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ORIGINAL RESEARCH

Prevalence and Pattern of Dyslipidemia and Its Associated Factors Among Patients with Type 2 Diabetes Mellitus in Jordan: A Cross-Sectional Study

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Background: Dyslipidemia and type 2 diabetes mellitus (T2DM) are growing health problems, particularly in developing countries. This study aimed to determine the prevalence and pattern of dyslipidemia and its associated factors among patients with T2DM.

Methods: A cross-sectional study was conducted among patients with T2DM attending Family Medicine Clinics in Jordan between August 2017 and March 2019. The socio-demographics, clinical features, medications, and laboratory findings were collected. These laboratory findings included high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), and triglycerides (TGs).

Results: A total of 870 patients with T2DM were included. The prevalence of dyslipidemia among patients with T2DM was 91.4%. The most common patterns of dyslipidemia were low HDL-C (66.2%), high LDL-C (62.1%), and hypertriglyceridemia (58.2%). Female gender, obesity, and hypertension were associated with diabetic dyslipidemia patterns. T2DM duration and poor glycemic control were associated with high LDL-C and hypercholesterolemia. Hypertriglyceridemia was associated with poor glycemic control and smoking.

Conclusion: Dyslipidemia is highly prevalent among patients with T2DM. Evidence –based interventions are needed to prevent and control dyslipidemia among patients with T2DM in Jordan.

Keywords: dyslipidemia, diabetes mellitus, cholesterol, triglycerides, prevalence

Introduction

Dyslipidemia is defined as an abnormal lipid profile characterized by the imbalance of lipids such as low high-density lipoprotein cholesterol (HDL-C), high low-density lipoprotein cholesterol (LDL-C), high total cholesterol (TC), and high triglycerides (TGs) levels.[1] Dyslipidemia and T2DM are growing public health problem, particularly in developing countries, including Jordan.[2–5] A recent study from Jordan indicated that hypercholesterolemia and hypertriglyceridemia patterns of dyslipidemia approximately doubled from 23.0% and 23.8%, in 1994 to 44.3% and 41.9% in 2017, respectively.[2]

Non-communicable diseases (NCDs) such as cardiovascular diseases (CVD) are highly prevalent and considered the leading cause of death in developing countries.[6,7] Dyslipidemia significantly contributes to CVD, T2DM and atherosclerosis development.[2–4] Even mild lipid profile abnormalities may increase the risk of CAD significantly in the presence of other CAD risk factors such as T2DM.[8]

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Different dyslipidemia patterns have been linked with gender and patients age groups. Besides T2DM, hypertension and obesity were found to be an independent factors for dyslipidemia.[2–4] The relationship between T2DM and dyslipidemia could be bidirectional. While the risk of coronary artery disease (CAD) is two to four-fold higher in subjects with T2DM,[9] several studies have shown a significant correlation between glycated Hemoglobin (HbA1c) and multiple lipid profile parameters in patients with T2DM s.[10–12] Thus, effective control of one could positively affect the other.

Although dyslipidemia is a modifiable CAD risk factor and its effective management could reduce morbidity and mortality rates,[13,14] dyslipidemia remains widely undiagnosed and uncontrolled in high-risk populations such as subjects with T2DM.[15]

This study aimed to determine the prevalence and pattern of dyslipidemia and its associated factors among patients with T2DM. Assessing the prevalence and pattern of dyslipidemia and its associated risk factors among patients with T2DM would help achieve the desired lipid parameters control, promote health, and, thus, reduce diabetic dyslipidemia incidence, prevalence, and complications.

Materials and Methods

Study Design

A cross-sectional study was conducted among patients with T2DM attending Family Medicine Clinics at King Abdullah University Hospital (KAUH) in Jordan between August 2017 and March 2019. KAUH is a tertiary teaching hospital located in Irbid governorate serving a population exceeding 2 million in the north of Jordan. The majority of them are Jordanians who are under the insurance cover of public universities, and ministry of health. Patients with T2DM who attended the Family Medicine Clinics between August 2017 and March 2019 were screened for this study. Eligibility criteria included patients previously diagnosed with T2DM based on the ADA criteria,[16] 30 years of age or older, having at least two laboratory measurements of lipid profile one year apart, and commencement of treatment at the KAUH family clinics. More strict inclusion criteria were conducted to rule out type 1 diabetes and latent autoimmune diabetes in adults (LADA). These criteria included DM diagnosis at the age of ≥30 years, having DM for more than 12 months, having at least two HbA1c readings ≥6.5, no insulin use in the first year after diagnosis, no history of ketosis or ketonuria, and C-peptide was normal to high at the time of DM diagnosis. Patients diagnosed with type 1 DM or LADA, pregnant women, and those without two lipid measurements approximately one year apart were excluded. Out of 4735 screened subjects with DM, 870 patients with T2DM were eligible and included in the study. The power of the study to estimate a prevalence of dyslipidemia of 50% within a margin of error of 5% al level of significance of 0.05 exceeds 80% for a sample of 870 patients.

