

## FREQUENCY OF HYPOTHYROIDISM IN PATIENTS WITH TYPE-II DIABETES MELLITUS

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### Abstract

**Objective:** To observe the frequency of hypothyroidism in patients with type-II diabetes mellitus.

**Study Design:** A Cross sectional observational study

**Study Duration:** 06 months

**Study Place:** Tertiary Care Hospital, Lahore

**Methods:** A cross-sectional observational study was conducted over six months in the Endocrinology Department of a tertiary care hospital in Lahore. Using WHO sample size calculator, a sample of 250 was calculated, keeping CI 95%. P value of less than 0.05 was set and ethical approval was obtained beforehand.

**Results:** 250 patients were included in our study, and among them 106 were males and 114 were females. 190 patients were euthyroid, 42 had subclinical hypothyroidism and 18 had overt hypothyroidism. Diabetes and hypothyroidism have relationship among them and it was evident during study, as hypothyroidism showed relation with disease activity, its duration, HBA1C levels, BMI and even gender i.e. female gender more prone to develop hypothyroidism.

**Conclusion:** Hypothyroidism is a much common disease among the T2DM. Early detection through the screening of thyroid in T2DM patients is needed regularly. Female gender is more prone to develop hypothyroidism, as well as its incidence rises with age. Early detection and treatment improves quality of life.

### INTRODUCTION

Hypothyroidism is a frequent endocrine disease where the thyroid gland fails to maintain the required level of thyroid hormones needed in the body. They are the hormones that are the main regulators of metabolism,

energy production, and a great number of other body functions, namely, thyroxine (T4) and triiodothyronine (T3). A low amount of hormones can slow down the metabolizing process and the

effects of it may be manifested in a great variety of symptoms and may influence several systems of the body. Hashimoto thyroiditis, an autoimmune disease, during which the immune system destroys thyroid tissue, is the most common cause of hypothyroidism in iodine-sufficient areas.<sup>1</sup> Poor dietary intake of iodine is a major cause in the iodine-deficient regions. Additional factors entail thyroid surgery, application of radioactive iodine, some drugs such as lithium or amiodarone, and inborn aspects such as maldevelopment of the thyroid gland (agenesis or dysgenesis). Such risk factors as female sex, mainly after the age of 60, family history of thyroid malady, and other autoimmune illnesses are to be considered. Hypothyroidism leads to the appearance of symptoms that seem to evolve gradually and, without further ado, can be confused with other medical conditions or aging processes. There are common symptoms such as fatigue,

weight gain, intolerance to cold, dry skin, constipation, depression, slowing of the heart rate, hoarseness, and inability to remember things. The women might become irregular in their menstruation, have lower fertility and in other cases lose or have problems in the course of pregnancy.<sup>2</sup> Without management, hypothyroidism may develop to worse life-threatening condition termed myxedema that is uncommon but fatal presenting itself in form of extreme drowsiness, hypothermia and coma. The average method of diagnosis is by measuring the level of thyroid-stimulating hormone (TSH) and free thyroxine (T4) in blood. High TSH with low free T4 confirms that the patient had primary hypothyroidism whereas mildly increased TSH accompanied with normal T4 indicates subclinical hypothyroidism. Proper therapy in hypothyroidism comes in the form of an oral drug called levothyroxine that is a substitute of T4. Levothyroxine is taken orally and should be taken daily to replace normal levels of hormone levels. This dose is modified according to periodic evaluation of both the TSH and the symptoms of the patients. The vast majority of people need life-long treatment, whereas some permanent types of hypothyroidism can be solved.<sup>3</sup> Treatment and the need to use medications regularly are essential to managing it successfully. The intake of levothyroxine ought to be on an empty stomach and at that there should be no co-consumption of substances that may inhibit the

intake of the drug like calcium or iron supplements. Women who are pregnant and have hypothyroidism should receive special care because the due health of both mothers and unborn children may be a disparity of thyroid hormones. Hypothyroidism is capable of causing individuals to have healthy and normal lives with proper management, even though due to poor treatment an untreated case can cause complications including cardiovascular illness, infertility, and mental impairment. The right candidates can have their hypothyroidism well managed and full recovery achieved through education, frequent medical check-up and symptom awareness.<sup>4</sup>

