



IJSRM

INTERNATIONAL JOURNAL OF SCIENCE AND RESEARCH METHODOLOGY

An Official Publication of Human Journals



Human Journals

Research Article

October 2019 Vol.:13, Issue:4

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Thyroid Autoantibodies in Type 1 DM Association with Duration of Disease



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Submission: 23 September 2019

Accepted: 28 September 2019

Published: 30 October 2019



HUMAN JOURNALS

www.ijsrm.humanjournals.com

Keywords: Autoimmune thyroiditis (AIT); Anti-glutamic acid decarboxylase (Anti GAD); Anti thyroglobulin antibodies (Anti-TG); anti-thyroid peroxidase antibodies (Anti-TPO); Glycated hemoglobin (HbA1c); Thyroid-stimulating hormone (TSH)

ABSTRACT

Autoimmune thyroiditis (AIT) in type 1 Diabetes Mellitus (T1DM) was studied in many cases, but the association between duration of type 1 DM and autoimmune thyroiditis not well clarified. However, very limited data are available from Saudi Arabia, despite an increase in the incidence of disease. This study aimed to find out the possible association between diabetes duration and thyroid antibodies; anti-Thyroid Peroxidase (anti-TPO) & anti-Thyroglobulin (anti-TG) and anti-glutamic acid decarboxylase (anti-GAD) in Saudi children with type 1DM. The study included 132 diabetics children selected from Najran area According to the duration of diabetes grouped into group 1: less than 2 years, group 2: 2 up to 5 years, group 3: 6 up to 10 years and group 4: more than 10 years. Blood levels of anti-TPO, anti-TG and anti-GAD antibodies were determined by ELISA and TSH using ELC while HbA1c was measured using chromatography technique. The highest serum GAD antibodies values were for group 1 (diabetic duration of fewer than 2 years). Results showed that the serum concentrations of Anti-TG Abs (U/ml) were significantly increased in group 1 (diabetic duration less than 2 years) compared with other groups of diabetic children ($P = 0.030$) and there were significant negative correlations between duration of diabetes and GAD, Anti-TG Abs and anti-TPO in type 1 DM children. In conclusion the highest titer of pancreatic autoantibodies & thyroid autoantibodies at the onset of T1DM also there was no significant association between duration of diabetes and thyroid-stimulating hormone levels in children with T1DM.

INTRODUCTION

The autoimmune destruction of pancreatic islet cells results in clinical form of Diabetes Mellitus (DM) known as type 1 diabetes mellitus (T1DM), associated with autoantibodies targeting components of insulin-producing cells: Anti-islet cell (ICA), anti-glutamic acid decarboxylase (anti-GAD), anti-tyrosine phosphatase (anti-IA2), and anti-zinc transporter 8 protein (ZnT8)[1][2]. Other autoimmune diseases such as Addison disease, Hashimoto thyroiditis, Graves disease, vitiligo, celiac disease, autoimmune hepatitis, myasthenia gravis, and pernicious anemia are associated with type 1 DM[3][4]. In particular, autoimmune thyroiditis (AIT) is the most common disorder associated with type 1 DM[5][6]. AIT is characterized by T and B-lymphocyte infiltration of the thyroid gland and the presence of autoantibodies to thyroid peroxidase (TPO Ab) and thyroglobulin (TG Ab)[7][8].

Also, recent studies have reported that the presence of glutamic acid decarboxylase antibodies (GADA) and human leukocyte antigen class II genes may influence the development or progression of AIT[5][9]. AIT and type 1 DM have a common genetic background and similar pathogenesis; hence, they could occur in the same individual or family. The prevalence of thyroid autoantibodies in children with type 1 DM ranges from 3% to 50% in different countries and populations, which is markedly higher than in the general population (range, 1% to 4%)[5][10][11][12]. Many studies in Saudi Arabia confirm an increased incidence of autoimmune thyroid diseases in type 1 DM, it showed a higher distribution of thyroid autoantibodies (anti-TPO and anti-TG) among type 1 DM patients 36.4% and 19.7% in contrast to lower distribution in apparently healthy controls 9.7% and 4.2% respectively[6] also reveal the association of autoimmune thyroid diseases with type 1 DM with respect to many factors such as gender [3][13]. The effect of duration of Diabetes Mellitus on both pancreatic & thyroid autoantibodies was not well demonstrated in literature so our study aimed to investigate the thyroid autoimmunity concerning long term duration of type 1 DM in Saudi children's in Najran area.

