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Dyslipidemia in Childhood Obesity: A Review

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Abstract

Childhood obesity has become epidemic in developed as well as developing countries. Apart from genetic factors, changes of lifestyle like consumption of excess calorie rich food, lack of physical activity and increased screen time are major contributing factors for childhood obesity. Many co-morbid conditions like cardiovascular, metabolic, neurological, hepatic, pulmonary, orthopedic, and renal disorders are associated with childhood obesity. It has both immediate medical complications as well as long term health consequences in later life. The most hazardous consequences like the cardiovascular disorder occur due to early athrosclerotic process which is accelerated due to dyslipidemia. As a result dyslipidemia is an important etiologic factor for development of cardiovascular disease (CVD), which is a leading cause of death in adulthood throughout the world. As abnormal vascular changes begins in childhood, and as dyslipidemia is an significant risk factor for CVD, screening and treatment of dyslipidemia in obese children and adolescents are an important health issue to prevent development metabolic syndrome and its consequences.

Key words: *Overweight, Obesity, Dyslipidemia, Childhood.*

Introduction:

The rate of obesity is rising alarmingly in many parts of the world.[1] Children and adolescent obesity is a significant health crisis throughout the world.[2] Childhood and adolescent obesity is a most important concern, not only because of immediate health problems, but also because of high possibility that it may continue into adulthood and affect long-term physical wellbeing.[3] The prevalence is maximum in western and industrialized nations.[4] A meta-analysis conducted in Indian subcontinent reported that the prevalence of overweight and obesity more among children of 10"18 year of age range and was higher among boys than girls.[5] A Bangladeshi meta-analysis showed that prevalence of overweight and obesity among children and adolescents of Bangladesh varied widely from 1.0% to 20.6% and 0.3% to 25.6% respectively and the pooled prevalence rates of overweight and obesity were 7.0% and 6.0% respectively.[6]

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Definition of Obesity:

Obesity in children and adolescents are approaching epidemic in developed as well as in developing countries.[3] Defining obesity in children is very intricate as precise assessment of body fat is very costly and fairly impractical.[7] Obesity is defined as an excessive accumulation of body fat.[8] For convenient reason, the definitions are generally based on anthropometry with waist circumference and BMI was most commonly used both clinically and in population based studies.[9] Overweight and obesity classification by center of disease control and prevention (CDC) is the most commonly used method. The CDC reference standard used the following cut-off points for classification: underweight (< 5th percentile), healthy weight (5th to < 85th percentile), overweight (85th to < 95th percentile) and obese (e" 95th percentile).[10]

Risk factors for obesity:

Genetic cause: Whitaker found that parental obesity was a more important predictor of offspring obesity and doubles the risk of adult obesity among both

obese and non-obese children less than 10 years of age.[11] Children with two obese parents are more fatty in childhood and also show a higher chance of tracking from childhood to adulthood.[12]

Adiposity rebound:
The adiposity rebound means the second rise in body mass index that occurs between 3 and 7 years and an early age of adiposity rebound predicts the later obesity.[13]

Infant Feeding: Review study done by Uwaezuoke et al. strongly supports the relationship between exclusivity of breastfeeding and lower risk of obesity.[14] Von Kries et al. in their study of 10,000 children in Bavaria found that the prevalence of obesity in children who had never been breast fed was 4.5% in comparison to 2.8% in breastfed children. An obvious dose-response consequence was identified for the duration of breast feeding on the prevalence of obesity where the prevalence was 3.8% for 2 months of exclusive breast feeding, 1.7% for 6-12 months, and 0.8% for more than 12 months. [15]

Fast food consumption: An international cross sectional study was done by Braithwaite et al.2014 among 72,900 children from 17 countries and 199,135 adolescents from 36 countries where frequent and very frequent fast-food consumption was reported in 23% and 4% of children, and 39% and 13% of adolescents, respectively. They also found that children in the frequent and very frequent groups had a BMI that was 0.15 and 0.22 kg/m2 higher than those in the infrequent group ($p<0.001$).[16]

Soft drinks: One prospective study has reported a positive association between consumption of sugar-sweetened drinks and obesity in children over 19 month's follow-up (mean change in BMI 0.18 kg/m2 for each daily serving).[17]

Portion size: large portions size of energy rich foods foster obesity-stimulating eating habit by increasing energy intake among children as young as 2 years of age.[18]

Physical activity and sedentary behavior: Less physical activity and more sedentary activities increase the incidence of overweight and obesity in children. Data suggests that reduced walking and cycling between the 1980s and 1990s, among children in the UK and USA, along with increasing use of cars increased the trend of obesity.[19]

