مدى الإصابة بمرض قصور الغدة الدرقية بين المراهقين المصابين بداء السكري من النوع الأول

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الخلاصة:

داء السكري من النوع الأول هو أحد أمراض المناعة الذاتية التي قد تكون مرتبطة باضطرابات المناعة الذاتية الأخرى مثل اضطرابات الغدة الدرقية. ركزت هذه الدراسة على مدى انتشار قصور الغدة الدرقية لدى سبعين من المراهقين العراقيين المصابين بداء السكري من النوع الأول (T1DM) .تم اختيار المشاركين عشوائيا من المركز التخصصي للغدد الصماء والسكري (مستشفى الكندي) / بغداد من المرضى القادمين للمتابعة الدورية في عيادة السكري. الفئة العمرية ما بين 10 – 19 سنة (55.7% إناث و44.3% ذكور)، تم تحليل عينات المصل لقياس نسبة الجلوكوز في الدم الصائمF.B.G ، الهيموجلوبين السكريHbA1c ، C–peptide، ثلاثي يودوثيرونين T3، هرمون الغدة الدرقيةT4 ، هرمون الغدة الدرقيةTSH ، قياس مضاد بيروكسيديز الغدة الدرقية(anti–TPO)، وتم حساب (مؤشر كتلة الجسم) لكل مشارك. كشفت نتائج الدراسة أن 18.6% من المشاركين أظهروا ضعفًا في التحكم في نسبة السكر في الدم نسبة (HbA1c> 10%) ، وكانت نتيجة اختبار 42% منهم إيجابية للأجسام المضادة لـــTPO ، وأظهر 76% من العينات مستويات منخفضة من الببتيد C بالإضافة إلى ذلك، كان لدى 24.3% من المراهقين المصابين بداء السكري من النوع الأول مستويات عالية من هرمونTSH ، وأظهر 83% منهم أجسامًا مضادة إيجابية لـــ TPO. تشير الدراسة الحالية إلى أن داء السكري من النوع الأول قد يؤثر على الغدة الدرقية ومستويات هرموناتها، مما قد يؤدي إلى خلل في الغدة الدرقية. تم تشخيص إصابة 21.5% من مجموعة المراهقين المصابين بداء السكري من النوع الأول بقصور الغدة الدرقية. تتوافق هذه النتائج بشكل وثيق مع العديد من الدراسات السابقة؛ ومع ذلك، لم يتناول أي منها المراهقين فقط على وجه التحديد.

الكلمات المفتاحية: المراهقين، هرمونات الغدة الدرقية، مرض السكري من النوع الاول، الببتيد C, مضاد بيروكسيديز الغدة الدرقية، مؤشر كتلة الجسم.

The Incidence of Hypothyroidism in Adolescents with Type 1 Diabetes Mellitus

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Abstract

Type 1 diabetes mellitus is an autoimmune disease that may be related to other autoimmune disorders like thyroid disorders. This study focused on the incidence of hypothyroidism in seventy Iraqi adolescents with Type 1 diabetes mellitus (T1DM). The participants were selected randomly from the Specialized Center for Endocrinology and Diabetes (Al-Kindi Hospital) / Baghdad, attending regular follow-up appointments at the diabetes clinic. The age range is between 10- 19 years old (55.7% females and 44.3% males), serum samples were analyzed for Fasting blood glucose F.B.G., glycated hemoglobin HbA_{1c}, C- peptide, triiodothyronine T3, thyroxine T4, thyroid stimulating hormone TSH, anti-thyroid-peroxidase (anti-TPO) measurements, as well as, the body mass index (BMI) was calculated for each participant. The study results revealed that 18.6% of participants exhibited poor glycemic control (HbA1c > 10%), 42% tested positive for anti-TPO antibodies, and 76% displayed low C-Peptide levels. Additionally, 24.3% of type 1 diabetic adolescents had high TSH levels and 83% of them showed positive anti-TPO antibodies. Current study indicates that type 1 diabetes mellitus may impact the thyroid gland and its hormone levels, potentially leading to thyroid dysfunction. 21.5 % of the adolescent diabetic type 1 patient group were diagnosed with hypothyroidism. These findings closely align with numerous prior studies; however, none have specifically addressed adolescents.

