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Review

# Current status on obesity in childhood and adolescence: Prevalence, etiology, co-morbidities and management

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ABSTRACT

Obesity and its associated co-morbidities increased throughout the world in the last 50 years, mainly due to increased amount of consumption of calorie-dense food and sedentary lifestyle. It is essential to combat with obesity at all available means and levels, including medical, societal and international measures. Childhood obesity persists into adulthood depending on the presence of parental obesity and severity of obesity. There are several windows of opportunity for interventions starting from pre-conception, to in-utero nutritional environment, from early infancy to adolescence to prevent obesity. In this paper, epidemiology, etiopathogenesis, co-morbidities, prevention and treatment of obesity in children will be reviewed.



## 1. General scope and epidemiology (Fig. 1)

Obesity is simply defined as excess amount of body fat and associated with number of health risks including Type-2 diabetes and cardiovascular problems. Obesity-related co-morbidities are among the leading public health problems worldwide since prevalence of obesity in adults as well as in children has been in rise in many countries over the last decades. In clinical practice, body mass index [(BMI) = weight (kilograms)/height (meters) squared], is the most commonly used surrogate measure of obesity in childhood. Calculated BMI value is plotted on published BMI reference standards. The definition of overweight/obesity varies according to the growth charts compiled by the Centers for Disease Control (CDC), the World Health Organization (WHO), and the International Obesity Task Force. The most commonly used definition of overweight is BMI between >85th and 95th percentile for age and sex and that of obesity is BMI ≥95th percentile for age and sex (CDC) (Shields and Tremblay, 2010). Severe obesity is defined as BMI ≥120 percent of the 95th percentile values corresponding to approximately the 99th percentile, or BMI Z-score ≥2.33 (ie, 2.33 standard deviations [SD] above the mean) (Skinner and Skelton, 2014; Flegal et al., 2009).

Although preventable, the prevalence of obesity has been continuously rising in both adults and children. According to WHO, worldwide obesity has more than doubled since 1980. Overall, 1.9 billion adults were overweight and 600 million of them were obese in 2014 covering 39% and 13% of total world's population respectively (www.who.int). This terrifying clinical picture also holds true for children. In year 2013, 43 million children under the age 5 were overweight/obese and this figure expected to reach 60 million by the year 2020 (de Onis et al., 2010). It is well known that many of the today's obese children and adolescents will become future's obese adults. The likelihood of persistence of childhood obesity into adulthood (tracking) depends on the age, the presence of parental obesity and severity of obesity (Guo et al., 1994; Parsons et al., 1999).

Once considered as a problem of developed world, some of the developed countries, succeeded in stopping or slowing down obesity epidemic in children and adolescents owing mostly to the effect of awareness campaigns and public health measures taken to prevent obesity. The prevalence of obesity in USA increased dramatically from 1970's to year 2000 (from 6.5 to 18.0 percent in children, and from 5.0 to 18.4 percent in adolescents) after which time it seems to stabilize and even decrease in some subgroups (Ogden et al., 2002, 2012, 2014). Reviewing the weight and height records of 11.1 million children aged 2–4 years who participated in federally funded health and nutrition programmes in 40 states, Pan et al. reported that from 2008 through 2011, the aggregated obesity prevalence decreased by 0.4–0.9% among all racial/ethnic groups except American Indians/Alaska Natives (Pan et al., 2015). The prevalence of obesity was 19.1% in young Southern Californians in

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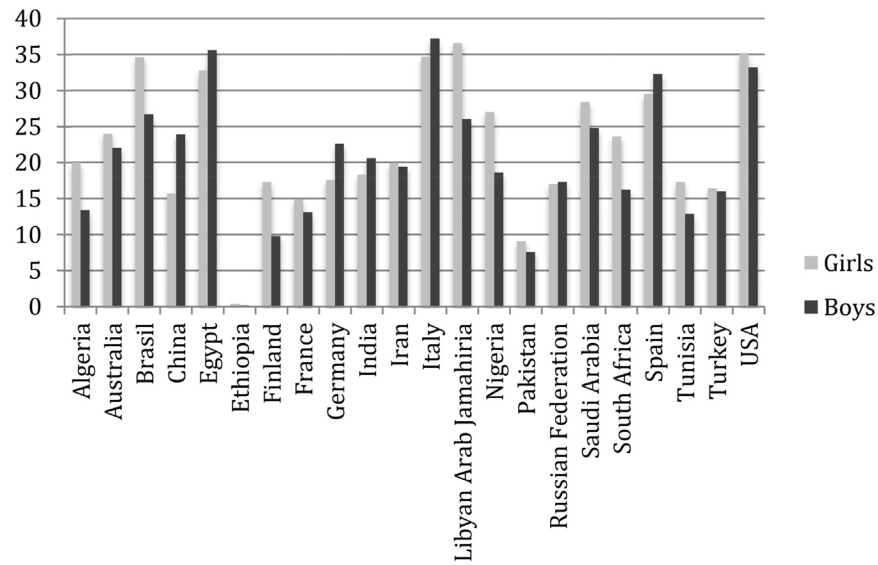



**Fig. 1.** The prevalence of childhood overweight and obesity in various countries in the world (data available from http://www.worldobesity.org/resources/trend-maps/).

year 2008 and decreased by 1.6% by 2013, corresponding to a relative decline of 8.4% (Koebnick et al., 2015). In a report from Israel, no increase in the prevalence of childhood obesity was observed between the years 2005–2007 and 2010–2012 (Almagor et al., 2015). Similarly, no difference in overweight prevalence between 2003 and 2011 among 12-year-old children in Sweden was reported (de Munter et al., 2016). Prevalence of overweight decreased in Dutch girls from 12.6% to 10.9% while it increased in children of immigrant descent from 14.6% to 21.4% from year 1999 through 2007 (de Wilde et al., 2014). Although, a third of children is obese/overweight, the trends showing that childhood overweight and obesity has also been stabilized recently with a small annual increase of 0.4% during 2004–2013 in England (van Jaarsveld and Gulliford, 2015).