One of the metabolic disorders is diabetes mellitus; it is a chronic disease with abnormalities in the quantity of blood glucose as a result of defects in the protective provision of insulin, the action of insulin, or both. It is among the commonest non-communicable diseases as well as it causes immense problems to the population health since it is linked with serious complications and also high death rates. Diabetes mellitus is predominantly two categories in terms of its major forms namely; type 1 diabetes and type 2 diabetes. Type 1 diabetes is an autoimmune disorder where the body destroys the insulin-producing beta cells at the pancreas leaving an absolute deficiency to insulin. It normally occurs during childhood or adolescent stage but it can also emerge in the adult stage. The most common type of diabetes leading to 90 percent of all cases with diabetes worldwide is type 2 diabetes that is described by insulin resistance as well as a relative insulin deficiency. This type is more prevalent in adults though it is being identified more in younger people including adolescents and even children because of more cases of obesity and lethargic living.<sup>5</sup> Beside these, there is gestational diabetes which may be manifested during pregnancy and predisposes one to type 2 diabetes in adulthood. The pathophysiology of diabetes is many-faceted wherein genetic, environmental, and lifestyle factors interact with each other. Sign and symptoms of diabetes mellitus are frequent urination (polyuria), excessive thirst (polydipsia), unintended weight loss, weakness, impaired visual perception, and delayed wound healing. Yet, more often than not, and more so with type 2 diabetes, the ailment can go unnoticed until years later without symptoms, and is only caused when complications occur. Chronic hyperglycemia may

cause the impairment of many organ systems, which leads to such complications as the development of cardiovascular disease, neuropathy, nephropathy, retinopathy, and the risk of infection. The management of diabetes constitutes a complex process involving lifestyle care, pharmacologic care, and monitoring. Control of all kinds of diabetes has its basis in lifestyle modification, especially on diet and regular exercise. Type 1 diabetes is a life-threatening disease, which requires the use of insulin in supplying the disease via insulin pump or injections.<sup>6</sup> In type 2 diabetes, initial medications can be oral hypoglycemic like metformin and insulin therapy can be adopted in case of failure to control glycemic level. It is very important to monitor blood glucose levels, glycosylated hemoglobin (HbA1c), blood pressure and lipid profile to evaluate the control and avoid complications. Other than the medical side, patient education and self-management are significant in the care of diabetes. Educational programs that show people on how to deal with their condition, how to read the nutrition labels, how to adjust their insulin dosages and other symptoms of hypo- and hyperglycemia can greatly increase the results. Diabetes is a problem that keeps on increasing in the world with most of the factors being as a result of populations getting old, urbanization, poor diets, and lack of physical exercise. Prevention measures are of paramount importance particularly towards type 2 diabetes and they involve adoption of healthy lifestyles, weight loss and early screening of people at risk. With high and ongoing care levels, majority of the people with diabetes are capable of controlling their conditions well and living good lives. There are however healthcare, medication, and educational inequality in wider swathes of the world that are still great hindrances to many, so we could use better public health policy and international collaboration in the fight against diabetes pandemic.<sup>7</sup>

In our study, we will see relationship between diabetes mellitus and hypothyroidism, and how various factors affect it.

## Methodology:

It was a descriptive, cross-sectional study with primary base in a tertiary care hospital Lahore equipped with an endocrinology and diabetes outpatient plan. The study was conducted from \_\_ to \_\_\_\_. The choice of this

setting was explained by the fact that it attracts a large portion of patients diagnosed with T2DM, so the final sample size and clinical data availability would be enough. The Institutional Review Board (IRB) gave the ethical clearance and signed informed consent was obtained by all the participating patients. Two hundred and fifty patients were recruited in the study, and sample size was calculated using WHO sample size calculator, keeping CI 95% and margin of error 5%. The sampling frame was predetermined using a target population whose characteristics included patients aged 30 years and above and who were diagnosed to have T2DM earlier and who were currently visiting the outpatient diabetes clinic during the study timeframe. Diagnosis T2DM was determined by the criteria provided by the American Diabetes Association (ADA): fasting plasma glucose 126 mg/dl or more, 2-hour plasma glucose 200 mg/dl or more during an oral glucose tolerance test, HbA1c 6.5 or more, and a random plasma glucose of 200 mg/dl or more in a patient with the typical diabetes symptoms showing hyperglycemic symptoms.