MATERIALS & METHODS

This study was a cross-sectional, case-control and hospital-based study carried out in Najran University Hospital & King Khalid Hospital in Najran City- Saudi Arabia from March 2017 to August 2018. All participant were from Najran province, the study included 132 Saudi children (76 male & 56 female) diagnosed as type 1 diabetes mellitus according to WHO

criteria [14] their ages ranged between 2 and 14years. According to the duration of diabetes, patients were divided into four groups: group 1: less than 2years, group 2: 2 up to 5years, group 3: 6 up to 10years and group 4: more than 10 years.

Exclusion criteria

Those with chronic diseases that may affect parameters understudies such as thyroid, renal, liver, anemia's disorders and any medication that may confuse the analytes under study were excluded from this study.

Sample collection and Biochemical Determination: In sterile condition and using a local antiseptic for skin following an overnight fast (8-12 hrs), 5mls of venous blood was collected from each participant and separated into 3mls as serum and 2mls as plasma in EDTA tubes. The serum samples were stored at -20 degrees centigrade in deep freezing until the whole collection of the samples.

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 TPO antibodies, TG antibodies, and GAD antibodies were measured by ELISA (Enzyme-Linked Immunosorbent Assay) from Abcam – UK.

Statistical analysis: Results of this study were statistically analyzed using statistical package for social science (SPSS) program. Significant differences between groups were assessed by one-way ANOVA and t-tests. A correlation matrix was done and the r values were obtained at the level of ($p < 0.05$) significance.

RESULTS AND DISCUSSION

RESULTS

A total of 132 Type 1 diabetics children (76 male & 56 female) were enrolled in the study and their mean age was (10.45 ± 3.92) years.

Table (1) shows the mean \pm SD of HbA1c% among the four studied groups of children. The four groups differed significantly from each other ($P = 0.032$). The highest values were for group 1 (diabetic duration of fewer than 2 years).

Table (1) also show the mean of serum levels of GAD (ng/ml) among the four studied groups of children. The four groups differed significantly from each other (P = 0.001). The highest values were for group 1 (diabetic duration less than 2 years) while the lowest values were for group 4 (diabetic duration of more than 10 years).

The serum concentrations of Anti- TG Abs (U/ml) were significantly increased in group 1 (diabetic duration less than 2 years) compared with other groups of diabetic children (P = 0.030), while the serum concentrations of Anti-thyroid peroxidase (U/ml) and TSH (μ IU/ml) was insignificantly increased in group 1 (diabetic duration less than 2 years) compared with other groups of diabetic children (P = 0.131) and (P = 0.566) respectively (Table 1).

For diabetic children, the results of Pearson’s correlation coefficients revealed a negative correlation between duration of diabetes mellitus and serum levels of GAD, Anti- TG Abs and Anti - thyroid peroxidase ($r = -0.642, P < 0.001; r = -0.548, P = 0.004; r = -0.177, P = 0.044$; respectively). While there was no significant correlation between duration of diabetes mellitus and the serum levels of TSH ($r = 0.048, P = 0.591$). (Table 2)

Table No. 1: Duration of diabetes and parameters among study groups.

Parameters	Duration of diabetes / years				P-value
	<2	2-5	6 <10	>10	
HbA1c%	10.50±1.8	9.90±1.4	9.40±1.7	10.0±2.0	0.032
GAD ng/ml	12.3±9.3	12.8±8.0	4.9±2.7	4.4±3.1	0.001
Antithyroglobulin Ab U/ml	30.9±48.3	17.3±33.4	11.0±23.0	9.5±21.0	0.030
Antithyroid peroxidase U/ml	127.6±152.4	83.6±113.5	57.0±102.3	85.8±135.3	0.131
TSH (μ IU/ml)	2.8±2.0	2.2±1.7	2.6±1.4	2.5±1.7	0.566

P-value less than 0.05 considered significant.