On the contrary, obesity trend is still on rise in low (LI) and middle-income (MI) countries. It has been noted that the prevalence of overweight/obesity in an LMI or LI country is similar to that in many western European countries 40 years ago (Poskitt, 2014). Urbanisation, so called westernisation with greater possession of domestic appliances – televisions, cars and electronic equipment leading to a sedentary life; food secure environment, easy access to processed food and sugar-sweetened beverages which increases caloric intake could somehow explain this rising trend. The fact that the prevalence tends to be higher in low socioeconomic groups in affluent countries (where calorie-dense processed food are cheap, but healthy fresh food are expensive) whereas higher in high socioeconomic groups in LI and MI countries (where healthy local food (low calorie) and water are more available than processed food, sugar-beverages, fast-food) supports this. Unfortunately, cultural perceptions of obesity indicating good nutrition, well-being and beauty together with public unawareness about the future problems related to obesity are the other factors that add to the rising tide of obesity in those countries. China could be one of the most obvious example for those countries in which obesity has entered into an epidemic stage. According to a recent study from Shandong, China; the prevalence of overweight and obesity (defined by WHO criteria) increased from 2.76% to 0.45% for boys, 2.46% and 0.11% for girls in 1985 to 20.30% and 18.16% for boys, 18.89% and 6.58% for girls in 2014, respectively (Zhang et al., 2015).

In transitional (between low to high income) countries figures show heterogeneity. The prevalence of overweight (including obese) children has been reported to range from 14.4% to 19.2% for boys and from 11.8% to 17.6% for girls in the transitional countries of Eastern and Central Europe which include Belarus, Bosnia Herzegovina, Bulgaria, Croatia, Czech Republic, Hungary, Latvia, Lithuania, Poland, Romania, Russian Fed., Slovakia, Slovenia and Turkey. Frequency Prevalence of overweight and obese children in Hungary increased between the 1980s and the beginning of the 2000s (Bodzsar and Zsakai, 2014). In Turkish children and adolescents, several local studies from different regions of the country performed between 2000 and 2010 demonstrated that prevalences of overweight and obesity in children aged 6–16 years vary between 10.3%–17.6% and 1.9%–7.8% respectively. The differences in the figures obtained in these regions are thought to be due to variations in the sampling of the subjects in regard to residential (urban vs rural) and economical conditions. The risk factors identified most commonly were; high income family, living in metropolis, having obese parents, large birthweight, consumption of soft beverages and time spent by TV and PC (Bereket and Atay, 2012).

In the Middle-Eastern countries, figure are more heterogenous. Obesity rates are alarmingly high in oil-rich countries, whereas they are lower in the middle-and low income countries. A total of 12,701 children (6281 boys and 6420 girls) with ages 1–18 years were screened in 2002 in different provinces of Saudi Arabia showed that the overall prevalence of overweight was 10.68 and 12.7 percent and that of obesity was 5.98 and 6.74 percent in the boys and girls, respectively (El-Hazmi and Warsy, 2002). Girls were more obese than boys. However, the situation is worsening, as a recent study in 6–10 years schoolchildren from Saudi Arabia, demonstrated the prevalence of overweight or obesity as 34.8% in girls and 17.3% in boys (Al-Mohaimeed et al., 2015). In Kuwait, the prevalence of overweight was 21.6% and obesity was 30.5% in 6–18 years of age and boys had a higher percentage of obesity (Elkum et al., 2015).

A meta analysis from Iran reported that the overall prevalence of obesity was 5.13% and 7.25% in 1995–1999 and 2005–2010, respectively. In the same period the prevalence of overweight remained relatively constant and estimated to be about 10.43% and 10.88%, respectively. Despite this relative stability, the authors drew attention to the point that until a few years ago underweight was the main nutritional problem of Iranian children. (Kelishadi et al., 2014). As one of the countries in Eastern Mediterranean area, studies in Lebanon also show, increase in obesity prevalence from 7.3% in 1997 to 10.9% in 2009 with the annual rates of change in obesity prevalence of +4.1% in children and adolescents (Nasreddine et al., 2012).

