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Original Research Paper

General Medicine

A STUDY OF PREVALENCE OF AUTOIMMUNE THYROID DISORDER IN TYPE 2 DIABETES MELLITUS

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ABSTRACT

BACKGROUND: Till date no clinical study has been conducted in Bikaner to know the prevalence of thyroid dysfunction in diabetes mellitus type and clinical correlation in between thyroid disorder and diabetes mellitus type 2. So I want to study the prevalence of thyroid dysfunction and auto antibodies in diabetes mellitus type 2. **METHODS:** This study was a cross sectional study. 234 adult ≥ 40 years of age with already diagnosed and newly diagnosed T2 diabetes mellitus (Criteria for the diagnosis of diabetes according to ADA 2017) were included. Detailed history and examination was done, Fasting blood samples of all the subjects were taken and at the same time samples were tested for HbA1C and thyroid profile (T3, T4 and TSH). The results were analyzed by EPI-Info software. **RESULTS:** 64.10% cases of TYPE2DM were normal thyroid function and 22.22% cases were overt hypothyroidism, 9.83% cases were sub clinical hypothyroidism, 1.28% cases secondary hypothyroidism and 2.56% cases were hyperthyroidism. **CONCLUSION:** It is concluded that thyroid dysfunction may be one of the factors of poor management of T2DM and worsening in complications of T2DM.

KEYWORDS : DM Type 2, Hypothyroidism, Hyperthyroidism.

INTRODUCTION

Diabetes Mellitus is a clinical syndrome characterized by hyperglycemia caused by absolute or relative deficiency of insulin. Lack of insulin affects the metabolism of carbohydrate, protein and fat and can cause significant decrease of water and electrolytes homeostasis[1]

Diabesity defined as obesity and type 2 diabetes is likely to be the greatest epidemic in human history[2] If the total number of diabetics in the world is to be collected in one country, it would be the third biggest country in the world.[2] In recent years, the prevalence of diabetes, as well as prediabetes, has significantly increased in India. A recent Indian Council of Medical Research sponsored study suggests the widespread seriousness of this condition across rural and urban areas with some areas showing prevalence as high as 13%.[3]

Thyroid disorders are also very common in the general population and it is second only to diabetes as the most common condition to affect the endocrine system. Many thyroid abnormalities may co-exist and interact with diabetes mellitus. Diabetes mellitus affects thyroid functions at many sites, from hypothalamic control of thyroid stimulating hormone (TSH), release to T3 production from T4 in the target t issues.

Autoimmunity has been implicated to be the major cause of thyroid-dysfunction associated diabetes mellitus. Autoimmunity in which circulating antibodies exist to numerous body tissue components destroy such tissues was stated to be the underlying mechanism behind the increase prevalence of thyroid disorders in type 1 diabetes mellitus ,despite the fact autoimmune thyroid diseases are know to be highly prevalent in all forms of the diabetes ; no specific reason has been adduced for an increased prevalence of thyroid disorders in type 2 diabetes mellitus. However, insulin; the hormone required for transporting glucose from plasma across cell membranes into the cytosol of many cells (including those of the skeletal muscle) is absolutely deficient in type 1 diabetics and relatively deficient in type 2 diabetics. Some authors have postulated that insulin treatment in type 1 diabetics and insulin resistance with resultant high plasma insulin levels in type 2 diabetes may equally predispose both groups to deranged thyroid function.

It is the only tertiary hospital in North Western Rajasthan and receives referral cases from all Bikaner division. Till date no clinical study has been conducted in this part to know the prevalence of thyroid dysfunction in diabetes mellitus type and clinical correlation in between thyroid disorder and diabetes mellitus type 2. So I want to study the prevalence of thyroid dysfunction and auto antibodies in diabetes mellitus type 2.

MATERIAL AND METHODS

Present study was conducted in Department of Medicine, This study was a cross sectional study.

Sample size: 234 OPD and IPD patients

Method of selection of subjects:

This study was include adults having type 2 DM attending medical outdoor or admitted in medicine wards. Before enrollment, details about nature and utility of present study was explained to all patients and informed consent was taken. All participants was subjected to detailed clinical examination and relevant investigations. Only after the inclusion and exclusion criteria's are met, the subjects was included in the study.

Inclusion criteria:

All adult ≥ 40 years of age with already diagnosed and newly diagnosed T2 diabetes mellitus (**Criteria for the diagnosis of diabetes according to ADA 2017)**

Exclusion criteria:

1. Pregnant women.
2. Patients who are under intensive care.
3. Patients with previous history of thyroid surgery.
4. Patients who are not willing to participate.
5. Connective tissue disorder.

