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The Correlation Between Type 2 Diabetes Mellitus and High-Density Lipoprotein (HDL) Cholesterol Levels

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Abstract

Objective: This study aimed to assess HDL cholesterol levels, identify specific lipid markers altered in individuals with type 2 diabetes mellitus (T2DM), and evaluate the correlation between HbA1C and HDL cholesterol.
Materials and Methods: Ninety-six volunteers aged 35-72 with confirmed T2DM underwent HDL cholesterol and HbA1c testing using the COBAS INTEGRA 400 PLUS device. Data on age, gender, diabetes status, and lipid profiles were collected in November 2023 to April 2024 from Layla Qasim Health Center located in Erbil, Iraq and then analyzed.
Results: The study found no statistically significant correlations between HbA1c levels and HDL cholesterol measures in the studied population. Dyslipidemia, characterized by reduced HDL cholesterol and hypertriglyceridemia, was prevalent among T2DM patients, particularly those with poorly controlled diabetes. The mean HbA1c level was higher in females, suggesting a potential association with dyslipidemia.
Conclusion: Dyslipidemia is a common complication in T2DM, with reduced HDL cholesterol and elevated triglycerides being key abnormalities. These findings underscore the importance of comprehensive lipid profiling and glycemic control in managing T2DM and mitigating associated cardiovascular risks. Early detection and treatment of dyslipidemia are crucial for preventing cardiovascular complications in T2DM patients. Further research is needed to elucidate underlying mechanisms and optimize therapeutic strategies.
Keywords: Type 2 diabetes mellitus (T2DM), dyslipidemia, HDL cholesterol, HbA1c, cardiovascular disease, lipid profile

Introduction

Type 2 diabetes mellitus (T2DM) is a complex condition, combination of resistance to the actions of insulin in liver and muscle together with impaired pancreatic β cell function leading to relative insulin deficiency (Galicia-Garcia et al., 2020). A report from the International Diabetes Federation Diabetes Atlas, 2020, has estimated approximately 463 million people with DM worldwide. Additionally, the number of patients with DM may reach 578 million by 2030 and 640 million by 2040 (Al Ghadeer et al., 2021).

Dyslipidemia, characterized by an abnormal lipid profile, is one of the major risk factors for cardiovascular disease in patients with diabetes, several factors are related to diabetic dyslipidemia including insulin effects on liver apoprotein production, regulation of lipoprotein lipase, actions of cholesteryl ester transfer protein (CETP), and peripheral actions of insulin on adipose and muscle tissue (Bhowmik et al., 2028). Metabolic syndrome with its associated insulin resistance leads to increased lipolysis by reducing inhibition of hormone-sensitive lipase in adipose tissue, thereby stimulating portal flux of free fatty acids to the liver (Roberts et al., 2013).

Hepatic lipase has greater activity against TG and will, thus, convert large HDL particles to small HDL particles, which are also cleared more rapidly from the circulation by the kidney, consequently reducing the concentration of HDL particles (HDL-P) (Bhowmik et al., 2028).

Although the prevalence of both type 1 and type 2 diabetes mellitus (DM) is increasing worldwide, the prevalence of T2DM is rising much more rapidly, presumably because of increasing obesity, reduced activity levels as countries become more industrialized, and the aging of the population (Mohammed et al 2019).

Several studies have found that around half of patients with T2DM are unaware of the potential complications associated with the condition (Sami et al, 2017).

T2DM can lead to numerous complications that contribute to illness and death. These complications can be divided into two categories, microscopic and macroscopic, microscopic complications consist of retinopathy, neuropathy, and nephropathy, while macroscopic complications encompass cardiovascular diseases, peripheral artery disease, and stroke (Cade, 2008). Furthermore, certain complications like dental issues and lowered immunity may also result from T2DM but do not neatly fit into these classifications (Galicia-Garcia et al., 2020). Gestational diabetes in women can lead to macrosomia. It is widely accepted that a high body mass index is a primary contributor to insulin resistance and the development of T2DM (Plows et al., 2018).