## 2. Etiopathogenesis

Obesity occurs as a result of complex interplay between genetic and environmental factors. Children with specific ethnic background such as American Indian, black, Mexican American and South Asians are more prone to develop obesity (Gurnani et al., 2015). Even in the same ethnic population, tendency to develop obesity varies among the families. Discerning genetic contribution to obesity is highly difficult since families share not only genetic material but also environments and nutritional habits. 30–50% of adiposity could be explained by heritable factors and up to now, eighteen genes associated with obesity have been identified by genome-wide association studies (Queiroz et al., 2015). Some single gene defects including leptin, leptin receptor, proopiomelanocortin, prohormone convertase 1, melanocortin receptors (MCR) 3 and 4, the transcription factor single-minded 1(SIM-1), TrkB and spesific syndromes such as Albright hereditary osteodystrophy (pseudohypoparathyroidism type 1a), Alström, Bardet-Biedl, Beckwith-Wiedemann, Carpenter, Cohen, Börjeson-Forssman-Lehmann, Prader-Willi, and WAGR (Wilms tumor, aniridia, genitourinary anomaly, mental retardation) syndromes are associated with obesity (Weiss and Lustig, 2014). Of the single gene defects, MCR4 is relatively common accounting for 4% of early onset cases of childhood obesity (Gurnani et al., 2015). Large deletions of chromosome 16p11.2 is found in some 0.7% of morbidly obese patients (Walters et al., 2010). All patients with syndromic forms of obesity could be identified by spesific dysmorphic features and also exhibit a certain degree of neurocognitive delay. Hypothyroidism, growth hormone deficiency, Cushing syndrome and hypothalamic obesity caused either by an intracranial tumor or rare ROHHAD (**R**apid onset **o**besity, **h**ypothalamic dysfunction, **h**ypoventilation, and **a**utonomic **d**ysfunction) syndrome are the other etiologies resulting in childhood obesity (Weiss and Lustig, 2014). Overall, less than 5% of cases of childhood obesity could be attributed to one of the specific causes mentioned above. Unfortunately, for the remaining large portion no single specific cause is present rather the condition result from the complex interactions of the child's genetic, ethnic, social and physical environment.

## 3. Risk factors for common (exogeneous) obesity (Fig. 2)

Environmental exposures during the fetal and early postnatal life could render the child to develop obesity by causing fetal metabolic programming via alteration of gene expression through epigenetic modifications. Mother's prepregnancy weight and weight gain during pregnancy is directly related to child's birthweight and/or weight during childhood (Lau et al., 2014). Small for gestational age or large for gestational age babies are more likely to develop obesity (Han et al., 2010). Studies regarding the correlations of childhood or adolescent BMI with gestational diabetes, maternal smoking during pregnancy, maternal preeclampsia and mode of delivery (Cesarian vs vaginal) give contradictory results (Lawlor et al., 2011; Davis et al., 2012; Ehrenthal et al., 2013; Black et al., 2015; Robson et al., 2015). It has been demonstrated in many studies that exclusive breast-feeding in the first 4–6 months of life has a protective role in the development of early childhood obesity (Chiasson et al., 2016; Zong et al., 2015). Earlier adiposity rebound (physiologic increase in slope of BMI curve) before the age 5 years has been shown to increase BMI and fat mass index at 15 years (Hughes et al., 2014).

As the child gets older, imbalance between energy intake and energy expenditure becomes more and more important in gaining weight. As for the energy intake part, high calorie-low nutrition processed foods, large portion sizes, rapid eating, fast food service, higher consumption of sugar sweetened beverages, skipping breakfast, absence of family at meal times, low intake of dairy products, fruit and vegetables are the factors associated with childhood obesity (Malik et al., 2013; Brown et al., 2015). Increased sedentary behavior with low level of physical activity such as playing video games, watching TV has strong association with development of obesity in children (Kaur et al., 2003; Stettler et al., 2004). Time spent watching TV has multiple effects, such as causing sedentary lifestyle, stimulating eating behavior by TV commercials of high-calorie foods targeted to children, and also causing children to sleep less (Güran and Bereket, 2011). Many studies have also demonstrated an association between short sleep duration and obesity (Lumeng et al., 2007). Chronic stress either personal or parental may lead to an increase risk of childhood obesity (Heerman et al., 2016). Some psychoactive drugs such as olanzapine, risperidone, antiepileptics and glucocorticoids are frequently associated with weight gain. The interest in linking obesity to viruses (adenovirus 36), gut microbiota and endocrine disrupting chemicals such as DDT has been increasing recently (Gabbert et al., 2010; Warner et al., 2014; Berger et al., 2014).