## Inclusion and Exclusion criteria:

### Inclusion Criteria:

1. Adult (age: 30 years and more) patients who have a definite diagnosis of having T2DM over 6 months of illness.
2. Written informed consent of patients.

### Exclusion Criteria:

1. Patients with diagnosed thyroid diseases under treatment.
2. Persons who have diabetes mellitus type 1.
3. Patients taking drugs with known thyroid effects (e.g amiodarone, lithium).
4. Pregnant or breast feeding women.
5. Patients having advanced stage 4 or more of chronic kidney disease, liver failure, or other serious systemic diseases that may have a role in affecting the levels of thyroid hormones.

The information was gathered using structured interviews, clinical assessment and in the laboratory. To collect demographic information (age, sex, residence), history of diabetes (duration, modes of treatment, adequate glycemic control), and other allied clinical variables including BMI, blood pressure, and lipid profile, a pre-determined questionnaire was filled in.

All the participants were fasted at least 8 hours the night before the collection of blood samples. On testing these samples, thyroid tests (TFTs) were done with serum thyroid-stimulating hormone (TSH), free thyroxine (FT4) and free triiodothyronine (FT3). The patients were categorized as below:

- Normal TSH, FT4 and FT3= euthyroid
- Subclinical hypothyroidism: Increased TSH and normal FT3 and FT4
- Overt hypothyroid: Increased TSH, low FT4 and /or FT3

The data was analyzed through excel sheets and SPPSS version 24. Data was arranged as per mean, median and standard deviation. Categorical variables were calculated as frequencies and percentages. Chi-square

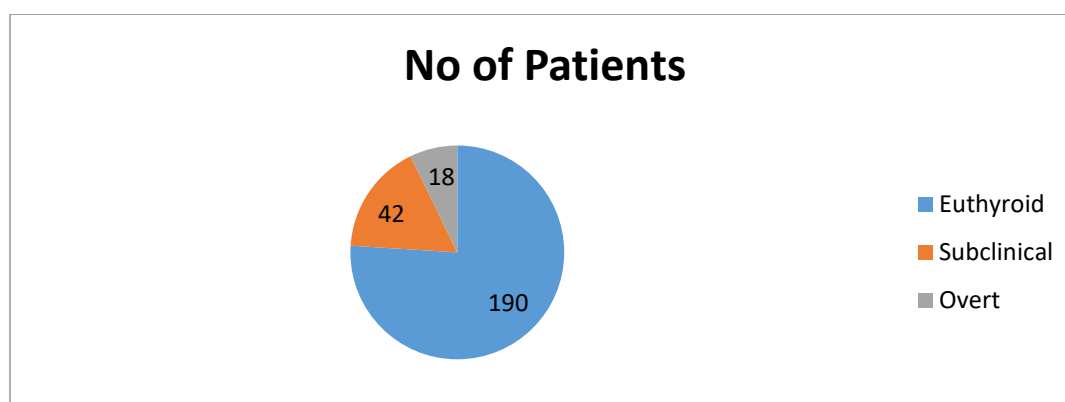
test and logic regression analysis were done. A result of  $p < 0.05$  was to be regarded as significant.

#### Results:

A total of 250 patients with type-II diabetes mellitus (T2DM) were included in our study. The mean age of participants was  $56.4 \pm 9.8$  years, with an age range from 32 to 75 years. Of the total sample, 144 (57.6%) were female and 106 (42.4%) were male.

Of the 250 patients with T2DM, testing of the thyroid showed following results and depicted in pie chart 1.1

1. Euthyroid (normal thyroid): 190 (76.0%)
2. Subclinical hypothyroidism, 42 patients (16.8%)
3. Overt hypothyroidism: 18 out of 250 patients (7.2 %)



Pie Chart 1.1 ( Thyroid function tests results)

Therefore, the frequency of a combined hypothyroidism (both subclinical and overt hypothyroidism) was 24.0 percent ( $n = 60$ ) among diabetic group.

