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Clinical evaluation of prevalence of the thyroid disorders in patients diagnosed with the type 2 diabetes mellitus in Bihar Region

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Abstract

Diabetes and thyroid dysfunction are the two most common endocrine disorders worldwide. Studies have shown that diabetes and thyroid dysfunction mutually influence each other and are associated with each other frequently. Subjects with diabetes have been found to have higher prevalence of thyroid dysfunction compared to the general population. But, the prevalence of thyroid dysfunction in subjects with diabetes has been found to differ widely between different studies. The reported prevalence of thyroid dysfunction is 10-24% in subjects with diabetes, while it is around 6-13% in subjects without diabetes. Studies have shown that thyroid dysfunction is more common in women with diabetes. A recent meta-analysis revealed a mean frequency of thyroid dysfunction of 11% in diabetes. Hence based on above findings the present study was planned for Clinical Evaluation of Prevalence of the thyroid disorders in Patients Diagnosed with the Type 2 Diabetes Mellitus in Bihar Region.

The present study was planned in Department of Internal Medicine, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar, India. In the present study 50 cases of diabetic patients were enrolled and evaluated. Diabetes was defined as per the American Diabetes Association criteria (Fasting plasma sugar ≥126 mg/dl, postprandial blood sugar ≥200 or Glycated hemoglobulin [HBA1c] ≥6.5% on 2 occasions). All the subjects underwent clinical and laboratory assessment. The demographic data included information regarding age, duration of diabetes, co-morbidities like hypertension, dyslipidemia, etc and presence of complications of diabetes. BMI was calculated using the height and weight of the subjects.

The data generated from the present study concluded that prevalence of thyroid dysfunction is significantly high in the studied subpopulation with type 2 diabetes. The most common abnormality is subclinical hypothyroidism and autoimmunity is the cause of thyroid dysfunction in large proportion of these subjects. Thyroid autoimmunity is common even in euthyroid subjects. The findings of this study indicate that screening for thyroid disease among patients with diabetes should be routinely performed to be able to identify thyroid autoimmunity and diagnose subclinical hypothyroidism early.

Keywords: Thyroid Disorders, Type 2 Diabetes Mellitus, Bihar Region, etc

1. Introduction

Thyroid disorders are very common in the general U.S. population, affecting up to 27 million Americans, although half that number remains undiagnosed. It is second only to diabetes as the most common condition to affect the endocrine system — a group of glands that secrete hormones that help regulate growth, reproduction, and nutrient use by cells. As a result, it is common for an individual to be affected by both thyroid disease and diabetes.

Since the thyroid gland plays a central role in the regulation of metabolism, abnormal thyroid function can have a major impact on the control of diabetes. In addition, untreated thyroid disorder can increase the risk of certain diabetic complications and can aggravate many diabetes symptoms. Luckily, abnormal thyroid function can easily be diagnosed by simple blood tests, and effective treatment is available. For all of these reasons, periodic screening for thyroid disorder should be considered in all people with diabetes.

The thyroid is a butterfly-shaped gland located in the neck, just below the Adam's apple and above the collarbone. It produces two hormones, thyroxine (T4) and triiodothyronine (T3), which enter the bloodstream and affect the metabolism of the heart, liver, muscles, and other organs. The thyroid gland operates as part of a feedback mechanism involving the hypothalamus, an area of the brain, and the pituitary gland, which is located within the brain.

Thyroid hormone regulates the way the body uses energy. It works by attaching to specific proteins called receptors that are present in cells throughout the human body. Therefore, thyroid hormone exerts wide-ranging effects in regulating the function of virtually every organ. Consequently, any changes in the blood level of thyroid hormone can affect many body systems and cause a wide range of symptoms.

People with diabetes have an increased risk of developing thyroid disorder. In the general population, approximately 6% of people have some form of thyroid disorder. However, the prevalence of thyroid disorder increases to over 10% in people with diabetes.

