Review

Pediatric obesity: a mini-review for pediatrician

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Abstract. Obesity is a multifactorial disease, and its prevalence in children has been increased over the last 30 years in Italy and many other European Countries. Obesity significantly impacts the quality of life of affected patients and health care systems. Obesity is related to several clinical comorbidities, especially metabolic syndrome and diabetes. The standard of care in this patient is still considered lifestyle changes and a healthy diet with regular physical activity to prevent associated metabolic complications (impaired glucose tolerance and type 2 diabetes) and reduce cardiovascular risk. Therefore, pediatricians should recognize potential risk factors (sedentary lifestyle, sugar, and fats-rich diet, genetic syndromes) and early signs of overweight and obesity to promptly address the child to a pediatric endocrinologist and a specialized reference Center. (www.actabiomedica.it).

Key words: Children, adolescents, type 2 diabetes, obesity, insulin resistance, metabolic syndrome

Introduction

Over the past three decades, childhood overweight and obesity have reached epidemic proportions worldwide ("globesity"), especially in some European countries, such as Mediterranean countries (1). In 2016, 124 million children and adolescents between 5 and 19 years were obese, and 213 million were overweight (2).

In children, obesity can also occur with metabolic complications such as impaired glucose tolerance and type 2 diabetes, growing cardiovascular risk, and significant impact on both physical and psychosocial health (3).

Obesity prevalence changes between different age groups: in the United States are obese 8.4% of children between 2-5 years, 20.5% of children between 6-11 years, 20.5% adolescents between 12-18 years (4).

The World Health Organization (WHO) is monitoring childhood overweight and obesity in Europe with the Childhood Obesity Surveillance Initiative (COSI) (Fig.1) (5). Italy is one of the most affected countries with other Mediterranean Countries (6).

Moreover, Italy is now working on a new surveillance system of the Superior Institute of Health (ISS) called "OKKio alla Salute" (7). This system collects data about children's lifestyle during primary school, such as weight, diet, and physical activity. Based on the values of the International Obesity Task Force (IOTF), during 2019 (6) were collected 53273 children and 20.4% of them resulted overweight, 9.4% obese, 2.4% severe obese (overweight girls 20.9%, overweight boys

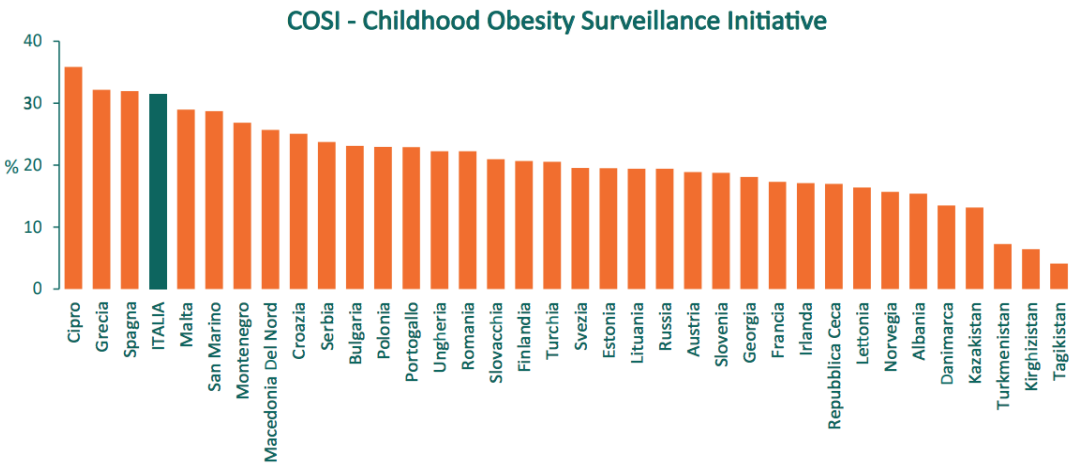

Figure 1. COSI Childhood Obesity Surveillance Initiative (2015-2017). Childhood Obesity Surveillance Initiative (COSI) Factsheet. Highlights 2015-17; 2018. www.euro.who.int (5).

20.0%; obese girls 8.8%, obese boys 9.9%) (Fig.2).