There is gender predilection in hypothyroidism and it was observed that it was extremely high in female T2DM patients:

- With the females ( $n = 144$ ):

1. Hypothyroid(subclinical + overt): 44 (30.6%)
  2. Euthyroid: 100 (69.4%)
- In men ( $n = 106$ ):
1. 16 (15.1%) Hypothyroid (subclinical + overt)
  2. Euthyroid 90 (84.9%)

Results of gender predilection as shown under the figure:

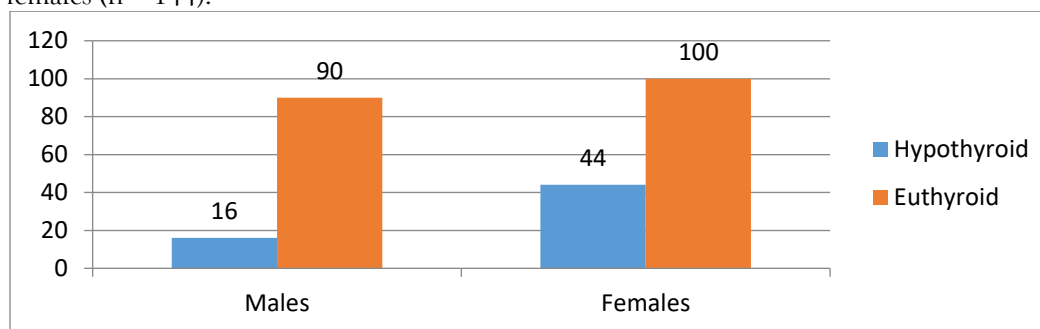


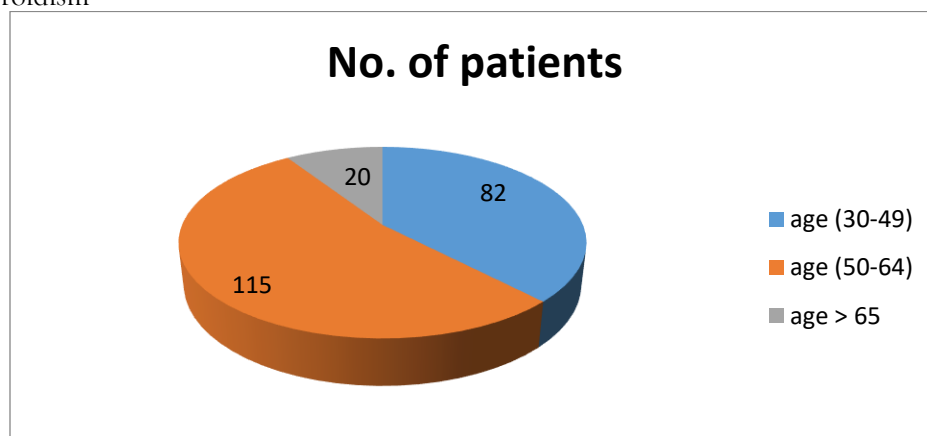
Figure 1.1 (Gender predilection of Hypothyroidism)

The variation on the prevalence of hypothyroidism by gender has been statistically significant (Chi-square test,  $p = 0.006$ ) In our study, we also found association of age with hypothyroidism in diabetic patients. The frequency of hypothyroidism increased with age is shown under and depicted in pie chart 1.2

- Patients aged 30–49 years ( $n = 82$ ): (12.2%) had hypothyroidism

- Patients aged 50–64 years ( $n = 115$ ): (26.1%) had hypothyroidism
- Patients  $\geq 65$  years ( $n = 53$ ): (37.7%) had hypothyroidism

There was a significant association between increasing age and prevalence of hypothyroidism (Chi-square test,  $p = 0.002$ ).