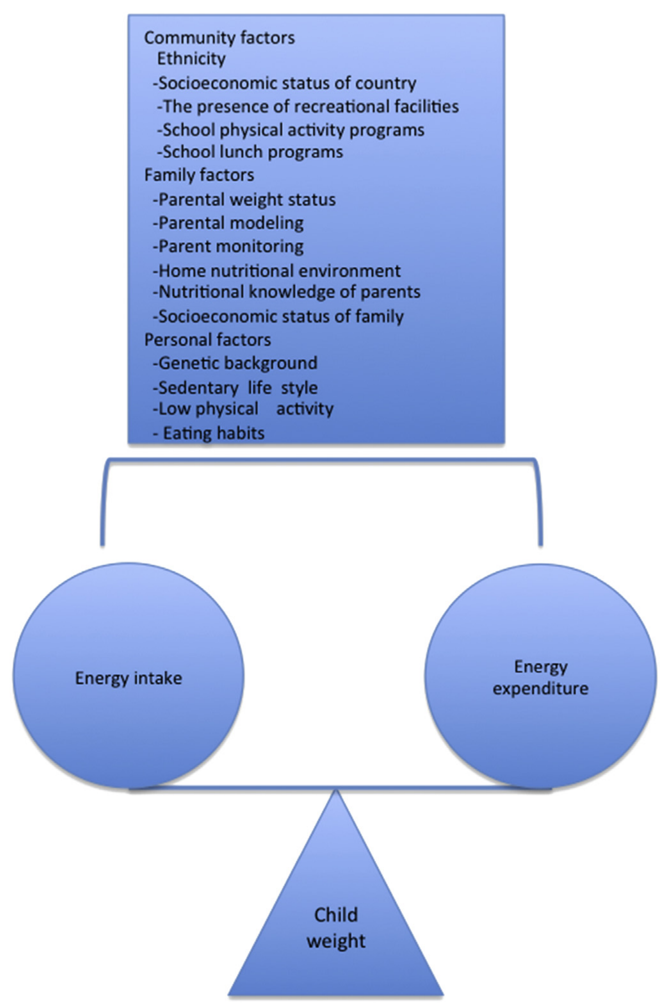



**Fig. 2.** Factors that affect a child weight by disturbing the balance between energy intake and energy expenditure.

## 4. Complications, co-morbidities of childhood obesity (Fig. 3, Table 1)

As the prevalence of obesity increases, complications and comorbidities related to obesity also increases. These life-long risks will affect both life expectancy and life quality of the population besides putting a huge economic burden on the finances of the world which are already limited especially in developing countries. These complications affect all systems in the body. In a study on 774 obese children, Maggio et al. reported that orthopedic problems are the most frequently seen medical complications (54%) followed by metabolic (42%) and cardiovascular disturbances (31%) (Maggio et al., 2014). Younger obese children below age 8 years most commonly suffer from orthopedic complications, the most frequent being genu valgum. The prevalence increased with weight status. Metabolic problems, such as abnormal glucose, insulin, TSH or ALT levels are more common in obese adolescents without difference among weight status. In the same study, so called non-medical conditions related to well-being, such as bullying, psychological complaints, shortness of breath or abnormal sleeping patterns, were present in the vast majority of the children (79.4%) (Maggio et al., 2014).

### 4.1. Metabolic & endocrine

Metabolic complications include insulin resistance, prediabetes, type II diabetes and metabolic syndrome. Standard technique for the measurement of insulin resistance, hyperinsulinemic euglycemic clamp, is not feasible for use in daily clinical practice. HOMA-IR (Homeostasis Model Assesment of Insulin Resistance), FIGR (Fasting glucose/insulin ratio), and QUICKI (Quantitative Insulin Sensitivity Check Index) are used as surrogate measures of insulin resistance in clinical settings.

Although varies with the ethnic, racial background, the age of studied population, the index used and the cut off values to define insulin resistance; about 1/3 of obese children had insulin resistance. In a study by Kurtoglu et al. 27.8% of girls and 37% of boys with obesity had insulin resistance during prepubertal ages (Kurtoglu et al., 2010). The prevalences increased to 66.7% and 61.7% for obese girls and boys, respectively during puberty. Insulin resistance with compensatory hyperinsulinemia is the first step that leads to prediabetes and type 2 diabetes. The children with prediabetes have increased risk for type 2 diabetes and include the children with fasting plasma glucose 100–125 mg/dl, 2-h plasma glucose on OGTT 140–199 mg/dl (Impaired glucose tolerance) or HbA1c 5.7–6.4%. The prevalence of impaired fasting glucose was reported to be 15.5%, 20.2% and 22.5% of overweight, obese and severely obese children respectively (Marcus et al., 2010). The prevalence of impaired glucose tolerance is similar and reported in 25% of children and 21% of obese adolescents (Sinha et al., 2002). Maggio et al. reported that abnormalities in glucose metabolism including IFG, IGT and T2DM were present in 16.1%, 11.7% and 7.8% of overweight, obese and extremely obese children, respectively.

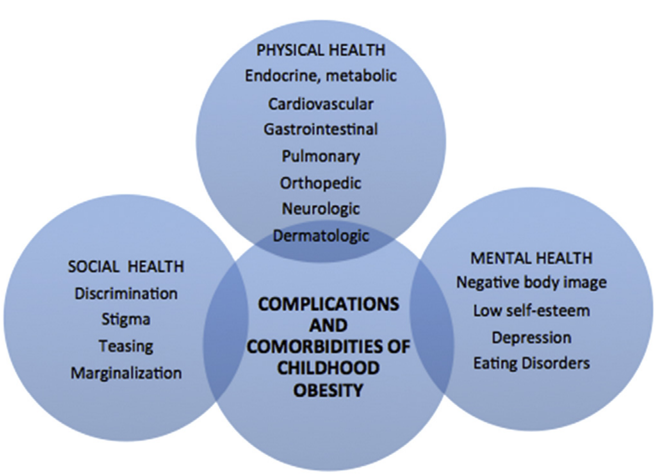



**Fig. 3.** Consequences of childhood obesity.

The prevalence of type 2 DM among children and adolescents rises in parallel with the rising epidemics of childhood obesity. The reported prevalence was 0.24 cases per 1000 individuals younger than 20 years in USA (Pettitt et al., 2014). In Europe, type 2 DM was reported to be present in 0.6/100,000 of Danish children and adolescents (Oester et al., 2015). The prevalence in obese children was reported to be 1–2% in various studies (Kurtoglu et al., 2010; Shah et al., 2009). The ratio of T2DM within children with DM also increases. In our center, this ratio increased from 1.3% to 5.3% between the years 1999–2013 (unpublished data).

