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The Comorbidities of Childhood Obesity

Author 1: Esther Ejiroghene Ajari

Email Address: estherejiroghene@gmail.com

Affiliations: (1) Faculty of Clinical Sciences, College of Medicine, University of Ibadan, Ibadan, Oyo State, Nigeria

(2) End Childhood Malnutrition and Diarrhea Initiative, The TriHealthon, Ibadan, Oyo State, Nigeria

Author 2: Babatunde Isaac Ademusire

Email Address: babatundeademusire@gmail.com

Affiliation: Faculty of Clinical Sciences, College of Medicine, University of Ibadan, Ibadan, Oyo State, Nigeria

Author 3: Abdulhammed Babatunde

Email Address: abdulhammedbabatunde99@gmail.com

Affiliation: Faculty of Clinical Sciences, College of Medicine, University of Ibadan, Ibadan, Oyo State, Nigeria

Corresponding Author: Esther Ejiroghene Ajari

Address: C1, Alexander Brown Hall, University College Hospital, Ibadan, Oyo State, Nigeria

Email Address: estherejiroghene@gmail.com

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Abstract

Childhood obesity is a preventable multi-systemic disease that has become an epidemic. In this narrative review, we showed evidence, in the literature, of the affectation of body systems by obesity. Co-morbid conditions of obesity in the cardiovascular, nervous, dermatological, respiratory, endocrine, reproductive, musculoskeletal, gastrointestinal, and renal systems, and its effects on mental health are discussed. Obesity ultimately reduces the quality of life of children and is a leading cause of preventable deaths. Effective measures aimed at the prevention of obesity and the treatment of its co-morbid conditions should be taken.

Keywords: Obesity, Childhood, Comorbidity, Malnutrition

Introduction

Obesity and overweight are nutritional disorders caused by energy imbalance between calories consumed and calories expended. Epigenetics also influences the transmission of the risk of developing obesity from parents to offspring (1). Single-nucleotide polymorphisms at genetic loci for adipokines and their receptors are linked to obesity (1).

In children greater than two years of age, a body mass index (BMI) of >30 kg/m2 is diagnostic of obesity, but not in children lesser than two years. Instead, a percentile scale based on the child's sex and age is used. In this population, BMI at the 85th to 94th percentile signifies overweight while BMI at or above the 95th percentile signifies obesity.

There has almost been a five-time increase in worldwide obesity since the 1970s (2). In the last three decades, the worldwide prevalence of obesity has increased by 47.1% for children, with 38 million under-five children and over 300 million aged 5-19 being reported as overweight or obese in 2019 (2). Asia accounts for almost half of these statistics (2).

Furthermore, obesity is a multi-system disease that kills more people than underweight. These deaths are linked to the co-morbidities associated with obesity. For every fivr-unit increase in BMI above the 25 kg/m^2 threshold, total mortality increases by 29%, vascular mortality by 41%, and

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diabetes-related mortality by 210% (3). Measures of central adiposity, such as increased waist circumference, predict these risks (3).

In this paper, we review evidence of the various co-morbidities associated with obesity according to the body systems.

Cardiovascular system

Childhood obesity is commonly associated with cardiovascular diseases which usually manifest after puberty and varies with BMI. Studies have shown the effects of obesity on the cardiac and vascular health of children, which results in the development of accelerated atherosclerosis enhanced by dyslipidaemia, which is usually evident during autopsy. Atherosclerosis, increased arterial stiffness, and vascular resistance result in increased afterload (2). These cardiovascular co-morbidities as well as ventricular hypertrophy, is not only peculiar to obese adults but also to children, and this worsens as the fat mass persists into adulthood (2). These co-morbidities increase the risk of hypertension in obese children and adolescents, which may pose a greater risk of early, and sometimes fatal, organ damage because of their exposure to high blood pressure at a very young age. (3).

In a study by Sorof et al. (2020), conducted to determine the prevalence of hypertension in school-aged children, five percent of the over 5000 children that participated in the study were found to have persistent high blood pressure, with obesity being the strongest risk factor (4). Mechanisms of childhood hypertension increase cardiac output and/or total peripheral resistance. Some of these mechanisms include increased sympathetic outflow, insulin resistance, renin-angiotensin-aldosterone system, vascular damage, sodium and water retention(5). Furthermore, impairment of cardiac structures by obesity in children also increases the risk of cardiac autonomic modulation (CAM) which results in increased sympathetic outflow and reduced parasympathetic innervation to the heart (6). This further contributes to other cardiovascular co-morbidities like coronary heart disease and hypertension in obese children.

