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RECENT ADVANCES IN ANTIOBESITY ACTIVITY ON CHILDREN AND ADOLESECENT

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Abstract

Obesity is a heritable condition that develops through the interactions of numerous genes and lifestyle factors, and its prevalence is steadily rising worldwide, leading to major health issues. A major challenge of the twenty-first century is the epidemic of childhood overweight and obesity, which has elevated to the status of a global public health emergency. Obesity in children and adolescents is a serious public health issue today, affecting both developed and developing nations. In 2016, there were more than 340 million overweight or obese children and teenagers worldwide, ages 5 to 19. Because adult obesity, early mortality, and disability, as well as early indicators of cardiovascular disease, can all be linked to childhood obesity, it is a serious burden. In Europe, childhood obesity is still a serious health issue that varies significantly between and within nations and populations. In Europe, there were more than 398,000 severely obese children aged 6 to 9 in 2019. In 2018, one in five youngsters in Southern European nations like Greece, Italy, Malta, San Marino, and Spain were obese. throughout recent years, a variety of programmes and initiatives have been introduced throughout Europe to combat childhood obesity. However, regionally, the fight against childhood obesity has advanced slowly and unevenly. The incidence of paediatric obesity and current initiatives to combat it in the European Region of the World Health Organisation (WHO) have been covered in this chapter.

Keywords: Obesity, overweight, childhood, adolescent, prevention.

1.INTRODUCTION

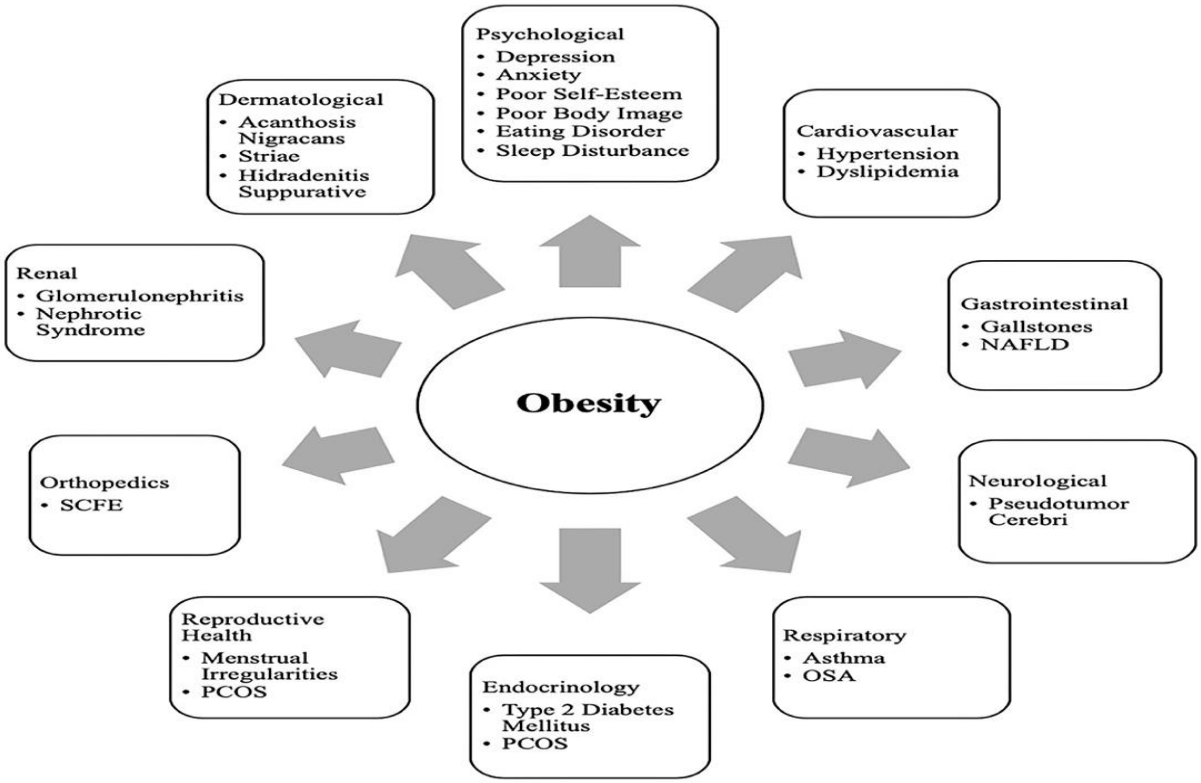
Children of all ages are impacted by the complicated problem of obesity (1-3). In the US, one-third of children and teenagers are considered to be either overweight or obese. Obesity is a complex interplay between biological, developmental, behavioural, genetic, and environmental factors; there is no single factor driving this epidemic. Recent research has shown that intrauterine and generational effects, as well as the role of epigenetics and the gut microbiota, all contribute to the obesity epidemic (5, 6). Other elements, such as being short for gestational age (SGA) at birth, formula feeding throughout infancy as opposed to breastfeeding, and early protein introduction in an infant's diet have reportedly been linked to weight increase that can last into adulthood (6–8). By increasing the burden of chronic non-communicable diseases, childhood obesity is becoming a serious public health concern (1, 8).

