ORIGINAL RESEARCH PAPER
VOLUME-6 | ISSUE-6 | JUNE-2017 | ISSN No 2277 - 8179 | IF : 4.176 | IC Value : 78.46
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

# Dyslipidemia in Children & Adolescents : Study, Diagnosis & Management

Pediatrics

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## ABSTRACT

The incidence and prevalence of obesity and dyslipidemia are increasing. Dyslipidemia is associated with significant comorbidities and complications, and with cardiovascular risk factors like obesity, diabetes mellitus, hypertension and smoking. The main objectives of this article is to describe the prevalence of dyslipidemia in children and adolescents attending our outpatient department and review the diagnosis and management of dyslipidemia in these.

## KEYWORDS:

### INTRODUCTION :

With socioeconomic development and the rapid increase of obesity for the past 20 years, the obesity rate has increased nearly 10-fold in children and adolescents [1,2]. The obesity rate of children is relatively high, especially in boys. The hypercholesterolemia was associated with cardiovascular disease (CVD). Atherosclerotic plaque is associated with the elevation of non-high density lipoprotein cholesterol (HDL-C) [3]. As the number of risk factors in CVD increased, the severity of asymptomatic coronary and aortic atherosclerosis was increased in youth [4]. Dyslipidemia is associated with cardiovascular risk factors (obesity, diabetes mellitus [DM], hypertension and smoking) [3,5]. Dyslipidemia is associated with carotid artery elasticity, intima-media thickness and brachial flow-mediated dilatation from childhood to adult- hood [6,7].

Therefore, the main objectives of this article are that to describe the prevalence of dyslipidemia in Children and adolescents attending our outpatient department and review the diagnosis and management of dyslipidemia in these.

### PREVALENCE OF DYSLIPIDEMIA IN CHILDREN AND ADOLESCENTS :

According to the 2012 report by Yang et al. [8], 19.7% of children and adolescents in our hospital (age 10-18 years) have at least 1 abnormal lipid profiles.

According to cutoff points and guideline of the American Heart Association (AHA) and National Cholesterol Education Program (NCEP), the prevalence of high low-density lipoprotein cholesterol (LDL-C) was 6.5%, that of high triglycerides (TG) was 4.7%, and that of low HDL-C was 7.1%. Totally, approximately 0.41% of study group were potentially possible for pharmacologic treatments [8]. In the study by Kim et al. [9], the dyslipidemia is increased with increasing body mass index (BMI) in male and female. The total cholesterol (TC) level was significantly increased with increasing BMI, especially in male. In our study, the prevalence of dyslipidemia was 25.2% in boys and 21.7% in girls and the more the frequency of dyslipidemia increased in overweight and obesity. The independent predictors of dyslipidemia were age and overweight /obesity in boys and girls.

### DIAGNOSTIC CRITERIA FOR DYSLIPIDEMIA :

The plasma levels of lipids and lipoproteins are influenced by various metabolic, genetic, and environ- mental factors. The lipid concentration is influenced by age, sex, and ethnicity. In 2011, the US National Institutes of Health Heart, Lung, and Blood Institute (NHLBI) experts revised the lipid cutoff values based on US normative data, categorised as the acceptable, borderline, and high [10]. Table 1 shows the more information.

The cut-off levels for LDL-C and TC according to the NCEP, American Academy of Pediatrics and NHLBI guidelines are similar. But, HDL-C <35 mg/dL and TG >150 mg/dL be regarded the abnormal in children and adolescents in AHA guideline [11].

