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Cross-Sectional Height-Specific Changes in Serum Lipid Concentrations in Cameroon Children

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Abstract

Background: Information on the relationship between height and changes in serum lipids in children is scarce in Cameroon. The aim of this study is to determine prevalence of dyslipidemia with respect to age and gender and assess the association between height increase and serum lipid changes in Cameroon children. **Methods:** This hospital-based cross-sectional analysis included 472 boys and 534 girls between the ages of 5 and 16 years. Body height, weight, and waist circumference (WC) of children were measured and z-scores calculated. Total cholesterol-TC, triglycerides-TG, low density lipoprotein cholesterol-LDL-C and high-density lipoprotein cholesterol-HDL-C concentrations in fasting blood samples were determined by enzymatic method using an automated clinical chemistry analyzer (RX Monaco, UK). Children were divided into increasing quartiles of height z-score. Multiple linear regression analysis was used to compare mean lipid concentrations across quartiles of height z-score after controlling for age, gender, body weight, WC and fasting blood glucose. **Results:** The prevalence of elevated TC and LDL-C were respectively 18.5% and 19.2% higher in girls than boys. Also, the prevalence of elevated TC and TG was highest among younger (5- to 9-year-old) girls and boys respectively. There was a significant decrease in mean TC (168.8 to 127.2 mg/dl; $p < 0.001$), TG (99.0 to 84.1 mg/dl; $p = 0.019$) and LDL-C (91.1 to 69.4 mg/dl; $p = 0.018$) in boys; and a significant decrease in mean TC (171.2 to 144.7 mg/dl; $p = 0.004$) and HDL-C (62.8 to 28.7 mg/dl; $p < 0.001$) in girls with increasing quartiles of height z-score. However, the decrease in HDL-C in boys ($p = 0.053$) and the decrease in TG ($p = 0.211$) and LDL-C ($p = 0.732$) in girls with increasing height were not significant. **Con-**

clusion: Serum lipids decreased with increasing height after controlling for different variables. This study indicates that short children have higher serum lipid concentrations and this may increase the risk of lipid disorders, which may persist into adulthood.

Keywords

Serum Lipids, Dyslipidemia, Height, Children, Cameroon

1. Introduction

Height is an important measure of nutrition status. It is determined by genetic predisposition and other environmental factors and it also reflects chronic disease in children and adults [1]. For instance, a recent study revealed that a one-standard deviation decrease in height (determined genetically) increased the risk of coronary artery disease (CAD) by 13.5% in adults [2]. Also, a systematic review and meta-analysis indicated that short height increased the risk of cardiovascular disease (CVD) mortality and coronary heart disease (CHD) by 1.55 and 1.49 times respectively when compared with the tallest subjects [3]. In another meta-analysis height had an inverse association with risk of stroke and CVD [4]. There is additional evidence from epidemiologic studies indicating that height is also inversely associated with dyslipidemia in both children and adults. In adults, a recent Korean study revealed that height had an inverse association with total cholesterol (TC), triglycerides (TG) and low-density lipoprotein cholesterol (LDL-C) and a positive association with high-density lipoprotein cholesterol (HDL-C) in men and women [5]. Also, a prospective cohort study indicated that a 6.7 cm increase in body height was associated with a 0.12 mmol/l decrease in serum cholesterol [6]. In children, shorter height increased the odds of hypercholesterolemia, hypertriglyceridemia and hyper-LDL-cholesterolemia by 2.3 to 7.0 times in boys, and in girls, only the odds of hyper-LDL-cholesterolemia increased by 3.12 times [5]. Also, a recent study showed that an increase of one standard deviation in body height lowered LDL-C by 0.049 mg/dl [7]. Previously, the Bogalusa Heart Study had shown that height is inversely associated with HDL-C and LDL-C in black and white adolescent males respectively [8]. However, this study did not control for the effect of confounding variables like dietary intake and tanner stage. In addition, studies in Japanese children had shown that height increase over a 3-year period had a negative association with TC, HDL-C [9] and LDL-C during puberty [10]. The decrease in serum lipid concentration during puberty has been attributed to the process of sexual maturation involving an increase in oestradiol and testosterone concentrations in girls and boys respectively [11] [12] [13]. Also, the secretion of growth hormone during this period promotes linear growth, and there is evidence that growth hormone secretion has a negative association with LDL-C [14]. The adverse lipid profile (dyslipidemia) and its association with shorter height from the above

