Forkert et al. Nutrire (2016) 41:15
DOI 10.1186/s41110-016-0017-7

Nutrire

REVIEW Open Access

Abdominal obesity and cardiometabolic risk in children and adolescents, are we aware of their relevance?

Elsie C. O. Forkert[1,2*], Tara Rendo-Urteaga[1,2], Marcus Vinicius Nascimento-Ferreira[1,2], Augusto Cesar Ferreira de Moraes[1,2,4], Luis A. Moreno[2,3] and Heráclito Barbosa de Carvalho[1]

Abstract

Obesity prevalence has increased worldwide over the last decades and has reached alarming rates in low middle-income countries. Childhood has been affected by this epidemic, leading to premature dramatic health problems. Adipose tissue is currently considered as an endocrine organ modulating an inflammatory state and important metabolic processes (insulin resistance, hypertension, glucose intolerance) leading to consequences of the cardiovascular system. This situation may be worst if the excess of body fat distribution such as abdominal obesity (AO) is involved because it is associated with a more atherogenic risk profile determining the cardiometabolic risks mainly in children and adolescents.

Hence, the knowledge regarding the association between AO and cardiometabolic factors aims to prevent and treat the obesity in this young population, avoiding early harmful consequences of adulthood health.

Keywords: Abdominal obesity, Adolescents, Children, Cardiometabolic risks, Prevalence

Background

Obesity is characterized by excessive accumulation of total body fat related to health problems and reduced quality of life in adults and children [1]. Besides, this condition adds greatly to the national health-care budgets [2].

The prevalence of obesity has increased in alarming rates in developing countries. In 2013, 42 million of children under the age of 5 were overweight or obese and the rate of increase was 30 % higher in low middle-income countries than that in developed countries (where no increase was observed after around 2000). If the trends continue by 2025, this rate may raise 70 million of patients worldwide [1].

Obesity per se, rather than the associated risk factors, is an independent predictor of some adverse cardiovascular events [3, 4] increasing threefold the mortality rate when compared with normal weight subjects [5]. In children and adolescents, obesity is associated with cardiometabolic risk factors such as dyslipidemia and type 2 diabetes, which are related with atherosclerosis development [6, 7]. High cardiovascular risk (assessed by Pathobiological Determinants of Atherosclerosis in Youth score) was associated with carotid intima-media thickening in obese adolescents with a fourfold higher risk of atherosclerosis [8]. The presence of overweight in adolescence was also associated with an increased risk of mortality from coronary heart disease in adulthood (women and men) regardless of the individual's weight in adulthood [9].

Otherwise, one of the most prevalent topics of discussion regarding excess body fat is the question of visceral fat depot or abdominal obesity (AO), also known as central obesity, central fat deposition, visceral obesity, visceral adiposity, visceral fat, truncal obesity, truncal fat, intra-abdominal fat, and its early effects on the metabolic changes in young populations [10]. Of note, cardiometabolic risk factors are more prevalent in children and adolescents with AO than those with overweight or general obesity [11]. So, it is important to estimate the association

* Correspondence: elsie@usp.br
[1]Department of Preventive Medicine, School of Medicine of the University of SãoPaulo, YCARE (Youth/Child and cArdiovascular Risk and Environmental) Research Group, Avenida Dr. Arnaldo, 455, Cerqueira Cesar, São Paulo, SP CEP 01246-903, Brazil
[2]Faculty of Health Sciences of the University of Zaragoza, GENUD (Growth, Exercise, Nutritionand Development) Research Group, Instituto Agroalimentário de Aragón (IA2), Zaragoza, Spain
Full list of author information is available at the end of the article

between AO and cardiovascular risk factors, especially in children and adolescents [9].

Abdominal obesity contribute to an inflammatory state and may cause abnormalities in health, triggering deleterious reactions related to insulin resistance (IR). Together with other factors as lipid abnormalities, fibrinolysis, oxidative stress, hypertension, hyperglycemia, or type 2 diabetes are positively associated with endothelial dysfunction, leading to early atherosclerosis [12].

Knowing the disorders related to excessive AO, which surround childhood and translate into chronic diseases in adulthood, it is urgent to approach them and to identify vulnerable points that could be addressed in prevention strategies. Therefore, the purpose of this paper is to review the existing knowledge regarding the association of AO with the main associated cardiometabolic risk factors such as disorders of glucose metabolism, lipid abnormalities, hypertension, and the metabolic syndrome (MetS) in children and adolescents.

