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Review

Overweight and obesity in childhood: Dietary, biochemical, inflammatory and lifestyle risk factors

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Obesity and overweight among children are global health challenges that are growing rapidly. Childhood obesity is strongly associated with adult obesity and posess serious health co-morbidities and psychosocial consequences. Growing evidence of high rate of dyslipidemia and hypertension along with impaired glycemic control have been reported in child obesity. Recent studies suggest the development of obesity-linked complications is related to the imbalance in the expression of pro- and anti-inflammatory adipokines. With increasing adiposity, the pro-inflammatory adipokines such as leptin are increased, while anti-inflammatory adipokines such as adiponectin are decreased. Weight gain could be associated with many factors including unhealthy dietary patterns and non-dietary factors as environmental factors as easy access to high caloric food; abnormal mealtime structure; sedentary lifestyle as television watching; and to less extent having overweight or obese mother/father. This review addresses the childhood obesity, focusing on dietary and non dietary causes and consequences. It also presents the effective ways to assess children's diets.

Abstract

1. Introduction

Child overweight and obesity prevalence has risen substantially in most high-income low-income and middle-income countries (Lobstein et al., 2015). Childhood obesity predisposes to insulin resistance and type 2 diabetes, hypertension, hyperlipidemia, liver and renal disease, and reproductive dysfunction. This condition also increases the risk of adult-onset obesity and cardiovascular disease, and impaired social, educational and economic productivity (Lanigan and Singhal, 2009).

Overweight and obesity are described as an excess of adipose tissue or body fat that present a risk to health (WHO, 2018). Internationally obesity in adults is defined by using the body mass index (BMI); which is calculated by dividing body weight (kg) by height squared (m^2) (WHO, 2018). However; definition of obesity in children is complicated since childhood period involve irregular changes in body shape and composition. World Health Organization (WHO) has published child growth standards based on BMI for age (WHO, 2018). Thus; obesity is defined as a BMI more than +2 SD; and overweight as a BMI more than +1 SD above the WHO growth reference median for 5–19 years old children (WHO, 2018).

Several methods were used to measure the degree of body fat. These anthropometric measurements techniques include; BMI; waist circumference (WC) and skin-fold thickness (Wells and Fewtrell, 2006); which are less accurate than the techniques that are used in research purposes such as densitometry (underwater weighing) Computed tomography (CT); Magnetic resonance imaging (MRI); Energy X-ray absorptiometry (DEXA) and bioelectrical impedance analysis (BIA) (Wells and Fewtrell, 2006). BMI failed to differentiate between fat and fat free mass. Also; BMI does not take into account the gender and age factors; where females naturally have a higher percentage of fat mass and lower percentage of fat free mass than males as well as the abdominal fat which increases dramatically with age (Wells, 2000). Nonetheless; BMI is widely used in clinical setting as it's increase is strongly associated with increase central and peripheral body fat and it is an effective tool for determining obesity and simply calculated (Ortega et al., 2016).

2. Causes of childhood obesity and overweight

Both between and within cultures; large variants in the frequency of overweight and obesity were documented (NCD-RisC, 2017). This is caused by variations in environmental exposures as well as genetic variations between populations (Hasselbalch, 2010). Thus; a complex

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interplay of non-modifiable genetic factors and modifiable environmental factors; has been suggested as the underlying cause of change in body weight (Lee and Ham, 2015; Syahrul et al., 2016).

