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# A RETROSPECTIVE STUDY ON THE THYROID DYSFUNCTION IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AND THE EFFECT OF DURATION OF DIABETES AND ANTI-GLYCEMIC MEDICATIONS ON MEAN HBA1C AND TSH LEVELS

**Dr. Zahoor Ahmed Khan[1], Dr. Nasrullah Zadran[2], Dr. Muhammad Mashood[3]**

[1] MO at BHU. 212/9.R Tehsil Fort Abbas Distt Bahawalnagar

[2] Khyber Medical College Peshawar

[3] BHU 297 HR Tehsil Fort Abbas Distt Bahawalnagar

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**Abstract:**

***Background:*** *The relationship between type 2 diabetes and thyroid disorders is well established and requires testing a diabetic patient for the presence of thyroid abnormalities.* ***Aim:*** *to check the presence of hypothyroidism or hyperthyroidism in a sample of patients with type 2 diabetes and to check if anti-glycemic drugs have any effect on average levels of TSH and A1c.*

***Methods:*** *This is a retrospective study of the documentation of 1,341 patients with type 2 diabetes at the Endocrinology and Diabetology department of Services Hospital Lahore for one-year duration from March 2019 to March 2020. The data was taken from patient registration software and analyzed for the presence of hypothyroidism or hyperthyroidism.*

***Results:*** *Out of 1,341 patients with type 2 diabetes, 108 had thyroid dysfunction (8%), 7% had hypothyroidism, and 1% had hyperthyroidism. Mean TSH levels were significantly lower with diabetes duration> 5 years in patients with hypothyroidism (p = 0.032) and lower when metformin was introduced to treat hypothyroidism (p = 0.036). In patients with hyperthyroidism, this effect did not occur.*

***Conclusion:*** *Thyroid disorders in patients with type 2 diabetes are underestimated in our country, mean TSH levels are lower in patients with hypothyroidism when metformin was used, and lower in patients with diabetes lasting more than 5 years.*

***Keywords:*** *Type 2 diabetes, Hypothyroidism, Hyperthyroidism, Metformin.*

**Corresponding author:**

**Dr. Zahoor Ahmed Khan,**

*MO at BHU. 212/9.R Tehsil Fort Abbas Distt Bahawalnagar*

QR code

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## INTRODUCTION:

Diabetes and thyroid diseases are the most common endocrine disorders in medical practice. The relationship between diabetes and thyroid disease was first described in 1979, and a number of studies have estimated the incidence of thyroid dysfunction in type 2 diabetics at 2.2-17%. Higher levels of HbA1c (A1c) are found in type 2 diabetic patients with thyroid dysfunction, and diabetes appears to affect thyroid function at two sites: first, in the hypothalamic control of TSH by TRH, and second, in peripheral tissues by converting T4 into T3. Hyperglycemia leads to decreased levels of T4, 5-deiodinase, low serum T3 levels, elevated levels of reverse T3, and low, normal, or high levels of T4. Thyroid hormone regulates metabolism, and diabetes alters the metabolism of many substances, including glucose, fatty acids, triglycerides, and lipoproteins. Thyroid hormones can also help regulate carbohydrate metabolism and pancreatic metabolism, while diabetes also affects the results of thyroid function tests to varying degrees. It's also worth mentioning that an underlying thyroid problem may go unrecognized due to the similarities between the signs and symptoms of thyroid disorders and diabetes. Hyperthyroidism refers to a hypermetabolic state characterized by excessive release of energy at rest, weight loss, lowered cholesterol, and increased lipolysis and gluconeogenesis, while hypothyroidism leads to decreased energy release, increased body weight, increased cholesterol, and decreased lipolysis and gluconeogenesis. . It is also mentioned that in euthyroid individuals there may be fluctuations in plasma thyroid hormone levels, correlated with changes in insulin secretion and sensitivity.

It has been observed that an overactive thyroid gland can worsen glycemic control and increase insulin requirements than expected. Thyroid function testing in patients with type 2 diabetes seems important, although it is not recommended in guidelines. It seems that diabetic thyroid dysfunction is more common in the elderly than in those under the age of 60. The incidence of thyroid dysfunction in patients with type 2 diabetes differs between the sexes between men and women and it is unclear whether there is a male or female predominance, although a study in Saudi Arabia found that primary hypothyroidism was male predominant, but it depends on the number and selection of patients as it is well known that in the non-diabetic population the number of women exceeds the number of men and it is well known that this also depends on many factors including ethnic, geographic and environmental origin including iodine consumption status and possibly other undiscovered factors. Hypothyroidism is the most common problem in people with type 2 diabetes compared to hyperthyroidism. Insulin and thyroid hormones are closely involved in cellular metabolism, therefore the excess or deficiency of any of these hormones leads to dysfunction of the others [10–13]. Metformin is the most commonly used blood glucose lowering drug in patients with type 2 diabetes and it has been found that diabetics treated with metformin had a smaller thyroid volume and a lower risk of nodule formation compared to controls. Metformin has also been found to have an isolated effect on lowering TSH levels in patients with hypothyroidism without changes in T3 and T4 levels. Metformin lowers gluconeogenesis, reduces insulin resistance, which has been found to occur more frequently in patients with hypothyroidism, and is also thought to alter the affinity and / or number of thyroid hormone receptors and increase central dopaminergic tone or activate TSH receptors and thus enhances the action of the thyroid hormone in the pituitary gland. In this study, we tried to estimate the incidence of both hypothyroidism and hyperthyroidism in a sample of patients with type 2 diabetes, and to determine the effect of antiglycemic drugs on mean TSH and A1c levels.

