

Research Article

Lipid/Lipoprotein Abnormalities Among Adult Type 1 Diabetics in Nigeria

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Abstract: Background: Dyslipidemia abounds among diabetics. However, these are poorly characterized among patients with type 1 diabetes (T1DM). The current study determined the pattern of dyslipidemia and their relationship with glycemic status among adult T1DM subjects. Methods: This survey was conducted retrospectively among 346 newly-diagnosed/treatment-naïve T1DM adults attending outpatient units of a third-level hospital in Nigeria. Patients' fasting plasma glucose and lipid parameters at the time of T1DM diagnosis were abstracted from their medical files. Lipid parameters included triglyceride (Tg), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C). Abstracted parameters were analyzed using descriptive and comparative statistics. Results: Of the 346 studied, 46.8% (n=162) were dyslipidemic (aged: 32.69±6.29) with female predominance (59.3%; p=0.018). Categorically, females predominated among isolated dyslipidemias while males predominated among the combined/mixed dyslipidemias. High plasma Tg concentration (n=142; 87.7%) was the most common isolated dyslipidemia without male/female difference (p>0.05); seconded by low HDL-C (n=80; 49.4%) with the females predominating (p<0.05). The most combined and mixed dyslipidemia was high plasma Tg/low HDL-C (total n=28, 17.3%; males n=16, 24.2% vs. females n=12, 12.5%; p=0.011) and high plasma Tg/high LDL-C/low-HDL-C (total n=30, 18.5%; males n=18, 27.3% vs. females n=12, 12.5%; p=0.001) concentrations, respectively with male predominance. The female dyslipidemias were younger with lower BMI, higher systolic blood pressure, glycemia, and mean plasma Tg levels (p<0.05). The overall dyslipidemias had poor glycemic status and their risk of dyslipidemia increases with worsening glycemia. Conclusion: Dyslipidemia was common and associated with poor glycemic status among the studied cohorts. This finding informs the need for more rigorous monitoring of dyslipidemia among T1DM subjects to reduce the risk of its complications.

Keywords: Diabetes, Type 1 Diabetes, Lipid/Lipoprotein Abnormalities

1. Introduction

Dyslipidemia (lipid/lipoprotein abnormalities) abound among patients with diabetes mellitus (DM) of type 1 (T1DM), type 2 (T2DM) and various other forms of DM. [1-5] These

abnormalities are cardinal components in the etiopathogenesis of a vast number of atherosclerotic vascular (microvascular and macrovascular) complications generally reported among patients with DM. [2, 3] Studies have also consistently demonstrated that lipid/lipoprotein abnormalities serve as mediators between DM and the these atherosclerotic vascular

complications. [3, 6].

Dyslipidemia in DM, which could either be quantitative, qualitative, or kinetic aberrations, are purported to be direct consequences of the relative/absolute deficiency of insulin hormone, characteristic of DM. [1, 4] The insulin deficiency alters the physiologic functions the hormone exercises over lipid/lipoprotein metabolism, thereby promoting atherosclerotic vascular complications. [1-4] The co-existence of atherosclerotic vascular complications occasioned by lipid/lipoprotein abnormalities significantly confers an increased risk of adverse health outcomes in the course of DM. [2-6].

Contrary to T2DM, studies on lipid/lipoprotein abnormalities among subjects with T1DM are limited in the literature. Moreover, the few published data had largely focused on childhood T1DM or had reported on DM generally without segregation. Furthermore, within the urban city of Uyo, Akwa Ibom State, South-south Nigeria, no study, to date, has been reported on lipid/lipoprotein abnormalities among subjects with T1DM.

Through this current study, we aimed to describe the lipid/lipoprotein abnormalities and their relationship with glycemic status among adults diagnosed with T1DM at a third-level hospital in Nigeria.

2. Materials and Methods

2.1. Study Design, Setting and Period

This was a retrospective, cross-sectional, descriptive hospital-based 5-year survey of the baseline lipid profile of newly diagnosed/treatment-naive T1DM subjects who had presented in the medical and general outpatient clinics of a third-level health facility located in Uyo, South-south Nigeria. In the health facility, all suspected non-pregnant DM patients are usually subjected to fasting glucose estimation to confirm DM status even if random plasma glucose value strongly suggests DM. The baseline lipid profile status is also determined, at DM confirmation, for all the newly diagnosed diabetics before commencement of treatment.

2.2. Ethical Considerations

The study protocol was reviewed and approved by the Institutional Research Ethics Committee. Informed consent was not deemed necessary since the study was a retrospective data-based one. However, all measures were observed to maintain the confidentiality of all subjects involved during the data acquisition.