Obesity increases the risk of developing a variety of health issues, including early puberty in children (9), irregular teen girls' periods (1, 10), obstructive sleep apnea (OSA), cardiovascular risk factors like prediabetes, type 2 diabetes, high cholesterol, hypertension, NAFLD, and metabolic syndrome (1, 2), and sleep disorders like OSA (1, 11). Additionally, psychological problems like eating disorders, sadness, anxiety, low self-esteem, and problems with body image and peer interactions can affect obese children and adolescents (12, 13). Interventions for the prevention of overweight and obesity have thus far generally centered on changes in an individual's behavior, such as increasing daily physical activity or improving diet quality while reducing excess calorie intake (1, 14, 15). These efforts, though, have not yielded much.

2.DEFINATION OF OBESITY

Body mass index (BMI), a low-cost approach for determining body fat in children over 2 years of age, is calculated using a formula based on height and weight (1, 15, 16). Directly calculating body fat can be done using advanced technologies, but they are expensive and not widely accessible. These techniques include using a calliper to measure skinfold thickness, bioelectrical impedance, hydrodensitometry, dual-energy X-ray absorption (DEXA), and air displacement plethysmography (2).

In the healthy paediatric population, BMI gives a reliable assessment of body fat indirectly, and research has established a correlation between BMI and future health concerns (16). In contrast to adults, children's BMI is represented by Z-scores or percentiles, which change depending on the child's age and gender. The World Health Organisation (WHO) recommends BMI Z-score cutoff points of >1.0, >2.0, and >3.0 to define at risk of overweight, overweight, and obesity, respectively (17). But when it comes to percentiles, overweight is defined as having a BMI over the 85th and above the 95th percentile (16,17). Although BMI Z-scores and BMI percentiles can be converted, the percentiles must be rounded and may incorrectly identify some children of normal weight as underweight or overweight (18). Therefore, it is advised that BMI Z-scores for children be utilised in research rather than BMI percentiles, which are better employed in clinical settings, to avoid these errors and facilitate understanding (17).



3.EPIDEMIOLOGY

Obesity is a prominent global cause of death that is preventable, and both adults and children are becoming more and more obese.[19] Since 1980, when the average percentage of adults with a BMI of 25 kg/m 2 was estimated to be 28%, the prevalence of overweight and obesity has rapidly increased around the world. [20] According to the most recent WHO figures, around 39% (1.9 billion) of persons over the age of 18 are overweight, and 13% (603.7 million) are considered obese.[19] As evidence of the upward tendency, it is predicted that by 2025 there will be three billion overweight people and over 700 million obese people worldwide. The prevalence of childhood obesity is likewise rising, with an estimated 42 million kids affected globally by new instances. Numerous studies have demonstrated the increased risk of diabetes mellitus (DM),[21] cardiovascular disease, cancer, musculoskeletal diseases, endocrine disorders, and psychological disorders in obese and overweight people.[22]

