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Association of thyroid disease in type 2 diabetes mellitus

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Abstract

Background: Diabetes Mellitus is characterized by absolute and relative deficiencies in Insulin action associated with chronic hyperglycemia and disturbances of carbohydrate, lipid and protein metabolism. Diabetic patients have a higher prevalence of thyroid disorders than normal population. Altered thyroid hormones have been described in patients with diabetes especially those with poor glycemic controls. The reported prevalence of thyroid dysfunction in diabetes varies from 2.2% to 17%. Others reported high prevalence of abnormal TSH concentration in 31% of type 2 DM. Diabetic women are more frequently affected than men, also hypothyroidism is more common than thyrotoxicosis.

Aims and Objective: To estimate thyroid hormone level in type 2 Diabetes Mellitus and determine the association of thyroid diseases in type 2 Diabetes Mellitus

Materials and methods: The study was a cross-sectional and comprised of 60 subjects, 30 known cases of Type 2 Diabetes who visited Diabetic Clinic, RIMS and another 30 apparently healthy individuals irrespective of age, sex and religion were selected for the study. After taking Informed written consent and detailed history from all the participants, Fasting 5ml venous blood was drawn from each subject under aseptic condition The serum thus collected were estimated for T3, T4 and TSH by using Microplate ELISA Kit.

Results: 66.7% of the cases had low T3 (i,e below 0.52ng/ml). 3.3% of control group had T3 above 1.85ng/ml. Mean±SD of T3 is found significantly lower in the case group than that of the controls($p < .001$). Mean±SD of T4 in case group was found higher than the control. Similarly TSH Mean±SD of case was also found significantly higher than control with P value .015. 73.33% of females and 60% of males show low T3,TSH level high in 80% of females as compared to males. Percentage of hypothyroidism increased in female group(40%) compared to males(20%).

Conclusion: 63.33% of type 2 diabetic patients have abnormal thyroid hormone level. Of which 30% has low levels of thyroid hormones and increased TSH. Hypothyroidism was the most common thyroid disorder associated with type 2 Diabetes and female patients are found more affected than male.

Keywords: Triiodothyronine(T3), Tetraiodothyronine (T4), Thyroid stimulating hormone(TSH), Type 2 Diabetes Mellitus.

Introduction

Diabetes mellitus (DM) is an important health problem affecting major population worldwide. DM is characterized by absolute and relative deficiencies in Insulin action associated with chronic hyperglycemia and disturbances of carbohydrate, lipid and protein metabolism. Defects in carbohydrate metabolism and consistent efforts of the physiological system to correct the imbalance in carbohydrate metabolism place an over-exertion on the endocrine system. The influence of endocrine and non-endocrine organs other than pancreas on DM is documented. Ocassionally, the endocrine disorders such as thyroid abnormalities may associate with DM[1].

Diabetic patients have a higher prevalence of thyroid disorders than normal population[2]. Hage M et al[3] also reported the association of thyroid disorders with DM. Insulin and thyroid hormones being intimately involved in cellular metabolism and thus excess or deficit of either of these hormones could result in the functional derangement of the other[4]. Altered thyroid hormones have been described in patients with diabetes especially those with poor glycemic controls[3].Thyroid disease is found commonly in most forms of diabetes and is associated with advancing age, particularly in type 2 DM and underlying autoimmune disease in type 1 DM[5].The reported prevalence of thyroid dysfunction in diabetes varies from 2.2% to 17% [6,7]. Others reported high prevalence of abnormal TSH(Thyroid stimulating hormone) concentration in 31% of type 2 DM. Diabetic women are more frequently affected than men, also hypothyroidism is more common than thyrotoxicosis. The researchers found that subclinical hypothyroidism affects almost one in 20 women with type 2 DM [8,9].