2.1. Genetic factors

There is cumulative evidence demonstrating that genetic background of individuals may play a role in development of obesity (Hasselbalch, 2010). Multiple genes may increase the susceptibility to obesity depending on the effect of environmental factors. The development within the field of molecular genetics allow to identify about 20 single nucleotide polymorphisms (SNPs) that are related to adiposity (Frayling et al., 2007). The SNPs with the largest risk on obesity and overweight is the rs9939609 which lies within the first intron of the fat mass and obesity associated (FTO) gene (Frayling et al., 2007). Thus, A allele found to be associated with an increase in BMI by 0.08–0.12 Z-score units (~0.2–0.4 kg/m^2) in children between 7 and 11 years old (Frayling et al., 2007). FTO gene is located on chromosome 16, is extensively expressed in several tissues, but its highest expression is in the brain, mainly the arcuate nuclei hypothalamus (Frayling et al., 2007). Other SNPs identified to be associated with increased BMI are; rs17782313, rs17700633 and rs12970134 near the melanocortin-4 receptor (MC4R) gene that also has been widely expressed in hypothalamus. Hypothalamus is essential in controlling of appetite, food intake and energy homeostasis by receiving neuronal and hormonal signals to regulate satiety and energy intake (Ramamoorthy et al., 2015).

2.2. Environmental factors

2.2.1. Family, socioeconomic and sociocultural factors

Parents are considered as providers; models; and regulators for their children. Therefore; specific family environment and characteristics may be a risk of childhood obesity and overweight (Bjelanovic et al., 2017).

Children learn what; when; and how much to eat from their direct experience with food as well as by observing the food habits of their families. Thus; previous studies have shown that one or both parent's obesity/overweight may be significant contributing factor for their children obesity/overweight (Bahreynian et al., 2017). This is can be seen in parent's eating habits; food choices/preferences; type and amount of food consumed as well as food preparation methods (Bjelanovic et al., 2017). Moreover; data suggest that family structure; income; working status and educational level of parents found to influence their weight which in turn may be effect children weight (Bjelanovic et al., 2017). For example; Musaiger (2011) conclude that obesity in Eastern Mediterranean Region has increased as income increased and widespread in urban areas more than in rural areas. Musaiger (2011) documented that nonworking women in Eastern Mediterranean Region were more susceptible to excess weight than working counterparts. Regarding the relationship between family structure and children weight; Schmeer (2012) found that children living with single mothers and extended family households have higher BMI and increased risk of obesity than those children in stable marriage households. Other socioeconomic factors that related to nutritional status of children are the commercial actions. These actions were focus on marketing of food with low cost and poor quality; resulting in increased energy intake; weight gain and chronic diseases.

Al-Kloub et al. (2010) believed that obesity among children in Jordan has been dramatically increased throughout the last three decades. Socioeconomic status; working of parents and fast food revolution may affect dietary habits of children as well as amount of energy they consume in school and out of home (Al-Kloub et al., 2010). Khader et al. (2011) found that those obese children belong to families with income above 300 JDs per month. This may be explained by higher food consumption by families with monthly income above 300 JD than those families with low income than 300 JDs per month. Another possible explanation is that families with high income frequently eat out of home where foods served in restaurants usually being high in calories and fat (Syahrul et al., 2016). Number of family members as well as parent's BMIs also found to be associated with overweight among Jordanian children (Khader et al., 2011).

2.2.2. Dietary factors

Dietary factors and its possible contributions of obesity rates have been extensively studied; where they found that dietary factors are strongly associated with overweight/obesity among school children (Powell and Nguyen, 2013; Lee and Ham, 2015).

When the energy intake exceeds the energy expenditure; over a long period of time; this extra energy balance results in deposition of fat in the adipose tissue. However; storage of extra energy as indispensable physiological activity improves survival during food deprivation periods. Humans have two main types of adipose tissues; white adipose tissue (WAT) and brown adipose tissue (BAT) (Choe et al., 2016). The key purposes of WAT are synthesis and storage of triacylglycerol (TAG) in cases of energy excess (lipogenesis); and hydrolysis of TAG during periods of energy deprivation (lipolysis) (Gregoire et al., 1998). Thus; glucose and fatty acids uptake and storage into adipocyte were regulated by insulin role which illustrated in Fig. 1 (Lewis et al., 2002). In obesity; adipose tissue expansion is driven by both hypertrophy and hyperplasia of adipocytes. Hypertrophic adipocytes occur through increase in adipocytes size when the synthesis of TAG exceeds TAG breakdown (Gregoire et al., 1998); whereas hyperplasic adipocytes occurs through increase in number and differentiation of preadipocytes (Gregoire et al., 1998). However; both adipocyte hypertrophy and hyperplasia are associated with adipocyte dysfunction which increased releasing of free fatty acids and proinflammatory adipokines; as well as increase cell hypoxia; and impaired insulin sensitivity (Choe et al., 2016). Animal experiments suggest that adipocyte hyperplasia may be followed hypertrophy and associated with more severity and less reversibility of metabolic concerns. As mentioned above children learn

