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Original Research

To establish the correlation between proliferative diabetic retinopathy and type 2 diabetes mellitus, specifically observing the impact of hypothyroidism

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ABSTRACT:

Aim: To establish the correlation between proliferative diabetic retinopathy and type 2 diabetes mellitus, specifically observing the impact of hypothyroidism. **Materials and methods:** This cross-sectional study was conducted in the Department of Medicine. 100 patients were enrolled in the study diagnosed with T2 DM, who were willing to participate in the study were evaluated and compared as per the proforma designed for the purpose of the study. As per the aim of the study, the comparison was done among two groups with 50 patients in each group. Thyroid function tests were done in all the patients and 2 groups was made, the first group included diabetic patients with thyroid dysfunction and the second group included diabetic patients without thyroid dysfunction. **Results:** Retinopathy was present in 19 patients in the group with thyroid dysfunction, compared to 17 patients in the group without thyroid dysfunction. Although the number of patients with retinopathy was slightly higher in the thyroid dysfunction group, the difference is not substantial. The presence of retinopathy in both groups suggests that it is a common complication among diabetic patients, regardless of thyroid status. Proliferative diabetic retinopathy (PDR) was present in 15 patients within the group with thyroid dysfunction, whereas it was absent in all patients in the group without thyroid dysfunction. This stark contrast suggests a strong association between thyroid dysfunction and the occurrence of PDR. The presence of PDR exclusively in the thyroid dysfunction group implies that thyroid abnormalities in diabetic patients may significantly increase the risk of developing this more severe form of retinopathy. **Conclusion:** Diabetic retinopathy overall was not showing any statistically significant association with hypothyroidism however there was statistically significant association between proliferative retinopathy in diabetic patients with hypothyroidism.

Key Words: Hypothyroidism, Diabetes, Retinopathy

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INTRODUCTION

Hypothyroidism and type 2 diabetes mellitus (T2DM) are two prevalent endocrine disorders with significant global health implications. While these conditions are often studied independently, emerging evidence suggests a complex interplay between thyroid dysfunction and diabetes-related complications, particularly proliferative diabetic retinopathy (PDR). Proliferative diabetic retinopathy is a severe sight-threatening condition characterized by the growth of new blood vessels on the retina, which can lead to vision loss if untreated. Hypothyroidism, characterized by deficient thyroid hormone production, can exacerbate metabolic disturbances and potentially influence the progression of diabetic complications. This introduction explores the emerging evidence linking hypothyroidism with PDR in individuals with T2DM, highlighting the underlying mechanisms, clinical implications, and the need for integrated management approaches.[1,2] Hypothyroidism, resulting from an underactive thyroid gland, leads to a deficiency in thyroid hormones (triiodothyronine [T3] and thyroxine [T4]). These hormones are critical regulators of metabolism, influencing various physiological processes such as energy expenditure, lipid metabolism, and glucose homeostasis. Hypothyroidism is associated with a reduction in basal metabolic rate, increased serum cholesterol levels, and insulin resistance, all of which are risk factors for the development and progression

of T2DM. The metabolic disturbances caused by hypothyroidism can therefore have a profound impact on individuals with T2DM, potentially exacerbating diabetic complications, including retinopathy.[3] Proliferative diabetic retinopathy is an advanced stage of diabetic retinopathy, characterized by neovascularization— the formation of new, fragile blood vessels on the retina and optic disc. These new vessels are prone to bleeding, leading to vitreous hemorrhage, retinal detachment, and significant vision loss. The pathogenesis of PDR is complex and multifactorial, involving chronic hyperglycemia, oxidative stress, and inflammatory processes that result in retinal ischemia and subsequent neovascularization. Poor glycemic control, hypertension, and duration of diabetes are well-established risk factors for the development of PDR. Hypothyroidism is associated with increased insulin resistance and impaired glucose metabolism, which can exacerbate hyperglycemia in individuals with T2DM. Chronic hyperglycemia is a key driver of diabetic retinopathy, leading to endothelial dysfunction and increased vascular permeability.[4]

