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Synergistic effects of Type 2 Diabetes and hypothyroidism on Dyslipidemia

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ABSTRACT

Two prevalent endocrine conditions that have a major impact on lipid metabolism and frequently result in dyslipidaemia are type 2 diabetes mellitus (T2DM) and hypothyroidism. The purpose of this study was to look at how T2DM and hypothyroidism affect lipid profiles in concert. Group A included only of T2DM, Group B consisted solely of hypothyroidism, Group C comprised of both T2DM and hypothyroidism, and Group D consisted of healthy individuals. Triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and total cholesterol (TC) were among the lipid parameters that were examined. The most severe dyslipidaemia was found in Group C, which had considerably higher levels of TC (245±4.78 mg/dl), LDL-C (156±2.39 mg/dl),

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and TG (234±5.37) than Groups A and B. Additionally, exacerbated lipid imbalances were linked to poor glycaemic management (higher HbA1c) in T2DM people (Groups A and C), whereas more severe lipid abnormalities were linked to higher thyroid-stimulating hormone (TSH) levels in hypothyroid participants (Groups B and C). These results show how the metabolic and endocrine systems are interdependent, and problems in one can worsen problems in the other. The combined effects of hypothyroidism and type 2 diabetes on dyslipidaemia highlight the significance of thorough screening and treatment of both disorders to lower the risk of cardiovascular disease and other associated problems. To clarify the underlying mechanisms and create focused therapies for patients with coexisting hypothyroidism and type 2 diabetes, more study is required.

Key word - Dyslipidemia, hypothyroidism, type 2 diabetes, cardiovascular disease.

Introduction

Increased low-density lipoprotein cholesterol (LDL), decreased high-density lipoprotein (HDL) cholesterol, and raised triglycerides are the hallmarks of dyslipidaemia. There is a reciprocal association between dyslipidaemia and diabetes. It might also contribute to or result from diabetes. Low-density lipoprotein (LDL) is increased, high-density lipoprotein (HDL) cholesterol is reduced, and triglycerides are elevated in diabetic dyslipidaemia. The risk of cardiovascular disease (CVD) is considerably increased by certain lipid abnormalities (1). One of the main risk factors for CVD is atherosclerosis, which is accelerated by elevated plasma lipids. The majority of cases of dyslipidaemia are really hyperlipidaemia, which can be categorised as primary (caused by genetic abnormalities) or secondary (resulting from underlying illnesses such as hypothyroidism, diabetes, or chronic alcoholism). (2)

Another prevalent metabolic condition, especially in older women, is hypothyroidism.(3) By directly or indirectly altering other regulatory hormones like insulin or catecholamines, thyroid hormones control important metabolic pathways. Changes in these hormones can result in thyroid illness.(4) Serum lipid profiles are clearly impacted by hypothyroidism; total cholesterol,

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especially Apo lipoprotein B (Apo-B) containing cholesterol such as TG and LDL-C, is usually elevated (5), although it is unknown how Apo A containing HDL-C is affected. Healthy people have a greater Apo A to Apo B ratio. (6,7,8) Compared to hypothyroid patients with TSH 4.0–10.0μIU/L, those with TSH >10 μIU/L have greater levels of lipoprotein cholesterol that contains Apo B (9,10,11). Apo B-containing lipoprotein cholesterol levels and blood serum TSH levels have a positive correlation (12,13), suggesting that elevated TSH raises the risk of dyslipidaemia, which could contribute to CVD. (14)

Cardiovascular illnesses are caused by a combination of hormone-induced haemodynamic alterations and metabolic abnormalities in hypothyroidism-induced dyslipidaemia. The two most common endocrine illnesses, hypothyroidism and type 2 diabetes mellitus, seem to be related. (15) The synthesis, utilisation, and absorption of glucose are all significantly influenced by thyroid hormones. Dysregulation of thyroid hormones can reveal hidden diabetes. The synthesis and release of triiodothyronine (T3) and thyroxin (T4), as well as the hypothalamic regulation of TSH, are all impacted by type 2 diabetes. A notable consequence of type 2 diabetes is a decrease in the amount of T3 in the blood. (16) This reciprocal association between T2DM and thyroid function highlights the intricate relationship between the two conditions and points up areas that need more study.