Data Collection and Laboratory Measurements

The electronic medical records of eligible participants were reviewed. Socio-demographics, comorbidities, chronic medications, including lipid-lowering, anti-hypertensive, and anti-diabetic medications, T2DM disease characteristics, clinical variables, and laboratory findings were extracted from the electronic medical records. The missing data in the medical records were obtained through direct communication with the patients.

Per hospital standards, a detailed history and examination are performed for all patients during each visit. HbA1c test is conducted for subjects with T2DM using the turbidimetric inhibition immunoassay (TINIA) method every three to six months or more frequent if the patient is not under control. Lipid profile is measured in the first visit of patients with DM and at least every six months using Beckman Coulter AU Clinical Chemistry analyzers (Beckman Coulter, Inc., 250 S. Kraemer Blvd., Brea, CA 92821, USA). Liver and renal functions and urine checks for microalbuminuria are tested on the first visit of the patient with DM and at least every year. Ophthalmologic examination of the fundus is performed for subjects with T2DM on the first visit and at least every two years or more frequently in case of retinopathy evidence.

Definition of Variables

The lipid profile abnormalities were defined according to the ADA report[17,18] and the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report.[19] Low levels of HDL-C were defined as ≤40 mg/dl (≤1.03 mmol/l) in men and ≤50 mg/dl (≤1.29 mmol/l) in women, high LDL-C levels were defined as ≥100 mg/dl

(≥2.59 mmol/l), hypercholesterolemia was defined as TC level ≥200 mg/dl (≥5.17 mmol/l), and hypertriglyceridemia was defined as TGs level ≥150 mg/dl (≥1.70 mmol/l). Dyslipidemia was defined as the presence of at least one of the previous four lipid abnormalities in the serum lipid profile. The TC to HDL-C ratio (TC/HDL ratio) was calculated and considered high if the ratio was ≥5.

The patients' age was divided by decades into six groups of 30–39, 40–49, 50–59, 60–69, 70–79, and ≥80 years. Also, the T2DM duration since diagnosis was categorized based on the median into two categories. The body mass index (BMI) was used to categorize the participants as defined by the World Health Organization (WHO) guidelines into three groups: Healthy weight (BMI = 18.5–24.9 kg/m^2), overweight (BMI = 25–29.9 kg/m^2), and obese with a BMI of 30 kg/m^2 or greater.[20] Smoking was classified into a current smoker (smoked at least 100 cigarettes in their lifetime and who currently smokes cigarettes); former-smoker (smoke-free for one year before enrollment); and never smoked participants (if they had never smoked or smoked less than 100 cigarettes in their lifetime).

Hypertension (HTN) was defined if it is documented in the patient medical record; or if the patient was on anti-hypertensive medications; or if systolic blood pressure (BP) values of ≥130 mmHg or diastolic BP of >80 mmHg on at least two occasions.[21] Ischemic Heart Disease (IHD) was defined as a documented previous diagnosis by angiography or electrocardiography. Diabetic retinopathy was defined as any degree of retinopathy detected by direct ophthalmoscopy carried out by an ophthalmologist.

Among patients with T2DM, the target HbA1c was determined to be ≤7% according to ADA guidelines. Thus, glycemic control was considered well-controlled with HbA1C levels ≤7%, while poor-controlled DM with HbA1C levels of >7%.[17] The albumin to creatinine ratio in an early morning spot urine sample equals 3–30 mg/mmol was defined as moderately increased albuminuria (ie, microalbuminuria) and >30 mg/mmol as severely increased albuminuria (ie, macroalbuminuria).[22]

Ethical Approval

This study protocol was ethically approved by the Institutional Review Board (IRB) at Jordan University of Science and Technology (20210096). This study was conducted following the 1975 Helsinki declaration, as revised in 2008, and its later amendments or comparable ethical standards. The informed consent from the study participants was waived due to the retrospective design of the study. The reason for consent form waiver is that most retrospective chart reviews involve a large number of records, and therefore the IRB would consider it impracticable to do the study if informed consent and authorization were required. The study involved minimal risk. The confidentiality of patient data was protected and medical records were password-protected. This work has been reported as a cross sectional study design based on STOBE 2019 guidelines (Strengthening the Reporting of Observational Studies in Epidemiology).

Statistical Analysis

The Statistical Package for the Social Sciences (IBM SPSS Corp., Chicago, Illinois, USA), Windows version 22.0, was used for data processing and analysis. Categorical variables were presented as frequencies and percentages, while continuous variables were described as mean (M) and standard deviation (SD). Chi-square test was used to compare the prevalence rates of dyslipidemia according to the studied characteristics.