2.3. Study Instruments and Population

The study utilized baseline lipid profile records and other related data of all the eligible subjects who presented with incident T1DM in the outpatient units of the hospital. All data were acquired from the Health Records (Department of Health Information Management) unit of the hospital.

2.4. Eligibility Criteria

The criteria for inclusion were as follows:

Newly diagnosed T1DM in UUTH between 1st January 2014 and 31st December 2018.

Aged ≥ 18 years old.

Confirmed regular clinic attendees following diagnosis.

Adequate baseline lipid profile records at the time of T1DM diagnosis.

Clinical/metabolic stability at the time of baseline lipid profile determination.

Nil record of exogenous insulin treatment before the time of baseline lipid profile determination.

Nil record of lipid-lowering medication before the time of baseline lipid profile determination.

The criteria for exclusion were as follows:

T2DM or any other DM variant.

Age < 18 years of age.

Positive pregnancy status

Patients with a fasting triglyceride level ≥ 4.5 mmol/l

Those with any other concurrent endocrinopathies at the point of data acquisition

Evidence of any chronic diseases – liver cirrhosis, chronic renal disease, cancer

Records with inadequate and incomplete dossiers.

2.5. Data Acquisition

All data, at the point of T1DM diagnosis, were retrieved from each case note and included age, gender, DM family history, cigarette/alcohol consumption, blood pressures (systolic/diastolic), weight (Wt), height (Ht), and calculated body mass index (BMI) using Wt/Ht^2 . Baseline fasting lipid profile (FLP) laboratory data retrieved were: diagnostic fasting plasma glucose (FPG) in mmol/l, triglyceride (Tg) in mmol/l, total cholesterol (TC) in mmol/l, and high-density cholesterol (HDL-C) in mmol/l. Low-density cholesterol (LDL-C) in mmol/l, was calculated using the Friedewald's formula if Tg value was less than 4.5 mmol/l. [7] The retrieved FPG and FLP data were those derived concurrently, before treatment, to confirm T1DM and to obtain baseline lipid profile status. Non-HDL-C was calculated by subtracting HDL-C from TC. Tg/HDL-C ratio was obtained by dividing Tg values by the HDL-C values. Non-HDL-C was calculated by subtracting HDL-C from TC.

Total Apolipoprotein B (ApoB), in g/l, was estimated using the following equations: $ApoB = 0.65 \times TC - 0.59 \times HDL-C + 0.01 \times TG$ when $TG < 270$ mg/dl (3.03 mmol/l) and $ApoB = 25.6 + 0.58 \times TC - 0.38 \times HDL-C - 0.06 \times TG$ when $TG > 270$ mg/dl (3.03 mmol/l). [8]

2.6. Data Stratifications

Age was stratified into five groups (< 29 , 30-39, 40-49, and > 50), BMI into four World Health Organization recommended groups (underweight < 18.5 , ideal weight 18.5-24.9, overweight 25-29.9, and obese > 30). [9] Blood pressure was stratified into three groups (normotensive, pre-hypertensive, and hypertensive) based on the Joint

National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) recommendations. [10] Glycemic status, estimated with FPG, was arbitrarily stratified into three (fair: 7.0-9.9 mmol/l, poor: 10-11.9 mmol/l, very poor>12.0 mmol/l) groups.

2.7. Laboratory Protocols

During the study period, specimen collection (following a 12-hour overnight fast) and laboratory protocols had been done using standardized and well-established methodologies. Fasting venous plasma glucose was determined using the enzymatic oxidase-peroxidase principle in fluoridated-plasma, while Tg, TC, and HDL-C were estimated based on the enzymatic principles in heparinized plasma, respectively. Laboratory analyses were carried out on Selectra ProM (ELITech Group, Holland) automated chemistry analyzer based on the aforementioned principles.

2.8. Laboratory Diagnosis

Diagnosis of T1DM was made using the World Health Organization guidelines in addition to the existence of the classic symptoms/signs of T1DM. [11]

Dyslipidemia was diagnosed based on the National Cholesterol Education Program/Adult Treatment Panel 111 (NCEP/ATP 111) guidelines if any of the following quantitative lipid/ lipoprotein cut-offs are met: Tg<1.7 mmol/l, TC>5.17 mmol/l, LDL-C>3.36 mmol/l, HDL-C<1.03 mmol/l (males), <1.30 mmol/l (females). [12]

2.9. Definition of Variables

T1DM cases were identified based on the following characteristics:

Diagnosed/managed by the specialist endocrinologist.

