

Evaluation of Thyroid Autoimmunity in Type 1 Diabetes Mellitus with Respect to Gender

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Abstract: **Background:** Type 1 diabetes mellitus (T1DM) is associated with autoimmune diseases such as thyroiditis. Autoimmune thyroiditis in type 1DM were studied in many cases, but the status of thyroid function and thyroid autoimmunity in respect to sex difference is not well clarified. However, very limited data were available from KSA, despite an increase in incidence of disease. **Objective:** The present study was aimed to compare and evaluate the thyroid function & autoimmune thyroiditis disorders between male and females in Saudi children with Type 1 DM and to evaluate their effect on HbA1c level as glycemic marker and Body Mass Index (BMI). **Method:** A clinical-based descriptive, analytical study was conducted during the period from March 2015 to August 2017. 132 patients with Type 1 DM (76 Males & 56 females) were selected as a test group compared with a control group which included 72 apparently healthy volunteers (40 males, 32 females), patients and controls were from Najran University Hospital & the King Khalid Hospital in Najran City- Saudi Arabia. The study excluded patients with thyroid disease, renal disease, liver disease, and anemia. HbA1c was measured using chromatography technique. The sera were used to assay the TSH concentrations using ELC (Electrochemiluminescent) technology while GAD antibodies, TPO antibodies & TG antibodies were measured by ELISA (Enzyme-Linked Immunosorbent Assay) from abcam –UK. The data were analyzed by SPSS. **Results:** Results of our study reveal that the concentrations of TSH, Anti-TG, Anti-TPO and Anti -GAD were found to be significantly increased in patients with type 1 DM, in comparison to control group (P value < 0.05). On the other hand the serum levels of anti- TPO and anti-TG concentration were significantly higher in diabetic female compared to diabetic male ($p < 0.05$). **Conclusions:** It could be concluded that thyroid antibodies (TG-Abs and TPO-Abs) were found to be highly significantly increased in type 1 diabetic female than male, our data support good recommendation for regular investigations of thyroid antibodies and thyroid function assessment in all patients with type 1.

Keywords: Thyroid Stimulating Hormone (TSH), Glycated hemoglobin (HbA1c), autoimmune thyroiditis (AIT), Type 1 diabetes mellitus (T1DM)

1. Introduction

Type 1 diabetes mellitus is very complicated disease that strongly associated with disorders organ-specific diseases such as autoimmune thyroid disease (ATD), pernicious anemia, and idiopathic adrenal insufficiency(1, 2), while ATD has been reported to be the most common coexisting autoimmune disease with type 1 diabetes mellitus(3). There is also an increased prevalence of thyroid antibodies in type 1 diabetic patients with ATD (4, 5). Unfortunately a recent study reported increasing in the incidence of the disease by 2-5% globally(6). However the prevalence in Saudi Arabia is higher in compare to other communities(7). Moreover the disease known to be associated with multiple autoimmune diseases world wide, such as Graves' disease, Hashimoto's thyroiditis, Addison's disease, vitiligo, celiac disease, autoimmune hepatitis, myasthenia gravis, and pernicious anemia. Perhaps the autoimmune thyroid diseases are the commonest (8), it estimated about 40% in cohort study in Germany and Austria(9). Both autoimmune thyroiditis and type 1DM are organ specific autoimmune disease mediated by T cells and probably they have same pathogenesis, their accompanied occurrence may explained by sharing some susceptibility genes(10).

The higher prevalence of thyroid auto antibodies as well as abnormal thyroid profiles was detected among type 1 DM

children and adolescence including their first-degree relatives(11, 12). As far as Anti-thyroid peroxidase (anti-TPO) is major thyroid autoantibodies(13). And anti-Thyroglobulin antibodies (anti-TG) were most commonly anti-thyroid antibodies associated with anti-pancreatic antibodies Anti-glutamic acid decarboxylase (Anti-GAD)(12) which are mainly linked to females and long standing diabetes(14). Recent studies reported an increase prevalence of thyroid auto antibodies associated with type 1 DM which explained by awareness of doctors about these combinations(15). Hashimoto thyroiditis is commonest clinical presentation among type 1 DM in contrast to Graves' disease, which is less frequent. Other more still there are contradicted results concerning distribution of goiter in type 1 DM versus non-DM(16). In previous report low T3 syndrome were detected in diabetic adolescences group, which were found to be associated with high level of glucose as well as HbA1c, so they recommend to do serial thyroid function test (T3, T4, TSH) as T3 level may be affected by metabolic control (11). On the other hand an increase prevalence of Graves' disease among type 1 DM associated with highly variable ages with patients, lead to a serious illness include metabolic disturbances which result from the association of both disease in one patient(17).

