Dyslipidaemia in Nigerian Children and Adolescents with Diabetes Mellitus: Prevalence and Associated Risk Factors

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Keywords

Dyslipidaemia · Diabetes mellitus · Children · Africa

Abstract

Background: Dyslipidaemia is prevalent in children and adolescents with type 1 diabetes and can worsen the presentation of chronic complications such as nephropathy, retinopathy, and neuropathy. The aim of this study is to determine the frequency of dyslipidaemia in children living with diabetes followed up at a paediatric endocrine clinic in southern Nigeria and to identify associations with demographic and clinical characteristics. **Methods:** The study is a cross-sectional, descriptive study of 22 children with diabetes followed up in a tertiary health care facility in southern Nigeria. Demographic data were retrieved from case files, and fasting lipid profile and HbA_{1c} levels were determined for all subjects. Lipid abnormalities were defined based on the Expert Panel on Integrated Guidelines for Cardiovascular Health Risk Reduction in Children and Adolescents. **Results:** Twenty-two subjects aged 7–18 years were studied (mean age: 14.94 ± 3.59 years). There were 12 (54.5%) females. Both genders were comparable regarding age ($p = 0.95$). Mean duration of diabetes was 3.37 ± 2.38 years. Prevalence of lipid abnormalities include: hypertriglyceridaemia (86.4%), hypercholesterolemia (22.7%), abnormal HDL-C (36.4%), high

LDL-C (13.6%), and non-HDL-C (22.7%). Hypercholesterolaemia was significantly higher in females ($p = 0.02$), and prevalence of hypertriglyceridaemia was higher in subjects ≥ 12 years ($p = 0.019$). There was no statistically significant difference in mean levels of various lipids between males and females. Six (27.3%) subjects had more than one lipid abnormality. There was no statistically significant association of lipid abnormalities with age, sex, weight category, and HbA_{1c} level. **Conclusion:** The commonest lipid abnormality was hypertriglyceridaemia. About a quarter of the subjects had more than 1 lipid abnormality. Programs should therefore be targeted at improved control of glycemia and lipid levels to delay and prevent chronic complications.

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Introduction

Dyslipidaemia is defined as any abnormality in plasma lipid levels such as decreased high-density lipoprotein (HDL), increased low-density lipoprotein (LDL), triglyceride, or total cholesterol levels [1, 2]. In youths and adolescents with type 1 diabetes, abnormal lipid levels are a major risk factor for cardiovascular disease later in life and can worsen the presentation of other chronic compli-

cations such as nephropathy, retinopathy, and neuropathy with adverse effects on quality of life and life expectancy [3, 4].

The effect of lipid abnormalities in diabetes may not be obvious in childhood but may start in childhood and track into adulthood [1, 5]. The prevalence of lipid abnormalities in children vary with a higher prevalence in children and youths living with diabetes. The frequency of dyslipidaemia in children with type 1 diabetes mellitus (T1DM) varies with prevalence rates as low as 3.8% and as high as 72.5% in different studies [4, 6, 7].

Lipid levels may be affected by several factors, such as glycaemic control, age, duration of diabetes, activity level, diet, and weight category [8]. According to the International Society for Pediatrics and Adolescent Diabetes (ISPAD), screening fasting lipid levels in children and adolescents is recommended from 11 years of age when diabetes is stabilized. However, in children with a family history of hypercholesterolaemia, early cardiovascular disease, or unknown family history, screening should start at 2 years of age [9]. The ISPAD guidelines were inconclusive regarding the other types of lipids but an LDL cholesterol level >2.6 mmol/L (100 mg/dL) was regarded as an indication for intervention to improve metabolic control [9].

In developing countries, reports on dyslipidaemia in diabetes have been mainly in adults. Studies in African children and adolescents living with T1DM are scarce. The pattern of dyslipidaemia in children living with diabetes in sub-Saharan Africa is not widely reported. So the aim of this study is to determine the frequency and pattern of dyslipidaemia in Nigerian children with diabetes followed up at a paediatric endocrine clinic in southern Nigeria and to identify associations with demographic and clinical characteristics.

Methodology

All subjects <18 years treated for diabetes mellitus (DM) with insulin from diagnosis and followed up in the paediatric endocrinology unit from January 1, 2013, till August 2016 were invited to participate in the study. Data on present age, sex, duration of diabetes, admission history, and insulin type and dose used in last month, and history of smoking was obtained from the patient's folder and patients. All patients had HbA_{1c} and fasting lipid profile done at no cost. Subjects 18 years and older, patients not receiving insulin, and those on lipid-lowering drugs were excluded from the study.