3.4 million fatalities worldwide due to obesity occur each year, or nearly 4% of all annual deaths. Consequently, it qualifies as a pandemic.[20] On a global scale, in 2015, among the 20 most populous nations, Egypt had the highest age-standardized adult obesity rate (35.3%; 95% confidence interval: 33.6-37.1), and the United States had the highest age-standardized childhood obesity rate (12.7%; 95% confidence interval: 12.2-13.2). In Bangladesh (1.2%; 95% uncertainty interval, 0.9-1.7) and Vietnam (1.6%; 95% uncertainty interval, 1.4-2.0), the prevalence was lowest among adults. Only the Democratic Republic of the Congo experienced no growth in the age-standardized prevalence of obesity between 1980 and 2015, while 13 of the 20 countries with the highest obesity rates did so. The greatest rates of obese youngsters were found in China and India in 2015, whereas the highest rates of fat adults were found in the US and China.[20], According to the American Medical Association, obesity is a disease as of 2013.[23], [24] Numerous physical and mental health concerns, including osteoarthritis, type 2 diabetes, obstructive sleep apnea, some types of cancer, depressive disorders, and cardiovascular illnesses, are all made more likely by obesity. [20], Obesity has been demonstrated to dramatically lower life expectancy as a result.[20], Obesity has been demonstrated to dramatically lower life expectancy as a result. [20] Affected people who are obese are more likely to develop metabolic syndrome, a group of illnesses that includes type 2 DM, hypertension, and hyperlipidemias. Obesity rates are rising globally and are hurting both the developed and developing world, despite once being thought to be an issue mainly in high-income nations. Urban areas have seen the most pronounced effects of these increases. Sub-Saharan Africa is the only area in the globe where obesity is still uncommon, but as sedentary lifestyles become more prevalent, the situation is slowly turning around.[25]

4.PATHOPHYSIOLOGY OF OBESITY

Numerous pathophysiological processes contribute to the emergence and maintenance of obesity. At the individual level, it is believed that the majority of cases of obesity are caused by a combination of high dietary energy intake and insufficient physical activity. Only a small percentage of instances are largely brought on by physical conditions, psychological disorders, or genetic susceptibility.[25] Therefore, a combination of hereditary and environmental variables contribute to obesity. Because not everyone who is exposed to the typical urban and rural environments develops obesity, this raises the possibility that there are underlying genetic factors at play. Leptin and melanocortin-4 receptors, which are expressed mostly in the hypothalamus and play a role in neuronal circuits regulating energy balance, are now known to play a role in rare monogenic forms of obesity, including those that lack them. The most frequent cause of monogenic obesity presently is heterozygous mutations in the melanocortin-4 receptor gene, which affect 2%–5% of children with severe obesity. [26] It has been discovered that individuals with two copies of the FTO gene (fat mass and obesity linked gene) weigh 3–4 kg more on average and are 1.67 times more likely to be obese. Numerous genetic syndromes, including Prader-Willi syndrome, Bardet-Biedl syndrome, Cohen syndrome, and MOMO syndrome, include obesity as a prominent characteristic. A single point DNA mutation is present in 7% of patients with early-onset severe obesity, which is defined as an onset before the age of 10 and a BMI that is more than three standard deviations over the value for a normal individual age-and-sex match.

Adiponectin, chemerin, perilipin-1, apelin, glucagon-like peptide-1 [GLP-1], cholecystokinin-pancreazymin, somatostatin, cortisol, glucose-dependent insulinotropic peptide, growth hormone, and catecholamines are among the other chemicals currently being studied as the molecular basis of obesity. However, there are

primarily five key endogenously produced chemicals that seem to tightly The following list of endogenous chemicals is provided: Endocannabinoids Leptin, Ghrelin, Obestat, and Nesfatin-1. These endogenous chemical compounds work on many pathway cascades within the central nervous system (CNS) and the periphery to promote or attenuate the development of obesity condition in addition to genetic factors that predispose to obesity. It is also worth mentioning here that leptin, obestatin, nesfatin-1, gastric inhibitory polypeptide/glucosedependent insulinotropic peptide [GIP], glucagon-like peptide-1 [GLP-1], adiponectin and chemerin are anti-obesogenic and anti-diabetogenic in activity, while ghrelin, endocannabinoids and perilipin-1 are pro-obesogenic and prodiabetogenic in activity.

5.CLINICAL COMORBIDITIES OF OBESITY IN CHILDREN

5.1Growth and Puberty

Children who gain too much weight may experience growth and pubertal development issues (27). Obesity in childhood can cause both boys and girls to have accelerated bone ages and linear growth acceleration during puberty (28). While children with obesity may have excessively high insulin levels, hyperinsulinemia is a natural condition that occurs during puberty (29). Because their adipose tissue produces more leptin than normal, obese people also experience leptin resistance (30, 29). The growth plates can be affected by the insulin and leptin levels, which can hasten bone ageing (30). For pubertal onset to occur at the typical time and pace, adequate nutrition is crucial. Early puberty can start because of excessive weight gain because of changed hormonal factors (27). Precocious puberty (PP), early adrenarche, or thelarche can all be symptoms of childhood obesity. In girls, the link between early pubertal changes and obesity is clear and extensively documented; in boys, the evidence is scant. According to a US research of boys of different racial backgrounds, overweight boys experienced early puberty while obese boys experienced delayed puberty. High leptin levels are present in PP-obese girls (32). Additionally, polycystic ovarian syndrome (PCOS) is more likely to occur in the future in obese females with early adrenarche (33). Issues With Sleep In kids and teenagers, obesity is a standalone risk factor for obstructive sleep apnea (OSA) (33). When compared to adolescents and adults, children with OSA have less harmful effects on cardiovascular stress and metabolic syndrome (32,33). Children who have OSA are more likely to experience aberrant behaviours and neurocognitive impairment than adults. However, obesity and OSA can both independently lead to oxidative systemic stress and inflammation in adolescents (34), and when this happens at the same time, it can have a more severe impact on metabolic dysfunction and long-term cardiovascular consequences (35).

