ASSOCIATION OF THYROID DYSFUNCTION WITH TYPE 2 DIABETES MELLITUS

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ABSTRACT

Objective: To determine association and to evaluate and compare the trends of thyroid dysfunction among patients with type 2 diabetes mellitus.

Study Design: Case control study.

Place and Duration of Study: Military Hospital Rawalpindi and chemical pathology department, Army Medical College Rawalpindi, from Nov 2014 to Nov 2015.

Material and Methods: A total number of 69 diagnosed patients with type 2 diabetes mellitus of either sex between age group of 30-60 years along with equal number of age and sex matched non-diabetic controls were included in the study. Fasting blood glucose and serum thyroid hormones (total T3, free T4 & TSH) in both groups were analyzed and compared for statistical significance at *p*-value <0.05. Chi-square test was used to compare frequencies of thyroid dysfunction among cases and controls.

Results: In patients 38 (55.1%) had thyroid dysfunctions including both subclinical and true thyroid disease while 31(44.9%) presented with normal thyroid profile. In control group 16 (23.2%) subjects were diagnosed for subclinical thyroid dysfunction while 53 (76.8%) controls had no dysfunction. No overt disease was found in control group. Among thyroid parameters, serum TSH and free T4 showed statistically significant differences among patients and controls (*p*-value <0.05). The patient group showed significantly higher frequencies of thyroid disease (*p*-value <0.001). Subclinical hypothyroidism was predominant disorder followed by subclinical hyperthyroidism.

Conclusion: This study suggests routine evaluation of thyroid dysfunction in diabetic patients to prevent diverse complications followed by co-existence of these common endocrine disorders. Type 2 diabetic patients are at more risk to develop thyroid dysfunction so routine assay of thyroid hormones in patients with type 2 diabetes mellitus is needed for timely therapeutic interventions.

Keywords: Hyperthyroidism, Hypothyroidism, Type 2 diabetes mellitus.

INTRODUCTION

Diabetes mellitus (DM) is the most common endocrine disorder which affects a large number of people worldwide with highest morbidity and mortality. It is a leading cause of death across the globe. According to WHO Fact Sheet (Nov 2014) out of 347 million diabetic patients worldwide, majority is suffering from type 2 diabetes which is predicted to become the seventh leading cause of death in the world by 2030. South Asian countries are included in highly diabetes mellitus prevalent societies with increasing number of difficult-to-treat diabetic patients[1].

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Thyroid disorders are found to be the most frequent endocrine disorders in the general population after diabetes. The metabolisms of deranged insulin and thyroid hormones can result in purposeful derangements of one another resulting in added risk towards prognosis of disease[2]. Diabetic patients with hyperthyroidism have poor glycemic control even on therapeutic doses during treatment while hypothyroidism with diabetes mellitus can lead to hypoglycemic episodes due to decreased insulin degradation along with added risk of dyslipidaemias. Raised serum thyroid hormones levels provoke gluconeogenesis in the liver and result in enhanced absorption of glucose through the intestine. It also affects insulin metabolism by increasing insulin resistance[3,4]. Thyroid hormones are thoroughly involved in cellular metabolism of

carbohydrate, lipids, and proteins along with insulin so surplus or deficiency of one of these hormones can produce the significant derangement of the others[5].

In different geographical regions of the world, a number of the studies have reported the different incidence and prevalence of thyroid dysfunction among diabetic patients[6,7].

Some recent regional studies have shown much higher prevalence of thyroid disease in patients with type 2 DM in the region of South Asia[8]. To the best of our knowledge, this study is first of its kind in our population.

This study was conducted to investigate and evaluate the associated tendencies of thyroid dysfunction with type 2 diabetes mellitus in our clinical set ups. Co-occurrence of these common endocrine conditions has significant impact on clinical manifestations and biochemical parameters of both the disorders which will further influence screening, diagnostic and therapeutic strategies.

MATERIAL AND METHODS

This case control study was conducted at Chemical Pathology Department, Army Medical College Rawalpindi and Military Hospital, Rawalpindi, over a period of one year from November 2014 to November 2015. Sampling technique was non-probability, convenient sampling. Sample size was calculated by WHO formula. A total of sixty-nine patients with type 2 diabetes mellitus fulfilling WHO criteria along with age and sex matched controls with no history of diabetes mellitus or thyroid dysfunction were enrolled from Military Hospital, Rawalpindi and Informed consent was obtained from each participant. All study subjects were evaluated clinically as well as biochemically through hormones assays in laboratory.

