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RESEARCH ARTICLE

Evaluation of Thyroid Function and Lipid Profile in Type 1 Diabetes Mellitus

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Abstract

Background: Diabetes mellitus and thyroid diseases are two common endocrinopathies seen in the general population. Asymptomatic Thyroid dysfunction reported more frequently in diabetic population particularly in type 1 diabetes. High frequency of Hashimoto's thyroiditis has been reported also in type1 diabetic disease.

Subjects and method: The present study evaluates the relation between the two diseases through investigating the levels of random blood sugar (RBS), HA1c, thyroid stimulating hormone (TSH), thyroid microsomal antibodies (TmAb) and lipid parameters in 60 type 1 diabetic children, 48 of them were well managed and 12 were uncontrolled cases. And 60 healthy controls aged between 4-16 years old.

Results: TSH was significantly elevated in patients mainly in the uncontrolled diabetic group, TmAb was detected in 41 of 60 patients, 78% of them were uncontrolled type 1 D.M. The difference were highly significant regarding TSH, free T4, and TmAb. Also the lipid profile showed highly significant difference between the cases and controls.

Conclusion: Serum TSH and TmAb levels are elevated in IDDM cases when compared to the controls. Among the uncontrolled IDDM cases, elevation in serum and LDL-cholesterol levels together with low level of HDL- C is highly significant in the cases with thyroid antibodies compared to the cases without antibodies.

Introduction

Diabetes mellitus is one of the commonest endocrinopathies seen in the general population affecting all age groups and both sexes (Muralidhara **et al., 2013**). Insulin and thyroid hormones are both involved in cellular metabolism, so any affection of either of these hormones could result in functional derangement of the other, so in diabetes thyroid function is also affected (Proces **et al., 2001**). Our study evaluates the relation between diabetes and thyroid dysfunction in previously euthyroid children, and on the other hand it will investigate how thyroid dysfunction could affect the glycemic control and lipid parameters in diabetic children.Incidence of goiter with diabetes under the age of 40 years was high (Michalek,2000**;** Nakazono,1983), Asymptomatic thyroid dysfunction found in about 3% of children with type 1 diabetes, more in females than in males (Perros, **1995**; Gray,1980).Moreover, 13 to 20% of type diabetic children have elevated blood TSH levels and anti-thyroid antibodies. Thyroid microsomal (peroxidase) antibodies are present in 5-40% of type 1 diabetic children and significant number of these children developed thyroid dysfunction (Eisenbarth,1998). Migual Fernandz Castaner et al reported that nearly one third of newly diagnosed type 1 diabetes patients children have coexistent thyroid dysfunction (Miguel **et al., 1999**). Adolescent girls and young women are especially affected (Holl **et al., 1999**). Type 1 diabetes in children often present with auto immune thyroid disorders (Roldan **et al., 1999**).Although many patients with Hashimoto's thyroiditis defined

by high titer of thyroid peroxidase (TmAb) or thyroglobin antibodies elevated TSH in the absence of medications, and / or positive history on exam in patients with insulin dependent D.M. and the onset may be insidious or asymptomatic for a long time (Kontiliness **et al., 1990**). Mostly Hashimoto's disease patients usually are hypothyroid but there is a sub group of euthyroid cases with high titres of thyroid auto antibodies and normal thyroid function who do not require medications.However, some of them become hypothyroid by time (Gleicher **et al., 1993**). The decreases in the basal metabolic rate due to untreated hypothyroidism cause serious illness and further complicate lipid metabolism and metabolic control (Floyd **and** Roberts **1992**).The lipid profile of children with type 1 diabetes mellitus is highly dependent on glycemic control, Individuals with poorly controlled type 1 D.M. show high levels of triglyceride, total cholesterol and variable concentration of high density lipoprotein cholesterol (HDL-C) compared with non-diabetic control subjects (Taskinen ,1992 ; Perez,1997) also diabetes mellitus has been found to be an important risk factor for macro vascular disease and increased risk of coronary heart disease at adult age (Gunczler **et al., 2001**).Altered lipid profile also reported in hypothyroidism (Laakso and Lehto,1977). So, dyslipidemia in type 1 D. M. with subclinical hypothyroidism superimposed becomes an interesting aspect of study. So, in this study we estimate the TSH and TmAb in type 1 D.M. and correlate them with lipid parameters to assess the thyroid dysfunction.

