Review Paper

Management of Obesity in Children: A Narrative Review

Seyyedeh Azade Hoseini Nouri[1], Manijeh Tabrizi[1], Marjaneh Zarkesh[1], Ali Talebi[1], Maryam Shahrokhi[2], Afagh Hassanzadeh Rad[1], Setila Dalili[1*], Ehsan Kazemnezhad Leili[1]

1. Pediatric Diseases Research Center, Guilan University of Medical Sciences, Rasht, Iran.
2. Department of Cinical Pharmacy, Faculty of Pharmacy, Guilan University of Medical Sciences, Rasht, Iran.

Use your device to scan and read the article online

Citation Hoseini Nouri SA, Tabrizi M, Zarkesh M, Talebi A, Shahrokhi M, Hassanzadeh Rad A, et al. Management of Obesity in Children: A Narrative Review. Journal of Pediatrics Review. 2022; 10(4):287-296. http://dx.doi.org/10.32598/jpr.10.4.584.5

http://dx.doi.org/10.32598/jpr.10.4.584.5

Article info:
Received: 26 Feb 2022
First Revision: 27 Aug 2022
Accepted: 30 Aug 2022
Published: 01 Oct 2022

Keywords:
Pediatric obesity, Child, Overweight, Bariatric surgery

ABSTRACT

Background: Over the past three decades, the prevalence of overweight and obesity in children and adolescents has increased up to 3 times. Obesity is a multi-systemic medical problem affecting all socioeconomic statuses and increases the risk of other severe comorbidities even in childhood. In 50% of cases, there is a persistence of obesity from childhood into adulthood. This narrative review aimed to define the etiology, risk factors, prevention, and management of obesity in children.

Methods: This narrative review was conducted through a literature search on articles in English with the keywords of pediatric obesity, child, overweight, and bariatric surgery in PubMed, Scopus, ISI Web of Sciences, Cochrane, and EMBASE databases from 2001 to 2021 for 4 categories of etiology, risk factors, prevention, and management of obesity in children. Scientific articles, systematic reviews, meta-analyses, consensus, recommendations, and international and national guidelines published on pediatric obesity were considered.

Results: In this narrative review, we first assessed relevant articles to define childhood obesity and mention its etiologies. We then discussed the probability of persistent obesity from childhood into adulthood and intergenerational and perinatal transmission risks. We also noticed syndromic obesity, evaluation of childhood obesity, and its complications along with medical/surgical interventions.

Conclusion: Metabolic programming in particular periods of life, such as before and during pregnancy, infancy, and at the age of rebound adiposity (5.5 years old), is necessary to prevent childhood obesity. Lifestyle changes, diet modifications, promoting exclusive breastfeeding, and increased activity are the main principles of preventing and managing obesity. It is prudent to rule out syndromic and endocrinologic causes of obesity in suspicious patients along with their management.

** Corresponding Author:*
Setila Dalili, Associate Professor.
Address: *Pediatric Diseases Research Center, Guilan University of Medical Sciences, Rasht, Iran.*
Tel: *+98 (911) 1411463*
E-mail: *setiladalili1346@yahoo.com*

Introduction

Obesity is a significant public health concern worldwide [1]. It is a multi-systemic medical problem affecting all socioeconomic groups and is associated with an increased risk of other severe comorbidities. It has a great negative impact on children and adolescents' physical, psychosocial, and quality of life [1]. Over the past three decades, the prevalence of overweight and obesity in children and adolescents dramatically increased up to 300% or even higher, particularly in low and middle-income countries [1, 2]. Over 22 million children under the age of 5 are obese, and 1 in 10 is overweight [2, 3]. In 2019, more than 398,000 children aged 6-9 years were severely obese in Europe [4]. Early identification and treatment are essential to prevent obesity-related comorbidities in early life [5]. There are various techniques to estimate total body fat, but direct measurement of total fat mass and body fat percent (%FAT) are inaccessible methods.

Body mass index (BMI) measurement is a simple and widely used screening tool for diagnosing and classifying obesity. It is calculated by dividing weight in kilograms by squared height. There is a difference between the classification of obesity based on BMI in children and adults. In adults, BMI <18.5 kg/m^2, 18.5-24.9 kg/m^2, 25-29.9 kg/m^2, and >30 kg/m^2 are mentioned as underweight, normal weight, overweight, and obese, respectively. However, the amount of total body fat varies at different childhood ages. This rate is normally higher in infancy and gradually decreases up to 5.5 years of age (adiposity rebound phenomenon) and then increases again up to adolescence. In girls, body composition changes appear to be of greater complexity during puberty, and fat accumulation is higher [6]. An increase in height occurs with weight gain in children during development and growth. Therefore, it is impossible to use only a specific BMI number to classify the obesity status of children [7]. Classification of body mass index status in children is based on sex and age-specific CDC or World Health Organization (WHO) curves. BMI less than 5%, 5%-85%, 85%-95%, and >95% are mentioned as underweight, normal weight, overweight, and obese, respectively. Obesity is divided into three categories in terms of severity as well. Class I is defined as BMI ≥95th to <120% of the 95th percentile. Severe obesity class II is defined as BMI ≥120% of the 95th percentile or BMI ≥35 (whichever is lower) and class III as BMI ≥140% of the 95th percentile or BMI ≥40 (whichever is lower) [5]. For infants (smaller than two years of age), the infants' weight to length percentile is used instead of BMI [8].