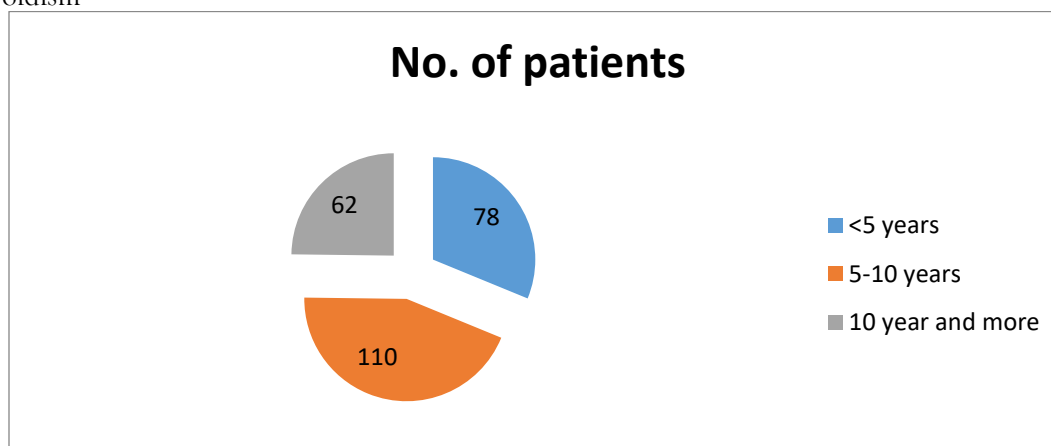
Pie Chart 1.2 (Hypothyroidism trend, Age wise )

Among 250 patients included in the study, another linkage was seen with the disease duration. The prevalence of hypothyroidism was also found to increase with longer duration of diabetes:

- <5 years duration ( $n = 78$ ): (12.8%) had hypothyroidism
- 5–10 years duration ( $n = 110$ ): (23.6%) had hypothyroidism

- 10 years duration ( $n = 62$ ): (38.7%) had hypothyroidism

The association between diabetes duration and hypothyroidism was statistically significant ( $p = 0.001$ ).



Pie Chart 1.3 ( Relationship between hypothyroidism and disease duration)

Patients with hypothyroidism had a higher mean Body Mass Index (BMI) compared to euthyroid patients:

- Mean BMI in hypothyroid group:  $29.2 \pm 3.8 \text{ kg/m}^2$  ( $n=135$ , 54%)

2. Mean BMI in euthyroid group:  $26.8 \pm 3.2$  kg/m<sup>2</sup>  
(n= 115, 46%)  
( $p < 0.001$ , independent t-test)

In terms of glycemic control, the mean HbA1c levels were slightly higher in the hypothyroid group:

- Hypothyroid patients:  $8.3 \pm 1.2\%$  (n= 141, 56.4%)
- Euthyroid patients:  $7.8 \pm 1.0\%$  (n= 109, 43.6%)  
( $p = 0.004$ )

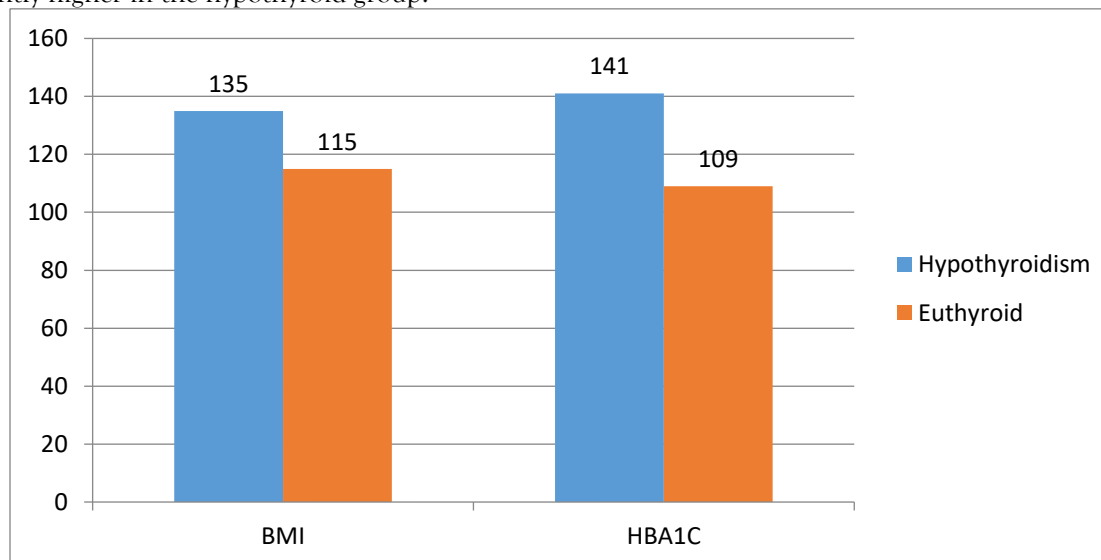


Figure 1.2 ( BMI and HbA1C relationship with hypothyroidism)