Since people with one form of autoimmune disorder have an increased chance of developing other autoimmune disorders, people with Type 1 diabetes have a higher risk of autoimmune thyroid disorder. Up to 30% of women with

Type 1 diabetes have some form of autoimmune thyroid disease. Postpartum thyroiditis, a form of autoimmune thyroid disease that causes thyroid dysfunction within a few months after delivery of a child, is three times more common in women with diabetes.

Although Type 2 diabetes is not an autoimmune disorder, there have been many reports showing a higher occurrence of thyroid diseases, particularly hypothyroidism, among people with Type 2 diabetes. The association between Type 2 diabetes and thyroid disorder, however, remains unexplained.

The extent to which each organ is affected varies widely between individuals, which is why thyroid dysfunction causes very different symptoms in different people. In general, the severity of symptoms of abnormal thyroid function depends on the severity of the actual condition, the length of time it has been present, and the person's age. As a result, it is difficult to correctly diagnose thyroid disorder based only on symptoms. Fortunately, precise measurement of thyroid function is now possible with the TSH blood test, a test that directly measures the amount of TSH produced by the pituitary gland.

Since normal thyroid function is essential to regulate energy metabolism, abnormal thyroid function may have profound effects on blood glucose control in diabetes. Both hyperthyroidism and hypothyroidism can affect the course of diabetes, but their effects are somewhat different.

Hyperthyroidism. Hyperthyroidism is typically associated with worsening blood glucose control and increased insulin requirements. The excessive thyroid hormone causes increased glucose production in the liver, rapid absorption of glucose through the intestines, and increased insulin resistance (a condition in which the body does not use insulin efficiently). It may be important to consider underlying thyroid disorder if a person has unexplained weight loss, deterioration in blood glucose control, or increased insulin requirements. Sometimes hyperthyroidism may even unmask latent diabetes.

Having diabetes increases a person's risk for heart disease, and many people with diabetes have a heart condition such as coronary heart disease or heart failure. Since hyperthyroidism causes rapid heart rate and increases the risk of abnormal heart rhythm, it may also bring on angina (chest pain), worsen heart failure or interfere with the treatment of heart failure, as well as further increase the risk of other heart problems.

Prolonged, untreated hyperthyroidism can cause excessive bone loss, leading to osteoporosis, or bone thinning. Osteoporosis raises the risk of bone fractures, making falling much more dangerous. People with diabetes who have peripheral neuropathy are at an increased risk for falls due to poor foot sensation and sometimes loss of proprioception, or loss of the stimuli that tell the brain where a body part is in space, in relation to other objects. Therefore, the combination of hyperthyroidism and diabetes, particularly when neuropathy is present, increases the risk of fractures that may result in disability, especially in the elderly.

Hypothyroidism rarely causes significant changes in blood glucose control, although it can reduce the clearance of insulin from the bloodstream, so the dose of insulin may be reduced. More important, hypothyroidism is accompanied by a variety of abnormalities in blood lipid levels. This includes increased total cholesterol and LDL (low-density lipoprotein or "bad") cholesterol levels, and increased triglyceride levels. The abnormal lipid pattern typical of Type 2 diabetes (low HDL, or "good" cholesterol; high triglycerides; and a high proportion of small, dense LDL particles) is usually worsened by hypothyroidism. These changes further raise the already high risk of cardiovascular diseases such as heart disease and stroke among people with diabetes.

Type 2 diabetes is characterized by insulin resistance, which may be combined with relatively reduced insulin secretion. The defective responsiveness of body tissues to insulin is believed to involve the insulin receptor. However, the specific defects are not known. Diabetes mellitus cases due to a known defect are classified separately. Type 2 diabetes is the most common type of diabetes mellitus. Many people with type 2 diabetes have evidence of prediabetes (impaired fasting glucose and/or impaired glucose tolerance) before meeting the criteria for type 2 diabetes. The progression of prediabetes to overt type 2 diabetes can be slowed or reversed by lifestyle changes or medications that improve insulin sensitivity or reduce the liver's glucose production [2].