Waist circumference is another screening tool for diagnosing obesity [9]. Waist circumference >40 inches (102 cm) in men and >35 inches (89 cm) in women is another criterion. In children, a waist-to-height ratio >0.459 (±0.017) for girls and >0.473 (±0.019) for boys is considered a valuable criterion of obesity [10]. This narrative review aimed to define the etiology, risk factors, prevention, and management of obesity in children.

Evidence acquisition

This study was conducted through a literature search of articles in English with the keywords of pediatric obesity, child, overweight, and bariatric surgery in PubMed, Scopus, ISI Web of Sciences, Cochrane, and EMBASE databases from 2001 to 2021.

Results

Multiple factors including genetic susceptibility and behavioral and environmental parameters are involved in the pathogenicity of overweight [3, 9]. Environmental factors including lifestyle changes, excessive calorie intake, low physical activity, greater hours of screen time, eating behaviors, and sleep disturbances might affect body weight [9]. Parental obesity [11], family eating behavior, and home environment are other contributing factors. The current evidence suggests that formula feeding increases the incidence of obesity during early ages. On the contrary, exclusive breastfeeding may prevent the development of obesity [12]. On the other hand, the early occurrence of adiposity rebound increases the risk of being overweight in adulthood. Muscle mass tends to decrease with age, which reduces metabolism and calorie need. So, even a tiny extra calorie can lead to overweight and obesity over time [3].

Over 90% of obesity cases are idiopathic. Syndromic, metabolic, and endocrine etiologies account for a small percentage of patients [3]. Some medications such as antidepressants, anticonvulsants, anti-diabetic drugs, antipsychotics, steroids, medroxyprogesterone, cyproheptadine, and beta-blockers might increase body weight. A relationship between obesity and psychological and behavioral problems such as attention deficit hyperactivity disorder has been suggested [13]. Appetite is affected by different hormones from the hypothalamus and the gastrointestinal tract and adipose tissue. As an appetite-stimulating hormone, ghrelin is secreted by the oxyntic glands of the stomach shortly before meal-

time. In contrast, leptin secretion from adipose tissue after eating affects the hypothalamus and appetite. In addition, peptide tyrosine (PYY), pancreatic polypeptide, oxyntomodulin, amylin, glucagon, glucagon-like peptide-1 (GLP-1), and GLP-2 are other hormones identified as anorexigenic [14].

Genetics certainly plays an essential role in the development of obesity. Many genetic polymorphisms responsible for obesity have not been yet identified [9]. *FTO* on q16 is a gene in charge of developing obesity [15]. Melanocortin 4 receptor mutation is the best-known monogenic disorder associated with obesity. POMC (Proopiomelan-ocortin) deficiency, leptin or leptin receptor mutations are other entities [16].

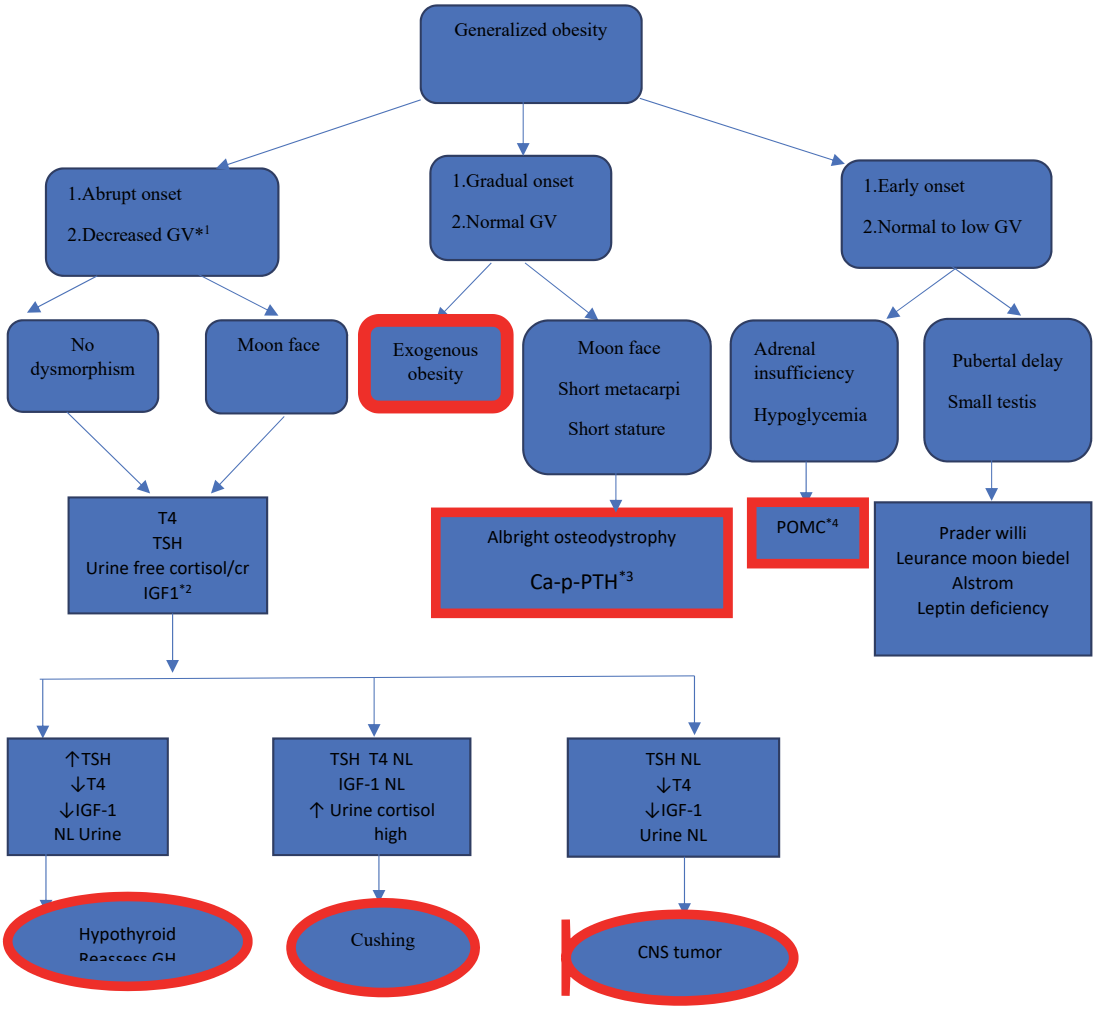
Endocrine disorders including hypothyroidism, hyperinsulinism, Cushing pseudohypoparathyroidism, and growth hormone deficiency as rare causes must be considered [3]. Gut microbiota is involved in synthesizing vitamins B12 and K and modulating gut permeability. It can modulate energy homeostasis through the absorption, breakdown, and storage of nutrients. It also causes an increase in insulin sensitivity and leptin levels and decreased ghrelin secretion. Gut microbiota might affect appetite by sending stimulatory signals for hunger to the brain and increasing GLP-1 and PYY secretion by enteroendocrine L-cells [17]. Pregnancy, quitting smoking, and stress are other contributing factors [18]. Adenovirus-36 infection is suggested to be associated with the development of obesity, although it has not been established yet [19].