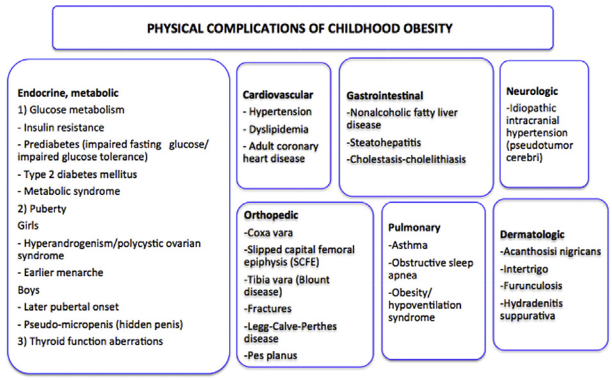
Metabolic syndrome defined as the co-presence of obesity, hypertension, abnormal glucose homeostasis and dyslipidemia is an important determinant of cardiovascular risks. The definition of metabolic syndrome in children and thus its prevalence differs depending on the criteria used (WHO, IDF, NHANES III or modified ATP III). In their systematic review, Friend et al. reported the prevalence of metabolic syndrome as 3.3%,11.9%, and 29.2% of normal-weight, overweight and obese children respectively (Friend et al., 2013). By using IDF criteria, Kurtoglu et al. reported a 34.6% prevalence rate for metabolic syndrome in 159 obese children at the age of 10–16 years (S1Akin et al., 2012). Çizmecioğlu et al. using IDF criteria found MS in 2.3% of Turkish schoolchildren aged 10–19 years, and 28% in obese children (Cizmecioglu et al., 2009).

### 4.2. Effects on puberty, PCOS and thyroid hormones

It has been known that body fat mass is among the critical factors for pubertal onset in girls (Frisch et al., 1973). BMI is negatively correlated with age at breast development and menarche in many studies. Kaplowitz et al. demonstrated that the mean BMI Z scores for each age are markedly greater in 6–9 year-old white girls with versus without breast development and the more advanced the breast development was the higher the BMI Z score was (Kaplowitz, 2008). They concluded that BMI is a significant predictor of breast development. A positive association was reported between BMI Z score and likelihood of having reached menarche by Anderson et al. (Anderson et al., 2003). Atay et al. found that in the same age groups, the premenarcheal girls have significantly lower BMI SD scores than the postmenarcheal girls (Atay et al., 2011). Although the mechanism has not been clearly elucidated yet, leptin has been shown to be the linkage between BMI and puberty. Secreted from the white adipose tissue in a pulsatile manner in direct proportion of the amount of total fat mass and acting on its receptors in hypothalamic arcuate and paraventricular nuclei, leptin stimulates GnRH, LH and FSH secretion. Besides its permissive effects on initiation of puberty, leptin has also direct effect on gonads, modulating proliferation, germ cell differentiation and steroidogenesis (Bereket and Atay, 2014).

Obese girls are also more prone to develop premature adrenarche and polycystic ovary syndrome (PCOS). Elevated DHEA and DHEAS level which appears to be due to enhancement of 17–20 lyase activity of CYP17 in adrenal gland, is the hallmark of premature adrenarche. Leptin might have a role in pathogenesis of premature adrenarche in obese girls since it has been demonstrated to stimulate the activity of CYP17 (Biason-Lauber et al., 2000). Affecting 3–8% of woman at reproductive age, PCOS is strongly associated with obesity. McManus et al. reported that 80% of

**Table 1**
Complications of childhood obesity in various systems of the body.




adolescents with PCOS was overweight/obese (McManus et al., 2013). Hyperinsulinemia with differential tissue sensitivity to insulin which induces ovarian hyperandrogenism in obese individuals is central to the development of PCOS.

Hyperthyrotropinemia, isolated TSH elevation, is commonly seen in obese individuals. Although the mechanism has not been elucidated yet, it is most probably an adaptive response of hypothalamo-pituitary-thyroid axis to increasing adipose tissue since it usually normalizes after weight loss (Santini et al., 2014).

### 4.3. Cardiovascular

Obesity affects cardiovascular system by causing hypertension, dyslipidemia, changes in cardiac structure and function. Hypertension in children is defined as the blood pressure over 95 percentile for age, sex and height. Obese children have about threefold higher risk of hypertension which increases with the severity of obesity. In their report, Maggio et al. calculated an odd's ratio of 2.5 for obese and 4.8 for extremely obese children for the presence of systolic hypertension (Maggio et al., 2014). The frequency of hypertension was 8.1, 16.2, 23.9% in overweight, obese and extremely obese, respectively.

Adipose tissue is hormonally active and induces a low grade chronic inflammation by secreting inflammatory factors such as monocyte chemo-attractant protein-1 (MCP-1), tumor necrosis factor-$\alpha$ (TNF-$\alpha$), and interleukin-6 (IL-6) (Chang et al., 2015). This elevated inflammatory cytokines together with hypoadiponectinemia, elevated leptin and insulin forms the hormonal milieu for this chronic inflammation in obese individuals leading to vascular injury and endothelial dysfunction which results in atherosclerosis and coronary artery disease. Obese children are more prone to have dyslipidemia (high LDL, high triglycerides and low HDL) which is one of the major risk factors for coronary artery disease. The prevalence of dyslipidemia reported in NHANES (the Nutrition Examination Survey) was 20.3% and 42.9% in nonobese and obese youth, respectively (US Department of Health and Human ServicesCenters for Disease Control and Prevention, 2010). There are other cardiovascular parameters affected in obese children such as decreased aortic diastolic velocity, increased carotid intima media thickness, decreased carotid artery compliance, decreased brachial artery flow-mediated dilatation, increased epicardial adipose tissue thickness and decreased left ventricular diastolic compliance. These parameters demonstrate the changes in cardiovascular structure and function and could be used in the risk assessment of future coronary artery disease.