Consistently on insulin therapy for at least a year following diagnosis.

Responding to insulin therapy for at least a year following diagnosis.

Nil history of being on any oral hypoglycemic agents following diagnosis.

Dyslipidemia was further categorized as follows:

Isolated (single quantitative abnormalities of plasma Tg, TC, LDL-C, HDL-C levels based on NCEP/ATP 111)

Combined (presence of any two isolated quantitative abnormalities of plasma Tg, TC, LDL-C, HDL-C levels)

Mixed (presence of any three isolated quantitative abnormalities of plasma Tg, TC, LDL-C, HDL-C levels).

2.10. Statistical Analysis

Data was managed using Statistical Package for Social Sciences software (IBM Corp., Armonk, NY, United States of America) version 21. Non-categorical variables were summarized using means and standard deviations; comparisons between two groups performed using Student's t-tests. Categorical variables are presented using frequencies (count) and relative frequencies (percentage); the between-group comparisons performed using chi-squared

tests (χ^2) with continuity correction applied when the expected frequency is between 5 and 10 or using Fisher's exact test when the expected frequency is less than 5. Cox proportional hazard regression models (1 and 2) were used to explore the linear trend between graded glycemic strata and varied lipid/lipoprotein-defined cutoff points.

Proportional-hazards assumption was explored using the Schoenfeld residuals and no significant deviations for all covariates in model 1 were observed. Two-tailed $p < 0.05$ was considered statistically significant.

3. Results

A total of 362 T1DM subjects were identified of which 346 (95.6%) met the eligibility criteria and were enrolled for the study. The remaining 16 (4.4%) of the total 362 were excluded.

Of the 346 enrolled (Table 1; Panel A), 162 (46.8%) were dyslipidemic while 184 (53.2%) were adyslipidemic (those without lipid/lipoprotein abnormalities). The females predominated among the dyslipidemic cohorts (females: 59.3% vs. males: 40.7%; $p = 0.018$) (Table 1; Panel A).

Depicted in Table 1, Panel B, isolated dyslipidemia ($n = 81$; 50%; $p < 0.001$) was the most frequent lipid/lipoprotein abnormality observed among all the study cohorts ($n = 346$) with female predominance ($n = 49$; 51%; $p < 0.001$). However, the frequency of the combined and mixed dyslipidemia were 22.8% ($n = 37$) and 27.2% ($n = 44$), respectively, and the males predominated ($p < 0.001$) (Table 1, Panel B).

Still on Table 1, following the subcategorization of lipid/lipoprotein abnormalities among the dyslipidemic cohorts, the most frequent isolated dyslipidemia was high plasma Tg ($n = 142$; 87.7%), seconded by low plasma HDL-C ($n = 80$; 49.4%) levels. The least isolated dyslipidemia was high plasma TC ($n = 64$; 39.5%) and high plasma LDL-C levels ($n = 49$; 30.2%), though without gender difference. The females had higher frequency of isolated high plasma Tg levels (males 83.3% vs. females 90.6%) without gender difference ($p = 0.224$) and a higher frequency of isolated low plasma HDL-C level (males 33.3% vs. females 58.4%) with significant gender difference ($p < 0.001$) (Table 1). Shown also in Table 1, the most frequent combined and mixed dyslipidemia was high plasma Tg/low plasma HDL-C (Total $n = 28$, 17.3%; males $n = 16$, 24.2% vs. females $n = 12$, 12.5%; $p = 0.011$) and high plasma Tg/high plasma LDL-C/low plasma HDL-C (Total $n = 30$, 18.5%; males $n = 18$, 27.3% vs. females $n = 12$, 12.5%; $p = 0.001$) levels, respectively, with the males predominating.

No difference was observed in the mean age of the dyslipidemic (32.69 ± 6.29 ; range 23-51) compared to the adyslipidemic (33.53 ± 6.48 ; range 20-51) cohorts ($p = 0.245$).

Similarly, no difference was observed in the mean values of SBP, DBP, BMI, and BMI between the dyslipidemic and adyslipidemic cohorts ($p > 0.05$) (Table 2). The dyslipidemic cohorts presented with higher glycemic status (FPG) than their adyslipidemic counterparts ($p < 0.05$) at the time of T1DM diagnosis (Table 2).

