The Association Between Type 2 Diabetes Mellitus and Levels of Total Cholesterol, Low-Density Lipoprotein (LDL) Cholesterol, Very Low-Density Lipoprotein (VLDL) and the Role of Dehydrated Vegetables in Glycemic Control

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KEYWORDS

Type 2 diabetes mellitus (T2DM), dyslipidemia, HbA1c, lipid profile, total cholesterol, LDL cholesterol, VLDL, cardiovascular disease, dehydrated vegetables

ABSTRACT

Objective: This study aimed to assess Total Cholesterol, Low-Density Lipoprotein (LDL) and Very Low-Density Lipoprotein (VLDL) Levels, identify specific lipid markers altered in individuals with type 2 diabetes mellitus (T2DM), and evaluate the correlation between HbA1C and total cholesterol, LDL cholesterol, and VLDL levels.

Materials and Methods: Ninety-six volunteers aged 35-72 with confirmed T2DM underwent total cholesterol, LDL, VLDL 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: Result: In our study, the prevalence of dyslipidemia among type 2 diabetes mellitus (T2DM) patients was 50.88%. This varied regionally, from 59.3% in China to 83.9% in Saudi Arabia. Dyslipidemia was more common in patients with poor blood glucose control. Weight and waist circumference were positively correlated with HbA1c levels, while age showed no significant effect on glycemic control. Women showed higher LDL and HbA1c levels than men. Although weak correlations were observed between HbA1c and LDL cholesterol, LDL was strongly correlated with total cholesterol and moderately with VLDL. Early detection and management of dyslipidemia is important to reduce the risk of cardiovascular disease in patients with T2DM.

Conclusion: Our study highlights the significant prevalence of dyslipidemia among patients with type 2 diabetes mellitus (T2DM), emphasizing the importance of lipid profile management to reduce the risk of cardiovascular disease. We found associations between weight, waist circumference and HbA1c levels, with gender differences in lipid profiles. While the association between HbA1c and LDL cholesterol was weak, early diagnosis and management of dyslipidemia could significantly reduce CVD risk, advocating a comprehensive strategy targeting both glycemic control and lipid management in T2DM patients.

1. 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).

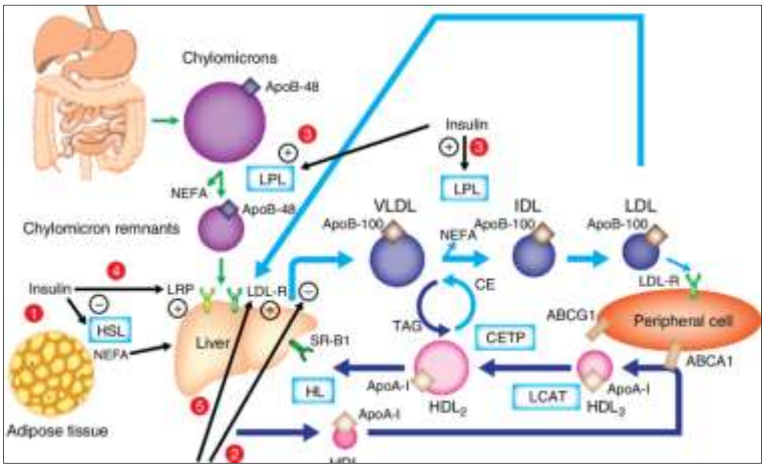

Figure 1. The primary actions of insulin on lipoprotein metabolism: An overview of human lipoprotein metabolism and the effects of insulin on lipoprotein metabolism. (1) Insulin inhibits hormone-sensitive lipase. (2) Insulin inhibits hepatic VLDL production. (3) Insulin activates LPL. (4) Insulin increases 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).

