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A Cross-sectional Study Investigating the Correlation between Subclinical Hypothyroidism and Type 2 Diabetes Mellitus at a Tertiary Care Facility in Kerala

Mohammed Ramees[1], Daniel Tony Kannampuzha[1], Ajay Mohan[2], Kiran Chandramohan[3], Jain Christy[4], Diana David[1]*

[1]Assistant Professor, Dept of Internal Medicine, Amala Institute of Medical Sciences, Thrissur, India
[2]Senior Resident, Department of Internal Medicine, Amala Institute of Medical Sciences, Thrissur, India
[3]Senior Resident, Department of Internal Medicine, Jubilee Mission Medical College and Research Institute, Thrissur, India
[4]Resident Medical Officer, ST Joseph Hospital Choondal, Thrissur, India

***Address for Correspondence:** Dr. Diana David, Assistant Professor, Dept Of Internal Medicine, Amala Institute of Medical Sciences, Thrissur, India
E-mail: dianadavid90@gmail.com

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ABSTRACT

Background: Subclinical hypothyroidism (SCH) is defined as elevated thyroid-stimulating hormone (TSH) and normal free thyroxine (FT4) levels. Several studies demonstrate a direct correlation between subclinical hypothyroidism and insulin resistance. To investigate the prevalence of SCH in patients with type 2 diabetes mellitus (T2DM) and its correlation with glycemic control.

Methods: This observational study included 475 participants, comprising 250 patients with T2DM and 225 non-diabetic controls. Subclinical hypothyroidism was defined as thyroid-stimulating hormone levels exceeding 4.0 mIU/L, accompanied by normal free T4 levels.

Results: The prevalence of SCH was similar in T2DM patients (28%) and non-diabetic controls (26.6%). However, poorly controlled T2DM patients (HbA1c≥9%) had a higher prevalence of SCH (50%) compared to well-controlled patients (HbA1c<7%, 21.4%).

Conclusion: The prevalence of SCH was similar in diabetic and non-diabetic groups. Our study revealed a greater than twofold increase in SCH prevalence among patients exhibiting poorly controlled diabetes (HbA1c≥9%) compared to those with well-controlled diabetes (HbA1c<7%). These results indicate that SCH presents a substantial risk for patients with inadequate glycemic control, and treatment of SCH could potentially enhance insulin sensitivity and facilitate glycemic control. Further prospective studies encompassing larger patient populations are recommended to comprehensively assess the correlation between HbA1c and SCH.

Key-words: Subclinical hypothyroidism, Thyroid-stimulating hormone (TSH), Type 2 diabetes mellitus (T2DM), Insulin resistance

INTRODUCTION

Subclinical hypothyroidism is a condition characterized by elevated serum thyroid-stimulating hormone (TSH) levels, with normal thyroxine (T4) and triiodothyronine (T3) levels. This condition is often referred to as "sub-clinical Hypothyroidism" (SCH). Despite its subtle clinical presentation, SCH affects a significant proportion of the global population, with prevalence estimates ranging from 4% to 20% in different populations. The clinical significance of SCH remains a topic of debate, with some arguing that it is a benign condition that does not require treatment. However, a growing body of evidence suggests that SCH is associated with various cardiovascular and metabolic disorders, including atherosclerosis, hypertension, dyslipidemia, and insulin resistance. Notably, a significant association has been observed between SCH and T2DM [1-5].

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Type 2 diabetes mellitus is a chronic metabolic disorder characterized by insulin resistance and impaired insulin secretion, affecting over 400 million people worldwide. The coexistence of SCH and T2DM has been reported in several studies, with prevalence estimates of SCH in type 2 diabetes mellitus patients ranging from 10% to 30%. The mechanisms underlying the association between SCH and T2DM are complex and multifactorial. Insulin resistance, a hallmark of T2DM, may contribute to the development of SCH by reducing the expression of thyroid hormone receptors and increasing the levels of inflammatory cytokines.

Conversely, SCH may exacerbate insulin resistance and contribute to the development of type 2 diabetes mellitus by reducing the expression of insulin receptors and increasing the levels of free fatty acids. Furthermore, SCH and T2DM share several common risk factors, including obesity, physical inactivity, and family history. The presence of SCH in T2DM patients may also be associated with poorer glycemic control, increased cardiovascular risk, and reduced quality of life [5-10].