The diagnosed and under treatment patients of type 2 diabetes mellitus from OPD of Military Hospital Rawalpindi were included in the study. All patients with history of type 1 diabetes mellitus, proven thyroid disorders and taking anti thyroid drugs or thyroid replacement therapy, pregnancy and gestational diabetes mellitus (GDM), history of thyroid surgery or radiation therapy to thyroid gland, drug history of glucocorticoids, oral contraceptives, estrogens, androgens and hormonal therapies, acute infection and inflammation, neoplastic diseases and any other systemic disease affecting serum thyroid hormone were excluded from the study.

Fasting venous blood sample was drawn and immediately transferred to respective vacutainers under sterile conditions for serum thyroid hormones and fasting plasma glucose analysis. Plasma glucose analysis was done on the same day while serum for thyroid profile was stored at -20^{0}C till biochemical analysis. Serum thyroid hormones (total T3, free T4 and TSH) were analyzed by using chemiluminescent enzyme immunoassay while plasma glucose was measured by the enzymatic colorimeteric method by using glucose (GOD-POD) kits on fully automated chemistry analyzer. Reference ranges mentioned on kit literature provided by manufacturer were used for diagnosis.

Data were analyzed on IBM statistical package for social sciences (SPSS), version 21. For quantitative data, means, medians, ranges (min-max) and standard deviations (SD) were calculated. Frequencies and percentages were calculated for qualitative variables. Mann-Whitney U test was applied for comparing fasting plasma glucose and serum thyroid hormones levels among cases and controls. Frequencies of thyroid dysfunction among cases and controls were compared by using Chi-square test. A p-value <0.05 was considered to indicate statistical significance.

RESULTS

A total of sixty-nine patients of type 2 diabetes mellitus fulfilling WHO criteria between age group of thirty to sixty years along with equal number of age and sex matched controls were included in this study. Out of total 69 patients, 35 (50.72%) males and 34 (49.3%) females along with equal number of sex matched

controls participated in the study. Mean and standard deviation age of the cases and control group was 46.55 ± 8.3 years and 47.00 ± 8.6 years respectively.

Mean fasting plasma glucose (FPG) levels in the patients was 6.01 ± 3.3 mmol/L while in controls it was 4.30 ± 0.9 mmol/L. The median value of FPG in patients was 5.7 mmol/L while this value in controls was 4.5 mmol/L. The mean value of serum free T4 in patients was 16.21 ± 8.9 pmol/L but in controls it was 19.29 ± 8.0 pmol/L. The median value of serum free T4 in patients and controls were 16.30 pmol/L and 19.0 pmol/L respectively. The control group showed much lesser value of TSH as compared to patients, in the patients mean serum TSH level was 4.01 ± 2.9 mIU/L while in controls it was 2.82 ± 1.6 mIU/L. The median value of TSH in patients was 3.9 mIU/L while in the controls it was 2.9 mIU/L (fig-1). Mann-Whitney U test revealed significant differences between FPG, serum free T4 and TSH levels among cases and controls (p<0.05). Mean serum total T3 levels showed no significant difference between patients and controls (p>0.05) (table-I).

Two gross categories of study participants were patients with thyroid dysfunctions and control, who had normal thyroid function. In group of patients 38 (55.1%) had thyroid dysfunctions including both subclinical and true thyroid disease while 31(44.9%) presented with normal levels of thyroid hormones. In control group 16 (23.2%) presented with subclinical thyroid dysfunction while 53 (76.8%) had no dysfunction. No overt disease was found in this group. Results of chi-square test were suggestive of significantly higher frequencies of thyroid dysfunction in type 2 diabetics than in non-diabetic controls (table-II).

Association of thyroid dysfunction with type 2 diabetes mellitus was studied by comparing sub-groups of thyroid function including hyperthyroid, hypothyroid and euthyroid groups. Among the patients with diabetes mellitus 14 (20.3%) had hyperthyroidism and 24

Table-I: Comparison of levels of biochemical parameters among patients and controls.