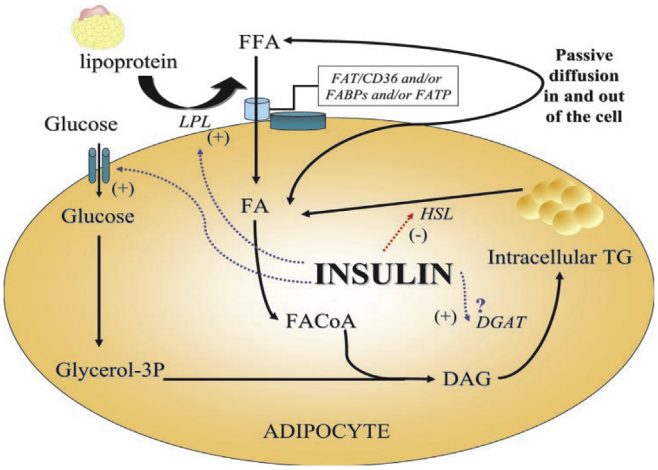

Fig. 1. Role of insulin in the stimulation of adipocyte glucose and fatty acid uptake and storage. Insulin regulate free fatty acid (FFA) uptake into the adipocyte by stimulating the lipoprotein lipase (LPL) to release FFA from lipoprotein triglycerides. Fatty acids (FA) then enter the adipocyte by diffusion (concentration gradient) and facilitated transport in the presence of fatty acid transporter (FAT)-CD36 and/or fatty acid binding proteins (FABPs) and/or fatty acid transporter protein (FATP). FA then esterified to form triglyceride (TG) in the presence of fatty-acyl-coenzyme A (FACoA). Insulin stimulates glucose transport into the adipocyte; thereby increasing the availability of glycerol-3 phosphate (Glycerol-3P) for triglyceride synthesis. Insulin may have a direct stimulatory effect on lipogenic enzymes such as diacylglycerol acyltransferases (DGAT). Intracellular lipolysis of triglycerides was reduced by inhibiting the hormone-sensitive lipase (HSL) which promoting adipocyte triglyceride storage (Lewis et al., 2002).

what; when; and how much to eat from their direct experience with food as well as by observing the food habits of their families. However; poor eating habits among children are common where they are failed to meet the recommended servings for grains; milk products; vegetables and fruit (Garnguet, 2004). In other hand; they increase consumption of sugar sweetened beverages; calorie dense snacks and eating out of home (Papandreou et al., 2016).

Many studies found that junk food consumption is linked with obesity (Bjelanovic et al., 2017; Albataineh et al., 2018). Junk food is known as easily available low cost food with low or no nutritive value. This food has high content of calories; salt; saturated fat and low content of iron; calcium and fiber (Horsu et al., 2015). Most common junk foods are fast food; carbonated and sugary drinks; chips; desserts; chocolates; etc.. In recent study in the Middle East displays that the risk of obesity and abdominal obesity were higher among students who regularly consume fast food; sweets and desserts; and consume extra soft drinks and chocolate than students who consumed them rarely (Albataineh et al., 2018). Large portion sizes of fast food and its high content of carbohydrate and fat amounts could induce child satiety; which in turn decrease the chance of children to eat healthier snacks (Powell and Nguyen, 2013).

