RELATIONSHIP OF GLYCEMIC CONTROL WITH THYROID HORMONE LEVELS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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ABSTRACT

Objective: To compare the results of thyroid function tests in euthyroid type 2 diabetic patients and normal healthy individuals on the basis of glycemic control.

Methodology: This case control study of 300 subjects; 150 with type 2 diabetes and 150 controls, paired by age and gender, was conducted at two teaching hospitals of Peshawar during February-July 2013. They were sampled to investigate the relationship of thyroid hormones with glycemic profile determinants. Fasting plasma glucose (FPG) and glycated hemoglobin (HbA1c) were measured. The concentration of thyroid stimulating hormone (TSH), total triiodothyronine (TT3) and thyroxine (TT4) were evaluated using a Radioimmunoassay procedure. Diabetics were further divided into 2 groups on the basis of their good/poor glycemic control as shown by their HbA1c. P value of <0.05 was considered significant for comparison.

Results: Serum concentration of TT3 and TT4 were significantly low and high, respectively, in diabetic group as compared with healthy controls on the basis of FPG and HbA1c ($p < 0.05$). While comparing diabetics on the basis of glycemic control, both TT3 and TT4 were significantly low in the group with poor glycemic control ($p < 0.05$). Diabetics with poor glycemic control had a raised mean TSH level (2.52 ±3.21) as compared with diabetics with good glycemic control (1.68 ±1.13) but the difference was not statistically significant.

Conclusion: Patients with type 2 diabetes were associated with a low TT3 and a high TT4 level, respectively, as compared to their normal controls in euthyroid diabetic patients.

Key Words: Type 2 diabetes mellitus, Glycemic control, Thyroid stimulating hormone, Total triiodothyronine, Thyroxine

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INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder of multiple etiologies with disturbances in carbohydrate, lipids and protein metabolism. Broadly it is divided into two types; Insulin dependent diabetes (type 1) and non-Insulin dependent diabetes (type 2)[1]. The prevalence of diabetes has been increasing at alarming rates all over the world and is estimated to rise to 552 million adults by 2030[2].

Diabetes mellitus and thyroid diseases tend to co-exist together and thyroid diseases are more common in diabetics than in general population[3,4]. Complications of diabetes mellitus are mainly associated with diabetic vasculopathy[5]. New addition to these complications is the thyroid dysfunction which is attributed by some of the recent studies[6]. Altered thyroid hormones have been described in patients with diabetes especially those with poor glycemic control. DM may affect thyroid function either at the level of hypothalamic control of TSH release or at the conversion of T4 to T3 in the peripheral tissue. It has been well documented that hyperglycemia leads to reversible reduction of the activity and hepatic concentration of T4-5-deiodinase, which leads to low serum concentration of T3 and low, normal, or high levels of T4[7].

Although related to glycemic control, the pathophysiology of thyroid hormone alterations in patients with diabetes mellitus has never been fully investigated. This makes it important for us to study the relationship between these two endocrine conditions.

METHODOLOGY

This case control study including 300 subjects; 150 patients with type 2 diabetes and 150 in control group, paired by age and gender, who met the study inclusion criteria was conducted at two tertiary care hospitals of Peshawar, Kuwait and Mercy Teaching Hospitals. The medical OPD and wards of the hospitals were selected. The study duration was from February to July 2013. The sampling technique applied was convenient sampling.

The nature of study was explained and consent was taken from each participant. To avoid the influence of confounding factors, the following patients were excluded from the study: smokers; patients taking any other medications or drugs; patients with stroke or heart diseases; and those with history of other illness. These can induce an alteration in the thyroid hormone levels. Data including demographic details, clinical history and physical examination, which were performed there and then, was recorded on a proforma designed for this study.

In this study, we also divided the diabetic population into two groups according to HbA1c levels, into good glycemic control i.e., HbA1c <6.5% and a poor glycemic control i.e., HbA1c >6.5%. From each subject (type 2 diabetics as well as from controls) 05 ml of venous blood was drawn under asceptic measures from antecubital vein in the morning after an overnight fast of 7-10 hrs. Serum was separated by centrifugation within 30-45 minutes. Glycemic profile including fasting plasma glucose (FPG) and glycated hemoglobin (HbA1c) levels were analyzed at the laboratory of Pakistan Medical Research Center (PMRC), Khyber Medical College (KMC), Peshawar.

Fasting plasma glucose (FPG) was measured on the day of collection by glucose oxidase method using Microlab 200 by semiautomatic chemistry analyzer. The samples were centrifuged at 4000 rmp and the serum was kept at -20°C until further use. HbA1c level was determined using kit Hemoglobin A1-test on Merck/ Microlab 200 on semiautomatic chemistry analyzer. Samples were also analyzed for thyroid function tests in radioimmunoassay laboratory (RIA-lab) at the institute of Radiotherapy and Nuclear Medicine (IRNUM), Peshawar, Pakistan. Serum TT_3, TT_4 and TSH were analyzed by RIA method using immunotech by Beckman Coulte.

Data analysis was conducted with statistical software, SPSS version 17.0. Significance was calculated by using independent t test and was defined as p value <0.05. Data was expressed as means and standard deviation (SD). All the results were presented in the form of tables.

RESULTS

The mean age of the cases was 51.53 ±8.70 years while that of control group was 48.97 ±9.02 years. There were 74 (49.33%) males and 76 (50.66%) females in the diabetic group while there were 76 (50.66%) males and 74 (49.33%) females in the control group.

