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Original Research Paper

General Medicine

LIPID PROFILE ANALYSIS IN A STUDY FOR PREVALENCE OF SUBCLINICAL HYPOTHYROIDISM IN TYPE 2 DIABETES MELLITUS

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ABSTRACT

Background and Objectives- Diabetes and hypothyroidism are common endocrine diseases that impact health and mortality. Glycaemic status affects thyroid hormone levels immensely. There is a paucity of studies from India that have investigated the prevalence of subclinical hypothyroidism in patients with type 2 diabetes mellitus. Subclinical hypothyroidism and dyslipidemia are two factors that may act synergistically in the elevation of cardiovascular risk in patients with type 2 diabetes mellitus. It is therefore important to analyze whether subclinical hypothyroidism is associated with changes in lipid profile. **Objective:** To determine the prevalence of subclinical hypothyroidism in type two diabetes mellitus patients. We also aim to examine the relationship between lipid profile and subclinical hypothyroidism in T2DM. **Methods-** Our study was conducted in the Department of Medicine of North Delhi Medical College & Hindu Rao Hospital, Delhi. A total of 150 with type 2 diabetes were screened for thyroid dysfunction, a group of 126 patients with normal thyroid function, a group of 13 patients with subclinical hypothyroidism, and a group of 11 patients with overt hypothyroidism were subjected to lipid profile. No patient had known dyslipidemia or was taking any lipid lowering medications. **Results –** 126 (84%) patients out of 150 were classified as euthyroid. 11(7.3%) and 13 (8.7%) patients had overt hypothyroidism and subclinical hypothyroidism respectively. There was a significant positive correlation between subclinical hypothyroidism and serum total cholesterol, LDL cholesterol, and triglycerides levels. There was a significant negative correlation with serum HDL cholesterol levels. **Conclusion-** The incidence of subclinical hypothyroidism in patients with type 2 diabetes mellitus was significantly increased with increasing age and in female patients. We conclude that subclinical hypothyroidism causes worsening dyslipidemia in type 2 diabetics.

KEYWORDS : Type 2 Diabetes Mellitus, Subclinical Hypothyroidism, Lipid Profile

INTRODUCTION

Diabetes Mellitus and hypothyroidism are common chronic endocrine diseases[1]. Both diseases immensely impact cardiovascular health and mortality[2]. Diabetes Mellitus is a heterogeneous group of diseases in which there is an underlying defect in glucose metabolism leading to chronic hyperglycemia. Diabetes Mellitus is diagnosed when fasting plasma glucose is >126 mg/dL or 2-h plasma glucose is >200 mg/dL during oral glucose tolerance test or HbA1c is >6.5% or if in a patient with classic symptoms of hyperglycemia, random plasma glucose is >200 mg/dL[3]. Subclinical hypothyroidism (SCHT) is a pure laboratory diagnosis when there is elevation in TSH with normal circulating free thyroid hormone concentrations[4]. SCHT is classified into two categories based to serum TSH level: mildly increased TSH levels (4.0–10.0 mU/l) and more severely elevated serum TSH concentrations (>10.0 mU/l). The former, the milder form, accounts for 90% of SCHT cases in the population. In individuals with established type 2 diabetes mellitus, a change in glycaemic control could herald the onset of SCHT[5]. SCHT has been recognized as an insulin-resistant state. Studies have shown that this is due to impaired insulin-mediated glucose utilization in peripheral tissues[6]. Numerous studies suggest that SCHT is associated with high cholesterol. Patients with SCHT have a higher risk of metabolic syndrome, atherosclerosis, and adverse cardiovascular events[7]. A meta-analysis confirmed increased serum total cholesterol, LDL cholesterol, and triglyceride levels in patients with SCHT[8]. Perturbation of the lipid profile is thought to be because of an altered adipokine profile, leading to changes in low-density lipoprotein (LDL) receptor affinity and lifespan. Inadequate T3-mediated signaling leads to lower levels of protein responsible for LDL to HDL conversion[9].

Type 2 diabetes mellitus is also associated with dyslipidemia, which increases the risk of cardiovascular disorders[10]. A recent meta-analysis has shown a higher prevalence of subclinical hypothyroidism in patients with type 2 diabetes mellitus[11]. Undiagnosed thyroid dysfunction may affect metabolic control and enhance cardiovascular, and other chronic complications in diabetic patients. Therefore, it is important to recognize the interdependent relationship between thyroid dysfunction and diabetes[12]. Subclinical hypothyroidism and dyslipidemia are two factors that may act synergistically in elevation of cardiovascular risk in patients with type 2 diabetes mellitus.