5.2 Other Comorbidities

The most significant cause of liver disease in children (37), NAFLD is connected to a clinical range of liver abnormalities, including obesity (36). Steatosis—increased liver fat without inflammation—and NASH—increased liver fat with inflammation and hepatic injury—are both symptoms of NAFLD. While NAFLD can develop into an advanced liver disease in certain individuals that requires a liver transplant (38,39), the risk of development during children is less clear (40). The metabolic syndrome, which includes central obesity, insulin resistance, type 2 diabetes, dyslipidemia, and hypertension, and NAFLD are all strongly related. Sedentary lifestyle practises may have a detrimental impact on the brain structure and executive functioning, although the direction of causality is unclear (41). Obese children are also at risk for slipping capital femoral epiphysis (SCFE).

6. CLINICAL COMORBIDITIES OF OBESITY IN ADOLESCENTS

6.1 Menstrual Irregularities and PCOS

Sexual steroid use can physiologically lead to weight increase and changes in body composition during the start of puberty that shouldn't interfere with regular menstruation (42). However, substantial weight gain in adolescent girls raises their risk for PCOS due to elevated testosterone levels and can cause irregular menstrual periods. They may also have polycystic ovaries, abundant body hair (hirsutism), and have incorrect body perceptions (43). Regardless of weight, adolescent females with PCOS are at an increased risk for developing insulin resistance. But gaining weight worsens their already severe insulin resistance and raises their chance of developing obesity-related comorbidities including metabolic syndrome and type 2 diabetes. A timely intervention (proper weight loss and use of hormonal treatments) might help restore menstrual cyclicity and ease future concerns about childbearing, even if the diagnosis of PCOS can be difficult at this age due to an overlap with anticipated pubertal changes.

In younger age groups, the definitions used to diagnose MS are debatable, and several classifications have been put out (44). This is because there is a large overlap between the characteristics of MS and normal growth during puberty due to the complicated physiology of growth and development. However, even before puberty, paediatric obesity is linked to an inflammatory state (45). Hyperinsulinemia throughout puberty and unhealthful sleep habits both raise the likelihood and severity of MS in obese children and adolescents (46). Although there is no agreed-upon diagnosis for MS in this age group, doctors should assess obese children and adolescents for MS risk factors and sleep habits and offer advice on weight management.

7. SOCIAL PSYCHOLOGY OF PEDIATRIC OBESITY IN CHILDREN AND ADOLESCENTS

Psychosocial consequences of obesity in children and adolescents may include depression, bullying, social isolation, low self-esteem, behavioural issues, unhappiness with one's body image, and a lower quality of life (43,46). Overweight and obesity are among the most frequent causes of bullying in children and adolescents at school when compared to counterparts who are of normal weight (47). Childhood obesity stigma, bullying, and teasing have widespread effects on performance and one's mental and physical well-being that can last throughout one's life. The psychological effects of obesity in teenagers are complex and inversely correlated (Figure 4). Due to their physical characteristics, obese teenagers may be more likely to experience psychological health problems such depression, negative body image or dissatisfaction, low self-esteem, peer victimisation or bullying, and interpersonal interaction challenges. In comparison to their non-obese/overweight peers, they may also show less resistance to difficult circumstances (43,48). Dissatisfaction with one's body image has been linked to continued weight gain, but it can also be linked to the emergence of mental health disorders, eating disorders, or disordered eating habits (DEH). An unhealthy diet, a sedentary lifestyle, and irregular sleep patterns are linked to mental health illnesses including depression. An individual's excessive value of their body form and weight may be linked to ED or DEH, which includes anorexia nervosa (AN), bulimia nervosa (BN), binge-eating disorder (BED), or night eating syndrome (NES) (49). If there is a strict focus on calorie intake or if a patient overcorrects and starts excessive self-directed dieting, the management of obesity can put a patient at risk for AN. Obesity-focused healthcare professionals frequently advise dieting to lose weight and then keep it off. Although some individuals may eventually adopt a tight diet (hypocaloric diet), this can result in an eating problem like anorexia nervosa. Adolescents persist in worrying about their weight and numbers as a result of this behaviour since it results in an unhealthy connection with food (50).