findings constitute a major contributor to the development of CVD and atherosclerosis [15] [16]. Atherosclerosis can start early in life and can persist until adulthood resulting in coronary atherosclerosis [17] [18]. Thus, in order to prevent cardiovascular diseases in adulthood, it is important for serum lipid levels to be checked during childhood and appropriate interventions carried out when necessary [17]. However, there is also evidence that some children can have elevated serum lipid levels that drop to acceptable levels later in life [19]. It can be hypothesized from the above findings that shorter children may tend to have higher levels of serum lipids. Information on this aspect is scarce in Africa and Cameroon in particular. In this study, the aim was to determine the prevalence of lipid disorders with respect to gender and age and assess the changes in serum lipid levels in relation to height-for-age in Cameroon children.

2. Materials and Methods

2.1. Study Design and Study Participants

This cross-sectional study was limited to children between the ages of 5 and 16 years who were recruited in-hospital (Bamenda Regional Hospital—BRH, Cameroon) during consultations from November 2021 to October 2022. The children and their parents/guardians were approached by laboratory technicians involved in data collection as they arrived the outpatient unit of the BRH and were provided with the consent information. Children were included in the study after their parents/guardians had provided informed consent and if the children had fasted overnight for at least twelve hours. Among the 1069 potential participants of the study, those with type 1 diabetes [20] and those with incomplete serum lipid data and anthropometric measurements (n = 63) were excluded. This eventually gave a sample that included 1006 children (472 boys and 534 girls).

2.2. Ethical Considerations

The study protocol was approved by the Ethical Review Committee/Institutional Review Board (IRB) of the Faculty of Health Sciences of The University of Bamenda (Ref. no. 2021/103H/UBa/IRB). Administrative clearance was also obtained from the North West Regional Delegation for Public Health. In addition, hospital clearance was obtained from the BRH. Lastly, all parents/guardians and children provided written informed consent and verbal assent respectively before data was collected.

3. Data Collection

3.1. Anthropometric Measurements

The body height of each participant was measured in bare feet using a portable stadiometer (SECA 213, Germany) to an accuracy of 0.1 cm. Body weight was also measured in bare feet and light clothing using a tetrapolar bioimpedance digital scale (Omron BF 511, Japan) to the nearest 0.1 kg. Body mass index

(BMI) was calculated as weight (kg) divided by the square of the height (m^2). The z-score of body height, weight and BMI were calculated using the WHO growth monitoring software (WHO Anthro) for children between 5 and 19 years [21]. This growth monitoring software makes use of the WHO 2007 child growth standards. The cases were sorted by increasing height z-score and then divided into increasing quartiles of height z-score. Waist circumference (WC) was also measured using a flexible inelastic waist circumference measuring tape (SECA 209, Germany) to the nearest 0.5 cm [22]. The WC readings were also converted to z-scores using LMS Growth software, which employs the UK 1990 growth reference standards as reported by McCarthy *et al.* [22].

3.2. Laboratory Measurements

The biochemical procedures were carried out in the laboratory of the BRH. Fasting veinous blood samples (5 ml) were obtained from the antecubital fossa using a vacutainer by laboratory technicians. The blood collected was allowed to coagulate. Centrifugation was carried at 3000 rpm for three minutes and serum was obtained using a pipette and transferred in to vials for lipid profile determination. The concentrations of TC, TG and HDL-C in serum were determined enzymatically using an automatic chemistry analyzer (Randox Monaco, UK). The instructions of the manufacturer were followed and the Randox Multisera level 2 and 3 were used for daily quality control monitoring. The Friedewald formular was used to calculate the concentration of LDL-C [23]. The study participants with at least one of the following lipid disorders were considered as dyslipidemic according to the Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents: hypo-HDL-cholesterolemia (<35 mg/dl), hyper-LDL-cholesterolemia (≥130 mg/dl), hypercholesterolemia (≥200 mg/dl), hypertriglyceridemia (≥100 mg/dl for children between 0 and 9 years and ≥130 mg/dl for children between 10 and 19 years) [24]. Fasting blood glucose was also determined using a blood glucose meter (Model G-425-3, LabPro Pharma, LLC, Houston, Texas, US).