Diagnosis

Obesity and overweight definition in childhood is more challenging than in adults. To measure body fat, we refer to the body mass index (BMI), calculated as body weight divided by height squared (kg/m^2). Ideal BMI changes during growth according to age and sex.

According to the Italian Society of Pediatrics (SIP) and the Italian Society of Pediatric Endocrinology and Diabetology (SIEDP), we use the following measure instruments (Table 1):

- 0-2 years: weight divided by height, OMS charts 2006;
- 2-5 years: BMI, OMS charts 2006;
- 5-18 years: BMI, OMS charts 2007;

Other useful instruments are:

- American charts of Center for Disease Control (CDC) from the Task Force of Endocrine Society;
- Charts of International Obesity Task Force (IOTF) (9);
- Cacciari's Italian charts (SIEDP) (10).

Pathogenesis

Obesity is a multifactorial disease resulting from genetic predisposition (30-40%) and environmental/behavioral factors (60-70%) (Fig. 3) (11).

There are some periods during life when the risk of developing obesity is higher:

1. intrauterine life: mother's diet and metabolism effects on fetus growth and glucose metabolism (13);
2. the first year of life: the protective effects of breastfeeding and behavioral learning during weaning, or adverse effects from the hyper-proteic diet anticipating the adiposity rebound (14);

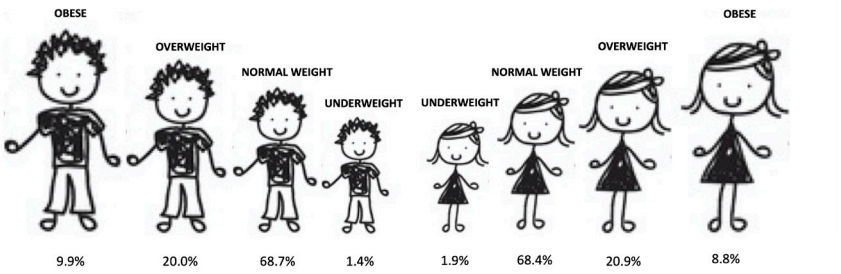

Figure 2. Weight status of Italian children according to sex. Data from "OKKio alla salute, 2019", a national surveillance system.

Table 1. Diagnosis of overweight and obesity according to SIP-SIEDP Consensus (8).

Age	0-2 years	2-5 years	5-18 years
Indicator	*Weight/height*	*BMI*	*BMI*
Reference system	OMS 2006	OMS 2006	OMS 2007
> 85° p (>1 DS)	Overweight risk	Overweight risk	Overweight
> 97° p (> 2 DS)	Overweight	Overweight	Obesity
> 99° p (> 3 DS)	Obesity	Obesity	Severe obesity

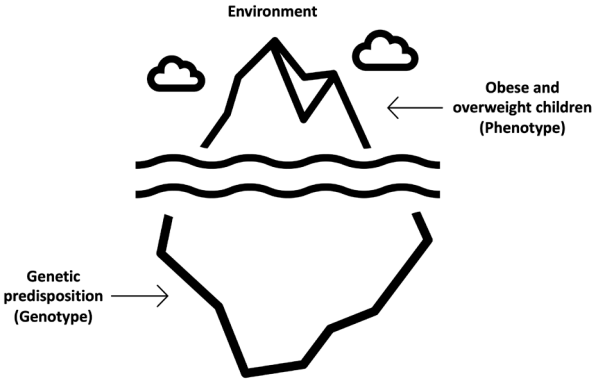

Figure 3. Relationship between genetic and environmental factors in obesity.

3. timing of adiposity rebound (AR): generally, after the first year of life, BMI decreases, then it usually stabilizes, and finally increases again around 5-6 years of age. When AR appears early, the risk of overweight, diabetes and cardiovascular disease becomes higher (14);
4. adolescence: body fat distribution and lifestyle alterations (lower physical activity and bad diet habits) (Fig. 4).