Type 2 diabetes is primarily due to lifestyle factors and genetics. A number of lifestyle factors are known to be important to the development of type 2 diabetes, including obesity (defined by a body mass index of greater than 30), lack of physical activity, poor diet, stress, and urbanization. Excess body fat is associated with 30% of cases in those of Chinese and Japanese descent, 60–80% of cases in those of European and African descent, and 100% of Pima Indians and Pacific Islanders. Even those who are not obese often have a high waist–hip ratio [3].

Dietary factors such as sugar-sweetened drinks is associated with an increased risk. The type of fats in the diet is also important, with saturated fat and trans fats increasing the risk and polyunsaturated and monounsaturated fat decreasing the risk. Eating lots of white rice also may increase the risk of diabetes, whereas substitution of brown rice or other whole grains for white rice may lower the risk of diabetes. A lack of physical activity is believed to cause 7% of cases [4]. Adverse childhood experiences (ACEs), including abuse, neglect, and household difficulties, increase the likelihood of type 2 diabetes later in life by 32%, with neglect having the strongest effect.

Thyroid disease is a medical condition that affects the function of the thyroid gland. The thyroid gland is located at the front of the neck and produces thyroid hormones that travel through the blood to help regulate many other organs, meaning that it is an endocrine organ. These hormones normally act in the body to regulate energy use, infant development, and childhood development. There are five general types of thyroid disease, each with their own symptoms. A person may have one or several different types at the same time. The five groups are:

1. Hypothyroidism (low function) caused by not having enough free thyroid hormones
2. Hyperthyroidism (high function) caused by having too much free thyroid hormones
3. Structural abnormalities, most commonly a goiter (enlargement of the thyroid gland)
4. Tumors which can be benign (not cancerous) or cancerous
5. Abnormal thyroid function tests without any clinical symptoms (subclinical hypothyroidism or subclinical

hyperthyroidism) [5].

In some types, such as subacute thyroiditis or postpartum thyroiditis, symptoms may go away after a few months and laboratory tests may return to normal. However most types of thyroid disease do not resolve on their own. Common hypothyroid symptoms include fatigue, low energy, weight gain, inability to tolerate the cold, slow heart rate, dry skin and constipation. Common hyperthyroid symptoms include irritability, anxiety, weight loss, fast heartbeat, inability to tolerate the heat, diarrhea, and enlargement of the thyroid. Structural abnormalities may not produce symptoms, however some people may have hyperthyroid or hypothyroid symptoms related to the structural abnormality or notice swelling of the neck. Rarely goiters can cause compression of the airway, compression of the vessels in the neck, or difficulty swallowing. Tumors, often called thyroid nodules, can also have many different symptoms ranging from hyperthyroidism to hypothyroidism to swelling in the neck and compression of the structures in the neck [6].

Diagnosis starts with a history and physical examination. Screening for thyroid disease in patients without symptoms is a debated topic although commonly practiced in the United States. If dysfunction of the thyroid is suspected, laboratory tests can help support or rule out thyroid disease. Initial blood tests often include thyroid-stimulating hormone (TSH) and free thyroxine (T4). Total and free triiodothyronine (T3) levels are less commonly used. If autoimmune disease of the thyroid is suspected, blood tests looking for Anti-thyroid autoantibodies can also be obtained. Procedures such as ultrasound, biopsy and a radioiodine scanning and uptake study may also be used to help with the diagnosis, particularly if a nodule is suspected.

Treatment of thyroid disease varies based on the disorder. Levothyroxine is the mainstay of treatment for people with hypothyroidism, while people with hyperthyroidism caused by Graves' disease can be managed with iodine therapy, antithyroid medication, or surgical removal of the thyroid gland. Thyroid surgery may also be performed to remove a thyroid nodule or to reduce the size of a goiter if it obstructs nearby structures or for cosmetic reasons [7].

The WHO report has shown a marked increase in the number of people affected with diabetes. Globally an estimated 422 million adults are living with diabetes mellitus, according to latest 2016 data from the WHO. Though diabetes mellitus is more common in developed countries, but the incidence is also increasing in the developing countries. This is due to the trend of urbanization and lifestyle changes, including increasingly sedentary lifestyles, less physically demanding work and changing dietary habits. Until recently, India had more diabetics than any other country in the world, according to the International Diabetes Foundation. Diabetes currently affects more than 62 million Indians 4 and nearly 1 million die every year.