Indeed; food is a powerful natural reward and habituation stimulus where several brain regions (limbic and cortical) and neurotransmitter (dopamine; serotonin; opioids and cannabinoids); in addition to the hypothalamus and neuropeptides (such as orexin; leptin and ghrelin); are involved in the rewarding effects of food (Cason et al., 2010). Foods rich in sugars and fat are strong rewards that stimulate releasing of dopamine to a level of pleasure. Dopamine is considered a crucial neurotransmitter that controls the reward system. However; Volkow et al. (2011) showed that dopamine levels and receptors were decreased in brain in the case of obesity. This hypothesis might be involved in the mechanism that elicits overeating in obese individuals.

Another factor that has been studied as a possible contributing factor of childhood obesity is skipping breakfast. Omission breakfast is found to be associated with an increased risk of becoming overweight or obese (Albataineh et al., 2018). Breakfast eating habit is described as protective agent in case of regular eating (Albataineh et al., 2018). Children who skip breakfast have double higher risk of becoming overweight than children who eat breakfast (Mushtaq et al., 2011). Thus; omission of breakfast is often associated with a decrease in diet quality during the day; since those children replace breakfast with snacking episodes and they choose sweet; salty and fatty foods rather than healthier snacks (Intiful and Lartey, 2014). Consequently; for each additional serving of sugar-sweetened drink the children consumed; BMI may increase by an average of 0.18 kg/m^2 (Ludwig et al., 2001).

Consuming large portions; as well as frequent snacking of high caloric foods; were resulting in excess total energy intake and consequently excess weight. For example; nowadays soft drinks available in 20 or 32 oz. bottles; while in past it is sold in 10 oz. or 12 oz. bottle (French et al., 2001). The most food groups that found to contribute of energy intake of children was breads and cereals; followed by fast food; sugar and sweets; meat and equivalent; milk and dairies; added fats and oils; and sugar sweetened beverages (Albataineh et al., 2018). Moreover; foods eaten out of home are often high in calories; total fat; saturated fat; cholesterol; and sodium; and low in fiber and calcium content (Musaiger, 2007).

2.2.3. Sleeping duration and quality

Insufficient sleep is associated with obesity and overweight among children (Liu et al., 2012; Tambalis et al., 2018). Sleep deprivation may have neuropeptides effect by its possible influence on levels of ghrelin and leptin which consequently may cause food intake disturbances; enhance the appetite and increase the consumption of total calories (Liu et al., 2012). Moreover; Tambalis et al. (2018) study the association between sleep duration and lifestyle profile. Inadequate sleeping hours (about 7 h/day) had a poorer physical activity; dietary habits and increased risk of overweight/obesity (Tambalis et al., 2018).

2.2.4. Watching television and obesity

Increased duration of watching television; playing video games; and using the internet are another reported contributing factors to augment the prevalence of sedentary lifestyle (Khader et al., 2011) which may increase the consumption of food in front of television and decreasing the time for physical activity. In addition; most foods that consumed by children during television viewing are sugar sweetened beverages; chocolates; sweets; potato chips and nuts (Musaiger, 2007). However; food advertisements may influence the food choices of children; which usually promote for fast foods; soft drinks; sweets; and chocolates purchasing and consumption (Madanat et al., 2007).

2.2.5. Physical activity level

Physical inactivity recognizes as one of the main risk factors of overweight and obesity (WHO, 2018). The effect of physical inactivity on the development of obesity in children is reported by many studies (Shook et al., 2015); as well as underlying reasons such as; increasing car use for transportation and increasing television watching hours (Musaiger, 2007). Indeed; physical activity is supposed to be key factor in defining the weight of children. However; Bjelanovic et al. (2017) concluded that physical activity effect varies depending on its type and level of intensity.

Recently; Shook et al. (2015) demonstrated that a relationship between energy intake; physical activity; appetite; and excess body weight has been detected. They found that individuals who are physically low active for one year have higher craving than those who are physically high active; which consequently result in higher BMI (Shook et al., 2015). A cohort study has been carried out for 32 years follow up on twins to investigate the role of physical activity on body weight with controlling of genetic cofactors (Leskinen et al., 2015). The authors revealed that twins on regular physical activity have significantly lower body weight than inactive co-twin (Leskinen et al., 2015).

