



Etiology and comorbidities of childhood obesity

Scott FI, Horton DB, Mamtani R, Haynes K, Goldberg DS, Lee DY, Lewis JD. Administration of Antibiotics to Children Before Age 2 Years Increases Risk for Childhood Obesity. *Gastroenterol Gastroenterology* 2016;151:120–9.

Scott et al. studied the association of antibiotic use before the age of two years with the risk of obesity in a large cohort. They found that exposure to antibiotics in the first two years of life is associated with an increase in the risk of early childhood obesity. They suggested that repeated antibiotic use—three or more courses—is highly responsible for an increased risk of obesity risk (1).

Clues of a drug's obesogenic effects by changing microbiota were previously shown in several laboratory investigations. The present study demonstrated this issue in humans while adjusting for multiple factors previously demonstrated to be associated with obesity.

Childhood obesity is one of the most serious public health problems in the 21st century. The problem is global and affects many low- and middle-income countries (2).

Body mass index (BMI) is the accepted standard measure of obesity for children aged two years and older (3). Other measures including weight-for-height and measures of regional fat distribution are used in the definition of obesity.

Because children grow, the norms for BMI in children vary with age and sex. There are published BMI reference standards for children between the ages of 2 and 20 years in different countries including Turkey (4,5).

Obesity is defined as BMI \geq 95th percentile for age and sex. Further, severe obesity is BMI \geq 120% of the 95th percentile.

The prevalence of obesity has increased worldwide. Globally, in 2015, the number of overweight children under the age of five years was estimated to be over 42 million. Children with obesity represent approximately 8.2%–8.5% of children (0–18 years of age) in Turkey (6).

The increased prevalence of childhood obesity has resulted in an increased prevalence of comorbidities associated with obesity. It has been demonstrated that a substantial component of adolescent obesity is established before the age of five years.

There is evidence about nutritional and environmental influences during critical periods in human development that can have permanent effects on an individual's metabolic syndrome and predisposition to obesity. These mechanisms have not been completely resolved. This "metabolic programming" may be responsible for a component of intergenerational transmission of obesity, with genetic and environmental factors. It is focused on gestation, infancy, and early childhood for understanding metabolic programming.

Several risk factors during the first 1,000 days of life—the period from conception to two years of age—are closely associated with later childhood obesity. These include higher maternal pre-pregnancy BMIs, prenatal tobacco exposure, maternal excess gestational weight gain, high infant birth weight, and accelerated infant weight gain. It has also been suggested that gestational diabetes, low strength of maternal–infant relationship, curtailed infant sleep, inappropriate bottle use, introduction of solid food intake before four months of age, and infant antibiotic exposure are risk factors for childhood obesity (7,8).

The causes of obesity are varied and complex. Obese children are influenced by environmental factors such as sedentary lifestyle and a greater-than-necessary caloric intake.

The risk of obesity increases by two- to three-fold if a child has one obese parent and by up to 15-fold if both parents are obese.

The increasing serving and consumption of foods with a high glycemic index, sugar-containing beverages, portion sizes of foods, and fast food service and diminishing family meals, decreasing physical activity, and

increasing use of computers have caused a rise in obesity. It has been suggested that the association of obesity with sugar-sweetened beverages is related to genetic predisposition.

Television viewing is an important environmental influence on the development of obesity during childhood. The duration of watching television directly increases the prevalence rate of obesity. Further, playing electronic games is associated with obesity during childhood.

There is some evidence of an association of shortened sleep duration with obesity. However, children with early bedtimes have a relative risk of adolescent obesity. Additionally, it has been shown that sleep deprivation is associated with increased food intake, weight gain, and higher leptin levels. Decreased insulin sensitivity, which is independent of adiposity, has been found to be associated with sleep-disordered breathing, sleep fragmentation, and intermittent hypoxemia in obese adolescents.

Some medications can cause weight gain, including certain psychoactive drugs (e.g., olanzapine and risperidone), anti-epileptic drugs, and glucocorticoids.

Other environmental factors such as gut microbiota, toxins, and viruses have been proposed as possible contributors to obesity. The role of these factors is still speculative, but they are supported by some evidence and continuing investigations. Studies in animals and humans have suggested that the administration of antibiotics during early life predisposes them to obesity later in life (1). It has been suggested that changes in gut microbiota are associated with weight loss and improvement in insulin sensitivity and induce the development of brown fat (7).