## MATERIALS AND METHODS:

This is a retrospective study of the documentation of 1,341 patients with type 2 diabetes at the Endocrinology and Diabetology department of Services Hospital Lahore for one-year duration from March 2019 to March 2020. The data collected included age, gender, duration of DM, TSH level, presence or absence of goiter, type of anti-glycemic therapy, HbA1c level from the data available in the records, unfortunately we could not have an evidence to label patient as hypothyroid or subclinical hypothyroid, so the total number included both hypothyroid and subclinical hypothyroid patients, the same was applied on those with hyperthyroidism. There was no evidence for the duration of thyroid dysfunction in the records but only the duration of type 2 diabetes was available. The record included 1341 type 2 diabetic patients 666 females (49.66%) and 675 males (50.34%), so the sex distribution was nearly equal. The age range was from 32-60 for hypothyroidism and 30-50 for hyperthyroidism. Pearson Chi square test was used for statistical analysis.

## RESULTS:

Table 1 showed the incidence of sex, age and disease among the sample. The age range was 30-75 years and was 32-60 for patients with hypothyroidism and 30-50 in female-dominated hyperthyroidism. The number of patients with hypothyroidism was 94 (7%) and 14 (1%) Hyperthyroidism.

**Table 1 shows some demographic data and disease prevalence (F=Female, M=Male)**

| Prevalence | No. and Percentage (%) | Gender (%) | Age range (year) |
|---|---|---|---|
| Total | 1341 | 666 F (49.66%) | 30-75 |
| | | 675 M (50.34%) | |
| Hypothyroidism | 94 (7%) | 84 F (89.36%) | 32-60 |
| | | 10 M (10.64%) | |
| Hyperthyroidism | 14 (1%) | 11 F (78.57%) | 30-50 |
| | | 3 M (21.43%) | |

In Table 2, 75.57% of patients with hypothyroidism had a predominance of a relaxed thyroid, 32.97% thyroid atrophy and 5.32% of the thyroid gland. Patients with hyperthyroidism were 11 (78.57%) diffusion goiters, and the rest had MNG 3 (21.43%).

**Table 2 shows the thyroid status. (MNG= Multi Nodular Goiter)**

| Status | Hypothyroidism (%) | Hyperthyroidism (%) |
|---|---|---|
| Diffuse goiter | 58 (61.7%) | 11 (78.57%) |
| Atrophy | 31 (32.97%) | ------- |
| Thyroidectomy | 5 (5.32%) | ------- |
| MNG | ------- | 3 (21.43%) |

Table 3 showed a link between diabetes duration and TSH and A1c levels. Regarding hypothyroidism, 48 patients have diabetes duration for 1-5 years with mean TSH of 13.1 while 46 patients have diabetes duration >5 years with mean TSH of 3.4 (p=0.032) and a mean A1c of 8.4% and 9.36% respectively (p=0.77).

**Table 3 shows the relation between diabetes duration and both TSH and A1c**

| Disease | Duration of diabetes (years) | Patient No. | TSH | A1c | p-value |
|---|---|---|---|---|---|
| Hypothyroidism | 1-5 | 48 | 13.1 | | 0.032 |
| | >5 | 46 | 3.4 | | |
| | 1-5 | 48 | ----- | 8.4 | 0.77 |
| | >5 | 46 | ----- | 9.36 | |
| Hyperthyroidism | 1-5 | 8 | 2.7 | ----- | 0.845 |
| | >5 | 6 | 1.625 | ----- | |
| | 1-5 | 8 | ----- | 9.6 | 0.56 |
| | >5 | 6 | ----- | 10.8 | |

While in hyperthyroid patients mean TSH with diabetes duration for 1-5 years was 2.7 with TSH mean of 1.625 in those with diabetes at duration >5 years (p=0.845) with mean A1c with diabetes duration for 1-5 years was 9.6% and with duration >5 years 10.8% (p=0.56).