The Role of Dehydrated Vegetables in Glycemic Control and Lipid Profile Management for Type 2 Diabetes Mellitus Patients

The composition and quality of a diet play a pivotal role in managing Type 2 Diabetes Mellitus (T2DM) due to their impact on glycemic control. According to the Medical Nutrition Therapy Guidelines for T2DM, it is advised to consume at least five servings of fruits and vegetables daily to achieve and maintain normal blood glucose levels (Malaysian Dietitian's Association, 2013). Likewise, the healthy plate model promoted by health organizations globally advocates for a balanced meal, suggesting that a single meal should include 25% carbohydrates, 25% protein, and 50% fruits and vegetables. Fruits and vegetables are essential sources of nutraceuticals and functional foods, being low in calories but high in dietary fiber and phytochemicals such as polyphenols. This diversity in nutrient intake supports various human physiological processes. Polyphenols are naturally occurring compounds found in large quantities in plant-based foods such as fruits, vegetables, legumes, and cereals. Acting as secondary metabolites, polyphenols help protect plants from ultraviolet radiation and pathogens. In food, polyphenolic compounds influence oxidative stability and sensory characteristics, including taste, flavor, color, and odor (Pandey and Rizvi, 2009). Fruits and vegetables play a crucial role in providing nutraceuticals and are essential components of a healthy diet, especially as recommended in medical nutrition therapy for type 2 diabetes mellitus (T2DM) to prevent hyperglycemia and associated complications. These foods are low in calories, high in dietary fiber, and rich in polyphenols, making them integral to a healthy lifestyle. Recently, there has been a growing research interest in exploring how polyphenols, including flavonoids and non-flavonoids, impact blood glucose levels (Zin CAJCM et al., 2022). Studies have shown that administering resveratrol, anthocyanin, and naringin to patients with prediabetes and diabetes can significantly reduce fasting blood glucose, glycated hemoglobin, and low-density lipoprotein cholesterol levels. Notably, resveratrol intervention has also been associated with decreased insulin levels, an effect not observed with other polyphenols. These beneficial effects of polyphenolic compounds on glycemic and metabolic parameters may be attributed to various pathophysiological mechanisms, such as the activation of regulatory proteins that enhance insulin signaling and ultimately reduce insulin resistance (Zin CAJCM et al., 2022).

Aim of the study

1. To assess the total cholesterol, LDL, and VLDL levels 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 total cholesterol, LDL, and VLDL levels.

2. Methodology

Methodology, volunteer selection and sample collection

For this research, ninety-six volunteers aged 35-72 with confirmed T2DM underwent total cholesterol, LDL, VLDL 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.:

3. Results and discussion

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
Total cholesterol mg/dl	Normal	78	81.25
	Abnormal	18	18.75
	Total	96	100
LDL mg/dl	Optimal	60	62.500

	Above optimal	25	26.042
	Border line high	8	8.333
	High	1	1.042
	Very high	2	2.083
	Total	96	100
VLDL	Normal	70	72.917
	Abnormal	26	27.083
	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
Total cholesterol mg/dl	Normal	78	81.25	150.55	25.921	144.70	156.39	95	200	104
	Abnormal	18	18.75	232.05	30.851	216.71	247.39	202	300	98
	Total	96	100	165.83	41.684	157.38	174.28	95	300	205
LDL mg/dl	Optimal	60	62.500	68.30	18.80	63.45	73.16	18.00	98.00	80
	Above optimal	25	26.042	114.40	7.93	111.13	117.68	103.00	127.00	24
	Border line high	8	8.333	139.04	6.56	133.55	144.52	130.00	151.00	21
	High	1	1.042	177.00				177.00	177.00	0
	Very high	2	2.083	221.90	4.10	185.05	258.75	219.00	224.80	5.8
	Total	96	100	90.54	36.62	83.12	97.95	18.00	224.80	206.8
VLDL	Normal	70	72.917	25.26	7.76	23.41	27.10	12.20	39.80	27.6
	Abnormal	26	27.083	65.16	22.75	55.97	74.35	40.92	121.58	80.66
	Total	96	100	36.06	22.31	31.54	40.58	12.20	121.58	109.38
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 total, LDL, and VLDL cholesterol levels and glycemic control by gender

	Gender		P-Value(Sig.)
	Male	Female	

	Mean	SD	Mean	SD	
Total cholesterol mg/dl	160.20	37.14	171.23	45.34	0.196 (NS)
LDL mg/dl	89.31	35.84	91.71	37.68	0.751(NS)
VLDL	35.85	22.96	36.27	21.90	0.927(NS)
HbA1c	7.92%	0.0174	8.23%	0.0199	0.422(NS)

Parameters measured:

Total cholesterol (mg/dL): Mean and SD of total cholesterol levels in milligrams per deciliter (mg/dL).