Material and methods -

Research Design:

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A cross-sectional investigation involving 280 participants from October 2023 to October 2024, was conducted at the Biochemistry department of Central Laboratory Katihar Medical College and Hospital, Bihar, in collaboration with the Medicine Department. The Study commenced after obtaining institutional ethical clearance.

Participant Selection:

Inclusion Criteria:

Participants diagnosed with Type 2 Diabetes Mellitus (T2DM) and hypothyroidism, aged 30-60 years. Willing participants who provided consent.

The study comprised four groups of 70 patients each:
Group A: T2DM only
Group B: Hypothyroidism only
Group C: Both T2DM and hypothyroidism
Group D: Healthy Individuals

Exclusion Criteria:

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People with comorbidities that affect lipid profiles, such as kidney or liver diseases, diabetic ketoacidosis, transplant rejection, or disorders of the central nervous system, as well as those with other endocrine or metabolic abnormalities, benign or malignant disorders, are not included. Pregnant women and individuals who have hypothyroidism as a result of thyroid surgery or radiation therapy are also covered by this. Additionally excluded are people on drugs that alter thyroid function testing, such as biotin and oestrogen.

METHODS:

The study was carried out following the acquisition of the required authorisations and institutional ethical clearance. Prior to enrolment, participants gave their informed consent. Clinical and biochemical thyroid function tests were performed on diabetes patients selected at random. Using BIOSYSTEM's patented kits and a fully automated "BA200 LED TECHNOLOGY" biochemistry analyser, biochemical tests were conducted.
With the exception of postprandial plasma glucose, all parameter estimations were performed using fasting data. (17) Trinder's GOD/POD approach was used to quantitatively measure fasting and postprandial plasma glucose. (18)

The "BECKMAN COULTER Access 2" competitive chemiluminescent immunoassay was used to quantify serum free T3 (FT3), T4 (FT4), and TSH (34). The CHOD-PAP approach, as outlined by Allian (19), was used to quantitatively measure total cholesterol (TC). Bucolo and David's GPO-ESPAS approach was used to quantitatively measure triacylglycerol (20). The PEG-PAP approach was used to quantitatively measure high-density lipoproteins. By deducting the cholesterol linked to HDL and very low-density cholesterol (VLDL), LDL levels were calculated using the Friedewald formula. MISPA-i2 was used to assess glycated haemoglobin.

Participants details: A total of 280 participants were included in the study. Demographic and clinical profiles of study participants (ages 30-60)

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Characteristic	Group A (T2DM)	Group B (Hypothyroidism)	Group c(T2DM+Hypothyroidism)	Group D(Healthy individual)
Age(Years)mean (SD)	50±9	51±8	52±7	48±9
Gender(F/M%)	55%/45%	40%/60%	48%/52%	53%/47%
BMI(kg/m2)mean (SD)	29.5±4.6	26.4±5.3	30.0±4.5	26.5±3.8
Duration of T2DM(years)	4.5	N/A	6.5±5.1	N/A
Duration of hypothyroidism(years)	N/A	6.0±3.0	8.0±3.0	N/A
TSH(m IU/L)mean(SD)	N/A	6.8±2.4	5.3±1.4	N/A
HbA1c(%)mean(SD)	8.9±2.3	N/A	9.5±1.4	N/A

Results and Data analysis:

This study's goal was to examine the relationship between type 2 diabetes, hypothyroidism, and their combined impact on dyslipidaemia in four different patient groups. SPSS Version 26.0 was used for statistical analysis. Means, standard deviations, and standard error of mean were computed as descriptive statistics. Group differences were examined using a one-way ANOVA and the Tukey's post hoc

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test. Pearson correlation coefficients were used to examine the correlations between lipid parameters, TSH, and HbA1c, and significance was determined at $p < 0.05$. Four groups were examined using the lipid panel, which included measurements of total cholesterol (TC), low density lipoprotein (LDL), high density lipoprotein (HDL-C), and triglycerides (TG). TC > 200 mg/dl, LDL > 100 mg/dl, HDL < 40 mg/dl for males and < 50 mg/dl for females, and TG >150 mg/dl were the criteria for dyslipidaemia.