Diabetes and thyroid dysfunction are the two most common endocrine disorders worldwide [8]. Studies have shown that diabetes and thyroid dysfunction mutually influence each other and are associated with each other frequently. Subjects with diabetes have been found to have higher prevalence of thyroid dysfunction compared to the general population. But, the prevalence of thyroid dysfunction in subjects with diabetes has been found to differ widely between different studies. The reported prevalence of thyroid dysfunction is 10-24% in subjects with diabetes, while it is around 6-13% in subjects without diabetes [9]. Studies have shown that thyroid dysfunction is more common in women with diabetes. A recent meta-analysis revealed a mean frequency of thyroid dysfunction of 11% in diabetes. Hence based on above findings the present study was planned for Clinical Evaluation of Prevalence of the thyroid disorders in Patients Diagnosed with the Type 2 Diabetes Mellitus in Bihar Region.

Methodology

The present study was planned in Department of Internal Medicine, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar, India. In the present study 50 cases of diabetic patients were enrolled and evaluated. Diabetes was defined as per the American Diabetes Association criteria (Fasting plasma sugar ≥126 mg/dl, postprandial blood sugar ≥200 or Glycated hemoglobulin [HBA1c] ≥6.5% on 2 occasions). All the subjects underwent clinical and laboratory assessment. The demographic data included information regarding age, duration of diabetes, co-morbidities like hypertension, dyslipidemia, etc and presence of complications of diabetes. BMI was calculated using the height and weight of the subjects.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Following was the inclusion and exclusion criteria for the present study.

Inclusion criteria: Cases of with diabetes of any duration; Age between 18 to 65 years.

Exclusion criteria: Symptoms of hypothyroidism, Presence of goiter, Family history of thyroid dysfunction, Subjects already on thyroxine replacement, Subjects on drugs like amiodarone or lithium.

Results & Discussion

Diabetes mellitus is one of the modern pandemics and an important health problem worldwide. Thyroid diseases and diabetes mellitus are the two most common endocrine disorders encountered in clinical practice which have been shown to mutually influence each other, and association between both the conditions has long been reported. Thyroid hormones contribute to the regulation of carbohydrate metabolism and pancreatic function and on the other hand, diabetes also affects thyroid function tests to a variable extent. However, underlying thyroid disorders may go undiagnosed because the common signs and symptoms of thyroid disorders are similar to those for diabetes and can be overlooked or attributed to other medical disorders. The recognition of this interdependent relationship between thyroid disease and diabetes is of importance to guide clinicians on the optimal management of both these conditions.

Table 1: Basic Characteristics

Parameters		No. of Cases
Age	<40 years	7
	41 to 50 years	12
	51 to 60 years	22
	>60 years	9
Duration	<1 year or New case	16
	2 to 5 years	19
	6 to 10 years	7
	11 to 15 years	8
	>15 years	0
Hypertension	No	29
	Yes	21
Dyslipidemia	No	27
	Yes	23
CAD	No	48
	Yes	2
Nephropathy	Macroalbuminuria	1
	Microalbuminuria	2
	Normoalbuminuria	47
Neuropathy	No	48
	Yes	2
Retinopathy	No	45
	Yes	5
BMI	Normal	10
	Overweight	25
	Obese	15
HbA1c	<6.5	12
	6.6 to 7.5	13
	7.6 to 8.5	13
	8.6 to 9.5	12

Table 2: Thyroid dysfunction

Thyroid function	No. of Cases
Euthyroid	37
Subclinical hypothyroidism	11
Clinical hypothyroidism	2
Subclinical hyperthyroidism	0
Clinical hyperthyroidism	0

Table 3: Thyroid autoimmunity and iodine deficiency

Thyroid function	No. of Cases
Anti TPO antibody positivity	6
Low urinary iodine (less than 100 mcg/L)	0

The difference may be attributed to variability in the iodine uptake by people of different areas. Thyroid hormone aids in regulation of pancreatic function and carbohydrate metabolism and diabetes is seen to affect thyroid function at variable levels. Therefore, many times thyroid disorders go undiagnosed owing to the common signs and symptoms. Unmanaged type I and type II diabetes result in a low T3 state which is characterised by low serum levels of total and free T3, increase in reverse T3 but serum T4 and TSH levels remain the same.4 There have been few studies in the past establishing the relationship between thyroid diseases and diabetes [10-12].