Dyslipidemia was also more common among hypothyroid patients, with hypothyroid patients showing high total cholesterol, LDL cholesterol and triglycerides and low HDL cholesterol, as compared to euthyroid group. ( $p < 0.03$ )

#### Discussion:

Over the past few years, a lot of interest has been expressed on the co-existence of hypothyroidism and type-II diabetes mellitus (T2DM) owing initially to mechanisms they share in pathophysiology and how each of them affects the others in paving the way into progression and management of the disease. The prevalence of hypothyroidism in T2DM patients has been reported widely in the past few years, and all of the mentioned studies proved that the number of patients with thyroid dysfunction was higher in diabetic groups than in the area of the general population. Possible causes of such an association, clinical implications and applicability of regular screening of thyroid in T2DM patients are discussed.<sup>8</sup> According to epidemiological data, it can be concluded that in people with T2DM, the chances of developing hypothyroidism in particular and thyroid failure in general are much higher. The prevalence of

the hypothyroidism in T2DM patients was reported between 10 to 25 percent depending upon the population surveyed, diagnostic criteria and the geographical location. To give an example, the predisposition of the thyroid dysfunction to the diabetics with type-II was 13.4 percent in the study of Celani et al. (1994), other publications have even higher percentages even among women and the older generations. In a study that was conducted in India in 2020 by Menon et al., it was observed that 21.5 percent of patients diagnosed with T2DM had hypothyroidism, which sheds light on the importance of regional epidemiologic data, given the fact that the dietary intake of iodine differs, as well as genetics and access to healthcare facilities.<sup>9</sup>

Hypothyroidism common to T2DM might occur partly due to similar risk factors and co-occurring mechanisms of pathogenesis. The two disorders are more common among older people and females. Autoimmunity is another critical connection, most notably in non-genetic-families of people with autoimmune thyroiditis (Hashimoto's disease). Despite type-II diabetes not being a classical autoimmune disorder as in the case of type-I diabetes, low grade, chronic inflammation and immune



dysregulation are characteristics of the metabolic syndrome and insulin resistance, and, potentially, as part of pathophysiology of metabolic syndrome may play into the role of dysfunction of the thyroid gland. Moreover, insulin and thyroid hormone work in mutual ways of metabolism of glucose and lipids. Hypothyroidism decreases glucose uptake and insulin production but raises insulin resistance and, therefore, may deteriorate the glycemic situation in patients with T2DM.<sup>10</sup>

Culturally, the co-morbidity of hypothyroidism among T2DM patients may make it very difficult to manage the disease. As a result of hypothyroidism, dyslipidemia may be worsened, weight increased, fatigue and bradycardia developed, which in addition to the resemblance to poorly controlled diabetes further exposes the patient to cardiovascular complications. In addition to that, hypothyroidism can worsen the insulin response and make glycemic control even more difficult and necessitate the change in antidiabetic treatment. Existent thyroid dysfunction might require the re-evaluation of the management of cardiovascular risk, as the thyroid dysfunction has a direct negative impact on lipid metabolism and blood pressure.

An extreme incidence of subclinical hypothyroidism (SCH) or increased TSH with normal free T<sub>4</sub> is common among T2DM patients. On the one hand, the treatment of overt hypothyroidism is obvious; on the other, DM T2 clinical decision-making concerning SCH is rather debatable. There are some studies which indicate that a little thyroid abnormalities may increase insulin resistance and elevate Metabolic outcome in diabetics as well.<sup>11</sup> The argument presented in favor of early intervention is evidenced by a meta-analysis showing that SCH is indeed correlated with elevated fasting blood glucose and a bigger insulin resistance index Han et al. (2015). On the other hand, it is claimed that conservative intervention should be applied, particularly in the case when increase of TSH is limited with no symptoms.<sup>12</sup>

With such associations and possible clinical relevance, a number of expert committees and research studies suggest that every T2DM patient should be tested using thyroid function tests. According to the American Thyroid Association, thyroid screening should be carried out to all adults at the age of 35 years

and every five years thereafter; however, the majority of endocrinologists recommend more frequent screening in T2DM patients, especially females and people with symptoms pointing to thyroid dysfunction.<sup>13</sup> When hypothyroidism in diabetics is diagnosed and treated at an early stage, a better metabolic process may result, lowering the cardiovascular risk, as well as increases the level of life quality.