Among the dyslipidemic cohorts, the age-group 30-39 years predominated (Table 2), The dyslipidemic cohorts also had non-significant a lower frequencies of overweight/obesity status but non-significant higher underweight and pre-hypertensive/hypertensive status compared to the adyslipidemic cohorts (p>0.05) (Table 2). Depicted in Table 2, the dyslipidemic cohorts had statistically significant higher frequencies of poor/very poor glycemic status (p<0.05) but lower frequency of family history of DM (p=0.014). The dyslipidemic and adyslipidemic cohorts were comparable regarding age, alcohol/cigarette consumption history, BMI, and blood pressure stratified data (p>0.05) (Table 2).

The dyslipidemic females were younger (females: 30.53±6.41 vs. males: 35.53±4.93 years) with lower BMI status but higher SBP, higher glycemic status, and higher plasma Tg levels compared to their dyslipidemic male cohorts

(p<0.05) (Table 3).

Based on Cox proportional regression model, the dyslipidemic cohorts with higher (poor/very poor) glycemic status had increased risk of abnormal lipid/lipoprotein parameters compared to those with lower (fair) glycemic status (Table 4). As noted in Table 4, the risk of abnormal lipid/lipoprotein parameters increases with worsening (from poor to very poor) glycemic status in Cox proportional regression models (Table 4). However, this trend demonstrated statistical significance only within the Tg (FPG=crude HR: 4.23 to 5.55; FPG=adjusted HR: 3.49 to 4.66; p trend<0.05) and within the male HDL-C (FPG=crude HR: 3.17 to 4.08; FPG=adjusted HR: 2.34 to 3.41; p trend<0.05) and female HDL-C (FPG=crude HR: 3.72 to 4.73; FPG=adjusted HR: from 2.91 to 3.62; p trend<0.05) lipid/lipoprotein fractions (Table 4).

Table 1. Lipid/lipoprotein status/abnormalities by gender.

Lipid/lipoprotein classes	All cohort, n=346	Males	Females	p-value
1. Lipid/lipoprotein status, n (%)				
a. Dyslipidemias**	162 (46.8)	66 (40.7)	96 (59.3)	0.018*
b. Adyslipidemias	184 (53.2)			
2. Categories of dyslipidemias, n (%)	n=162			0.001*
a. Isolated	81 (50)	32 (48.5)	49 (51.0)	
b. Combined	37 (22.8)	16 (24.2)	21 (21.9)	
c. Mixed	44 (27.2)	18 (27.3)	26 (27.1)	
3. Subcategories of dyslipidemias				
a. Isolated dyslipidemias, mmol/l, n (%)				
High Tg (>1.7)	142 (87.7)	55 (83.3)	87 (90.6)	0.224
High TC (>5.17)	64 (39.5)	28 (42.4)	36 (37.5)	0.624
High LDL-C (>3.36)	49 (30.2)	20 (30.2)	29 (30.2)	1.000
Low HDL-C (<1.03* ¹ , <1.30)* ²	80 (49.4)	22 (33.3)	58 (58.4)	<0.001*
b. Combined dyslipidemias, mmol/l, n (%)				
High Tg & low HDL-C	28 (17.3)	16 (24.2)	12 (12.5)	0.011*
High Tg & high TC	9 (5.6)	0 (0)	9 (9.4)	NA
c. Mixed dyslipidemias, mmol/l, n (%)				
High Tg, high LDL-C, & low HDL-C	30 (18.5)	18 (27.3)	12 (12.5)	0.001*
High Tg, high TC, & low HDL-C	11 (6.8)	0 (0)	11 (11.5)	NA
High TC, high LDL-C & low HDL-C	3 (1.9)	0 (0)	3 (3.1)	NA

*Statistical significance; **As defined by the NCEP/ATP 111*¹males; *²females; Tg: Triglyceride; TC: total cholesterol; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; NA: Not applicable.

Table 2. Comparative analyses of variables by lipid/lipoprotein status.

Variables	Dyslipidemias, n=162	Adyslipidemias, n=184	p-value
Age, years	32.69±6.29	33.53±6.48	0.245
Age range	23 - 51	20 - 51	
SBP, mmHg,	119.80±8.17	118.55±8.94	0.368
DBP, mmHg,	78.76±6.98	77.27±7.18	0.125
BMI, kg/m ²	24.13±3.84	24.92±3.65	0.197
FPG, mmol/l	11.56±2.10	9.93±1.40	0.005*
Age stratum, years, n (%)			0.771
≤29	61 (37.7)	57 (31.0)	
30-39	72 (44.4)	94 (51.1)	
40-59	28 (17.3)	26 (14.1)	
≥50	1 (0.6)	7 (3.8)	
DM family history, n (%)			0.014*
Positive	30 (18.5)	52 (28.3)	
Negative	84 (51.9)	99 (53.8)	
NA/No Response	48 (29.6)	33 (17.9)	
Alcohol consumption, n (%)			0.270
Never-drinker	124 (76.5)	145 (78.8)	
Past/present-drinker	38 (23.5)	39 (21.2)	
Cigarette consumption, n (%)			0.519
Never-smoker	151 (93.2)	171 (92.9)	