Lipids are carried in body fluids in the form of lipoprotein particles, which are categorized based on density, ranging from chylomicrons to VLDL, intermediate-density lipoprotein (IDL), LDL, and HDL (Feingold, 2024). Insulin plays a crucial role in regulating lipid metabolism (Zhang et al., 2022). The primary actions of insulin on lipoprotein metabolism are illustrated in Figure 1. In adipose tissue, insulin acts as an inhibitor of lipolysis by suppressing hormone-sensitive lipase activity. This action promotes the storage of triacylglycerols in adipocytes and decreases the release of circulating NEFA from adipose tissue (Chakrabarti et al., 2013).

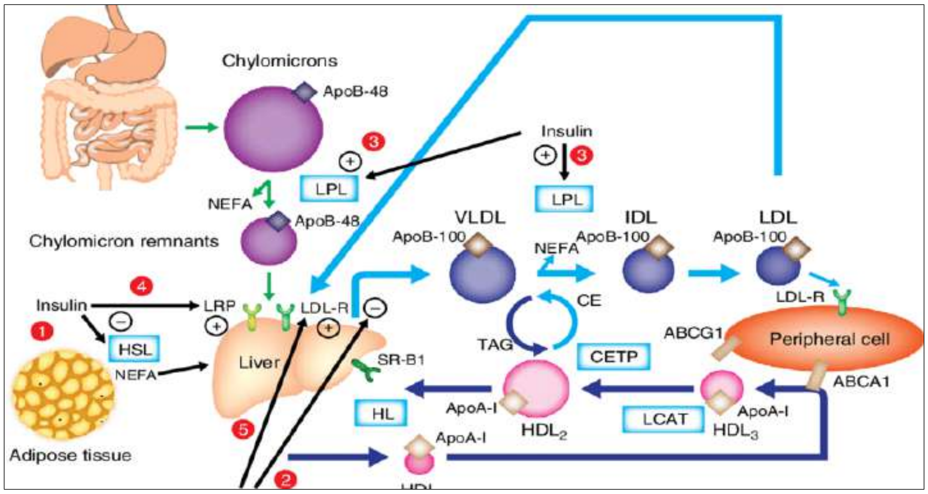

Figure 1. The primary actions of insulin on lipoprotein metabolism: An overview of human lipoprotein metabolism and the effects of insulin on lipoprotein metabolism. (1) Insulin inhibits hormone-sensitive lipase. (2) Insulin inhibits hepatic VLDL production. (3) Insulin activates LPL. (4) Insulin increases LRP expression on the plasma membrane. (5) Insulin increases LDL receptor (LDL-R) expression. CE, cholesterol ester; CETP, cholesteryl ester transfer protein; HDLn, nascent HDL HL, hepatic lipase; HSL, hormone-sensitive lipase; LPL, lipoprotein lipase; SR-B1, scavenger receptor B1; TAG, triacylglycerol (Vergès, 2015)

Lipid abnormalities commonly found in individuals with diabetes, often referred to as "diabetic dyslipidemia," typically involve elevated total cholesterol (T-Chol), high triglycerides (TG), reduced high density lipoprotein cholesterol (HDL-C), and increased levels of small dense LDL particles. Low density lipoprotein cholesterol (LDL-C) levels may be moderately raised or normal (Schofield et al., 2016). These lipid disturbances in T2DM are not just quantitative but also affect their qualitative and kinetic properties. Such abnormalities are prevalent among people with T2DM and prediabetes, although the lipid profile can differ across ethnicities, economic backgrounds, and access to healthcare (Ozder, 2014).

Dyslipidemia is a significant contributor to cardiovascular diseases in individuals with T2DM. Diets high in calories and low in fiber contribute to fat accumulation in T2DM, promoting insulin resistance and leading to lipotoxicity (Tangvarasittichai, 2015). The alterations in lipid composition in T2DM are linked to increased fatty acid levels due to insulin resistance. Insulin resistance or deficiency impacts critical enzymes and pathways involved in lipid metabolism (Savage et al., 2007). The lipid particle composition seen in diabetic dyslipidemia is more atherogenic compared to other forms of dyslipidemia (Dixit et al., 2014).

1.5- Aim of the study

1. To assess the HDL cholesterol level of individuals with T2DM.
2. Identification of specific lipid markers that are significantly altered in individuals with T2DM.
3- To Assess the Correlation between HbA1C and HDL Cholesterol level.