In cases of hypothyroidism there is decrease in glucose absorption from gastrointestinal tract along with increased glucose accumulation and decreased disposal of glucose.10 In a study conducted by Nobre *et al.* [13] around 12.5 % of diabetic patients had thyroid disorders. According to Ashok *et al* subclinical hypothyroidism was the most common disorder amongst diabetic patients, in around 7.5 % of total cases. This subclincal hypothyroidism generally leads to dyslipidemia. This clearly evident from our study as the levels of total cholesterol, LDL was raised in diabetic group. Diabetes leads to an increased risk of nephropathy, cerebrovascular accidents, neuropathy, retinopathy etc. Increased amount of dyslipidemia associated with hypothyroidism further exarcebates these complications associated with diabetes. This increases the risk of cardiovascular diseases by 2-4 times amongst diabetics [14]. Increased risk of nephropathy was shown in patients with type 2 diabetes and subclincal hypothyroidism by Chen HS *et al.* [15] According to Den Hollander *et al.* [16] there was a case in which treatment of hypothyroidism improved renal function in patients with diabetes.

Basic understanding of the physiology and pathology of thyroid functions and current knowledge and appropriate use of thyroid investigations helps the physician to make a reasonable diagnosis of a thyroid disorder. It is very important to note that every abnormal result of the thyroid investigation should be correlated with the clinical setting and unnecessary and prolonged treatment should not be undertaken by the treating physician.

There is inter-dependence between insulin and thyroid hormones for normal cellular metabolism so that diabetes mellitus and thyroid diseases can mutually influence the other disease process. When diabetes occurs in euthyroid individuals, it results in altered thyroid function tests with no clinical dysfunction. In a patient with preexisting Graves Oribitopathy, the risk of visual loss is increased and chances of visual recovery is less if co-existing diabetes is present. When hyperthyroidism occurs in the setting of euglycemia, 2-3% of these individuals may become diabetic. Hyperthyroidism results in deterioration of diabetic control while hypothyroidism increases the susceptibility to hypoglycemia in diabetic patients thereby complicating the diabetic management in these individuals.

In a study conducted by Bharat *et al*, the levels of TSH significantly increased amongst diabetic patients but T3 levels showed no significant change amongst diabetics and non diabetics. Various mechanisms have been implicated in the alteration of thyroid hormone levels amongst diabetics. Firstly, it could be due to medications like phenythiourea which decrease the levels of T4 and thus increases TSH level [17]. Secondly insulin is anabolic in nature and TSH is a protein and hence it enhances TSH turnover. Diabetics are mostly associated with stress which can lead to changes in the hypothalmo pituitary axis. Recently another pathway which is mediated by C peptide has also been shown to influence the thyroid status. It increases the activity of sodium potassium ATPase pump which leads to increase in protein synthesis.

Diabetes mellitus is an important health problem affecting major populations worldwide. The influence of endocrine and non-endocrine organs other than the pancreas on diabetes mellitus is documented. Occasionally, other endocrine disorders such as abnormal thyroid hormone levels are found in diabetes. The major alterations in thyroid7 hormone system are a reduction in the TSH stimulation of the thyroid gland, probably caused by central hypothyroidism, and in the peripheral generation of T3 from T4.

Conclusion

The data generated from the present study concluded that prevalence of thyroid dysfunction is significantly high in the

studied subpopulation with type 2 diabetes. The most common abnormality is subclinical hypothyroidism and autoimmunity is the cause of thyroid dysfunction in large proportion of these subjects. Thyroid autoimmunity is common even in euthyroid subjects. The findings of this study indicate that screening for thyroid disease among patients with diabetes should be routinely performed to be able to identify thyroid autoimmunity and diagnose subclinical hypothyroidism early.

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