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Research Article

Hypothyroidism in Saudi patients with type 1 Diabetes Mellitus

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ABSTRACT

Background and objective: The associations between type 1 diabetes mellitus (T1DM) and hypothyroidism (HT) have long been reported. Thus, we conducted a cross sectional study to find out the prevalence of HT in patients with T1DM.

Design:A "cross-sectional study " was conducted in the Diabetes center at King Fahad Armed Forces Hospital, Jeddah, Saudi Arabia from January 2018 to March 2019. Thyroid stimulating hormone (TSH), free thyroxin (FT4) and HbA1c were measured.

Results: A total of 124 (50.6%) patients with T1DM and 121 (49.4%) patients with no history of T1DM as control group were included in this study. Average age of patients with of T1DM compared to patients without T1DM was statistically non-significant (15.6±2.1 and 16.1±1.9 respectively, p=0.2). There was statistically non-significant more frequent of females compared to males in patients with T1DM (54% vs. 46%) p=0.8. Mean of TSH was statistically non-significant different in patients with T1DM when compared with those withoutT1DM (3.6±7.5 vs. 3.5±14.7 respectively) p=0.9.

There was a statistically significant higher prevalence of HT among T1DM (16.1% vs. 6.6%) p=0.03. Mean age of diabetic patients with HT compared to patients without HT was statistically non-significant (15.6 ±2.6 and 16.0±1.9 respectively, p=0.4). There was statistically non-significant more frequent of females compared to males in diabetic patients with HT (70% vs. 30%) p=0.2. Mean TSH was statistically non-significant different in diabetic patients with than without HT (13.0 ±15.8 vs. 2.7 ±10.7 respectively) p<0.0001.

In addition, there was statistically non-significant different between diabetic patients with and without HT (13.0 ±2.4 vs. 13.8 ±3.2 respectively) p=0.4. Mean HbA1c was statistically non-significant different between diabetic patients with than without HT (8.6 ±2.5 vs. 8.3 ±1.8 respectively) p=0.4.

Using a multivariate regression model, age, gender and HbA1c were the independent predictors of diabetic patients with HT. In the constructed model, we found that age, gender and HbA1c were statistically non-significant to be independent predictors of diabetic patients with HT.

Conclusion: The frequency of primary hypothyroidism was high with poor glycemic control in patients with T1DM.

Keywords: Cell wall; Ionic liquid;Polysaccharide; Wood.

Introduction

Diabetes mellitus (DM) and thyroid diseases are common endocrine disorders. They have been shown to influence each other and associations between both conditions have long been reported[1,2].

Insulin and thyroid hormones are being intimately involved in cellular metabolism, excess or deficit of either of these hormones could result in functional derangement of the other[3]. As such, the fact that insulin and thyroid hormone influence each other's actions assumes great significance.

Thyroid disorders are highly prevalent in the general population while the reported prevalence of hypothyroidism (HT) among general pediatric population is 0.1 to 2%[4-6].

The immune-mediated destruction of pancreatic islet cells causes type 1 diabetes mellitus (T1DM). Autoimmune thyroid disorders (AITD) and T1DM have a common genetic background and similar pathogenesis; hence, they could occur in the same individual or family[7].AITD are the most prevalent immunological diseases in patients with T1DM[1-4,8].

Nearly one third of all newly detected T1DM patients have co-existent AITD and a high prevalence of thyroid dysfunction which is predominantly HT[1-4,8-10].

HT is prevalent among pediatric patients with T1DM; the prevalence of hypothyroidism in patients with T1DM is much higher ranging from 3 to 30%[11,12].A collaborative study of the AASGPED-Alpe Adria Study Group of Pediatric Endocrinology and Diabetology showed in a cross-sectional study involving 1419 children with T1DM, where 3.5% had Hashimoto's thyroiditis[13].

Cross-sectional studies have reported a prevalence of HT in 12–24% of female and 6% of male patients with T1DM[1-2,8,14]. The Kingdom of Saudi Arabia (KSA), which is the largest country in the Middle East that houses approximately four-fifths of the Arabian Peninsula, supports a population of more than 33 million people, of whom 26% are aged < 14 years[15].