3. Consequences of childhood obesity and overweight

Overweight and obesity in children have been associated with long-term morbidity and mortality. Childhood obesity has been linked to various medical; psychological and social conditions (Jansen et al., 2008). Several organs and metabolic processes are get dysfunction by excess body fat; which could cause severe complications that might be extent to death (Sahoo et al., 2015). Children who are obese are more likely to develop diabetes. About 55% of alteration in insulin sensitivity in children can be elucidated by total adiposity (Chiarelli and Marcovecchio, 2008). Obesity related insulin resistance are complicated including increase production and releasing of free fatty acids; adipokines and many hormones by adipose tissue (Chiarelli and Marcovecchio, 2008). Also; obese children may have an increased risk of developing cardiovascular diseases and their associated factors (hyperglycemia; dyslipidemia; and hypertension) (Khader et al., 2011); blood pressure; and fatty liver disease (Félix et al., 2016). Breathing problems are another health consequence of childhood obesity; such sleep apnea and asthma; where sleep apnea may be occurred due to fat tissue accumulation around the neck that pressing and reducing the airway (Schwab et al., 2003). However; the most important long-term concern of childhood obesity is its persistence into adulthood (Schore, 2012). Thus; overweight or obesity as well as other complications are likely to be more severe in adulthood.

Social stigmatisation or discrimination are psychosocial complication that facing obese children (American Academy of Pediatrics, 2014). Accordingly; these psychosocial problems may decrease the child confidence; increased risk of depression as well as increased risk of being socially isolated (American Academy of Pediatrics, 2014).

Obese and overweight children are also more likely to have poor academic performance (Schwimmer et al., 2003). Thus; those children

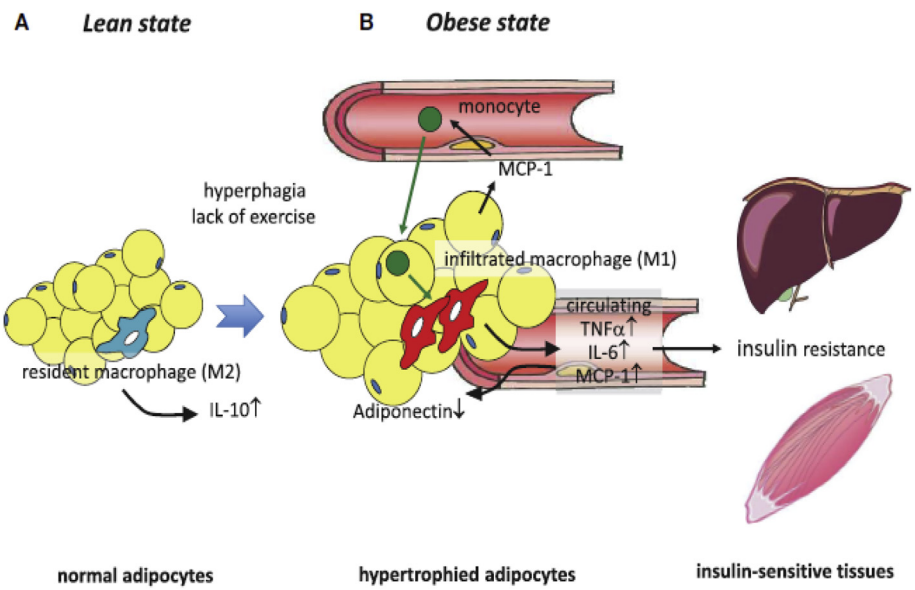

Fig. 2. Obesity-induced macrophage infiltration causes insulin resistance. (A) In a lean state; the abundant macrophages are M2 macrophages that contribute to insulin sensitivity by secreting IL-10. **(B)** Obesity induces MCP-1 excretion to the circulation; leading to the recruitment of circulating monocytes to adipose tissues. Infiltrated monocytes differentiate into activated M1 macrophages; which vigorously secrete proinflammatory cytokines such as TNFa; IL-6; and MCP-1; thus contributing to low-grade inflammation in adipose tissue and a decrease of adiponectin cause insulin resistance in liver and skeletal muscle by acting as insulin resistance-inducing adipokines (Tateya et al., 2013).

were found to be four times more to have difficulties at school comparing to their normal weight counterparts (Schwimmer et al., 2003).