### 4.4. Gastrointestinal

Nonalcoholic fatty liver disease (NAFLD) defined as the accumulation of triglycerides in the liver in the absence of alcohol consumption or other liver pathologies that causes fat deposition such as Reye syndrome, fatty acid oxidation defects, urea cycle defects, drugs (valproate, salicylate, steroids etc.), total parenteral nutrition and phosphorous intoxication. The clinical spectrum varies from steatosis and steatohepatitis to cirrhosis. In a recent meta-analysis, the prevalence of NAFLD in general pediatric population was reported to be 7.6% (Anderson et al., 2015). In the same study, the prevalence of NAFLD in lean, overweight and obese children was 2.3, 12.5 and 36.1%, respectively. The odd's ratio for NAFLD in overweight and obese children was 13.4 when compared to normal weight children. Cholelithiasis, the other gastrointestinal complication of obesity, was reported in 6.1% of obese adolescents (Nunes et al., 2014). The risk for developing gallstones is about twofold greater in moderately obese boys whereas the risk is about sixfold in moderately obese girls (Koebnick et al., 2012).

### 4.5. Pulmonary

Overweight/obese children have a greater risk of incident asthma, more severe or frequent symptoms, and a decreased response to inhaled steroids In a population based study of 681,122 individuals aged 6–19 years, 10.9% had current asthma. 46.5% of those with current asthma was overweight/obese and adjusted odds of asthma for overweight, moderately obese, and extremely obese youth compared to those of normal weight were 1.22, 1.37, and 1.68, respectively. In the same study, increasing BMI was also associated with more frequent ambulatory and emergency department visits, as well as increased inhaled and oral corticosteroid use (Black et al., 2012).

Obstructive sleep apnea (OSA) and obesity-hypoventilation syndrome are the two important respiratory hazards of obesity. OSA is 4–6 fold more common in obese children and adolescents (Gurnani et al., 2015).

### 4.6. Orthopedic

Genu valgum, pes planus and hyperlordosis are the most frequent three orthopedic complications of childhood obesity (Maggio et al., 2014). Obese children are also more prone to develop slipped capital femoral epiphysis, Blount disease, scoliosis and spondylolisthesis. Due to reduced bone mass relative to body surface area resulting from lack of exercise and associated vitamin D deficiency, obese children are more susceptible to fractures when compared to non-obese ones.

### 4.7. Neurologic

Idiopathic intracranial hypertension (IIH) is strongly associated with obesity. In a recent study of 78 children with IIH aged 11–19 years, the adjusted odds ratios for IIH with increasing weight class were 1.00, 3.56 (1.72–7.39), 6.45 (3.10–13.44), and 16.14 (8.18–31.85) for underweight/normal weight, overweight, moderately obese and extremely obese, respectively (Brara et al., 2012).

### 4.8. Dermatologic

Obesity induces skin problems by posing mechanical stress and also change in hormonal milieu such as elevated DHEAS level. Complications related to skin have been classified according to their pathophysiologic origin as being associated with insulin resistance (IR), hyperandrogenism, skin folds, mechanical causes, and hospitalization (Gómez et al., 2014). Gomez et al. studied 109 overweight/obese individuals (13 children) and reported that acanthosis nigricans, skin tags, keratosis pilaris, and plantar hyperkeratosis were seen in 97%, 77%, 42% and 38% of the patients respectively. They found a significant and independent association between number of skin tags, AN neck severity score, AN distribution and insulin levels. Although less common than adults, acanthosis is also prevalent in adolescents and younger children. Ng HY et al. demonstrated that adolescents aged 12–18 years, compared with children aged 5–11 years, were more likely to have acanthosis nigricans (63% vs 47%; $P < 0.001$) and insulin resistance (Ng et al., 2014). Guran et al. have demonstrated that, the presence of acanthosis among obese children is associated with more severe obesity and more unfavorable lipid profile (Guran et al., 2008).

### 4.9. Psychosocial

Obesity may have serious psychosocial impacts. An inverse relationship between BMI and health related quality of life in the subscales of Physical well-being and Self-perception was reported (Helseth et al., 2015). Anxiety, depression, low self-esteem, distorted body image, stigmatization, eating disorders (bulimia, binge eating), school absenteeism, poor academic performance are other psychosocial consequences related to obesity.

## 5. Prevention and societal issues

Noncommunicable diseases (NCD) constitute one of the major challenges in the twenty-first century and have major social and economic impacts worldwide, particularly on developing countries. In the declaration of United Nation General Assembly in 2011, a concern on rising levels of obesity in different regions, particularly among children and youth was noted. It was also stated that obesity, an unhealthy diet and physical inactivity have strong linkages with the four main non-communicable diseases and are associated with higher health costs and reduced productivity (www.who.int/nmh). The World Health Organization (WHO) Global Strategy on Diet, Physical Activity and Health is one of the underheadings of a broader "Global Action Plan for the prevention and control of noncommunicable diseases 2013–2020" which aims to achieve the commitments of the UN Political Declaration on NCDs which was endorsed by Heads of State and Government in September 2011 (www.who.int). Many regional initiatives, (e.g. the European Charter on Counteracting Obesity, the Aruba Call for Action on Obesity, Plan of Action for the Prevention of Obesity in Children and Adolescents in Brasil, Reducing Obesity Rates in Illinois: The Path to Enhanced Physical Education, Healthy Nutrition and Active Life Program of Turkey: Obesity Prevention and Control Programme of Turkey) try to take measures to implement recommendations of the WHO in order to establish healthy nutrition and lifestyle for their own population and combat obesity (www.worldobesity).