Studies indicate, in the recent decades, a significant increase in prevalence and incidence rates of T1DM in different cities of KSA, mainly among the children and adolescents[16,17]. Thus, it becomes imperative to study interrelationship between the two entities[18].

Therefore, the aim of this study was to evaluate the prevalence of HT in patients with T1DM.

Materials and Methods

This cross-sectional study was performed in Jeddah, KSA between January 2018 to March 2019. T1DM was diagnosed by physicians based on American Diabetes Association criteria and matched for age and sex patients with no history of T1DM were analyzed as the control group[19].

Patients enrolled into the study were between 12 to 19 years old and had a health profile in King Fahad Armed Forces Hospital with regular attending to the diabetes center. Individuals with history of recent or acute illness and history of taking drugs affecting thyroid function were excluded.

Thyroid stimulating hormone (TSH) was measured with a chemiluminescent immunoassay method (CMIA) (Architect i2000 system, Abbott, USA). Serum free thyroxine (FT4) was estimated by radioimmunoassay.

The assays have intra- assay precision of 4.3%. TSH levels between 0.22-4.2 mIU/L and Free T4 12.0-22.0 pmol/L were regarded normal[20].Hypothyroidism was defined as elevated TSH >4.2 mIU/l[21]. HbA1c was measured with high performance liquid chromatography and expressed as percentage.

The study was approved by the ethical board of King Fahad Armed Forces Hospital.

Statistical Analysis

Data are presented as means ± standard deviation (SD) or numbers (%). Quantitative variables were compared between two groups by using the Student's test. Differences in categorical variables were analyzed using the chi-square test.

Logistic regression analysis was carried out to identify the independent predictors of T1DM with HT considering age, gender and HbA1c as risk factors and to estimate odds ratio (OR) and 95% CI. P value <0.05 indicates significance.

The statistical analysis was conducted with SPSS version 23.0 for Windows.

Results

A total of 124 (50.6%) patients with T1DM and 121 (49.4%) patients with no history of T1DM as control group were included in this study. Average age of patients with T1DM compared to control was statistically non-significant (15.6±2.1 and 16.1±1.9 respectively, p=0.2) (Table 1).

There was statistically non-significant more frequent of females compared to males in patients with T1DM (54% vs. 46%) p=0.8. Mean of TSH was statistically non-significant different in patients with T1DM when compared with those withoutT1DM (3.6±7.5 vs. 3.5±14.7 respectively) p=0.9.

Table 1: Demographic characteristics of patients with and without type 1 diabetes [mean±standard deviation or number (%)].

Parameters		Type 1 diabetes	Non-Type 1 diabetes	P value
Numbers		124 (50.6)	121 (49.4)	
Age (years)		15.6±2.1	16.1±1.9	0.2
Gender	Male	57 (46)	58 (47.9)	0.8
	Female	67 (54)	63 (52.1)	
TSH (mIU/l)		3.6±7.5	3.5±14.7	0.9
FT4 (pmol/l)		13.5±2.4	13.8±3.6	0.5
Hypothyroidism		20(16.1)	8(6.6)	0.03

There was a statistically significant higher prevalence of HT among T1DM in comparison to control group (16.1% vs. 6.6%) p=0.03.

(Table 2) showed the clinical and biochemical characteristics of patients with T1DM with and without HT. Compared patients with T1DM with and without HT.

Table 2: Clinical characteristics of patients with type 1 diabetes with and without hypothyroidism [mean±standard deviation or number (%)].

Parameters		Type 1 diabetes		P value
		with hypothyroidism	without hypothyroidism	
Numbers		20 (8.2)	225 (91.8)	
Age (years)		15.6 ±2.6	16.0 ±1.9	0.4
Gender	Male	6 (30)	109 (48.4)	0.2
	Female	14 (70)	116 (51.6)	
HbA1c (%)		8.6 ±2.5	8.3 ±1.8	0.4
TSH (mIU/l)		13.0 ±15.8	2.7 ±10.7	<0.0001
FT4 (pmol/l)		13.0 ±2.4	13.8 ±3.2	0.4

Mean age of diabetic patients with HT compared to patients without HT was statistically non-significant (15.6 ±2.6 and 16.0±1.9 respectively, p=0.4).