### SCREENING GUIDELINES :

As the guidelines of the AHA and NCEP, the current recommendations for screening are based on the family history or the risk factor of CVD and dyslipidemia. In selective screening, fasting lipid panels should be assessed in children aged over 2 years with risk factors. Fasting TC, TG and HDL-C should be checked. The LDL-C is calculated using the Friedewald equation: LDL-C=TC (HDL-C+TG/5). If TG is >400 mg/dL, this formula cannot be used. The sensitivity of assays to determine LDL-C concentrations is lower than that obtained using the Friedewald equation. The direct LDL-C assays were limited in dyslipidemia screening of children [12]. Non-HDL-C is atherogenic and the better predictor of dyslipidemia in adult, but is also related to non-lipid cardiovascular risk factors in adulthood [14]. The 2011 NHLBI guidelines additionally recommend “universal screening” [10]. In 2010, the results of the Coronary Artery Risk Detection in Appalachian Communities project indicated that the selective screening would have missed many with significant dyslipidemia and failed to detect the genetic dyslipidemias which require pharmacologic treatment. The universal screening would enable for proper intervention and prevention of future atherosclerotic disease [14].

Cholesterol levels are reasonably consistent over 2 years of age. Cholesterol levels are not routinely measured before the age of 2 years because no formal treatment is recommended for this age group. Ten years of age (range, 9-11 years) has been proposed as an appropriate time to check the lipid profile [15].

Because TC and LDL-C level reduced by 10-20% during adolescence [10], children at risk for familial dyslipidemia should ideally be screened before adolescence (age 2 and 10 years). If results during puberty are normal, blood checking should be repeated on the end of puberty (age 16 years in girls and 18 years in boys). In universal screening, non-fasting TC and HDL-C can be checked, which this is meaningful in children than a fasting lipid profile.

## MANAGEMENT OF DYSLIPIDEMIA :

### LIFESTYLE CHANGES :

The primary treatment for dyslipidemia in children and adolescents is lifestyle changes, primarily dietary, and increased physical activity. The increasing of physical activity are correlated with decreased body fat and BMI, higher HDL-C levels, lower TC, TG and LDL-C levels, decreased insulin resistance and lower blood pressure in childhood and adolescence [10]. Children and adolescents should be encouraged the moderate and vigorous physical activity every day. Sedentary time for watching television, internet, and playing video games should be reduced as much as possible (<2 hours/day) [10].

### DIETARY TREATMENT :

The NCEP experts recommend dietary treatment aged over 2 years [13]. The first approach to therapy for children with dyslipidemia is a modified diet containing decreased amounts of cholesterol, total fat, saturated and transfat. The intake of simple sugars is decreased and that of complex carbohydrates are increased. The limiting protein intake is not recommended. Adequate calories should be provided to maintain the normal development and growth.

The Cardiovascular Health Integrated Lifestyle Diet (CHILD)-1 diet by the NCEP pediatric panel is as follows: total fat (25-30% of total daily calories); saturated fat (8-10% of daily kcal/estimated energy requirements); avoiding trans-fat, <300 mg/day from cholesterol; dietary fiber (14 g/1,000 kcal); fat-free unflavoured milk; limiting sodium intake and sweetened juice (no added sugar) <120 mL/day. The CHILD-2 diet is consisted with CHILD-2-LDL and CHILD-2-TG. The CHILD-2 diet recommends: 25-30% of total calories from fat; <7% from saturated fat; <10% from monounsaturated fat; and avoiding trans-fat. The CHILD-2-LDL recommends: plant sterol and stanol esters up to 2 g/day; water-soluble fiber psyllium, dose of 6 g/day (2-12 years) and 12 g/day (>12 years). The CHILD-2-TG recommends: decreasing sugar and sugar-sweetened beverages; replacing simple with complex carbohydrates; and increasing dietary fish to increase omega-3 fatty acid intake [13].

### PHARMACOLOGIC TREATMENT :

When to initiate medication?

Pharmacologic treatment of dyslipidemia is recommended in children aged ≥10 years with fail to the diet treatment and lifestyle changes after 6-12 months. Pharmacologic treatment for lower LDL-C is started in children without other CVD risk factors if the LDL-C is persistently ≥190 mg/dL despite a dietary intervention. Pharmacologic treatment is started, if the post-dietary LDL-C is ≥160 mg/dL with an at least 1 risk factors for CVD, a family history of CVD or metabolic syndrome. In children with DM, the medication should be considered when LDL-C is ≥ 130 mg/dL [10,11,16,17].