LDL (Low-Density Lipoprotein) (mg/dL): Mean and SD of LDL levels in milligrams per deciliter (mg/dL).

VLDL (Very Low-Density Lipoprotein): Mean and SD of VLDL levels.

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 Total Cholesterol, LDL, and VLDL levels 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	
Total cholesterol mg/dl	158.18	26.47	163.48	49.04	169.97	33.73	177.11	65.73	165.83	41.68	0.622(NS)
LDL mg/dl	89.76	29.17	82.92	37.90	93.35	32.03	109.92	56.99	90.54	36.62	0.247(NS)
VLDL	28.14	14.92	40.71	20.14	34.89	25.34	41.80	29.43	36.06	22.31	0.190(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 Total Cholesterol, LDL, and VLDL levels 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.

Total cholesterol levels increase with age, with the highest mean value observed in the 65+ age group.

Low-density lipoprotein (LDL) levels show a slight increase in the 65+ age group compared to other age groups.

Very low-density lipoprotein (VLDL) levels also demonstrate some variability 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).

Table 5. Correlation matrix of Total Cholesterol, LDL, and VLDL levels and HbA1c levels

Correlations		**total cholesterol mg/dl**	**TG mg/dl**	**HDL mg/dl**	**LDL mg/dl**	**VLDL**	**HbA1c**
Total cholesterol mg/dl	Pearson Correlation	1	.312**	.207*	.848**	.312**	0.179

	P-Value		0.002	0.043	0	0.002	0.082
LDL mg/dl	Pearson Correlation	.848**	.206*	0.138	1	.206*	0.087
	P-Value	0	0.044	0.181		0.044	0.399
VLDL	Pearson Correlation	.312**	1.000**	-.426**	.206*	1	0.036
	P-Value	0.002	0	0	0.044		0.73
HbA1c	Pearson Correlation	0.179	0.036	0.101	0.087	0.036	1
	P-Value	0.082	0.729	0.328	0.399	0.73	

Total Cholesterol vs. Other Parameters: Total cholesterol shows significant positive correlations with TG, HDL, LDL, and VLDL, indicating a moderate to strong positive relationship with these parameters.

LDL (Low-Density Lipoprotein) vs. Other Parameters: LDL demonstrates a very strong positive correlation with total cholesterol and moderate positive correlations with TG and VLDL.

VLDL (Very Low-Density Lipoprotein) vs. Other Parameters: VLDL shows positive correlations with total cholesterol, TG, and LDL. The correlation with TG is very strong

HbA1c (Glycated Hemoglobin) vs. Lipid Profile: HbA1c exhibits weak positive correlations with all lipid parameters, though none of these correlations are statistically significant.

Overall, the correlation matrix provides insights into how various components of the lipid profile are related to each other and to HbA1c levels.

