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Diagnostic Criteria and Lipid Screening of Dyslipidemia in Children

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Obesity is associated with significant morbidities and life-threatening conditions. Evidence shows that obesity in the pediatric population has increased by ten folds recently. This has been attributed to the remarkable recent alternations in socioeconomic factors and the overall increase in the incidence of obesity among the different populations. The pathogenesis of atherosclerosis and cardiovascular diseases is usually initiated in childhood. Previous studies indicates that early identification and proper treatment of dyslipidemia in the pediatric population can significantly reduce the risk of developing cardiovascular diseases and associated morbidities. Therefore, it is

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vital to screen children's lipid profiles to identify dyslipidemia and apply better interventions. This can significantly reduce the risk of premature cardiovascular diseases and accelerated atherosclerosis. The present study aims to identify the diagnostic criteria and various lipid screening approaches proposed in the literature to identify dyslipidemia in children. Two main approaches for screening dyslipidemia in children were reported. These include universal and selective screening approaches. While the latter is recommended to identify high-risk children, universal screening is also recommended to identify children missed by targeted screening (usually treated by pharmacological modalities).

Keywords: Dyslipidemia; screening; diagnosis; pediatrics; adolescence; children.

1. INTRODUCTION

Evidence shows that obesity in the pediatric population has increased by ten folds recently [1, 2]. This has been attributed to the remarkable recent alternations in socioeconomic factors and the overall increase in the incidence of obesity among the different populations. Furthermore, adult investigations shows that the risk of cardiovascular diseases is significantly associated with dyslipidemia. In this regard, it has been further shown that cardiovascular disease risk significantly decreases by properly managing dyslipidemia [3-6]. The pathogenesis of dyslipidemia is usually triggered during childhood and adolescence. Therefore, screening children's lipid profiles is vital to identify dyslipidemia and apply better interventions. This can significantly reduce the risk of premature cardiovascular diseases and accelerated atherosclerosis [4].

Different screening approaches of lipid profiles were proposed in the literature. The main approaches include targeted and universal approaches aiming at identifying children with dyslipidemia to help healthcare authorities and professionals plan for proper management and interventional modalities. In addition, different screening approaches have been proposed for a specific function aiming at adequately identifying these children [7]. The present study aims to identify the diagnostic criteria and various lipid screening approaches proposed in the literature to identify dyslipidemia in children.

2. OVERVIEW AND DIAGNOSTIC CRITERIA

The prevalence of dyslipidemia has been reported among various epidemiological studies in the literature. Estimates in the United States show that around 20% of children in the United States have at least one abnormality in their lipid values [8-11]. In this context, it has been shown that the prevalence of high low-density lipoprotein cholesterol (LDL-C), ≥130 mg/dL, high triglyceride, ≥130 mg/dL, high total cholesterol, ≥200 mg/dL, high non-high-density lipoprotein cholesterol (non-HDL-C), ≥145 mg/dL, and reduced HDL-C, <40 mg/dL, are 6.4%, 10.2%, 7.1%, 6.4%, and 12.1%, respectively. It should be noted that a child can have one or more of these abnormalities. Based on data between 1996 and 2006 from the United States National Health and Nutrition Examination Survey (NHANES), it has been indicated that adolescents with increased body mass index (BMI) were more likely to have a higher incidence of lipid abnormalities [12]. In this context, it has been reported that the prevalence of obesity (defined as BMI >95th percentile), overweight (defined as BMI ranges between 85th and 95th percentile), and normal weight was 43%, 22%, and 14%, respectively, among adolescents. Other investigations from various worldwide countries also reported similar rates of dyslipidemia among the pediatric population [13, 14].

It is widely known that various factors can significantly affect the plasma levels of lipoproteins and lipids. These factors include different environmental, genetic, and metabolic parameters. Therefore, different characteristics should be used to evaluate the presence of dyslipidemia in the pediatric population. However, there are some controversies between the different studies regarding the proposed ranges of these parameters, indicating the need for future studies. It should be noted that the definition of dyslipidemia has some considerations before discussing the diagnostic criteria and approaches of lipid screening in the pediatric population [15]. Among the different investigations in the literature, including the National Health and Nutrition Examination Survey and the Lipid Research Clinics Prevalence Study, it has been reported that the prevalence and epidemiology of dyslipidemia are