Obesity can lead to an inflammatory environment since childhood. Inflammation is the biological answer to foreign "disruptors" such as bacteria, tissue damages, fasting, or overfeeding. Since 1970s, it is known that adipose tissue releases a higher level of cytokines (TNF-α, NF-kB, etc.), but at the same time, inflammatory cytokines increase the level of free

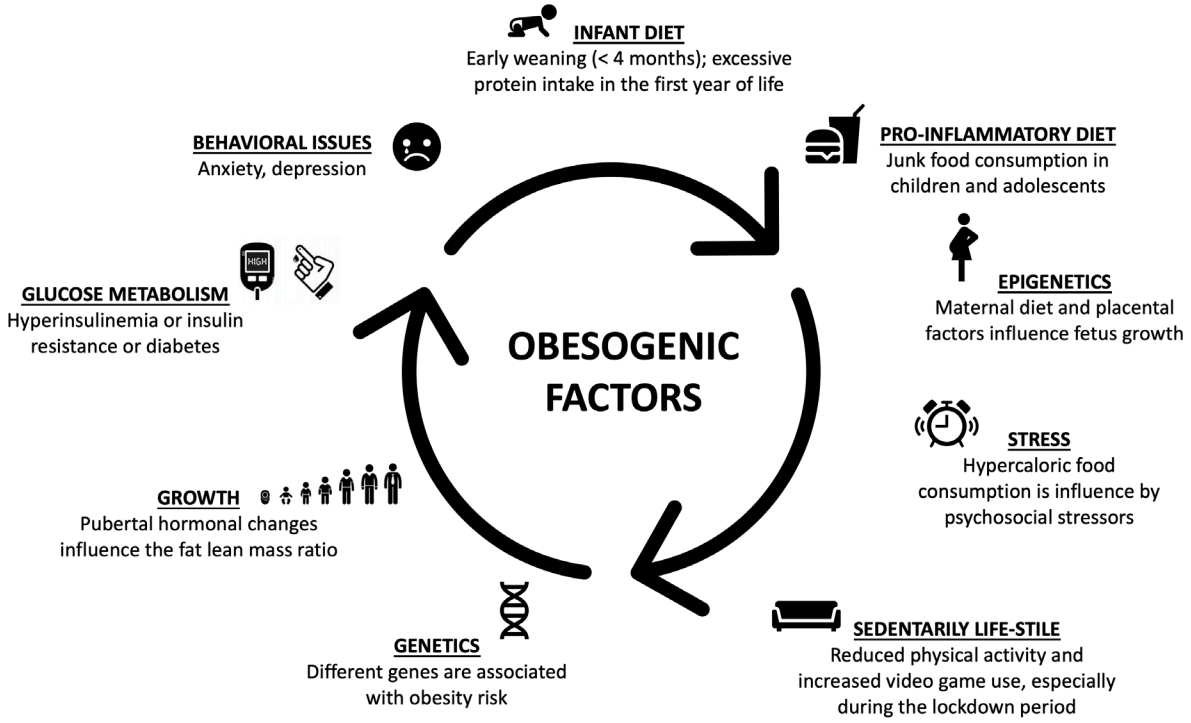

Figure 4. Multifactorial Development of Obesity.

fatty acids in blood (16,17). There is a complex and intricate connection between the immune system and adipose tissue. The understanding of the events that initiate metabolic inflammation ("metainflammation") can support the identification of targets for preventing metabolic disease and its adverse effects on health (18).

Comorbidities

Overweight and obesity are risk factors for glucose metabolism abnormalities (19), such as impaired fasting glucose (IFG) and impaired glucose tolerance (IGT); these conditions are also known as "pre-diabetes," and they can lead to type 2 diabetes (T2D). The diagnosis of pre-diabetes or T2D is based on the oral glucose tolerance test (OGTT) (Table 2). The prevalence of IFG and IGT between obese adolescents is, respectively, 16.8% and 6.6% (19).

Insulin resistance (IR) is defined as the decreased tissue response to insulin-mediated cellular actions and is the opposite of insulin sensitivity (19). In this condition, higher insulin levels are released to reach average plasma glucose initially, but this mechanism leads to metabolic complications and, finally, diabetes and cardiovascular disease. The gold standard to measure IR is the euglycemic- hyperinsulinemic clamp technique, but it usually is preferred to use some indexes such as *Matsuda Index* (20) or the *Homeostatic Model of Assessment-insulin resistance* (HOMA-IR) (21). HOMA-IR index is defined as fasting plasma glucose multiplied by fasting plasma insulin (mg/dL or mmol/L). High HOMA-IR index indicates low insulin sensitivity (insulin resistance). Because of IR, obese children and adolescents have also altered lipids profiles, usually higher triglycerides, and LDL concentrations with lower HDL concentrations (Table 3). Plasma lipids abnormalities can cause liver steatosis and non-alcoholic fatty liver disease (NAFLD) (22).