Variables	Dyslipidemics, n=162	Adyslipidemics, n=184	p-value
Past/present-smoker	11 (6.8)	13 (7.1)	
BMI stratum, n (%)			0.482
Underweight	9 (5.6)	2 (1.1)	
Ideal weight	80 (49.4)	90 (48.9)	
Overweight	66 (40.7)	78 (42.4)	
Obese	7 (4.3)	13 (7.1)	
Blood pressure stratum, n (%)			0.784
Normotensive	116 (71.7)	134 (72.9)	
Pre-hypertensive	5 (2.5)	2 (1.6)	
Hypertensive	41 (25.9)	47 (25.5)	
FPG stratum, mmol/l, n (%)			<0.001*
Fair (7.90 – 9.9)	37 (22.8)	121 (65.8)	
Poor (10.0 – 11.9)	60 (37.0)	44 (23.9)	
Very poor (≥ 12.0)	65 (40.2)	19 (10.3)	

*Statistical significance; BMI: body mass index; FPG: Fasting plasma glucose.
mmol/l: millimole per liter; SBP: systolic blood pressure; DBP: diastolic blood pressure.
BMI: body mass index; FPG: Fasting plasma glucose; mmHg: millimeter mercury.
mmol/l: millimole per liter; NA: No available data

Table 3. Comparative analyses of the clinical, glycaemic/lipid variables among the male/female dyslipidemic cohorts.

Variables, mmol/l	Males, n=66, m \pm sd	Females, n=96, m \pm sd	p-value
Age, years	35.53 \pm 4.93	30.72 \pm 6.41	0.004*
BMI, kg/m ²	25.80 \pm 2.72	22.97 \pm 4.10	<0.001*
SBP, mmHg	113.25 \pm 7.37	122.19 \pm 8.41	<0.001*
DBP, mmHg	76.63 \pm 6.48	77.71 \pm 8.84	0.090
FPG, mmol/l	11.14 \pm 1.73	12.76 \pm 2.43	0.030*
Tg, mmol/l	2.25 \pm 0.43	2.39 \pm 0.38	0.046*
TC, mmol/l	4.87 \pm 0.67	4.97 \pm 0.77	0.362
LDL-C, mmol/l	2.80 \pm 0.65	2.85 \pm 0.81	0.056
HDL-C, mmol/l	1.18 \pm 0.25	1.25 \pm 0.23	0.521
Apo B, g/l	1.30 \pm 0.11	1.32 \pm 0.10	0.367
Tg/HDL-C ratio	3.10 \pm 0.85	3.02 \pm 0.72	0.301
Non-HDL-C, mmol/l	3.20 \pm 0.82	3.21 \pm 0.71	0.284

*Statistical significant (p<0.05); BMI: body mass index; SBP: systolic blood pressure.
DBP: diastolic blood pressure; FPG: fasting plasma glucose; Tg: Triglyceride.
TC: total cholesterol; LDL-C: low-density lipoprotein cholesterol.
HDL-C: high-density lipoprotein cholesterol; ApoB: Apolipoprotein B.
kg/m²: kilogram per meter squared; mmHg: millimeter mercury.
mmol/l: millimole per liter; g/l: gram per liter; m \pm sd: mean \pm standard deviation.

Table 4. Relationship between lipid/lipoprotein cutoffs and glycaemic grades among the dyslipidemic cohorts.