Nonetheless, there are still issues associated with introducing the idea of widespread screening, particularly in poor-resource countries. Lack of awareness, cost and access to laboratories where early detection can be carried out may be a hindrance. Secondly, different diagnostic standards in the determination of prevalence and reference ranges in the laboratories can create under diagnosis or over treatment.<sup>14</sup>

In addition, the effects of comorbid hypothyroidism in diabetics drizzle to the mental health and quality of life. It is common to find fatigue, depression, cognitive slowing, and diminished physical activity among the patients of hypothyroid, and this can severely affect diabetes self management and treatment adherence. An existing depression symptom and cognitive impairment in diabetics can be worsened with the presence of thyroid dysfunction. That is why the comprehensive approach to the management of diabetic individuals is needed, where the usual exercise psychological assessment and education of the patient regarding the signs and symptoms of the thyroid illness is expected.<sup>15,16</sup>

In clinical practice, the question how often the T2DM patients should be screened regarding the problems with the thyroid gland is debatable. Although others may suggest selection of screening by risk factors and symptoms, increasing evidence toward high prevalence and clinical significance has caused many researchers to suggest universal screening at the time of diagnosis of diabetes and subsequent re-evaluation thereafter. Hypothyroidism in diabetics when diagnosed and treated early has been linked to good glycemic control, a decrease in insulin demands, and an improvement in lipid profiles which help in the control of the disease and in preventing long-term comorbidities.<sup>17,18</sup>

In simple words the frequent occurrence of hypothyroidism and type-II diabetes mellitus is a

clinically important association which has far-flung implications. The thyroid dysfunction significantly affects the results of diabetes intimately<sup>1</sup>, including metabolic effects, cardiovascular risks and quality of life. Being aware of this association and regularly screening and treating thyroid disease in the patients with diabetes can work to the benefit of patients, lower the complication rates and overall healthcare delivery to this high-risk patients group.<sup>19</sup>

In our study, Out of 250 T2DM patients, 24.0% were found to have hypothyroidism, with a higher frequency among females, older individuals, those with longer diabetes duration, and patients with dyslipidemia. These findings underscore the importance of routine thyroid function screening in the management of type-II diabetes, especially in high-risk subgroups.

Conflict of study: Nil

Funding: Nil

### Conclusion:

It is concluded that hypothyroidism is highly prevalent among people with type-II diabetes mellitus (T2DM) than among the general population and both overt and subclinical hypothyroidism present extra clinically related issues. This comorbidity may be attributed to the similarity in the metabolic and endocrine processes, which may have the effect of hindering blood sugar regulation and predispose one to complications. Thyroid function is expected to be done regularly in T2DM patients in order to assist in early detection and proper care. Hypothyroidism has the potential of exacerbating insulin resistance, dyslipidemia, and cardiovascular risks which are already high among the diabetics. Research studies conducted have revealed that the complications that are likely to occur include hypertension, atherosclerosis along with endothelial dysfunction which are further aggravated by thyroid dysfunction. Additionally, hypothyroidism influences antidiabetic medications (e.g., insulin, glyburide) metabolism and excretion of the medications, which predisposes to the development of adverse drug effects, such as hypoglycemia. Even gender differences contribute to this issue, which is why women have more chances of experiencing hypothyroidism, and such cases may be caused by anti-thyroid peroxidase antibodies. This evidence demonstrates the necessity of sex and

individual-specific treatment of T2DM along with other thyroid conditions. Additional studies are required to clarify the ideal screening rates, assessing the advantages of early intervention, and comprehension of the long-term consequence of the thyroid hormone replacement therapy on the diabetic outcomes.

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