Thus, knowing the prevalence of SCHT in patients with T2DM along with its association with lipid profile parameters is profoundly important to enhance the knowledge of the interrelation between diabetes, SCHT, and dyslipidemia. Through this study we aim to determine the prevalence of subclinical hypothyroidism in type two diabetes mellitus patients. We also aim to examine the relationship between lipid profile and subclinical hypothyroidism in T2DM patients.

MATERIALS AND METHODS

This observational descriptive study was conducted from January 2021 to May 2022 in the department of General Medicine of North Delhi Medical College & Hindu Rao Hospital, Delhi after ethical committee approval.

Patients attending the outpatient department and admitted patients in the general medicine department were included in the study. The study was approved by the ethics committee, and patients gave their informed consent before blood sampling. Variables recorded included demographic and anthropometric data, time since onset of diabetes, the antidiabetic treatment used, and other laboratory data.

Inclusion Criteria

Patients who are diagnosed with Type 2 Diabetes mellitus according to ADA criteria. Patients with age at onset of Type 2 Diabetes mellitus > 35 years.

Exclusion Criteria

1. Patients with history of a known thyroid disease or previous history of thyroid surgery.

2. Patients with biochemical or clinical features of hyperthyroidism.
3. Patients with hyperglycemic emergencies or a critical illness like malignancy, heart failure.
4. Patients taking drugs that alter thyroid hormone levels.
5. Pregnant females and females on oral contraceptives.
6. Patients with a personal or family history of other autoimmune disorders.
10. Patients on treatment with lipid lowering drugs or prior history of taking lipid lowering drugs.
11. Patients with diagnosed Primary dyslipidemias.

Definitions

Each patient was classified based on the laboratory reference range:

- Euthyroidism - TSH value between 0.270–4.20 mIU/L a free T4 value between 0.93-1.7 ng/dl.
- Overt hypothyroidism - TSH value >4.2 mIU/L and a T4 <0.93 ng/dl.
- Subclinical hypothyroidism - TSH value >4.2 mIU/L and a normal T4 (0.93–1.7 ng/dl).

Methodology

All participants were subjected to basic clinical examination along with lipid profile, glycemic profile, and thyroid profile. Autoimmunity was assessed by measuring thyroid peroxidase antibodies. Cholesterol was estimated by the cholesterol oxidase method, HDL by the direct immune-inhibition method, and LDL by direct measurement. Based on lipid profile parameters, patients were classified as:

- Total Cholesterol- < 200 mg/dl and ≥ 200 mg/dl
- LDL < 100 mg/dl and ≥ 100 mg/dl
- HDL < 40 mg/dl and ≥ 40 mg/dl
- Triglycerides < 100 mg/dl, 100 – 149 mg/dl and, ≥ 150 mg/dl

Statistical Analysis

The data generated from the study were entered into MS Excel and analyzed using SPSS statistical package version 28.0. Continuous variables were expressed as mean and SD values and categorical variables were expressed as percentages. ANOVA test was applied for continuous variables, and the chi-square test was used for categorical variables at a 95% confidence interval. The level of significance in all tests was p value < 0.05.

RESULTS

Table 1 –prevalence Of Scht In T2dm:

Thyroid Status	Frequency	Percent
Euthyroid	126	84.0
Overt Hypothyroidism	11	7.3
Subclinical Hypothyroidism	13	8.7
Total	150	100.0

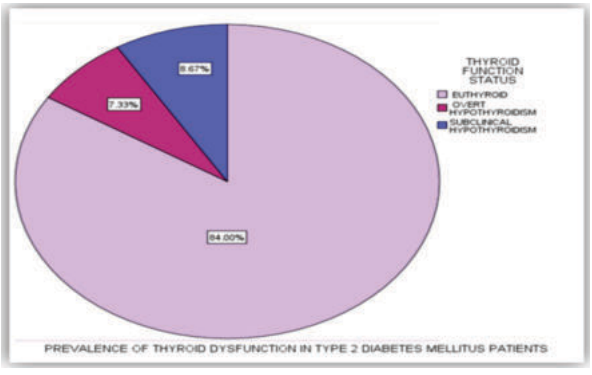

Chart 1 - Prevalence Of Scht In T2 Dm :

Table 2 – Thyroid Function And Lipid Profile

A. Table 2.1 – Total Cholesterol And Thyroid Status

		Thyroid Status			Total
		Euthyroid	Overt Hypothyroidism	Subclinical Hypothyroidism	
Total Cholesterol	<200 mg/dl	104	1	2	107
	≥ 200 mg/dl	22	10	11	43
Total	126		11	13	150

Table 2.2 – Mean Total Cholesterol

Serum Total Cholesterol (mg/100 ml)				
Thyroid Status	Mean	N	Std. Deviation	% of Total N
Euthyroid	181.87	126	45.126	84.0%
Overt Hypothyroidism	233.36	11	44.608	7.3%
Subclinical Hypothyroidism	248.31	13	44.303	8.7%
Total	191.40	150	49.894	100.0%

X^2 (2, N = 150) = 48.478, p = <0.001.