There was statistically non-significant more frequent of females compared to males in diabetic patients with HT (70% vs. 30%) p=0.2. Mean TSH was statistically non-significant different in diabetic patients with than without HT (13.0 ±15.8 vs. 2.7 ±10.7 respectively) p<0.0001.

In addition, there was statistically non-significant different between diabetic patients with and without HT (13.0 ±2.4 vs. 13.8 ±3.2 respectively) p=0.4. Mean HbA1c was statistically non-significant different between diabetic patients with than without HT (8.6 ±2.5 vs. 8.3 ±1.8 respectively) p=0.4.

In order to identify the independent factors affecting diabetic patients with HT, a multivariate regression model was constructed using diabetic patients with HT as the dependent factor.

The constructed model is shown in table 3. Age, gender and HbA1c were the independent predictors of diabetic patients with HT.

In the constructed model, we found that age, gender and HbA1c were statistically non-significant to be independent predictors of diabetic patients with HT; female gender (OR: 2.377, 95% CI: 0.850-6.650, P=0.1), age (OR: 1.064, 95% CI: 0.846-1.339, P=0.6) and HbA1c (OR: 0.908, 95% CI: 0.695-1.188, P =0.5).

Table 3: Regression analysis using type 1 diabetes with hypothyroidism as the dependent variable.©

Parameters	Coefficients	Standard error	Expo(B)	95% CI	P value
Age (years)	0.062	0.117	1.064	0.846-1.339	0.6
Gender	0.886	0.525	2.377	0.850-6.650	0.1
HbA1(%)	-0.096	0.137	0.908	0.695-1.188	0.5

Conclusion

Diabetes mellitus and thyroid disorders are two of the most common endocrine disorders[1,2]. An association between diabetes and thyroid disease has long been recognized, although the reported prevalence of HT in diabetic populations varies widely between studies[1,2,5,6,8,13,14,18,22-25].

Functional impairments of thyroid glands, especially HT, have been promulgated to be more common amongst diabetes mellitus patients. In the current study, HT was a prevalent problem among patients with T1DM, complicating 16.1% of these patients.

This was higher than other studies; based on a 2010 review 3–8% of pediatric patients with T1DM have been reported to develop HT.11 The NHANES III reported a prevalence of HT in 4.6% of the U.S. population[26].

While a recently published review and a meta-analysis reported a much higher rate of 7–30% for the prevalence of hypothyroidism in patients with T1DM[12,27].

The heterogeneity in the reported prevalence of HT in these studies could be due to the variable population characteristics including age and ethnicity of patients, the differences in study design including the cut-off levels and classification of the disease with different definitions including autoimmune, subclinical, and clinical hypothyroidism[11,12,27].

Recent studies have revealed some genes that might be responsible for the joint susceptibility to T1DM and autoimmune thyroid dysfunction; HLA class II loci, CTLA4, INS, PTPN22, and FOXP3, are among the identified genes.

These genes have been recognized as the key role players in the regulation of the immune response; these genes are involved in the differentiation, regulation, activation and function of regulatory T-cells, and their polymorphism have been linked to a number of autoimmune diseases including T1DM and AITD[28-35].

Although there is general agreement that the high prevalence of HT in T1DM subjects justifies screening in all patients, it is not clear which is the best procedure and how often to perform it[36,37].

The American Diabetes Association, International Society for Pediatric and Adolescent Diabetes and several authors recommend annual screening for thyroid disease in all T1DM subjects with TSH measurement[38-40].

The mean age of patients of T1DM with HT was 15.6 ±2.6 years and 16.0 ±1.9 years for patients with T1DM without HT (p=0.4). The logistic regression of patients of T1DM with HT versus patients with T1DM without HT on age, gender, and HbA1c level were statistically non-significant predictors of HT in the multivariable model (p=0.6, p=0.1, and p=0.5 respectively).

