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Dyslipidemia in children with chronic kidney disease

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Dyslipidemia, a known risk factor for atherosclerosis, is frequent among both adults and children with chronic kidney disease. Here, we describe the prevalence and pattern of dyslipidemia from a cross-sectional analysis of 391 children aged 1–16 years, enrolled in the multicenter Chronic Kidney Disease in Children (CKiD) study, with a median glomerular filtration rate (GFR), measured by the plasma disappearance of iohexol, of 43 ml/min per 1.73 m^2. Multivariate analysis was applied to adjust for age, gender, body mass index (BMI), GFR, and the urinary protein/creatinine ratio. Proteinuria was in the nephrotic range in 44 and the BMI exceeded the 95th percentile in 57 patients of this cohort. Baseline lipid analysis found a high prevalence of hypertriglyceridemia in 126, increased non-HDL-C in 62, and reduced HDL-C in 83. Overall, 177 children had dyslipidemia, of whom 79 had combined dyslipidemia. Lower GFR was associated with higher triglycerides, lower HDL-C, and higher non-HDL-C. Nephrotic-range proteinuria was significantly associated with dyslipidemia and combined dyslipidemia. Compared with children with a GFR >50, children with a GFR <30 had significantly increased odds ratios for any dyslipidemia or for combined dyslipidemia. Hence, among children with moderate chronic kidney disease, dyslipidemia is common and is associated with lower GFR, nephrotic proteinuria, and non-renal factors including age and obesity.

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Individuals with chronic kidney disease (CKD) suffer an exceptionally high burden of atherosclerotic cardiovascular disease (ASCVD).[1] Dyslipidemia, a known risk factor for atherosclerosis, is frequent among both adults and children with CKD.[2,3] In addition, there is evidence to suggest that dyslipidemia contributes to the initiation and progression of CKD itself.[4–9] Although CKD patients are commonly burdened with multiple cardiovascular risk factors, dyslipidemia is an important focus of clinical CKD research, as it is both highly prevalent and a potentially modifiable exposure.

Accelerated atherosclerosis in children with CKD is likely. Within the general population, atherosclerosis begins during childhood and dyslipidemia is a risk factor for its development.[10–12] Young adult survivors of childhood end-stage renal disease (ESRD) experience an extremely high rate of premature mortality because of ASCVD, their principal cause of death.[13–16] However, compared with the adult population, data about dyslipidemia in children with CKD remain scarce.

The primary aim of this cross-sectional investigation was to describe the prevalence and pattern of dyslipidemia in children with moderate CKD using data collected on participants in the Chronic Kidney Disease in Children (CKiD) Study. We also aimed to identify clinical and laboratory factors associated with dyslipidemia in children with CKD.

RESULTS

As of May 2009, 574 children had completed a baseline study visit in CKiD. A subset of 427 children with known age, sex, race, and CKD diagnosis had complete lipid and glomerular filtration rate (GFR). After excluding 11 children currently taking lipid-lowering medication and 25 children known not to be fasting, 391 children remained for analysis. In 29% ($n=112$) of this group, fasting status was not recorded, whereas the remainder (71%, $n=279$) of the children were confirmed to be fasting. Of all GFR measures, 94% ($n=368$) were direct (iGFR) by plasma iohexol disappearance.

Characteristics of the study population are shown in Table 1, including overall lipid measures. In general, the population had a slight male predominance, was mostly Caucasian, and was skewed toward overweight. A significant minority (31%) had moderate or nephrotic-range proteinuria.

Table 1 | Study population characteristics (*N*=391)

Characteristic	Median [IQR] or % (*n*)
Age (years)	12 [8,15]
Male	60% (236)
Race	
White	71% (277)
Black	15% (57)
Other/mixed	15% (57)
Hispanic ethnicity[a]	14% (55)
GFR (ml/min per 1.73m^2)[b]	43 [32,55]
Glomerular CKD	19% (76)
Proteinuria (Up/c; mg/mg)[a]	*0.4 [0.2,1.2]*
Normal (Up/c < 0.2)	27% (103)
Mild (0.2 ⩽ Up/c < 1.0)	42% (160)
Moderate (1.0 ⩽ Up/c < 2.0)	19% (72)
Nephrotic (Up/c ⩾ 2.0)	12% (44)
BMI percentile[a,c]	61 [32,85]
Overweight (85 < BMI percentile ⩽ 95)[c]	10% (37)
Obese (BMI percentile > 95)[c]	15% (57)
Triglycerides (mg/dl)	106 [75,141]
Total cholesterol (mg/dl)	174 [154,194]
HDL cholesterol (mg/dl)	47 [40,55]
non-HDL cholesterol (mg/dl)	126 [107,147]

