

A Study of Thyroid Dysfunction in Type 2 Diabetes Mellitus in Tertiary Care Center

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ABSTRACT

Introduction: Type 2 diabetes mellitus and thyroid disorders are the most common endocrine disorders and growing problem in our country. We have observed that many diabetes mellitus patients are associated with thyroid dysfunction. However, the prevalence of thyroid dysfunction in these patients has not been investigated. We conducted this study to study the proportion of Thyroid dysfunction in patients with type 2 Diabetes.

Materials and methods: The current study was a prospective, cross-sectional study. All the type-2 Diabetic patients and normal subjects with no diabetes attended to the outpatient clinic and admitted in the General Medicine department at Kasturba hospital, Manipal was considered as the study population. After obtaining informed written consent, a structured questionnaire was used to analyse the patient's chief complaints, General and local examination was performed by measuring BMI, waist circumference. Lab investigations were recorded. Analysis based on patient's lab values for FBS, PPBS, HbA1C AND TSH, LIPID PROFILE.

Results: The mean age of subjects in cases was 55.98 ± 11.19 years and it was 54.54 ± 10.08 years in controls. The difference in the proportion of gender between study groups was statistically not significant, the difference in weight and BMI between the two groups was statistically significant. There was no statistically significant difference in cholesterol, triglyceride, LDL between two groups. The difference in the proportion of thyroid dysfunction between the two groups was statistically significant.

Conclusion: The present study showed a high prevalence of thyroid dysfunctions in patients of type 2 DM.

Keywords: Diabetes Mellitus, Thyroid Dysfunction FBS, PPBS, HBA1C, BMI, Waist Circumference.

INTRODUCTION

One of the primary health problems presents globally which is assuming epidemic proportions is Diabetes Mellitus.¹ It was 366 million in 2011², 382 million in 2013³, and 415 million in 2015.⁴ It is estimated that it would increase by 2045 to 629 million⁵, 4 out of 5 persons affected by diabetes mellitus are reported to be from low income and middle-income countries. Globally, India is emerging as a leader in diabetes mellitus, with the maximum number of subjects with diabetes next only to China.^{6,7}

Several micro and macrovascular complications of diabetes arise with the increasing duration of diabetes and poor glycaemic control.⁸ Globally, the most commonly prevalent endocrine disorders are Thyroid diseases. Around forty-two million people were estimated to be suffering from thyroid diseases in India. Thyroid disease has higher widespread

among the diabetic population as compared to the population with normal individuals.⁹⁻¹¹

The thyroid hormones play an important part in key metabolic pathways as the balance is controlled by them by regulation of expenditure and storage of energy.¹² "metabolism is regulated by TH primarily by actions in the brain, brown fat, white fat, liver, skeletal muscle, and pancreas".¹² Although the autoimmune mechanism is very clear in establishing the association between Type I diabetes and Thyroid dysfunction¹³, the connection between Type II Diabetes mellitus and Thyroid dysfunction is still not completely understood.¹⁴ It is very complex and involves many variables such as synthesis of TRH, the circadian rhythm of TSH, insulin resistance, autoimmunity, and the use of metformin.¹⁴

The co-existence dysfunction of thyroid in type 2 diabetes mellitus will worsen the macro vascular and microvascular complications, morbidity, mortality, and quality of life.¹⁴ Detecting dysfunction of the thyroid gland in type 2 DM will inform clinicians to give optimal treatment for metabolic conditions since thyroid condition such as hypothyroidism will delicate achievement of glycaemic target and other comorbidities. "Functional changes in the thyroid gland may be related to metabolic syndrome with its associated factors which include obesity, insulin resistance (IR), raised blood pressure, lipid and glucose metabolism abnormalities, and cardiovascular dysfunction"^{15,16}

Since much of the focus is given to major microvascular and macrovascular complications in diabetes, the focus on thyroid dysfunction and its effect on various end organs in diabetes have not been studied in detail. There is death of research studies which have reported the relationship between various metabolic parameters and Thyroid dysfunction in subjects with Type 2 DM.^{11,17}

So, we did evaluation thyroid dysfunction prevalence in subjects with Type 2 Diabetes mellitus and determined the correlation between various metabolic parameters such as Lipid profile, FBS, Body Mass Index (BMI), PPBS, HbA1C,

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Waist circumference and Thyroid dysfunction measured using levels of thyroid hormones.

