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RESEARCH ARTICLE

Prevalence of thyroid peroxidase autoantibodies in children and adolescence associated with Type 1 diabetes in Gezira state-Sudan

***Abubakr, I, Mohamed[1]. Alneil, A, Hamza[2]**

1. Department of Clinical Laboratory Sciences, Buraydah Private Collage Alquasim- Saudi Arabia.

2. Head department of Clinical laboratory Sciences, Buraydah Private Collage Alquasim- Saudi Arabia.

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Corresponding Author
Abubakr, I, Mohamed
Bakoor79@gmail.com

00966533755192

Abstract

Objective: Auto immune thyroiditis (AIT) is more frequently occurred among children with type1 diabetes mellitus. The aim of this study was to assess the presence of thyroid autoantibodies among children with type 1 diabetes in Gezira state-Sudan.

Materials and methods: 145 diabetic children (68 male and 77 female) attending for regular follow-up in the diabetic center in Wad-Medani pediatric hospital were enrolled in cross sectional descriptive study. Measurement of serum anti-TPO autoantibodies and serum TSH were carried out using immunological techniques (ELIZA)

Results: The mean age of total study subjects was 12 ±3.9 years (range 3-18) and the median duration of diabetes was 4 years (range 1-16). Out of 145 patients, 7.5% (11) had positive antibodies. However, the prevalence of positive antibodies in females were reach (72.6 %) as compared to males (27.3) (*P*=0.219). Anti-TPO auto antibodies presented early within the first 5 years are less than those present later (27.3%
versus 72.6%, p= 0.032) and the prevalence of these antibodies increased after the age of 10 years in both males and females (*P*= 0.753). The anti-TPO autoantibodies titer means for the positive and negative groups were (250.7±130.4 and 17.0±11.4 *P*=0.000) respectively. Serum TSH level was found abnormal in 45% of the anti TPO positive cases (5 out of 11).

Conclusion: Study concluded that the prevalence of thyroid autoantibodies associated with diabetes duration and more developed with progress in a lifetime. The present study revealed that the presence of these antibodies were also harmful by gender and age of the patient. Therefore, the measurement of anti-TPO autoantibodies may be an earlier marker for thyroid abnormalities alongside with serum TSH screening and this will be helpful in early diagnosis of disease and patient management.

Introduction

Autoimmune diseases affect a substantial percentage of the population, providing a strong impetus for research into ways whereby such diseases can be detected, prevented and even cured.[1-2] However, autoimmune thyroid disease (AITD) is the most frequent autoimmune disease associated with type 1 diabetes mellitus. The screening and diagnosis of AITD are based on the assessment of autoantibodies to thyroid peroxidase (anti-TPO) and thyroglobulin (anti-TG). The prevalence of these autoantibodies is dependent on gender, age of patient, and age at the onset of diabetes. It also varies in different geographic regions and is known to be higher in regions with higher iodine intake. [3] The prevalence of thyroid autoantibodies in children with type1diabetes mellitus (T1DM) varies between 3% and 50% in different countries.[4-5]

In recent years detection of antibodies against thyroid peroxidase (anti-TPO), a major antigen for microsomal antibody, appears to obviate the need for autoantibodies against microsomes (AMA) and autoantibodies against thyroglobulin (ATA) measurement because of the improvement in specificity and sensitivity of the method.[6]

The prevalence of anti-TPO antibodies in type1 diabetic patients who are clinically euthyroid have been reported to vary from 10% to 21.8%, but progression to overt thyroid disorders in individuals with significant titers of anti-TPO occurs in about 50% of them within 3-4 years. The diagnosis of thyroid dysfunction is often made late in type1 diabetic population. Up to now, there is no consensus about either the monitoring of autoimmune thyroid disease or the time point of therapeutic intervention in patients with type1 DM unless clinical symptoms of hypo or hyperthyroidism appear. [7]

Thyroid diseases affect approximately 10-15% of patients with diabetes mellitus whereas in non-diabetics, the prevalence is approximately 6%. The prevalence is much more in type-1 than type-2 DM. Mode of association between DM and thyroid diseases are more complex and very unclear. Neither DM nor thyroid disorders present homogenous histologic unit, pathogenesis of different types of DM as well as thyroid diseases is diverse. Therefore, even the relations between them are different.[8]