3.3. Statistical Analysis

All statistical analyses were performed using IBM-SPSS version 21.0 (IBM, 1 New Orchard Road Armonk, New York 10504-1722, US). The distribution of continuous variables was checked for normality using the Kolmogorov Smirnov (*K-S*) test. Comparisons of mean concentrations of serum lipids between boys and girls and also between two age groups (5 - 9 and 10 - 16 years) were carried out using the independent samples *t*-test and data has been reported as mean (minimum - maximum). Also, the proportions of children with abnormal lipid levels were calculated and the data has been presented as % (95% CI). The comparison of proportions was carried out using the Chi square test. In addition, the comparison of means of serum lipid concentrations across increasing quartiles of height z-score was carried out using general linear models. In this analysis, the

serum lipids (TC, TG, LDL-C and HDL-C) were modeled as dependent variables and quartiles of height z-score as the independent variable. The model was adjusted for covariates including; age, gender, body weight, waist circumference and fasting blood glucose. The unadjusted and adjusted mean concentrations of serum lipids across quartiles of height-z-score have been presented with their corresponding standard errors and *p*-values for trend. The cut-off for statistical significance was set at $p < 0.05$.

4. Results

4.1. Summary Characteristics of the Study Population

The summary characteristics of the study population have been presented in Table 1 below. With respect to gender, girls were significantly older ($p < 0.001$) and heavier ($p = 0.008$) than boys. Also, the girls had significantly higher mean serum TC ($p = 0.002$), TG ($p = 0.004$) and LDL-C ($p = 0.003$) concentrations than the boys. The boys had a higher mean HDL-C concentration than girls. However, this difference was not significant ($p = 0.241$). In addition, the mean waist circumference (WC) was significantly higher for girls ($p < 0.001$) than boys. The mean blood glucose was significantly higher in boys ($p < 0.001$) than girls. With respect to age groups, the mean concentrations of serum lipids decreased slightly among children between the ages of 10 and 16 years. However, these differences were not statistically significant ($p > 0.05$) when compared with

Table 1. Summary characteristics of the study population with respect to gender and age group.

Variables	Boys		Girls	
	5 - 9 years	10 - 16 years	5 - 9 years	10 - 16 years
n	240	232	194	340
Height (cm)	134.8 (125.0 - 145.0)	155.5 (133.0 - 178.0)	132.1 (128.0 - 153.0)	154.9 (131.0 - 167.0)
Height z-score	0.5 (−1.8 - 2.6)	−0.4 (−2.1 - 1.2)	0.2 (−0.8 - 2.5)	−0.2 (−2.1 - 1.7)
Weight (kg)	29.3 (22.0 - 38.0)	50.7 (25.0 - 76.0)	29.6 (22.0 - 38.0)	51.5 (25.0 - 87.0)
Weight z-score	0.3 (−1.2 - 1.7)	0.2 (−2.2 - 2.5)	0.2 (−2.0 - 1.5)	0.3 (−2.9 - 2.7)
BMI (kg/m^2)	16.2 (10.9 - 21.3)	20.3 (12.9 - 27.3)	16.9 (12.1 - 20.7)	21.2 (11.6 - 33.2)
BMI z-score	−0.3 (−5.4 - 2.2)	0.5 (−2.8 - 2.5)	0.2 (−3.2 - 1.9)	0.3 (−4.2 - 2.8)
Waist circumference (cm)	60.9 (54.0 - 67.0)	68.4 (54.0 - 85.0)	61.8 (54.0 - 70.0)	70.9 (53.0 - 90.0)
Waist circumference z-score	1.0 (−0.7 - 1.9)	0.5 (−1.7 - 2.2)	1.2 (−0.4 - 2.5)	1.3 (−1.5 - 3.2)
Total cholesterol (mg/dl)	157.2 (96.2 - 228.2)	150.6 (89.3 - 281.1)	171.7 (63.0 - 229.0)	159.5 (78.5 - 237.0)
Triglycerides (mg/dl)	96.9 (40.4 - 224.0)	83.1 (31.7 - 275.9)	111.1 (24.0 - 389.3)	90.6 (54.6 - 117.5)
LDL-C (mg/dl)	83.3 (33.8 - 167.4)	79.4 (37.3 - 228.8)	103.2 (19.2 - 241.8)	86.9 (24.6 - 209.8)
HDL-C (mg/dl)	57.3 (−46.9 - 106.0)	51.9 (−76.7 - 201.0)	50.4 (−42.9 - 98.6)	50.3 (−33.7 - 89.3)
Blood glucose (mg/dl)	117.0 (87.0 - 152.0)	107.1 (79.0 - 189.0)	106.4 (84.0 - 137.0)	107.0 (71.0 - 154.0)