4. Childhood underweight

Underweight can negatively affect the physical growth and the psychological development of children; as well as it is strongly correlated with an increased risk of morbidity and mortality. Underweight is often verified for growth monitoring purposes and is considered as a sign of under-nutrition in children (McDonald et al., 2013).

The inadequate dietary intake in children is often mixed; underlying medical conditions and environmental or psychosocial problems which consequently may lead to low caloric intake and low weight gain (Liu et al., 2015). However; inadequate intake can be due to 1) Social and family factors such as poverty and level of mother's education (Syahrul et al., 2016). 2) Health problems such as immune system problem (as food allergies); digestive problem (as food intolerances) or pains associated with eating (as dental caries) 3) Behavioral problems as over consumption of juice that may decrease appetite or picky eating behavior (Lee and Ham, 2015). 4) Increased nutrients need or loss due to high requirements for growth and metabolism during childhood or increase metabolic requirements secondary to underlying disease (USDA, 2015).

Underweight as a result of malnutrition in children may cause growth retardation; iron-deficiency anemia; repeated infections; and more frequent and severe illness due to several organs dysfunction compared to normal weight children (McDonald et al., 2013). In addition; underweight children may later in life have muscle weakness; low bone density; late maturation; and low work productivity (Pasricha and Biggs, 2010).

5. Dietary patterns changes in children

Wide transition in dietary pattern and nutrition from traditional; healthy and natural food to foods high in fat; sugar and salt throughout the developed and developing countries has been studied globally. This transition affects all age groups and communities in which the risk of obesity increased dramatically and consequently the chronic diseases including diabetes; hypertension; and stroke. Most of the developing countries in Middle East and North Africa region (World Bank, 2017); have been hit by this transition which increases the level of obesity and under-nutrition. Children are known to be irresponsible and can't meet their overall requirements by themselves that required for normal growth and development (Mohammad et al., 2013). They need more and more care in their schools and homes. Thus, unhealthy eating patterns can result in impaired motor and cognitive development (Kanjilal et al., 2010).

6. Biochemical and inflammatory parameters

The relationship of obesity with various biochemical and inflammatory parameters was studied by many studies (Mohammadi et al., 2016; Zyl et al., 2017). The dysmetabolic parameters of obese children highlight the assessment of biochemical and inflammatory measures to evaluate the obesity status and any related health complications (Weiss et al., 2004).

6.1. Biochemical parameters and children weight

Childhood obesity strongly correlates with decline in insulin sensitivity and glucose intolerance (Assuncão et al., 2018). The prevalence of the metabolic syndrome is increased with obesity in children as well as with increasing insulin resistance (Weiss et al., 2004). Similarly; a large-scale study on metabolic syndrome among 19593 children aged 6–18 years; confirmed the strong correlation between obesity and metabolic syndrome (Chen et al., 2012). A recent study on obese Brazilian children and adolescents to assess the glucose alteration and insulin resistance; found that hyperinsulinemia was observed in almost 30% of children and adolescents studied and 52.2% showed a significant increase in the homeostasis model assessment of insulin resistance (HOMA-IR) index; while no significant alteration detected in blood glucose; which indicated that high blood glucose levels may cause increase in insulin production. However; after a certain period; this compensatory process of increase in insulin level is lost; follow-on hyperglycemia; glucose intolerance; and finally type II diabetes (Assuncão et al., 2018). One of explanations about relation between obesity and insulin resistance is that as obesity result in increase in visceral and intraperitoneal adipose depots; consequently release high level of circulating free fatty acids and inflammatory factors; which in turn causes peripheral and hepatic insulin resistance (Shah et al., 2014). Fig. 2 shows the relationship between obesity and insulin resistance. High rate of hyperlipidemia along with impaired glycemic control have been reported in obesity (Mohammadi et al., 2016). Szternel et al. (2015) observed that hypercholesterolemia; hypertriglyceridemia and high low-density lipoprotein cholesterol (LDL-C) levels but not high-density lipoprotein cholesterol level (HDL-C); are dominant lipid abnormality

