Normal function Mean ± SD	
	8.29 ± 0.84	7.19 ± 1.06	0.001*

* Significant difference is at the P-value < 0.05 level. HbA1c: Glycated heamoglobin.

Table 4. Correlations of HbA1c with TSH and T4*.

Biomarker	TSH		T4	
	Correlation	P-value	Correlation	P-value
HbA1c	0.409	0.001*	- 0.093	0.203

* Correlation is significant at the P-value < 0.05. HbA1c: Glycated heamoglobin; TSH: Thyroid-stimulating hormone; T4: Thyroxine.

Among children with TIDM in this study, 13.2% were diagnosed with thyroid dysfunction (hypothyroidism and subclinical hypothyroidism). This prevalence differs from an Iraqi study, which has reported that a prevalence of overt hyperthyroidism with TIDM was found among 13.4%, overt hypothyroidism 51.2%, and subclinical hypothyroidism 34.1% [15]. Other studies have reported prevalences of thyroid dysfunction of 18% and 9.9%, respectively [15, 16]. Notably, children with TIDM are 24 times more likely to develop thyroid dysfunction than those without diabetes [17]. Differences in the reported prevalence across studies may be attributed to variations in population samples, age, ethnicity, study designs, and disease definitions (e.g., autoimmune, subclinical, and clinical hypothyroidism).

The current study aligns with the findings of Ridha et al.'s study, which reported that the most affected age group was 5-10 years (46%) [14]. A slight female predominance was observed in this study, which is consistent with previous studies [14, 15, 18].

This study aligns with the common belief that the consanguineous marriage carries a high risk of certain disorders (like TIDM) in future children. As such, the present study found that 12.6% had a family history of TIDM, while 1.6% had a family history of vitiligo. These findings differ from a study by Shuhoub et al., which reported that 63.7% of Egyptian patients had a positive family history of DM, 19.8% had positive consanguinity, and 8% had a family history of thyroid disease [18]. Other studies have also reported varying percentages [14, 15]. It is advisable to avoid consanguineous marriage in families with a high risk of autoimmune diseases.

In the current study, DKA was the first clinical manifestation in about 60% of children. Comparatively, Fatourechiet et al., found that DKA was the first presentation in 37.2% of TIDM patients [15], while Shuhoub et al. reported a prevalence of 40.1% [18]. Several factors might contribute to the variability in these results, including sample size, study design, disease severity, treatment type, comorbid conditions, educational level, ethnicity, and environmental differences. The higher presentation of DKA in kids with TIDM necessitates increasing awareness among parents to avoid such serious complications through keeping their eyes on the dietary restriction of high or rich glucose diets and regular checking of blood sugars, as well as avoiding missing or giving low doses of insulin.

The current investigation was consistent with other studies. These studies demonstrated the significant correlation between hypothyroidism and a higher incidence of DM in the first-degree relatives compared to TIDM patients without thyroid diseases [15, 19]. On the other hand, no significant association have found between thyroid dysfunction and family history of DM or consanguinity, but a significant association with DKA as a first presentation [18].

Sex is the factor that has not been significantly associated in TIDM children with thyroid dysfunctions, a finding supported by previous research [20]. Differences in sex associations across studies may be due to sample sizes, study designs, variations in laboratory measurement methods, different reference ranges, the presence of comorbid conditions, and disease duration. Routine screening for thyroid dysfunction is crucial for early detection in TIDM patients. The American Thyroid Association (ATA) currently recommends thyroid screening in children and adolescents with TIDM [21].

Our findings were nearly similar to other studies. A study reported that anti-TPO positivity was 17.3% and anti-TG positivity was 28% [14]. Similarly, Alomrani et al. found positive serum anti-TPO Ab in 15% of TIDM children, with no antibodies detected in the control group [22]. Several studies have reported varying anti-TPO antibody positivity rates in DM patients [15, 23]. Regarding thyroid antibody distribution, and glycemic control, a study observed a progressive increase in anti-TG titers with poor glycemic control, though the result was not significant (P-value = 0.15) [14]. In the case of hypothyroidism and its relationship with anti-TPO and anti-Tg antibodies, it was concluded that both antibodies have a significant correlation with chronic autoimmune hypothyroidism in about 52% of the patients [24].

Similar to our results, studies found that TIDM children with thyroid dysfunction had significantly higher HbA1c levels [15, 18, 25]. HbA1c levels were significantly correlated with TSH, whereas no significant association was found between HbA1c and T4 levels. In contrast, other studies have reported a negative correlation between TSH and HbA1c, with no significant correlation between HbA1c and T4 [25, 26].

This study has several limitations. Firstly, the small sample size was examined. Secondly, the cross-sectional design, which prevents establishing causal relationships. Lastly, a single-center study, which may not reflect broader population trends.

CONCLUSION

The prevalence of thyroid dysfunction in children with TIDM is a common problem. The thyroid dysfunction was included in this study were mainly due to hypothyroidism and subclinical hypothyroidism. Patients with thyroid dysfunction had a higher rate of DKA, hospital admission, and a higher rate of chest infection. Further large-scale and multicenter studies are recommended to further investigate the relationship between TIDM and thyroid dysfunction and validate these findings.

ETHICAL DECLARATIONS

Acknowledgments

None.

Ethics Approval and Consent to Participate

The study received approval from the Ethical Approval Committee of the University of Anbar (reference number: 159 on 25-9-2022). Informed consent was obtained from the parents of each patient.

Consent for Publication

Not applicable.

Availability of Data and Material

Data generated during this study are available from the corresponding author upon reasonable request.

Competing Interests

The authors declare that there is no conflict of interest.

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Authors' Contributions

All authors made significant, direct, and intellectual contributions to the design, implementation, and writing of this study. The authors have read and approved the final version of the manuscript.

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