Values = mean (min - max).

those of the younger children (5 to 9 years). Mean blood glucose concentration was significantly higher ($p = 0.002$) among the younger children (5 to 9 years) than those who are 10 to 16 years.

4.2. Prevalence of Lipid Disorders with Respect to Gender and Age

The prevalence of lipid disorders in relation to gender and age is presented in Table 2. There was an 18.5% increase in the prevalence of hypercholesterolemia (TC ≥ 200 mg/dl) in girls when compared with boys ($X^2 = 20.187$, $p < 0.001$). Also, the prevalence of hyper-LDL-cholesterolemia significantly increased by 19.2% in girls ($X^2 = 28.053$, $p < 0.001$) than boys. Hypertriglyceridemia was also higher for girls than boys. However, this difference was not statistically significant ($X^2 = 0.207$, $p = 0.649$). The prevalence of hypo-HDL-C was higher in boys (36.0%) than girls (33.0%). However, the difference was not significant ($X^2 = 0.519$, $p = 0.471$). The prevalence of dyslipidemia was highest among the younger children than their older peers. For instance, the prevalence of hypercholesterolemia and hypertriglyceridemia was highest among 5- to 9-year-old girls and boys respectively. On the contrary, the prevalence of hypo-HDL-cholesterolemia was highest among the 10- to 16-year-old boys. It is also important to note that the prevalence of combined dyslipidemia in the whole sample was 19.3%. On a gender basis, combined dyslipidemia was higher among girls (21.0%) than boys (17.4%).

4.3. Height Increase and Serum Lipid Concentrations

Table 3 shows the relationship between height increase and serum lipid concentrations in the study participants. The mean body height for the first, second, third and fourth quartiles of height z-score were 138.2, 141.8, 145.9 and 148.1 cm respectively for the whole sample. When the study participants were classified according to increasing quartiles of height z-score, inverse relationships were observed with serum lipids. In boys, there was a significant decrease in the adjusted mean TC, TG and LDL-C concentrations with increasing height quartiles. Body height in boys was also inversely related with HDL-C. However, this relationship

Table 2. Prevalence of lipid disorders in relation to gender and age.

Variables	Boys		Girls	
	5 - 9 years	10 - 16 years	5 - 9 years	10 - 16 years
n	240	232	194	340
TC ≥ 200 mg/dl	24.2 (17.4 - 32.6)	19.0 (12.9 - 27.1)	57.7 (44.8 - 67.1)	30.0 (23.6 - 37.3)
TG ≥ 100 mg/dl and ≥130 mg/dl	56.7 (47.7 - 65.2)	37.1 (28.5 - 46.1)	45.4 (35.8 - 55.3)	51.2 (43.7 - 58.6)
LDL-C ≥ 130 mg/dl	12.9 (8.0 - 20.2)	10.8 (6.4 - 17.7)	40.2 (31.0 - 50.2)	25.9 (19.9 - 33.0)
HDL-C < 35 mg/dl	25.0 (18.0 - 33.6)	46.7 (37.9 - 55.6)	32.9 (24.4 - 42.8)	32.9 (26.3 - 40.3)

Values = % (95% CI).

was not significant. In girls, there was a significant decrease in the adjusted mean TC and HDL-C concentrations with increase in height.