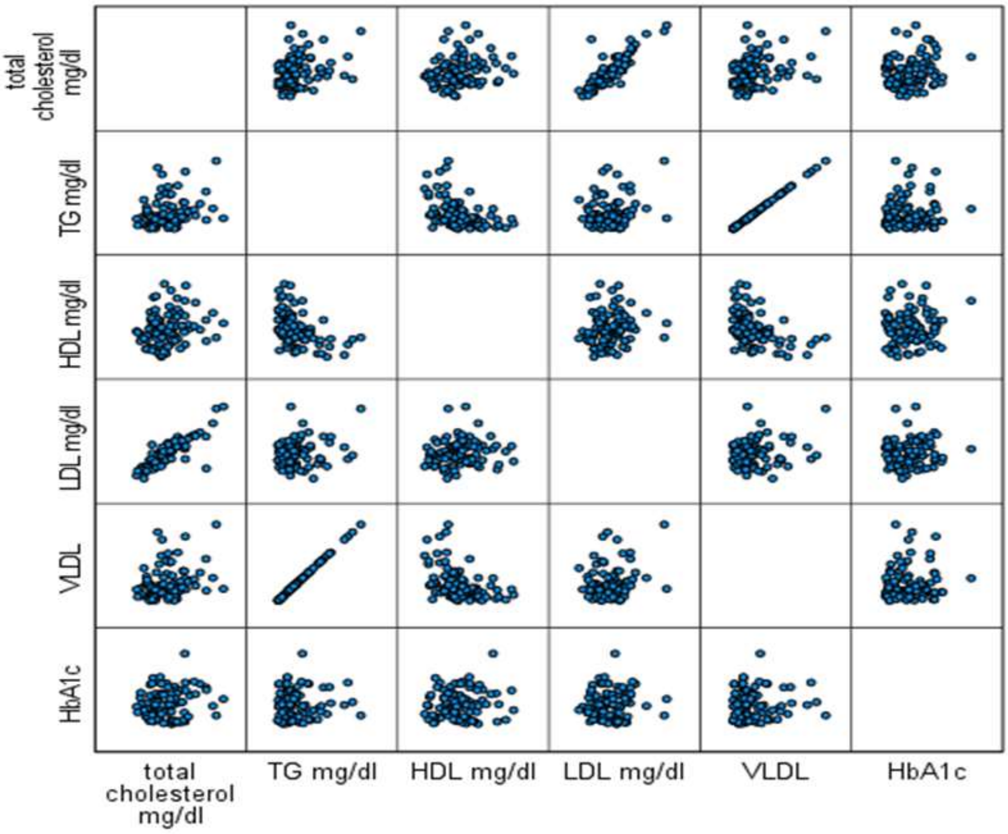

Figure 2. Correlation Matrix of Lipid Profile and HbA1c Levels

Table 6. Correlation Analysis of HbA1c with Total Cholesterol, LDL, and VLDL Variables

Variable		**HbA1c**	**Sig.**
Total cholesterol mg/dl	Pearson Correlation	0.179	(NS)
	P-Value	0.082	
LDL mg/dl	Pearson Correlation	0.087	(NS)
	P-Value	0.399	
VLDL	Pearson Correlation	0.036	(NS)
	P-Value	0.73	

This correlation analysis examines the relationship between HbA1c levels and Total Cholesterol, LDL, and VLDL levels variables.

Total Cholesterol (mg/dl): Pearson Correlation: 0.179, Significance (Sig.): Not significant (NS), P-Value: 0.082.

LDL Cholesterol (mg/dl): Pearson Correlation: 0.087, Significance (Sig.): Not significant (NS), P-Value: 0.399.

VLDL Cholesterol: Pearson Correlation: 0.036, Significance (Sig.): Not significant (NS), P-Value: 0.73.