Almost 25% of obese children and adolescents are affected by hypertension (23). It is estimated that ten units BMI higher mean ten mmHg systolic blood pressure (SBP) and three mmHg diastolic blood pressure (DBP) higher, and this trend remains later in the adult life (24) (Table 4).

Obesity plays a central role in metabolic syndrome (MS) development, which is a complex condition characterized by a combination of some risk factors such as high waist circumference (WC), abnormal blood levels of triglycerides, HDL-cholesterol, altered blood pressure, and glucose metabolism abnormalities (IR). There are many definitions of MS (Table 5).

Treatment options

Treatment of obesity in children and adolescents could be more complex than in adults, and it requires

Table 2. Diagnostic criteria of IFG, IGT, T2D (8).

Prediabetes	1. IFG: fasting plasma glucose (almost 8:00 am) 100- 125 mg/dl (5.6- 6.9 mmol/l) 2. IGT: plasma glucose 140- 199 mg/dl ,after 2 hours from OGTT 3. 3. HbA1c value: 5.7- 6.4 % (39-47 mmol/mol)
Type 2 diabetes	1. random plasma glucose ≥ 200 mg/dl with diabetes symptoms 2. fasting plasma glucose ≥ 126 mg/dl 3. plasma glucose ≥ 200 mg/dl ,after 2 hours from OGTT 4. HbA1c value ≥ 6.5 % (48 mmol/mol)

Table 3. Values for lipidic plasma levels proposed by *Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents (8).*

	Acceptable	Borderline	Abnormal
Total cholesterol (mg/dL)	< 170	170-199	≥ 200
LDL- cholesterol (mg/dL)	< 110	110-129	≥ 130
Non HDL- cholesterol (mg/dL)	< 120	120-144	≥ 145
Triglycerides (mg/dL):			
- 0-9 years	< 75	75-99	≥ 100
- 10-19 years	< 90	90-129	≥ 130
HDL- cholesterol (mg/dL)	>45	40-45	< 40

Table 4. Definition of abnormalities of blood pressure (8)**.**

Normal blood pressure	SBP and DBP < 90° percentile for sex, age, height
Normal- high blood pressure	SBP and DBP ≥ 90° percentile for sex, age, height
Hypertension (I)	SBP and DBP ≥ 95° percentile for sex, age, height but < 99°
Hypertension (II)	SBP and DBP ≥ 99° percentile for sex, age, height

Table 5. Diagnostic criteria for metabolic syndrome in children (19).

	Cook et al., 2003 (NCEP)	Weiss et al., 2004 (NCEP)	Zimmet et al., 2007 (IDF)	Ahrens et al., 2014 (IDEFICS)
Waist circumference	≥ 90°pct		≥ 90°pct	≥ 90° (95°) pct
Systolic blood pressure	≥ 90°pct	≥ 95° pct	≥ 130 mmHg	≥ 90° (95°) pct
Diastolic blood pressure	≥ 90°pct	≥ 95° pct	≥ 85 mmHg	≥ 90° (95°) pct
Triglycerides	≥ 1.24 mmol/L	≥ 95° pct	≥ 1.7 mmol/L	≥ 90° (95°) pct
HDL-cholesterol	1.03 mmol/L	5° pct	1.03 mmol/L	10° (5°) pct
Glucose homeostasis	IFG ≥ 6.11 mmol/L	IGT (ADA criteria)	IFG ≥ 5.6 mmol/L	HOMA-IR or IFG
Body mass index		Z score ≥ 2		≥ 90° (95°) pct

HDL, high-density lipoprotein; IFG, fasting glucose; IGT, impaired glucose tolerance; HOMA-IR, homeostatic model assessment of insulin resistance, NCEP, national cholesterol education program, IDF, international diabetes federation, IDEFICS, Identification and prevention of dietary and lifestyle-induced health effects in children and infants.