In this study, the female patients with T1DM were predominated versus male group. Patients who were females were 2.4 times as likely to develop HT as patients who were without HT (95% CI 0.850-6.650), controlling for age and HbA1c (p=0.1).

It was just like the previous research from brazil and inconsistent to other two studies from KSA where the male patients were dominant[41-43].

Cross-sectional studies have reported a prevalence of HT in 12–24% of female and 6% of male patients with T1DM[1,2,8]. However, gender bias may happen[44].

The difference in sex hormones may partly explain the sex-difference in the relationship between thyroid hormone levels[45]. However, because levels of sex hormones such as testosterone and estrogen were not measured in this study, further research is needed to explore this issue. In addition, because the sample size was smaller for males (30%) than in females (70%), the precision and statistical power of the analysis may be lower for males.

We aimed to identify the prevalence of HT in patients with T1DM in Saudi patients in hospital-based health care setting. In our study, the observed population reflects a selected yet comprehensive group of patients rather than the general population.

This study had limitations stemming from its small sample size and cross-sectional study design and therefore may underestimate the true prevalence of HT in patients with T1DM. Prospective longitudinal studies with more patients would be needed to characterize the prevalence of HT in patients with T1DM.

In conclusion, our results showed that HT occurred more

frequently in patients with T1DM females. Therefore, regular screening of thyroid function may be considered in all T1DM patients. In the absence of registry data, larger cooperative studies involving diverse population samples from multiple centers could help to provide further information on the true relation nationally.