	NCEP/ATP 111 Lipid/lipoprotein Cut-offs, mmol/l				
	Tg>1.7	TC>5.17	LDL-C>3.36	HDL-C<1.03* ¹	HDL-C<1.30* ²
Model 1	***HR; 95% CI	***HR; 95% CI	***HR; 95% CI	**HR; 95% CI	**HR; 95% CI
Glycaemic stratum					
Fair (Reference)	1.0	1.0	1.0	1.0	1.0
Poor	4.23; 2.73-6.23*	1.24; 0.57-2.34	1.83; 0.55-3.08	3.17; 1.73-5.33*	3.72; 1.97-6.11*
Very poor	5.51; 3.34-7.72*	1.41; 0.69-2.87	2.13; 1.14-3.95	4.08; 1.86-6.22*	4.73; 1.22-7.88*
P Trend	<0.001*	0.090	0.074	<0.001*	<0.001*
Model 2					
Glycaemic stratum					
Fair (Reference)	1.0	1.0	1.0	1.0	1.0
Poor	3.49; 2.34-4.58*	1.13; 0.34-2.54	1.56; 0.45-2.87	2.34; 0.98-3.79*	2.91; 1.84-4.13*
Very poor	4.66; 2.75-6.92*	1.20; 0.48-2.66	1.67; 0.69-3.11	3.41; 1.09-5.76*	3.82; 1.71-5.71*
P Trend	<0.009*	0.225	0.361	<0.001*	0.017*

FPG: fasting plasma glucose; Tg: Triglyceride; TC: total cholesterol; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol;
NCEP/ATP 111: national cholesterol education program/adult treatment panel 111; *¹males; *²females; HR: hazard ratio.

*Statistical significant (p<0.05).

***Adjusted for age, sex, BMI, alcohol/cigarette consumption, and DM family history (excluded those without responses/data to DM family history).

**Adjusted for age, BMI, alcohol/cigarette consumption, and DM family history (excluded those without responses/data to DM family history).

4. Discussion

In this current study, using the NCEP/ATP 111 guidelines, we had explored the pattern of lipid/lipoprotein abnormalities among newly-diagnosed/treatment-naïve T1DM adult attendees of a third-level hospital in Nigeria. To the best of our knowledge, no data exist on lipid/lipoprotein abnormalities among subjects with adult-onset T1DM within the studied region. Hence, we anticipated the current study to bridge this gap and constitute baseline data for future studies regarding lipid/lipoprotein abnormalities among adult subjects diagnosed with T1DM within the studied region.

The overall frequency of lipid/lipoprotein abnormalities obtained from the current study was 46.8%. Similar rates had previously been reported from the United States (47%) and Mexico (47%), respectively. [13, 14] In contrast, three other studies with higher rates, were recently reported from Brazil, China and also in another study from the United States. [15-17] Homma et al reported 66.1% from Brazil among adults ≥ 19 years of age, Lou et al reported 65.3% from China, and Abeg et al reported 64% from the United States. [15-17] The disparity in frequency might partly be explained by the observed different cutoff points of lipid indices used in these various studies. [18] Furthermore, our estimate of 46.8% remains comparable to the rate recently reported among the general adult population within the studied region. [19]

Following the categorization of patterns of lipid/lipoprotein abnormalities in the current study, abnormal high plasma Tg status was observed to be the most common isolated abnormality; seconded by isolated abnormal low plasma HDL-C fractions. Furthermore, the most common combined and the mixed lipid/lipoprotein abnormalities were the high plasma Tg/low plasma HDL-C and high plasma Tg/high plasma LDL-C/low plasma HDL-C lipid/lipoprotein fractions, respectively. From the foregoing, abnormal high plasma Tg status remained a common factor within the isolated, the combined, and the mixed lipid/lipoprotein abnormalities in the current study.

The finding of mostly high Tg-associated abnormalities is consistent with similar lipid/lipoprotein patterns reported recently, though among children and adolescents, in association with T1DM within the studied region. [20] In contrast, most other studies, mainly within the western populations had reported more frequencies of isolated high LDL-C abnormalities among T1DM cohorts. [15, 17] The prominence of high Tg abnormalities, in the current study, may be adduced to the carbohydrate-enriched dietary patterns prevalent within the studied region, as suggested by Jaja et al. [20] Some other authors had postulated the insulin deficiency state as a major factor and inferred that the high Tg status is a nidus for other lipid/lipoprotein abnormalities in T1DM. [21]

Female predominance was observed among the overall dyslipidemics in the current study and among those with isolated abnormal high plasma Tg concentrations, which is in line with previous data. [20, 22] Our findings might be, to a certain extent, explained by the high magnitude of insulin resistance and the direct impact of insulin resistance and

hormonal status on enzymes implicated in lipid/lipoprotein metabolism in females. [16, 23] However, the males predominated among those with combined high plasma Tg/low plasma HDL-C and mixed high plasma Tg/high plasma LDL-C/low plasma HDL-C lipid/lipoprotein abnormalities. This finding has potential clinical consequence, given the well-known relationship between combined and mixed lipid/lipoprotein abnormalities and their various adverse vascular events in DM [2-6].