More than 50% of childhood obesity extends to adulthood. This highlights the importance of prevention and control during childhood [20, 21]. Early age onset (preschool age <5 years) [22], severity from class II onwards [23], and having obese parents are important risk factors in this setting.

Maternal weight, cesarean section delivery, and birth weight seem to have an increasingly important role in pediatric overweight and obesity. The composition of the neonatal intestinal microbiota, which tends to be affected by maternal factors before pregnancy, has paramount importance. Pre-pregnancy overweight and obesity and gestational weight gain can change the gut microbiota in early life. Infants with overweight and obesity at the mean age of 3.7 months and those born to mothers with overweight and obesity have a high level of Lachnospiraceae bacteria (phylum firmicutes) in their gut. The abundance of Lachnospiraceae and Rikenellaceae in gut microbiota positively correlates with maternal BMI. As the major taxonomic groups in the human gut, they degrade complex polysaccharides to short-chain fatty acids, including acetate, butyrate, and propionate, which might be used as a source of energy by humans [24]. Both small and large for gestational age (SGA, LGA) infants are at risk of childhood obesity. It has been proven that higher neonatal adiposity is significantly associated with higher overall BMI and more likelihood of overweight and obesity from 2 to 6 years [25, 26]. In SGA infants, rapid catch-up growth in the first few months after birth (cell division period) has been reported as a long-term risk for truncal obesity. Rapid and marked postnatal increase in lipoprotein lipase and insulin-like growth factor-1 is mentioned as a mechanism for subcutaneous central fat accumulation in SGA infants [25].

A complete history and examination are essential in the evaluation of any obese child for appropriate management. Information regarding the age of obesity onset, diet, appetite, screen view and meal time, activity, sleep, socioeconomic status, having obese parents or siblings, menstrual cycle, and bulimia is mandatory. It is also necessary to ask about the use of drugs inducing hyperphagia (i.e. corticosteroids, sodium valproate, risperidone, phenothiazines, ciproeptadine), history of irradiation, seizure, and other CNS symptoms, signs of obstructive sleep apnea, snoring/noisy breathing, asthma, obesity hypoventilation syndrome, dyspnea after moderate efforts, wheezing, chest pain, and developmental milestones.

In the physical examination, estimating BMI and the severity of obesity is necessary. Accurate measurement of weight, height, growth velocity (GV), and head circumference must be done. Obesity has been identified as a primary risk factor for pre-HTN and HTN in childhood (7-30%), Therefore, accurate measurement of blood pressure (percentile of systolic and diastolic blood pressure adjust for age, height, and sex) should be done [27]. Ocular and or auditory exams are mandatory. Considering dysmorphic features, poly-syndactyly, acral edema, adenotonsillar hypertrophy, acne, hirsutism, acanthosis nigricans, striae, male pattern baldness, tanner stage, cryptorchidism or hypogonadism, abnormal fat distribution, hepatomegaly, and orthopedic exam (hip/knee/foot) seems to be important. In exogenous obesity, bone age is advanced, and linear growth increases. Endocrinological etiologies should be considered if an obese child has decreased linear growth or delayed bone age [27]. Genetic causes should be considered in patients with early obesity before the age of 5 or rapid progression, associated with developmental delay, reduced height



Journal of Pediatrics Review

Figure 1. Childhood obesity management algorithm [28-30]
*1Growth velocity,*2 Insulin-like growth factor1, 3*Parathyroid hormone, 4* Pro-opiomelanocortin deficiency.

velocity or short stature short, dysmorphic features, delayed cognitive development, or hyperphagia [8].