Multivariate analysis was performed to determine factors associated with each lipid abnormality outcome variable (low HDL-C, high LDL-C, hypercholesterolemia, and hypertriglyceridemia) among T2DM patients while simultaneously controlling for probable confounders. A backward stepwise method was selected. The potential predictor variables included age groups, gender, BMI categories, smoking status, comorbidities, T2DM duration for longer than 10 yrs, glycemic control, diabetic complications, lipid-lowering medications (statins and fibrates), anti-diabetic medications, and use of Beta-blockers. These variables were entered into the model as independent explanatory variables. After that, the independent variable with a significance level of ≥0.2 was excluded at each step until the final most parsimonious model was obtained. The magnitude of the associations was presented by the adjusted odds ratio (OR), and the statistical significance was assessed by the 95% confidence intervals (CI) and p-values.

Results

Participants' Characteristics

A total of 870 individuals were included in the analysis with a mean (SD) age of 61.15 (10.94) years. Almost 53.9% of patients were males. The mean (SD) of BMI among patients with T2DM was 30.5 (6.1) kg/m^2. The vast majority of patients with T2DM were overweight or obese. Table 1 and Supplementary Table 1. demonstrates the sociodemographic characteristics, clinical features, medications, vital signs, and laboratory findings of the patients.

Among T2DM patients, the mean (SD) of diabetic duration since diagnosis was 11.9 (7.7) years and ranged from one to 43 years. Diabetic nephropathy and retinopathy were the most common diabetic complications (23.7% and 17.4%; respectively). Despite that more than half of patients were using Insulin, approximately two-thirds of them (68.4%) were poorly controlled with an HbA1c mean (SD) of 8.3 (2.2) (Table 1, Supplementary Table 1).

Table 1 Patients' Demographics, Clinical and Laboratory Characteristics

Variable	N (%)
Age (years), m ± SD	61.15 ± 10.94
Gender	
Women	401 (46.1)
Men	469 (53.9)
BMI (kg/m^2), m ± SD (Total n. = 752)	30.50 ± 6.05
Healthy weight (BMI≤24.9)	137/752 (18.2)
Overweight (BMI, 25–29.9)	262/752 (34.8)
Obese & Morbid obese (BMI≥30)	353/752 (46.9)
Comorbidities	
HTN	712 (81.8)
IHD	274 (31.5)
Stroke	81 (9.3)
CKD	47 (5.4)
Lipid lowering Medications	
Statins	597 (68.6)
Fibrates	44 (5.1)
Diabetes duration (yrs), m ± SD (Total n. = 731)	11.87 ± 7.65
Longer than 10 yrs	378/731 (51.7)
Vital Signs and Laboratory Findings	
Systolic BP (mmHg), m ± SD	134.32 ± 18.41
Diastolic BP (mmHg), m ± SD	81.38 ± 10.43
FBS (mg/dL), m ± SD	10.11 ± 4.78
HbA1c (%), m ± SD	8.33 ± 2.19
HbA1c ≤7%	275 (31.6)
HbA1c >7% (poor-controlled DM)	595 (68.4)

Patterns of Dyslipidemia

Among patients with T2DM, 795 (91.4%) patients had dyslipidemia. The most common forms of dyslipidemia were low HDL-C (66.2%) and high LDL-C (62.1%). Around 69.4% of patients with T2DM had two or more lipid abnormalities, 40.3% had three or more abnormalities, and 14.0% had all four lipid parameters abnormal. Table 2 shows the lipid profile values, dyslipidemia patterns, and TC/HDL ratio among T2DM participants

Dyslipidemia According to the Studied Characteristics

Table 3 depicts the prevalence rates of dyslipidemias among patients with T2DM by their socio-demographics, clinical characteristics, and comorbidities. The prevalence rates of high LDL-C, hypercholesterolemia, and hypertriglyceridemia significantly differed according to age, where they reached their peaks at the age group of 40–49 years, then decreased among the older age groups. A similar difference in the prevalence rates of high TC/HDL ratio with age was noticed where the prevalence increased until the age group of 40 to 49 years, then decreased again. However, the prevalence of low HDL-C significantly increased until the age of 59 years, and then it plateaued approximately throughout the older age groups. Female patients with T2DM had statistically significantly higher rates of all dyslipidemia patterns than men ($p \leq 0.006$), with exception of high TC/HDL ratio ($p=0.236$).