Compared to the male dyslipidemic cohorts, the female dyslipidemic cohorts presented in poor/very glycemic status and with lower mean age/BMI status, but with higher mean plasma Tg levels ($p < 0.05$). These are some of the unfavorable prognostic features reported among T1DM cohorts. [15] Consistent with our findings, Homma et al had previously reported higher frequencies of poor glycemic status, higher mean Tg levels, and lower BMI status among young adult females (≥ 19 years) with T1DM in their study. [15]

The female dyslipidemics also presented with higher mean systolic blood pressure, which may be related to the higher vascular events reported among pre-menopausal T1DM females compared to T1DM males. [24]

Studies have shown that in T1DM, poor glycemic status increases plasma Tg and decreases HDL-C levels with modest influence on LDL-C. [16, 22] Consistent with the aforementioned studies, most of the dyslipidemics in the current study presented in poor glycemic status, and their dyslipidemic risk increases with worsening glycemia, however, the trend showed statistical significance only within the plasma Tg and HDL-C lipid/lipoprotein fractions. Additionally, poor glycemic status, determined using varied indices, has consistently shown associations with various unfavorable lipid/lipoprotein patterns. [15, 16, 22] Conversely, improvement in glycemic status in T1DM tends to promote favorable lipid/lipoprotein patterns. [25]

In the current study, we also observed when compared to the dyslipidemic cohorts, that the adyslipidemic cohorts reported a higher frequency of positive DM family history which may reflect their favorable healthy-lifestyle predisposition, probably prompted by their awareness of DM family history, thereby limiting the incidence of lipid/lipoprotein abnormalities among the adyslipidemic cohorts. This fact is evidenced by studies demonstrating enhanced awareness of DM risk factors and a greater likelihood of engagement in certain favorable health-protective behaviors among individuals with positive DM family history compared to those without DM family history. [26]

The current study was limited by some factors that are worthy of note. Firstly, it is a retrospective study conducted in a single health care setting whose findings may not necessarily be reflective of the entire population in the studied region. The reliance of FPG as an index of glycemic status, instead of glycated hemoglobin (HbA1c), was another limitation of the study. HbA1c testing, being an expensive test around the studied region, is not routinely done during DM diagnosis in the study center for now due to limited financial capacity on the part of the

patients. However, HbA1c testing is currently employed for long-term blood glucose monitoring in the study center.

5. Conclusion

Based on the findings of the current study, we conclude that lipid/lipoprotein abnormalities are common among our studied cohorts and compares with the literature. Abnormal high plasma Tg concentration was most common isolated dyslipidemia observed which was more pronounced among the younger females. The most combined and mixed dyslipidemia documented was a high plasma Tg/low HDL-C and high plasma Tg/high LDL-C/low-HDL-C concentrations, respectively with the males predominating. Overall, the dyslipidemics had poor glycemic status and their risk of dyslipidemia increases with worsening glycemia.

Hence, during the evaluation of adult patients with T1DM, early identification of lipid/lipoprotein abnormalities in this at-risk group may help to prevent or delay the onset of macrovascular and microvascular complications.

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Conflict of Interest

The authors declare that they have no competing interests.