Necessary laboratory tests based on the patient's examinations are: FBS, HbA1C (no consensus), glucose tolerance test (GTT), homeostatic model assessment, insulin level, lipid profile, liver, and thyroid function tests, Ca, P, PTH, vitamin D (no consensus), FSH, LH, DHEAS, testosterone, serum leptin, insulin growth factor 1 (IGF-1), insulin growth factor- binding protein-3 (IGFBP-3), and urine cortisol. Many centers consider OGTT levels in children with severe obesity or obesity with several risk factors for diabetes. The OGTT is recommended after the age of 10 years or at the onset of puberty or for children with fasting plasma glucose ≥100 mg/dL or HbA1c ≥5.7-6.4% or at least one of the following risk factors: 1) Family history of T2DM in first- or second-degree relatives; 2) Race/ethnicity (African American, Latino, Native American, Asian American, or Pacific Islander), 3) Signs of insulin resistance (high blood pressure, hyperlipidemia, polycystic ovary syndrome, acanthosis nigricans, or small for gestational age at birth), 4) Maternal history of maternal gestational diabetes, 5) Non-alcoholic liver disease, 6) TG/HDL-cholesterol ≥2.2, and 7) Fasting plasma glucose ≥86 mg/dL, 8-TG >100 mg/dL and fasting plasma glucose >80 mg/dL (Figure 1).

Assessment of liver function tests and liver ultrasound are essential for the presence of Non-Alcoholic Fatty Liver (NAFLD) in overweight or obese children with BMI ≥85th with risk factors and children with BMI ≥95th percentile (AMA, Health Resources and Services Administration, and CDC). NAFLD increases the risk of cancer and cirrhosis. Screening for cholelithiasis is not recommended. The lipid profile test should be reassessed after 3 years if even the first results were nor-

Table 1. Syndromic causes of obesity and their manifestations

Syndromes	Manifestations
Prader Willi	PWS is caused by missing or non-working genes on chromosome 15. Hypotonia, feeding difficulties, short stature, and small genitalia in infancy. Hyperphagia leads to obesity, childhood behavioral problems, and intellectual disabilities.
Alstrom syndrome	The autosomal recessive genetic disorder, early obesity, early-onset type 2 diabetes, dilated cardiomyopathy, hypogenitalism, retinitis pigmentosa, cone-rod dystrophy resulting in blindness, sensorineural hearing loss, and deafness.
Cohen syndrome	Autosomal recessive disorder (mutation in *COH1* gene at 8q22), hypotonia, obesity, pigmentary retinopathy, progressive myopia, bull's-eye" maculopathy, slender extremities, joint hyperextensibility, skeletal abnormalities, non-progressive intellectual disability, benign neutropenia, microcephaly, and characteristic facial gestalt.
Bardet Biedel syndrome	Autosomal recessive, truncal obesity, intellectual disability, renal anomalies, rod/cone dystrophy, and retinal degeneration leading to night blindness, polydactyly in 70% of patients, and hypogonadism.
Carpenter syndrome	Autosomal recessive, also called acrocephalopolysyndactyly type II, obesity, craniosynostosis, brachydactyly, syndactyly, male hypogonadism, and developmental problems.
Albright hereditary osteodystrophy	Paternal mutation in the *GNAS1* gene on chromosome 20q 13.2. It is characterized by the phenotype of pseudohypoparathyroidism type 1A, short stature, obesity, round face, subcutaneous ossifications, short fourth and fifth metacarpi hearing disability, mental retardation, and lens clouding.
Biemond syndrome	Obesity, brachydactyly, iris coloboma, nystagmus, strabismus, hypogonadism, cerebellar ataxia, and intellectual disability.
Rohhad syndrome	The rare and potentially fatal disease, rapid-onset obesity with hypothalamic dysfunction, central hypoventilation, diabetes insipidus, hypothyroidism, GH deficiency, premature puberty, and neural crest tumor.
Borjeson-Forssman	Intellectual disability, obesity, seizure, hypogonadism, distinctive facial features (coarse face), ptosis, nystagmus, hyperopia, retinal disorder, and skeletal abnormalities.
Pro-opiomelanocortin deficiency	X-linked disorder, hypotonia, microcephaly, developmental delay, obesity, hypoglycemia, hypothyroidism, GH deficiency, adrenal insufficiency, red hair, light skin pigmentation, liver disease, and cholestasis.

GH: Growth hormone.

Journal of Pediatrics Review

mal. Tg/HDL-C >2.2 is a marker of atherogenic dyslipidemia and needs cardiac evaluation. In the presence of obstructive sleep apnea symptoms/signs, transcutaneous saturation of O_2 and systemic/pulmonary pressure measurement by a cardiologist should be determined. Determining bone age is also one of the most important assessments to assess height and the puberty process. Bone densitometry is not recommended as a routine evaluation for obese children. A referral to a psychologist is needed in the suspicious of depressive and or anxious symptoms due to anxiety disorder, dysmorphophobic traits, suicidal risk, and eating disorders [29, 30].

Over 25 syndromic types of obesity have been identified (Table 1). They are characterized by early childhood obesity associated with abnormal findings including dysmorphic features, hearing loss, visual impairment, short stature, mental retardation, hypogenitalism, and organ involvement (kidney and heart, etc.). Prader Willi is the most common genetic disorder associated with hypotonia, FTT, short stature, and small genitalia in infancy. Hyperphagia leads to obesity and childhood behavioral problems, and intellectual disabilities occur.