Subjects and methods:

Our study is carried out on known type 1 diabetic children attending the outpatient department of pediatric department, Zagazig university hospital, Zagazig, Egypt in the period from March 2013 to December 2013 . This study was conducted on 60 children type 1 D.M; 48 of them were well managed (Group A) and 12 were uncontrolled cases (Group B). 60 healthy children age and sex matched (4-16 years old) were used as a control group. Among these 60 diabetic children 42 of them were females and 18 were males. Patient with complicated type 1 D.M. or any other children with coincident disease were excluded from the study. Venous blood samples were collected from these subjects. The samples were processed for estimation of serum thyroid stimulating hormone (TSH), thyroid microsomal antibodies (TmAb), free thyroxine, total serum cholesterol, serum triglycerides, high density lipoprotein (HDL- cholesterol) , low density lipoprotein (LDL-cholesterol),low density lipoprotein (VLDL-cholesterol), Random blood sugar, and HA1C%. Fasting urine sugar, ketone bodies and albumin level at urine were assessed by dipstick method. TmAb ,TSH and freeT4 were done using the ELFA technique (Enzyme Linked Fluorescent Assay) on VIDAS analyzer, the reagents supplied by biomerieux SA while blood glucose and lipid profile parameters were estimated on Coobas 6000, Roche diagnostics.

Statistical analysis

The Statistical software namely SPPS 10.0 were used for the analysis of the data and Microsoft Word and Excel have been used to generate graphs, tables etc. Student t test of independent samples has been used to find the significance of difference between the cases and controls for various parameters and between the group A and Group B in cases. The significance level of 5% is taken as critical value to see the difference between the mean values of cases and controls (Bernard,2000).

Results

Table (1) showed, there were non-significant difference among the studied groups as regard to sex and age

Table (2) showed , there were significant difference in cases group compared to control group as regard to the mean values ± SD levels, RBS (T=8.337,P<0.001) , HA1c% T=16.118,P<0.001),TSH (T=10.455,P<0.001), FreeT4(T=15.031,P<0.001), TmAB(T=11.247,P<0.001), Total Cholesterol (T=14.002,P<0.001) ,LDL-C(T=6.614,P<0.001), HDL-C (T=15.240,P<0.001), while there were no significant difference as regard VLDL-C (T=1.53,P=0.062) and TG (T=1.15,P=0.101)

Table (3) According to HA1C patients group divided to controlled and the uncontrolled diabetic patients there were significant difference in both groups as regard to the mean values ± SD levels, RBS (T=15.249,P<0.001) , HA1c% T=18.004,P<0.001), TSH(T=83.848,P<0.001) ,FreeT4(T=34.408,P<0.001), TmAB(T=27.24,P<0.001), Total Cholesterol (T=20.683,P<0.001) ,LDL-C(T=50.79,P<0.001), HDL-C (T=26.615,P<0.001), while there were no significant difference as regard VLDL-C (T=1.23,P =0.079) and TG (T=0.73,P=0.084) .

Table (4) showed significant correlation between the high level of thyroid antibodies and the high LDL-C, VLDL, and low level of HDL-C .

Table (1):- Demographic data of patients and control.