Material and Methods

Methodology, volunteer selection and sample collection

For this research, ninety-six volunteers aged 35-72 with confirmed T2DM underwent HDL cholesterol and HbA1c testing. Data on age, gender, diabetes status, and lipid profiles were collected in November 2023 to April 2024 from Layla Qasim Health Center located in Erbil, Iraq and then analyzed.

Procedure

Blood samples were collected by drawing venous blood from volunteers and placed into tubes. The samples were then centrifuged at 2500-3000 rpm to separate components. Subsequently, the samples were processed using the COBAS INTEGRA 400 PLUS device equipped with specific test kits for the required tests. The HbA1c test results were also obtained using the same device.

Results

Table 1. Descriptive statistics for demographic and health profile distribution

		N	%
Age	35 - 44	21	21.875
	45 - 54	33	34.375
	55 - 64	33	34.375
	65+	9	9.375
	Total	96	100
HDL mg/dl	At risk	25	26.042
	Normal	66	68.750
	Desirable	5	5.208
	Total	96	100
HbA1c	Control	34	35.417
	Non-Control	62	64.583
	Total	96	100

Table 2. Summary statistics of participant characteristics and biomarkers

		N	%	Mean	SD	95% Confidence Interval for Mean		Min.	Max.	Range
						Lower Bound	Upper Bound			
Age	35 - 44	21	21.875	40.52	2.732	39.28	41.77	35	44	9
	45 - 54	33	34.375	49.12	2.713	48.16	50.08	45	54	9
	55 - 64	33	34.375	60.09	2.337	59.26	60.92	56	64	8
	65+	9	9.375	69.33	2.693	67.26	71.40	66	73	7
	Total	96	100	52.91	9.427	51.00	54.82	35	73	38
HDL mg/dl	At risk	25	26.042	29.55	3.74	28.01	31.09	22.60	34.70	12.1
	Normal	66	68.750	44.64	7.14	42.88	46.39	35.00	64.50	29.5
	Desirable	5	5.208	66.42	7.22	57.45	75.39	55.20	72.90	17.7
	Total	96	100	41.84	10.84	39.65	44.04	22.60	72.90	50.3
HbA1c	Control	34	35.417	6.15%	0.0056	0.0596	0.0634	0.0529	0.0700	0.0171
	Non-Control	62	64.583	9.14%	0.0143	0.0877	0.0950	0.0719	0.1500	0.0781
	Total	96	100	8.08%	0.0187	0.0770	0.0846	0.0529	0.1500	0.0971

Table 3. Comparison of HDL cholesterol and glycemic control by gender

	Gender				P-Value (Sig.)
	Male		Female		
	Mean	SD	Mean	SD	
HDL mg/dl	40.13	10.31	43.49	11.18	0.130(NS)
HbA1c	7.92%	0.0174	8.23%	0.0199	0.422(NS)

Parameters measured:

1. HDL (High-Density Lipoprotein) (mg/dL): Mean and SD of HDL levels in milligrams per deciliter (mg/dL).
2. HbA1c: Mean and SD of HbA1c levels, which is a measure of glycemic control over a period of time.

The "NS" (non-significant) notation next to the p-values indicates that there is no statistically significant difference observed between male and female subjects for the respective parameter at the given significance level.

Table 4. Comparison of HDL cholesterol level and glycemic control across age group

	Age groups										**P-Value**
	35 - 44		**45 - 54**		**55 - 64**		**65+**		**Total**		
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	
HDL mg/dl	43.18	8.50	39.83	10.41	43.76	13.39	39.08	4.50	41.84	10.84	0.386(NS)
HbA1c	0.076	0.016	0.081	0.016	0.083	0.023	0.083	0.019	0.081	0.019	0.566(NS)

This table compares HDL cholesterol level and glycemic control across different age groups. The data is presented as mean values with standard deviations (SD). The age groups are categorized as 35-44, 45-54, 55-64, and 65 and above.

High-density lipoprotein (HDL) levels don't exhibit a consistent pattern across age groups.
Hemoglobin A1c (HbA1c), a marker of glycemic control, does not show significant differences across age groups.

The "P-Value" column indicates the statistical significance of the differences observed across age groups. In this case, all the p-values are above 0.05, indicating that the observed differences are not statistically significant (NS).