The mean values for each group are shown in the Table .1

Table 1. Comparison of lipid levels among groups (Mean value with Standard deviation & SEM)

LIPID PARAMETER	GROUP A (T2DM)	GROUP B (Hypothyroidism)	GROUP C (T2DM + Hypothyroidism)	GROUP D (Healthy)	P-value
Total Cholesterol (mg/dl)	225 ± 4.18 *35	210± 3.11 *26	245± 4.78 *40	180±4.18 *35	<0.001
LDL-C (mg/dl)	134±2.87 *24	130±2.74 *23	156± 2.39 *20	95± 2.15 *18	<0.001
HDL-C (mg/dl)	35±1.19 *10	36± 0.84 *7	31± 0.96 *8	53± 1.19 *10	<0.001
Triglycerides (mg/dl)	185± 4.78 *40	162 ±3.79 *35	234±5.37 *45	125±2.98 *25	< 0.001

*****standard deviation, ± standard error of mean

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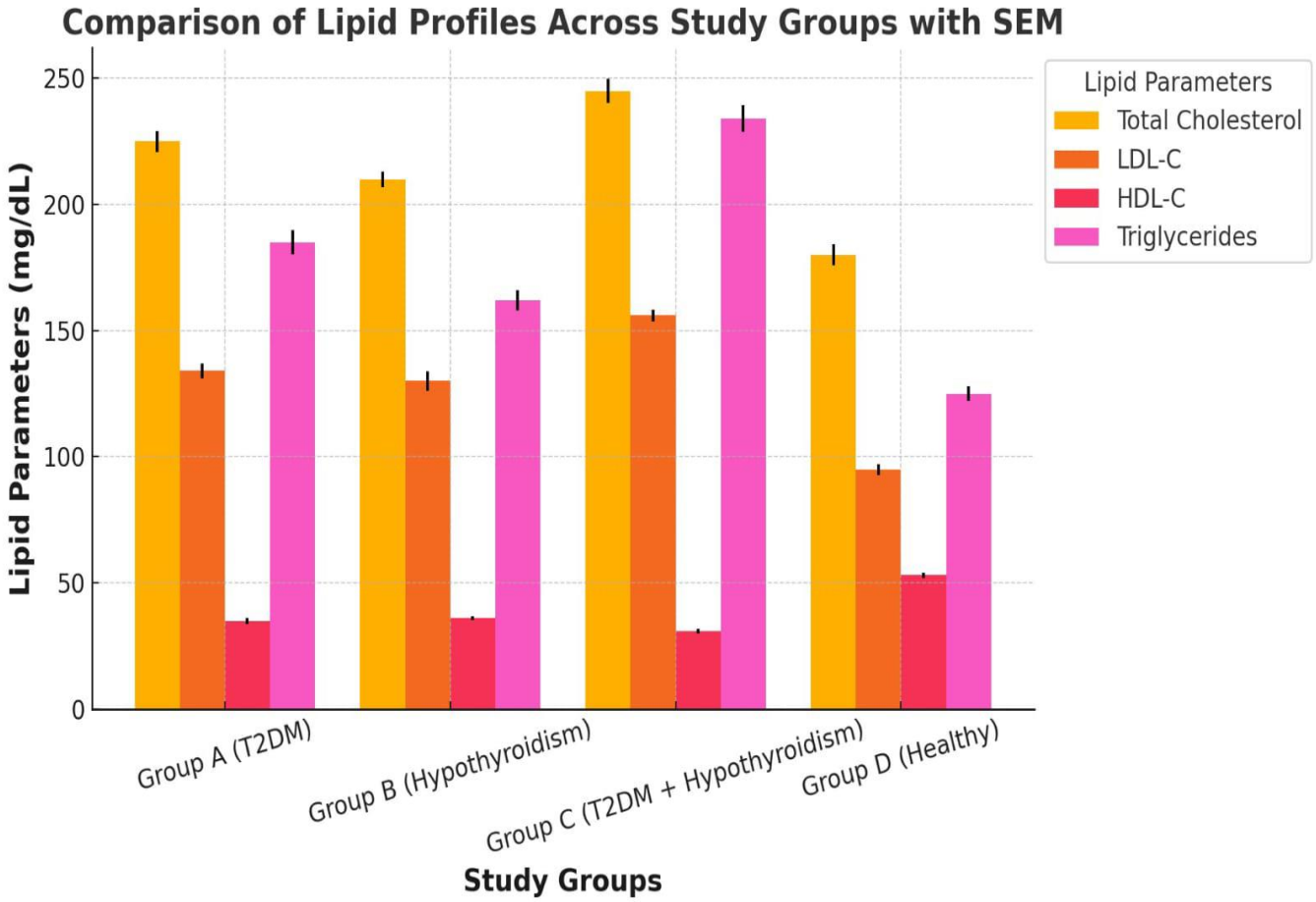
Total cholesterol, LDL-C, and triglyceride levels were considerably higher in study groups A (T2DM), B (Hypothyroidism), and C (T2DM+Hypothyroidism) than in healthy individuals (P <0.001). The sick groups showed a considerable drop in HDL-C levels.