Alstrom syndrome is characterized by early obesity, cardiomyopathy, hypogenitalism, retinitis pigmentosa, and deafness in 80%-90% of patients, although height is generally unaffected.

Cohen syndrome is diagnosed by a constellation of symptoms consisting of pigmentary retinopathy and progressive myopia, slender extremities, joint hyperextensibility, neutropenia, microcephaly, and characteristic facial gestalt.

The cardinal features of Bardet Biedel syndrome are truncal obesity, intellectual disability, renal anomalies, retinal degeneration leading to night blindness, and polydactyly in 70% of patients. Cardinal features including craniosynostosis, brachydactyly, syndactyly, and male hypogonadism are characteristic of the carpenter syndrome.

Albright hereditary osteodystrophy is due to a paternal mutation in the *GNAS1* gene on chromosome 20q 13.2. It is characterized by short stature, round face, short fourth and fifth metacarpi hearing disability, and lens clouding. Down, Klinefelter, and Turner syndrome, along with their typical symptoms, increase the risk of obesity [31]. The characteristics and symptoms of the above-mentioned syndromes are listed in Table 1.

Any suspicion of syndromic or monogenic forms of obesity must be confirmed by genetic investigations.

Assessment for obesity risk (dietary habits, eating patterns, daily physical activity, and duration and quality of nocturnal sleep) is mandatory during routine well-child care. Observing proper dietary habits and exercise and nutrition counseling should continue even if BMI is normal. The initial screen for comorbidities, earlier follow-ups, and specific behavioral and eating patterns modification for at least 6 months are recommended if BMI is >85% or rising sharply.

Age-appropriate sharing of responsibility between child and parents, continuous monitoring of weight, healthy diet, and adequate physical activity are recommended for children with stable BMI after 6 months.

In cases with an increasing BMI despite the above recommendations after 6 months, it is mandatory to consider more frequent visits, more specific goals for diet and activity, and repeated screening for comorbidities. In adolescents with severe or refractory obesity, pharmacotherapy or surgery is considered after 6 months [32].

Changes in lifestyle and eating habits of the child are the main principles for gradual weight loss. Of course, this requires the cooperation of the whole family. The child should maintain weight loss alongside proper height growth. A low-calorie diet is not effective in the long term and failure of weight loss and progression into more complicated forms is common. Considering child and family dietary habits, meal composition, frequency of food intake, food preferences, or aversions can help regulate the regime. The diet should include the following combination 1 g/kg/day protein, carbohydrates 45%-60% of total calories, lipids 20%-35% of total calories, and saturated fatty acids <10% of total calories. The child should have breakfast, and 5 meals per day and should avoid high-energy and low-nutrient density foods consumption and eating between meals. Physical exercise (combining aerobic and resistance exercises, at least 2 weekly sessions with a duration >60 min) and reduced television or screen view time are recommended to associate with diet [29, 30]. Familial behavior therapy is important for achieving excellent results.

Bariatric surgery can control weight in obese patients and is associated with a 50% decrease in mortality rate [33]. Surgery might be a suitable option in adolescents with a BMI ≥35 kg/m^2 who have significant comorbidities like type 2 diabetes mellitus, OSA, severe nonalcoholic steatohepatitis, or symptomatic pseudotumor cerebri [34, 35]. It should be considered in adolescents who meet the criteria for surgery in case of failed attempts for weight loss. In this case, a multidisciplinary team consisting of a psychologist, nutritionist, physiotherapist, endocrinologist, pulmonologist, gastroenterologist, cardiologist, and specialized surgeon is needed. There is a controversy regarding the allowed age of bariatric surgery due to concerns about the negative impact of calorie restriction on target adult height. On the contrary, it has been noted that vertical sleeve gastrectomy (VSG) in preadolescent patients has no significant adverse effect on adult stature [36, 37]. Before surgery, a comprehensive psychological evaluation should be done to evaluate post-surgical dietary acceptance.

Roux-en-y gastric bypass (RYGB), laparoscopic adjustable gastric banding (AGB), and laparoscopic VSG are the most frequent surgeries. AGB has not been approved by Food and Drug Administration (FDA) in adolescents. VSG is now the most commonly used procedure due to fewer complications and similar weight loss compared to RYGB. In VSG, the surgeon removes approximately 60%-80% of the fundus and body of the stomach [37, 38]. Correcting minerals and vitamins such as iron, vitamin D, B1, and B12 must be considered to avoid postoperative nutritional deficiencies. There is a concern about the probability of unplanned pregnancy following massive weight loss, so it is advised to have reliable contraception in the first two years after bariatric surgery [39]. Postoperative visits should be done regularly, and any deficiencies in nutrients must be corrected. Long-term follow-up studies showed a significant decrease in comorbidities [37, 40].

Pharmacotherapy can only be offered for the treatment of obese children after the failure of the diet and lifestyle changes, if the potential benefits outweigh the risks, especially in severe obesity with cardiometabolic, hepatic, or respiratory disorders. It is noteworthy that in the case of ignoring behavioral modifications, more significant weight gain may be occurred after discontinuation of pharmacotherapy. Even with drug continuation, weight loss stops around 6 to 9 months after treatment. Losing weight >2kg in the first month, and >4%-5% baseline weight between 3 to 6 months shows the success of treatment. However, a reduction of 5% to 10% of body weight can substantially reduce the risk of diabetes, hypertension, and cardiovascular diseases [41]. Drugs cause weight loss through different mechanisms. Some of them reduce energy intake and baseline metabolism, while others affect intestinal or renal tubular reabsorption, or act as anorexiant agents.