MATERIAL AND METHODS

The current study was a prospective, cross-sectional study. This study was conducted in the Department of General Medicine at Kasturba Hospital, Manipal. The data collection for the study was done between September 2017 to June 2019. All the type-2 Diabetic patients and normal subjects with no diabetes aged more than 30yrs attended to the outpatient clinic and admitted in the General Medicine department at Kasturba hospital, Manipal was considered as the study population. Patients with Type 2 diabetes and normal subjects aged more than 30 years irrespective of glucose control and treatment (OHA/insulin) were included in the study, Exclusion criteria included patients of type 1 diabetes mellitus, previously on medications affecting thyroid dysfunction and pregnant females. The general and local examination was performed by measuring BMI, waist circumference. Analysis based on patient's lab values for FBS, PPBS, HBA1C AND TSH, Lipid Profile.

Approval of the study was obtained by the institutional human ethics committee. Informed written consent was obtained from all the study participants, and only those participants willing to sign the informed consent were included in the study. The risks and benefits involved in the study and the voluntary nature of participation were explained to the

participants before obtaining consent. The confidentiality of the study participants was maintained.

RESULTS

Table I: Comparison of cases and controls

A total of 496 subjects were included in the final analysis. Out of the 496 subjects, 248 were cases (Type 2diabetes Mellitus) and the remaining 248 were controls.

The mean age of subjects in cases was 55.98 ± 11.19 years and it was 54.54 ± 10.08 years in controls. The difference in the age between the two groups was statistically not significant (P-Value 0.131). Among the cases, 162 (65.32%) participants were male and 86 (34.67%) participants were female. Among the controls, 169 (68.14%) participants were male and 79 (31.85%) participants were female. The difference in the proportion of gender between study groups was statistically not significant (P-value 0.505). (Table 1)

The mean height in cases was 161.02 ± 8.3 cm, it was 161.01 ± 7.79 in controls. The mean weight in cases was 69.2 ± 12.64 kg, it was 65.47 ± 10.86 in controls. The difference in weight between the two groups was statistically significant. (P-value <0.001). The mean BMI in cases was 26.21 ± 4.7 , it was 24.8 ± 4.15 in controls. The difference in BMI between the two groups was statistically significant. (P-value <0.001). The mean waist circumference in cases was 92.82 ± 13.6 , it was 93.39 ± 12.53 in controls. The difference in waist circumference between the two groups was statistically not significant. (P-value 0.632). (Table 2)

The median FBS in cases was 133 (IQR 102 to 175.5), it was 106.5 (IQR 94 to 119) in controls. The median PPBS in cases was 184 (IQR 137.75 to 250.75), it was 137 (IQR 111 to 166) in controls. The median HBA1C in cases was 7.5 (IQR 6.5 to 9.4), it was 5.6 (IQR 5.2 to 6) in controls. The median cholesterol in cases was 155 (IQR 121 to 194), it was 163.5 (IQR 137 to 194) in controls. The median Triglycerides in cases was 134 (IQR 96.775 to 199), it was 122.5 (IQR 89

Parameter	Group		P-value
	Cases (N=248)	Control (N=248)	
Age	55.98 ± 11.19	54.54 ± 10.08	0.131
Gender			
Male	162 (65.32%)	169 (68.14%)	0.505
Female	86 (34.67%)	79 (31.85%)	

Table-1: Comparison of age, gender between cases and controls (N=496)

Parameter	Group		P-value
	Cases (N=248) (Mean± SD)	Control (N=248) (Mean± SD)	
Height (in cm)	161.02 ± 8.3	161.01 ± 7.79	0.988
Weight (in kg)	69.2 ± 12.64	65.47 ± 10.86	<0.001
BMI	26.21 ± 4.7	24.8 ± 4.15	<0.001
Waist circumference	92.82 ± 13.6	93.39 ± 12.53	0.632

Table-2: Comparison of mean of anthropometric parameters between the study groups (N=496)

Parameter	Group		P-value (Mann Whitney U test)
	Cases (N=248) Median (IQR)	Control (N=248) Median (IQR)	
FBS	133 (102, 175.5)	106.5 (94, 119)	<0.001
PPBS	184 (137.75, 250.75)	137 (111, 166)	<0.001
HBA1C	7.5 (6.5, 9.4)	5.6 (5.2, 6)	<0.001
Cholesterol	155 (121, 194)	163.5 (137, 194)	0.082
Triglycerides	134 (96.775, 199)	122.5 (89, 178.75)	0.054
HDL	34 (26, 42)	36 (30, 47)	<0.001
LDL	92.9 (68.15, 120)	97.2 (72.1, 119)	0.289

Table-3: Comparison of the median of clinical parameters between cases and controls (N=496)

Parameter	Group		Chi square	P value
	Cases (N=248) Median (IQR)	Control (N=248) Median (IQR)		
Thyroid dysfunction				
Yes	50 (20.16%)	23 (9.27%)	11.710	<0.001
No	198 (79.84%)	225 (90.73%)		
Type of Thyroid				
Hyperthyroidism	5 (2.02%)	3 (1.20%)	12.223	0.016
Hypothyroidism	11 (4.44%)	5 (2.02%)		
Subclinical Hyperthyroidism	1 (0.4%)	0 (0%)		
Subclinical Hypothyroidism	33 (13.31%)	15 (6.05%)		
ND	198 (79.84%)	225 (90.73%)		