The first report showing the association between Diabetes and thyroid dysfunction was published in 1979 [6,7]. Since then a lot of studies in different countries have tried to estimate the prevalence of thyroid dysfunction among diabetic patients [6,7,10]. The reports were varied in different countries in their prevalence estimates. The prevalence rate of thyroid dysfunction in Diabetic patients still remains controversial. Moreover, not many studies have been done in thyroid dysfunction in type 2 DM. The present study aimed to determine the association of thyroid dysfunction in type 2 Diabetic patients.

Materials and methods

The study was a cross- sectional, carried out in the department of Physiology in collaboration with the department of Medicine, Regional Institute of Medical Sciences(RIMS), Imphal, after getting approval from the Institutional Ethical Committee (Board of Ethics, RIMS)

The study group comprised of 60 subjects, 30 known cases of Type 2 Diabetes who visited Diabetic Clinic, RIMS and another 30 apparently healthy individuals irrespective of age, sex and religion were selected for the study. Informed written consent was taken from all the participants. Detailed history such as age, sex, religion, occupation, duration of diabetes, dietary habits, history of thyroid disease etc was recorded. Thorough general and systemic examination was done to exclude chronic kidney disease and vascular disease. All the patients were screened with Ultrasonography to rule out adrenal mass, weight, height, mode of treatment for DM were also recorded.

Fasting 5ml venous blood was drawn from each subject under aseptic condition and collected in sterile vial. The

collected samples were allowed to clot and centrifuged at 3000rpm for 30 minutes. The serum thus collected was estimated for T3, T4 and TSH by using Microplate ELISA Kit of ELISCAN by RFCL Limited.

Statistical methods: The data collected were analyzed using SPSS software. Results were reported as Mean±SD for quantitative variables and no. of cases along with percentage for the categorical/qualitative variables. The group means were compared by Independent sample t - test and F - test (Analysis of variance- ANOVA). For categorical variables, Chi square test was applied. All the comparisons are two sided and P value of <0.05 and <0.01 are use as the cut off values for significant and highly significant respectively.

Results

Table 1: Distribution of study group according to demographic profile

Demographic profile		Cases(n=30)	Control(n=30)	Chi square or t- value	df	P - value
Sex	Male	15(50.0%)	15(50.0%)	No test required		
	Female	15(50.0%)	15(50.0%)			
Age (years)	20-30	-	12(40.0%)	21.600	4	< .001
	30-40	2(6.7%)	4(13.3%)			
	40-50	11(36.7%)	9(30.0%)			
	50-60	6(20.0%)	4(13.3%)			
	60-72	11(36.7%)	1(3.3%)			
Age (yrs)	Mean±SD	52.70±9.89	37.47±10.93	5.657	58	< .001
Height(cm)	Mean±SD	160.07±7.46	155.57±6.72	2.453	58	.017
Weight(Kg)	Mean±SD	67.33±6.87	59.43±11.44	3.241	58	.002
BMI	Mean±SD	26.33±2.75	24.24±4.34	2.219	58	.030
SBP(mmHg)	Mean±SD	131.67±6.89	121.33±10.74	4.416	58	< .001
DBP(mmHg)	Mean±SD	84.67±5.07	77.33±5.20	5.524	58	< .001

SD : Standard deviation, df : degree of freedom, P : observed level of significance, Chi square(applied in categorical variable); t- test (applied in continuous/quantitative variable i,e Mean±SD)

Table 2: Distribution according to thyroid hormone levels.

Thyroid profile		Cases(n=30)	Control(n=30)	Chi square or t- value	df	P- value
T3 ng/ml	Below 0.52	20(66.7%)	-	No test is appropriate		
	0.52 - 1.85	10(33.3%)	29(96.7%)			
	Above 1.85	-	1(3.3%)			
T3 ng/ml	Mean±SD	0.543±0.360	1.341±0.366	8.89	58	< .001
T4 µg/dl	4.4 - 11.6	8(26.7%)	28(93.3%)	27.77	1	< .001
	Above 11.6	22(73.3%)	2(6.7%)			
T4 µg/ml	Mean±SD	12.762±2.923	8.480±2.137	6.47	58	< .001