Keywords: Adolescents, Thyroid hormones, Type 1 diabetes mellitus, C-Peptide, anti-thyroid-peroxidase, body mass index.

Introduction

Autoimmune thyroid disease (AITD) and Type 1 diabetes mellitus (T1DM) are two endocrine disorders that are closely related, Studies indicate that 15-30% of patients with type 1 diabetes mellitus (T1DM) also have autoimmune thyroid disease (AIT). [1,2] Diabetes mellitus is a group of metabolic disorders characterized by elevated blood sugar

levels (hyperglycemia). This condition results from problems with insulin secretion, its action, or a combination of both.[3]. The new Classification for DM has been proposed by the American Diabetes Association (ADA) and the World Health Organization (WHO). There are many types of diabetes: TIDM, T2DM, gestational diabetes, and other specific types. Impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) are stages of disordered carbohydrate metabolism. [4,5]. Type 1 diabetes mellitus (T1DM) is characterized by a complete deficiency of insulin resulting from an autoimmune attack on the pancreatic beta cells. This autoimmune response leads to the infiltration of the islets of Langerhans by activated T lymphocytes, a condition known as insulitis. Over time, this sustained immune attack causes a gradual reduction in the population of beta cells, ultimately resulting in absolute insulin deficiency. The loss of beta cells can be caused by autoimmune diseases, viral infections, or, in rare instances, genetic factors.[6-8] . Markers indicating immune destruction of B-cells include islet cell autoantibodies and autoantibodies to insulin. The rate of B-cell destruction varies significantly; it tends to be rapid in some individuals, particularly infants, children, and adolescents, while in others, especially adults, it occurs more slowly. [9,10]. According to a report by the World Health Organization (WHO) in 2024, adolescence is the phase of life between childhood and adulthood, specifically spanning ages 10 to 19. In this age group, some patients with T1DM, particularly children and adolescents, may experience ketoacidosis as the first indication of the disease. Others might demonstrate mild fasting hyperglycemia, which can quickly escalate to severe hyperglycemia and/or ketoacidosis, especially in response to infections or other sources of stress. [11,12] Type 1 diabetes has many effects on the hypothalamus -pituitary-gonadal axis, particularly if the disease is poorly controlled [13]. Griffin et al. noted that the onset of diabetes before puberty can disrupt the hypothalamic-pituitary-gonadal axis. This disruption may delay ovarian maturation and the production of sex hormones. Additionally, diabetes can lead to weight loss, which reduces body fat that is crucial for menarche to occur.[14]. Hypothyroidism may be due to thyroid failure (primary), pituitary failure (secondary), or hypothalamic failure (tertiary). Primary hypothyroidism with reduced circulating thyroid hormone results in an increased production of thyroid-stimulating hormone (TSH) by the pituitary [15] T3 and T4 are synthesized in the thyroid gland and released into blood circulation. The thyroid gland is the only source of T4 and

20% of T3, the other 80% of T3 being generated in peripheral tissues from T4 [16]

Subjects and methods

Inclusion criteria: This study was conducted between 2024 and 2025. Seventy adolescent subjects with type 1 diabetes attending regular follow-up appointments at the diabetes clinic were selected from The Specialized Center for Endocrinology and Diabetes, the group consists of individuals aged between 10 and 19 years, including 39 females and 31 males (mean age value= 13.65±3.2,), as control group, twenty-five subjects were selected to match the age of those in the studied group (mean age value= 14.72±4.1). The local ethics committee of the Specialized Center for Endocrinology and Diabetes approved the study, as well as, all participants' parents.

Methods

A sufficient amount (6-10 ml) of venous blood was obtained from adolescent participants with type 1 DM. The fasting blood glucose (F.B.G.) was measured using the procedure provided by the Randox reagent kit manufacturer, and glycated hemoglobin HbA_{1c} was calculated using the Variant Hemoglobin A_{1c} program developed by BIO-Rad. Thyroid Stimulating Hormone TSH, total Thyroxine T_4, and Triiodothyronine T_3 were estimated by Micro ELISA redder Biokit (U.S.A). Serum anti-thyroid peroxidase (TPO) antibodies were assessed using AESKU Diagnostics a-TPO kits from Germany. This solid-phase enzyme immunoassay employs recombinant technology., the Normal range for anti-TPO antibody was less than 40 IU/ ml, borderline (40-60) and the positive result was > 60 IU/ml. and C peptide levels were estimated by using Mercodia C-peptide ELISA (UK).