The studies show an increasing incidence of SCH over recent decades. Large population screenings report an overall prevalence ranging from 4% to 10%, though this varies by age, sex, and race. Further research is needed to determine the prevalence of SCH in diabetic patients with varying levels of glycemic control, as current knowledge is limited. Conduct a comparative analysis of the prevalence of subclinical hypothyroidism (SCH) in patients with type 2 diabetes mellitus (T2DM) and non-diabetic control groups. Assess the correlation between SCH and glycemic control among patients with type 2 diabetes mellitus.

MATERIALS AND METHODS

Place of study- This observational study was conducted at the Outpatient Department (OPD) of Amala Institute of Medical Sciences, Thrissur, India, over one year from July 2023 to August 2024.

Included criteria- The study population comprised 250 (52.63%) diabetic and 225 (47.36%) non-diabetic participants. Study variables included age, BMI, blood pressure, HbA1c, BUN, lipid profile, and thyroid profile. SCH was defined as a thyroid-stimulating hormone (TSH) level exceeding 4.0 mIU/L with a normal free thyroxine (T4) level (0.7–1.4 ng/dL). The diabetic group was further categorized by HbA1c level: Group 1 (well-controlled, <7%), Group 2 (7–8.9%), and Group 3 (poorly controlled >9%).

Exclusion criteria- Clinical hyperthyroidism or hypothyroidism (FT4 > 1.9,<0.9 ng/dL), severe anemia, chronic kidney disease, abnormal liver function tests, individuals with chronic infections, acute illness, and pregnant women.

Research design- A total of 475 outpatients, comprising 250 diabetic patients (52.63%) and 225 non-diabetic controls (47.36%), were enrolled using convenience sampling. The study included participants who were assessed for variables such as age, body mass index (BMI), blood pressure, HbA1c, blood urea nitrogen (BUN), lipid profile, and thyroid profile. Subclinical hypothyroidism was defined by a TSH level exceeding 4.0 mIU/L, with a normal free T4 level (0.7–1.4 ng/dL).

The diabetic group was further subdivided into three categories based on their HbA1c levels: Group 1 (well-controlled, HbA1c<7%), Group 2 (moderately controlled, HbA1c 7–8.9%), and Group 3 (poorly controlled, HbA1c>9%). Exclusion criteria included clinical hyperthyroidism or hypothyroidism (FT4 levels >1.9 or <0.9 ng/dL), severe anemia, chronic kidney disease, abnormal liver function tests, chronic infections, acute illnesses, and pregnant women.

Statistical Analysis- The extent of the study involved 475 participants, including 250 individuals with Type 2 diabetes mellitus (T2DM) and 225 non-diabetic controls. The study focused on assessing the prevalence of subclinical hypothyroidism and its association with various factors such as glycemic control, age, BMI, and thyroid function. Statistical analysis, using Chi-square tests, was conducted to determine the significance of the relationship between T2DM and SCH.

RESULTS

In the diabetic group, the prevalence of subclinical hypothyroidism (70) was 57% among females(n=40) and 42% among males(30) (Fig. 1).

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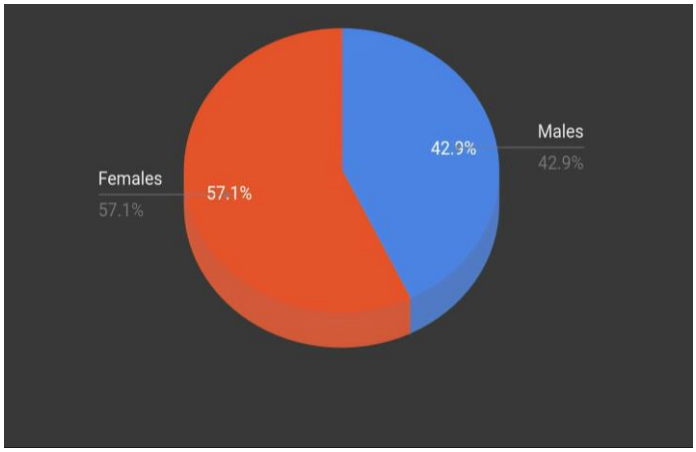

Fig. 1: Prevalence of Subclinical Hypothyroidism in Female and Male Participants within the Diabetic Group

In non-diabetic groups, the prevalence of SCH(60) is 56.7% in females (n=34) and 43.33% in males (n=26) (Fig. 2).