Orlistat as an intestinal lipase inhibitor is the only FDA–approved medication for obesity in children <16 years old that reduces fat absorption. It has proven benefits

regarding glycemia, lipids, and blood pressure. Unfortunately, it frequently causes gastrointestinal upset and is often not tolerated by patients.

Liraglutide, a glucagon-like peptide-1 (GLP-1) receptor agonist is a drug that increases insulin secretion and hinders glucagon release. It is administered by an initial dose of 0.6 mg/day for the first week, which increases by 0.6 mg/day/week and stops at 3.0 mg/day. However, gastrointestinal side effects (nausea, vomiting), the need for a daily injection, and the cost may limit its use.

The effect of administering phentermine (a norepinephrine-releasing agent which suppresses appetite) in combination with extended-release topiramate (a carbonic anhydrase inhibitor) is more significant than orlistat. However, clinicians have to consider side effects such as tachycardia, depression, anxiety, and cognitive disorders. Phentermine alone can only be administered for up to 3 months in obese children, but phentermine plus topiramate is used for chronic conditions. It is noteworthy that phentermine is contraindicated in the case of hypertension or cardiovascular diseases.

The combination of naltrexone and bupropion produces similar weight loss as orlistat by suppressing appetite, but owing to the uncertainty about cardiovascular outcomes, it is preferred to use orlistat or liraglutide rather than naltrexone-bupropion.

FDA-approved short-term (i.e. 12 weeks) use of sympathomimetic drugs like phentermine, benzphetamine, phendimetrazine, and diethylpropion. Orlistat, metformin, or liraglutide, alone or in combination. They are the treatment of choice in overweight or obese patients with polycystic ovarian syndrome.

In patients with a high risk of diabetes, metformin, acarbose, and thiazolidinediones could be considered. Green tea, *Garcinia cambogia* (hydroxycitric acid), conjugated linoleic acid, and chitosan are ineffective for weight loss. In addition, the efficacy and safety of chromium, Gambisan, *Hoodia Gordonii*, and *Cynanchum auriculatum* are still unproven [42, 43].

Considering the prevalence of obesity as a pre-inflammatory state, we expect numerous chronic somatic complications in younger ages [9]. Concerning complications are cardiovascular diseases [44], metabolic syndrome, hepatic steatosis, cholelithiasis, gastroesophageal reflux disease, Blount disease, slipped capital femoral epiphysis, OSA, asthma, osteoarthritis, menstrual abnormalities, certain cancers, and premature death. Obese children might have disturbed psychological functions, which commonly present with low self-esteem, bulimia, anxiety, and depression [2, 3, 9]. Regarding the outbreak of COVID-19, we have to keep in mind that in addition to the above-mentioned complications, obesity can significantly increase COVID19-related morbidity and mortality [45].

Conclusion

Given the increasing prevalence of obesity, its related morbidity-mortality in children, and the likelihood of an extension of obesity to adulthood, early detection, and control of BMI trajectory in childhood, especially <5 years, is of great importance. In this regard, metabolic programming in particular periods of life is essential. Promoting lifestyle changes, diet modification, exclusive breastfeeding, and increased activity are the main principles for preventing and treating obesity. Early diagnosis of endocrine and rarely monogenic cases of obesity might be helpful to control long-term complications. As it was mentioned, bariatric surgery and pharmacotherapy can be considered in particular patients as well.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this research.

Funding

This research did not receive any grant from funding agencies in the public, commercial, or non-profit sectors.

Authors' contributions

All authors equally contributed to preparing this article.

Conflicts of interest

The authors declared no conflict of interest.

References

1. Lee EY, Yoon KH. Epidemic obesity in children and adolescents: Risk factors and prevention. Front Med. 2018; 12(6):658-66. [DOI:10.1007/s11684-018-0640-1] [PMID]

2. Raj M, Kumar RK. Obesity in children & adolescents. IJMR. 2010; 132(5):598-607. [Link]

3. Xu S, Xue Y. Pediatric obesity: Causes, symptoms, prevention, and treatment. Exp Ther Med 2016; 11(1):15-20. [DOI:10.3892/etm.2015.2853] [PMID] [PMCID]

4. Nittari G, Tomassoni D, Di Canio M, Traini E, Pirillo I, Minciacchi A, et al. Overweight among seafarers working on board merchant ships. BMC Public Health. 2019; 19(1):1-8. [DOI:10.1186/s12889-018-6377-6] [PMID] [PMCID]

5. Güngör NK. Overweight and obesity in children and adolescents. J Clin Res Pediatr Endocrinol. 2014; 6(3):129. [DOI:10.4274/jcrpe.1471] [PMID] [PMCID]

6. Hillman JB, Biro FM. Dynamic changes of adiposity during puberty: Life may not be linear. J Adolesc Health. 2010; 47(4):322-3. [DOI:10.1016/j.jadohealth.2010.06.023] [PMID] [PMCID]