Screen time: Screen media exposure is one of the best predictable causes of obesity in children and similarly, obesity is one of the recognized effects of screen media exposure.[20] A prospective cohort of over 700 children aged 10–15 years done by Gortmaker et al. showed a strong dose–response relationship between hours of television viewing and the prevalence of overweight and obesity, even after adjusting the confounding variables.[21]

Social Deprivation:
In most Western countries children from poor socio-economic environments have a higher risk of developing obesity than those from more rich groups.[22] This is expected to be more prominent in lower socioeconomic groups where limited money forces the poor to buy foods richer in energy (high in fat and sugar) to satisfy hunger; which are much cheaper than less fattening foods (like fruits and vegetables).[23]

Consequences of obesity:
The climbing trend of childhood obesity has been accompanied by higher rates of the co morbidities and the appearance of new or newly identified notorious health hazards. These conditions include sleep apnea, asthma, fatty liver disease, gastro-esophageal reflux, gallstone, Type 2 diabetes, cardiovascular disease, dyslipidemia, glucose intolerance and insulin resistance, menstrual abnormalities and orthopedic problems etc.[24] Above all the most worrying is that many of these children have risk factors for adult cardiovascular disease (CVD) and early signs of atherosclerosis.[25] The bunch of cardiovascular risk factors includes hypertension, hypertriglyceridemia, low HDL cholesterol and hyperinsulinaemia which is usually termed as the metabolic syndrome, is especially common among obese children.[26] Overweight or obese children are at increased risk of dyslipidemia especially if they have increased body fat proportion.[27] Obesity-related dyslipidemia is principally characterized by elevated levels and abnormal composition of plasma free fatty acids and triglycerides, low-density lipoprotein (LDL) and decreased levels of high-density lipoprotein (HDL).[28] This has been called atherogenic dyslipidemia because of its potential to accelerate atherosclerosis.[29]

Dyslipidemia: A disorder of lipid and lipoprotein metabolism which includes lipoprotein over production or deficiency. According to the National Cholesterol Education Program (NCEP) dyslipidemia

is defined as HDL-C <40 mg/dl and Total Cholesterol e"200 mg/dl, LDL-C e"130 mg/dl and Triglyceride levels 130 mg/dl, respectively.[30] National Health and Nutrition Examination Survey (NHANES), establishing cutoff points for TC, LDL-C, HDL-C and TG levels according to age and sex: for boys aged 12–16, 223–233 mg/dl for TC, 144–153 mg/dl for LDL-C and 163–195 mg/dl for TG; and for girls, 208–225 mg/dl, 136–145 mg/dl and 158–180 mg/dl for TC, LDL-C and TG, respectively. HDL-C only shows variation in boys, with values 39–46 mg/dl, The low HDL-C curve for males declined a little until 16 years of age, after that no change occurs throughout the young adulthood but the female curve for low HDL-C remains almost static level during adolescence.[31] Bogalusa Heart Study and the Lipid Research Clinics Study had developed a cut off points for normal lipid values and dyslipidemia is identified if one or more of these lipid, lipoprotein levels are abnormal.

†The cut points for high and borderline high represent approximately the 95th and 75th percentiles, respectively. Low cut points for HDL–C represents approximately the 10th percentile.

Prevalence of dyslipidemia in childhood obesity:

Elmaoðullarý et al in their study found that dyslipidemia prevalence was 43% in obese children and adolescents. They also observed that hypertriglyceridemia was the most frequent lipid abnormality and the frequency of dyslipidemia was related with older age and higher BMI.[33] A Turkish study showed 42.9% dyslipidemia in school aged obese children.[34] Another study done by Hashemipour et al. reported as 69.9% dyslipidemia in 2064 obese Iranian children.[35] Korsten-Reck et al.2008 in their study found 45.8% of the overweight children had an abnormal lipid profile. A German study showed that about 40% of the children had high total cholesterol and about 30% had high LDL-C and TG and more than 20% of the children had a HDL-C value.[36] An Indian study reported dyslipidemia in 63% of children and high LDL cholesterol being the most frequent lipid abnormality.[37]

Mechanisms of dyslipidemia in obesity

Energy in excess of the body's needs is assimilated by fat cells in the form of fatty acids and stored as triglycerides in lipid droplets. When required for the body the intracellular triglyceride stores are hydrolyzed to liberate free fatty acids that are transported to different tissues and oxidized to produce energy. [38] Free fatty acids (FFA) released from adipose tissue results in enhanced delivery of FFA to the liver. The enhanced FFA leads to increased level of triglyceride (TG) and very-low-density lipoprotein (VLDL) production in the liver as well as inhibition lipolysis in adipose tissue and skeletal muscle, thus promoting hypertriglyceridemia.[28] Furthermore the increased VLDL can inhibit lipolysis in the liver that also leads to hypertriglyceridemia. The TG in VLDL is exchanged for cholesteryl esters from low-density lipoproteins (LDL) and high-density lipoproteins (HDL) by the cholesteryl ester transport protein, producing TG-rich LDL and HDL. The TG in the LDL and HDL is then hydrolyzed by hepatic lipase, producing both small, dense LDL and HDL. LDL particles and the decreased HDL concentration are associated with a greater risk of atherosclerosis and cardiovascular disease. [39, 40]