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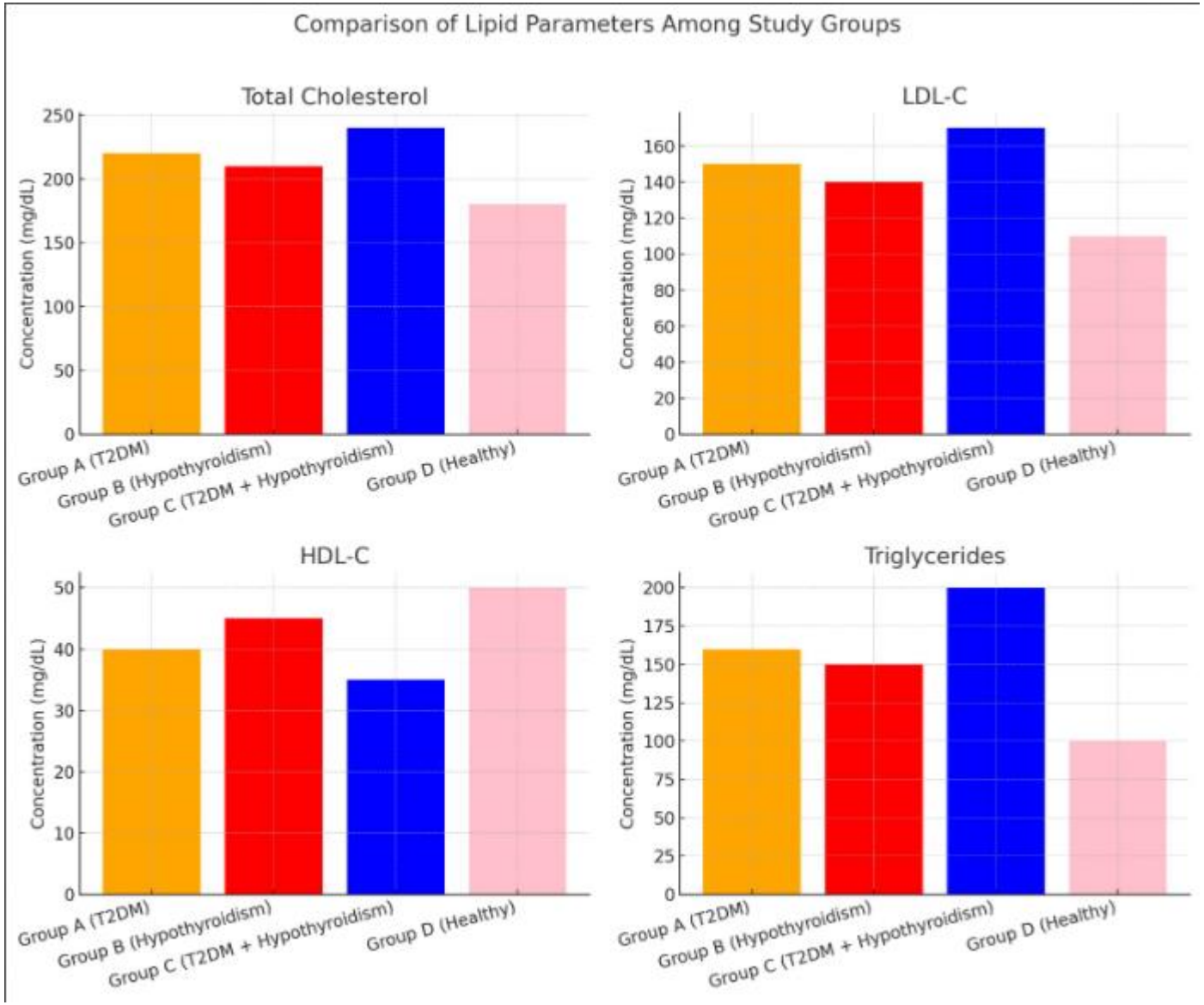