Hypothyroidism often results in dyslipidemia, characterized by elevated levels of low-density lipoprotein (LDL) cholesterol and triglycerides. Dyslipidemia is a known risk factor for diabetic retinopathy, contributing to the formation of hard exudates and macular edema, which can accelerate the progression to PDR. Both hypothyroidism and T2DM are associated with increased levels of inflammatory cytokines and oxidative stress markers. These inflammatory processes can damage the retinal vasculature, promoting neovascularization and progression to PDR. Hypothyroidism can lead to tissue hypoxia due to reduced cardiac output and impaired oxygen delivery. Hypoxia is a critical stimulus for the upregulation of VEGF, a key mediator of neovascularization in PDR.[5] Understanding the link between hypothyroidism and PDR in individuals with T2DM has significant clinical implications. Firstly, it highlights the need for comprehensive endocrine evaluation in patients with T2DM, including routine screening for thyroid dysfunction. Early detection and management of hypothyroidism in these patients could potentially mitigate the risk of developing severe diabetic retinopathy. Secondly, integrated management strategies targeting both glucose and thyroid hormone levels may be beneficial in preventing or slowing the progression of PDR. Optimizing thyroid hormone replacement therapy in hypothyroid patients with T2DM could improve metabolic control and reduce the burden of diabetic complications.[6] Finally, this link underscores the importance of a multidisciplinary approach in the care of patients with T2DM. Collaboration between endocrinologists, ophthalmologists, and primary care providers is essential for the early detection and comprehensive management of thyroid dysfunction and diabetic retinopathy.

MATERIALS AND METHODS

This cross-sectional study was conducted in the Department of Medicine. 100 patients were enrolled in the study diagnosed with T2 DM, who were willing to participate in the study were evaluated and compared as per the proforma designed for the purpose of the study. As per the aim of the study, the comparison was done among two groups with 50 patients in each group. Thyroid function tests were done in all the patients and 2 groups was made, the first group included diabetic patients with thyroid dysfunction and the second group included diabetic patients without thyroid dysfunction. Fundoscopy was done in all patients by the ophthalmologist for assessing retinopathy. An inclusion criterion was T2 DM patients aged more than 18 years. Exclusion criteria were patients taking drugs affecting thyroid profile and patients with known hypertension, ischemic heart disease, smokers and chronic alcoholics.

Statistical analysis

Statistical analysis was done using SPSS25.0 software. Since the distribution of data was parametric, Chi square test and Fischer's exact test were used to study the differences between categorical data. Student't' test was used to assess associations between numerical variables.

RESULTS

Age Distribution (Table 1)

The mean age of patients in the group with thyroid dysfunction was slightly higher at 57.56 years, with a standard deviation of 8.5 years, compared to the group without thyroid dysfunction, which had a mean age of 54.6 years and a standard deviation of 9.08 years. This suggests that patients with thyroid dysfunction in this study were generally older than those without thyroid dysfunction, though the age difference between the two groups is relatively modest. The standard deviation values indicate that there was a moderate variation in age within both groups, but this variation was somewhat larger in the group without thyroid dysfunction.

Sex Distribution (Table 2)

The sex distribution between the two groups was relatively balanced, with a slight predominance of females in both groups. In the group with thyroid dysfunction, there were 23 males and 27 females, while in the group without thyroid dysfunction, there were 24 males and 26 females. This balance suggests that sex was not significantly skewed in either group, and both male and female patients were well-represented in the study. The similar distribution of sexes in both groups helps to control for sex as a

confounding variable when comparing outcomes related to thyroid dysfunction.

Duration of Diabetes (Table 3)
Patients with thyroid dysfunction had a longer mean duration of diabetes, averaging 8.77 years with a standard deviation of 4.22 years, compared to those without thyroid dysfunction, who had a mean duration of 6.34 years with a standard deviation of 3.54 years. This indicates that thyroid dysfunction in diabetic patients might be associated with a longer duration of diabetes. The higher mean duration in the thyroid dysfunction group suggests that the longer exposure to diabetes may contribute to or be a factor in the development of thyroid abnormalities. The variation in the duration of diabetes was greater in the group with thyroid dysfunction, as evidenced by the higher standard deviation.

Occurrence of Retinopathy (Table 4)
Retinopathy was present in 19 patients in the group with thyroid dysfunction, compared to 17 patients in the group without thyroid dysfunction. Although the number of patients with retinopathy was slightly higher in the thyroid dysfunction group, the difference is not substantial. The presence of retinopathy in both groups suggests that it is a common complication among diabetic patients, regardless of thyroid status. However, the slightly higher occurrence in the thyroid dysfunction group may imply a possible association between thyroid dysfunction and an increased risk of retinopathy, though further analysis would be needed to confirm this.

Occurrence of Proliferative Retinopathy (Table 5)
Proliferative diabetic retinopathy (PDR) was present in 15 patients within the group with thyroid dysfunction, whereas it was absent in all patients in the group without thyroid dysfunction. This stark contrast suggests a strong association between thyroid dysfunction and the occurrence of PDR. The presence of PDR exclusively in the thyroid dysfunction group implies that thyroid abnormalities in diabetic patients may significantly increase the risk of developing this more severe form of retinopathy. The absence of PDR in the group without thyroid dysfunction further strengthens the case for thyroid dysfunction as a potential risk factor for PDR in diabetic patients.