Management of dyslipidemia in childhood obesity

Treatment for combined dyslipidemia of obesity is primarily lifestyle modification which is often highly

Acceptable, Borderline High, and High Plasma Lipid and Lipoprotein Concentrations (mg/dl) for Children and Adolescents [32]

Category	Low† (mg/dl)	Borderline low(mg/dl)	Acceptable (mg/dl)	Borderline† high(mg/dl)	High† (mg/dl)
Youth up to 19 years					
Total Cholesterol			< 170	170-199	≥200
LDL-C			<110	110-129	≥130
HDL-C	<40		>45	40-45	
Triglyceride(0-9 years)			<75	75-99	≥100
Triglyceride(10-19 years)			<90	90-129	≥130

effective.[41] Numerous studies have shown considerable improvements in combined dyslipidemia in response to weight loss, change in diet and increased physical activity. Moreover, loss of weight as little as 5% results in a 20% decrease in triglycerides and an 8 to 10 % increase in HDL-C.[42] In the absence of significant weight loss, regular bouts of aerobic activity had been found to reduce lipids.[43]

Diet composition: Obese individuals can lose weight by caloric restriction which is the key determinant of weight loss.[44]

These diet recommendations are those recommended for all healthy children over age 2 with specific differences focused on appropriate portion size and limitation of simple carbohydrate intake.[41]

Teach portions based on estimated energy requirements for age/gender/activity level.

Primary beverage: Fat-free unflavored milk No sugar-sweetened beverages; encourage water intake.

Limit refined carbohydrates (sugars, baked goods, white rice, white bread), replacing with complex carbohydrates (brown rice, whole grain bread, whole grain pasta).

Encourage dietary fish content

Fat content: Total fat 25–30% of daily kcal/Estimated energy requirement.

Saturated fat </= 8% of daily kcal/ Estimated energy requirement.

Cholesterol <300 mg/d

Avoid *trans* fats as much as possible.

Mono- and polyunsaturated fat up to 20% of daily kcal/ Estimated energy requirement.

Encourage high dietary fiber intake from naturally fiber-rich foods (fruits, vegetables, whole grains) with a goal of "age plus 5 g/d."

Activity recommendations for obese children [45, 46]

- Take activity and screen time history from child and parent(s) at each visit
- In children over age 6 y, prescribe moderate to vigorous activity* 1 h/d, with vigorous intensity physical activity** on 3/7 days
- Combined leisure screen time should not exceed 2 h/d
- Match physical activity recommendations with energy intake
- No TV in child's bedroom

* Examples of moderate to vigorous physical activities are walking briskly or jogging. **Examples of vigorous physical activities are running, playing singles tennis or soccer.

Drug Therapy for Combined Dyslipidemia

Drug therapy for management of dyslipidemia in childhood is very limited.[47] Rarely medication are considered in children with hypertriglyceridemia and combined dyslipidemia in whom diet and physical activity interventions are found unsatisfactory.[41] Medical intervention is recommended e"10 years old children with insufficient response to diet and lifestyle modification therapy over a period of at least 6-12 months. The choice of drug therapy depends upon the age, gender, lipid profile and family history of the patient.[48]

Statin therapy appears to be the rational choice for treatment of combined dyslipidemia if drug therapy is needed. Statin therapy decreased LDL cholesterol by 20 to 50% but change in TG is much less consistent.[49] Adverse effects are rare in children and adolescent.

There are some studies which suggest that Omega 3 fatty acids can decrease body fat in children; though very few data are available and most of them are conducted over short time periods with small sample sizes which makes it difficult to draw definite conclusions. Garcia-Cervera et al. in their study showed that intake diet of omega-3 polyunsaturated fatty acids decreased body mass index and cholesterol in a dose-dependent approach.[50]

Preliminary data suggests that Fibrates may also be potentially useful to decrease dyslipidemia.[51] Niacin is the most effective HDL enhancer and is suggested only as adjunctive therapy in children under supervision of a lipid specialist.[48]

Conclusion:

Detection and treatment of obese children with dyslipidemia is vital to reduce future cardiovascular disease burden. Treatment should be designed to lose weight by healthy dietary practice with a reduction in total calorie intake and increasing physical activity. Drug therapy can be started if lifestyle modification is unsatisfactory. Statins are the most important lipid lowering drugs but the addition of fibrates and others may be considered if necessary.

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