7. Vanderwall C, Randall Clark R, Eickhoff J, Carrel AL. BMI is a poor predictor of adiposity in young overweight and obese children. BMC Pediatr. 2017; 17(1):1-6. [DOI:10.1186/s12887-017-0891-z] [PMID] [PMCID]

8. Cuda SE, Censani M. Pediatric obesity algorithm: A practical approach to obesity diagnosis and management. Front Pediatr. 2019; 6:431. [DOI:10.3389/fped.2018.00431] [PMID] [PMCID]

9. Sahoo K, Sahoo B, Choudhury AK, Sofi NY, Kumar R, Bhadoria AS. Childhood obesity: Causes and consequences. Fam Med Prim Care Rev. 2015; 4(2):187. [DOI:10.4103/2249-4863.154628] [PMID] [PMCID]

10. Irenewati S, Arkhaesi N, Wistiani W. Association of BMI measurements to waist circumference and waist-to-height ratio in overweight and obese children. Paediatr Indones. 2020; 60(3):131-136. [DOI:10.14238/pi60.3.2020.131-6]

11. Koomanaee S, Tabrizi M, Naderi N, Rad AH, Moghaddam KB, Dalili S. Parental anthropometric indices and obesity in children. Acta Med Iran. 2016:270-5. [Link]

12. Yopiana E, Dewi YL, Murti B. Relationship between formula milk and the incidence obesity in children under five: Meta-analysis. Med J Indones. 2020; 5(04):299-307. [DOI:10.26911/theijmed.2020.05.04.05]

13. Kousha M, Dalili S, Kiani SA, Zare M, Karambin MM, Heidarzadeh A, et al. BMI changes in children and adolescents with attention deficit hyperactivity disorder before and after treatment with methylphenidate. Iran J Pediatr. 2018; 28(2):e7954. [DOI:10.5812/ijp.7954]

14. Obradovic M, Sudar-Milovanovic E, Soskic S, Essack M, Arya S, Stewart AJ, et al. Leptin and obesity: Role and clinical implication. Front Endocrinol. 2021; 12:585887. [DOI:10.3389/fendo.2021.585887] [PMID] [PMCID]

15. Lan N, Lu Y, Zhang Y, Pu S, Xi H, Nie X, et al. FTO: A common genetic basis for obesity and cancer. Front Genet. 2020; 11:559138. [DOI:10.3389/fgene.2020.559138] [PMID] [PMCID]

16. Nordang GB, Busk ØL, Tveten K, Hanevik HI, Fell AK, Hjelmesæth J, et al. Next-generation sequencing of the monogenic obesity genes LEP, LEPR, MC4R, PCSK1 and POMC in a Norwegian cohort of patients with morbid obesity and normal weight controls. Mol Genet Metab. 2017; 121(1):51-6. [DOI:10.1016/j.ymgme.2017.03.007] [PMID]

17. Petraroli M, Castellone E, Patianna V, Esposito S. Gut microbiota and obesity in children: The state of the art. Front Genet. 2021; 9:193. [DOI:10.3389/fped.2021.657020] [PMID] [PMCID]

18. Coleman C. Stress and Obesity. An ecological approach to obesity and eating disorders; 2020.

19. da Silva Fernandes J, Schuelter-Trevisol F, Cancelier AC, Goncalves e Silva HC, de Sousa DG, Atkinson RL, et al. Adenovirus 36 prevalence and association with human obesity: A systematic review. Int J Obes. 2021; 45(6):1342-56. [DOI:10.1038/s41366-021-00805-6] [PMID] [PMCID]

20. Narzisi K, Simons J. Interventions that prevent or reduce obesity in children from birth to five years of age: A systematic review. J Child Health Care. 2021; 25(2):320-34. [DOI:10.1177/1367493520917863] [PMID] [PMCID]

21. Maring B, Greenspan LC, Chandra M, Daniels SR, Sinaiko A, Prineas RJ, et al. Comparing US paediatric and adult weight classification at the transition from late teenage to young adulthood. Pediatr Obes. 2015; 10(5):371-379. [DOI:10.1111/ijpo.274] [PMID] [PMCID]

22. Rundle AG, Factor-Litvak P, Suglia SF, Susser ES, Kezios KL, Lovasi GS, Cirillo PM, Cohn BA, Link BG. Tracking of obesity in childhood into adulthood: Effects on body mass index and fat mass index at age 50. Child Obesity. 2020; 16(3):226-33. [DOI:10.1089/chi.2019.0185] [PMID] [PMCID]

23. Cunningham SA, Kramer MR, Narayan KM. Incidence of childhood obesity in the United States. N Engl J Med. 2014; 370:403-11. [DOI:10.1056/NEJMoa1309753] [PMID] [PMCID]

24. Paolella G, Vajro P. Maternal microbiota, prepregnancy weight, and mode of delivery: Intergenerational transmission of risk for childhood overweight and obesity. JAMA Pediatr. 2018; 172(4):320-2. [DOI:10.1001/jamapediatrics.2017.5686] [PMID]

25. Hong YH, Chung S. Small for gestational age and obesity related comorbidities. Ann Pediatr Endocrinol Metab. 2018; 23(1):4-8. [DOI:10.6065/apem.2018.23.1.4] [PMID] [PMCID]

26. Moore BF, Harrall KK, Sauder KA, Glueck DH, Dabelea D. Neonatal adiposity and childhood obesity. Pediatrics. 2020; 146(3):e20200737. [DOI:10.1542/peds.2020-0737] [PMID] [PMCID]