in obese/overweight children.

In other recent study; BMI was found to be associated with obesity-related cardiovascular risk factors including; systolic and diastolic hypertension; hypo-HDL; elevated TG/HDL ratio; metabolic syndrome; and reduced β cell function in children (Mameli et al., 2018). Also; a cross-sectional study conducted on obese children and adolescents in United Arab Emirates; defined that for each 1 cm increase in waist circumference (used as indices for defining abdominal obesity) dyslipidemia increase by 1.020 (OR = 1.020; 95% CI (1.001; 1.039); P = 0.041) (Deeb et al., 2018).

6.2. Inflammatory parameters and children weight

Adipose tissue has also been recognized as an endocrine organ. Adipokines are peptides induce adipose tissue to control different biological processes in targets organs such as brain, liver, immune system and muscle. Adipokines include leptin, adiponectin, fibroblast growth factor 21 (FGF21), retinol-binding protein 4 (RBP4), dipeptidyl peptidase 4 (DPP-4), bone morphogenetic protein (BMP)-4, BMP-7, vaspin, apelin, and progranulin. Levels of adipokines are altered in case of adipose tissue dysfunction and that may contribute to a spectrum of obesity-associated diseases (Klöting and Blüher, 2014). However, at early stages in obesity, obesity-associated inflammation has positive effect on the body. Literature suggest that adipose tissue hypoxia is the origin of inflammation in obesity. Thus, obesity-associated inflammation boosts energy expenditure by enhancing fuel mobilization and heat production (Ye, 2011).

Leptin and adiponectin are adipocyte-derived biologically active peptides that are found to be implicated in the pathogenesis of obesity as the adipocyte mass is distinctly altered (Guerre-Millo et al., 2002). Thus; with increasing adiposity; the pro-inflammatory adipokines such as leptin are increased; while anti-inflammatory adipokines such as adiponectin are decreased (Matsubara et al., 2002). Pediatric studies; also confirmed that both high levels of circulating leptin and low adiponectin levels were associated with obesity/overweight (Eldosouky et al., 2018). High leptin levels may also induce secretion of proinflammatory cytokines such as tumor necrosis factor- α (TNF-α) and interlukin-6 (IL-6) that contribute to insulin resistance and metabolic syndrome (Sainz et al., 2015). In contrast; adiponectin deficiency may lead to the occurrence of metabolic disorders. Recently a study has been conducted on 168 overweight and obese Saudi children and 126 controls to evaluate the correlation between serum leptin; its gene expression; and risk of childhood overweight and obesity (Eldosouky et al., 2018). The authors revealed that obese/overweight children have higher leptin level and higher gene expression than control (Eldosouky et al., 2018). In general; leptin can suppress food intake and stimulate energy expenditure by its action on the hypothalamus. Thus; the main signaling pathways of leptin are JAK/STAT; AMPK and insulin signaling (Marroquí et al., 2012). By JAK/STAT pathway the signals were imports from outside to inside the cell then into the nucleus; to stimulate the transcription of DNA and increase cell activity. When leptin attached to its receptor (OB-Rb); phosphorylation of the associated JAKs stimulated. The activated OB-Rb/JAK complex is then stimulates the phosphorylation of STAT3 and promotes its dissociation from the leptin receptor to form dimers that move into the nucleus. These hetero-dimers cooperate with specific DNA elements where it works as a transcription factor to regulate gene expression; like neuropeptide Y (NPY) and suppressor of cytokine signaling 3 (SOCS3) which mediated the anorexigenic effects of leptin (Marroquí et al., 2012); as shown in Fig. 3. Data propose that leptin effects may be more efficient when fat mass and nutrients are low (low leptin state) more than in state of satiety when leptin serum is high. During obesity it is suggested that leptin may be secreted in insufficient levels. Otherwise; as body fat increase serum leptin increase; but leptin shows inefficient effects may be due to leptin resistance (Heymsfield et al., 1999). Leptin resistance is commonly used to define states of high level of leptin with low or absence of response.