Statistical Analysis: The data analyzed by Duncan's multiple range test at ($p < 0.05$) was considered statistically significant, and classified as highly significant when ($p < 0.001$), using SPSS software version 24. All analyses were conducted three times.

Results and Discussion

Seventy adolescent subjects with type 1 diabetes aged from 10 to 19 years and twenty-five age and sex-matched controls were included in the study **(Table 1)**. No notable differences were observed between groups in age and sex regarding the demographic characteristics of the study population. The distribution of the groups being studied based on BMI (kg/m2) based on WHO presents no significant difference ($p > 0.05$), and 54.3% of the diabetic adolescents' group had normal B.M.I values (Table 2). The

results in **(Table 3)** indicated highly significant differences ($p<0.001$) in F.B.G concentrations (227.1±24.3 mg/dl) in comparison with the control group, notably highly significant differences also were obtained in HbA_1c % 8.2±2.8, C-peptide 0.87±0.24 ng/ml, thyroxine hormone T_4= 61.45±11.50 nmol/L, and Anti-TPO 53.5±21.3 IU/ml respectively. While no significant differences ($p >0.05$) were obtained in TSH= 4.12±1.1 and T_3= 2.13±0.88 concentrations. The results of Anti-TPO show that 42% of patients have tested positive, 8 (11.4%) of patients exhibited poor glycemic control (HbA1c > 10%) at Anti-TPO levels of more than 60 IU/ml, while 17 (56.7%) of the adolescent diabetic group considered good glycemic control at Anti-TPO levels less than 40 IU/ml, and 30 (42%) of the patients' group had Anti-TPO positive levels (of more than 60 IU/ml) **(Table 4)**. The results in **(Table 5)** illustrate the distribution of thyroid hormone concentrations according to Anti- TPO levels, 24.3 % of adolescent diabetic patients had been high TSH concentrations, and 83% of them diagnosed with a positive value of anti-TPO antibodies, while 30% had low or normal T4 concentrations.

Table 1: Distribution of studied groups based on age, gender, duration of DM, and the age at onset of diabetes type 1

Variables	Type 1 Diabetic group (No.70)	Control group (No.25)	*P*-Value
Age	13.65±5.1	14.72±4.3	NS
Sex (female/male)	39/31 (55.7%) ♀ (44.3%) ♂	15/10	NS
Duration of DM (range)	7.27±2.4 (1-16)	-	-
Age at DM onset	6.34±3.2 (1-12)	-	-

NS: Not Significant

Table 2: Distribution of the studied groups based on their body mass index (BMI) (kg/m2) according to WHO 2024 [17]

BMI	Type 1 Diabetic group		Control group		*P*-Value
	No.	%	No.	%	
Underweight <18.5	10	14.3	0	0	-
Normal weight 18.5-24.9	38	54.3	19	76.0	0.543
Overweight 25-29.9	14	20.2	6	24.0	0.654
Obese ≥30	8	11.2	0	0	-
Total	**70**	**100**	**25**	**100**	

Table 3: Summary statistic table for the studied clinical parameters as compared by groups using t-test

Variables	Type 1 Diabetic group (No.70)	Control group (No.25)	*P*-Value
F.B.G. mg/dl	227.1±24.3	93.5±11.9	0.000
HbA_1c %	8.2±2.8	4.9± 0.8	0.000
C- peptide ng/ml	0.87±0.24	2.82±1,33	0.000
TSH mIU/ml	4.12±1.1	2.66±0.62	0.062
T3 nmol/L	2.13±0.88	2.21±0.39	0.765
T4 nmol/L	61.45±11.50	125.53±13.36	0.000
Anti-TPO IU/mL	53.5±21.3	23.4±7	0.000

Table 4: Summary statistic table for Anti- TPO in adolescents' diabetic groups according to HbA_{1c} % using F-test