Furthermore, studies have shown that overweight/obese children are at higher risk than the general population of developing idiopathic intracranic hypertension (7,8). The prevalence of obesity

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among children suffering from idiopathic intracranic hypertension have been shown to be as high as 75% in a study (7). However, the sample size of this study is relatively small. Moreover, at onset of idiopathic intracranic hypertension, overweight/obese children have been shown to have more symptoms of the disease than children with appropriate weight for age (8). Additionally, although there is no consesus as to whether the degree of obesity affects the severity of idiopathic intracranic hypertension symptoms and the disease outcomes, particularly visual field defects, some researchers have suggested that it does (8).

In addition, obese children suffer from abnormal lipid profile characterized by low HDL and high LDL in the blood which increases the risk of fat deposition in coronary arteries and carotid arteries. Atherosclerosis, dyslipidaemia, structure damage of the myocardium and vascular wall are disorders associated with obesity in children and may be complicated by diabetes mellitus or family history of hypocholesterolaemia (3). Children with atherosclerosis may not present with any clinical symptoms until adulthood, when the plaque has significantly narrowed the vessel increasing the risk of developing coronary artery diseases or even sudden cardiac death as young adults (9).

Moreover, researchers have pegged childhood obesity as a predictor of cardio-metabolic disease occurence in adults.

However, some children who are obese from childhood till adulthood may never develop any cardio-metabolic co-morbidity and have higher chance of remaining healthy later in life (10). This condition is known as “Metabolically healthy obesity” (10). Although this may be rare but it affirms that not all obese children have higher risk of cardiovascular co-morbidities, as compared to children with appropriate weight for age.

Nervous system

Morphological alteration in the brain may also arise as a result of obesity in children. According to a study of the differences in morphology of brain substances among children, there was significantly increased volume of amygdala and nucleus accumbens in obese children (mean age: 13.8+/-1.9), and a reduced gray matter mass, without any relationship with age or gender (11). The effect(s) of these differences has not been elucidated and more research is required to confirm this association on a larger study size.

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Mental health

Obesity not only increases the risk of cardio-metabolic disorders but also have significant effect on the psychological and social well-being of children. It can either be a primary or secondary co-morbidity or even both. Psychological co-morbidities of childhood obesity include depression, anxiety, low self-esteem, compromised perceived Quality of Life (QoL), behavioural disorders (12). These may be as a result of other predisposing factors such as stigmatization, isolation, "body-shaming", teasing and other negative behaviours from peers and the society in general. Hussein et al. (2020), studied the correlation between obesity and common psychiatric disorders in 60 obese (BMI >95 percentile) and 60 normal children. There was a significant correlation between obesity, depression and low self-esteem ($P<0.05$) with girls being more vulnerable than boys (13).

Moreover, obesity is a recognized cause of low self-esteem in childhood, particularly among boys, and white and Hispanic girls aged 13-14 years (14). Low self-esteem is a risk factor for loneliness, nervousness, smoking and alcohol intake (14). Although anxiety and oppositional defiant disorder were also more prevalent in obese children, the difference was not statistically significant. Furthermore, bullying of obese children was a major risk factor that contributed to development of depression among them. (13).

Additionally, eating disorder and Attention Deficit/Hyperactivity Disorder are other comorbidities associated with childhood obesity. Overweight girls, regardless of clinical status, experience binge eating (15), more depressive symptoms (16), and have a lower quality of life, compared to their peers of normal weight (17). In a study carried out on 26 school-aged children (8-17 years) hospitalized for obesity (BMI >85%) over 4 year period, 57.7% suffered from Attention Deficit/Hyperactivity Disorder (ADHD), a significantly higher prevalence when compared to a 10% prevalence among the same age group inthe general population ($p< .0001$), with the boys to girls ratio being 2:1 (18). Loss of control (LOC) over eating, an example of an eating disorder that is associated with obesity in children, also contributes to increased adiposity in the body. This kind of reciprocal relationship between obesity and LOC is also reported for depression and ADHD because as much as children with obesity have higher prevalence of these conditions than children

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with appropriate weight for age, those with these conditions tend to also have higher BMI than the general population (19). This can be attributed to the fact that depression, LOC and ADHD often cause inactivity, overeating, insomnia and low self-esteem, which are factors that reduce the amount of calories used daily, and ultimately result in overweight/obesity.