inconsistent among the different populations. It has been furtherly shown that ethnicity, race, and sex significantly contribute to hugely variable lipid profiles among children [16-18]. In this context, a previous study reported that the estimated 10th percentile for HDL-C and the -95th percentiles for LDL-C and TC was 38 mg/dL, 129 mg/dL, and 203 mg/dL, respectively. This is similar among various investigations in the literature and studies from the United States for children. It has been furtherly reported that the estimated 95th and 90th percentiles for TG concentrations were 185 mg/dL and 150 mg/dL, respectively. Previous studies also evidenced that non-HDL-C values of 145 mg/dL remarkably corresponded to the approximate values of the 90th and 95th percentiles [19, 20]. Different societies also reported that they concluded that the National Heart Lung and Blood Institute (NHBLI) guidelines for managing and preventing dyslipidemia-induced adulthood cardiovascular diseases. Medical interventions and lifestyle modification were the main themes for achieving a successful intervention based on these guidelines [21].

In Table 1, we have listed the variables currently reported for screening and evaluating dyslipidemia in pediatric settings based on recent guidelines and reports in the literature [21, 22]. It should be noted that the optimal cutoff of TG is inconsistent among the various reports in the literature. This is because of the inconsistency of the dietary components among the different populations worldwide. For instance, it has been suggested that a cutoff of 150 mg/dL for TG can more appropriately predict and evaluate dyslipidemia in children because of the high carbohydrate dietary component in this population [19, 23]. On the other hand, other previous studies suggested that increased TG levels are directly correlated with the increased routine consumption of alcohol, fructose, and simple sugars [24, 25]. Moreover, studies showed that TG is usually considered a significant component in lifestyle modification. Accordingly, it has been suggested that a cutoff of >130 mg/dL should be considered for TG when evaluating hypertriglyceridemia in pediatric settings. However, it should be noted that evidence for these conclusions is lacking. Therefore, further research is encouraged to empower the current literature, especially young children.

There is also epidemiological evidence indicating favorable trends in dyslipidemia prevalence and associated abnormalities among the pediatric population. For instance, it has been demonstrated that the trends of dyslipidemia among pediatrics were notable based on BMI and ethnicity parameters. In addition, estimates of trends between 1999 and 2016 from data from the NHANES database show that among pediatric patients (6-19 years old), trends show favorable outcomes regarding the levels of lipids in these patients and the estimated unfavorable measures. For example, it has been shown that HDL-C levels have significantly increased from 52.5 mg/dL to 55.0 mg/dL between 2007-2008 and 2015-2016, respectively. It was further reported that total cholesterol levels also showed favorable trends, with a significant reduction from 164 mg/dL to 155 mg/dL between 1999-2000 and 2015-2016, respectively [9, 26].

3. LIPID SCREENING

Screening the general population and a selected population are two distinct approaches that have been described in the literature for detecting dyslipidemia in children. Evidence shows that it is advisable to conduct screening approaches for high-risk children. Some of the reported risk factors include the presence of hyper-cholesterolemia and having a family history of cardiovascular diseases [27].

As a result of the increasing trends in the incidence of diabetes mellitus, obesity, and metabolic syndrome among pediatric patients, it has been recommended that additional parameters should further evaluate the screening process of children at high risk of developing these events. These include hypertension, insulin resistance, hyperglycemia, LDL levels, high levels of triglycerides, and elevated HDL-C levels. As previously mentioned, evidence shows that there are two main patterns in the process of lipid screening, including universal and selective screening approaches. It should be noted that conducting the selective lipid screening is mainly based on risk factors and/or family history of cardiovascular diseases and dyslipidemia. During this approach, it has been indicated that the fasting lipid panel should be evaluated in children >2 years old and have different risk factors for dyslipidemia and cardiovascular diseases. In this context, it has been suggested that the fasting levels of HDL-C, triglycerides, and total cholesterol should be evaluated in these children. By performing the Friedewald equation, it would be easy to calculate LDL-C or total cholesterol levels (HDL-C+triglycerides/5). However, it should be noted that the formula

cannot be applied in cases when the triglycerides levels exceed 400 mg/dL. Evidence shows that the estimated sensitivity for the Friedewald equation when estimating the serum values of LDL-C is higher than the sensitivity of other parameters used to evaluate it. It has been shown that direct assays for LDL-C are usually limited by some parameters when screening for dyslipidemia in children. It has been furtherly reported that non-HDL-C levels are good predictors of atherosclerosis. Besides, it has been proven that they can effectively predict dyslipidemia in adults. However, these levels might be associated with other non-lipid cardiovascular risk factors in this population [28-30].