The six main classes of dyslipidemia therapy in children: the 3-hydroxy-3-methyl-glutaryl-coenzyme A (HMG-CoA) reductase inhibitor (statins), bile acid sequestrants (cholestyramine and colestipol), cholesterol absorption inhibitor, niacin (nicotinic acid), fibric acid derivatives and omega-3 fatty acids. Each drug is described below.

3-hydroxy-3-methyl-glutaryl-coenzyme A reductase inhibitor (statins):

HMG-CoA reductase inhibitor (statins) are the most commonly used medication to treat the dyslipidemia in children and adults. Statins can competitively inhibit HMG-CoA reductase which the first enzyme of the HMG-CoA reductase pathway. By inhibiting HMG-CoA reductase, the statins block the pathway of cholesterol synthesis in the liver. Atorvastatin, lovastatin, pravastatin, rosuvastatin, and simvastatin are currently approved by the US Food and Drug Administration for adolescents. Side effect of statin is limited and does not affect the growth or pubertal maturation. The increasing in liver enzyme up to 3 times the normal level has been reported in adolescents treated with simvastatin (40 mg/day) and atorvastatin (20 mg/day) [18,19]. Although rare, the asymptomatic increasing (over 10-fold) of creatine kinase (CK), has been reported in adolescents treated statins [20]. Liver function tests and CK assessment is recommended every 3-4 months in children. Because the cholesterol synthesis takes place mostly at night, the statin is usually taking at night for maximise their effect.

**Bile acid sequestrants (cholestyramine and colestipol):**

The cholestyramine and colestipol are bile acid binding resins, as bile acid sequestrants. This medication can bind the bile salt in the gastrointestinal (GI) tract and prevent the reuptake. This medication leads to depletion of bile salts and increased conversion of cholesterol to bile in the liver. The decreasing cholesterol level in hepatocytes leads to up-regulation of LDL-C receptor and increased clearance of LDL from the circulation [21]. Because the bile acid sequestrants are stayed in the GI tract, there was no systemic side-effects. But, the adverse GI effects such as gas, bloating, constipation, and cramps are common and the compliance is poor with interruption rates ranging from 20% to 30%. This agent can bind fat soluble vitamins. This effect would result in a vitamin deficiency, and so checking blood levels and possible supplementation has been suggested.

**Cholesterol absorption inhibitors (ezetimibe) :**

Cholesterol absorption inhibitor is newly developed medication which inhibiting the uptake of cholesterol. This blocks the uptake of cholesterol, thereby reducing the incorporation of cholesterol esters into chylomicron particles. This medication can decrease cholesterol absorption and decrease cholesterol delivery to the liver. The net result is a reduction in circulating LDL particles. This drug class is approved in children aged >10 years, as an adjuvant to statins. Co-administration of ezetimibe with the simvastatin is well tolerated, safe and resulted in higher LDL-C decrease compared with the simvastatin alone in adolescents (aged 10-17 years) with familial hypercholesterolemia studied as long as 53 weeks [22].

**Niacin (nicotinic acid) :**

Niacin (vitamin B3) acts by decreasing the hepatic production and release of very-low-density lipoprotein (VLDL). This agent can reduce the LDL-C and TG levels and this is the most potent HDL-C enhancer; however, this is of limited use because the significant side effect. The most common side effects are hepatic failure, hyperglycemia, flushing, myopathy, hyperuricemia, and gastrointestinal issues. Colletti et al. [23] reported that six children (29%) had reversible dose-related elevations of serum aminotransferase levels and the niacin treatment was stoped in 8 children (38%) because of flushing, GI trouble, headache, or elevated aminotransferase levels.