Table 2 Lipid Profile and Patterns of Dyslipidemia in Patients with Type 2 Diabetes

Variable	N (%)
Lipid profile values (mg/dl), m ± SD	
HDL-C	41.38 ± 13.28
LDL-C	115.99 ± 40.91
TC	176.86 ± 49.96
TGs	206.07 ± 205.19
Patterns of dyslipidemia, n (%)	
Low HDL-C	576 (66.2)
High LDL-C	540 (62.1)
Hypercholesterolemia	250 (28.7)
Hypertriglyceridemia	506 (58.2)
Combinations of dyslipidemia patterns, n (%)	
None	75 (8.6)
One	191 (22.0)
Tow	253 (29.1)
Three	229 (26.3)
All four	122 (14.0)
TC/HDL ratio	
Ratio value, m ± SD	4.64 ± 2.14
High ratio (≥5), n (%)	289 (33.2)

Abbreviations: N, number; HDL-C, High-density lipoprotein-cholesterol; LDL-C, Low-density lipoprotein-cholesterol; TC, Total cholesterol; TGs, Triglycerides; m ± SD, mean ± standard deviation.

Table 3 Prevalence Rates of Dyslipidemia Patterns Among Patients with Type 2 Diabetes According to Studied Characteristics

	Low HDL-C M<40; F<50 mg/dl n (%)	High LDL-C ≥ 100 mg/dl n (%)	Hypercholesterolemia ≥ 200 mg/dl n (%)	Hypertriglyceridemia ≥ 150 mg/dl n (%)	Dyslipidemia ≥ 1 abnormality n (%)	High TC/HDL Ratio ≥ 5 n (%)
Overall	576 (66.2)	540 (62.1)	250 (28.7)	506 (58.2)	795 (91.4)	289 (33.2)
Age groups (years)						
30–39	13 (52.0)	16 (64.0)	8 (32.0)	14 (56.0)	20 (80.0)	9 (36.0)
40–49	49 (53.8)	72 (79.1)	40 (44.0)	62 (68.1)	85 (93.4)	39 (42.9)
50–59	194 (70.5)	188 (68.4)	87 (31.6)	171 (62.2)	260 (94.5)	99 (36.0)
60–69	177 (64.4)	165 (60.0)	74 (26.9)	151 (54.9)	249 (90.5)	84 (30.5)
70–79	121 (70.8)	90 (52.6)	34 (19.9)	93 (54.4)	155 (90.6)	52 (30.4)
≥80	22 (66.7)	9 (27.3)	7 (21.2)	15 (45.5)	26 (78.8)	6 (18.2)
p-value	0.025	<0.001	0.002	0.076	0.010	0.084
Gender						
Women	288 (71.8)	273 (68.1)	144 (35.9)	253 (63.1)	380 (94.8)	125 (31.2)
Men	288 (61.4)	267 (56.9)	106 (22.6)	253 (53.9)	415 (88.5)	164 (35.0)
p-value	0.001	0.001	<0.001	0.006	0.001	0.236
Body Mass Index (BMI) (kg/m2) (Total n. = 752)						
Healthy weight, n=137	68 (49.6)	64 (46.7)	27 (19.7)	50 (36.5)	100 (73.0)	35 (25.5)
Overweight, n=262	179 (68.3)	153 (58.4)	68 (26.0)	153 (58.4)	244 (93.1)	86 (32.8)
Obese, n=353	252 (71.4)	239 (67.7)	114 (32.3)	234 (66.3)	340 (96.3)	132 (37.4)
p-value	<0.001	<0.001	0.014	<0.001	<0.001	0.042
Smoking Status						
Never smoked	382 (66.4)	359 (62.4)	170 (29.6)	324 (56.3)	519 (90.3)	176 (30.6)
Former smoker	76 (60.8)	73 (58.4)	28 (22.4)	66 (52.8)	115 (92.0)	40 (32.0)
Current smoker	118 (69.4)	108 (63.5)	52 (30.6)	116 (68.2)	161 (94.7)	73 (42.9)
p-value	0.297	0.637	0.231	0.009	0.186	0.011