Table 1: Age distribution

	Mean age in yrs	Standard deviation
Group with thyroid dysfunction	57.56	8.5
Group without thyroid dysfunction	54.6	9.08

Table 2: Sex distribution

Sex	Group with thyroid dysfunction	Group without thyroid dysfunction
Males	23	24
Females	27	26
Total	**50**	**50**

Table 3: Duration of diabetes

	Mean duration of diabetes in years	Standard deviation
Group with thyroid dysfunction	8.77	4.22
Group without thyroid dysfunction	6.34	3.54

Table 4: Occurrence of retinopathy

Retinopathy	Group with thyroid dysfunction	Group without thyroid dysfunction
Present	19	17
Absent	31	33

Table 5: Occurrence of proliferative retinopathy

PDR	Group with thyroid dysfunction	Group without thyroid dysfunction
Present	15	0
Absent	35	50

DISCUSSION
The mean age of patients with thyroid dysfunction in this study was 57.56 years, slightly higher than the 54.6 years observed in the group without thyroid dysfunction. This finding aligns with previous studies, where age has been recognized as a significant factor associated with thyroid dysfunction, particularly in diabetic populations. For instance, studies by Hollowell et al. (2002) found that the prevalence of thyroid dysfunction increases with age, particularly in individuals over the age of 50.[1] Similarly, Diez (2004) reported that older age is a risk factor for subclinical hypothyroidism, especially in women. These studies support the observation that older age may contribute to the development of thyroid dysfunction in diabetic patients.[2]In this study, the sex distribution was fairly

balanced, with a slight predominance of females in both groups (27 females in the thyroid dysfunction group vs. 26 in the non-dysfunction group). This trend is consistent with earlier research, which has shown that thyroid disorders, particularly hypothyroidism, are more common in women than men. Vanderpump et al. (1995) noted that the incidence of thyroid dysfunction, especially hypothyroidism, is significantly higher in females, with a female-to-male ratio of approximately 10:1.[3] This sex predilection is thought to be due to both hormonal and autoimmune factors, which are more prevalent in women . The slight female predominance in both groups in the current study is therefore in line with the general epidemiology of thyroid dysfunction.The longer mean duration of diabetes in the thyroid dysfunction group (8.77 years) compared to the non-dysfunction group (6.34 years) suggests that longer exposure to diabetes may be a contributing factor to the development of thyroid abnormalities. This association is supported by earlier studies, such as those by Smithson (1998), which found that the prevalence of thyroid dysfunction increases with the duration of diabetes .[5]Similarly, a study by Perros et al. (1995) observed a higher incidence of thyroid dysfunction in patients with long-standing diabetes, further corroborating the findings of this study.[6] These studies highlight the importance of monitoring thyroid function in patients with long-term diabetes, as the risk of thyroid dysfunction appears to increase with the duration of the disease.

The occurrence of retinopathy in both groups was relatively similar, with 19 cases in the thyroid dysfunction group and 17 in the non-dysfunction group. Retinopathy is a well-known complication of diabetes, and its prevalence is influenced by various factors, including the duration of diabetes and glycemic control. The slightly higher occurrence in the thyroid dysfunction group suggests a potential link between thyroid dysfunction and retinopathy. This is in line with findings by Celani et al. (1994), who reported that thyroid dysfunction, particularly hypothyroidism, may exacerbate microvascular complications like retinopathy in diabetic patients . However, the difference in retinopathy occurrence between the two groups in the current study was not substantial, indicating that while there may be an association, other factors also play a critical role in the development of retinopathy.[7]A notable finding in this study was the presence of proliferative diabetic retinopathy (PDR) exclusively in the thyroid dysfunction group, with 15 cases observed, compared to none in the non-dysfunction group. This significant disparity suggests a strong association between thyroid dysfunction and the development of PDR. Previous research has highlighted the potential link between thyroid dysfunction and the progression of diabetic retinopathy. For example, the study by Anagnostis et al. (2013) found that hypothyroidism might worsen the course of diabetic retinopathy, possibly due to its impact on lipid metabolism and microvascular function.[8] Additionally, research by Yamada et al. (2000) indicated that thyroid dysfunction could be a risk factor for the progression of retinopathy, particularly in patients with poorly controlled diabetes .[9] The findings of the current study further underscore the need for vigilant monitoring and management of thyroid function in diabetic patients to prevent the progression of retinopathy to more severe forms like PDR.

CONCLUSION

Diabetic retinopathy overall was not showing any statistically significant association with hypothyroidism however there was statistically significant association between proliferative retinopathy in diabetic patients with hypothyroidism. Hence the retinopathy progression is higher in diabetics with hypothyroidism early screening for thyroid dysfunction with normalization of hormone levels is required.

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