4.4. Prevalence of Lipid Disorders in Relation to Height-for-Age

Figure 1 shows the prevalence of lipid disorders in relation to increasing height-for-age in boys and girls. The prevalence of hypercholesterolemia decreased significantly with increasing quartiles of height z-score in both boys (*p*

Table 3. Changes of serum lipid concentration in relation to height.

Height quartiles	N	TC (mg/dl)		TG (mg/dl)		LDL-C (mg/dl)		HDL-C (mg/dl)	
		Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted
Boys									
First	108	169.1 (5.4)	168.8 (4.0)	103.0 (5.7)	99.0 (5.1)	94.5 (7.5)	91.1 (4.2)	58.4 (2.2)	63.0 (5.0)
Second	134	154.0 (3.5)	156.6 (4.2)	86.7 (6.7)	88.3 (5.7)	79.6 (2.5)	81.1 (4.7)	57.1 (2.6)	53.7 (5.4)
Third	101	151.6 (4.3)	152.4 (4.5)	85.2 (5.2)	87.8 (6.3)	78.3 (2.9)	78.8 (4.3)	52.1 (9.2)	55.6 (4.8)
Fourth	129	133.2 (4.3)	127.4 (4.9)	86.1 (5.3)	84.1 (5.3)	66.6 (3.1)	69.4 (5.2)	49.6 (2.9)	41.0 (5.9)
p-value for trend		0.007	< 0.001	0.019	0.039	0.002	0.018	0.704	0.053
Girls									
First	140	171.3 (2.7)	171.2 (4.4)	102.3 (5.7)	98.4 (7.9)	99.3 (6.8)	96.6 (5.8)	60.8 (2.2)	62.8 (4.5)
Second	130	166.4 (3.4)	167.6 (4.1)	104.2 (5.9)	97.3 (7.6)	94.3 (5.2)	91.6 (5.3)	54.5 (4.8)	57.0 (4.7)
Third	158	169.3 (4.9)	168.3 (4.0)	94.0 (2.4)	91.9 (6.9)	87.4 (3.1)	92.3 (6.1)	50.3 (4.5)	48.3 (4.4)
Fourth	106	142.9 (6.1)	144.7 (4.6)	92.6 (6.4)	95.0 (7.1)	87.9 (7.4)	91.2 (5.4)	31.4 (5.5)	28.7 (4.9)
p-value for trend		<0.001	0.004	0.034	0.211	0.123	0.732	<0.001	<0.001

Values = mean (standard error). The mean serum lipid concentrations were adjusted for age, gender, body weight, waist circumference and fasting blood glucose.

