



RESEARCH ARTICLE

STUDY OF AUTOIMMUNE THYROIDITIS IN TYPE 1 DIABETIC PATIENTS

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ABSTRACT

Context: Autoimmune thyroiditis (AIT) is a group of inflammatory thyroid disorders with either hyperthyroid, euthyroid or hypothyroid state. The aim of this study is to detect the subclinical thyroiditis among type 1 diabetic patients and to study the correlation of the thyroid antibodies to duration of diabetes. The study problem was that the modes of association between DM and thyroid diseases are more complex and unclear. **Aims:** This study was carried out to evaluate the associations between thyroiditis and duration of diabetes mellitus. The importance of the study was that the thyroid diseases affect approximately 10-15% of patients with diabetes mellitus whereas in non-diabetics the prevalence is approximately 6%. **Settings and Design:** A case-control and hospital-based analytical study was conducted from January 2015 to November 2017. **Methods:** Two hundred and five Sudanese children with T1DM were selected as test group and 100 apparently healthy volunteers as controls both groups were age and sex matched. In all participants, the following antibodies were surveyed: Anti-glutamic acid decarboxylase (anti-GAD), thyroglobin antibodies (TG), HbA1c (%) and TSH. **Statistical Analysis Used:** The quantitative variables were expressed as a mean and standard deviation and the qualitative variables in contingency tables. Student's t-test and 2 tests were used to assess the differences between the groups. The level of significance was established as $P < 0.05$. **Results:** means of serum levels of anti GAD, anti TG, HbA1c & TSH were statistically significant increased in diabetic patients in comparison to controls (8.86 ± 9.233) versus (3.00 ± 1.40), $p=0.00$ (6.49 ± 8.80) versus (2.70 ± 1.26), $p=0.00$, (12.42 ± 1.99) versus (5.39 ± 0.37) $p=0.00$, (2.25 ± 0.98) versus (2.06 ± 1.10) $p=0.04$ respectively also these were strong correlation between (anti GAD and anti TG) and duration of diabetes ($r 0.54$, $p=0.00$), (0.59 , $p=0.00$) respectively. **Conclusions:** Serum level of TSH and HbA1c are important tests for monitoring diabetic patients with thyroid disorders. Early detection of auto antibodies (TG antibodies and GAD antibodies) provides a prognostic value for the prediction of autoimmune thyroiditis in type I diabetes mellitus children and the duration of disease should be considered.

INTRODUCTION

Diseases of thyroid gland are amongst the most abundant endocrine disorders in the world second only to diabetes. 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 Diabetes. Modes of association between DM and thyroid diseases are more complex and very unclear (Perros, 1995). Autoimmune thyroiditis is a group of inflammatory thyroid disorders with either hypothyroid, euthyroid or hyperthyroid state (Kordonouri, 2002). Type-1 Diabetes is often accompanied by autoimmune diseases. Autoimmune thyroid diseases are amongst the most common (De Block, 2003). Recent studies confirm an increased incidence of autoimmune thyroid diseases even in type-2 Diabetes. The occurrence of common features of autoimmune diseases and the co association of multiple autoimmune diseases in the same individual or family supports the suggestion that there may be common genetic factors (Kordonouri, 2002).

Thus there are a limited number of studies thoroughly analyzing the risk factors related to the development of thyroid antibodies in children with Type 1 Diabetes (Kordonouri, 2002). It is noteworthy that there are also very few studies on the effect of thyroid antibody positivity on the growth and body mass index (BMI) status of children and with type 1 Diabetes (Kordonouri, 2002). Therefore the aims of the present study were to detect and to evaluate anti GAD antibodies, anti TG antibodies and to assess thyroid functions in patients with type 1 diabetes in relation with the duration of diabetes, the body mass index and glycemic control.

MATERIALS AND METHODS

This is descriptive an analytic and hospital based- case control study that was conducted, in Jabir Abuelez diabetes center, Omdurman pediatrics hospital and GaferIbnaof pediatrics hospital, in Khartoum state -Republic of Sudan from January 2015 to November 2017. The study samples comprised 205 Sudanese patients with type 1 diabetes mellitus (101 Male & 104 female) clinically diagnosed as type 1 diabetes

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mellitus according to WHO criteria in contrast, 100 healthy volunteers (43males, 57 females) were involved as a control group. Both groups were age and sex matched and their ages.

Inclusion criteria: Those with other types of diabetes mellitus, thyroid disease, renal disease, liver disease, anaemia and any medication that may be affect the Parameters 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 Jabir Abuelez diabetes center, Omdurman pediatrics hospital and GaferIbnaof pediatrics 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 (8-12 hrs), 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. The serum samples were stored at -20 degree 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 GAD antibodies & TG antibodies were measured by ELISA (Enzyme-Linked Immunosorbent Assay) from abcam –UK. Our data in this study was 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).

RESULTS

Table 1 showed that there was no statistical difference in the values of age and BMI between type-1 DM and control groups. There was a significant increase in the values of anti-GAD and anti-TG antibodies in type-1 DM when compared to controls. Moreover there was a significant increase in the values of TSH and HbA1c% in type-1 DM when compared to controls. Table 2 showed a significant strong correlation between the GAD & TG antibodies with duration of diabetes.