Comorbidities						
Hypertension						
Yes	517 (72.6)	461 (64.7)	216 (30.3)	453 (63.6)	699 (98.2)	256 (36.0)
No	59 (37.3)	79 (50.0)	34 (21.5)	53 (33.5)	96 (60.8)	33 (20.9)
p-value	<0.001	0.001	0.027	<0.001	<0.001	<0.001
Hx of Ischemic heart disease (IHD)						
Yes	212 (77.4)	189 (69.0)	93 (33.9)	189 (69.0)	273 (99.6)	116 (42.3)
No	364 (61.1)	351 (58.9)	157 (26.3)	317 (53.2)	522 (87.6)	173 (29.0)
p-value	<0.001	0.004	0.021	<0.001	<0.001	<0.001
Hx of Stroke						
Yes	67 (82.7)	59 (72.8)	31 (38.3)	60 (74.1)	81 (100.0)	35 (43.2)
No	509 (64.5)	481 (61.0)	219 (27.8)	446 (56.5)	714 (90.5)	254 (32.2)
p-value	0.001	0.036	0.046	0.002	0.004	0.045
Hx of Chronic Kidney Disease (CKD)						
Yes	36 (76.6)	26 (55.3)	13 (27.7)	28 (59.6)	44 (93.6)	15 (31.9)
No	540 (65.6)	514 (62.5)	237 (28.8)	478 (58.1)	751 (91.3)	274 (33.3)
p-value	0.122	0.327	0.867	0.840	0.574	0.845
Diabetes Situation						
Diabetes duration (yrs) (Total n. = 731)						
≤ 10 yrs, n=353	233 (66.0)	189 (53.5)	67 (19.0)	195 (55.2)	321 (90.9)	93 (26.3)
> 10 yrs, n=378	253 (66.9)	276 (73.0)	163 (43.1)	239 (63.2)	351 (92.9)	161 (42.6)
p-value	0.791	<0.001	<0.001	0.028	0.340	<0.001
Glycemic control (based on HbA1c)						
Well-controlled (HbA1c≤7%)	174 (63.3)	130 (47.3)	38 (13.8)	133 (48.4)	241 (87.6)	61 (22.2)
Poor-controlled (HbA1c>7%)	402 (67.6)	410 (68.9)	212 (35.6)	373 (62.7)	554 (93.1)	228 (38.3)
p-value	0.214	<0.001	<0.001	<0.001	0.007	<0.001

(*Continued*)

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Table 3 (Continued).

	Low HDL-C M<40; F<50 mg/dl n (%)	High LDL-C ≥ 100 mg/dl n (%)	Hypercholesterolemia ≥ 200 mg/dl n (%)	Hypertriglyceridemia ≥ 150 mg/dl n (%)	Dyslipidemia ≥ 1 abnormality n (%)	High TC/HDL Ratio ≥ 5 n (%)
Diabetes Complications						
Retinopathy						
Yes	110 (72.8)	112 (74.2)	58 (38.4)	107 (70.9)	145 (96.0)	65 (43.0)
No	466 (64.8)	428 (59.5)	192 (26.7)	399 (55.5)	650 (90.4)	224 (31.2)
p-value	0.054	0.001	0.004	0.001	0.025	0.005
Peripheral Vascular Disease (PVD)						
Yes	45 (83.3)	46 (85.2)	25 (46.3)	40 (74.1)	54 (100.0)	26 (48.1)
No	531 (65.1)	494 (60.5)	225 (27.6)	466 (57.1)	741 (90.8)	263 (32.2)
p-value	0.006	<0.001	0.003	0.014	0.020	0.016
Peripheral Neuropathy						
Yes	41 (70.7)	43 (74.1)	29 (50.0)	45 (77.6)	56 (96.6)	34 (58.6)
No	535 (65.9)	497 (61.2)	221 (27.2)	461 (56.8)	739 (91.0)	255 (31.4)
p-value	0.455	0.050	<0.001	0.002	0.146	<0.001
Nephropathy						
Yes	131 (63.6)	123 (59.7)	58 (28.2)	120 (58.3)	183 (88.8)	64 (31.1)
No	445 (67.0)	417 (62.8)	192 (28.9)	386 (58.1)	612 (92.2)	225 (33.9)
p-value	0.364	0.424	0.833	0.976	0.136	0.453

Abbreviations: T2DM: N, number; BMI, Body mass index; HTN, Hypertension; IHD, Ischemic heart disease; CKD, chronic kidney disease; BP, Blood pressure; FBS, Fasting blood sugar; Hb, Hemoglobin; m ± SD, mean ± standard deviation.

Abnormal BMI was significantly associated with all patterns of dyslipidemia in T2DM patients. The prevalence rates of low HDL-C and high LDL-C were significantly higher among obese and overweight diabetic participants than those with normal BMI ones. Similarly, the highest proportions of hypercholesterolemia, hypertriglyceridemia, and high TC/HDL ratio were noticed among patients with T2DM and obesity (p=0.014, p<0.001, p=0.042; respectively). The difference in the prevalence of dyslipidemias was not statistically significant by smoking status except for hypertriglyceridemia and high TC/HDL ratio.

The rates of four dyslipidemia patterns and high TC/HDL ratio were significantly higher in subjects with T2DM who have comorbidity of HTN, IHD, or stroke than in those who did not have one of these comorbidities.

Dyslipidemia Patterns by Clinical Characteristics

Significant associations of dyslipidemia with prolonged T2DM duration and poor glycemic control were observed. Having T2DM for longer than 10 years was significantly associated with higher prevalence rates of high LDL-C (73.0%), hypercholesterolemia (43.1%), hypertriglyceridemia (63.2%), and high TC/HDL ratio (42.6%) than those with a DM duration of ≤10 years since diagnosis (53.5%, 19.0%, 55.2%, and 26.3%; respectively).