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

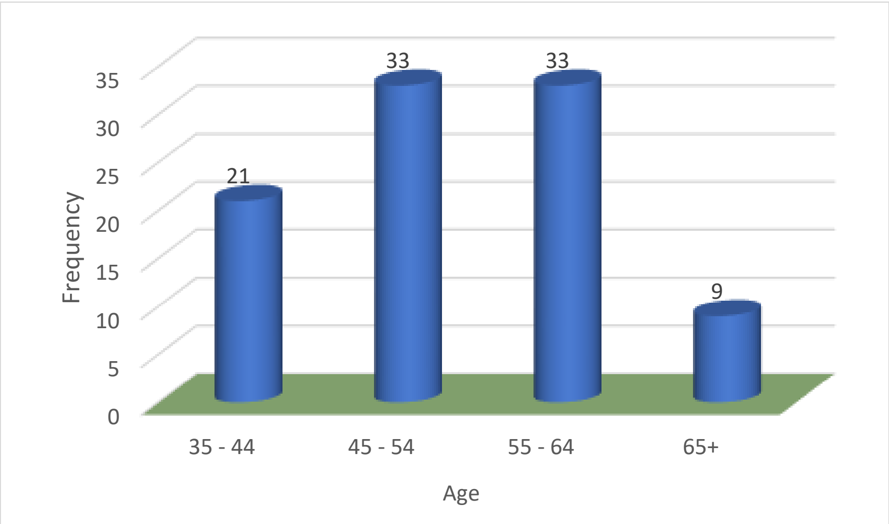

Figure 3. Bar chart for Age distribution

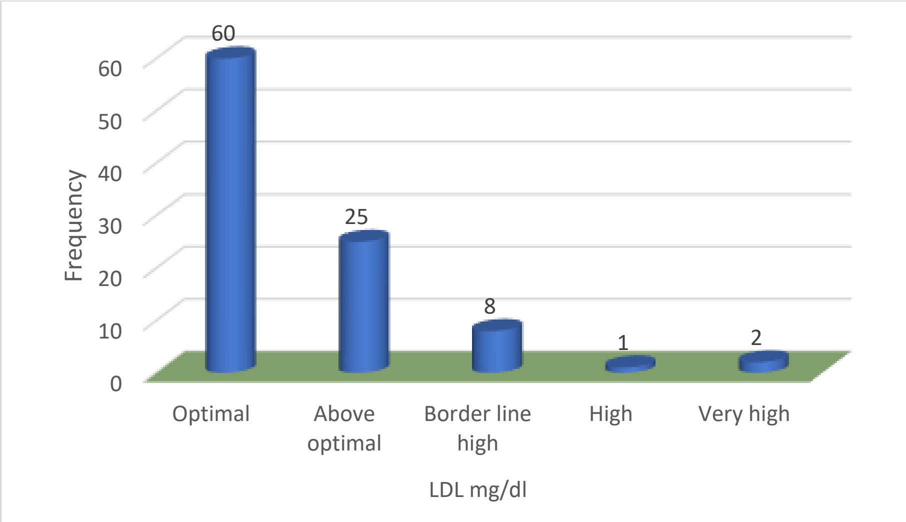

Figure 4. Bar chart for LDL distribution

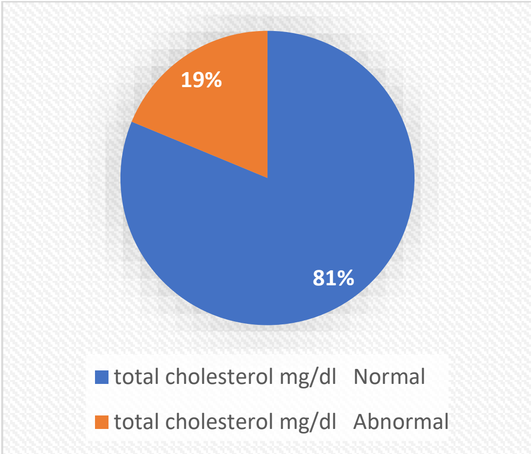

Figure 5. Pie chart for total cholesterol distribution

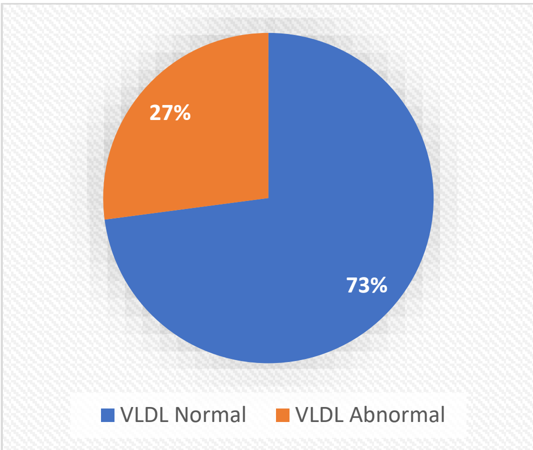

Figure 6. Pie chart for VLDL distribution

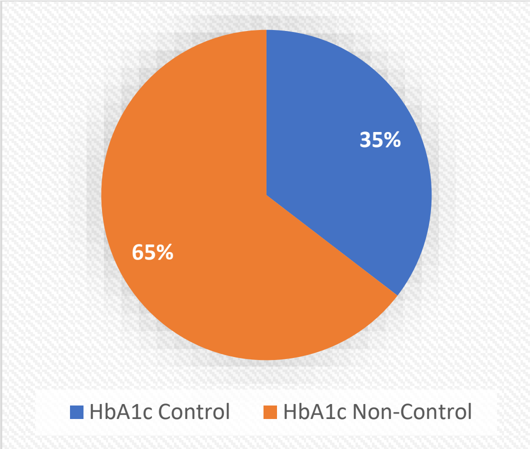

Figure 7. Pie chart for HbA1c distribution

Discussion

Dyslipidemia has long been recognized as a significant risk factor for diabetes, alongside hyperglycemia and hypertension. The increased risk of cardiovascular disease (CVD) in patients with type 2 diabetes mellitus (T2DM) is partly attributed to abnormalities in the lipid profile associated with T2DM (AL-Bahrani et al., 2022).