27. Bell CS, Samuel JP, Samuels JA. Prevalence of hypertension in children: Applying the new American Academy

of Pediatrics clinical practice guideline. Hypertension. 2019; 73(1):148-52. [DOI:10.1161/HYPERTENSIONAHA.118.11673] [PMID] [PMCID]

28. Estrada E, Eneli I, Hampl S, Mietus-Snyder M, Mirza N, Rhodes E, et al. Children's Hospital Association consensus statements for comorbidities of childhood obesity. Child Obes. 2014; 10(4):304-17. [DOI:10.1089/chi.2013.0120] [PMID] [PMCID]

29. Valerio G, Maffeis C, Saggese G, Ambruzzi MA, Balsamo A, Bellone S, et al. Diagnosis, treatment and prevention of pediatric obesity: Consensus position statement of the Italian society for pediatric endocrinology and diabetology and the italian society of pediatrics. Ital J Pediatr. 2018; 44(1):1-21. [DOI:10.1186/s13052-018-0525-6] [PMID] [PMCID]

30. Singhal V, Schwenk WF, Kumar S. Evaluation and management of childhood and adolescent obesity. Mayo Clin Proc. 2007; 82(10):1258-64. [DOI:10.4065/82.10.1258] [PMID]

31. Chung WK. An overview of mongenic and syndromic obesities in humans. Pediatr Blood Cancer. 2012; 58(1):122-8. [DOI:10.1002/pbc.23372] [PMID] [PMCID]

32. Spear BA, Barlow SE, Ervin C, Ludwig DS, Saelens BE, Schetzina KE, et al. Recommendations for treatment of child and adolescent overweight and obesity. Pediatrics. 2007; 120(Suppl 4):S254-88. [DOI:10.1542/peds.2007-2329F] [PMID]

33. Wolfe BM, Kvach E, Eckel RH. Treatment of obesity: Weight loss and bariatric surgery. Circ Res. 2016; 118(11):1844-55. [DOI:10.1161/CIRCRESAHA.116.307591] [PMID] [PMCID]

34. Consensus Development Conference Panel. Gastrointestinal surgery for severe obesity. Ann Intern Med. 1991; 115(12):956-961. [DOI:10.7326/0003-4819-115-12-956] [PMID]

35. Pratt JS, Lenders CM, Dionne EA, Hoppin AG, Hsu GL, Inge TH, et al. Best practice updates for pediatric/adolescent weight loss surgery. Obesity. 2009; 17(5):901-910. [DOI:10.1038/oby.2008.577] [PMID] [PMCID]

36. Alqahtani AR, Antonisamy B, Alamri H, Elahmedi M, Zimmerman VA. Laparoscopic sleeve gastrectomy in 108 obese children and adolescents aged 5 to 21 years. Ann Surg. 2012; 256(2):266-73. [DOI:10.1097/SLA.0b013e318251e92b] [PMID]

37. Inge TH, Courcoulas AP, Jenkins TM, Michalsky MP, Helmrath MA, Brandt ML, et al. Weight loss and health status 3 years after bariatric surgery in adolescents. NEJM. 2016; 374(2):113-23. [DOI:10.1056/NEJMoa1506699] [PMID] [PMCID]

38. Aggarwal S, Kini SU, Herron DM. Laparoscopic sleeve gastrectomy for morbid obesity: A review. Surg Obes Relat Dis. 2007; 3(2):189-94. [DOI:10.1016/j.soard.2006.10.013] [PMID]

39. Miller RJ, Xanthakos SA, Hillard PJ, Inge TH. Bariatric surgery and adolescent gynecology. Curr Opin Obstet. 2007; 19(5):427-33. [DOI:10.1097/GCO.0b013e3282efb285] [PMID]

40. Olbers T, Beamish AJ, Gronowitz E, Flodmark CE, Dahlgren J, Bruze G, et al. Laparoscopic Roux-en-Y gastric bypass in adolescents with severe obesity (AMOS): A prospective, 5-year, Swedish nationwide study. Lancet Diabetes Endocrinol. 2017; 5(3):174-83. [DOI:10.1016/S2213-8587(16)30424-7]

41. Melmed S, Polonsky KS, Larsen PR, Kronenberg HM. Williams textbook of endocrinology E-Book. Amsterdam: Elsevier Health Sciences; 2015. [Link]

42. Kliegman RM, Behrman RE, Jenson HB, Stanton BM. Nelson textbook of pediatrics e-book. Amsterdam: Elsevier Health Sciences; 2007. [Link]

43. Styne DM, Arslanian SA, Connor EL, Farooqi IS, Murad MH, Silverstein JH, et al. Pediatric obesity-assessment, treatment, and prevention: An Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2017; 102(3):709-57. [DOI:10.1210/jc.2016-2573] [PMID] [PMCID]

44. Dalili S, Rezvani SM, Dalili H, Amiri ZM, Mohammadi H, Medghalchi A, et al. Cardio-metabolic risk factors in Iranian children: Where we are and the others? Acta Medica Iranica. 2014:831-6. [Link]

45. Ho JSY, Fernando DI, Chan MY, Sia CH. Obesity in COVID-19: A Systematic Review and Meta-analysis. Ann Acad Med Singap. 2020; 49(12):996-1008. [DOI:10.47102/annals-acadmedsg.2020299] [PMID]

This Page Intentionally Left Blank