Environmental chemicals, such as the pesticide dichlorodiphenyltrichloroethane or bisphenol A (BPA), may trigger obesity. Cans and plastic packaging contain BPA. Experimental studies have shown that BPA is a selective modulator of estrogen receptors and that it accelerates adipogenesis and body growth. Moreover, an association of urinary BPA concentrations with obesity or obesity-related diseases has been demonstrated.

Genetic factors play a role and interact with environmental factors to result in obesity. It has been suggested that heritable factors are responsible for 40%–85% of the variation in adiposity, but molecular mechanisms for these factors have yet to be determined.

Specific syndromes and single-gene defects are related to childhood obesity. Children with genetic syndromes associated with early-onset obesity and characteristic findings on physical examination. These findings are dysmorphic features, short stature, developmental delay, intellectual disability, retinal changes, or deafness. Prader–Willi syndrome is the most common of these.

Endocrine causes of weight gain are identified in less than 1% of obese children. Cortisol excess, hypothyroidism, growth hormone deficiency, and pseudohypoparathyroidism type 1a are primary considerations among the endocrine causes of obesity. Hypothalamic lesions may cause rapidly progressive severe obesity. In the pediatric age group, hypothalamic obesity is most often seen after the surgical treatment of craniopharyngiomas.

Obese children are at risk of a number of medical conditions that can lead to further morbidity and mortality. The comorbidities of obesity in childhood affect the cardiovascular, endocrine, gastrointestinal, pulmonary, orthopedic, neurologic, dermatologic, and psychosocial systems.

Formerly, type 2 diabetes mellitus and steatohepatitis were considered as “adult diseases,” but now, they are frequently seen in obese children. It is known that obesity during adolescence increases the risk of premature death during adulthood.

Childhood obesity is associated with an increased risk of major cardiovascular events during adulthood, independent of the adult obesity status.

Hypertension is probably the most common comorbidity associated with obesity. Obese children are three times more likely to have hypertension than non-obese children. More than 50% of obese children have lipid abnormalities in a fasting lipid profile. One of the following is seen: elevated concentration of serum low-density lipoprotein cholesterol, total cholesterol, and triglycerides and decreased concentration of high-density lipoprotein cholesterol. Obese children also have risk factors for atherosclerosis such as endothelial dysfunction, carotid intima-media thickening, the development of early aortic and coronary arterial fatty streaks, decreased arterial distensibility, and increased left atrial diameter (7).

The principal endocrine comorbidities of obesity are impaired glucose tolerance, type 2 diabetes mellitus, metabolic syndrome, and polycystic ovary syndrome.

The prevalence of impaired glucose tolerance among obese children ranges from 7% to 25%, and the prevalence of type 2 diabetes ranges from 0.5% to 4%.

Metabolic syndrome is more common in obese children. It is characterized by abdominal obesity, hyperglycemia, dyslipidemia, and hypertension, which are risk factors for type 2 diabetes and atherosclerotic cardiovascular disease.

Obese adolescent girls are at an increased risk of hyperandrogenism and early-onset polycystic ovary syndrome.

Fatty livers were found in 40% of obese children. This prevalence varies by ethnicity. Of these obese children, approximately 10%

have mildly elevated serum aminotransferase concentrations, which are usually caused by nonalcoholic fatty liver disease.

Asymptomatic gallstones can be detected in approximately 2% of obese adolescents.

Sleep apnea diagnosed by polysomnography was seen in approximately 10% of obese children.

Orthopedic comorbidities of obesity are slipped capital femoral epiphysis and tibia vara (Blount disease). The prevalence of fractures, genu valgum, musculoskeletal pain (e.g., back, leg, knee, ankle, and foot), impaired mobility, and lower extremity malalignment is high in obese children.

Psychosocial consequences of childhood obesity are common. Alienation, anxiety, distorted peer relationships, distorted body image, poor self-esteem, and depression are frequently seen. The risk of psychosocial morbidity increases with increasing age and is higher among girls than boys (7).

Despite some limitations, interventions to prevent childhood obesity are generally effective. The strategies supported most by the literature are school-based programs that enhance physical activity, nutrition education, and the quality of food served at school and, additionally, parent-focused interventions designed to encourage children to be more active.

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Received: 20.02.2017 **Accepted:** 27.02.2017

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• Available online at www.turkjgastroenterol.org • DOI: 10.5152/tjg.2017.010317