Material and Methods

Materials & methods

An across sectional hospital based study was conducted to assess the presence of serum anti –TPO antibodies in children and adolescent associated with type1 diabetes mellitus. This study was carried out in Wad-Medani Pediatric Teaching Hospital during the period from June to August 2011. A total of 145 (68 male and 77 female, ages below 18 years) children and adolescence patients with type 1 diabetes registered at the outpatient clinic were selected to be the subject for this study. All patients were diagnosed with type 1 diabetes according to standard criteria, which included polyuria, polydipsia, and polyphagia and weight loss as well as plasma glucose concentration ≥ 11 mmol/l or (200mg/dl). All the subjects were screened for thyroid autoimmune disease by measuring the anti-TPO autoantibodies titer and TSH concentration level in plasma.

Blood collection and serum preparation

Venipuncture technique was used and blood specimens were collected in plain container. Serum was separated by blood centrifugation at 3000 rpm for 5 minute; then used to estimate serum TPO antibodies and serum TSH level.

Anti-TPO antibodies measurement

Anti-TPO antibodies were measured by using an ELISA technique (EUROIMMUN, Lubeck, Germany) which provides a semi quantitative or quantitative in vitro assay for human autoantibodies of the IgG class against thyroid peroxidase (TPO) in serum or plasma. The (cut-off) recommended by EUROIMMUN is 50 IU/ml. EUROIMMUN recommends the cutoff value enable clinical discrimination were :< 50 IU/ml (negative) and >50 IU/ml (positive) for anti-TPO antibodies. The test linearity is up to 500 IU/ml and the detection limits is approximately 5 IU/ml.

Thyroid function test (TSH level) measurement

ELISA technique (Bio-Line S.A- Bruxelles – Belgium) was used for TSH concentration measurement. The Bio-Line TSH-ELISA is a solid phase enzyme amplified sensitivity immunoassay performed on microtiter plates. Calibrators and samples react with the capture monoclonal antibody (M Ab 1) coated on microtiter well and with a monoclonal antibody (M Ab 2) labeled with horseradish peroxidase (HRP). The detection limit was 0.05 mIU/ml and the reference values recommended by the manufacturers were: 0.27 – 4.2 mIU/ml.

Statistical analysis

The study data was analyzed by using SPSS program to compute descriptive parameters including mean and frequencies, and inferential statistics was used including student's t test to test the significance of the differences between the mean values of two continuous variables and Chi-squire test (X^2) test the difference in proportions categorical variables between two groups. The level of confidence (P<0.05) was considered as cutoff value for significance.

Results

The mean age of the study subjects was 12 ±3.9 years (range 3-18) and the median duration of diabetes was 4 years (range 1-16). Out of 145 patients, 11(7.5%) had positive anti-TPO autoantibodies while 134 (92.5%) were antibodies negative. The mean age of the subjects with type 1 DM who had anti-TPO positive was 12.8 ± 3 years (range 8-17) versus who had negative 12.0±4 years (range 3-18) and the median duration of diabetes was 8±3.9 years versus 4 ± 3.4 years in those with positive and negative anti TPO antibodies. The anti-TPO autoantibodies titer mean of the positive and negative groups were found to be (250.7 ±130.4 and 17.0±11.4, P= 0.000) respectively. (Table1) shows the characteristics of the study subjects (positive/negative) for Anti-TPO.

Of 11 subjects with anti-TPO positive, 3 (27.3%) developed antibodies within 5 years of the onset of diabetes and 8 (72.6%) after 5 years of duration of diabetes and this difference was statistically significant ($P< 0.05$) (figure1). The anti-TPO antibodies appeared more often after 10 years old in both sexes 72.6% (8/11) versus their appearance before 10 years 27.3% (3/11). The difference was not statistically significant ($P< 0.05$) (figure 2). The association between demographic characteristics of anti-TPO (positive/ negative) groups was shown in table 2. Abnormal TSH level was observed in 5 of the anti TPO positive subjects. One of the 5 cases had high concentration of TSH (> 100 mIU/ml) compared to the mean of 7.6±1.7 for the other cases shown in table 1