A chi-square test of independence was performed to examine the relationship between serum total cholesterol and the prevalence of thyroid dysfunction in the form of SCHT and overt hypothyroidism. The relation is statistically significant (p = <0.001).

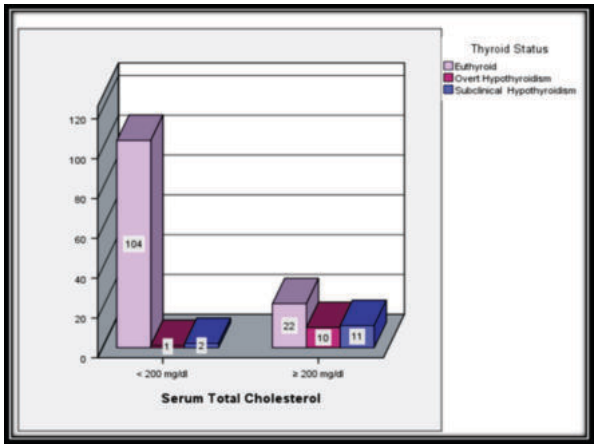

Chart 2 – Total Cholesterol And Thyroid Function

B. Table 3.1- Serum Hdl And Thyroid Function

		Thyroid Status			Total
		Euthyroid	Overt Hypothyroidism	Subclinical Hypothyroidism	
SERUM HDL	< 50 mg/dl	40	10	10	60
	≥ 50 mg/dl	86	1	3	90
Total	126		11	13	150

Table 3.2 – Mean Serum Hdl

SERUM HDL (mg/100 ml)				
Thyroid Status	Mean	N	Std. Deviation	% of Total N
Euthyroid	43.22	126	6.391	84.0%
Overt Hypothyroidism	35.45	11	3.532	7.3%
Subclinical Hypothyroidism	36.23	13	4.304	8.7%
Total	42.05	150	6.628	100.0%

X^2 (2, N = 150) = 22.840, p = <0.001.

A chi-square test of independence was performed to examine the relationship between serum HDL and the prevalence of thyroid dysfunction in the form of SCHT and overt hypothyroidism. The relation is statistically significant (<0.001).

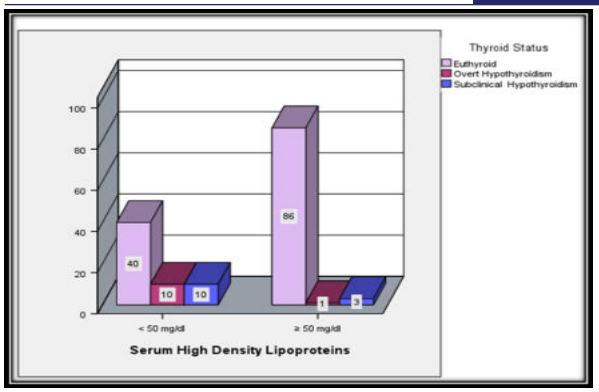

Chart 3 – Serum Hdl And Thyroid Function

C. Table 4.1 – Serum Triglycerides And Thyroid Function

		Thyroid Status			Total
		Euthyroid	Overt Hypothyroidism	Subclinical Hypothyroidism	
SERUM TRIGLYCERIDES	< 100 mg/dl	19	0	0	19
	100 – 149 mg/dl	84	1	0	85
	≥ 150 mg/dl	23	10	13	46
Total		126	11	13	150

Table 4.2 – Mean Serum Triglyceride

SERUM TRIGLYCERIDES (mg/dl)				
Thyroid Status	Mean	N	Std. Deviation	% of Total N
Euthyroid	130.14	126	26.750	84.0%
Overt Hypothyroidism	180.36	11	15.015	7.3%
Subclinical Hypothyroidism	180.00	13	16.946	8.7%
Total	138.15	150	31.259	100.0%

X^2 (4, N = 150) = 57.329, p = <0.001.

A chi-square test of independence was performed to examine the relationship between serum TGs and the prevalence of thyroid dysfunction in the form of SCHT and overt hypothyroidism. The relation is statistically significant (<0.001).