Universal screening was also previously recommended in the available guidelines for screening dyslipidemia in children. Regarding the efficacy and potentials of this approach, it has been reported that it can detect many pediatric patients with significant dyslipidemias that might be routinely missed by selective screening, in addition to detecting genetic dyslipidemias in the high-risk population [21, 31]. In this context, estimates show that 30-60% of children with dyslipidemias can be missed by the routinely targeted lipid screening approaches based on a family history of cardiovascular diseases and hypercholesterolemia [21, 31, 32]. As a result, it has been shown that around 51% of children suffering from untreated or missed dyslipidemia will eventually develop a cardiovascular disease by 50 years of age, of whom 5% will develop it by 30 years only [33]. This indicates the importance of universal screening approaches. This can remarkably enhance the process of management and treatment based on recommendations from the Coronary Artery Risk Detection in Appalachian Communities project [21, 34].

Projections show that the incidence and risk of atherosclerosis and cardiovascular diseases can be significantly reduced by implying better interventions using these screening results. Studies show a linear trend in cholesterol levels in the earliest two years. Therefore, it has been suggested that no screening measures should be conducted to evaluate cholesterol levels before two years of age because no apparent treatment guidelines are suggested during this period. Assessment and screening of the lipid profile have been recommended to be conducted at ten years old. Evidence shows that total cholesterol and LDL-C levels are usually altered (with an estimated 10-20% reduction in adolescence). Accordingly, it has been suggested that screening and assessment of these variables should be conducted as early as 2-10 years of age, especially among children with an increased risk of having familial dyslipidemia. It has been recommended that routine check-ups and screening be further conducted after adulthood (16-18 years old) when the lipid screening approaches before this age indicate normal findings. When conducting the universal screening, the measurement of fasting levels of HDL-C and total cholesterol for assessing lipid profiles in children has been suggested as better approaches than non-fasting ones [21].

It should be noted that different subtypes are included under non-HDL-C, including very-low-density lipoprotein, intermediate-density lipoprotein, lipoprotein (a), and LDL-C. Accordingly, it has been concluded that non-HDL-C can effectively replace LDL-C in predicting dyslipidemia. In this regard, studies show that non-HDL-C can be a significant predictor for adulthood dyslipidemia and cardiovascular diseases. It should be noted that when the estimated non-HDL-C levels are >145 mg/dL, it is essential to perform extra two fasting lipid panels (with ≤ 2 - ≥12 weeks intervals). Clinical examination can also be a valuable tool for screening dyslipidemia in children. However, it is only valid for clinically-apparent

Table 1. Variables and measures that define dyslipidemia in pediatrics

Variable*	Borderline	Acceptable	Abnormal
Total cholesterol	170-199	<170	≥ 200
HDL-C	40-45	>45	<40
Non-HDL-C	120-144	<120	≥ 145
LDL-C	110-129	<110	≥ 130
Triglyceride			
10-9 (yeas)	90-129	<90	≥ 130
0-9 (years)	75-99	<75	≥ 100

**All variables are measured by mg/dL; HDL-C: high-density lipoprotein cholesterol; non-HDL-C: non–high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol. These findings are mainly adapted from the National Heart, Lung, and Blood Institute (NHLB) guidelines.*

atherosclerotic cases, while no value has been reported in cases of familial hypercholesterolemia. Genetic screening might also help identify patients with familial hypercholesterolemia. Population-based mass screening for related genetic mutations is recommended in some guidelines to identify these cases. Cascade screening is another potential approach. However, it is not widely used and needs further reporting for future implementations [7, 31, 35, 36].

4. CONCLUSION

The pathogenesis of atherosclerosis and cardiovascular diseases is usually initiated in childhood. Evidence indicates that early identification and proper treatment of dyslipidemia in the pediatric population can significantly reduce the risk of developing cardiovascular diseases and associated morbidities. This indicates the importance of screening lipid profiles in these children, which we have reviewed in the current study. Two main approaches for screening dyslipidemia in children were reported. These include universal and selective screening approaches. While the latter is recommended to identify high-risk children, universal screening is also recommended to identify children missed by targeted screening (usually treated by pharmacological modalities).

CONSENT AND ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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