Table-4: Comparison of thyroid dysfunction and type of thyroid between group (N=496)

Diabetic retinopathy	Thyroid dysfunction		Chi-square	P-value
	Yes(N=50)	No(N=198)		
NPDR	19 (38%)	43 (21.71%)	15.733	<0.001
PDR	9 (18%)	12 (6.060%)		
No	22 (44%)	143 (72.22%)		
Type of thyroid				
	Hypothyroidism (N=44)	Hyperthyroidism (N=6)	Euthyroidism (N=198)	*
NPDR	17 (38.63%)	2 (33.33%)	43 (21.71%)	
PDR	9 (20.45%)	0 (0%)	12 (6.060%)	
No	18 (40.90%)	4 (66.66%)	143 (72.22%)	

*No statistical test was applied- due to 0 subjects in the cells

Table-5: Comparison of diabetic retinopathy between thyroid dysfunction (N=248)

Parameter	Spearman rho's correlation	P-value
FBS	0.012	0.795
PPBS	-0.013	0.779
HBA1C	0.027	0.553
Cholesterol	0.000	0.998
Triglycerides	0.036	0.419
HDL	-0.014	0.748
LDL	-0.027	0.543

Table-6: Correlation between TSH and clinical parameters (N=496)

to 178.75) in controls. The median HDL in cases was 34 (IQR 26 to 42), it was 122.5 (IQR 36 (IQR 30 to 47) in controls. The median LDL in cases was 92.9 (IQR 68.15 to 120), it was 97.2 (IQR 72.1 to 119) in controls. There was a statistically significant difference in FBS, PPBS, HBA1C, HDL between two groups (P-value <0.05). There was no statistically significant difference in cholesterol, triglyceride, LDL between two groups. (P-value >0.05). (Table 3)

Among cases, 50 (20.16%) had thyroid dysfunction. Among controls, 23 (9.274%) had thyroid dysfunction. The difference in the proportion of thyroid dysfunction between the two groups was statistically significant. (P-value 0.001). (Figure 1)

Among cases 5 (2.016%) had hyperthyroidism, 11 (4.435%) had hypothyroidism, 1 (0.403%) had subclinical hyperthyroidism, 33 (13.30%) had subclinical hypothyroidism. Among controls 3 (1.209%) had hyperthyroidism, 5 (2.016%) had hypothyroidism and 15 (6.048%) had subclinical hypothyroidism. (Figure 2)

Among people with thyroid dysfunction, 19 (38%) had NPDR, 9 (18%) had PDR. Among people without thyroid dysfunction 43 (21.71%) had NPDR and 12 (6.060%) had PDR. The difference in the proportion of diabetic retinopathy between people with and without thyroid dysfunction was statistically significant. (P-value <0.001). (Table 4)

Among people with hypothyroid 17 (38.63%) had NPDR, 9 (20.45%) had PDR. Among people with hyperthyroidism 2 (33.33%) had NPDR. Among people with euthyroidism, 43 (21.71%) had NPDR and 12 (6.060%) had PDR. (Table 5, Figure 3)

There was a weak positive correlation between TSH and FBS (r_s value: 0.012, P-value: 0.795). There was a weak negative correlation between PPBS and TSH (r_s value: -0.013, P-value: 0.779). There was a weak positive correlation between HBA1C and TSH (r_s value: 0.027, P-value: 0.553). There was weak no correlation between Cholesterol and TSH (r_s value: 0.000, P-value: 0.998). There was a weak positive correlation between Triglycerides and TSH (r_s value: 0.036, P-value: 0.419). There was a weak negative correlation between HDL and TSH (r_s value: -0.014, P-value: 0.748). There was a weak negative correlation between HDL and TSH (r_s value: -0.027, P-value: 0.543). (Table 6)

DISCUSSION

The co-existence of thyroid dysfunction in type 2 DM patients will worsen the macrovascular and microvascular complications, morbidity, mortality, and quality of life.¹⁴ Since much of the focus is given to these major complications, the focus on thyroid dysfunction and its effect on various end

organs in diabetes have not been studied in detail.

We did a Single-Centre prospective, cross-sectional study in the Department of General Medicine on 248 type-2 Diabetes mellitus patients and 248 normal subjects without type-2 diabetes presenting to the outpatient clinic. A total of 496 subjects were included in our final analysis, out of which 248 (50%) were cases of Type 2 diabetes mellitus and the remaining 248 were controls. 65.32% were males in the diabetic group, while 68.14% of controls were males in our study. We found no significant difference between the 2 study groups with respect to gender distribution and mean age. Telwani AA et al¹¹, and Pasupathi P et al¹⁸, and Jalal MJ et al¹⁹, also observed that the two groups were comparable in their studies.