Treatment, general well-being, and the risk of adult obesity can all be improved with support and attention to underlying psychological issues (49). The complexity of the various psychological problems that can have an impact on the clinical care provided to an obese adolescent is illustrated in the diagram above. Eating family meals together can improve overall dietary intake due to enhanced food choices mirrored by parents. It has also may serve as a support to individuals with DEHs if there is less attention to weight and a greater focus on appropriate, sustainable eating habits (45).

8.TREATMENT

8.1 Prevention and Anticipatory Guidance

Early childhood and adolescent obesity must be recognised and treated with preventative strategies (50, 51). It is well known that early AR increases the likelihood of adult obesity. As a result, health care professionals who work with children must concentrate on metrics like BMI while also anticipatorily offering nutritional counselling without stigmatising or criticising the parents of children who are overweight or obese. Ironically, despite their efforts to combat the obesity pandemic, healthcare professionals frequently engage in stigmatising and weight-biasing behaviours. According to research, the language used by medical professionals when discussing a patient's body weight can increase stigma, lessen motivation for weight loss, and even lead to patients avoiding regular preventive care. Ironically, healthcare personnel frequently engage in stigmatising and weight-biasing actions despite their efforts to tackle the obesity pandemic. The language used by medical practitioners when discussing a patient's body weight, it has been found, can promote stigma, decrease motivation for weight loss, and even cause patients to forego routine preventative care.

After trying food and lifestyle changes without success, a structured weight-management programme using a multidisciplinary approach is the next step. The best results are linked to an interdisciplinary team that meets 1-2 times each week and includes a doctor, nutritionist, and psychologist. Patients with significant obesity, though, do not respond well to this course of treatment. Although healthier lifestyle recommendations for weight loss are the current cornerstone for obesity management, they often fail. As clinicians can attest, these behavioural and dietary changes are hard to achieve, and all too often is not effective in patients with severe obesity. Poor compliance with the advised lifestyle adjustments and physiological responses that oppose weight reduction are the main reasons why substantial weight loss cannot be sustained over the long term. The participants on the reality TV programme "The Biggest Loser" are overweight or obese people who are trying to lose weight in order to win cash. Due to a significantly reduced resting metabolic rate, "The Biggest Loser" contestants who underwent metabolic adaptation (MA) after significant weight reduction gained back more weight than they lost after six years. MA is a physiological reaction that results in a lower basal metabolic rate in those who are or have lost weight. In MA, the body changes how well it converts the food consumed into energy; this is a reaction to calorie restriction as well as a natural defence mechanism against famine. During calorie restriction, plasma leptin levels significantly drop, suggesting that this hormone may be responsible for the decline in energy expenditure (53).

9. PHARMACOLOGICAL MANAGEMENT

Pharmacological therapy plays a limited part in the management of childhood and teenage obesity. The sole FDA-approved drug for weight loss in children and adolescents aged 12 to 18 is orlistat, however it comes with unfavourable side effects. Another medication, metformin, has been used in young patients with insulin resistance symptoms; it is not FDA-approved, but it may have some effect on weight. The FDA has approved the phentermine/topiramate combination (Qsymia) for weight loss in obese people who are 18 years of age and older. Over a two-year period, studies have shown a weight decrease of 9–10%. However, females should exercise caution because it has the potential to cause congenital defects, particularly if used during the first trimester of pregnancy (45).

Academic researchers and business partners recently presented novel therapies at the EASL conference that target the intestinal content, intestinal microbiota, intestinal mucosa, and peritoneal cavity among other levels of the gut-liver axis. The scope of these therapeutic approaches inside the gut-liver axis was vast and included everything from novel medications preserving the intestinal mucosa lining to re-establishing intestinal barriers to enhancing the gut flora. Hydrogel technology, which includes fibres and high viscosity polysaccharides that absorb water in the stomach and increase volume, hence improving satiety, was one of the therapeutic possibilities for individuals with metabolic syndrome. Additionally, a clinical research employing docosahexaenoic acid (DHA) on obese pregnant women revealed that the DHA-treated mothers had offspring with decreased adiposity at ages 2 and 4. Probiotics have recently become more important in the fight against obesity. It has been demonstrated that probiotics change the gut flora, which enhances nutritional absorption and intestinal digestion. The management of paediatric obesity may involve probiotic intervention (54). In addition, vitamin E's significance in treating obesity-related comorbidities such diabetes,

