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Impact of Autoimmune Thyroiditis in Patients with Type 1 Diabetes

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Abstract: ***Context: Diabetes Mellitus, the most common non-communicable disease and the diseases of thyroid gland are amongst the most abundant endocrine disorders in the world second only to 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 type 1 diabetes mellitus and thyroid dysfunction. 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 2016. Methods: Two hundred and five Sudanese patients with T1DM were selected as test group 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), immunoglobulin A (IgA), HbA1c (%) and TSH. Statistical Analysis Used: The quantitative variables were expressed as a mean and standard deviation and the qualitative variables incontinency tables. Student's t-test and x^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 were statistically significant increased in diabetic patients in compression to control group AD, TG, HbA1c % and TSH (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-0.00 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 patients.***

Keywords: Serum TSH, HbA1c, Thyroiditis, type 1 DM

1. Introduction

Diabetes mellitus, often simply referred to as diabetes—is a group of metabolic diseases in which a person has high blood sugar, either because the body does not produce enough insulin, or because cells do not respond to the insulin that is produced. This high blood sugar produces the classical symptoms of polyuria (frequent urination), polydipsia (increased thirst) and polyphagia (increased hunger) [1].The term diabetes mellitus describes a metabolic disorder of multiple etiologies characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolisms resulting from defects in insulin secretion, insulin action, or both. The effects of diabetes mellitus include long–term tissue damage; dysfunction and failure of various organs [2].There are two main types of diabetes. Type 1diabetes usually develops in childhood and adolescence and patients require lifelong insulin injections for survival. Type 2 diabetes usually develops in adulthood and is related to obesity, lack of physical activity, and unhealthy diets. This is the most common type of diabetes (representing 90% of diabetic cases worldwide) and its treatment may involve lifestyle changes and weight loss alone, or oral medications or even insulin injections [2][3].

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 [4].

Autoimmune thyroiditis is a group of inflammatory thyroid disorders with either hypothyroid, euthyroid or hyperthyroid state [5]. Type-1 Diabetes is often accompanied by autoimmune diseases. Autoimmune thyroid diseases are amongst the most common [6]. 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 [5].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 [5]. 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 [5].Therefore the aim of the present study was to detect and to evaluate anti GAD antibodies, anti TG antibodies and to asses thyroid functions in patients with type 1 diabetes in relation to the body mass index and glycemic control.

2. 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 Gafer Ibnaof pediatrics hospital, in Khartoum state -Republic of Sudan from January 2015 to November 2016.

The study samples comprised 205 Sudanese patients with type 1 diabetes mellitus (101Male &104 female) clinically diagnosed as type 1 diabetes mellitus according to WHO criteria 18; in contrast, 100 healthy volunteers (43males,

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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 Gafer Ibna of 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 for5 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 (Electrochemiluminescen technology) while GAD antibodies & TG antibodies were measured by ELISA (Enzyme-Linked Immunosorbent Assay) from abcam – UK. Our data in 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

Two hundred and five Type 1 diabetic patients and one hundred matched controls were participated in this study. In the present study, males constitute 49.3% (n=101) of the test group and 43% (n=43) of the control group, while females constitute 50.7% (n=104) of the test group and 57% (n=57) of the control group. 41.5% (n=85) of patients had a family history of diabetes while 58.5% (n=120) had no family history of diabetes.

Table (1) shows baseline characteristics of the study group (diabetic patients and controls). This table shows insignificant difference (P=0.71) between the mean of age of the test group and the control group (12.88±3.91 years) versus (12.79±5.11 years), respectively. No significant difference in BMI between study group and healthy control group (17.48±3.20 mean ± S.D, versus 18.42±4.01, $p < 0.07$).

Table (2) shows a significant difference (P = 0.04) between the mean of the serum levels of TSH of the test group and the control group, there also a significant difference (P=0.00) between the mean of serum levels of GAD of the test group and the control group, moreover there was a significant increased in serum level of TG in comparison to control group (P=0.00), and HbA1c %was significantly higher in diabetic group than that of healthy control group (12.42±1.99, versus5.39±0.37, $p < 0.001$), which are demonstrated by (table-1).

Table 1: Basic characteristic of diabetic patients 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
BMI(Kg/m2)	17.48±3.20	18.42±4.01	0.07

* The means is a significant difference between different values, (P<0.05)

Table 2: Means of parameters among diabetic patients and control group

Variable	Test group (n=205)	Control group (n=100)	P value
GAD (U/ml)	8.86±9.23	3.00±1.40	0.00
TG (%)	6.49±8.80	2.70±1.26	0.00
HbA1c (%)	12.42±1.99	5.39±0.37	0.00
TSH (μlU/ml)	2.25±0.98	2.06±1.10	0.04

* The means is a significant difference between different values, (P<0.05)

4. Discussion

Diabetes is recognized as one of the leading causes of morbidity and mortality in the world. Type 1diabetes 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 Type1diabetes [7]. Type 1 diabetes mellitus is strongly associated with other organ-specific diseases such as Autoimmune Thyroid Diseases [ATD] [8], while ATD has been reported to be the most common coexisting autoimmune disease with type 1diabetes mellitus [9]. Tasi et al [10] 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 [11].

In the present study there is 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 [15], McCrimmon et al [16] and Perros et al [4], 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. Subclinical thyroid

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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 is 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 [17], 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 1diabetic 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 autoantibodies.

The result of current study shows 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 ElHefnawy et al [12], G. S. R. Kedari [13] and Lindberg B et al [18], 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 1diabetes mellitus. There is 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 antigens present in the tissues prone to autoimmune disease, or ethnic variations, difference in iodine intake, and a more sensitive assay in the latter study or alternatively immunological abnormalities present at diagnosis of T1DM before the start of insulin treatment.

The present data clearly demonstrated that there is a highly significant of HbA1c % of the test group and that of the control group this result is compatible with the result obtained by Hicham et al [19] who reported that the mean value of HbA1c % is significantly raised in the diabetic patients with type 1 when compared to healthy controls ($P < 0.001$.

Our study concluded that thyroid antibodies (TG-Abs & GADAbs) are significantly increased in type 1 diabetic patients with expecting of thyroiditis even in the subclinical state and elevated of TSH indicated that sever 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 at yearly intervals [20].

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