Although many researches proved the association of auto thyroid antibodies with type 1DM, but there are debates

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concerning subclinical thyroiditis and their role in glyceemic control as well as disease complication(7, 18).

Saudi children with type1 diabetes known to be have very poor glyceemic control that may result in worse diabetic complications(19), other more a new form of diabetes were very common in Saudi adolescence represented about one-third of diabetic patients called double diabetes (T1 DM&T2 DM); The patients presented with both feature of T1 DM &T2 DM make the glyceemic control challengeable (20). So extensive research needed to understand the hidden pathophysiology beyond the problem, so our study aimed to evaluate the thyroid function and thyroid autoimmunity in type 1 diabetic children in respect to sex difference may give an idea about the impact of autoimmune thyroiditis in diabetic children in Saudi Arabia.

2. Materials and Methods

Our study was case -control study that was conducted in Najran University Hospital & King Khalid Hospital in Najran City- Saudi Arabia from March 2015 to August 2017. All participant in this were from Najran area, the study included 132 Saudi children (76Male & 56 female) diagnosed as type 1 diabetes mellitus according to WHO criteria 18were selected as a test group compared with a control group which included 72 apparently healthy volunteers (40 males, 32 females), all patients were age and sex matched, their ages ranged between 2 and 14 years.

Patients with chronic diseases that may be distributed our study this included thyroid, renal, liver, anaemias disorders and any medication that may be infused the analytes under study were exclude from this study.

An interview with a questionnaire to obtain the clinical data was done for each participant in this study, clinical history and examination of the test group and the controls were done by physicians working in Najran University Hospital & King Khalid Hospital.

Weight was measured using electronic digital scales. Height was measured using a wall mounted stadiometer. BMI was subsequently calculated as weight (kg) per height (m²).

In sterile condition and using a local antiseptic for skin following an overnight fast (8-12hrs), 5mls of venous blood was collected from each participant and separated into 3mls as serum and 2mls as plasma in EDTA tubes. For serum preparation the blood samples were separated after complete clotting by centrifugation at 4000 rpm for 5 minutes and serum was obtained. From EDTA tubes HbA1c was measured using chromatography technique (boronate affinity chromatography). The sera were used to measure the concentrations of TSH using ELC (Electrochemiluminescence technology) while GAD antibodies, TPO antibodies & TG antibodies were measured by ELISA (Enzyme-Linked Immunosorbent Assay) from abcam -UK. Results of this study were statistically analyzed using statistical package for social science (SPSS) program. Independent t-test and Persons correlation coefficients were used; significance levels were set at (P < 0.05).

3. Results

Results of this study demonstrated the baseline characteristics and biochemical parameters of test group and controls, which were highly different between the test group and control group. Also there was a significant differences in concentrations of these characteristics and biochemical parameters between male and females.

Table-1 showed that there was no significant difference between T1DM and control group regarding age (P value =0.12), while there was a significant decrease in the BMI in type1diabetic patients when compared to the control group (P value =0.009), moreover TSH and HbA1c% levels were significantly elevated in type 1 DM patients in comparison to control group (P value = 0.001), the concentrations of Anti-TG, Anti-TPO and Anti -GAD were found to be significantly increased in patients with type 1 DM, in comparison to control group (P value =0.003, P value =0.001 and P value = 0.001) respectively.

Table-2 shows Mean ± S.D of parameters under study in diabetic male compared to diabetic females , age was not significantly different between males and females (P value =0.112), while that the BMI was significantly increased in males when compare to the females with type1DM (P value =0.035), moreover HbA1c% was significantly elevated in males when compared to female group (P value = 0.004), There was no statistically difference between the two diabetic groups regarding serum TSH level(P value = 0.052) However, the mean levels of anti- TPO and anti-TG concentration were significantly higher in diabetic female compared to diabetic male (p<0.05). No statistically significant differences in the mean levels of anti-GAD concentration was observed between male and female with type 1 diabetes, although there was a slight trend towards higher values in females.