Data was collected over 3 months from August to October 2016. Informed consent was obtained from all participants. All parents who gave their consent for the study were instructed concerning fasting by the patient for 12 h the night before presenting

for sample collection. All patients were evaluated and weight and height were measures according to a standard protocol, and BMI and height z scores were determined using WHO Anthroplus Software. BMI z score was classified into weight categories of low weight, normal weight, overweight, and obesity. Weight status was classified as underweight z score of <-1 , normal weight as z score from -1 to $+1$, overweight as $+1$ to $+2$, and obesity as z score ≥ 2 [10].

Fasting lipid levels were determined using a Randox reagent kit (Liverpool, UK) and HbA_{1c} by the BIO-RADin2it™ analyzer (UK). Lipid abnormalities were defined based on the Expert Panel on Integrated Guidelines for Cardiovascular Health Risk Reduction in Children and Adolescents [11]. Lipid levels were classified into normal and abnormal levels. Abnormal levels were described as total Cholesterol ≥ 200 mg/dL, triglyceride ≥ 150 mg/dL, HDL-C ≤ 45 mg/dL, and LDL-C ≥ 130 mg/dL. Non-HDL-C ≥ 130 mg/dL was used by adding 30 mg/dL to ISPAD target LDL of 100 mg/dL [9]. Dyslipidaemia was diagnosed when one or more lipid values were abnormal [1]. HbA_{1c} was classified as normal if $<7.5\%$ and abnormal if $\geq 7.5\%$ [7]. Subjects were also classified into groups <12 years and from 12 to 19 years of age. Duration of diabetes was classified into <5 years and ≥ 5 years.

Data was entered into a spreadsheet, and analysis was done using SPSS version 20 (Chicago, IL, USA). Descriptive and comparative analyses were performed using descriptive statistics. Means were compared using independent t test, and the χ^2 test and Fisher's exact t test were used to compare proportions.

Results

Twenty-two subjects were analyzed (age range: 7–18 years; mean age: 14.94 ± 3.59 years); their mean duration of diabetes was 3.37 ± 2.38 years. There were 12 females (54.5%) in the study population, and their mean age of 14.99 ± 3.70 years was not significantly different from the mean age of 14.88 ± 3.64 for males ($p = 0.95$). There was no history of smoking in any subject studied.

Table 1 shows the demographic and clinical parameters by gender. The mean duration of DM, HbA_{1c}, total cholesterol, triglycerides, and non HDL-C were higher in females; however, these findings were not statistically significant. Mean levels of total cholesterol, triglycerides, HDL-C, LDL-C, and non HDL-C of the study population were 154 ± 48.64 , 214 ± 73.00 , 54.19 ± 15.65 , 76.85 ± 37.30 , and 100.38 ± 45.45 respectively.

Nineteen (86.4%) subjects had at least 1 abnormal lipid value while 6 (27.3%) subjects had 2 or more lipid abnormalities; only 2 (9.0%) subjects had no lipid abnormality. Tables 2 and 3 show the prevalence of different lipid abnormalities by sex and age group, respectively. The commonest dyslipidaemias were hypertriglyceridaemia in 19 (86.4%) and low HDL-C level in 8 (36.4%). The prevalence of hypercholesterolaemia was significantly

Table 1. Demographic and clinical parameters of the subjects

Mean parameters	Total	Female	Male	<i>p</i> value
Subjects, <i>n</i>	22 (100%)	12 (54.5%)	10 (45.5%)	
Age, years	14.94±3.6	14.96±3.7	14.88±3.6	0.95
Duration of DM, years	3.37±2.4	3.85±2.7	2.75±1.9	0.28
Height <i>z</i> score	-0.86±1.82	-0.40±1.86	-1.44±1.66	0.18
BMI <i>z</i> score	0.00±1.25	1.00±1.04	0.00±1.4	
Insulin dose, units/kg/day	0.83±0.39	0.80±0.45	0.87±0.32	0.70
HbA _{1c} , %	7.92±2.12	8.57±2.18	7.09±1.80	0.096
Total cholesterol, mg/dL	154.08±48.64	159.47±63.16	147.08±19.18	0.557
Triglycerides, mg/dL	212.20±76.74	233.73±77.94	184.22±68.96	0.128
HDL-C, mg/dL	54.19±15.66	53.72±14.21	54.80±18.15	0.87
LDL-C, mg/dL	76.85±37.30	77.77±46.56	75.66±22.53	0.897
Non-HDL, mg/dL	100.38±45.45	106.66±56.90	92.22±24.51	0.463

Means ± SD are shown except for subject number and BMI *z* score (median).