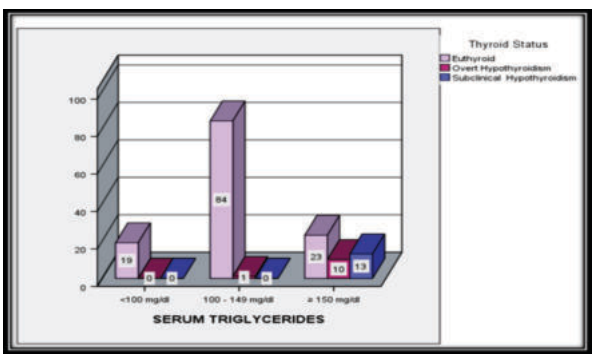

Chart 4 – Serum Triglycerides And Thyroid Function

D. Table 5.1 - Serum And Ldl And Thyroid Function

		Thyroid Status			Total
		Euthyroid	Overt Hypothyroidism	Subclinical Hypothyroidism	
SERUM LDL	<100 mg/dl	29	0	0	29
	≥ 100 mg/dl	97	11	13	121
Total		126	11	13	150

Table 5.2 – Mean Serum Ldl

SERUM LDL (mg/dl)				
Thyroid Status	Mean	N	Std. Deviation	% of Total N
Euthyroid	117.60	126	22.343	84.0%
Overt Hypothyroidism	162.64	11	21.355	7.3%
Subclinical Hypothyroidism	162.92	13	17.713	8.7%
Total	124.83	150	27.404	100.0%

X^2 (2, N = 150) = 6.848, p = <0.033.

A chi-square test of independence was performed to examine the relationship between serum LDL and the prevalence of thyroid dysfunction in the form of SCHT and overt hypothyroidism. The relation is statistically significant (<0.033).

DISCUSSION

Out of 150 individuals included in our study 126 (84%) patients had normal thyroid function. Thirteen (8.7%) individuals had the diagnosis of SCHT. Eleven individuals (7.3%) had overt hypothyroidism. Other studies have also reported a similar prevalence of SCHT in patients with T2DM[13,14].

There was a significant increase incidence of thyroid dysfunction, both overt and subclinical with age[15].

In our study, 71 individuals out of 150 were males, and 79 were females. Among patients with SCHT, only 3 subjects were males, accounting for 23.07% of participants with SCHT. The prevalence of SCHT in patients with type 2 DM is significantly more in females.

Dyslipidemia is defined as an abnormal lipid profile characterized by high total cholesterol (TC), high low-density lipoprotein cholesterol (HDL), high triglycerides (TG), and low high-density lipoprotein cholesterol (LDL)[16].

A study from Ukraine found that total cholesterol values in patients with T2DM combined with SCHT were significantly higher compared to those with T2DM alone. Most patients with a combined course of T2DM and SCHT had low HDL levels and high TG levels[17]. The present study co-related best with a case-control study from Chennai[18]. Our study showed a significantly increased total cholesterol, triglycerides, LDL, and lower HDL cholesterol in patients with SCHT as compared to euthyroid patients with type 2 DM.

In an observational study from China, TC and LDL values in T2DM patients with SCHT were significantly higher than those in diabetics without SCHT. While HDL and TG levels were not different between the two groups[19].

In another study, Patients with SCHT had lipid profile parameters that were not significantly different from those found in euthyroid patients[20].

Wang et al[21], also reported a greater prevalence of elevated total and LDL cholesterol levels, and decreased HDL cholesterol levels, in diabetic women with subclinical hypothyroidism as compared to euthyroid diabetic women.

CONCLUSION -

In the current study, SCHT was positively associated with lipid dysregulation in T2DM patients as there was a positive significant relationship between SCHT and TG, LDL-C and TC in addition to a negative significant correlation between SCHT and HDL-C among T2DM patients.

Limitations

1. Given the overlap of type 1 and type 2 diabetesmellitus, it

is difficult to clinically classify patients into either type in the absence of islet autoantibody testing.

2. Insulin resistance of diabetic patients could not be estimated in our study. Thus, the effects of insulin sensitivity on the relationship between thyroid function and serum lipids cannot be analysed.

CONCLUSION

1. This study demonstrated that SCHT is a common thyroid dysfunction in T2DM patients. In addition, gender and age were independently correlated with SCHT.
2. SCHT was significantly associated with lipid profile derangements in T2DM patients.

Recommendation -

The increased frequency of thyroid dysfunction in type 2 diabetes calls for a systematic approach to thyroid testing.

These results also support the possible need for early replacement therapy with levothyroxine in diabetic patients with subclinical hypothyroidism for the prevention of diabetic dyslipidemia. This conclusion can only be reliably drawn from adequate prospective clinical studies on a sufficiently large sample size.

Conflict of interest:

Nothing to declare

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