For each patient the following data was collected: Age, Sex, biochemical parameters (complete blood count including hemoglobin, total and differential leucocyte count, total platelet count, HBA1c, fasting plasma glucose, blood urea, serum creatinine, aspartate aminotransferase, alanine aminotransferase, total bilirubin,T3,T4.TSH,AntiTPO,and Anti TGA antibody, urine analysis),Complete physical examination of each participant will be done.

RESULTS

Table 1. General characteristic of patients

General characteristic	No of patients	95% confidence level
Age group(Yrs)		
41—50	48	14.31-24.84%
51—60	83	30.35-43.22%
61—70	68	24.11-36.22%
71 — 80	29	7.74-16.34%
>80	6	0.95-5.50%
Gender		
Male	120	41.31-54.47%
Female	114	45.53-58.69%
BMI (kg/m^2)		
18 – 24.9	95	35.13-48.20%
25 – 29.9	108	38.07-51.25%
30 – 39.9	33	9.68-18.99%

Age of the patients were varied from 40 years to 85 years with maximum number of patients were observed in the age group 51- 60 years. The mean ages of the patients were 58.18 ± 10.08. 112 patients were males and 122 patients females. The mean BMI of T2DM cases was high (26.21 ± 3.13 kg/m^2). The mean value of HbA1c was 8.81 ± 1.96%. The mean value of FBS was 126.31 ± 29.76 mg/dl and of PPBS 216.29 ± 52.82 mg/dl.

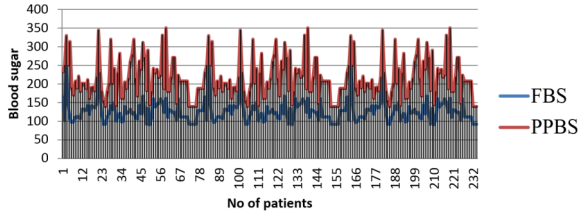

Fig.1. Sugar level of diabetes type 2 patients

Table 2 – Anti TPO wise distribution

Anti TPO	No. of cases	95% confidence level
Positive	45	75.13-85.61%
Negative	189	14.39-24.87%

In present study maximum 80.73% cases of TYPE2DM were anti TPO negative and only 19.23% cases were anti TPO positive.

Table 3. – Distribution of cases according to thyroid hormone abnormality

Thyroid Disorder	No. of cases	95% confidence level
Euthyroid	150	57.59-70.25%
Hyperthyroidism	6	0.95-5.50%
Overt Hypothyroidism	52	17.06-28.10%
Secondary Hypothyroidism	3	0.27-3.70%
Sub clinical Hypothyroidism	23	6.33-14.38%

In present study maximum 64.10% cases of TYPE2DM were normal thyroid function and 22.22% cases were overt hypothyroidism, 9.83% cases were sub clinical hypothyroidism, 1.28% cases secondary hypothyroidism and 2.56% cases were hyperthyroidism.

Table 4– Association between thyroid disorder and anti TPO.

Thyroid Disorder	Anti TPO		Total
	Positive	Negative	
Euthyroid	0	150	150
Hyperthyroidism	3	3	6
Overt Hypothyroidism	13	39	52
Secondary Hypothyroidism	3	0	3
Subclinical Hypothyroidism	20	3	23
Total	45	189	234

Chi-square=144.77, df=4	p-value=0.001

In present study out of 23 cases of Subclinical Hypothyroidism, 20 cases were ant-TPO positive and 3 cases were anti-TPO negative. The association between thyroid disorder and anti-TPO was stastically significant.

DISCUSSION

Among the endocrinal metabolic diseases diabetes occupies the major share. India is the diabetes capital of the world. Diabetes mellitus is a complex multifactorial disease with varying etiologies but in most of the cases there is genetic predisposition. It has been associated with various physiologic changes in different organ systems of human body. The varying complications are associated with the morbidity and mortality associated with diabetes. According to recent estimates, overall prevalence of T2DM was 4.3% in India.[4] In recent study, about 42 million people in India suffer from thyroid diseases. The prevalence of overt hypothyroidism in India is 3.9%. The prevalence of subclinical hypothyroidism is also high in our study, the value being 22.22%. The prevalence of subclinical and overt hyperthyroidism in India is 1.6% and 1.3%.[4] T2DM has an intersecting underlying pathology with thyroid dysfunction. Altered thyroid hormones have been described in patients with diabetes especially those with poor glycemic control. In diabetic patients, the nocturnal TSH peak is blunted or abolished and the TSH response to thyrotropin releasing hormone is impaired. Reduced T3 levels have been observed in uncontrolled diabetic patients and it become normal with improvement in glycaemic control. This "low T3 state" could be explained by impairment in peripheral conversion of T 4 to T 3. The abnormal thyroid hormone level may also be the outcome of various medications that the diabetic patients were receiving. For example, it is known that insulin, an anabolic hormone enhances the level of FT4 while it suppresses the level of T3 by inhibiting hepatic conversion of T4 to T3. On the other hand some of the oral hypoglycaemic agents such as the phenylthioureas (sulfonylureas) are known to suppress the level of FT4 and T4, while causing raised levels of TSH. [4]