hyperlipidemia, NASH, and cardiovascular risk has recently been documented. Tocopherols and tocotrienols are both found in vitamin E, which is a lipid-soluble substance. Tocopherols interact with cellular lipids and shield them from oxidative damage through their lipid-soluble antioxidant capabilities (53). Studies have summarised the role of vitamin E in the management of obesity, metabolic, and cardiovascular disease (55). In metabolic disease, vitamin E has an impact on a number of critical pathways. Therefore, proper vitamin E supplementation has been recommended as a suitable therapy to aid in the treatment of obesity and its related comorbidities. Nevertheless, some clinical studies using vitamin E supplements produced inconsistent findings (55). Although vitamin E is known to be an antioxidant that guards against oxidative damage, its exact mechanism of action is still not well understood.

9.1 Bariatric Surgery

Since the early 2000s, bariatric surgery has become more often used to treat severe obesity. There are greater results for losing weight and treating obesity-related comorbidities in adults if it is done early. The current criteria for bariatric surgery include adolescents with a BMI >35, at least one severe comorbid condition (such as Type 2 Diabetes, severe OSA, pseudotumor cerebri, or severe steatohepatitis), or a BMI of 40 or higher with additional conditions (such as hypertension, hyperlipidemia, mild OSA, insulin resistance, glucose intolerance, or a reduced quality of life as a result of weight). These patients must have finished the most of their linear growth and committed to a structured weight-loss programme for 6 months before contemplating bariatric surgery (54,56).

The patient must also see a paediatrician or physician with expertise in adolescent medicine, endocrinology, gastrointestinal, and nutrition, as well as a licenced dietician, a mental health professional, and an exercise specialist, in addition to a licenced bariatric surgeon. A mental health professional is crucial because people who are obese and have depression may still require ongoing mental health care even after weight loss surgery (34). There are three procedures that can be used: laparoscopic Sleeve Gastrectomy (LSG), Gastric Banding, and Roux-en-Y Gastric Bypass (RYGB). Children under the age of 18 may currently use RYGB and LSG (56). Gastric banding is not currently an FDA-recommended surgery in the US for patients under the age of 18. One research had several repeat procedures and indicated that it was not a good option for obese adolescents, despite modest improvements in BMI and the severity of comorbidities (57).

Studies and clinical trials have demonstrated that RYGB offers superior results over LSG for excess weight loss and the correction of obesity-related comorbidities. LSG is often a safer option and might be recommended more frequently. Given that fewer surgeries are carried out on adolescents than on adults, the impact of bariatric surgery on the gut-brain axis is yet unclear. Increased fasting and post-prandial PYY and GLP-1 were observed in those who received RYGB, which may have contributed to the rapid weight loss. Patients who had gastric banding experienced this effect less frequently. Higher amounts of bile acid (BA) subtype were seen in adult patients in a different investigation, which raised the possibility that BA had a part in the surgical weight reduction response following LSG (57). Bariatric surgery should be considered sooner rather than later since adolescents have lower surgical complication rates than their adult counterparts (59). Nutritional deficiencies in iron, calcium, vitamin D, and vitamin B12 are complications following surgery that require constant monitoring (57, 59, 60). Although the 5-year statistics for gastric bypass in severely obese teenagers is encouraging, lifelong outcomes are still unknown, and the psychosocial elements involved in adolescent adherence post-surgery are difficult and unreliable.

10. CONCULSION

Childhood and adolescent obesity cannot be prevented by one simple change. Youth eating habits are influenced by biological, cultural, and environmental variables, such as the availability of high-density food options. For kids and teenagers, physical activity is a less desirable option because of media devices and related screen time. This evaluation serves as a prompt to take immediate action. Clarification is required regarding the necessity of interventions to alter the obesogenic environment through the implementation of policies pertaining to the food sector and in schools. GLP-1 agonists have been shown in clinical studies to be beneficial in helping children lose weight, but they have not yet received FDA approval. It would be

revolutionary to develop probiotic or faecal transplant therapies to alter the gut flora in order to treat obesity or overweight. For the time being, multidisciplinary lifestyle programmes, pharmacotherapy, and ongoing clinical research show promise.

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