There are many actions to be taken in the prevention of obesity at personal, familial, community and governmental levels. All these actions are interrelated. Actions related to personal and familial life starts from early, even antenatal, life of the individual since metabolic programming which predisposes future obesity and metabolic derangements is known to develop during this period. Increase in BMI of women in childbearing age directly influences next generations as we already know that maternal weight influences birthweight of the child hence future risk of obesity in the child. Therefore prevention should start from decreasing the obesity rates among women of childbearing age. In the low income countries, and high income countries young women usually work, however, in middle income and especially traditional countries such as those in middle-east, the ratio of young women in work is low. Easy availability of calorie-dense foods and sedentary lifestyle in these women are the main reasons for escalating rates of overweight/obesity among women which reached to >40% in many countries in the Middle East (Yumuk, 2005; Kilpi et al., 2014). Furthermore, keeping gestational weight gain within suggested limits of guidelines is important in this sense. Exclusive breastfeeding for the first six months of life, avoiding bottle feeding and early introduction of solids before 3–5 months might have a substantial effect in prevention of future obesity (Brown et al., 2015). It must be stressed that 36.3 million (63%) of children younger than 6 months in LMI countries were not exclusively breastfed (Victoria et al., 2016). Therefore, it is important to take effective measures to increase exclusive breastfeeding in these countries. Taking measures for building up healthy eating habits during childhood is also essential. Some of those include eating together with family at structured meals and snacks, avoiding TV viewing especially during meals, providing a perspective on portion size, encouraging fruits and vegetables, limiting eating at restaurants especially fast foods, offering foods in a variety of ways, avoiding soft sweetened beverages and demonstrating positive parent modeling. Parents should be a role model rather than being restrictive. They should set some rules and teach how to plan and prepare proper meals, then allow their child to take responsibility for choosing their meals. Moderate to vigorous physical activity for at least 60 min become important in school-aged children and adolescents. For achievement of this level of physical activity, it is essential to organise suitable environment within and outside the school. Involving peer groups to these activities will be particularly helpful for adolescents. Adolescents may also benefit from technology in this respect (Brown et al., 2015). Exergaming, use of electronic games designed to promote physical exercise, has been shown to increase energy expenditure and time spent on physical activity (Lamboglia et al., 2013).

Governments, especially those of developing countries must produce sustainable policies to combat obesity. These policies should include the fields of health, education, nutrition, agriculture and finance (Poskitt, 2014). Since undernutrition is also a problem in these LI and MI countries, it is important to provide nutrition security which means 'the assured supply, availability, and affordability of adequate food for a healthy diet' (Lobstein et al., 2015). It was demonstrated that soft drink consumption has been declining or stable in many high income countries in recent years. However, worldwide sales have been increasing as a result of increasing consumption in low and middle-income countries (Lobstein et al., 2015). Soda and chocolate bar otomatis are taking their place in especially private schools in middle income countries. Advertisements of these products go in parallel with the sales in certain, as reported by Pan Arab Research Center (McManus et al., 2007). Establishment of strict regulatory rules regarding the investments for marketing and advertisements of soft beverages, processed foods, breastmilk substitutes are important. Not only establishment of these rules, but also implementing them despite all the pressures is also essential, since food industry is in a tremendous effort on a governmental and societal level to offset these kind of obesity-preventive measures being taken.

Since women are primarily taking the responsibility of raising the child in these developing countries, giving a priority to educate and financially support the women for preparation of healthy foods at home instead of consuming energy-dense, nutrient poor, commercially branded processed foods should be aimed.

Creating public awareness about healthy lifestyle, nutrition, obesity, its complications and its costs to individual, family, population and to whole world is needed. Both social and traditional media should be activated in this regard. Besides this, building recreational places for physical activity in schools and neighbourhood, providing fresh fruits and vegetables for school meals and snacks, avoiding commercial food and drink dispensers in schools are some of the actions necessary to prevent obesity.

## 6. Treatment

Treatment of childhood obesity is mainly based on non-pharmacologic interventions. These include modification of diet, energy expenditure and use of behavioral strategies such as goal setting, reward systems, self-monitoring, stimulus control and contracting to enhance and provide maintenance of these changes.

Dietary intervention, supervised by a dietician if possible, is essential for weight management. A primary focus on health improvement rather than weight loss would be beneficial. Commonsense dietary approaches include setting a calorie range (1200–1500 kcal), modifying dietary content by limiting sugar-sweetened beverages, fast foods and increasing fruit and vegetable intake, reducing snacks and portion sizes.

Although essential, dietary intervention is not enough and should be supported by physical activity intervention programmes. 60 min of vigorous activity daily is recommended for school-aged children (>5 years) and adolescents. According to AAP, schools should provide at least 30 min of structured physical activity during school days. Younger children should have 180 min of any intensity physical activity or unstructured free play. Screen time should be limited to less than 2 h/day (Gurnani et al., 2015).

Psychological interventions are necessary to achieve and maintain this lifestyle modification. Only 5% of people maintain their weight loss, if not supported by behavioral strategies (Miller et al., 2004). In a recent meta-analysis, family-based behavioral treatment (FBT) and Parent-Only Behavioral Treatment for children were found to be well-established psychological treatments of overweight and obesity in child and adolescent populations (Altman and Wilfley, 2015). Furthermore the success in the child is strongly associated with weight loss in the parents. Weight change in the parent can predict weight change in the child (Wrotniak et al., 2004).