There were significant positive correlations of DM duration with LDL-C (r=0.200, p<0.001), TC (r=0.173, p<0.001), and TC/HDL ratio (r=0.138, p<0.001). Also, a weak positive correlation was observed between DM duration and TGs but did not reach statistical significance (r=0.066, p=0.076).

Compared to the well-controlled patients with T2DM, poorly controlled T2DM patients had significantly higher proportions of high LDL-C (68.9% vs 47.3%), hypercholesterolemia (35.6% vs 13.8%), hypertriglyceridemia (62.7% vs 48.4%), and high TC/HDL ratio (38.3% vs 22.2%) (p<0.001 for each). However, Low HDL-C prevalence did not differ significantly by DM duration and glycemic control. Table 3 shows the prevalence of dyslipidemia patterns among patients with T2DM by their T2DM characteristics and complications based on univariate analyses.

Regarding diabetic complications, high LDL-C, hypercholesterolemia, hypertriglyceridemia, and high TC/HDL ratio were significantly more prevalent among diabetic participants having retinopathy, PVD, or peripheral neuropathy than those with no such diabetic complications ($p \leq 0.05$).

Approximately two-thirds of the diabetic participants (n=608, 69.9%) used lipid-lowering medications. Out Of the 597 (68.6%) statins used T2DM participants, 20.3% had hypercholesterolemia, and 28.1% had a high TC/HDL ratio compared to 47.3% and 44.3% among participants not taking statins ($p<0.001$ for each). Also, low HDL-C and high LDL-C were significantly lower prevalent among subjects with T2DM on statins than those not taking statins (Low HDL-C: 63.1% vs 72.9%, $p=0.005$; High LDL-C: 52.8% vs 82.4%, $p<0.001$). Hypertriglyceridemia prevalence was lower among the diabetic participants on statin therapy (56.3%) than those without statin therapy (62.3%); however, the difference did not reach statistical significance ($p=0.096$). There were no significant differences in prevalence rates of high LDL-C, hypercholesterolemia, and high TC/HDL ratio by fibrates therapy. The prevalence of dyslipidemia patterns in the diabetic population was not significantly different by diabetes medications. However, the prevalence of low HDL-C was significantly lower among subjects with T2DM with Metformin therapy (64.4%) than those with no such medication (73.1%) ($p=0.028$) (Supplementary Table 2).

Multivariate Analysis of Factors Associated with Dyslipidemias

Table 4 and Supplementary Table 3 illustrate Multivariate analysis findings for low HDL-C, high LDL-C, hypercholesterolemia, and hypertriglyceridemia. Female gender, being obese, having HTN, and using Beta-blockers appeared as common factors associated with having an abnormal value in all four lipid parameters. Statins therapy was a significant factor with decreased odds of low HDL-C, high LDL-C, and hypercholesterolemia (p<0.001 for each), while fibrates were associated with decreased odds of low HDL-C (p<0.001) and hypertriglyceridemia (p=0.034). Also, being on insulin was associated with decreased odds of high LDL-C (p<0.001) and hypercholesterolemia ($p=0.002$).

Having diabetic disease for more than ten years and poor glycemic control were associated with high LDL-C and TC. Also, poor glycemic controlled T2DM patients were 1.71 times more likely to have hypertriglyceridemia (95% CI 1.165–2.514; $p=0.006$). T2DM with co-morbid IHD or stroke was significantly associated with low HDL-C, high LDL-C, and hypercholesterolemia ($p<0.05$).

Table 4 Multivariate Analysis of Factors Associated with Low HDL, High LDL, Hypercholesterolemia, and Hypertriglyceridemia Among Patients with Type 2 Diabetes

Variable	Adjusted Odds Ratio	95% Confidence Interval	*p*-value
Low high-density lipoprotein-cholesterol (Low HDL-C)			
Gender (Female)	1.828	1.256–2.660	0.002
Body Mass Index (BMI)			
Healthy weight	REF	REF	REF
Overweight	1.829	1.097–3.051	0.021
Obese	1.775	1.079–2.919	0.024
Hypertension	2.184	1.342–3.553	0.002
Hx of Ischemic Heart Disease	1.701	1.084–2.671	0.021
Hx of Stroke	2.226	1.076–4.603	0.031
High low-density lipoprotein-cholesterol (High LDL-C)			
Gender (Female)	1.912	1.280–2.857	0.002
Body Mass Index (BMI)			
Healthy weight	REF	REF	REF
Overweight	1.421	0.841–2.400	0.189
Obese	1.878	1.123–3.142	0.016
Hypertension	2.778	1.557–4.959	0.001
Hx of Ischemic Heart Disease	3.325	2.052–5.387	<0.001
Hx of Stroke	4.653	2.118–10.222	<0.001
Diabetes duration > 10 yrs	2.533	1.670–3.842	<0.001
Poor-controlled diabetes (HbA1c>7%)	2.369	1.527–3.676	<0.001
Hypercholesterolemia			
Gender (Female)	1.540	1.018–2.331	0.041
Body Mass Index (BMI)			
Healthy weight	REF	REF	REF
Overweight	1.457	0.863–2.459	0.159
Obese	1.687	1.023–2.784	0.043
Hypertension	2.128	1.142–3.965	0.017
Hx of Ischemic Heart Disease	2.088	1.266–3.445	0.004
Hx of Stroke	1.994	1.011–3.932	0.046
Diabetes Duration > 10 yrs	3.337	2.141–5.200	<0.001
Poor-controlled Diabetes (HbA1c>7%)	4.074	2.375–6.987	<0.001