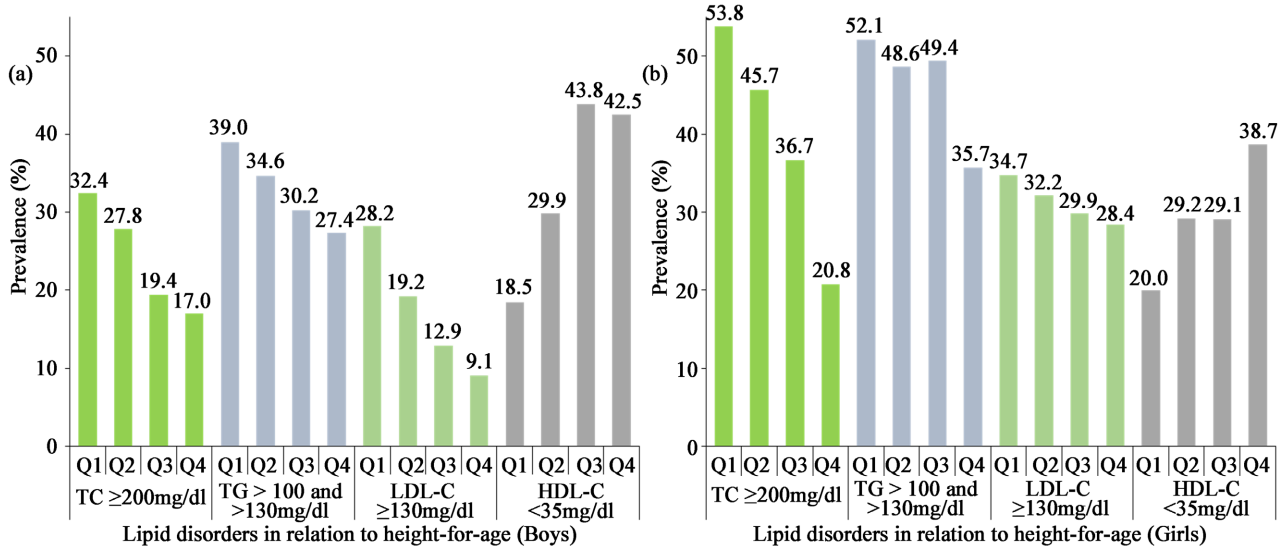

Figure 1. Prevalence of lipid disorders in relation to height-for-age in boys (a) and girls (b).

for trend < 0.001) and girls (p for trend = 0.002). Also, the prevalence of hypertriglyceridemia decreased with increase in height in boys (p for trend = 0.009) and girls (p for trend = 0.041). In addition, the prevalence of hyper-LDL-cholesterolemia significantly decreased with increasing quartiles of height-z-score in boys (p for trend = 0.001) and girls. However, in girls, the decrease observed was not statistically significant (p for trend = 0.699). In the case of hypo-HDL-cholesterolemia, the prevalence increased with increase in height for both boys (p for trend = 0.002) and girls (p for trend < 0.001).

5. Discussion

This study set out to determine the prevalence of lipid disorders with respect to gender and age and also to determine the changes in serum lipid concentrations with respect to increased height-for-age. On a gender basis, the prevalence of hypercholesterolemia, hyper-LDL-cholesterolemia and hypertriglyceridemia were generally higher for girls than boys. However, the prevalence of hypo-HDL-cholesterolemia was higher in boys than girls. This finding is in line with that of a recent study in which the prevalence of elevated TG and LDL-C increased by 1.7% and 3.3% respectively in girls compared to boys and the prevalence of low HDL-C increased by 6.7% in boys compared to girls [25]. This can be explained by the fact that the levels of serum lipids are influenced by sex hormones during puberty and adolescence [26]. For example, a previous report had indicated that lower LDL-C and HDL-C were associated with an increase in plasma concentrations of estrogen and progesterone in girls and testosterone in boys [11] [27]. Also, changes that occur in the expression of some genes like apoA-1 and ABCA1 that occur during development, have been linked to alterations in esterified cholesterol concentrations and a reduction in HDL-C production [28].

With respect to age, the prevalence of elevated TC, TG and LDL-C decreased and low HDL-C increased among boys between the ages of 10 and 16 years when compared with their younger peers. In girls, the prevalence of elevated TC and LDL-C decreased among those between the ages of 10 and 16 years. These also correspond with the observed decrease in mean concentrations of TC, TG and LDL-C among the older children in this study, though not statistically significant. There is evidence indicating that serum lipids usually peak in children between the ages of 9 and 10 years, and then decrease after [11]. A recent German Health Survey for children and adolescents revealed that serum lipid concentrations increased in children up to the age of 9 years and lower lipid measures were observed in children between the ages of 10 and 17 years [29]. Also, a previous report had shown that during adolescence, serum LDL-C and HDL-C decrease in children, with boys experiencing a more remarkable decrease in HDL-C [13] [30]. This is in line with the current study in which a higher prevalence of hypo-HDL-cholesterolemia was observed among the older boys (10 to 16 years). The decrease in serum lipids observed in older children observed in

this study could be explained by the fact that during puberty, hormonal alterations occur, which are linked to growth spurt and sexual maturation. These physiological processes lead to an increased in cholesterol requirement for the synthesis of cellular membranes in growing cells and tissues, which eventually lead to lower levels of lipids [8] [31].