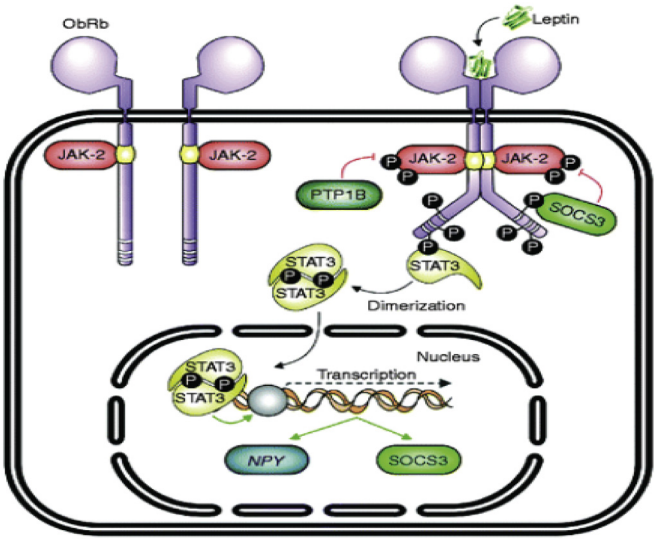

Fig. 3. The JAK/STAT pathway (Marroquí et al., 2012).

Several possibilities have been suggested that may lead to the development of leptin resistance these are; failure of leptin to cross the blood brain barrier and thus failed to act on its target neurons; decline in the expression of leptin receptors and failure of leptin signaling pathway at central and peripheral levels (Martin et al., 2000).

Resistin; a cysteine-rich adipokine; is reported to be involved in the development of obesity and insulin resistance. Studies reported that resistin is expressed only in rodent adipocytes but not human adipocytes, where in humans it is expressed in the macrophages. However, obese individuals who are likely to have more macrophages infiltration in adipose tissue exhibited increase in expression of resistin in adipose tissue compared to lean individuals (Park and Ahima, 2013). Studies show that levels of serum resistin in obese and overweight individuals was higher compared with lean adults as well as in children and adolescents (Mantovani et al., 2016). While resistin concentrations of obese children similar to normal weight children; it is found to be associated with central obesity; lipid metabolism; and insulin resistance. Thus; the researchers suggested that resistin concentrations are associated not only to overall fat but also to fat distribution (Simões et al., 2018).

7. Conclusion

Pediatric obesity is a complex epidemic consequently impaired metabolic and cardiovascular health. Healthy diet during childhood is recommended to control weight and prevent obesity for healthy adulthood and lifelong. Early identification of biochemical and inflammatory markers with combination of interventions can offset chronic inflammatory state and the consequent comorbidities. This review aimed to highlight the causes and consequences of and biochemical markers associated with weight gain in children.

Authors' contributions

All authors have strictly contributed to the study protocol, data collection and analysis, and writing and revising the article. All approved the final version to be published.

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Ethical approval

This research did not request ethical approval.

Availability of data and materials

Data and materials are available upon request.

Consent for publication

The Author agrees to deliver to the responsible Editor(s) on a date to be agreed upon the manuscript created according to the Instructions for Authors.

Conflicts of interest

The authors declare that there is no conflict of interest.

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