

## Obesity and Metabolic Dysregulation in Childhood: A Review

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### Abstract

Obesity these days had become a major health problem with prevalence both in developed as well as in developing countries. Overweight and obese children are likely to stay obese into adulthood [1]. While overweight and obesity are themselves risk factors to develop non communicable diseases like diabetes and cardiovascular diseases (CVD) at younger age, their association with metabolic dysregulation further increases the risk. The objective of this article is to identify the causes of obesity, to highlight its association with metabolic dysregulation and to suggest ways to prevent it, so as decrease co-morbidities associated with it

**Keywords:** Overweight; Obesity; Metabolic Dysregulation; BMI

### What is overweight and obesity?

Overweight is defined as BMI > 85<sup>th</sup> percentile and obesity as BMI >95<sup>th</sup> percentile [2]. However as per age specific cut offs for overweight and obesity, overweight is defined as BMI > 23 kg/m<sup>2</sup> of adult equivalent and obesity is defined as > 28 kg/m<sup>2</sup> of adult equivalent [3].

### What are the causes of obesity?

The main causes of obesity are

- Changing lifestyle which promotes more of indoor activities and decrease outdoor activities.
- More intake of junk food and carbonated drinks.
- Lack of physical exercise.
- Genetic factors.
- Excessive screen time, hence decreasing time for physical activity (National health and nutritional examination survey (NHANES) has shown a strong correlation between physical activity and overweight. Physical activity has been shown to prevent and to treat obesity [4].

### What is metabolic syndrome?

Metabolic syndrome (MS) refers to constellation of findings related to reduced insulin sensitivity and increased risk of CVD. It includes obesity, insulin resistance, glucose intolerance, hypertension, dyslipidemia, hyperandrogenism and polycystic ovary syndrome in women.

### Why is there growing concern about metabolic syndrome?

There is growing evidence on the prevalence of components of MS among obese children and adolescents. Obesity and metabolic syndrome are associated with endothelial dysfunction, atherogenic dyslipidemia and increases the risk of development of cardiovascular diseases and type 2 diabetes mellitus (T2DM) [5,6]. Obesity has a negative effect on immunity due to alterations in lymphoid tissue architecture and increase fat deposition in bone marrow and thymus hence causing changes in distribution of leukocyte subsets and lymphocyte activity [7-9]. Metabolic syndrome further promotes increase of proinflammatory mediators in adipose tissue which block the production of insulin sensitizing adipokines like adiponectin [10]. Further metabolic syndrome is characterized by low plasma HDL levels which has anti-inflammatory and immunoregulatory properties [11]. HDL neutralizes LPS, located on outer membrane of gram negative bacteria, thus protecting against endotoxin induced inflammation and shock [12]. Low HDL levels in obese persons may fail to effectively sequester LPS, further causing metabolic disease progression and immune cell activation [13-15].

Obesity and metabolic syndrome are independent risk factors for chronic kidney disease (CKD) and end stage renal disease (ESRD) [16-18]. Obesity related kidney disease, now termed as obesity related glomerulopathy (ORG) has histological finding of increased glomerular size and glomerular sclerosis [19,20]. These occur before decreased kidney function and often presents as isolated proteinuria with or without renal insufficiency.

### How obesity is linked to metabolic syndrome?

Metabolic syndrome is caused by insulin resistance which is induced by circulating free fatty acids (FFA) from adipose tissue mass. FFA reduce insulin sensitivity by inhibiting insulin-mediated glucose uptake hence causing hyperinsulinemia. Besides obesity causes increased secretion of adipokines which affect food intake and cause changes in vascular system which results in endothelial dysfunction and atherosclerosis [21].

Risk factors for metabolic syndrome have origin in prenatal and early post-natal period. Maternal gestational diabetes, low birth weight, infant feeding practices and early adiposity rebound are associated with development of obesity and metabolic syndrome later in life. Both genetic and environmental factors have been linked to obesity as well as metabolic syndrome. Environmental factors include short duration of sleep, unhealthy eating habits, excessive screen time and tobacco smoke exposure. Genome wide linkage analyses have shown common genetic factors responsible for individual components of the metabolic syndrome. Besides blood pressure, lipid profile and obesity are themselves highly heritable and show significant family aggregation.

### What are the comorbidities associated with obesity and metabolic syndrome?

Comorbidities associated with obesity, insulin resistance and metabolic syndrome include obstructive sleep apnea, polycystic ovary syndrome, nonalcoholic fatty liver disease (NAFLD), type 2 DM. Besides this obese people are at greater risk for depression and social stigma related to being overweight also contributes to mental illness.

### Does obesity lead to depression in children?

Obesity and stress have been linked through many ways. Stress, causing increase in peripheral cortisol and catecholamine levels result in increased insulin secretion and decrease in growth hormone and sex steroid secretion causing accumulation of fat in visceral adipose tissue [22-24].

Stress and depression causing disturbance in the circadian rhythm of cortisol secretion may contribute to development of central obesity and metabolic syndrome [25,26]. Studies have shown high prevalence of anxiety and depression in overweight and obese children [27,28].