Also, obese children have a higher risk of a wide range of psychosocial and mental health disorders than normal weight children. In a study of about 43,297 children between ages 10 and 17 years, randomly selected by a telephone interview of parents or guardians in 2007 NSCH, there was a significant association ($p < 0.001$) between obesity and mental and psychosocial conditions, which include internalizing problem, externalizing problem, repeat grade, school problems, conduct disorder, learning disability and developmental delay together with ADHD (P .003), and depression (p .006), while anxiety was reported to have no significant association with BMI (20).

Dermatological system

Many skin disorders are associated co-morbidities of obesity in adulthood and some have been reported also in children. Skin tags (40%), striae distensae (32%), plantar hyperkeratosis (20%), hyperhidrosis (24%) and acanthosis (12%) were the dermatoses (percentage of subjects) that were significantly associated with obesity (>95th percentile) in a study of 65 overweight and obese children (aged 8-15years) at the Department of Dermatology, University Federico II, Naples, Italy. However, none of the 30 children with appropriate weight for age, in the control group, had these dermatoses (21). There was also no observed sex difference in skin diseases in obese children (21).

According to a retrospective cohort study of 248,775 children, aged 5-17 years, skin infections caused by bacteria, fungi and candidiasis were significantly associated ($p < 0.001$) with obesity (BMI > 95th percentile) while cutaneous viral infections showed an inverse relationship. Other risk factors for bacterial infections are female sex, diabetes, and white race. Pruritus, atopic dermatitis (22), psoriasis, seborrheic dermatitis, hidradenitis, hyperhidrosis and mechanical cutaneous changes were also significantly higher in obese children than those with normal BMI(23).

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Also, acanthosis nigricans, a hyperpigmented, papillomatous, velvety cutaneous thickening is also a known dermatological co-morbidity of obesity in children and an independent risk factor for metabolic disorders (hyperinsulinemia, insulin resistance, elevated triglycerides) in obese children (24). Some cutaneous features and skin diseases are associated with genetically induced childhood obesity. Generalised hypopigmentation and acanthosis nigricans are seen in Prader-Willi syndrome, regional hyperpigmentation in fragile X syndrome, atomic eczema in MOMES syndrome, hypohidrosis, nipple hypoplasia in ulnar-mammary syndrome and obesity syndromes which are commonly associated with disorders of pigmentation (25).

Additionally, psoriasis, a common chronic immune-mediated inflammatory skin disorder which reduces quality of life of children, is a notable co-morbidity of obesity in children as demonstrated by many studies (26,27)

Respiratory system

New-onset asthma in children has been reported to be associated with increased BMI and females are at a greater risk than their male counterparts (28). In 2019, Deng et al. meta-analysed 18 articles involving 73,252 children to find the association between overweight or obesity on childhood asthma and discovered that obese children are 1.40 times more likely to develop asthma than normal children (29). Obese children are at higher risk of obstructive sleep apnea (OSA), obesity hypoventilation syndrome (OSH), and more severe asthma than children with normal BMI, and therefore present with more serious symptoms, and require more medication and oxygen when managed in intensive care unit (30).

In the past few decades, the prevalence of obstructive sleep apnea syndrome (OSAS) continues to increase with childhood obesity and therefore is considered to be a co-morbidity. Some of the possible mechanisms are blockage of airway by tonsillar and adenoidal hypertrophy, and reduced lung compliance by increased chest wall weight and ventilator instability (31). Interestingly, not all studies have found a correlation between childhood obesity and obstructive sleep apnea. For example, according to a study on 340 children between 2 and 10 years of age, comprising of 170 children with sleep-disordered breathing and 170 healthy children, done to determine the rate of obesity in these two groups of children, 25.9% of the study group was obese while 74.1% was not,

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and it was concluded that there was no significant difference in the two groups (32). The study result might have been skewed by limitations and small study size and therefore may not be enough to reach a general conclusion. Other studies suggested that childhood obesity is linked to OSAS/OSA although the pathophysiology has not been elucidated and obese children with OSAS present more severely and require expert clinical management (28,31). Furthermore, increased chest and abdominal wall weight in obese children result in decreased lung volume ad expiratory flow when subjected to submaximal exercise which further increase inactivity and the risk of other complications as a result of low oxygen saturation (28).