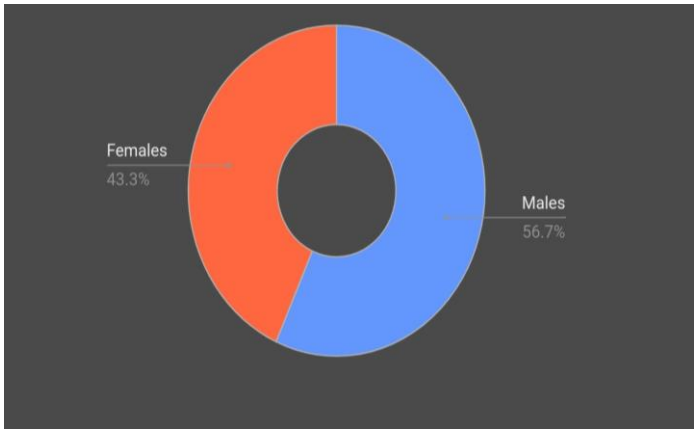

Fig. 2: Prevalence of Subclinical Hypothyroidism in Female and Male Participants in the non-diabetic Group

In the diabetic cohort, 28% (70 of 250) of participants exhibited SCH, while in the non-diabetic control group, 26.66% (60 of 225) exhibited SCH. Statistical analysis revealed no significant difference in SCH prevalence between the two groups (p=0.442) (Fig. 3).

Diabetic patients were categorized into three subgroups based on HbA1c levels. The poorly controlled glycemic group (HbA1c≥9%) exhibited a higher prevalence of subclinical hypothyroidism (50.0%, n=35) compared to the well-controlled diabetic group (HbA1c<7%, 21.42%, n=15) and the group with HbA1c 7-8.9% (28.57%, n=20) (Fig. 4).

The prevalence of subclinical hypothyroidism increased with higher HbA1c levels; the odds ratio for HbA1c≥9% was 2.40 compared to HbA1c<7%, which had an odds ratio of 1.18.