The goal setting for childhood obesity management should be SMART (**S**pecific, **M**easurable, **A**chievable, **R**elevant, **T**imely). A stepwise manner is logical. Weight maintenance should be the start, escalating the goal to not more than 0.5 kg/week (Gurnani et al., 2015).

Pharmacotherapy may be an adjunct to standard lifestyle modification in some selected children. However, options for pharmacologic therapy in childhood obesity are very limited. Orlistat, an intestinal lipase inhibitor, is the only drug approved by FDA for children >12 years of age. Reported BMI change with orlistat changes between 0.5 and 4.2 kg/m$^2$ (Rogovik and Goldman, 2011; Ozkan et al., 2004). Side effects include flatus, borborygmi and abdominal cramps. Fecal incontinence with oily discharge can be rather troubling. It can be recommended to adolescents with BMIs 2 or more units above the 95th percentile who continue to gain weight despite a 12-month trial of lifestyle modifications (Wrotniak et al., 2004). A multivitamin containing 5000 IU of vitamin A, 400 IU of vitamin D, 300 IU of vitamin E, and 25 μg of vitamin K should be added for adolescent use (Rogovik and Goldman, 2011).

Metformin is approved by FDA in the treatment of children ≥10 years of age with type 2 diabetes. Its use in obese children without type 2 diabetes has revealed a modest reduction in BMI when combined with lifestyle interventions. In a meta analysis of fourteen randomized clinical trials, a BMI reduction of −1.38 (95% CI, −1.93 to −0.82) from baseline compared with control at six months was reported. However, studies of one year of treatment did not report similar significant results (McDonagh et al., 2014). Gastrointestinal side affects such as nausea, flatulence and diarrhea are relatively common occurring in approximately 26% of patients (Ozkan et al., 2004). Metformin increases urinary excretion of vitamins B1 and B6. Vitamin B12 deficiency is also seen. Thus, prophylactic multivitamin should be added to metformin therapy. Lactic acidosis which is the most feared side effect, has not been reported in children so far.

Although approved for the treatment of adult type 2 diabetes, exenatide, a GLP1 agonist, has also been used in clinical trials for its potential to reduce weight. Kelly et al. reported that compared to control, exenatide significantly reduced BMI (−1.7 kg/m$^2$, body weight (−3.9 kg) and fasting insulin (−7.5 mU/L)) in twelve children aged 9–16 years with extreme obesity (Kelly et al., 2012).

Topiramate is a novel anticonvulsant, which blocks voltage-dependent sodium channels, enhances the activity of the GABAA receptor (Nasreddine et al., 2012). It has been shown to cause an average reduction in body mass index of 3.2 (dosages above 200 mg) to 6.1 (dosages below 50 mg) every six months of treatment in 47 children followed in a psychiatry clinic (Shapiro et al., 2016). Topiramate is promising especially in the treatment of antipsychotic-induced obesity.

Some other drugs including Lorcaserin, phentermine, phentermine/topiramate, and naltrexone SR/bupropion SR have been approved by FDA for treatment of obesity in adults (Boland et al., 2015). No clinical trials related to these drugs in children and adolescents have been published yet.

Oxyntomodulin, one of the several gut hormones which modulate appetite, is an analog of PYY(3–36). In a 4-week, randomized double-blind study in adults, it has been shown to reduce weight by 2.3 ± 0.4 kg (Wynne et al., 2005).

### 6.1. Bariatric surgery

Surgical procedures including laparoscopic adjustable gastric banding, sleeve gastrectomy, Roux-en-Y gastric bypass are effective for weight reduction in adolescents. In their meta analysis, Black et al. reported a significant decrease in BMI of −13.5 kg/m$^2$, at 1 year of surgery (Black et al., 2013). Although the data about resolution of comorbidities is poor as they stated, improvement in metabolic and psychosocial comorbidities have also been reported. Despite this dramatic reduction in weight, complications related to surgical procedures may be significant. Thus, indications for bariatric surgery in adolescents requires strict definitions. BMI greater than 35 kg/m$^2$ with severe comorbidities or BMI greater than 40 kg/m$^2$ with mild comorbidities are suggested as possible indications for bariatric surgery. Besides these, the patients must have attained 95% of adult stature before surgery, have failed to attain a healthy weight with previous lifestyle and pharmacologic interventions, have healthy mental status to provide informed assent and adhere to pre and postoperative rules (Hsia et al., 2012). Although Roux-en-Y gastric bypass remains the gold standard procedure for both adolescents and adults, no clear guidelines to choose a specific bariatric procedure for a specific adolescent patient have been described yet. These procedures should be done only in centers experienced with bariatric surgery and a multidisciplinary approach is essential to cope with pre and postoperative problems.

## 7. Conclusion

Obesity brings an enormous amount of problems in regard to personal and social life. Dealing with these complicated problems requires a huge medical, social and financial support. It is obvious that trying to prevent obesity would be more logical and cost-effective than to treat its complications. Unfortunately, no single intervention can halt the rising tide of obesity in childhood. The prevention requires a whole-of-government, inter-governmental actions in which policies regarding all the relevant sectors primarily take health into account. And lastly, the governments of LI and MI countries should be supported vigorously by international organizations such as the WHO, UNICEF, UN in regard to knowhow, finance and human resources to combat obesity. Pediatricians are the key health-workers in this combat who monitor growth and development of the child from birth. Early preventive measures for under-risk children should be discussed with family in each visit and proper guidance should be provided throughout childhood.

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