Discussion

Auto immune diseases affect a substantial percentage of the population and it is well known that certain autoimmune diseases occurs in association with each other's such as auto immune thyroid disease (ATD), pernicious anemia, celiac disease and idiopathic renal insufficiency but the most common combination is type1 DM and ATD. 9

In the present study the prevalence of anti-TPO antibodies observed in children and adolescents with type 1 DM was found to be 7.5 % which is similar to prevalence found in Khartoum state children (6%) 10, Saudi Arabian children (8%) 11, and Egyptian children (12%)12. However, previous studies on prevalence of thyroid autoimmunity in children and adolescents with type 1 DM have shown various results depending on methodology, age, duration of DM onset and ethnicity of the patients studied. 14

The results of this study showed that the anti-TPO autoantibodies were more common in females than males with a ratio of 8:3 but no statistical significance was observed. Similar were also reported from different countries which indicating that ATD was more common in diabetic females than males, were female sex was reported as an important risk factor for ATD15,16,17 and the production of serum anti TPO is inheritable in the autosomal fashion in females than males. 10, 18

The present result also showed that anti TPO antibodies developed more often with the increase of age after 10 years. This finding is similar to the results that reported in previous studies.10, 13, 19

As it was reported in previous studies that the overall prevalence of thyroid autoimmune antibodies appeared to increase over time10, the result of this study showed that 72.7% of antibodies positive children developed anti-TPO autoantibodies within more than 5 years of the onset of diabetes.

Also, in literature reported that the elevated serum TSH levels associated with the degree of anti-thyroid antibody positive may be due to the direct involvement of auto antibodies in the pathophysiologic mechanisms of thyroid gland destruction or may be to the association of these antibodies with tissue destruction by thyroid infiltrating T cells. 12 However, in this study abnormal serum TSH level was observed in 5 of the anti TPO positive subjects. One of the 5 cases had high concentration of TSH (> 100 mIU/ml) compared to the mean of 7.6±1.7 for the other cases. From previous literature review it was found that these findings were agreed with other reports as in Shiva et al study in Tahran20, it was agreed in that disease was more prevalent in females than males, and the prevalence of ATD varies world- wide depending on the age, gender, and ethnic background of the studied subjects. 21

Conclusion

Study concluded that autoimmune thyroid disease in Sudanese children and adolescents with type 1 diabetes mellitus was 8%. The disease is more common in females than males. Subjects who are positive for anti-TPO antibodies have a significant susceptibility to sustain thyroid dysfunction. This study confirms the association between autoimmune hypothyroidism and type 1diabetes mellitus. So, the measurement of anti-TPO autoantibodies may be an earlier marker for thyroid abnormalities alongside with serum TSH screening in early stage of age may play crucial role in the management of type 1 diabetes in children.

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Table 1: characteristics of the study subjects (positive/negative) for Anti-TPO

Characteristics	Anti TPO positive (n=11)	Anti TPO negative(n= 134)	P- value
Age, years			
Means ± SD	12.8±3	12.0±4	0.416
Range	8-17	3-18	
Diabetic duration, year			
Means ± SD	7.6±3.8	4.0±3.4	0.034
Range	1-14	1-16	
Anti-TPO titer			
Means ± SD	250.7±130.4	17.0±11.4	0.000
TSH conc.			
Means ± SD	7.6±1.7		

P value based on Student's t-test: significant at ($p< 0.05$), Anti-TPO titer cutoff (>50 IU/ml

Table 2: Demographic characteristics and association between anti-TPO (positive/ negative) groups

Characteristics	Anti-TPO Positive		Anti-TPO Negative		Total Subjects		X^2	P
	No.	%	No.	%	No.	%		
Sex								
Male	3	27.3	65	48.5	68	46.9	1.84	0.175
Female	8	72.6	69	51.5	77	53.1		
Age categories								
< 10	3	27.3	45	33.6	48	33.1	0.183	0.669
> 10	8	72.6	89	66.4	97	66.9		
Diabetic duration								
<5	3	27.3	81	60.4	84	58	4.59	0.032
>5	8	72.6	53	39.6	61	42		

P value based on chi squire test: significant at ($p< 0.05$)