**Fibric acid derivatives :**

The fibric acid derivatives (gemfibrozil and fenofibrate) are usually used to treat hypertriglyceridemia in adult. This can reduce the hepatic production of TG by increasing oxidation of fatty acids in the muscle and liver and can reduce the rate of hepatic lipogenesis. This is also believed to increase HDL-C through a complex mechanism regulated by the nuclear transcription activator, peroxisome proliferator-activated receptor-α [24]. Fibric acid derivatives agents mainly affect TG and HDL-C. Although rare, rhabdomyolysis and myopathy may occur, particularly when used with a statin.

**Omega-3 fatty acids :**

The omega-3 fatty acids (eicosapentaenoic acid and docosahexaenoic acid) have been studied for ef- fect of reducing TG level in adult. In adult, omega-3 fatty acids (2-4 g/day) reduced TG levels (30-40%) and increased HDL-C (6-17%) [10]. The typical dose of omega-3 fish oils (1 g per capsule) is 1-4 g/day; its side effect is intermittent gastrointestinal issues.

## CONCLUSION :

Obesity is rising issue that has various risk factors that are associated with various comorbid conditions. In this article, we highlight about the prevalence of dyslipidemia in children and adolescents as well as the diagnosis and management of same. Paediatricians should be aware of the diagnosis and management of dyslipidemia as per the new protocols.

## REFERENCES:

1. . . . Park YS, Lee DH, Choi JM, Kang YJ, Kim CH. Trend of obesity in school age children in Seoul over the past 23 years. Korean J Pediatr 2004;47:247-57.
2. . . . Kim YS, Park MJ. Time trend in height, weight, BMI and waist circumference of Korean adolescents; from the Korean National Health and Nutrition Examination Survey (KNHNES), 1998, 2001 and 2005. J Korean Soc Pediatr Endocrinol 2007;12:142-9.
3. . . . McGill HC Jr, McMahan CA, Zieske AW, Sloop GD, Walcott JV, Troxclair DA, et al. Associations of coronary heart disease risk factors with the intermediate lesion of atherosclerosis in youth. The Pathobiological Determinants of Atherosclerosis in Youth (PDAY) Research Group. Arterioscler Thromb Vasc Biol 2000; 20:1998-2004.
4. . . . Berenson GS, Srinivasan SR, Bao W, Newman WP 3rd, Tracy RE, Wattigney WA. Association between multi- ple cardiovascular risk factors and atherosclerosis in children and young adults. The Bogalusa Heart Study. N Engl J Med