TSH µIU/ml	0.39 - 6.16	7(23.3%)	18(60.0%)	8.29	1	.004
	Above 6.16	23(76.7%)	12(40.0%)			
TSH µIU/ml	Mean±SD	9.457±3.574	7.182±3.420	2.51	58	.015

* P value < 0.05 is taken as significant

Table 2 shows that 66.7% of the cases had low T3 (i,e below 0.52ng/ml). However, only 3.3% of control group had T3 above 1.85ng/ml. Mean±SD of T3 is found to be significantly lower in the case group than that of the controls(p < .001). Mean±SD of T4 in case group was found higher than the control. Similarly TSH Mean±SD of case was found significantly higher than control with P value .015.

Table 3 : Distribution of cases according to patient's profile

Patient's profile		Cases (n=30)
DM mode of treatment	Insulin	4(13.33%)
	Oral	26(86.67%)
Treatment outcome	Controlled	23(76.67%)
	Uncontrolled	7(23.33%)

Table 4 : Percentage of normal and abnormal thyroid function in case group

		Thyroid hormones		Chi square or t- value	df	P- value
		Abnormal hormone levels	Euthyroid			
Sex	Male	8(53.34%)	7(46.66)	1.292	1	.256
	Female	11(73.34%)	4(26.66%)			
Total		19(63.34%)	11(36.66%)			

Table 5: Percentage distribution of thyroid hormone levels in case group

Parameters	Male (n=15)	Female (n=15)
Low T3	9(60%)	11(73.33%)
Total low T3	20(66.7%)	
High TSH	11(73%)	12(80%)
Total high TSH	23(76.6%)	
Euthyroid	7(46.66%)	4(26.7%)
Total Euthyroid	11(36.66%)	
Hypothyroid	3(20%)	6(40%)
Total hypothyroid	9(30%)	
Hyperthyroid	0	0

73.33% of females and 60% of males show low T3,TSH level high in 80% of females as compared to males. Percentage of hypothyroidism increased in female group(40%) compared to males(20%) as shown in table 6.

Discussion

In the present study, the thyroid hormones were estimated in both the cases and controls group to reveal the thyroid function. It was observed that 66.7% of the case group had T3 below 0.52ng/ml and 33.3% had T3 in the range between 0.52 - 1.85ng/ml. Whereas in the control group, 96.7% had T3 between the range of 0.52 - 1.85ng/ml except in one individual where T3 was found above 1.85ng/ml. Thus, mean±SD was found to be lowered in case group compared to the control($p < .001$).

In 73.3% of cases, T4 was found above 11.6µg/dl whereas 93.3% of the control group had T4 value within 4.4 - 11.6µg/dl. Therefore, mean±SD of T4(12.762±2.923)µg/dl of case group was found much higher than mean±SD(8.480±2.137)µg/dl of control group.

The present study also observed higher mean±SD of TSH (9.457±3.574)µIU/ml of cases than control where mean±SD was found to be 7.182±3.420µIU/ml. The difference was statistically significant ($p = .004$) which is consistent with the work of Swamy RM et al [11] and Smithson MJ[10] .T3 in the case group mean±SD was reduced significantly ($p<.001$) which is in agreement with Swamy RM et al [11] and Munoz NA et al [12] ,but the mean±SD of T4 was increased significantly which may be due to uncontrolled diabetic conditions of the cases. In the present study, there are 23.3% cases of uncontrolled diabetes.

Marked hyperglycemia causes reversible reduction of the activity and hepatic concentration of T4-5'-deiodinase,low serum concentration of T3, elevated levels of reverse T3 and low, normal or high T4 [13]. Since thyroid hormone regulate metabolism and diabetes can alter metabolism of foodstuff and further affect the diabetic patients associated with thyroid disease [14].The present study observed 63.34% abnormal thyroid hormone,30% hypothyroidism and 0% hyperthyroidism among the case group. Although there is variation, this finding can be correlated with the reports of other studies [10,14].