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References

- [1] Athyros VG, Doumas M, Imprialos KP, Stavropoulos K, Georgiou E, Katsimardou A, et al. Diabetes and lipid metabolism. *Hormones* 2018; 17: 61-7.
- [2] Eid S, Sas KM, Abcouwer SF, Feldman EL, Gardner TW, Pennathur S, et al. New insights into the mechanisms of diabetic complications: role of lipids and lipid metabolism. *Diabetologia* 2019; 62: 1539-49.
- [3] Poznyak A, Grechko AV, Poggio P, Myasoedova VA, Alfieri V, Orekhov AN. The Diabetes Mellitus–Atherosclerosis Connection: The Role of Lipid and Glucose Metabolism and Chronic Inflammation. *Int J Mol Sci.* 2020; 21: 1835. DOI: 10.3390/ijms21051835.
- [4] Filippatos T, Tsimihodimos V, Pappa E, Elisaf M. Pathophysiology of Diabetic Dyslipidaemia. *Curr Vasc Pharmacol* 2017; 15: 566-75.
- [5] Soran H, Schofield JD, Adam S, Durrington PN. Diabetic dyslipidaemia. *Curr Opin Lipidol* 2016; 27: 313-22.
- [6] Parhofer KG. Interaction between glucose and lipid metabolism: more than diabetic dyslipidemia. *Diabetes Metab J* 2015; 39: 353-62.
- [7] Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem* 1972; 18: 499–502.
- [8] Hwang Y-C, Ahn H-Y, Lee WJ, Park C-Y, Park SW. An equation to estimate the concentration of serum apolipoprotein B. *PLoS One* 2012; 7: e51607.
- [9] Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. *World Health Organ Tech Rep Ser* 1995; 854: 1-452.
- [10] Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, et al. The Seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure: the JNC 7 report. *JAMA* 2003; 289: 2560–72.
- [11] World Health Organization. Definition and Diagnosis of Diabetes Mellitus and Intermediate Hyperglycemia: Report of a WHO/IDF Consultation. Geneva: World Health Organization; 2006.
- [12] Expert panel on detection, evaluation, and treatment of high blood cholesterol in adults. Executive summary of 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. *JAMA* 2001; 285: 2486–97.
- [13] Wadwa RP, Kinney GL, Maahs DM, et al. Awareness and treatment of dyslipidemia in young adults with type 1 diabetes. *Diabetes Care* 2005; 28: 1051-6.
- [14] González Virla B, Mercado Atri M, Molina Ayala M. Prevalence of metabolic syndrome in patients with type 1 diabetes. *Gac Med Mex* 2012; 148: 137-43.
- [15] Homma TK, Endo CM, Saruhashi T, Mori AP, Noronha RM, Monte O, Calliari LE. Dyslipidemia in young patients with type 1 diabetes mellitus. *Arch Endocrinol Metab* 2015; 59: 215-9.
- [16] Luo SH, Yang DZ, Wei XY, Ai HY, Lin QY, Liu ZY, et al. Association of insulin resistance with dyslipidemia in adults with type 1 diabetes. *Zhonghua Yi Xue Za Zhi* 2019; 99: 2665-9.
- [17] Abed E, LaBarbera B, Dvorak J, Zhang Y, Beck J, Talsania M. Prevalence of dyslipidemia and factors affecting dyslipidemia in young adults with type 1 diabetes: evaluation of statin prescribing. *J Pediatr Endocrinol Metab* 2019; 32: 327-34.
- [18] Stankute I, Dobrovolskiene R, Danyte E, Razanskaite-Virbickiene D, Jasinskiene E, Mockeviciene G, et al. Factors Affecting Cardiovascular Risk in Children, Adolescents and Young Adults with Type 1 Diabetes. *J Diabetes Res* 2019; 2019: 9134280. DOI: 10.1155/2019/9134280.
- [19] Noubiap JJ, Bigna JJ, Nansseu JR, Nyaga UF, Balti EV, Echouffo-Tcheugui JB, et al. Prevalence of dyslipidaemia among adults in Africa: a systematic review and meta-analysis. *Lancet Glob Health* 2018; 6: e998-e1007.
- [20] Jaja TC, Yarhere IE. Dyslipidaemia in Nigerian Children and Adolescents with Diabetes Mellitus: Prevalence and Associated Risk Factors. *Int J Diabetes Metab* 2019; 25: 45-51.

- [21] Verges B. Lipid disorders in type 1 diabetes. *Diabetes Metab* 2009; 35: 353-60.
- [22] Kim SH, Jung IA, Jeon YJ, Cho WK, Cho KS, Park SH, et al. Serum lipid profiles and glycemic control in adolescents and young adults with type 1 diabetes mellitus. *Ann Pediatr Endocrinol Metab* 2014; 19: 191-6.
- [23] Millstein RJ, Pyle LL, Bergman BC, Eckel RH, Maahs DM, Rewers MJ, et al. Sex-specific differences in insulin resistance in type 1 diabetes: The CACTI cohort. *J diabetes Complications*. 2018; 32: 418-23.
- [24] Huxley RR, Peters SA, Mishra GD, Woodward M. Risk of all-cause mortality and vascular events in women versus men with type 1 diabetes: a systematic review and meta-analysis. *Lancet Diabetes Endocrinol* 2015; 3: 198-206.
- [25] Shamir R, Kassis H, Kaplan M, Naveh T, Shehadeh N. Glycemic control in adolescents with type 1 diabetes mellitus improves lipid serum levels and oxidative stress. *Pediatr Diabetes* 2008; 9: 104-9.
- [26] Baptiste-Roberts K, Gary TL, Beckles GL, Gregg EW, Owens M, Porterfield D, Engelgau MM. Family history of diabetes, awareness of risk factors, and health behaviors among African Americans. *Am J Public Health* 2007; 97: 907-12.