(*Continued*)

Table 4 (Continued).

Variable	Adjusted Odds Ratio	95% Confidence Interval	*p*-value
Hypertriglyceridemia			
Gender (Female)	2.005	1.325–3.035	0.001
Body Mass Index (BMI)			
Healthy weight	REF	REF	REF
Overweight	2.031	1.206–3.422	0.008
Obese	2.670	1.598–4.461	<0.001
Smoking Status			
Never smoked	REF	REF	REF
Former smoker	1.174	0.706–1.950	0.537
Current smoker	2.527	1.496–4.270	0.001
Hypertension	3.054	1.816–5.136	<0.001
Poor-controlled diabetes (HbA1c>7%)	1.712	1.165–2.514	0.006

Abbreviations: n, number; HDL-C, High-density lipoprotein-cholesterol; LDL-C, Low-density lipoprotein-cholesterol.

Age was significantly associated with high LDL-C. Current smokers were more likely to develop hypertriglyceridemia (adjusted OR, 2.527; 59% CI 1.496–4.270, p=0.001) than ex-smokers and those who never smoked. In contrast, age and smoking were not significant risk factors for other dyslipidemia patterns (Table 4, Supplementary Table 3).

Discussion

These findings of this cross-sectional study shed light on dyslipidemia as a widely prevalent uncontrolled health problem among the Jordanian T2DM population (91.4%). Female gender, obesity, cardiovascular comorbidities, prolonged T2DM duration, poor glycemic control, and the use of statins, fibrates, insulin, and Beta-blockers were associated with dyslipidemia among patients with T2DM.

Compared to a previous similar study conducted in Jordan between June 2005 and July 2006 on Jordanian patients with T2DM, remarkable declines in the prevalence rates of dyslipidemia patterns are observed. The frequency of low HDL-C declined from 83.9% in 2005–2006 to 66.2% in 2017–2019; high LDL-C prevalence decreased from 91.5% to 62.1%; hypercholesterolemia prevalence declined from 77.2% to 28.7%; and the frequency of hypertriglyceridemia decreased from 83.1% to 58.2%.[23] This decline could be attributed to the differences in cohorts' characteristics. In the Abdel-Aal et al. T2DM cohort, most patients were overweight or obese (90.9%) compared to 81.7% in our cohort, and they included more women and younger patients. Besides, Abdel-Aal et al study showed higher rates of diabetic nephropathy, retinopathy, and hypothyroidism, which are associated with a higher prevalence of dyslipidemia. From another insight, this decline over the last decade could be attributed to the development of healthcare systems in Jordan.[24]

In contrast, a more recent study conducted on Jordanian T2DM patients by AL-Eitan et al in 2014 reported dyslipidemia patterns frequency similar to our findings.[25] The authors found that 87.3% of T2DM participants had dyslipidemia which approximates our findings of 91.4%. Also, similar to our results, they reported low HDL-C and high LDL-C as the most common form of dyslipidemia, with prevalence rates of 62.0% and 60.3%, respectively.[25]

However, the current study revealed that dyslipidemias are highly prevalent among T2DM patients, which indicated a remarkable association between dyslipidemia and T2DM. This finding is in line with the reports from our region and other countries.[26–32] There are variations in the frequency and phenotype of dyslipidemia patterns among studies in the literature that could be attributed to different populations' characteristics, studies design, racial differences, lifestyle patterns, therapeutic approaches and investigation methods across these studies.[33,34]

A remarkable finding of this study was that the prevalence rates of all dyslipidemia patterns declined after 60 years of T2DM patients' age, with observed prevalence peaks at the age group of 40–49 years for high LDL-C, hypercholesterolemia, hypertriglyceridemia, and high TC/HDL ratio. Similar findings were reported previously,[2,35,36] These findings could be explained by the higher mortality rate of subjects with T2DM with dyslipidemia before the age of 60; thus, survival or attrition bias cannot be excluded.[35]

