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ASSOCIATION OF THYROID DISORDERS AND TYPE 2 DIABETES MELLITUS – BEYOND COINCIDENCE-A HOSPITAL BASED STUDY FROM SUB-HIMALAYAN REGION

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Abstract

Introduction: The global burden of type 2 Diabetes Mellitus of 2010 was around 285 million people which is projected to increase to 438 million in 2030, a 65% increase. The burden of both type 2 diabetes mellitus and thyroid disorders in India is on the rise but their association has rarely been studied. Patients with type 2 diabetes mellitus have a higher prevalence of thyroid disorders, hypothyroidism being the most common disorder. **Objectives:** To study the profile of thyroid disorders in patients with type2 diabetes mellitus. **Material and methods:** In this study 100 patients with type 2 diabetes mellitus attending outpatient clinic and admitted at a tertiary care hospital in North India were investigated for fasting blood sugar (FBS), glycosylated haemoglobin (HbA1c), thyroid stimulating hormone (TSH), free triodothyroxine (Ft3), free thyroxine (Ft4), antithyroperoxidase (anti-TPO) and antithyroglobulin (anti tg) levels. **Results:** Twenty four (24%) patients were observed to have thyroid dysfunction. Hypothyroidism was found to be the most common thyroid disorder (19%). Eleven (11%) of them had overt hypothyroidism and eight (8%) had subclinical hypothyroidism. Anti–TPO antibodies were found in 9 (47.36%) cases of hypothyroidism while anti-Tg antibiodies were found in three (15.78%) cases of hypothyroidism. Similar number of patients had both anti TPO and anti-Tg antibodies**. Conclusion:** Patients with type 2 diabetes mellitus should be screened for thyroid disorders as this can help in better understanding and management of these patients.

Key words: Type 2 diabetes mellitus, hypothyroidism, hyperthyroidism, antithyroperoxidase antibody, antithyroglobulin antibody

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Introduction:

Non communicable diseases are the leading cause of death in the world. Diabetes mellitus attributes to 3 % of this burden. [1,2] Diabetes mellitus is the biggest endocrine driver of global burden of disease 2010.[3] Thyroid disease is considered to be a both nutritional and non -communicable disease. Although it does not lead to significant mortality but contributes to sequel leading to various disabilities. Goitre due to iodine deficiency contributes to 2.72% of the sequel which is almost similar to that of uncomplicated diabetes mellitus.[4])

The correlation of diabetes mellitus and thyroid disorders is widely known and it was first studied in 1979. (5) Type 2 diabetes mellitus patients have a higher prevalence of thyroid disorders because patients with single organ specific autoimmune disease are usually at risk of other autoimmune disorders. (6) Thyroid disorders affect diabetes control. Diabetes mellitus appears to influence thyroid function at two sites; firstly at the level of hypothalamic control of TSH release and secondly at the conversion of T4 to T3 in the peripheral tissues.(7) Hyperthyroidism is associated with worsening of glycemic control and increased insulin requirements.(8) Reduced glucose absorption from gastrointestinal tract accompanied by prolonged peripheral glucose accumulation, gluconeogenesis, diminished hepatic glucose output and reduced disposal of glucose are hallmarks of hypothyroidism. (9) The study conducted by Perros P et al in 1995 found that 13.4% patients of type2 diabetes mellitus had thyroid dysfunction. (10)

Although a study has been done in patients of type 1 diabetes mellitus but association of autoimmune thyroid disorders with type 2 diabetes mellitus has rarely been studied in the state of Uttrakhand. Sub-Himalayan region is considered to be the goitre belt of India therefore this study was undertaken to evaluate the prevalence of thyroid dysfunction and thyroid autoantibodies in patients of type 2 diabetes mellitus and to assess various demographic and biochemical parameters in patients of type 2 diabetes mellitus with and without thyroid dysfunction.

Material and methods:

This observational study was conducted in the department of medicine at a tertiary care hospital, Dehradun. Hundred (100) patients with type 2 diabetes mellitus attending outpatient department and medical wards in a span of one year from October 2009 to October 2010 participated in the study. Written informed consent was taken obtained all the patients with type 2 diabetes mellitus. The study protocol was approved by the ethical committee of the hospital. The diagnosis in each case was established using American Diabetes Association (ADA) classification of diabetes mellitus (2009). [(11)] Blood samples were taken for TSH, Ft3, Ft4, FBS, HBA1c, antiTPO and antiTg. The demographic data was obtained from the patients.