Parameters	FPG (mmol/L)	Total T3 (nmol/L)	free T4 (pmol/L)	TSH (m IU/L)
Mean ± SD				
Patients	6.01 ± 3.3	2.52 ± 1.9	16.21 ± 8.9	4.01 ± 2.9
Controls	4.30 ± 0.9	2.12 ± 0.9	19.29 ± 8.0	2.82 ± 1.6
Median (Min-Max)				
Patients	5.7 (2.0 -18)	2.1 (1-7)	16.3 (3-33)	3.9 (0.1-9)
Controls	4.5 (2.5-6.7)	2.2 (1-4)	19.0 (3-40)	2.9 (0.2-7.7)
p-value	*0.001	0.751	*0.042	*0.027

*Significant *p* value <0.05

Table-II: Frequencies of thyroid dysfunction among patients and control groups.

Groups	Euthyroid n (%)	Hyperthyroid n (%)	Hypothyroid n (%)	Total n(%)	*p*-value (Chi-square test)
Patients	31 (44.9%)	14 (20.3%)	24(34.8%)	69 (100%)	**<0. 001
Controls	53 (76.8%)	8 (11.6%)	8 (11.6%)	69 (100%)	
Total	84 (60.9%)	22 (15.9%)	32 (23.2%)	138 (100%)	

*Significant *p*-value < 0.05

Table-III: Frequencies of subclinical and overt thyroid dysfunction in patients and controls.

Thyroid dysfunction	Patients (n=69)			Controls (n=69)		
	Subclinical n (%)	overt n (%)	Total n (%)	Subclinical n (%)	Overt n (%)	Total n (%)
Hypothyroidism	17 (70.84%)	7 (29.2%)	24 (34.78%)	8 (100%)	0(0.00%)	8 (11.6%)
Hyperthyroidism	10 (71.4%)	4 (28.6%)	14 (20.28%)	8 (100%)	0(0.00%)	8 (11.6%)
Total	27 (39.13%)	11(15.94%)	38 (55.06%)	16 (23.2%)	0(0.00%)	16(23.2%)

(34.8%) were hypothyroid while 31 (44.9%) patients had normal serum levels of thyroid hormones. Hypothyroidism was the predominant disorder in group of patients. On the other hand out of sixty-nine non-diabetic healthy controls 8 (11.6%) were sub-clinically hyperthyroid and 8 (11.6%) had subclinical hypothyroidism while 53 (76.8%) showed normal thyroid function. No overt thyroid disease was found in this group (*p*-value <0.001) (table-III).

Both patients and controls were also studied for frequencies of subclinical and overt thyroid dysfunction. Subclinical hypothyroidism was predominant disorder. In patients group, out of total hypothyroid patients 17 (70.8%) had subclinical hypothyroidism while in control group 8 (100%) participants presented with subclinical hypothyroidism. Overt hypothyroidism was found in 7 (29.2%) of patients out of total hypothyroid patients. Subclinical hyperthyroidism was found in 10 (71.4%) patients while 4 (28.6%) presented with overt hyperthyroidism out of total hyperthyroid patients. In group of patients 11 (15.94%) were found with overt thyroid disease. No member in control group presented with overt thyroid disease (table-III).

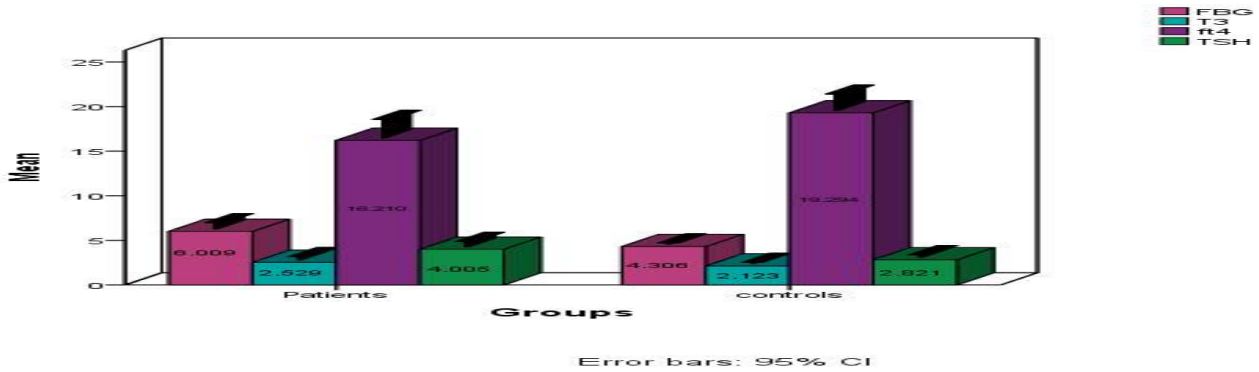

Figure: Mean serum levels of biochemical parameters among patients and controls.