Abbreviations: BMI, body mass index; CDC, Centers for Disease Control and Prevention; CKD, chronic kidney disease; GFR, glomerular filtration rate; HDL, high-density lipoprotein; IQR, interquartile range; Up/c, protein: creatinine ratio.
[a]Missing data: Hispanic ethnicity, *n*=3; Up/c, *n*=12; BMI percentile, *n*=16.
[b]*n*=368 (94%) directly measured by iohexol plasma disappearance; *n*=23 (6%) based on estimating equation.
[c]Age- and gender-specific BMI percentiles were calculated using 2000 CDC standard growth charts for United States children.[57]

Triglycerides

Figure 1a shows the relationship between triglyceride (TG) levels and GFR. Univariately, log(TG) and GFR displayed a linear relationship, with TG levels increasing on average 8% (95% confidence interval (CI): 5%, 11%) for every 10 ml/min per 1.73 m^2 decrease in GFR (Table 2a). Although a relationship was suggested between elevated TG and subnephrotic proteinuria, this was clearer in subjects with nephrotic-range proteinuria, who displayed TG levels on average 55% higher (95% CI: 32, 84) than those with normal protein: creatinine ratio (Up/c). The prevalence of hypertriglyceridemia in children with nephrotic-range proteinuria was 61%, as compared with 21, 30, and 24% in children with normal, mild, and moderate proteinuria, respectively.

After multivariate adjustment, higher TG levels continued to be associated with increased age, decreased GFR, proteinuria, and being either overweight or obese (Table 2a). Children who were overweight or obese, or had nephrotic proteinuria, had TG levels on average 30% higher than those of children with normal weight and normal Up/c, a magnitude of association greater than that for a 30 ml/min per 1.73 m^2 decrease in GFR (23%, not shown in table). Higher TG levels were associated with mild proteinuria (18% increase in TG) and nephrotic proteinuria (34% increase in TG), but not with moderate proteinuria (3% increase in TG). Restricting analysis to the 279 children who self-reported overnight fasting did not qualitatively change the reported associations.

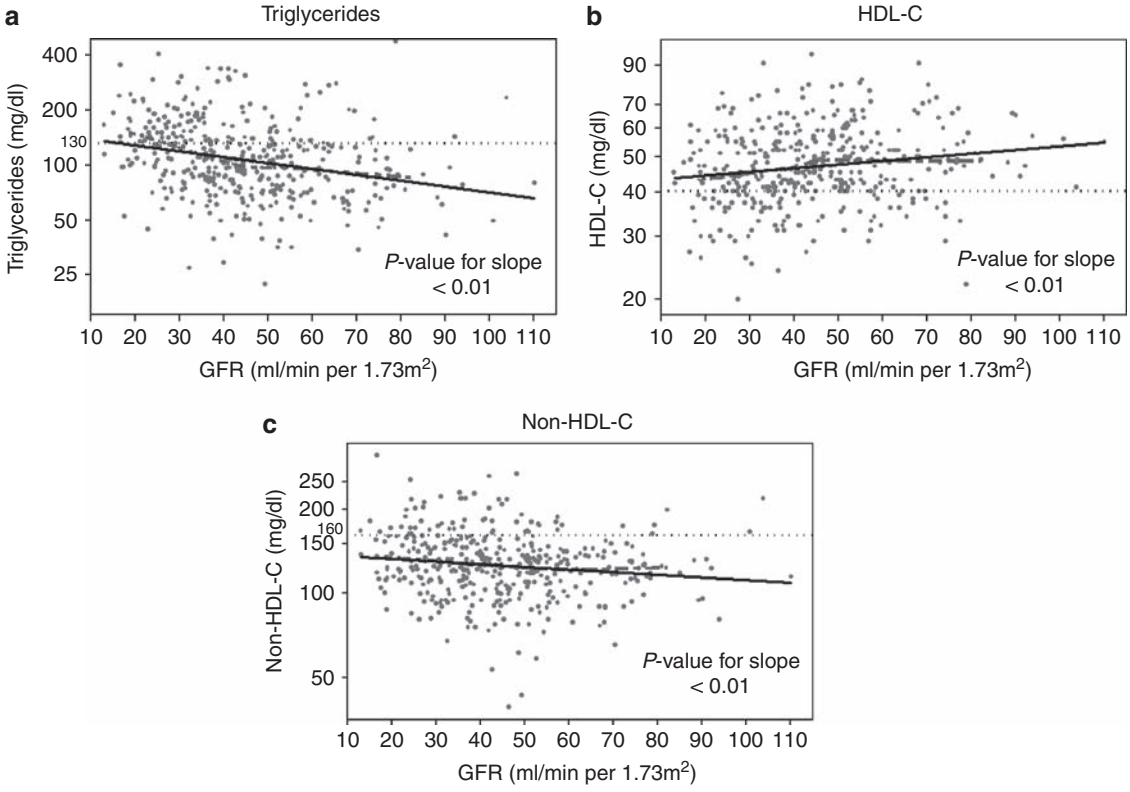

Figure 1 | Relation of lipid measurements to GFR. (**a**) Triglycerides. (**b**) HDL–C. (**c**) Non-HDL–C. GFR, glomerular filtration rate; HDL–C, high-density lipoprotein cholesterol.