An important finding of this study is that after controlling for confounding variables like age, gender, body weight, waist circumference and fasting blood glucose, inverse relationships were observed between height and mean serum lipid concentrations. The mean serum TC, TG, LDL-C and HDL-C concentrations significantly decreased with increasing quartiles of height z-score in boys. In girls, height had an inverse relationship with TC and HDL-C. Also, in both boys and girls, the prevalence of hypercholesterolemia, hypertriglyceridemia and hyper LDL-cholesterolemia were lower in taller children and the prevalence of hypo-HDL-cholesterolemia was higher in taller children. The above findings are in line with previous observations. For instance, a previous study in Japan indicated that height was inversely associated with TC and HDL-C in boys and girls [26]. Also, the Bogalusa Heart Study revealed that the observed changes in height over a five-year period had negative associations with TC, LDL-C and HDL-C in boys [8]. In addition, a three-year follow-up study in Japan showed that height was inversely associated with TC in pubertal children [9]. Moreover, a recent study has indicated that shorter height was associated with adverse lipid profiles in adolescents [5].

The above findings suggest that children with a higher height-for-age might also have lower concentrations of atherogenic lipids and children with a lower height-for age might have higher concentrations of atherogenic lipids. In fact, some authors had indicated that height and age should be considered in the evaluation of serum lipids in children [26]. Evidence indicates that growth spurt during puberty is negatively associated with changes in serum lipid levels [8]. Bone growth is influenced by increased growth hormone secretion during puberty and growth hormone has a lipolytic effect, which eventually improves lipid profiles [14]. Therefore, it can be suggested that pubertal children with sufficient growth hormone will experience an optimal growth and have acceptable lipid profiles [5]. The skeletal system is also involved in lipid metabolism. Osteocalcin is a hormone found in bone, which contributes to the expression of adiponectin gene in bone cells [32]. Adiponectin raises the level of serum HDL-C and reduces the concentration of serum TG [33]. Therefore, children with a high concentration of osteocalcin and experiencing a rapid growth velocity [34] are likely to have acceptable lipid profiles [35]. A recent study had investigated the relationship between height and CAD using a genetic approach [2]. The study revealed that height-related single nucleotide polymorphisms (SNPs) were significantly associated with CAD, and this represented a 13.5% increase in the risk of CAD for each one-standard deviation decrease in height. Also, this association was partly

attributed to the relationship between shorter height and elevated levels of TG and LDL-C [2].

6. Limitations of the Study

A limitation of this study is that the sample is not representative of Cameroon children. It is also not possible for causal relationships between height and adverse lipid profiles to be established because of the cross-sectional design of the study. Also, the effects of tanner stage, dietary intake and other lifestyle factors were not controlled for in the analysis. However, this study has assessed the relationship between height and dyslipidemia in Cameroon children for the first time and has controlled for confounding variables like age, gender, body weight, waist circumference and fasting blood glucose.

7. Conclusion

To conclude, this study has shown that the prevalence of dyslipidemia is generally higher for girls than boys. Also, the prevalence of dyslipidemia was higher among the younger children than their older peers. In addition, this study provides evidence that children with shorter heights have elevated levels of serum lipids, which may track to adulthood. Longitudinal studies with larger samples are needed in the future to track serum lipid changes with chronological age in children and adolescents.

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Availability of Data

Data and material are available from the corresponding author upon reasonable request.

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Authors Contributions

LKN was responsible for the conception and design of the study, direct collection of data and processing, statistical analysis and drafting of the manuscript. LLN contributed to the conception and design of the study and participated in data collection as well as interpretation of data and drafting of manuscript. TBC and EAR contributed to the conception and design of the study as well as interpretation and analysis of data. All authors revised the manuscript and gave a final approval of the submitted version.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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