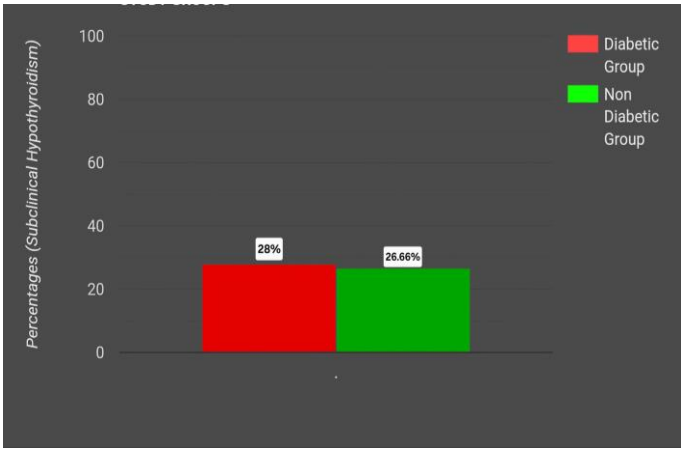

Fig. 3: Prevalence of Sub-Clinical Hypothyroid among study groups

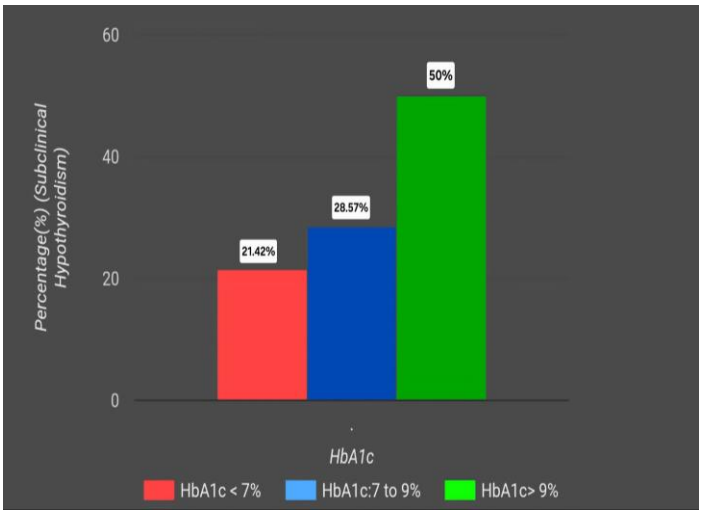

Fig. 4: Prevalence of subclinical hypothyroidism among diabetic study groups

DISCUSSION

This study found no difference in SCH prevalence between patients with T2DM and healthy controls. Existing literature indicates a higher frequency of thyroid dysfunction in diabetic populations; however, many studies included both type 1 and type 2 diabetics and lacked control groups. Our findings align with Ishay *et al.* [6] report showing a significant association between SCH and glycemic control in T2DM. Furthermore, Maratou *et al.* [7] demonstrated comparable insulin resistance in SCH patients and those with hypothyroidism. El-Eshmawy *et al.* [8] also reported positive correlations between TSH levels and insulin resistance. The interplay between SCH and T2DM appears complex and warrants further investigation to elucidate the underlying mechanisms.

Optimal control of glucose is a daunting task without a clear understanding of the precise dynamics of poor glycaemic control in people with type 2 diabetes (T2DM).

Epidemiological studies in different populations Mahmood *et al.* [11]; Ahmad *et al.* [12]; Khattab *et al.* [13]; Al Balushi *et al.* [14]; Shaikh *et al.* [15]; Sanal *et al.* [16] have identified several factors that are related to poor glycaemic control. However, most of these studies have been conducted on patients in Western countries.

Our study has a strength for large sample size, but it should be noted that this study has some limitations. Firstly, a blood test for thyroid function was done for a single time. Secondly, this was a cross-sectional study; therefore, it could not determine the causal relationship between SCH and glycemic control. Well-designed prospective studies are warranted to confirm the association between SCH and glycemic control in patients with T2DM [17]. Furthermore, future studies will be required to determine whether thyroid hormone replacement therapy can improve glycemic control in diabetic patients with SCH. Lastly, medications being taken by the patients were not checked, which may affect thyroid function- multivitamins and/or health supplements.

Patient medication regimens, including multivitamins and supplements, were not reviewed, potentially influencing thyroid function assessments. This observational study design precludes establishing causality between SCH and glycemic control; thus, well-designed prospective studies are needed to confirm this association in type 2 diabetes mellitus patients [18]. Patient medication regimens, including multivitamins and supplements, were not reviewed, potentially influencing thyroid function assessments.

CONCLUSIONS

The prevalence of SCH was comparable in diabetic and non-diabetic cohorts. Our study demonstrated a more than twofold increase in SCH prevalence among patients with poorly controlled diabetes (HbA1c≥9%) compared to those with well-controlled diabetes (HbA1c<7%). These findings suggest that SCH may pose a significant risk for patients with poor glycemic control and that its treatment could potentially improve insulin sensitivity and facilitate effective glycemic control. Further prospective studies involving larger patient populations are recommended to more thoroughly evaluate the relationship between HbA1c and SCH.

CONTRIBUTION OF AUTHORS

Research concept- Mohammed Ramees, Daniel Tony Kannampuzha

Research design- Kiran Chandramohan, Jain Christy, Diana David

Supervision- Daniel Tony Kannampuzha

Materials- Ajay Mohan, Kiran Chandramohan, Jain Christy

Data collection- Daniel Tony Kannampuzha

Data analysis and Interpretation- Kiran Chandramohan, Diana David

Literature search- Ajay Mohan, Kiran Chandramohan, Jain Christy

Writing article- Mohammed Ramees, Daniel Tony Kannampuzha

Critical review- Jain Christy, Diana David

Article editing- Mohammed Ramees, Daniel Tony Kannampuzha

Final approval- Kiran Chandramohan, Diana David

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