

## Chapter 3: Assessment of lipid status in children with CKD

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**3.1: In children with newly identified CKD (including those treated with chronic dialysis or kidney transplantation), we recommend evaluation with a lipid profile (total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides). (1C)**

### RATIONALE

Young adults with eGFR <15 ml/min/1.73 m<sup>2</sup> have at least 10-fold higher risk for CVD mortality compared to the general population.<sup>54</sup> Many recent studies document the prevalence of CVD risk factors in children with CKD. However, due to limited follow-up, few studies demonstrate the association of dyslipidemia with clinical CVD events in adolescents or young adults, especially in the setting of CKD.

In the general pediatric population, lipid levels in childhood are predictive of future lipid levels and subsequent cardiovascular events.<sup>55</sup> The Pathobiological Determinants of Atherosclerosis in Youth (PDAY) study shows that initial fatty streaks seen in adolescents with normal kidney function develop into atheromatous plaques in young adults.<sup>56</sup> Over 50% of children 10–14 years old had early fatty streaks, and 8% had fibrous plaques, thus confirming that atherosclerosis begins in childhood.<sup>56</sup> Additional longitudinal studies demonstrate an association between childhood lipid levels and adult onset coronary artery disease.<sup>57–59</sup> Moreover, this atherosclerotic process is likely accelerated in nephrotic syndrome, proteinuric states and chronic kidney disease due to abnormal lipid metabolism and other atherogenic risk factors, thus putting children and adolescents at risk for developing CVD as they age into adulthood. In the Bogalusa Heart Study, body mass index, LDL-C, and systolic blood pressure were associated with atherosclerotic disease of the aorta and coronary vessels of children.<sup>56,57</sup> Recent studies of subclinical atherosclerotic CVD in children with familial hypercholesterolemia found an increase in intimal medial thickness of the aorta and carotid arteries compared to that of healthy young children.<sup>60</sup> Thus, atherosclerotic disease appears to begin in childhood, and dyslipidemia in children may play an important role in the early pathogenesis of atherosclerosis.

In children with CKD, the relationship between dyslipidemias and subsequent atherosclerotic clinical events is not known due to short follow-up in observational studies or clinical trials. Recently, the Cardiovascular Risk Reduction in High-Risk Pediatric Patients: A Scientific Statement from the American Heart Association Expert Panel on Population and

Prevention Science stated that CVD prevention in many chronic pediatric conditions was warranted given the high risk of developing disease as adults.<sup>61</sup>

The recent National Institutes of Health Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents in 2011 addressed specific questions of screening for dyslipidemias in children and adolescents and also treatment of dyslipidemias.<sup>7</sup> Cholesterol and its metabolism are important in children as cholesterol is the basis of cell membranes, myelin formation, subcellular organelles and steroid hormones which are all key for natural growth and development. Based on growth and development, lipid levels vary depending on age, puberty, and gender.<sup>62</sup> Lipid levels are very low at birth and increase during the first year of life [mean TC of 3.9 mmol/l (150 mg/dl), LDL-C 2.6 mmol/l (100 mg/dl), and HDL-C 1.4 mmol/l (55 mg/dl)] where they remain fairly constant till age 12 and are slightly lower in girls than boys. During puberty, there is a decrease in TC, LDL-C, and a slight decrease in HDL-C in boys. After puberty, TC and LDL-C increase to adult levels in boys and girls. Boys continue to have a slightly lower HDL-C than girls. Due to these variations in levels, former guidelines used the 95th percentile for age and gender to determine the upper limit of acceptable values. More recently, age- and gender- specific curves for lipoproteins linked to CVD risk over 15–20 years<sup>55,58</sup> have been used instead. A simplified and more practical approach has been to define acceptable, borderline high and high lipid concentration for children and adolescents based on these curves<sup>7</sup> (see Table 5).