Women, obese, and hypertensive patients were at higher risk for developing the four dyslipidemia patterns. The effect of gender on dyslipidemia in T2DM patients remains controversial. Several studies conducted in different countries reported higher prevalence rates of dyslipidemias in females than males.[23,37,38] On the other hand, other studies reported no association.[39,40] However, the observed gender-based difference in our results could be attributed to the post-menopausal state of female subjects, which is associated with low estrogen production, thus, an unfavorable lipid profile.[41] Obesity and hypertension are well-identified risk factors for dyslipidemia by many studies including international guidelines and ours.[2–4,23,36,40,42,43,48] Our study results also indicated that current smokers were more likely to develop hypertriglyceridemia, which was reported elsewhere.[25,36,40]

In the present study, poor glycemic control was an independent risk factor for developing high LDL-C, hypercholesterolemia, and hypertriglyceridemia among T2DM patients. This finding confirms earlier results by others.[10,39,44] In addition, it has been estimated that a decline in the HbA1c level by 0.2% could lower the mortality rate by 10%.[45] But other studies disputed the significant difference between the serum concentrations of cholesterol and triglycerides with relation to HbA1c level.[23,46]

Of notice, approximately two-thirds of the T2DM patients in this study did not achieve the glycemic controlling goal, with a reported mean (SD) HbA1c of 8.33 (2.19). This finding reflects the poor glycemic status of most subjects with T2DM in our study, which is concordant with the findings of earlier studies from Jordan.[23,25] This finding could be attributed to poor drug compliance, an unhealthy lifestyle, and high BMIs.

Our data identify that prolonged T2DM duration was an independent risk factor for developing high LDL-C and hypercholesterolemia. As well it was correlated with TC/HDL ratio. Similar evidence has been reported by other studies.[39,40,47] While a previous study found that T2DM duration was not significantly related to high LDL, and low HDL-c.[23]

The current study findings indicate significant associations between certain microvascular and macrovascular diabetic complications with different dyslipidemia patterns in T2DM patients. These findings are consistent with other studies,[36,48,49] which in all indicate a bidirectional association between dyslipidemia and diabetic complications.

Statin therapy was a significant protective factor from low HDL-C, high LDL-C, and hypercholesterolemia, while fibrates were an effective protective medication from low HDL-C and hypertriglyceridemia. The efficacy and safety of statins have already been well documented in subjects with T2DM.[50,51] Therefore, most subjects with T2DM should receive statin therapy.[52,53] Also, we have observed that insulin therapy was a significant protective factor from high LDL-C and hypercholesterolemia. These findings are in agreement with a previous study reporting anti-atherogenic effects and lipid metabolism activation with insulin therapy.[54]

Study Strengths and Limitations

This study had several strengths. It updates our knowledge regarding dyslipidemia patterns and their associated factors among patients with T2DM. The study included participants with at least two laboratory measurements of lipid profile one year apart rather than single values. This study has some limitations. First, this study did not include individual changes over time with no follow-up of patients. Thus, this study could not judge whether dyslipidemia developed before or after the studied factors, and the temporal sequence from cause to effect could not be established. Second, most of the patients' information was obtained from electronic hospital records. Thereby, potential confounders were not adjusted in this study, such as a family history of dyslipidemia, patients' compliance with their medications, and adherence to a healthful diet and exercise program. Third, we did not measure Glutamic Acid Decarboxylase (GAD) or islet cell autoantibodies to exclude those other than T2DM patients. However, we rely on the age, insulin history, T2DM duration, absence of ketosis events history or ketonuria, and C-peptide test result at the time of T2DM diagnosis to exclude the probability of T1DM and LADA among our patients. Fourth, some types of selection bias cannot be excluded because

the study subjects attended family medicine clinics at a tertiary hospital and were already under medical care. Fifth, the representativeness of our sample may be limited since this was a single-center based study.

Conclusion

Dyslipidemia is highly prevalent among patients with T2DM Female gender, overweight or obesity, HTN, prolonged T2DM duration, poor glycemic control, and diabetic vascular complications were associated with a higher risk of dyslipidemia patterns. In contrast, lipid-lowering medications and insulin could effectively manage dyslipidemia.

A change in the therapeutic approach used for subjects with T2DM is recommended, emphasizing the cornerstone roles of healthy lifestyle modifications and pharmacological interventions toward decreasing T2DM dyslipidemia incidence, prevalence, and complications. Prospective and longitudinal follow-up studies from different centers are strongly recommended.

Data Sharing Statement

The datasets used and analyzed during the current study are available from the corresponding author on a reasonable request.

Ethics Approval

All procedures performed in this study involving human participants were reviewed and ethically approved by the Institutional Review Board (IRB) at Jordan University of Science and Technology (JUST), Irbid, Jordan (20210096). This study was conducted following the 1975 Helsinki declaration, as revised in 2008, and its later amendments or comparable ethical standards.

Consent to Participate

Informed consent from the participant was waived by the IRB due to the retrospective design of the study.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors declare that they have no competing interests in this work.

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