Table 1: Baseline characteristics and biochemical parameters of the test group and the control group

Parameters	Test group Mean ± SD	Control group Mean ± SD	P-value
Age	10.5 ± 3.92	10.6 ± 2.27	0.12 (N.S)
BMI	17.48 ± 1.76	18.10 ± 1.42	0.009 (S)
HbA1c	9.90 ± 1.79	4.53 ± 0.46	0.001 (H.S)
TSH(μU/ml)	2.65 ± 1.67	1.81 ± 0.87	0.001 (H.S)
Antithyroglobulin-Ab U/ml	16.21 ± 32.51	4.48 ± 8.13	0.003 (S)
Anti- thyroid peroxidase U/ml	84.92 ±126.88	15.93 ± 31.29	0.001 (H.S)
GAD ng/ml	7.30 ± 6.78	2.33 ± 1.60	0.001 (H.S)

S = Significant; H.S = Highly significant; N.S = Not significant

- The table shows the mean ± SD.
- P value Less than 0.05 considered significant.

Table 2: Comparison between male & female in the test group

	56)	76)	
	Mean ± SD	Mean ± SD	
Age	10.92±4.67	9.82±2.50	0.112(N.S)
BMI	17.18 ± 1.71	17.83±1.77	0.035(S)
HbA1c	9.56±1.88	10.41±1.54	0.004(S)
TSH(μU/ml)	2.88±1.92	2.35±1.20	0.052(N.S)
Antithyroglobulin Ab U/ml	21.06±38.168	9.63±21.34	0.045(S)
Anti - thyroid peroxidase U/ml	113.42±148.14	46.25±75.99	0.001(H.S)
GAD ng/ml	8.23±7.82	6.62±5.87	0.179(N.S)

S = Significant; H.S = Highly significant; N.S = Not significant

- The table shows the mean ± SD.
- P value Less than 0.05 considered significant.

Discussion

Our present study represents the evaluation of thyroid function and its auto-immune features in Saudi children with type 1 DM compared to apparently healthy controls and also in diabetic males compared to diabetic females. However there were no significant difference between T1DM children and unaffected control group regarding age, while that the BMI was increased in study group than control group, also in both diabetic groups (male & female), the BMI was found to be higher in diabetic male patients than that of diabetic female group. The HbA1c was statistically significant increased in female diabetic patients than that of diabetic male patients. In the present study, the serum level of TSH was significantly higher in diabetic patients compared to unaffected controls in general. But serum TSH concentration in diabetic male was not statistically different from that of diabetic female, in spite of this the serum TSH concentration is higher in diabetic females than males, this indicate that diabetics female may develop subclinical hypothyroidism rather than diabetic males, this result is in accordance with the results of other studies done by Perros et al (21) who reported that subclinical hypothyroidism was found in 6.5% of type-1 diabetic female patients. The present study demonstrated that the values of anti-TPO, anti-TG and GAD antibodies were significantly increased in type-1 DM when compared to the control group so autoimmune thyroid diseases are common in patients with type-1 DM (15, 22) this results were in concordance to Schroner et al (17) who found that the incidence of autoimmune thyroid disorders in 40% patients of type-1 DM. The serum thyroid antibodies (Antithyroglobulin Ab and Anti - thyroid peroxidase) were found to be higher in both diabetic patients groups, while that, the GAD-antibodies was decreased in the male diabetic patients group than female diabetic group in spite of no significant difference in both groups (15, 22).

Based on autoantibody positivity and TSH concentration, autoimmune thyroid disease (AITD) was higher in women. This is in agreement with previous finding done by PRÁZNY *et al*, (23) who found that anti-TG concentration was significant elevated in diabetic female compared to diabetic male, However they reported that no significant difference was found in the value of anti-GAD between male and female in the diabetic group. But our result was disagree

with this finding regarding anti-TPO bodies we found that it was significant increase in diabetic female patients than that in diabetic male patients and PRÁZNY *et al* reported that there were no significant difference between them.

Conclusion

It could be concluded that thyroid antibodies (TG-Abs and TPO-Abs) were found to be highly significantly increased in type 1 diabetic female than male, our data support good recommendation for regular investigations of thyroid antibodies and thyroid function assessment in all patients with type 1 diabetes.

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