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References

1. Feely J, Isles TE (1979) Screening for thyroid dysfunction in diabetics. Br Med J 1:1678. Link: https://urlzs.com/VnmY8
2. Gray RS, Irvine WJ, Clarke BF(1979)Screening for thyroid dysfunction in diabetic's British medical journal 2: 1439. Link: https://urlzs.com/Cp6FS
3. Satish R, Mohan V(2003) Diabetes and thyroid disease: a review. Int J Diab Dev Countries 23: 120-123. Link:https://urlzs.com/goJbK
4. Wang C, Crapo LM (1997) The epidemiology of thyroid disease and implications for screening. Endocrinol Metab Clin North Am 26:189–218. Link: https://urlzs.com/sXGAw
5. Hunter I, Greene SA, MacDonald TM, Morris AD(2000) Prevalence and etiology of hypothyroidism in the young. Arch Dis Child 83: 207–210. Link: https://urlzs.com/Z2iAL
6. Shriraam M, Sridhar M(2014) Subclinical hypothyroidism in children. Indian Pediatr 51: 889–895. Link: https://urlzs.com/5GzJz
7. Kahaly GJ, Hansen MP(2016) Type 1 diabetes associated autoimmunity. Autoimmun Rev 15: 644-648. Link: https://urlzs.com/KowwL
8. Perros P, McCrimmon RJ, Shaw G, Frier BM(1995)Frequency of thyroid dysfunction in diabetic patients: value of annual screening. Diabet Med12:622–627. Link: https://urlzs.com/YjiEH
9. Fernandez CM, Molina A, Jimenez LL, Gomez JM, Soler J(1999) Clinical presentation and early course of Type 1 diabetes in patients with and without thyroid autoimmunity. Diabetes Care22: 377- 381. Link: https://urlzs.com/yS2Dy
10. Balducci-Silano PL, Connor E, Maclaren NK. Association between insulin dependent diabetes mellitus (Type 1) and other autoimmune diseases. In: Diabetes Mellitus, a fundamental and clinical Text. Le Roith D, Taylor SI, Olefsky JM (eds). Lippincott-Raven, Philadelphia. 2002: 401-19.
11. Brenta G(2010) Diabetes and thyroid disorders. Br J Diabetes Vasc Dis10: 172–177. Link: https://urlzs.com/Ls5do
12. Joffe BI, Distiller LA. Diabetes mellitus and hypothyroidism: Strange bedfellows or mutual companions? World J Diabetes. 2014;5: 901–904. Link: https://urlzs.com/z4SRD
13. G. Radetti, C. Paganini, L. Gentill et al., "Frequency of Hashimoto's thyroiditis in children with type 1 diabetes mellitus," Acta Diabetologica.1995;32(2):121–124.
14. Duckworth WC, Badlissi J, Kitabchi AE: Thyroid function in diabetes. In The Thyroid Gland. Vanmiddleworth L, Ed. Chicago, Year Book Medical.1986;247–261.
15. United Nations, Department of Economic and Social Affairs, Population Division. World Population Prospects: The Revision.2017.
16. A. M. Habeb, M. S. F. Al-Magamsi, S. Halabi, I. M. Eid, S. Shalaby, and O. Bakoush, "High incidence of childhood type 1 diabetes in Al-Madinah, North West Saudi Arabia (2004- 2009)," Pediatric Diabetes.2011;12(8):676–681.
17. M. Alotaibi, L. Alibrahim, and N. Alharbi, "Challenges associated with treating children with diabetes in Saudi Arabia," Diabetes Research and Clinical Practice.2016;120:235–240.
18. Shah SN. Thyroid disease in diabetes mellitus. JAPI. 2007; 32:1057-1059.
19. American Diabetes Association. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes—2019. Diabetes Care. 2019; 42: S13-S28
20. Dos Remedios LV, Weber PM, Feldman R, Schurr DA, Tsoi TG. Detecting unsuspected thyroid dysfunction by the free thyroxine index. Arch Intern Med 1980;140:1045-9.
21. Garber JR, Cobin RH, Gharib H, Hennessey JV, Klein I, Mechanick JI, Pessah-Pollack R, Singer PA, Woeber for the American Association of Clinical Endocrinologists and American Thyroid Association Taskforce on Hypothyroidism in Adults KA. Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. Thyroid. 2012; 22(12):1200-35.
22. Riley WJ, Maclaren NK, Lezotte DC, Spillar RP, Rosenbloom AL: Thyroid autoimmunity in insulin-dependent diabetes mellitus: the case for routine screening. J Pediatr.1981; 99:350–354
23. Mouradian M, Abourizk N: Diabetes mellitus and thyroid disease. Diabetes Care.1983; 6:512–520
24. Nerup J, Binder C: Thyroid, gastric and adrenal auto-immunity in diabetes mellitus. Acta Endocrinol.1973; 72:279–286
25. Nabarro JD, Mustaffa BE, Morris DV, Walport MJ, Kurtz AB: Insulin deficient diabetes: contrasts with other endocrine deficiencies. Diabetologia.1979;16:5–12
26. Hollowell J. G., Staehling N. W., Flanders W. et al., "Serum TSH, T4, and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III)," Journal of Clinical Endocrinology and Metabolism. 2002; 87(2):489–499.
27. Shun CB, Donaghue KC, Phelan H, Twigg SM, Craig ME. Thyroid autoimmunity in Type 1 diabetes: systematic review and metaanalysis. Diabet Med. 2014;31: 126–35.
28. Balsamo C, Zucchini S, Maltoni G, Rollo A, Martini AL, Mazzanti L, et al. Relationships between thyroid function and autoimmunity with metabolic derangement at the onset of type 1 diabetes: a cross-sectional and longitudinal study. J Endocrinol Invest. 2015;38: 701–7.
29. Golden B, Levin L, Ban Y, Concepcion E, Greenberg DA, Tomer Y. Genetic analysis of families with autoimmune diabetes and thyroiditis: evidence for common and unique genes. J Clin Endocrinol Metab. 2005;90: 4904–11.
30. Ikegami H, Awata T, Kawasaki E, Kobayashi T, Maruyama T, Nakanishi K, et al. The association of CTLA4 polymorphism with type 1 diabetes is concentrated in patients complicated with autoimmune thyroid disease: a multicenter collaborative study in Japan. J Clin Endocrinol Metab. 2006;91: 1087–92.
31. Dultz G, Matheis N, Dittmar M, Röhrig B, Bender K, Kahaly GJ. The protein tyrosine phosphatase non-receptor type 22 C1858T polymorphism is a joint susceptibility locus for immunthyroiditis and autoimmune diabetes. Thyroid. 2009;19:143–8.
32. Villano MJ, Huber AK, Greenberg DA, Golden BK, Concepcion E, Tomer Y. Autoimmune thyroiditis and diabetes: dissecting the joint genetic susceptibility in a large cohort of multiplex families. J Clin Endocrinol Metab.2009;94: 1458–66.
33. Inoue N, Watanabe M, Morita M, Tomizawa R, Akamizu T, Tatsumi