**Table 4 shows the effect of metformin on mean TSH and A1c levels**

| Disease | Patient No. | TSH | p-value | A1c | p-value |
|---|---|---|---|---|---|
| Hypothyroidism | With metformin (62) | 4 | 0.036 | 10.7 | 0.2 |
| | without (32) | 7.6 | | 10.317 | |
| Hyperthyroidism | with metformin (2) | 1.3 | 0.19 | 10.7 | 0.027 |
| | without (12) | 1.39 | | 10.317 | |

Table 4 detected the effect of metformin on mean TSH and A1c levels. The significant effect of metformin (p-0.036) on the reduction of mean TSH in patients with hypothyroidism had no significant effect on mean A1c (p-0.2). Two (14.28%) of the 14 patients with hyperthyroidism had 12 (85.71) remaining metformin. Average TSH levels (p-0.19) have no significant impact, but have a significant impact on A1c levels (p-0.027). This means that the mean a1c reaches 12 patients using insulin, even though 2 patients have metformin. Table 5 showed A1c levels in patients with hypothyroidism and hyperthyroidism with diabetes. Patients with a1c8 in both diseases are 65 (60.18%).

**Table 5 shows the A1c level in both diseases**

| Disease | A1c<7% (Patient No.) | A1c=7-8% (Patient No.) | A1c>8% (Patient No.) |
|---|---|---|---|
| Hypothyroidism | 20 (21.28%) | 19 (20.21%) | 55 (58.51%) |
| Hyperthyroidism | 2 (14.29%) | 2 (14.29%) | 10 (71.42%) |
| Total | 22 (20.37%) | 21 (19.44%) | 65 (60.18%) |

## DISCUSSION:

Based on patient records, this indicator included the total number of cases because we had no idea about the percentage of patients with subclinical or clinical hypothyroidism and it was not clear whether thyroid function was performed in diabetic patients suspected of having thyroid problems and whether thyroid problems were diagnosed for the first time or before thyroid problems were diagnosed. , but the duration of diabetes was visible in the records[9-10]. The total number of patients with type 2 diabetes was 666 women (49.66%). were, so the incidence of the disease is almost identical in both sexes, their age ranges from 30 to 75, hypothyroidism in 94 patients (7%) hyperthyroidism (1%) 14 patients. This frequency is significantly lower for hypothyroidism than in other studies, ranging from 22-56.82% to 6-8.15% for hyperthyroidism (clinical + subclinical). In practice, the thyroid problem pays little attention to type 2 diabetes. Our study shows that the low number of type 2 thyroid dysfunction is underestimated, and several fractions of this type of 2 diabetics are tested for thyroid problems. In our study, there are 58 patients with hypothyroidism (61.7%) distributed goiter, 31 (32.97%) thyroid atrophy and only 5 (5.32%) previous thyroid gland. In patients with hyperthyroidism 11 (78.57%) and 3 (21.43%) mng, as shown in Table 2. This means that a total of 108 patients (66.3%) 69 patients are most likely autoimmune diffusion goiters 032) although there is no statistically significant difference between mean A1c (TSH 6 vs 15.15.15)(p-0.032) mean A1c (TSH 6 vs 15.1) (p-0.032), There is no statistically significant difference from the mean A1c (A1c p-0.77) and both groups have a high A1c, however, it is clear that people with diabetes in Table 3 are 33.4% compared to 33.4% over 5 years, with an average level of A1C higher than in Although the mean difference in average TSH in patients with hyperthyroidism (p-0.845) and A1c (p-0.56) also does not appear in Table 3, which means that a1c is higher than in people under 5 years of age (10.8 vs. 9.6). Among the 94 patients with hypothyroidism in this study, there are 32 other agents, including metformin for treatment, including metformin, the effect of metformin on reducing TSH levels is very clear (p-0.036), a1c levels are almost identical (p-0.2)[11-12]. This is clear in Table 4, which shows that 2 out of 14 hyperthyroidisms are metformin's, and the remaining 12 are insulin. This means that although most insulin is found, metformin has reached A1c levels despite the use of a minority of patients (p-0.027), although there is no significant difference between average TSH (p-0.19). Hyperthyroidism causes a hypermetabolic condition that causes excessive secretion of thyroxine, increased lipolysis and gluconeogenesis. This explains why most of our patients with hyperthyroidism are treated with insulin[13-14]. In other studies, the effect of TSH metformin has been observed to decrease in patients with hypothyroidism. Fournier, et al., found that metformin use in patients with type 2 diabetes was associated with a higher rate of lower TSH levels. Nurcheshmeh, et al. In his study, he mentioned that metformin can reduce TSH levels even in patients with subclinical hypothyroidism and co-existent metabolic syndrome.[15] This reflects a wide change in the number between different studies, depending on a number of factors such as the use of insulin or oral diabetes medications and aversion to insulin treatment when necessary.

## CONCLUSION:

This study showed that the prevalence of thyroid dysfunction in type 2 diabetic patients in our country is underestimated, and metformin has a significant TSH lowering effect in hypothyroid patients. We encourage checking more type 2 diabetic patients for thyroid problem as much as it is feasible, as this is cost-effective.

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