Table 2. Prevalence of lipid abnormalities by sex

Lipid type	Total	Female	Male	χ^2 (<i>p</i> value)
Total cholesterol				5.39 (0.02)
Normal	17 (77.3%)	7 (58.3%)	10 (100%)	
Abnormal	5 (22.7%)	5 (41.7%)	0 (0%)	
Triglycerides				0.206 (0.650)
Normal	3 (13.6%)	2 (16.7%)	1 (10%)	
Abnormal	19 (86.4%)	10 (83.3%)	9 (90%)	
HDL-C				1.473 (0.225)
Normal	14 (63.6%)	9 (75%)	5 (50%)	
Abnormal	8 (36.4%)	3 (25%)	5 (50%)	
LDL-C				2.895 (0.089) ^a
Normal	19 (86.4%)	9 (75%)	10 (100%)	
Abnormal	3 (13.6%)	3 (25%)	0 (0%)	
Non-HDL-C				1.691 (0.193)
Normal	17 (77.3%)	8 (66.7%)	9 (90%)	
Abnormal	5 (22.7%)	4 (33.3%)	1 (10%)	

Numbers of subjects are shown. ^a Fisher's exact test.

higher in females ($p = 0.02$). There was no difference in the prevalence of other lipid abnormalities between the sexes. The prevalence of hypertriglyceridaemia in subjects ≥ 12 years was significantly higher than in subjects < 12 years ($p = 0.019$). There was no statistically significant difference in the prevalence of other lipid abnormalities according to age group (Table 3).

Table 4 shows the difference in mean variables between subjects with ≥ 2 and < 2 dyslipidaemias. There was no statistically significant difference in the mean HBA_{1c},

age, BMI percentile, and insulin dose between both age groups. In view of the fact that only 2 subjects did not have dyslipidaemia, subjects who had more than 1 dyslipidaemia and only 1 or none were compared. Table 5 shows the difference in proportion by age, sex, and other characteristics between subjects with ≥ 2 dyslipidaemias and 1 or no dyslipidaemia. More females, more subjects ≥ 12 years and more subjects who are overweight and obese had ≥ 2 dyslipidaemias. But these findings were not statistically significant.

Table 3. Prevalence of lipid abnormalities by age group

Lipid type	Total	<12 years	≥12 years	χ^2 (p value)
Total cholesterol				0.014 (0.905)
Normal	17 (77.3%)	3 (75%)	14 (77.7)	
Abnormal	5 (22.7%)	1 (25%)	4 (22.3%)	
Triglycerides				5.489 (0.019)
Normal	3 (13.6%)	2 (50%)	1 (5.6%)	
Abnormal	19 (86.4%)	2 (50%)	17 (94.4%)	
HDL-C				0.273 (0.601)
Normal	14 (63.6%)	3 (75%)	11 (61.1%)	
Abnormal	8 (36.4%)	1 (25%)	7 (38.9%)	
LDL-C				0.772 (0.380) ^a
Normal	19 (86.4%)	4 (100%)	15 (83.3%)	
Abnormal	3 (13.6%)	0 (0.0%)	3 (16.7%)	
Non-HDL-C				1.436 (0.230) ^a
Normal	17 (77.3%)	4 (100%)	13 (72.2%)	
Abnormal	5 (22.7%)	0 (0%)	5 (27.8%)	

Numbers of subjects are shown. ^a Fisher's exact test.

Table 4. Characteristics of subjects based on number of lipid abnormalities

Variable	<2 lipid abnormality	≥2 lipid abnormalities	t test (p value)
Mean age	15.15±3.6	14.78±3.7	0.238 (0.814)
Mean HbA _{1c}	7.5±2.3	7.7±1.9	-1.63 (0.872)
Mean duration of DM	3.31±2.4	2.88±1.6	0.448 (0.659)
Mean BMI percentile	57.25±30.8	66.38±31.9	-0.642 (0.529)
Mean weight	48.15±13.7	52.75±19.6	-0.634 (0.534)
Mean height	151.46±15.6	149.88±15.9	0.225 (0.825)
Mean insulin/kg/day	0.923±0.49	0.571±0.64	1.478 (0.157)

Discussion

This report reveals a high prevalence of dyslipidaemia in the subjects studied. Eighty-six percent of subjects with T1DM had dyslipidaemia, and this high rate of dyslipidaemia has been reported by other studies in children with T1DM [7, 11, 12]. In their study on dyslipidaemia in Brazilian children with T1DM, Homma et al. [7] reported that 72.5% of the subjects had dyslipidaemia. Similarly, looking at the significance of lipid abnormalities in children with insulin-dependent DM, Rahma et al. [13] reported a prevalence of 66%.