K, et al. Association of functional polymorphisms related to the transcriptional level of FOXP3 with prognosis of autoimmune thyroid diseases. Clin Exp Immunol 2010;162: 402–6.

34. Burn GL, Svensson L, Sanchez-Blanco C, Saini M, Cope AP. Why is PTPN22 a good candidate susceptibility gene for autoimmune disease? FEBS Lett. 2011;585: 3689–98.

35. Yeşilkaya E, Koç A, Bideci A, Camurdan O, Boyraz M, Erkal O, et al. CTLA4 gene polymorphisms in children and adolescents with autoimmune thyroid diseases. Genet Test. 2008;12: 461–4.

36. Jaeger C, Hatziagelaki E, Petzoldt R, Bretzel RG: Comparative analysis of organspecific autoantibodies and celiac diseaseassociated antibodies in type 1 diabetic patients, their first-degree relatives, and healthy control subjects. Diabetes Care.2001; 24:27–32

37. Glastras SJ, Craig ME, Verge CF, Chan AK, Cusumano JM, Donaghue KC: The role of autoimmunity at diagnosis of type 1 diabetes in the development of thyroid and celiac disease and microvascular complications. Diabetes Care.2005; 28:2170–2175

38. Silverstein J, Klingensmith G, Copeland K, Plotnick L, Kaufman F, Laffel L, Deeb L, Grey M, Anderson B, Holzneister LA, and Clark N: ADA statement. Care of children and adolescents with type 1 diabetes. Diabetes Care.2005; 28 :186 –212

39. Hansen D, Bennedbaek FN, Hoier-Madsen M, Hegedu SL, Jacobsen BB(2003) A prospective study of thyroid dysfunction, morphology and autoimmunity in young patients with type 1 diabetes. Eur J Endocrinol148:245–251. Link: https://urlzs.com/8i6ue

40. Hoffman RP (2003) Thyroid stimulating hormone screening is more sensitive for detecting thyroid abnormalities in children and adolescents with type 1 diabetes (Letter). Diabetes Care26:255. Link: https://urlzs.com/wKo21

41. Nasir AAJ, Sharifah DA Al Issa, Abdullah NA Al Jurayyan, Hessah MNAl Otaibi, Amir MI Babiker(2015) Thyroid Disorders Associated with Type 1 Diabetes Mellitus in Children and Adolescents from Central Province Saudi Arabia Int.J.Curr.Res.Biosci.Plantbiol 2: 45-49. Link:https://urlzs.com/Ew6X9

42. Elhashimie H, Elagab EAM, Mohammed HB, Abdelgader AE, Elhussein AB, et al. (2017) Distribution of Thyroid Autoantibodies in Saudi Children with Type 1 DM and their Effect on Glycemic Control. Biomedical & Pharmacology Journal10:29-35. Link: https://urlzs.com/M3FYP

43. Alves C, Santos LS, Toralles MB(2016) Association of type 1 diabetes mellitus and autoimmune disorders in Brazilian children and adolescents. Indian journal of endocrinology and metabolism 20:381-386. Link: https://urlzs.com/ZG25Q

44. Gale EA, Gillespie KM (2001) Diabetes and gender. Diabetologia 44:3-15. Link: https://urlzs.com/7cexP

45. Korenchevsky V, Hall K (1941) Correlation between sex hormones, thyroid hormones and desoxycorticosterone as judged by their effects on the weights of organs of gonadectomized rats. Biochem J 35:726–735. Link: https://urlzs.com/Bz38h