With regard to anthropometric variables, there was a significant difference in weight and BMI. The diabetic subjects had a higher mean BMI (26.21) compared to controls (24.8), and this difference of 1.41 was statistically significant (<0.001). With regards to laboratory parameters, the median FBS, PPBS, HbA1C levels were higher in the diabetic group compared to controls, and this difference was statistically significant (<0.001). The median HDL level was higher in controls compared to cases with statistical significance.

Thyroid dysfunction is more common among diabetic females. The most common thyroid dysfunction observed was subclinical hypothyroidism. There association of Thyroid dysfunction with Insulin resistance. Association of Hyper- and hypothyroidism with insulin resistance has been considered to be the major cause of impaired glucose metabolism in T2DM¹⁴.

The prevalence of thyroid dysfunction in cases was 20.16% while it was only 9.27% in controls in our study. This higher prevalence of thyroid dysfunction in cases compared to controls was statistically significant (<0.001) in our study. Jalal MJ et al¹⁹, in their study also observed that thyroid dysfunction was found to be more in type 2 DM (16%) than in healthy controls (4%) which were significant. Telwani AA et al¹¹, also observed that the prevalence of thyroid dysfunctions was high in diabetic patients compared to controls (29% versus 9%, P-value <0.001). Deshmukh V et al¹⁵, in their study, observed that about 121 out of 432 patients (28%) were diagnosed with Thyroid dysfunction. Similarly, Chang CH et al¹⁶, in their study, also observed that patients with metabolic syndrome were at (21%) excess risk of developing subclinical hypothyroidism.

In our study, among the spectrum of thyroid disorders, Subclinical hypothyroidism was the most commonly observed disorder in both cases (13.3%) and also controls (6.048%) which was similar to that of observed by Jalal MJ et al.¹⁹ In cases, only 2% were hyperthyroid, but 4.4% were hypothyroid with only one case (0.4%) of subclinical hyperthyroidism. Similarly, in the study by Telwani AA et al¹¹, the most common thyroid disorder in diabetic patients was subclinical hypothyroidism (16%) while the least common was hyperthyroidism (1%). In our study, in controls, only 1.2% were hyperthyroid, 2% were hypothyroid with none cases of subclinical hyperthyroidism.

Present study results showed that the difference in the proportion of diabetic retinopathy between people with and without thyroid dysfunction was statistically significant. Our results matched with Chandrakumar SV et al²⁰, who found a significant association between subclinical and overt hypothyroidism with the development of diabetic retinopathy. Obaid N et al²¹, concluded that thyroid dysfunction was found insignificant number of patients with diabetic retinopathy.

In our study, no statistically significant difference found between the cases with and without thyroid dysfunction with respect to median laboratory parameters like FBS, PPBS, HbA1C and lipid levels. Telwani AA et al¹¹, in their study, observed that prevalence of thyroid disorders in diabetics were significantly more in patients with age ≥ 50 years, more in females, more in patients with BMI ≥ 30 and more in diabetic patients with duration of diabetes ≥ 5 years. There was no statistically significant correlation between laboratory parameters and TSH levels in this study. The levels of serum T3 and T4 were significantly low while serum TSH levels were significantly high in the diabetic group compared to the control group in the study by Telwani AA et al¹¹. In the study by Jalal MJ et al¹⁹, the mean thyroid-stimulating hormone (TSH) levels in people with diabetes with thyroid dysfunction.

Wolffenbittel BHR et al²², in their study, observed that higher FT3 levels are related with Metabolic Syndrome (MetS). Only in men, lower FT4 is related to MetS. In the highest FT3 and FT3FT4 quartiles, there is a 50-80% increased risk of having MetS compared to the lowest quartile. Khatiwada S et al²³, in their study, observed that "Thyroid dysfunction, particularly subclinical hypothyroidism is common among metabolic syndrome patients, and is associated with some components of metabolic syndrome such as waist circumference and HDL cholesterol". In our study, there was a weak positive correlation between levels of FBS, HbA1C, Triglycerides and TSH levels while there was a very weak negative correlation between levels of PPBS, HDL, LDL and TSH levels. Gyawali P et al²⁴, in their study, observed that "Patients with MetS had subclinical hypothyroidism greatly.

CONCLUSION

The present study showed a high prevalence of thyroid dysfunctions in patients of type 2 DM. Hence, screening for thyroid dysfunction in diabetic patients should be performed routinely, so as to recognize these dysfunctions early, thus helping in improving the quality of life and reducing the morbidity rate in them.

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