Results from a cohort study,of 3,960 8-year-old children, to determine the relationship between BMI and general health, health related problems, and respiratory infections showed a significant association between obesity and bronchitis (95% confidence interval) (33). Although non-obese children also had respiratory infections during the study but the duration and severity of these infections were more in the obese children (33). This suggests that obesity reduces the body's immune response to infections.

Gastrointestinal system

Cholelithiasis in children is usually due to haemolytic disorders (34). However, obesity is responsible for 8-33% of cholelithiasis, and this is due to the excretion of cholesterol in bile in excess of the rate of bile acid and phospholipid secretion (34,35). Risk factors for the development of cholelithiasis in obese children are insulin resistance,metabolic syndrome, and subsequent weight loss (34,35).

Non-alcoholic steatohepatitis is seen in about 38% of children with obesity (35). Increased lipolysis and insulin resistance are implicated in the pathogenesis of steatohepatitis in obese children (34,35). Other risk factors for steatohepatitis include diabetes mellitus, hyperlipidaemia, and rapid weight loss (35). Non-alcoholic steatohepatitis can progress to hepatic fibrosis and cirrhosis in severe cases, as previously mentioned above (34–36).

Furthermore, gastro-oesophageal reflux disease (GERD) is more likely to occur in obese children when compared to their normal-weight counterparts (37) and this may be due to the compression

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of the stomach by the adjacent adipose tissue as seen in obese children with the resulting increase in stomach pressure, opening of the lower oesophageal sphincter, and acid reflux into the oesophagus (37,38).

Hypovitaminosis D is also a co-morbidity of childhood obesity and this may be due to the fact that vitamin D is stored excessively in the adipose tissue of obese children (39). More so, children who are overweight or obese are twice more likely to suffer from iron deficiency than those who are not (39,40) because obesity inhibit iron absorption by a pathway mediated by inflammation (39,41).

Furthermore, abdominal obesity in children is associated with non-alcoholic fatty liver disease (NAFLD), which is an early manifestation of ectopic lipid deposition in the liver (46). NAFLD is the most common liver disease among obese children in North America and some other regions (46). The spectrum of NAFLD ranges from steatosis to steatohepatitis to fibrosis and even cirrhosis (46).

Renal system

Obesity-related glomerulopathy, end-stage renal disease (ESRD) and chronic kidney disease (CKD) can occur secondary to obesity (42). Obesity induces renal injury by causing hyperinsulinaemia, which via different pathways such as the stimulation of inflammatory cytokines, induction of apoptosis, glomerular hyperperfusion and hyperfiltration, causes renal damage (42). Obesity is not only a risk factor for the development of ESRD and CKD in childhood but also causes a worsening of these conditions (42,43). Other risk factors for the development of ESRD and CKD in obese children are hyperinsulinaemia, hypertension, microalbuminuria, impaired glucose metabolism, and dyslipidaemia (42).

Endocrine system

Obesity has multiple negative impacts on the glucose-insulin axis and non-esterified fatty acid metabolism. This leads to peripheral insulin resistance and abnormal lipolysis (43). Furthermore, obesity leads to hyperinsulinaemia (43).

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Metabolic syndrome is also another endocrine-related co-morbidity of obesity. There is evidence that truncal fat and insulin resistance are the primary causes of this syndrome, where hyperglycaemia, dyslipidaemia, and hypertension exist alongside obesity (44). In addition, the concentration of adipokines such as leptin, adiponectin, retinol binding protein-4, chemerin, tumor necrosis factor alpha (TNFα), and interleukin 6 (IL-6) can be used to predict the risk of an obese child developing metabolic syndrome (44).

Recently, scientists have demonstrated that insulin resistance and increased visceral and total body fat can lead to the development of Impaired Glucose Tolerance, which can progress to Type 2 Diabetes Mellitus (45).

Other endocrine co-morbidities associated with obesity include Cushing syndrome and hypothyroidism [43].