Patients with type 2 diabetes mellitus were classified as:

- Euthyroid – when Ft3, Ft4 and TSH were normal.
- Overt hypothyroidsm: when TSH more than 10 µIu/ml, Ft3 less than 2pg/ml and Ft4 less than 0.6ng/ml.
- Subclinical hypothyroidism: when TSH more than 4.25 µIu/ml and less than 10 mIu/ml and Ft3 and Ft4 were normal.
- Overt hyperthyroidism: when TSH less than 0.3 µIu/ml, Ft3 more than 4.2pg/ml and Ft4 more than 1.7ng/ml.

- Subclinical hyperthyroidism: when TSH less than 0.3 µiu/ml and Ft4 normal.

The values of anti TPO more than 50 Iu/ml and anti- Tg more than 100Iu/ml were considered to be positive. Both the tests were done using EUROIMMUN KIT.

TSH, Ft3 and Ft4 were estimated using chemiluminescence technique.

Patients of type 1 diabetes mellitus, secondary diabetes, gestational diabetes mellitus, thyroid malignancies, subjects not willing to take part and pregnant and lactating females were excluded from the study.

Statistical analysis was done using unpaired t test and chi square test.

Results:

Table 1: Demographic and biochemical parameters of type 2 diabetes mellitus patients with or without thyroid dysfunction

Characteristics	Normal thyroid function (n=76)	Abnormal thyroid function (n=24)	p value
Demographics			
Age	**57.49±9.76**	**58.87±6.30**	**0.517**
Sex (m:f)	**34:42**	**10:14**	**0.132**
Duration	**6.64±5.11**	**8.42±4.66**	**-**
Anthropometry			
Weight (in kg)	**64.81±9.95**	**71.37±13.86**	**0.012**
Height (in cm)	**161.03±8.24**	**161.08±8.25**	**0.982**
BMI	**25.07±3.92**	**27.54±5.12**	**0.014**
WHR	**0.83±0.097**	**0.91±0.16**	**0.003**
Biochemical			
FBS	**179.76±42.1**	**215±60.11**	**0.002**
HBA1c	**8.24±1.72**	**8.27±1.52**	**0.93**
Microvascular Complications	**12(50%)**	**24(31.5%)**	**0.001**
Macrovascular Complications	**1(4.1%)**	**14(18.42%)**	**0.001**

Out of 100 patients with type 2 diabetes mellitus who fulfilled the inclusion criteria, 24(24%) had thyroid dysfunction.

Table 2: Thyroid function tests in type 2 diabetes mellitus and prevalence of thyroid autoantibodies

Antibody	Hypothyroid		Hyperthyroid	
	Subclinical (n=8)	Overt (n=11)	Subclinical (n=5)	Overt
Anti TPO	**3 (37.5%)**	**6 (64.5%)**	**0**	**0**
Anti Tg	**1 (12.5%)**	**2 (18.1%)**	**0**	**0**
Both	**1 (12.5%)**	**2 (18.1%)**	**0**	**0**

Table 2 shows profile of thyroid function tests in patients with type 2 diabetes mellitus and prevalence of thyroid autoantibodies. Thyroid dysfunction was found in 24 (24%) cases of which 19 (89.16%) had hypothyroidism and 5 (20.8%) had hyperthyroidism (subclinical). Three (37.5%) patients of hypothyroidism had anti-TPO positive antibodies and one (12.5%) had anti-Tg positive antibodies. Thus, patients of hypothyroidism had more prevalence of anti TPO antibodies.

Seven (9.2%) patients of type 2 diabetes mellitus with normal thyroid function were found to have positive anti-TPO antibodies and two (2.6%) patients had positive anti-Tg antibodies. 50% patients with thyroid dysfunction had microvascular complications (neuropathy, nephropathy, retinopathy) whereas only few patients(4.1%) had macrovascular complications (peripheral arterial disease, cerebrovascular, cardiovascular). Thus

significant association was found between thyroid dysfunction and complications of type 2 diabetes mellitus.

Discussion:

In our study thyroid dysfunction was found in 24% (n=24) patients of type 2 diabetes mellitus. This is consistent with the previous studies done which reported thyroid dysfunction in 12.5% to 30% of patients with type 2 diabetes mellitus. [12-17] The simultaneous occurrence of idiopathic or primary hypothyroidism and diabetes mellitus has received scant attention in medical literature. Few cases of this combination have been reported in the last decade, although recently the co-existence of diseases of the pituitary, thyroid, parathyroids, adrenals and pancreas has been noted. [18]