However, lower prevalence rates of dyslipidaemia have also been reported by other studies [6, 12, 14, 15]. The reports by Bulut et al. [14] in children with T1DM and Demirel et al. [15] in Turkish adolescents with T1DM noted dyslipidaemia in 26.2 and 30.3%, respectively. The dif-

ference in prevalence recorded by different studies may be due to various reasons, which include differences in target age, diets, treatment regimens, and glycaemic control, and also differences in the reference ranges used by the different studies. In the USA, in a study investigating cardiovascular risk factors in 11,348 children and adolescents aged 2–18 years with T1DM, Redondo et al. [6] reported a prevalence of dyslipidaemia of 3.8%. He attributed the low prevalence to the fact that most of the subjects were young and the low prevalence of obesity in the study subjects.

Looking at the pattern of dyslipidaemia in this study, hypertriglyceridaemia was the commonest dyslipidaemia. The mean triglyceride level in the group was higher than the normal value in the guideline [11]. More than 80% of the subjects in this study had hypertriglyceridaemia, which is much higher than the values from other studies [7, 13]. Hypercholesterolaemia has been reported

Table 5. Relationship between clinical characteristics and dyslipidemia

Parameters	<2 lipid abnormalities	≥2 lipid abnormalities	<i>p</i> value
Sex			0.264
Male	9 (90%)	1 (10%)	
Female	7 (58.3%)	5 (41.7%)	
Age			0.730
<12 years	3 (75%)	1 (25%)	
≥12 years	13 (72.2%)	5 (41.7%)	
Duration of diabetes			0.542
<5 years	12 (70.6%)	5 (29.4%)	
≥5 years	4 (80.0%)	1 (20.0%)	
HbA _{1c}			0.666
<7.5%	6 (75%)	2 (25%)	
≥7.5%	10 (71.4%)	4 (28.6%)	
Weight category			0.769 ^a
Underweight	1 (100%)	0 (0%)	
Normal weight	11 (73.3%)	4 (26.6%)	
Overweight/obesity	4 (66.7%)	2 (33.3%)	
Total	16 (100%)	6 (100%)	

Numbers of subjects are shown. ^a Fisher's exact test.

as the commonest type of dyslipidaemia in several studies [13, 15, 16]. In the study by Bulut et al. [14], hypercholesterolaemia was the commonest dyslipidaemia while hypertriglyceridaemia was reported in only 12.9% of subjects. Mona et al. [12] in Egypt reported high LDL-C and low HDL-C as the commonest dyslipidaemias, and hypertriglyceridaemia was reported in <5% of subjects. However, in a report of lipid profiles in children with T1DM in Erbil, Alrabaty et al. [17] reported hypertriglyceridaemia as the highest dyslipidaemia. The reasons for the difference in the prevalence of dyslipidaemias may not be very obvious but may be due to differences in the diets, age, glycaemic control, and other associated disease conditions. In this study, although the dietary pattern was not specifically studied, carbohydrates are a dominant part of our diet; suboptimal insulin therapy and poor glycaemic control are also typical and reported in DM children in Africa [18] and may account for the high prevalence of hypertriglyceridaemia compared to other studies. Triglycerides are a flexible source of energy and can be converted to glucose by the liver and readily stored in the adipose tissue usually in the presence of adequate insulin. Recently eaten foods and drinks (i.e., within the last few hours) can lead to increased levels, which underscores the need for fasting before samples are taken. Although the subjects in this study had fasting lipids taken, the immediate explanation for the high triglyceride levels

may be the background poor glycaemic control usually reported in African subjects with diabetes.

Non-HDL-C, a reflection of highly atherogenic apolipoprotein B and LDL-C, track into adulthood and can usually predict the severity of atherosclerosis in adults [19, 20]. In this study, 5 (22.7%) subjects had abnormal levels of these highly atherogenic lipids. In the study amongst Turkish children with T1DM, increased LDL-C was reported in 10.4% of the subjects, which is in agreement with our study. Higher LDL-C prevalence rates of 20.51 and 44% were reported in Cairo [12] and Brazil [7], respectively. The higher values reported in the latter is because a lower cutoff (100 mg/dL) was used for LDL-C compared to the 130 mg/dL used in this study. According to the ISPAD guidelines on dyslipidaemia, a high LDL-C (>100 mg/dL) is an indication for intervention to improve metabolic control with diet and increased exercise. Statin should be considered in children if LDL-C does not reduce to <130 mg after nonmedical intervention [9]. In this study, 13.6% of the subjects had high LDL levels and therefore will require intervention.