DISCUSSION

In the present study, evaluation of thyroid function tests was carried out to determine association between thyroid dysfunction and type 2 diabetes mellitus. This aspect is required to be considered because every year increasing number of patients with poorly controlled diabetes report in hospitals and most of them are continued undiagnosed for thyroid disease in spite of its high prevalence in type 2 diabetes mellitus, particularly in South Asia[9,10]. Thyroid dysfunction, if left untreated in patients of type 2 diabetes, can lead to early development of complication of diabetes. Diabetes mellitus and thyroid disorders are two main endocrine disorders interconnected to each other and encountered in our clinical setups. Their association is yet poorly understood although it is coupled with vascular complications leading to high mortality and morbidity[11]. Micro-angiopathies and atherogenesis can develop early in diabetes mellitus, associated with thyroid dysfunction which affects the impact of therapy on course of both the disorders[12].

Previous similar studies in different geographical regions conducted by Papazafir-opoulou et al, Radaideh et al ,Singh et al, Ghazali et al, , Demitrost et al and Diaz et al reported higher frequencies of thyroid disorders in type 2 diabetes mellitus as from 12.3% to 32.4% in their regions[13-16].

A number of studies conducted in South Asia have shown much higher prevalence in contrast to rest of the world. Some regional studies also have shown higher prevalence of thyroid disease in patients of type 2 DM. A study conducted as joint venture of medicine and surgery departments of R.G.Kar Medical College Kolkata, India reported 65.83% prevalence of

thyroid dysfunction in type 2 diabetics[8]. Same author reported frequency of 75% in a later study. This study concludes that there is much greater occurrence of thyroid disorder in diabetic patients in this part of the world in contrast to Europe and US[10]. Other regional studies also reported high prevalence of thyroid disease in diabetic patients. Bharadiya and Taksali reported prevalence of 53.33% and 55% respectively[9,12]. In these studies non-diabetic control groups also had thyroid dysfunction, especially subclinical thyroid disease. This finding was consistent with results of this study. Incidence of subclinical thyroid disease in control group indicates high prevalence of thyroid disease in our population. This finding was supported by some local studies conducted for prevalence of thyroid disease in our population. A screening study conducted by Alam et al at Liaqat National Medical College in collaboration with Lyari General Hospital, Karachi for prevalence of thyroid disease revealed much higher frequencies of both subclinical and true thyroid disease. Subclinical thyroid disease was found in 22% of females and 15% of male participants. Frequencies of true thyroid disease were 44.69% and 20.40% in females and males respectively. These results are indicative of higher prevalence of thyroid disease in this region[17].

In the present study significant differences were observed in the thyroid profiles among patients and healthy controls. In this study serum levels of TSH and fT4 have shown significant disparity among patients and controls which was also supported by outcome of previous studies while T3 levels showed no significant difference which differs from respective studies[18,19]. The reason for this difference could be the difference in sample size used in those studies and different factors affecting peripheral conversion of T4 to T3. Another reason may be different ethnicity of the study participants in those studies. Pasupathi et al investigated the effects of diabetes mellitus on thyroid hormone levels. In their study, the levels of TSH and free T4 had significant difference in diabetic patients as compared to control subjects, the finding corresponds to the objective of the present study that type 2 DM is associated with thyroid disease. Serum T3 levels did not differ significantly between cases and control groups which were supportive of observations in the present study[20]. In a comparative analysis, Islam et al, reported that patients with type 2 diabetes had significantly lower serum FT4 levels compared with the control subjects. The finding was in accordance to the present the study[5]. All the above studies support the hypothesis that an association exists between thyroid dysfunction and diabetes mellitus. No study is carried out in Pakistan previously to assess and evaluate the association of these two common endocrine disorders. This study highlighted the important derangements in serum levels of thyroid hormones along with significantly high frequencies of thyroid dysfunction in patients with type 2 diabetes mellitus.

CONCLUSION

This study demonstrates the more deranged biochemical parameters of thyroid profile in type 2 diabetics and reflects significantly higher frequencies of thyroid disorders in patients of type 2 DM in contrast to control group. It emphasizes that evaluation of thyroid dysfunction should be considered in patients of diabetes mellitus, especially poorly controlled type 2 DM to reduce the complications followed by co-existence of these two common endocrine disorders.

CONFLICT OF INTEREST

The study has no conflict of interest to declare by any author.

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