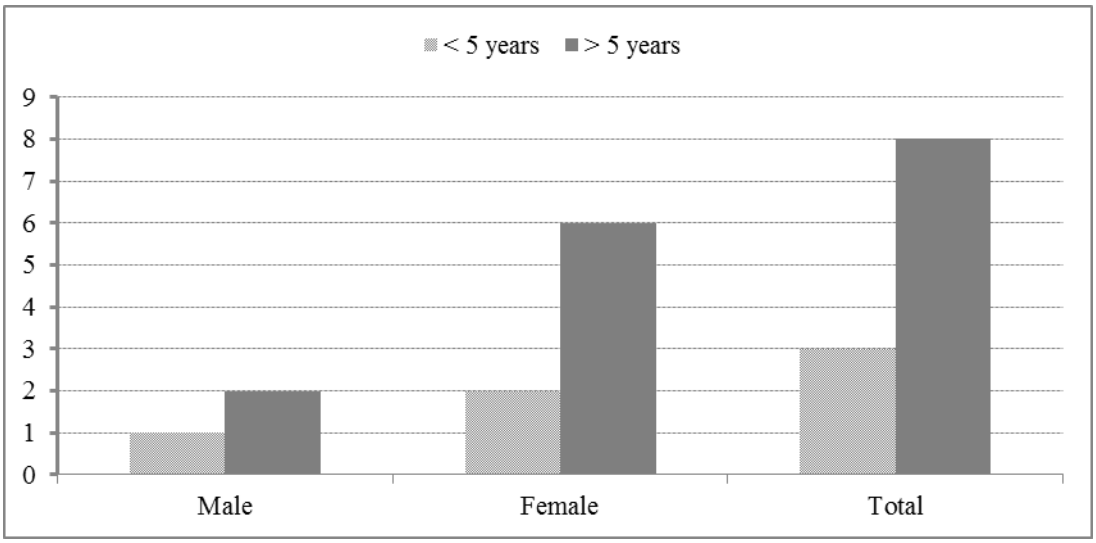

Figure 1: Association of positive Anti-TPO with duration of diabetes among 3 male and 8 females with type1 diabetes in the cross sectional study group p< 0.05

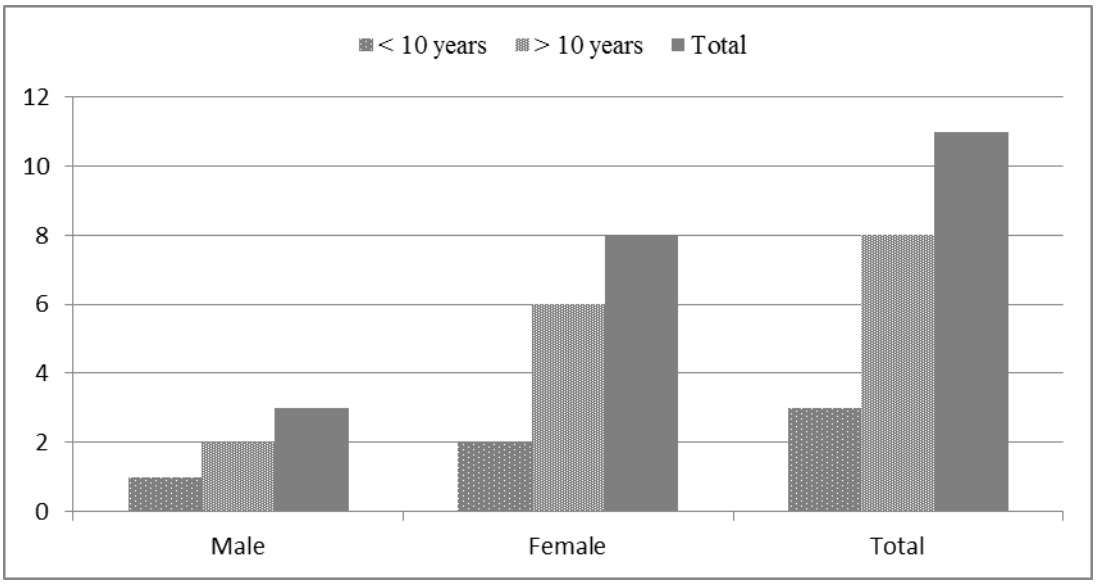

Figure 2: Association between Anti-TPO and the age categories in the positive group p< 0.05