13.3% of the cases were on Insulin and 86.67% on oral hypoglycemic drugs. Insulin is capable of raising the level of TSH and suppressing the level of T3. Apart from the physiological impact of diabetes on TSH, Insulin administration could also have influenced its level. The higher the standard deviation(±3.574)µIU/ml of TSH observed among the diabetic in the study may be due to the influence of the Oral hypoglycemic agents given to the diabetic patients which also correlate with the findings of Udiong CEJ et al [15].TSH mean±SD was found higher in females as compared to males.

Guney E et al [13] reported that treatment of diabetes with sulfonylureas led to increased incidence of goiter and hypothyroidism. This might be the cause of low T3(66.7%) and high T4(73,33%) found among the 30 cases. Singh G et al [14] reported only low but no change in T4 in their study.

There is a decrease TRH synthesis in diabetes mellitus [16,17] or modified TRH synthesis which could be responsible for variation in thyroid hormone levels and the glycemic status of the diabetics studied may have a role. Glycemic status is influence by Insulin, which is known to modulate TRH and TSH levels [15].

The incidence of hypothyroid is higher in females(40%) than in males(20%) which is similar with the findings of Udiong CEJ et al [15]. This could be due to higher prevalence of obesity in female diabetics that was recorded from the calculated BMI [16] . In the present study, the mean±SD of BMI of diabetics were found higher in females (27.124±2.907) than

males(25.53±2.425).This is in agreement with the findings of other studies [15,16] .

It has been reported that thyroid disease was associated with both type 1 and type 2 diabetes [17] .The present study detected hypothyroidism in 30% of diabetic patients. Swamy RM et al [11] reported 12.06% hypothyroidism in his study, Whereas Perros et al [18] reported 13.4%. According to Papazafiropoulou A et al [8] ,12% of diabetic patients were associated with hypothyroidism.

The high prevalence of abnormal thyroid function could have been resulted from the influence of poorly controlled diabetes on thyroid hormone concentrations [19,20] . In the present study,63.34% of the cases had abnormal thyroid hormone levels. Udiong CEJ et al [15] reported a prevalence of 46.5% abnormal hormone levels among the diabetic patients. Therefore, the findings of the present study were in consistent with their work. These abnormalities may be influenced by local diets, standard of living and sedentary lifestyle. It might also be the outcome of various medications that the diabetic patients received. Suzuki et al [17] attributed the abnormal thyroid hormone levels found in diabetes to the presence of Thyroid Hormone Binding Inhibitor (THBI) ,an inhibitor of extra thyroidal conversion enzyme of T4 to T3 and dysfunction of the hypothalamus- hypophyseal-thyroid axis. Stress which is associated with DM may also cause changes in the hypothalamus, anterior-pituitary axis. It appeared that the presence of subclinical and hyperthyroidism might result from hypothalamus-hypophyseal-thyroid axis disorder as suggested by Celani et al [21] and Guney E et al [13] .This present study did not find any incidence of hyperthyroidism in the diabetic cases.

The limitation of the present study is that it is a cross sectional study with lesser sample size and hence follow up may be required to substantiate the findings. Evaluation of glycosylated haemoglobin level, reverse T3 level, kidney function test and lipid profiles of the diabetic patients were not determined as information from these could help in various aspects.

Conclusion

The present study observed that 63.33% of type 2 diabetic patients have abnormal thyroid hormone level. Of which 30% has low levels of thyroid hormones and increased TSH. Therefore, hypothyroidism was the most common thyroid disorder associated with type 2 Diabetes and female patients are found more affected than male.

So, it is important that all patients with Diabetes should be screened for thyroid function as failure to recognize the presence of abnormal thyroid hormone level in type 2 Diabetes may be a primary cause of poor management often encountered in some treated type 2 Diabetes.

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