Many studies document the prevalence of dyslipidemias among children with CKD and ESRD.<sup>63,64</sup> As in adults, the pattern of dyslipidemias in children with CKD is greatly influenced by the underlying pathogenesis and duration of CKD, severity of proteinuria, and treatment.<sup>63,64</sup> Due to this variability, the prevalence of hypercholesterolemia ranges from 39% to 65% in children with CKD. Among 391 children from the North American observational cohort study, CKiD (Chronic Kidney Disease in Children), TG and non-HDL-C levels increased as the measured GFR declined in this cross sectional study population.<sup>63</sup> Conversely, HDL-C was lower for those with a lower GFR. Factors that impacted TG, HDL-C and non-HDL-C levels were primarily GFR, significant proteinuria and obesity by multivariate analyses.<sup>63</sup> Over half the population had no evidence of dyslipidemias and of the remainder, 25% had a single abnormal lipid level, and the other 25% had at least 2 abnormal lipid levels.<sup>63</sup> The most

**Table 5 | Plasma lipid concentrations for children and adolescents<sup>7</sup>**

Category	Acceptable	Borderline High (75%)	High (95%)
Total Cholesterol	<4.4 (<170)	4.4–5.2 (170–199)	>5.2 (≥200)
LDL-C	<2.8 (<110)	2.8–3.3 (110–129)	≥3.4 (≥130)
Non-HDL-C	<3.1 (<120)	3.1–3.7 (120–144)	≥3.8 (≥145)

Abbreviations: LDL-C, low-density lipoprotein cholesterol; Non-HDL-C, non-high-density-lipoprotein cholesterol.

Values given are in mmol/l (mg/dl). Values for plasma lipid and lipoprotein levels are from the National Cholesterol Education Program (NCEP) Expert Panel on Cholesterol Levels in Children. Non-HDL-C values from the Bogalusa Heart Study are equivalent to the NCEP Pediatric Panel cut points for LDL-C.

common abnormality was hypertriglyceridemia.<sup>63</sup> The frequency of these abnormalities suggests that clinicians should measure lipid levels at baseline in children with CKD to screen for underlying secondary causes of dyslipidemia.

As for adults, there is no direct evidence indicating that measurement of lipid status will improve clinical outcomes. However, such measurement is minimally invasive, relatively inexpensive, and has potential to improve the health of people with secondary dyslipidemia. In the judgment of the Work Group, children with CKD (and their families) place a high value on this potential benefit and are less concerned about the possibility of adverse events or inconvenience associated with baseline measurement of lipid levels. In the judgment of the Work Group, these considerations justify a strong recommendation despite the low quality of the available evidence.

### **3.2: In children with CKD (including those treated with chronic dialysis or kidney transplantation), we suggest annual follow-up measurement of fasting lipid levels. (Not Graded)**

#### **RATIONALE**

Few data document how frequently the clinical lipid status changes in children with CKD, although it is clear that abnormal levels (once documented) are likely to persist. Unlike adults, growth and development in children have potential to influence lipid levels over time. Therefore, the Work Group recommends that fasting lipid levels be followed in children with CKD to screen for underlying secondary causes of dyslipidemia.

The ideal frequency of follow-up for fasting levels of LDL-C, HDL-C and serum TGs is unknown. These levels could be assessed annually in most children with CKD.

However, more frequent (or less frequent) follow-up measurements may be appropriate based on the clinical status of the patient, and the potential for such follow-up measurements to influence management.<sup>65</sup> Possible changes in management in response to such measurements could include therapeutic lifestyle measures (see Recommendation 6.1) or statin regimens for children with very high LDL-C levels (see Recommendation 4.1).

#### **Considerations for International Settings**

Similar to those for Chapter 1.

#### **Suggested Audit Criteria**

Similar to those for Chapter 1.

#### **KEY POINTS**

- Dyslipidemia is common in children with CKD.
- All children with CKD should be screened for dyslipidemias at presentation.
- Because growth and development as well as modality switches may influence lipid metabolism, lipids could be regularly evaluated during follow-up and when children initiate dialysis or receive a kidney transplant.

#### **RESEARCH RECOMMENDATION**

- Future studies should be conducted to determine the prevalence of dyslipidemias among children initiating dialysis or receiving a kidney transplant.

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