In our study, the overall prevalence of dyslipidemia in type 2 diabetic patients was 50.88%. This prevalence varies considerably across different studies and regions: 73% in Karbala, 70.5% in Basra, 69.3% in Nigeria, 83.9% in Saudi Arabia, and 59.3% in China. These differences may be due to differences in lifestyle factors, dietary habits, and genetic predisposition (AL-Bahrani et al., 2022).

Our study found a strong association between dyslipidemia and poor blood glucose control in patients with type 2 diabetes, with dyslipidemia being more common in those with poorly controlled diabetes (Nnakenyi et al., 2022; Hussain et al., 2017). Many studies have indicated that maintaining HbA1c levels up to 7.0% can reduce the risk of cardiovascular complications (Hussain et al., 2017; Bonilha et al., 2021).

Weight is another factor that showed a statistically significant positive correlation with HbA1c levels. In addition, a significant positive correlation was found between HbA1c and waist circumference (AL-Bahrani et al., 2022).

In our study, HbA1c, a marker of glycemic control, did not show significant differences across age groups, although younger individuals tended to have slightly better glycemic control than older ones.

Low-density lipoprotein (LDL) cholesterol levels showed a slight increase in individuals aged 65 and older. Additionally, women with diabetes had slightly higher mean and standard deviation (SD) levels of LDL compared to men. Higher mean HbA1c levels in females were also reported, similar with previous studies that have noted a significant association between female gender, poor glycemic control, and hyperlipidemia. These gender differences may be attributed to the effects of sex hormones on body fat distribution, influencing lipid profiles (AL-Bahrani et al., 2022).

Total cholesterol shows significant positive correlations with LDL, and VLDL, indicating a moderate to strong positive relationship with these parameters.

The associations between HbA1c and the LDL cholesterol level in T2DM were evaluated in this study. HbA1c showed weak positive correlations with LDL parameter, although none of these correlations were statistically significant. LDL showed a very strong positive correlation with total cholesterol and a moderate positive correlation VLDL.

An important factor in the change of LDL phenotype in T2DM is reduced insulin sensitivity. Insulin resistance decreases LDL particle size, as insulin resistance becomes more severe, LDL particle size decreases further (Bonilha et al., 2021). Early detection and treatment of dyslipidemia in diabetes may significantly reduce CVD risk, with up to 90% of CVD potentially preventable if risk factors are managed effectively (Hussain et al., 2017).

4. Conclusion and future scope

In conclusion, our study highlights the significant prevalence of dyslipidemia among type 2 diabetes mellitus (T2DM) patients, with 50.88% of participants having it. This prevalence is consistent with other studies, although regional variations are evident due to differences in lifestyle, diet, and genetics. The strong association between dyslipidemia and poor blood glucose control emphasizes the importance of lipid profile management to reduce the risk of cardiovascular disease (CVD) in patients with diabetes.

Our findings also reveal that weight and waist circumference are positively correlated with HbA1c levels, indicating that obesity and central adiposity contribute to poor glycemic control. Gender differences were observed, with women showing higher levels of LDL cholesterol and HbA1c, presumably due to hormonal effects on lipid distribution and lipid metabolism.

While the association between HbA1c and LDL cholesterol levels was weak and not statistically significant, the strong association between LDL and total cholesterol, as well as the effect of insulin resistance on LDL particle size, underscores the complex interplay between lipid metabolism and insulin sensitivity in T2DM. Early detection and management of dyslipidemia in diabetic patients can significantly reduce CVD risk, potentially preventing up to 90% of cardiovascular events if risk factors are effectively controlled. These findings advocate comprehensive strategies targeting both glycemic control and lipid management to improve cardiovascular outcomes in patients with T2DM

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