The most probable mechanism leading to hyperglycemia in thyroid dysfunction could be attributed to perturbed genetic expression of a constellation of genes along with physiological aberrations leading to impaired glucose utilization and disposal in muscles, overproduction of hepatic glucose output, and enhanced absorption of splanchnic glucose. These factors contribute to insulin resistance. Insulin resistance is also associated with thyroid dysfunction. Both hyperthyroidism and hypothyroidism have been associated with insulin resistance which has been reported to be the major cause of impaired glucose metabolism in T2DM. The state of art evidence suggests a pivotal role of insulin resistance in underlining the relation between T2DM and thyroid dysfunction. A plethora of preclinical, molecular, and clinical studies have evidenced an undeniable role of thyroid malfunctioning as a comorbid disorder of T2DM.

In present study maximum 80.73% cases of TYPE2DM were anti TPO negative and only 19.23% cases were anti TPO positive.

A study conducted by Palma CC et al in 2013 year prevalence of anti TPO antibodies was 10.8%.[5]

In our study maximum 64.10% cases of Type 2 DM were normal thyroid function and 22.22% cases were overt hypothyroidism, 9.83% cases were sub hypothyroidism, 1.28% cases secondary hypothyroidism and 2.56% cases were hyperthyroidism.

Kiran Babu *et al* [6] reported 28% of thyroid dysfunction in T2DM case with 13.2% having hypothyroidism, 8.8% having hyperthyroidism and low T3 syndrome in 5.8%. Celani M F *et al* [7] reported 31.4% thyroid dysfunction in T2DM cases. Out of

these, Subclinical hypothyroidism was most common (48. 3%), followed by subclinical hyperthyroidism (2 4. 2%) and by definite hypothyroidism (23. 1%). Definite hyperthyroidism was found in 4 patients (4. 4%).

Dysregulated glucose disposal and metabolism in adipocytes, muscles, and liver, along with impaired insulin secretion by the pancreatic beta cells, constitute the four major organ system abnormalities which play a definitive role in the pathogenesis of T2DM. It is worth considering that insulin resistance has been a proven condition in hyperthyroidism as well as hypothyroidism[8]

Insulin resistance has been shown to be caused in hypothyroidism in various *in vitro* and preclinical studies where it was found that peripheral muscles became less responsive in hypothyroid conditions. A possible role of dysregulated metabolism of leptin has been implicated for such pathology.[8]

The pathological features of T2DM include increased intestinal glucose absorption, reduced insulin secretion, and change in the cell mass. Further, symptoms also include increased insulin degradation, increased glucagon secretion, increased hepatic glucose production, enhanced catecholamines, and insulin resistance. These factors have been investigated to be an integral part of hyperthyroidism as well. Hence, an intersection of pathological basis occurs which gives us cue to an array of physiological aberrations which are common in hyperthyroidism and T2DM [8]

Insulin resistance and cell function are inversely correlated with TSH which may be explained by insulin-antagonistic effects of thyroid hormones along with an increase in TSH. The higher serum TSH usually corresponds to lower thyroid hormones via negative feedback mechanism. As TSH increased, thyroid hormones decreased and insulin antagonistic effects are weakened. These observations demonstrate that insulin imbalance is closely associated with thyroid dysfunction and the phenomenon is mediated via cell dysfunction (T2DM).[8]

Both T2DM and hypothyroidism are associated with high BMI and insulin resistance while hyperthyroidism is mostly associated with low BMI because of high metabolic rate. So because of common pathophysiology of T2DM is more commonly associated with hypothyroidism compare to hyperthyroidism.

So it is evident from the above discussion that thyroid dysfunction was more common in T2DM than non diabetics. The results of the present study are more or less correlated with the various national and international studies.

CONCLUSION

Maximum number of T2DM patients had subclinical hypothyroidism19.23% cases were anti TPO positive. It is concluded that thyroid dysfunction may be one of the factors of poor management of T2DM and worsening in complications of T2DM.

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