- The comparison of lipid profiles among the four study groups revealed significant variations.

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- Total cholesterol and LDL-C levels were highest in Group C (T2DM + Hypothyroidism), lowest in Group D (Healthy).
- HDL-C was highest in Group D and lowest in Group C, further emphasizing the unfavorable lipid profile in Group C.
- Triglyceride levels were also highest in Group C and lowest in Group D.
- Overall Group D demonstrated the healthiest lipid profile, highlighting the adverse effects of T2DM and hypothyroidism on lipid metabolism.

Group C has the most severe dyslipidaemia when compared to healthy controls, while Groups A, B, and C all have raised cholesterol, LDL-C, and triglycerides, according to the graph that compares lipid parameters across groups. Group C (T2DM+ Hypothyroidism) had the most severe dyslipidaemia, with significantly higher TC, LDL-C, and TG levels than the other groups, according to an analysis of the lipid profiles of the four groups.

The four groups' lipid profiles varied significantly, according to the study. The greatest total cholesterol levels were found in those with T2DM+hypothyroidism (245±4.78 mg/dl), followed by those with T2DM (225±4.18 mg/dl) and hypothyroidism (210±3.11 mg/dl). The lowest cholesterol values (180±4.18 mg/dl) were seen in healthy people. Accordingly, group D had the lowest levels of LDL cholesterol (95±2.15 mg/dl), whereas group C had the greatest levels (156±2.39 mg/dl), with minor increases in groups A (134±2.87 mg/dl) and B (130±2.74 mg/dl). In comparison to groups A (35±1.19 mg/dl) and B (36±0.84 mg/dl), group C had the lowest levels of HDL-C, which is known for its protective function in heart health, at 31 mg/dl. Conversely, the greatest HDL values (53±1.19 mg/dl) were found in healthy individuals.

Additionally, triglyceride levels were higher in group C (234±5.37 mg/dl), group A (185±4.78 mg/dl), and group B (162±3.79 mg/dl), but the lowest amounts were seen in healthy individuals (125±2.98 mg/dl). According to these findings, those with type 2 diabetes,

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hypothyroidism, or both are more likely than healthy people to have a lipid profile that is out of balance, with higher levels of total cholesterol, LDL, and triglycerides and lower levels of HDL-C. A P value of less than 0.001 indicated that all differences were statistically significant. Relationships between HbA1c and lipid markers in type 2 diabetes (Groups A and C)

Table 1. presents the correlation data:

Lipid parameter	r- value	p-value
Total cholesterol	0.60	P < 0.001
LDL –C	0.68	P < 0.001
HDL-C	0.45	P < 0.01
Triglycerides	0.65	P <0.001

Strong positive relationships were seen between HbA1c and LDL cholesterol ($r=0.68$, $p<0.001$) and triglycerides ($r=0.65$, $p<0.001$) in Groups A (T2DM) and C (T2DM+ Hypothyroidism). These results imply that in T2DM patients, worsened dyslipidaemia is linked to inadequate glycaemic management.