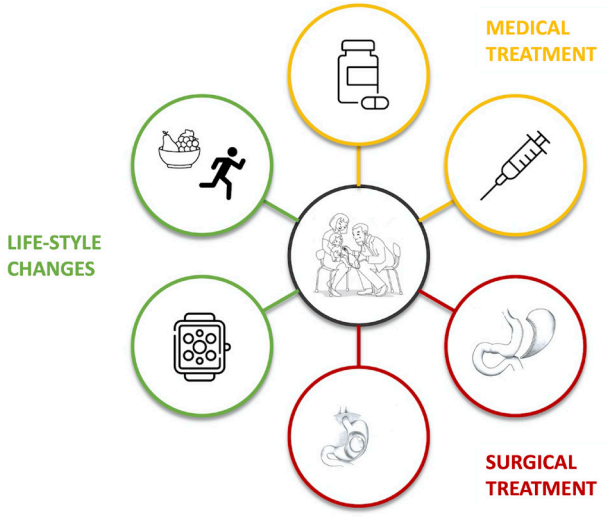

Figure 5. Obesity treatment options.

changes in diet, activity, and lifestyle (Fig. 5).

- The standard therapy is represented by lifestyle intervention, involving both patient and family. Particularly, it is necessary to provide diet and nutritional education and advise physical activity to reach a gradual BMI reduction and teach a healthy lifestyle for long-term weight loss maintenance. It is essential to keep the growth rhythm with an excellent weight-to-height ratio. Such efforts aim to decrease energy intake while improving the nutritional quality of foods consumed. When needed, could also be proposed a family-based behavioral weight loss treatment that is a multicomponent intervention targeting parents and children.
- Pharmacologic options are minimal. The pharmacological approach is proposed for obese youths who respond sub-optimally to behavioral therapy and only for children and adolescents with high BMI and comorbidities. Orlistat is the only medication approved for long-term pediatric obesity treatment (it can be used only for children older than 12 years). A lipase inhibitor reduces about 30% of lipids intestinal absorption, improving diet compliance (25,26). A new pharmacologic treatment option is liraglutide, a glucagon-like peptide 1 (GLP-1) analog that increases the post-prandial insulin level in a glucose-dependent manner, reduces glucagon secretion, delays gastric emptying, and induces weight loss through the reduction in appetite and energy intake. It is approved by the FDA and EMA for obesity treatment in adult patients as an add on treatment to lifestyle therapy. In a 2020 trial, the use of liraglutide plus lifestyle therapy led to a significant reduction of BMI in obese adolescents (27).
- Adolescents with severe, refractory (according to some guidelines ≥ 12 months of behavioral therapy) obesity or with comorbidities may be candidate for metabolic and bariatric surgery (MBS) or device therapy. However, data of these approaches are limited compared with behavioral interventions. The indications for surgery are 1) BMI ≥ 35 Kg/m^2 with one of T2M, severe obstructive apnea, benign intracranial hypertension, NAFLD (with Ishak score > 1) or 2) BMI ≥ 40 Kg/m^2 with minor complications such as mild obstructive apnea, impaired glucose tolerance.
- New polysaccharide complexes: since treatment op-

tions are minimal, a new approach has been proposed, such as polysaccharide complexes that work on the bowel mucosa like a sticky gel reducing postprandial plasma glucose level and the speed of carbohydrates absorption. They also reduce appetite and lipids absorption, promoting bowel transit.

Conclusions

Pediatric obesity is a silent pandemic with a dangerous rising prevalence, especially in developed countries. Obesity significantly impacts the quality of life of affected patients and health care systems. Obesity is related to several clinical comorbidities, especially metabolic syndrome and diabetes. Therefore, pediatricians should recognize potential risk factors (sedentary lifestyle, sugar, and fats-rich diet, genetic syndromes) and early signs of overweight and obesity to promptly address the child to a pediatric endocrinologist and a specialized reference Center. Early prevention is the key to avoiding clinical and phycological complications in the brief and long period.

Conflict of Interest: Each author declares that they do not have commercial associations that might pose a conflict of interest in connection with the submitted article.

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