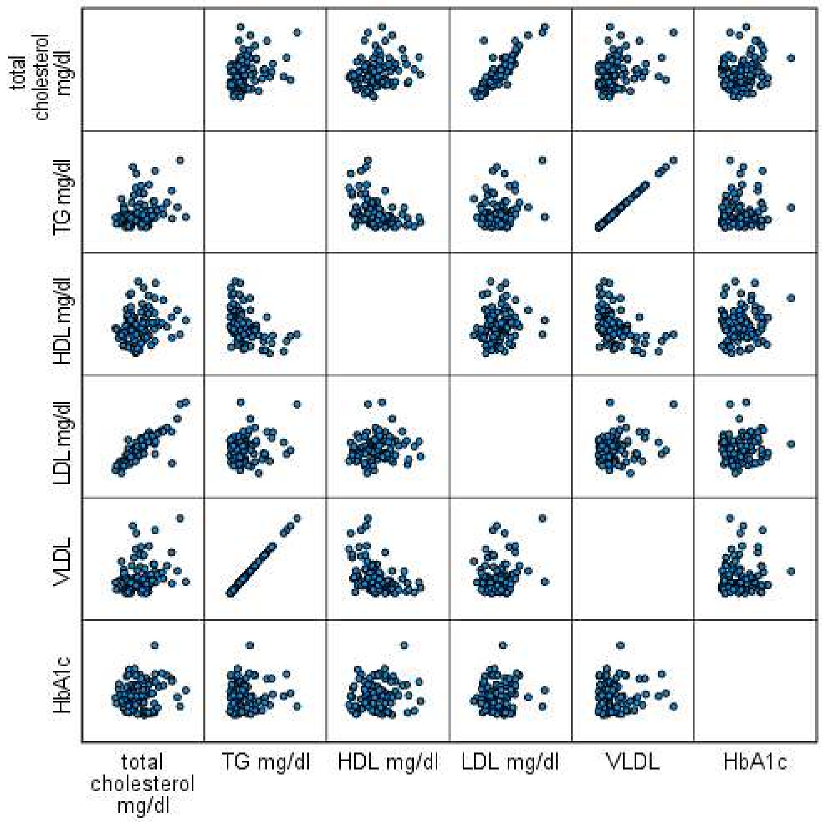

Figure 2. Correlation Matrix of Lipid Profile and HbA1c Levels

Table 5. Correlation analysis of HbA1c with HDL cholesterol variables

Variable		HbA1c	Sig.
HDL mg/dl	Pearson Correlation	0.101	(NS)
	P-Value	0.328	

This correlation analysis examines the relationship between HbA1c levels and HDL cholesterol variables.

HDL Cholesterol (mg/dl): Pearson Correlation: 0.101, Significance (Sig.): Not significant (NS), P-Value: 0.328.

In summary, none of the correlations between HbA1c levels and the HDL Cholesterol variables are statistically significant based on the provided P-Values. This suggests that there is no strong linear relationship between HbA1c and HDL Cholesterol measures in the studied population.