Table 2. Correlation between TSH and dyslipidemia among hypothyroidism (group B+C)

Lipid parameter	r- value	p-value

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Total cholesterol	0.58	P<0.01
LDL-C	0.55	P <0.01
HDL-C	0.30	
Triglycerides	0.40	P <0.05

Groups B (Hypothyroidism) and C (T2DM+ Hypothyroidism) exhibited significant positive correlations between TSH levels and both LDL-C ($r=0.55$, $p < 0.01$) and TC ($r=0.58$, $p <0.01$). Elevated TSH levels were linked to deteriorating lipid profiles, particularly in cases of comorbid T2DM and hypothyroidism.

DISCUSSION

Interconnected Pathways: Dyslipidemia, T2DM, and Hypothyroidism

This study sheds light on the intricate interactions among hypothyroidism, dyslipidaemia, and Type 2 Diabetes Mellitus (T2DM). The results highlight how these metabolic diseases affect cardiovascular health and general well-being in subtle but important ways. The study shows how lipid profiles are impacted by T2DM and hypothyroidism, both separately and in combination. Insulin resistance, a

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common feature of type 2 diabetes, interferes with lipid metabolism, raising triglycerides (TG) and low-density lipoprotein cholesterol (LDL-C) while lowering high-density lipoprotein cholesterol (HDL-C). At the same time, hypothyroidism prevents the breakdown of lipoproteins, which raises LDL-C and total cholesterol (TC) levels. The most severe cases of dyslipidaemia were seen in subjects with both diseases (Group C), suggesting that these disorders work in concert. Hypothyroidism and type 2 diabetes mellitus (T2DM) have a major impact on dyslipidaemia and frequently make lipid abnormalities worse. Nearly 50% of patients with type 2 diabetes have dyslipidaemia, which is characterised by increased tiny dense LDL particles, decreased HDL-C, and raised triglycerides. Karale et al. (2019). (20)

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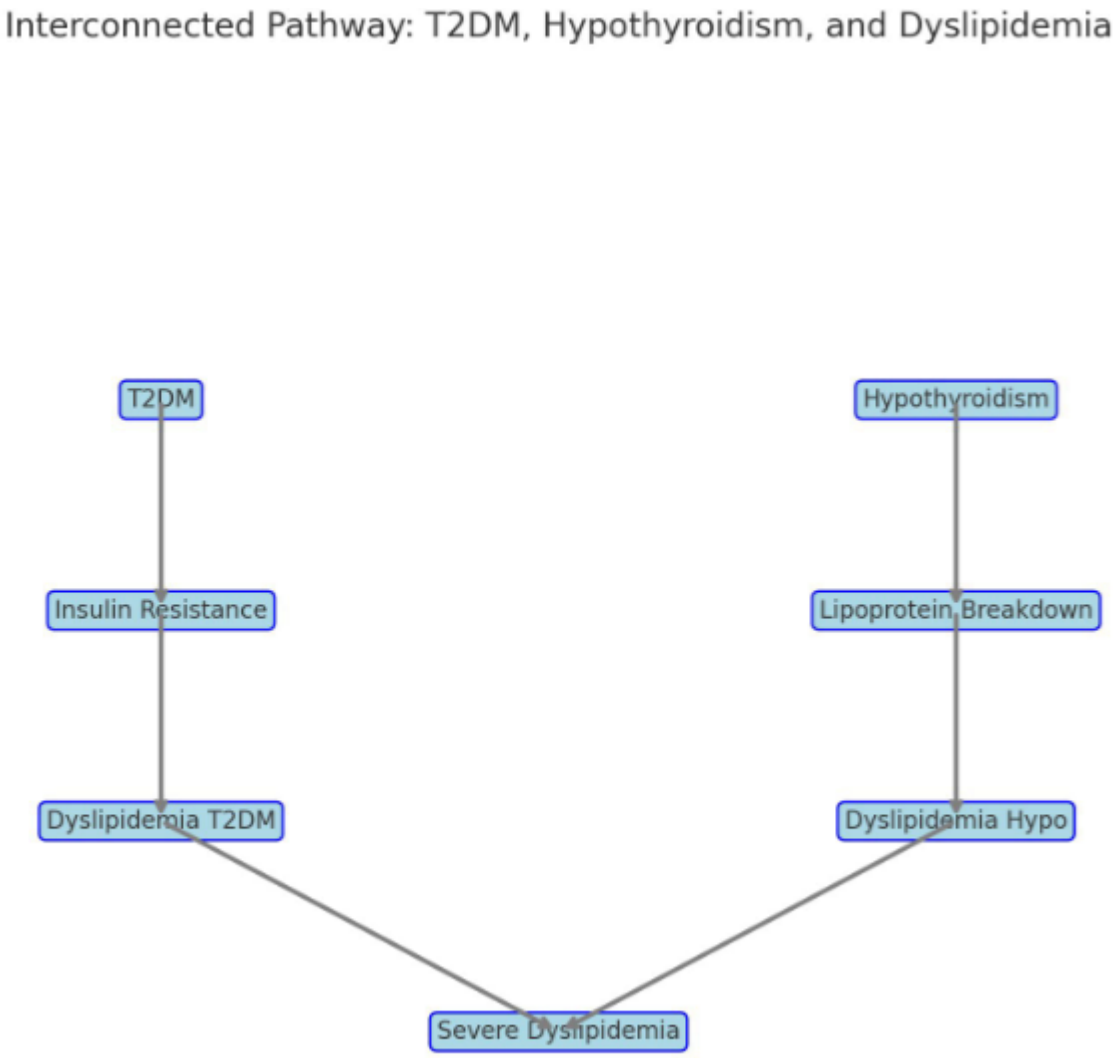