1998;338:1650-6.
5. . . . McGill HC Jr, McMahan CA, Zieske AW, Malcom GT, Tracy RE, Strong JP. Effects of nonlipid risk factors on atherosclerosis in youth with a favorable lipoprotein profile. Circulation 2001;103:1546-50.
6. . . . Li S, Chen W, Srinivasan SR, Bond MG, Tang R, Urbina EM, et al. Childhood cardiovascular risk factors and carotid vascular changes in adulthood: the Bogalusa Heart Study. JAMA 2003;290:2271-6.
7. . . . Juonala M, Viikari JS, Rönnemaa T, Marniemi J, Jula A, Loo BM, et al. Associations of dyslipidemias from childhood to adulthood with carotid intima-media thickness, elasticity, and brachial flow-mediated dila- tation in adulthood: the Cardiovascular Risk in Young Finns Study. Arterioscler Thromb Vasc Biol 2008; 28:1012-7.
8. . . . Yang S, Hwang JS, Park HK, Lee HS, Kim HS, Kim EY, et al. Serum lipid concentrations, prevalence of dyslipi- demia, and percentage eligible for pharmacological treatment of Korean children and adolescents; data from the Korea National Health and Nutrition Examination Survey IV (2007-2009). PLoS One 2012; 7:e49253.
9. . . . KimSH,AhnBC,JoungH,ParkMJ.Lipidprofilesand prevalence of dyslipidemia in korean adolescents. Endocrinol Metab 2012;27:208-16.
10. . . Expert Panel on Integrated Guidelines for Cardiovas- cular Health and Risk Reduction in Children and Adolescents; National Heart, Lung, and Blood Insti- tute. Expert panel on integrated guidelines for car- diovascular health and risk reduction in children and adolescents: summary report. Pediatrics 2011;128(Suppl5):S213-56.
11. . . Kavey RE, Daniels SR, Lauer RM, Atkins DL, Hayman LL, Taubert K; American Heart Association. American Heart Association guidelines for primary prevention of atherosclerotic cardiovascular disease beginning in childhood. Circulation 2003;107:1562-6.
12. . . Yu HH, Markowitz R, De Ferranti SD, Neufeld EJ, Farrow G, Bernstein HH, et al. Direct measurement of LDL-C in children: performance of two surfac- tant-based methods in a general pediatric population. Clin Biochem 2000;33:89-95.
13. . . Srinivasan SR, Frontini MG, Xu J, Berenson GS. Utility of childhood non-high-density lipoprotein cholesterol levels in predicting adult dyslipidemia and other car- diovascular risks: the Bogalusa Heart Study. Pediatrics 2006;118:201-6.
14. . . Ritchie SK, Murphy EC, Ice C, Cottrell LA, Minor V, Elliott E, et al. Universal versus targeted blood choles- terol screening among youth: The CARDIAC project. Pediatrics 2010;126:260-5.
15. . . Wald DS, Bestwick JP, Wald NJ. Child-parent screen- ing for familial hypercholesterolaemia: screening strat- egy based on a meta-analysis. BMJ 2007;335:599.
16. . . Daniels SR, Greer FR; Committee on Nutrition. Lipid screening and cardiovascular health in childhood. Pediatrics 2008;122:198-208.
17. . . Kwiterovich PO Jr. Recognition and management of dyslipidemia in children and adolescents. J Clin Endocrinol Metab 2008;93:4200-9.
18. . . de Jongh S, Ose L, Szamosi T, Gagné C, Lambert M, Scott R, et al; Simvastatin in Children Study Group. Efficacy and safety of statin therapy in children with familial hypercholesterolemia: a randomized, dou- ble-blind, placebo-controlled trial with simvastatin. Circulation 2002;106:2231-7.
19. . . McCrindle BW, Ose L, Marais AD. Efficacy and safety of atorvastatin in children and adolescents with fami- lial hypercholesterolemia or severe hyperlipidemia: a multicenter, randomized, placebo-controlled trial. J Pediatr 2003;143:74-80.
20. . . Avis HJ, Vissers MN, Stein EA, Wijburg FA, Trip MD, Kastelein JJ, et al. A systematic review and meta-anal- ysis of statin therapy in children with familial hypercholesterolemia. Arterioscler Thromb Vasc Biol 2007;27:1803-10.
21. . . Shepherd J, Packard CJ, Bicker S, Lawrie TD, Morgan HG. Cholestyramine promotes receptor-mediated low- density-lipoprotein catabolism. N Engl J Med 1980; 302:1219-22.
22. . . van der Graaf A, Cuffie-Jackson C, Vissers MN, Trip MD, Gagné C, Shi G, et al. Efficacy and safety of co- administration of ezetimibe and simvastatin in adoles- cents with heterozygous familial hypercholesterolemia. J Am Coll Cardiol 2008;52:1421-9.
23. . . Colletti RB, Neufeld EJ, Roff NK, McAuliffe TL, Baker AL, Newburger JW. Niacin treatment of hyper- cholesterolemia in children. Pediatrics 1993;92:78-82.
24. . . Auwerx J, Schoonjans K, Fruchart JC, Staels B. Transcriptional control of triglyceride metabolism: fi- brates and fatty acids change the expression of the LPL and apo C-III genes by activating the nuclear receptor PPAR. Atherosclerosis 1996;124(Suppl):S29-37.