Table 1. Basic characteristic means of parameters among diabetic children and control group

Variable	Test group (n=205)	Control group (n=100)	P. value
Age (years)	12.88±3.91	12.79±5.11	0.71 (N.S)
BMI(Kg/m2)	17.48±3.20	18.42±4.01	0.07 (N.S)
GAD (U/ml)	8.86±9.23	3.00±1.40	0.00(H.S)
TG (%)	6.49±8.80	2.70±1.26	0.00(H.S)
HbA1c (%)	12.42±1.99	5.39±0.37	0.00(H.S)
TSH (µU/ml)	2.25±0.98	2.06±1.10	0.04 (S)

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

Table 2. Correlation between autoimmune antibodies duration in the test group

Antibodies	Duration	
	r. value	p. value
GAD- Antibodies	0.54	0.00 (H.S)
TGA- Antibodies	0.59	0.00(H.S)

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

DISCUSSION

Diabetes is recognized as one of the leading causes of morbidity and mortality in the world. Type 1 diabetes usually develops in childhood and adolescence. The World Health Organization estimates that about 171 million people worldwide are diabetics, about 10% of these affected by Type 1 diabetes (King, 1998). Type 1 diabetes mellitus is strongly associated with other organ-specific diseases such as Autoimmune Thyroid Diseases [ATD] (Munichoodappa, 1990), while ATD has been reported to be the most common coexisting autoimmune disease with type 1 diabetes mellitus (Mimura, 1990). Tasi et al (Tsai, 1993), found that there was also an increased prevalence of thyroid antibodies in type 1 diabetic patients with ATD. The reasons for the increased frequency remain obscure; it was thought to result from a generally increased propensity to react against certain antigens, or from a genetically impaired ability to acquire tolerance to some auto antigens, or perhaps from certain common antigens present in the tissues prone to autoimmune disease (Norden, 1983). In the present study there was a significant increase in the means of serum levels of TSH in the test group when compared with the control group (P = 0.04).

This result is compatible with the results obtained by Radaideh et al [9], McCrimmon et al (McCrimmon, 1995) and Perros et al (1995) who reported that the mean value of the serum levels of TSH is high in diabetic patients when compared to healthy controls and the measuring of TSH is provide a major advance in the diagnosis of thyroid disorders and subclinical thyroid dysfunction. The present study found that about 4.5% of type 1 diabetic patients had subclinical thyroiditis when this was compared to study done by Simthson (Simthson, 1998), who found a primary hypothyroidism in 2.5%, and subclinical hypothyroidism in 2% of mixed diabetic patients. Subclinical thyroid dysfunction can only be diagnosed by abnormal TSH while the serum levels of FT3 and FT4 are normal and by definition, the patients are usually asymptomatic. In the present study there was a significant difference between the means of serum levels of GAD of the test group and the control group (P=0.00), this result agrees with the results of Prazny M et al (2005), who reported that the prevalence of islet auto antibodies to GAD was found in more than 60 % of our type 1 diabetic patients.

The elevation of serum levels of GAD in type 1 diabetic patients is most probably due to autoimmune endocrine diseases in which immune dysregulation results in certain organ-specific aggression, and is characterized by the presence of auto antibodies. The result of current study showed a significant difference between the means of serum levels of TG of the test group and the control group (P=0.00), This result agrees with the result of G. S. R. Kedari (Kedari, 2010), and Lindberg B et al (Lindberg, 1997). Who reported that, type 1 diabetes mellitus is strongly associated with other organ-specific diseases such as ATD, pernicious anemia, and idiopathic adrenal insufficiency, while ATD has been reported to be the most common coexisting autoimmune disease with type 1 diabetes mellitus. There was also an increased prevalence of thyroid antibodies in type 1 diabetic patients with ATD. The Possible explanations for the wide range of thyroid antibodies prevalence in type 1 diabetes mellitus was thought to result from a generally increased propensity to react against certain antigens, or from a genetically impaired ability to acquire tolerance to some auto antigens, or perhaps from

certain common. In the present study there is a significant moderate positive correlation between the serum levels of GAD in U/ml and the duration of diabetes in years ($r = 0.54$, $P = 0.00$), however, the result of Prazny M et al (Prazny, 2005), reported a significant inverse relationship was observed between the concentration of anti-GAD and duration of diabetes ($r = -0.47$, $P < 0.002$). The present study showed a significant, moderate positive correlation between the serum of TG % and the duration of diabetes in years ($r = 0.59$, $P = 0.00$). This result agrees with the result of Kordonouri et al [2], De Block et al [3] and Kostas et al, [15] who suggests that autoimmune disease is the final phase of a process starting with auto recognition, passing through immunity with the appearance of auto antibodies, and finally leading to cell destruction and autoimmune disease. Our study concluded that thyroid antibodies (TG-Abs & GADAbs) were significantly increased in type 1 diabetic patients with expecting of thyroiditis even in the subclinical state and elevated of TSH indicated that severe thyroid disorders in those patients and high HbA1c % level in our case study reflect uncontrolled and severity of diabetes. Recommendation could be to perform measurement of thyroid antibodies (TG-Abs & GAD-Abs), regularly for every type 1 diabetic patient beside HbA1c %. Patients with positive antibodies should be monitored for TSH elevation (Kedari, 2010).

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