High body mass index was found to be significantly associated with thyroid dysfunction in our study. Similar results were observed in a study conducted on Chinese population where higher TSH levels were found in patients with metabolic syndrome. [19] Pre diabetic conditions like impaired glucose tolerance and impaired fasting glucose are also on the rise, indicating the possibility of further rise in the prevalence of diabetes mellitus. Metabolic syndrome, which is a constellation of cardiovascular risk factors, of which hyperglycemia and insulin resistance are components, is also widely prevalent. The conversion to diabetes is enhanced by the low thresholds for the risk factors, such as age, body mass index and upper body adiposity. With a high genetic predisposition and the high susceptibility to the environment results, the Indian population faces a higher risk for diabetes and its associated complications. Early diagnosis of high risk groups and appropriate intervention by lifestyle modification may be a solution for the disease burden. [20]

The association of thyroid autoantibodies with type 1 diabetes mellitus is well known but the relationship with type 2 diabetes mellitus is unexplained. In our study 37.5% patients of hypothyroidism had positive anti-Tpo antibodies . A similar study conducted by Alnaqdy et al demonstrated prevalence of thyroid autoantibodies in patients of type 2 diabetes mellitus. This association was more often expressed in older females with type 2 diabetes mellitus. The association of thyroid antibodies with type 1 is to be expected due to autoimmune nature of disease; the relationship with type 2 DM is unexplained. [21]

Poorly controlled diabetes with or without its complications, may produce changes in thyroid function tests that occur in non thyroidal illnesses. Our study reported that 50% patients with type 2 diabetes mellitus who had hypothyroidism were found to have microvascular complications. Subclinical hypothyroidism can elevate serum LDL cholesterol and worsen pre-existing dyslipidemia, further increasing the risk of atherosclerosis. [22] SchronerL et al observed that the prevalence of subclinical and overt hypothyroidism was found to be 24% patients of type 2 diabetes mellitus. It was 7

times more common in women, with a significant increase in older age. Unrecognized hypothyroidism in diabetics can cause unsatisfying compensation of diabetes mellitus and can result in frequent and prolonged hypoglycemia. Even subclinical hypothyroidism has a negative influence on lipid metabolism and it is an independent risk factor for myocardial infarction. [23] In a study conducted by Hak et al found that women with subclinical hypothyroidism and antibodies to thyroid peroxidase had a greater prevalence of aortic atherosclerosis than euthyroid women without antibodies to thyroid peroxidase. It was observed that subclinical hypothyroidism is highly prevalent among elderly women and is associated with a greater frequency of aortic atherosclerosis and myocardial infarction. [24] The presence of anti-thyroid peroxidase (TPO) antibodies is helpful in predicting the development of autoimmune thyroid disorders, especially hypothyroidism. Patients who have anti-TPO antibodies should be screened for thyroid dysfunction on a regular basis, so early detection and treatment is possible. [25] A study was made by Gray et al of the clinical features of diabetics with coexisting Graves' disease or primary hypothyroidism. Those with Graves' disease developed thyroid dysfunction and diabetes at an earlier age than patients with primary hypothyroidism. In contrast to the general diabetic population, 87% of diabetics with thyroid disease were female, 56% required insulin treatment and of patients requiring insulin, the median age at diagnosis of diabetes was 36 years. The diabetics mellitus with associated autoimmune thyroid disease exhibit marked female preponderance with a female to male ratio 6.4:1. [26] A study conducted by Canaris et al found that the proportion of subjects with an elevated TSH level was greater among women than men and increased with advancing age. Of the group who reported taking thyroid medication, nearly 40% had an abnormal serum TSH level. One consequence of declining thyroid function is rising serum lipid levels, as observed in this study. Most hypothyroid individuals had an elevated lipid level. [27] Small et al concluded that type 2 diabetes mellitus should be added to the list of conditions in which diminished TRH evoked TSH secretion may occur. [28]

In our study a significant relationship existed between thyroid dysfunction and complications of type 2 diabetes mellitus. But the study conducted by Papazafiropoulou A et al did not support this result. [5]. The bias in our study could be because this was a hospital based (tertiary care centre) study so chances of finding complications were more. The limitation of this finding is that it could not be ascertained that whether these complications were due to diabetes alone or due to associated thyroid dysfunction. In a study conducted by Menon et al which included 971 subjects excluding subjects with abnormal thyroid function found that the prevalence of anti-TPO and anti-TG antibodies was 9.5% and 8.5%. [29]

Conclusion:

The association of type 2 Diabetes mellitus and thyroid dysfunction is beyond a mere co-existence. Hence thyroid status should be screened in all the patients of type 2 DM for better control of blood sugar and its complications. This association could be attributed to presence of autoantibodies.

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