We also observed that the mean values of most lipids were higher in females than males, and more females (41.7%) had more than 1 dyslipidaemia than males (10%). The higher prevalence of dyslipidaemia in females has also been observed in other studies [7, 21]. In the study by Homma et al. [7] in Brazilian children with T1DM, a

higher prevalence of dyslipidaemia (87%) and a lower prevalence of HDL-C were observed in females. Franca and Alves [21] also reported higher dyslipidaemia prevalence in females (34.7%) and males (25.3%). However, in the study in Turkish children by Bulut et al. [14], prevalence of dyslipidaemia was similar in both males and females: 26.2% in females versus 26.1% in males. The reason for the higher tendency to dyslipidaemia in females may have several reasons. Pérez et al. [22], for example, have suggested that in women diabetes has a greater impact on cardiovascular risk than in men. They also noted that women have a higher atherogenic risk than men even when diabetes was well controlled for.

In this study, the mean age was similar for females and males, but females had a higher mean BMI *z* score and HbA_{1c} level, and mean lipid levels were also higher in females than males. Although not looked at in this report, females of the same age are more likely to be more advanced in puberty than males of that age with a possible effect of estrogen on BMI and glycaemic control [23]. In this study, there was no significant relationship between HbA_{1c}, age, duration of diabetes, and weight category and dyslipidaemia. This is similar to observations made by Homma et al. [7] in Brazilian children. However, a relationship has been described between dyslipidaemia and glycaemic control shown by HbA_{1c} in some studies [4, 23, 24]. In our study, a higher prevalence of dyslipidaemia was reported in females who had a higher mean HbA_{1c}, but there was no statistically significant difference between subjects who had optimal HbA_{1c} <7.5% and subjects with HbA_{1c} ≥7.5%. Guy et al. [4] and Teles and Fornés [25] stated that poor glycaemic control was related to higher serum lipid levels. Ladeia et al. [26] also found a significant correlation between glycaemic control and lipid profiles.

Autoimmune comorbidities and micro- and macrovascular complications were not looked at in this study due to the financial burden on the investigators. Further limitations were the poor knowledge and awareness of the nutrient content of local foods, and family knowledge of cardiovascular risk factors were also limitations of the data collected for this study. Most subjects in this study were regarded as T1DM, but no test was performed to confirm the presence of T1DM.

Limitations

BMI is a measure of adiposity and correlates with total body fat. Body fat mass distribution was not considered in this study as weight loss was a frequent feature in children and adolescents living with T1DM. Abdominal obesity was also not a significant feature in T1DM.

The ISPAD guideline mentioned only LDL-C in its guideline hence the use of a more comprehensive panel.

Diet was not looked at in this study because details on caloric and nutrient contents of most of our diets are not known and preparation methods vary, which could affect nutrient content.

Waist circumference was not measured in this study; however, even though there was no statistically significant difference regarding weight, the prevalence of dyslipidaemia was higher in overweight/obese than normal weight or underweight subjects.

Most of the subjects enrolled had T1DM. Diagnosis was basically clinical. However, subjects included in this study are only those who have been on only insulin from diagnosis. No subject was on metformin therapy.

Lifestyle and physical activity was not mentioned for patients enrolled in the study as well as blood pressure values and their percentiles.

A prospective and case-control study involving a larger sample will be needed to be able to draw more definite conclusions on dyslipidaemia in children and adolescents living with diabetes in Africa.

Conclusion

The commonest lipid abnormality was hypertriglyceridaemia. About a quarter of our subjects had more than one lipid abnormality. Programs should therefore aim to improve lipid levels to delay and prevent chronic complications.

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Statement of Ethics

All parents whose children were studied gave informed consent. Ethical clearance for this study was obtained from the Ethical Committee of the University of the Port Harcourt Teaching Hospital.

Disclosure Statement

The authors have nothing to disclose.

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Author Contributions

Both authors developed and carried out sample collection. Literature review was done by Dr. Tamunopriye Jaja, and both authors did the data analysis and read through the final paper.

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