Sex	**Cases (No.&%)**	**Control (N o.&%)**	**χ^2**	**P.value**
Male	18 (30.0)	20 (33.3)	0.15	0.69
Female	42 (70.0)	40 (66.7)		
Total	60 (100.0)	60 (100.0)		
Age in years	**Mean±SD**	**Mean±SD**	**T**	**P.value**
	9.02±3.3	9.73±3.5	1.145	0.255

Table (2): biochemical parameters in cases and control

Biochemical parameters	**Cases(no=60) Mean±SD**	**Control (no=60) Mean±SD**	**T**	**P.value**
RBS mg/dl	192.77±80.7	105.05±11.5	8.337	**<0.001**
HA1c %	6.3±0.8	4.5±0.3	16.118	**<0.001**
TSH uIU/ ml	4.8±2	2±0.3	10.455	**<0.001**
Free T4 nmol/l	69.6±12.3	93.9±2.5	15.031	**<0.001**
TmAB IU/ml	36±12.4	17.7±1.6	11.247	**<0.001**
Total Cholesterol mg/dl	197.2±43.6	117±8	14.002	**<0.001**
LDL-C mg/dl	149±36.7	50.5±6.2	6.614	**<0.001**
VLDL-C mg/dl	29.8±5.1	27.5±8	1.53	**0.062**
HDL-C mg/dl	44±7.5	60±3.3	15.240	**<0.001**
TG mg/dl	165.4±13.6	159.9±21.9	0.73	**0.101**

Table (3): biochemical parameters in controlled and uncontrolled diabetic patients according to HA1c.

parameter	**uncontrolled type 1 Diabetics (no = 12)**	**Controlled type 1 Diabetics (no.=48)**	**T**	**P.value**
	Mean±SD	**Mean±SD**		
RBS mg/dl	335.9±75.8	157±17	15.249	**<0.001**
HA1c %	7.8±0.4	5.9±0.3	18.004	**<0.001**
TSH uIU/ ml	8.8±0.2	3.8±0.2	83.848	**<0.001**
Free T4 nmol/l	45.8±3.3	75.5±2.5	34.408	**<0.001**
TmAB IU/ml	59.8±3.5	30±3.3	27.24	**<0.001**

Total Cholesterol mg/dl	278.3±15.9	176.9±15	20.683	**<0.001**
LDL-C mg/dl	173.3±14.7	142.8±12.9	50.79	**<0.001**
VLDL-C mg/dl	39.1 ±3.3	33.9±9	1.23	**0.079**
HDL-C mg/dl	29.8±3.2	47.5±1.7	26.615	**<0.001**
TG mg/dl	189.2±7	179.9±14.9	1.15	**0.084**

Table (5):- correlation between TmAb and lipid profile parameters in uncontrolled diabetic group.

lipid profile parameters	TmAb	
	(r)	p. value
Total Cholesterol	0.57	0.053
LDL-C	0.581	0.048*
VLDL-C	0.641	0.025*
HDL-C	0.681	0.015*
TG	0.362	0.247

Discussion:

Data on RBS and HbA1C levels in controls and cases indicates a poor glycemic control in our cases. Glycemic state strongly influences the serum T_3 levels and TSH levels and poorly controlled diabetes results in a low T_3 level (Schlienger **et al., 1982**). In hypothyroidism that is coincident with type 1diabetes, the synthesis and release of insulin is decreased accounting for impaired glycemic control as well as recurrent hypoglycaemia due to decreased hepatic output (Mohn **et al., 2002**). In addition to the impact of altered thyroid status per se on diabetes, hypothyroidism with a decrease in the secretions of growth hormone and glucocorticoids further affects glucose homeostasis (Dimitriadis and Raptis,2001 ; Tosi,1996). TSH levels show highly significant elevation in cases compared to the controls. TSH values in cases in the present study are clearly suggestive of the hypothyroid state that is commonly associated with type 1 diabetes mellitus. There are a number of reports on the TSH levels in type 1 diabetes mellitus and many of them have recorded elevated TSH levels (Nakazono,1983; Perros ,1995; Flatau, 2000 ; Ditta, 2001). TSH levels are recorded to be higher in female type 1 diabetic cases (Perros **et al., 1995**), which show no difference between genders in our study. In euthyroid individuals with diabetes mellitus the serum T_3 levels, basal TSH levels and TSH response to TRH may all be strongly influenced by the glycemic control. Poorly controlled diabetes may also result in impaired TSH response to TRH or loss of normal nocturnal TSH peak. TSH responses and low T_3 state may normalize with good glycemic and/or diabetes control. The normal nocturnal TSH peak may not be restored in C-peptide negative patients i.e. patients with totally absent pancreatic b cell function (Schlienger **et al., 1982**).The association between type 1 diabetes and autoimmune thyroid disease has long been recognized and a high prevalence of thyroid antibodies has been found (8 to 44%) in several studies (Darendeliler ,1994; Lorini, 1996; Lindberg, 1997) is an indicator of thyroid autoimmune disease or Hashimoto's disease. In the present study thyroid microsomal antibody (TmAb) titre values in serum recorded a high significant elevation in cases when compared to the controls, mainly in the uncontrolled diabetic group. This was reported together with high levels of TSH and T4. Nearly 7% of our type 1 diabetic cases have co-existent thyroid antibodies (TmAb) together with high TSH level. As is reported in the literature (Erin, 1998), elevation in TmAb titres is encountered only in type 1 diabetic cases with increased TSH values. About $1/4^{th}$ of Thai patients with type 1 diabetes without thyroid disease had thyroid antibodies (Rattarasarn, 2001). A strong association between autoimmune thyroid antibodies (TmAb) and type1 diabetes has been indicated by Umpierrez et al (Umpierrez **et al.,** 2003).The present investigations on serum lipid profile in type 1 diabetic cases compared to the controls report a highly significant elevation in total cholesterol and LDL- cholesterol. The serum levels of triglycerides and VLDL-cholesterol though elevated are not statistically significant. The values of HDL- cholesterol are highly significant lowered and this recorded mainly in the uncontrolled diabetic patients. Among persons with type 1 diabetes mellitus, the decrease in basal metabolic rate (BMR) due to untreated hypothyroidism that commonly occurs may cause serious illness and

further complicate lipid disturbances (Erin **et al.,** 1998), but unlike in NIDDM, the prevalence of dyslipidaemia in IDDM is not large. Gray et al (1981) have reported elevated total cholesterol and triglyceride in diabetics with increased level of TSH and dyslipidaemia is dependent on glycemic control. In the cases of subclinical hypothyroidism (increased TSH), elevated total cholesterol, triglycerides and LDL-C with comparable HDL-C have been reported by Nadia Caraccio et al (2002). Antonio Perez et al (2000) have cited several papers in which individuals with poorly controlled type 1 diabetes mellitus show high levels of total cholesterol and triglycerides with variable concentrations of HDL cholesterol. They have also reported elevated LDL-C and triglyceride levels with low HDL-C levels in IDDM cases. Dyslipidaemia is indicated to normalize to some degree with good glycemic control and lipidemic changes appear to be more evident in females (Perros **et al.,** 2003). Indeed more frequent dyslipidaemic disorders in IDDM cases is low HDL-C, low prevalence of hypertriglyceridaemia and higher incidence of elevated total cholesterol. The recorded dyslipidemic state in our uncontrolled diabetic patients with thyroid antibodies and subclinical hypothyriodism of increased LDL-C and lowered HDL-C levels giving more risk to coronary heart disease in diabetics in general and in type 1 diabetic cases with thyroiditis (hypothyroidism) in particular, the results of this and other similar studies strongly project the need for evaluation of lipid profile as well as thyroid status in type 1 diabetic cases. Indeed several studies have suggested a need for regular screening of type 1 diabetics for TSH levels and lipid profile.

Conclusion

- Insulin dependent D.M type specially with uncontrolled blood glucose levels an important risk factor for thyroid gland dysfunction and dyslipidaemia
- Regular screening is recommended for all diabetic children to assess lipid profile, thyroid function and if presence of thyroid autoantibodies

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