Reproductive System

Although, it begins typically in adolescence, polycystic ovarian disease is a common abnormality associated with childhood obesity (47). It is often accompanied by hyperinsulinaemia and hyperandrogenism. Scientists postulate that high circulating insulin levels play a key role in ovarian cyst development due to the anabolic effect of insulin on the ovaries(47). Moreover, obesity can worsen the symptoms of polycystic ovarian disease by increasing insulin resistance and aggravating metabolic syndrome and diabetes, thus starting a vicious cycle which can lead to infertility (47).

In addition, obesity is a physiological trigger of menarche before ten years of age (48). Obesity is also associated with oligomenorrhea, amenorrhea and increased risk of complicated pregnancies (48). Furthermore, recent evidences have emerged in support of the theory that childhood obesity is associated with increased risk for impaired oocyte maturation, ovulation, implantation and oocyte quality when puberty is attained (48).

Musculoskeletal system

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Obesity is associated with high frequency and severity of orthopaedic disorders in children. These disorders occur due to increased stress and strain on bones and cartilages which are not designed to accommodate excess weight (49). The most common orthopaedic disorders include bowing of the femurs and tibia which can result in Blount syndrome (overgrowth of the medial aspect of the proximal tibial metaphysis) and slipped capital femoral epiphysis due to increased weight on the growth plate of the hip joint (49).

Obesity during the growth spurt phase may increase the risk of fractures from falls (50). This is due to the weight/bone mass imbalance, which also places increased levels of stress on developing bones and joints (50). This can, in turn, result in joint damage and even osteoarthritis in the later years. The recurrence of these fractures and bone disorders can lead to the increased need for complex surgeries and joint replacements in order to manage paediatric trauma. This need, thus, amplifies the physical and financial burden of childhood obesity.

Chronic nonspecific musculoskeletal pain in children has been reported as a common co-morbidity associated with obesity. Children suffering from this kind of pain usually have increased tendencies to be anxious, depressed and take part in lesser activities (51). The sites of pain in this population include the neck and musculoskeletal sites such as the lower back, knees, ankles and feet (51). Additionally, some studies did not specify the site of the reported nonspecific musculoskeletal pain (51).

Recent evidences identified the lower extremities as the most frequent site of this type of pain. An estimated prevalence of this form of lower limb pain among children aged 6-10 years is 24% (51). Childhood obesity is also associated with foot pain, and with the risk of joint pain increasing by 10% for every 10kg increase in weight and every 3% increase in BMI (51).

Childhood obesity also correlates with decrease in balance and range of motion (52). This commonly results from excessive anatomical and mechanical strain on the lower limbs, leading to pes valgus, pes planus, genu valgum, etc (52). The dynamic impairment associated with childhood obesity can also manifest as shortening of the hip flexor and knee extensors, especially the

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quadriceps and psoas muscles (53). This can, in turn, result in hyperlordosis (pronounced curve in the lumbar spine) or retropatellar symptoms (anterior knee pain).

Childhood obesity is sometimes associated with early onset of osteoarthritis, especially of the knee, vertebrae and feet (53). The symptoms of osteoarthritis are accelerated by both the mechanical factors and hormonal changes associated with obesity (53).

Some other well-established orthopaedic comorbidities associated with childhood obesity include Perthes' disease, Osgood Schlatter's disease, Scheuermann's disease and calcaneal apophysitis (54). Again, in these conditions, the lower extremities are mainly affected (54).

Conclusion

With more children becoming obese every year, obesity had reached epidemic proportions and is a major public health challenge. As demonstrated by this review, obesity is a multi-systemic disease with affectation of all body systems. Some of these co-morbidities occur in childhood while others are delayed till later life. Nevertheless, obesity remains a leading cause of preventable deaths.

As such, at the individual level, children should be encouraged to eat healthier foods and do regular exercise. At the community level, policies that support obesity prevention should be implemented (1). This may include increasing the amount of tax fees associated with pro-obesity activities carried out by parents e.g. acquisition of fast food, personal transportation vehicles etc. Also, anti-obesity lifestyles should be promoted in the curriculum of all schools. Additionally, non-governmental organization working to reduce the prevalence of childhood obesity should receive adequate financial and technical support from the government.

Moreover, the co-morbidities associated with obesity should be routinely investigated and promptly treated.

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Authors contribution

All authors contributed equally to this research

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