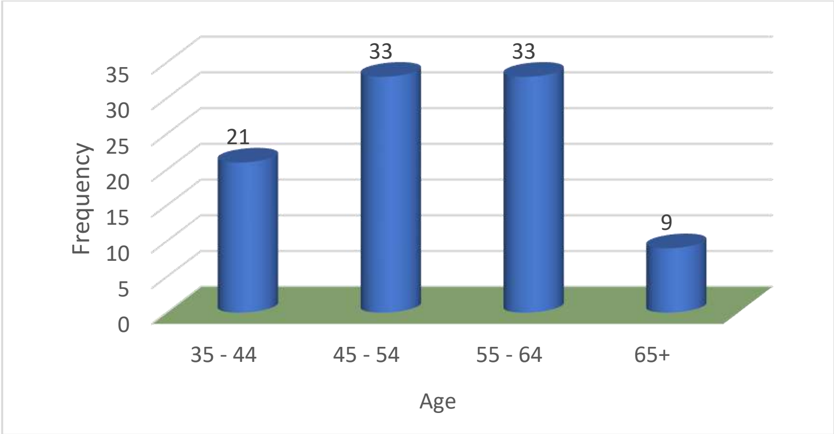

Figure 3. Bar chart for age distribution

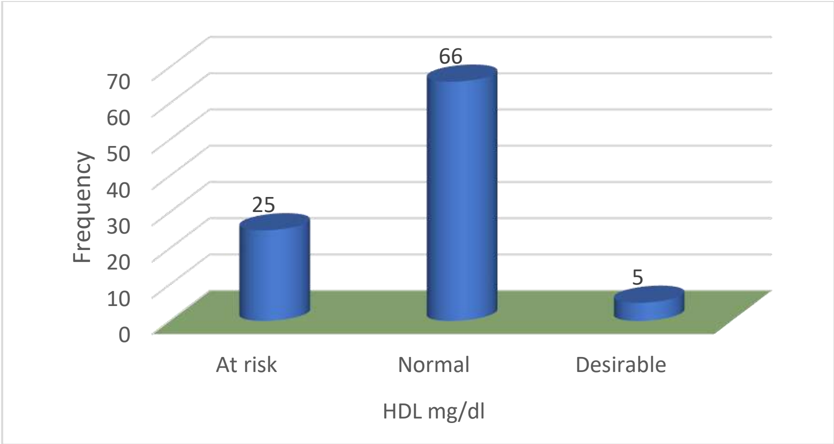

Figure 4. Bar chart for HDL distribution

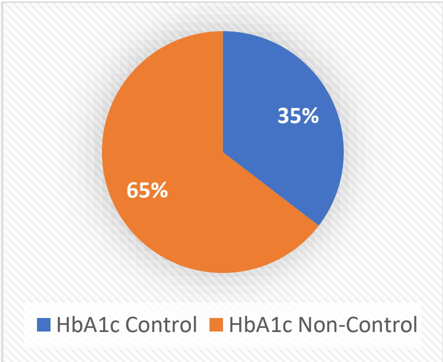

Figure 5. Pie chart for HbA1c distribution

Discussion

The increased risk of cardiovascular disease (CVD) in individuals with T2DM is partly due to abnormalities in HDL cholesterol levels associated with T2DM. This study found that the prevalence of dyslipidemia among T2DM patients was 50.88%, varying across different regions, Karbala (73%), Basrah (70.5%), Nigeria (69.3%), Saudi Arabia (83.9%), and China (59.3%) (AL-Bahrani et al., 2022). These differences in prevalence may be attributed to lifestyle, dietary habits, and genetic factors. A key lipoprotein abnormality observed was decreased HDL cholesterol levels, with dyslipidemia more prevalent among those with poorly controlled diabetes.

Glycemic control, as measured by HbA1c levels, is crucial in managing diabetes. The Diabetes Complications and Control Trial identified HbA1c as the gold standard for glycemic control, with an 18% increased risk of CVD for every 1% rise in HbA1c levels. Other studies indicate that weight is a modifiable factor affecting HbA1c levels, with statistically significant positive correlations observed between HbA1c and both weight and waist circumference (Shen et al., 2023). Dietary behavior also impacts diabetes control (Shen et al., 2023).

Age does not significantly affect HbA1c levels in this study, though younger individuals generally exhibit slightly better glycemic control. Contradictory findings exist regarding age and glycemic control across different regions. Women tend to have higher mean HbA1c levels, which has been associated with poorer glycemic control in females. The effects of sex hormones on body fat distribution may contribute to differences in lipid profiles among women (Alzahrani et al., 2019).

HbA1c shows weak positive correlations with lipid parameters, although these correlations are not statistically significant. Early detection and treatment of dyslipidemia associated with diabetes are essential steps in reducing CVD risk. Prevention strategies can potentially avoid up to 90% of CVD cases by addressing established risk factors (Khavandi et al., 2017; Rippe, 2018).

Conclusion

In conclusion, this study identified hypertriglyceridemia (27%) and low HDL-C (26%) as the most prevalent lipid abnormalities among the subjects, followed by hypercholesterolemia (19%). Additionally, a higher mean HbA1c level was observed in females, with HbA1c directly correlating with dyslipidemia in T2DM and aiding in the assessment of micro- and macrovascular risk. The study suggests that cardiac complications may be driven by the dyslipidemia insulin resistance (IR)-hyperinsulinemia cycle, known as the "vicious cycle hypothesis." Insulin resistance is implicated as the primary cause of dyslipidemia in T2DM. Enhanced understanding of lipid disorders in T2DM is important for improving the management of diabetic dyslipidemia and associated cardiovascular risks.

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