		Glycated Hemoglobin A_{1c}						P-Value LSD (F-test)
		Good glycemic control		Fair glycemic control		Poor glycemic control		
		No.	%	No.	%	No.	%	
Anti-TPO IU/ml	**<40**	17	56.7	5	18.5	4	30.8	0.000
	borderline (40-60)	8	26.7	5	18.5	1	7.7	0.000
	> 60	5	16.6	17	63	8	61.5	0.000
		30	100%	27	100%	13	100%	

Table 5: Summary statistic table for Anti- TPO in adolescents' diabetic groups according to thyroid hormones

		Thyroid Hormones					
		TSH		T4		T3	
		Low or Normal No. (%)	High No. (%)	Low or Normal No. (%)	High No. (%)	Low or Normal No. (%)	High No. (%)
Anti-TPO IU/ml	**<40**	24 (34.3)	2(2.9)	25(35.7)	4(5.7)	31(44.3)	1(1.4)
	borderline (40-60)	13(18.6)	1(1.3)	11(15.7)	0(0.0)	5(7.1)	3(4.3)
	> 60	16(22.9)	14(20)	21(30)	9(12.6)	24(34.3)	6(8.6)
		70(100%)		70 (100%)		70(100%)	

In type 1 diabetes mellitus (T1DM), insulin deficiency arises from the autoimmune destruction of pancreatic beta cells. Insulin is crucial for the metabolism of carbohydrates and fats. Weight loss in T1DM occurs due to the body's inability to metabolize glucose combined with the lack of insulin, which

causes the body to metabolize its fat reserves for energy.[18] In common adolescents and children with T1DM are either at the lower end of the normal range or underweight [19] Contrary to traditional clinical teaching recent studies indicate that children with T1DM often have body mass index BMI equal to or higher than the general population [20], our results show that most diabetic participants had normal and overweight BMI, this agrees with Manyanga et al study in 2016 which stipulated: (Not as skinny as we used to think body mass index in children and adolescents with T1DM) [21] Diabetic adolescents with T1D display a high risk of developing diabetes-related complications, the risk increases markedly as glycated hemoglobin (HbA1c) increases. (18.6%) were poor glycemic control in the studied patients' group, these adolescents with diabetes showed a below-average quality of life-related to their health [22].

The present statistical results illustrated that a high incidence of low C-peptide levels (76%) in studied participants was found substantiating that adolescent patients have type 1 diabetes. A significant correlation was found between C-peptide levels and diabetes classification and diagnosis [23]

This study aimed to figure out the connection between thyroid hormone levels and type 1 diabetes in adolescents aged 10 to 19 years. the results indicated that adolescents with T1DM had higher levels of anti-TPO antibodies than the healthy group. There are significant correlations between thyroid autoantibodies and the risk of thyroid dysfunction in patients with Type 1 diabetes. Additionally, it has been shown that Type 1 Diabetes Mellitus (T1DM) is strongly associated with autoimmune disorders. [14,24] The high incidence of autoimmune disorders in these patients remains unclear. It may stem from a change in response to specific antigens, a genetic inability to develop tolerance to autoantigens, or common antigens found in persons who are sensitive to these diseases [25] Thyroid-stimulating hormone is a frequently ordered blood test that acts as a highly sensitive marker for primary hypothyroidism. The current results closely align with studies conducted on Egyptian and Iraqi adults in 2010 and 2016, respectively [26,27]. No significant difference in T3 and TSH levels between the studied groups was found. It agrees with a study conducted in India, in 2008 by Palanisamy et al [28]. Muneera Fadhil Ridha et al. in 2019 found that “TSH concentration was high in 16% of the studied patients and all of them had positive autoimmunity”, in our study TSH concentration was high in 24.3% and 83% of them had positive auto anti-TPO [29].

This is consistent with other literature indicating that autoimmune disorders typically produce signs of hypothyroidism (such as Hashimoto's thyroiditis) and, less frequently, signs of hyperthyroidism (like Graves' disease or the hyperactive phase of Hashimoto's thyroiditis).[30]

Conclusion

The screening for hypothyroidism in adolescents with type 1 diabetes involves various factors, including the age of diabetes onset, the duration of diabetes, glycemic control levels, body mass index, and the presence of anti-TPO antibodies. The correlation between T1DM and thyroid diseases is candid; however, based on the factors analyzed in this study, there is a need for more scientific explanations and research involving larger sample numbers.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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