### What screening to be done for obesity and metabolic syndrome?

Obesity prevention in childhood and adolescence should be first line approach to decrease the risk of metabolic syndrome and CVD. Primary care clinicians should perform annual obesity screening

for all children by using BMI and children with BMI at or greater than 95th percentile should be referred for weight management program and dietary counseling should also be provide to such children.

In addition to obesity screening, children should be screened annually for elevated blood pressure. Lipid profile should be done for all children between 9 - 11 years of age and those with family history of dyslipidemia. Screening for glucose intolerance and type 2 DM, should also be done using fasting glucose levels, oral glucose tolerance test, HbA1C levels and random glucose levels.

### What are the treatment options for obesity and metabolic syndrome?

Treatment options mainly include dietary modifications, lifestyle modifications as well as pharmaco-therapeutic interventions.

CHILD-1 (Cardiovascular health integrated lifestyle diet-1), a diet consisting of evidence based recommendation for dietary changes to reduce cardiovascular risk in pediatric population [29].

CHILD-1 involves 5 different age groups from birth to 21 years of age. Following table is based on the recommendations for each group with certain modifications proposed.

Lifestyle interventions include increase in physical exercise decrease in screen time, decrease intake of artificially-sweetened beverages. Children should be encouraged to be active for weight control and for physical well-being. The WHO recommends atleast 30 minutes of cumulative moderate exercise for all ages; and for children an additional 20 minutes of vigorous exercise three times a week [30].

Pharmacotherapeutic options to treat obesity are limited in children. FDA has approved only orlistat for weight loss in adolescents > 12 years of age. Orlistat is an intestinal lipase inhibitor causes 3% weight loss at 6 months of age based on initial weight. Bariatric surgery although effective, is reserved for severely affected adolescents.

### Summary

Metabolic dysregulation and metabolic syndrome reflects the effect of insulin resistant on human physiology.

- Risk factor are mostly multiple and cluster together, aim should be to prevent obesity and promote a healthy lifestyle.
- Focus for clinical screening and treatment should be on cardiometabolic risk factors.
- Screening should be done for obesity, glucose abnormalities, hypertension, dyslipidemia.

Age	Dietary Recommendations
Birth to 6 months	<ul style="list-style-type: none"> <li>• Colostrum to be fed</li> <li>• No top feeds</li> <li>• Initiate breastfeeding as soon as possible after birth</li> <li>• Infants should be exclusively breast fed until 6 months of age</li> </ul>
6 - 12 months	<ul style="list-style-type: none"> <li>• Continue breast feeding until 24 months of age.</li> <li>• Start home based easily available complementary diet at 6 months of age</li> <li>• No restriction in fat intake without medical recommendation.</li> <li>• Water should be encouraged.</li> <li>• Limit other types of drinks to 100% fruit juice, intake of which should be limited to 4 ounces/day or less.</li> <li>• Avoid sweetened beverages.</li> </ul>
12 - 24 months	<ul style="list-style-type: none"> <li>• Switch to reduced fat milk (2% to fat free).</li> <li>• Limit or avoid sugar sweetened drinks.</li> <li>• Water should be encouraged.</li> <li>• Transition to table food with total fat content of 30% of daily kcal/estimated energy requirement (EER), saturated fat content of 8-10% of daily kcal/EER and monounsaturated and polyunsaturated fat content of up to 20% of daily kcal/EER.</li> <li>• Avoid trans fat as much as possible.</li> <li>• Total daily cholesterol less than 300 mg</li> </ul>
2 - 10 years	<ul style="list-style-type: none"> <li>• Fat free milk.</li> <li>• Limit or avoid sugar sweetened drinks.</li> <li>• Water should be encouraged.</li> <li>• Limit total fat to 25-30% of daily kcal/EER, saturated fat content of 8-10% of daily kcal/EER and monounsaturated and polyunsaturated fat content of up to 20% of daily kcal/EER.</li> <li>• Avoid trans fat as much as possible.</li> <li>• Total daily cholesterol less than 300 mg</li> <li>• Encourage high dietary fiber intake from foods.</li> </ul>
11 - 21 years	<ul style="list-style-type: none"> <li>• Fat free milk.</li> <li>• Limit or avoid sugar sweetened drinks.</li> <li>• Water should be encouraged.</li> <li>• Limit total fat to 25-30% of daily kcal/EER, saturated fat content of 8-10% of daily kcal/EER and monounsaturated and polyunsaturated fat content of up to 20% of daily kcal/EER.</li> <li>• Avoid trans fat as much as possible.</li> <li>• Total daily cholesterol less than 300 mg</li> <li>• Encourage high dietary fiber intake from foods.</li> </ul>

Table

- Children with the presence of multiple components of metabolic syndrome are at maximum risk and need most intensive intervention efforts to achieve risk reduction.
- Increasing awareness of comorbid conditions such as NAFLD, PCOS, obstructive sleep apnea, mental health disorders enables pediatricians to refer to specialists as needed.

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