Table No. 2: Correlation between duration and parameters in diabetic children

Duration	Diabetic children	
	r. value	p. value
GAD ng/ml	-0.642	0.000
Antithyroglobulin Ab U/ml	-0.548	0.004
Antithyroid peroxidase U/ml	-0.177	0.044
TSH (μ IU/ml)	0.048	0.591

P-value less than 0.05 considered significant.

DISCUSSION

Autoimmune thyroid diseases are common in Type 1 diabetic patients. The most frequent of them is chronic autoimmune thyroiditis[15]. The results of this study found that the serum thyroid antibodies: Anti thyroglobulin antibodies (Anti-TG) & anti-thyroid peroxidase antibodies (Anti-TPO) and Anti-glutamic acid decarboxylase (Anti GAD) were found to be significantly higher in group 1 (diabetic duration less than 2 years) compared with other groups of diabetic children. Also, there was a negative correlation between the duration of diabetes mellitus and serum levels of GAD, Anti- TG Abs and Anti - TPO. These results were consistent with those of Rochmah *et al*[16] found the thyroid dysfunction apparent at diabetes onset or years thereafter and Peak of autoimmune thyroiditis incidence in the early until mid-puberty. Shiva *et al*[7] assessed the prevalence of anti- TPO and anti- TG in newly diagnosed type one diabetic child in North-West Iran, they clear that the studied children had raised levels of one or both of mentioned antibodies at the onset of diabetes. Kordonouri *et al*[12] who found that the clinical or subclinical hypothyroidism requiring treatment with L-thyroxine occurred during the first five years of diabetes and for early detection of autoimmune thyroiditis in children with T1DM, measurement of anti-TPO and TSH at T1D onset and in yearly intervals after the age of 12 years is recommended.

G. Hwang *et al*[5] results found the prevalence of at least one thyroid antibody was 30.4%. Patients with thyroid antibodies had a significantly higher frequency of GADA at the time of the diagnosis. Autoimmune thyroiditis was more prevalent in the older age group. GADA was a significant risk factor for the development of thyroid autoantibodies after the diagnosis of type 1 DM (odds ratio, 4.45; 95% confidence interval, 1.399–14.153).

From our results, mainly the negative correlations between duration of Type 1 DM & autoantibodies and matched similar data of previous literature it was clear that the peak of thyroid autoantibodies and pancreatic autoantibodies (GAD) in type 1 DM present at the onset of diabetes and few years after then the titer of autoantibodies decrease with long – term of diabetes duration.

Our results found the serum levels of TSH (μ IU/ml) were insignificantly increased in group 1 (diabetic duration less than 2 years) compared with other groups of diabetic children and there was non-significant correlation between duration of diabetes mellitus and the serum levels of TSH ($r = 0.048$, $P = 0.591$), these results agreed with results of Rochmah *et al*[16]

who found that there was no significant association between duration of diabetes and thyroid-stimulating hormone concentration ($r = -0.068$; $P = 0.703$).

CONCLUSION

This work revealed that serum anti- GAD & anti- TG levels were significantly higher among group 1 (diabetic duration less than 2 years) diabetics children while serum anti- TPO and TSH levels were insignificant increases. This study provides further evidence supporting that the high titer of pancreatic autoantibodies & thyroid autoantibodies at the onset of T1DM also there was no significant association between duration of diabetes and thyroid-stimulating hormone levels in children with T1DM.

ACKNOWLEDGMENT

This work was funded by a grant from the Deanship of Scientific Research, Najran University, KSA (NU/MID/14/036).

Disclosure: None declared.

Ethical approval: Permission of this study was obtained from the research and ethics committee of Najran University, KSA. All patients were assured that all their obtained information will be handled in a confidential atmosphere and it will not affect their life after taking verbal and written consent.

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