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Patients with diabetes often have hypothyroidism, especially subclinical hypothyroidism, which leads to lipid dysregulation. In 2011, Julieette A. and P. (21). Interestingly, lipid profiles seem to be more affected by the combination of T2DM and hypothyroidism than by either condition alone. According to a study, individuals with both hypothyroidism and type 2 diabetes had considerably greater levels of LDL-C (236.17±4.093 mg/dl) and total cholesterol (337.92±4.793 mg/dl) than those with either condition alone. In 2018, Ghosh et al. (15). According to a different study, patients with both illnesses had mean cholesterol levels of 488.3±144.43 mg/dl and triglyceride levels of 354.30±128.57 mg/dl, which were considerably higher than those with T2DM alone. Singh and colleagues, 2020.(22)This group's lipid imbalance illustrates how the metabolic and endocrine systems are interdependent, with problems in one system exacerbating problems in the other.

Impact of Glycemic and Thyroid Regulation

Poor blood sugar control exacerbates lipid abnormalities, according to the relationship between HbA1c and lipid markers in T2DM patients (Groups A and C). This supports past findings that chronic hyperglycemia worsens lipid profiles by causing inflammation and oxidative stress [23]. Similarly, TSH levels and lipid abnormalities were significantly correlated in hypothyroid subjects (Groups B and C). It is well established that elevated TSH impairs LDL receptor function, lowering cholesterol excretion and raising the risk of cardiovascular disease [24]. Dyslipidaemia is a risk factor that can lead to major health catastrophes like heart attacks or strokes, so it's more than just a test result. This emphasises how important it is to control thyroid and glycaemic function since they have a direct impact on cholesterol levels. Changes in lifestyle can significantly lower the risk of cardiovascular disease. For others, reaching lipid targets may need the use of pharmaceutical solutions such as fibrates or statins [25].

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Summary & Conclusion

The combination of T2DM and hypothyroidism appears to have a synergistic effect on dyslipidaemia, resulting in more severe lipid abnormalities, according to the study mentioned above. This study emphasises how patients with Type 2 Diabetes Mellitus (T2DM) and hypothyroidism, especially when these conditions coexist, are significantly impacted by aberrant lipid levels. Subjects with T2DM, hypothyroidism, or both had a considerably higher prevalence and severity of dyslipidaemia, with combined diseases showing the most severe cases. Poor glycaemic management (higher HbA1c) was linked to negative lipid profiles in type 2 diabetes, whereas raised TSH levels were linked to higher LDL and cholesterol levels in hypothyroidism. The study shows links between thyroid function, blood sugar control, and lipid abnormalities, illustrating the intricate interactions that occur within metabolic health. Lowering long-term heart disease risks and improving the general health of people with these disorders may be possible with an integrated, customised approach comprising several medical specialities.

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Conflict of interest

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There are no conflicts of interest

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