Controls had mean fasting plasma glucose of 82.0 ±13.52 mg/dl and diabetics had a mean FPG of 188 ±90.36 mg/dl with a significant p value of 0.0001. In case of glycated hemoglobin, controls had a mean HbA1c of 5.19 ±3.90% which is normal and diabetics had a mean of 7.91 ±1.79% with a significant p value of 0.0001.

Table 1 shows a low serum T3 level in diabetics as compared to control group with a significant p value of 0.01. Regarding serum T4, the comparison between two groups was significant with a p value of 0.03. However, the comparison between the means of two groups on TSH levels was non-significant.

Table 2 describes the comparison of TFT levels between type 2 diabetics based on glycemic control. According to our results, the only significant difference was in T3 i.e., p value of 0.02.

DISCUSSION

Diabetes is an alarming disorder of the third world[1]. The present study was carried out to look at the possible relationship between glycemic control and thyroid functions in euthyroid type 2 diabetics. The literature is extensive when issues about thyroid dysfunction and type 2 diabetes are concerned; however it is scarce when looking at euthyroid individuals. In Pakistan, studies have previously been performed on diabetes and lipid abnormalities, on thyroid abnormalities like hypothyroidism and subclinical hypothyroidism but not on the relationship of glycemic control in euthyroid type 2 diabetics and thyroid hormones.

Table 1: Comparison of TFT levels between controls and type 2 diabetics

Parameters	Control subjects Mean ±SD (n=150)	Diabetic subjects Mean ±SD (n=150)	P value
T3 (nmol/l)	1.89 ±0.23	1.80 ±0.36	0.01
T4 (nmol/l)	102 ±14.34	107 ±24.53	0.03
TSH (µIU/ml)	2.01 ±0.96	2.3 ±2.93	0.19

Table 2: Comparison of TFT levels between type 2 diabetics based on glycemic control

Parameters	Good Glycemic Control Mean ±SD (n=32)	Poor Glycemic Control Mean ±SD (n=118)	P value
T3 (nmol/l)	1.93 ±0.39	1.76 ±0.34	0.02
T4 (nmol/l)	109.0 ±26.1	108.0 ±24.49	0.82
TSH (µIU/ml)	1.68 ±1.13	2.52 ±3.21	0.14

In our study there was a significant low serum T3 levels in diabetics as compared to controls. This finding is in accordance with the study of Islam et al[8] who reported that patients with diabetes had a significant lower serum T3 levels as compared to controls. Similar results of low T3 were reported by the study of Moura-Neto et al[9] in which diabetic patients had significantly lower levels of TT3 as compared to healthy controls. Similarly, low T3 levels have been reported in subjects with type 1 diabetes and were associated with glycemic control[10]. It is unclear, however, if the same associations found in our study are present in patients with type 1 diabetes, as the pathogenesis of type 1 and type 2 diabetes are different.

In the present study, there was a significant raised serum TT4 levels in diabetics as compared to controls. This finding is in accordance with the study of Farasat et al[11]. They reported that patients with diabetes had significantly raised serum T4 levels as compared to controls with a p value of 0.02. This finding was also in accordance with other studies[8,12].

But our findings are contrary to the findings of Uppal et al[13] who conducted a study on 120 diabetics and 117 healthy controls. They found a low serum T4 levels in diabetics as compared to controls but with a non-significant p value. Moura-Neto et al[9] conducted a study in Brazil on 52 diabetics and 52 healthy controls. They found a low serum TT4 level in diabetics as compared to healthy controls (6.35 Vs 7.11µg/dL; p=0.006). Other studies also observed a low TT4 levels in diabetics as compared to healthy controls[14-16].

In our study, there was a raised mean TSH levels (2.3 ±2.93 Vs. 2.01 ±0.96, p value=0.19) in diabetics as compared to controls with a non-significant p value. These findings were supported by the study of Uppal et al[13] who reported raised mean TSH levels in diabetics as compared to controls with a non-significant p value. Other studies like Moura-Neto et al[9] and Islam et al[8] have found the same results with a non-significant p value. Some other studies like Farasat et al[11], Saha et al[17] and Bharat et al[18] showed a significantly raised TSH levels in diabetics as compared to healthy controls. These findings were contrary to the study done in Calabar, Nigeria by Udiong et al[19] in 2007 on diabetics and healthy controls. They have found a low mean TSH level in diabetics as compared to healthy controls.

In euthyroid individuals with diabetes mellitus, the serum T3 levels, basal TSH levels and TSH response to thyrotropin releasing hormone (TRH) all are strongly influenced by the glycemic status[17,18]. Patients with poor glycemic control had a low TT3 levels as compared to patients with good glycemic control. This is consistent with other studies[9,11,13,17]. Patients with poor glycemic control had a low TT4 levels as compared to patients with good glycemic control. This was also found in other studies[13].

Patients with poor glycemic control had a raised TSH level as compared to patients with good glycemic control. The levels of TSH in our study were not significant. This finding is not consistent with the reports of Celani et al[16], Smithson[21] who recorded varied levels of thyroid hormones in diabetic subjects. Similar findings were observed by Bazrafshan et al[22] in their study of 2001 type 2 diabetics showed the relationship between thyroid dysfunction and type 2 DM.

CONCLUSION

Patients with Type 2 diabetes had a low TT3 and a high TT4 level, respectively, as compared to their normal controls in euthyroid diabetic patients.

RECOMMENDATIONS

We recommend that screening for thyroid function tests should be done routinely in all diabetic patients especially in patients with uncontrolled diabetes. Further studies with larger sample sizes are needed to further elaborate the issue.

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CONTRIBUTORS

SW conceived the idea, planned the study, and drafted the manuscript. MA and FK helped acquisition of data and did statistical analysis. All authors contributed significantly to the submitted manuscript.