Obesity prevalence and risks in children and adolescents

The worldwide prevalence of overweight and obesity among children and young adults has increased in the last years. In children under 5 years, the prevalence of overweight and obesity in 1990 was 4.2 %, increasing to 6.7 % in 2010, and in 2020, it could reach 9.1 % [13]. Among adolescents, the rate of increase of obesity was about 12 % (from 1980 to 2000) [14]. The scenario recently changed, because in low middle-income countries, the tendency of childhood overweight and obesity seems to rise quickly, especially in urban areas, reaching about 30 % more when compared with developed countries [15, 16].

Thereby, from around 2005, Latin America has shown trends of increase in overweight/obesity similar to those previously observed in Western Europe and North America, where a plateau level was reached [17]. Thus, currently the prevalence of overweight in children from Latin America is over 25 %,whereas in adults, it is higher than 50 %.The prevalence of obesity in children also reached more than 3 % (exception in Peru where for preschool children it is less than 2 %), and in adults, this prevalence is higher than 25 % [18]. In Brazilian children, overweight prevalence ranged from 25 to 40 % and among adolescents, it is 22 % in boys and 19.4 % in girls [18]. Recently, a meta-analysis conducted in Brazil showed that the overall prevalence of obesity among children/adolescents was 14.1 %. Among boys, it was 16.1 % and for girls, it was 15 %, showing the highest prevalence in the southeastern regions, mainly in the South region [19].

Concerning childhood overweight/obesity in European countries (2009–2010), Norway showed the lowest prevalence (15 %), while Italy the highest prevalence (36 %) [17]. In the majority of the countries (except Italy, Czech Republic, and Slovenia), the prevalence was higher in females than that in males. In the USA, data from 2009–2010 showed that 34 % of children aged 5–17 years were affected by this epidemic [14, 17].

According to Zhang et al., the prevalence of obesity is increasing among children and adolescents from rural area as well, alerting for an urban-rural disparity ever closer [20]. In children and adolescents from low middle-income countries, obesity carries on a problem, especially to those with fairly high socioeconomic status [21]. In contrast, developed economies with children in lower socio-economic status tend to show a higher prevalence of obesity [17]. Despite efforts applied to recognize this epidemic and to deal with, there is no decrease noted in its occurrence, but at least a leveling off in its prevalence [14]. Although, a stability of obesity in this young population from developed countries is supported by Rokholm et al. [22], it must be kept in mind that the prevalence is higher than ever before.

Nowadays, it is known that the adipose tissue is an essential endocrine organ [10]. It takes an important place in the body related with the destination of excess dietary lipids, which might determine body homeostasis maintenance or the production and regulation of certain hormones, modulating an inflammatory state and important metabolic processes (insulin resistance, atherogenesis (endothelial dysfunction)), leading to detrimental consequences of the cardiovascular system [23].

Overweight/obese children show early changes on left cardiac structures that were not explained by blood pressure [24] besides significant impairment of vascular function as arterial wall stiffness [25]. That supports an attainable cumulative cardiovascular effect of childhood obesity on adult cardiovascular outcomes. Thus, overweight and obesity during childhood and adolescence increase the risk of long-term obesity, leading to chances of harmful consequences [23, 26].

Abdominal obesity and cardiometabolic risk factors

The pathophysiologic mechanisms linking childhood obesity to cardiovascular abnormalities have not been clearly established. Body fat distribution plays an important role on the endothelial damage because obese subjects are more prone to such dysfunction. Particularly, AO has been identified as a determinant of arteriosclerosis development [27].

Abdominal obesity is associated with a more atherogenic risk profile (Fig. 1) because it increases the cardiometabolic risk factors (lipid profile, systolic hypertension, and abnormal fasting blood glucose) both in children and adolescents [28–31]. Furthermore, approximately 16 to 18 % of children and adolescents have AO [32]. In adolescents, the prevalence of AO is higher in low middle-income countries, varying from 3.8 to 51.7 %, than in high-income countries (8.7 to 33.2 %) [33], as it was also noticed in American children and adolescents [34].

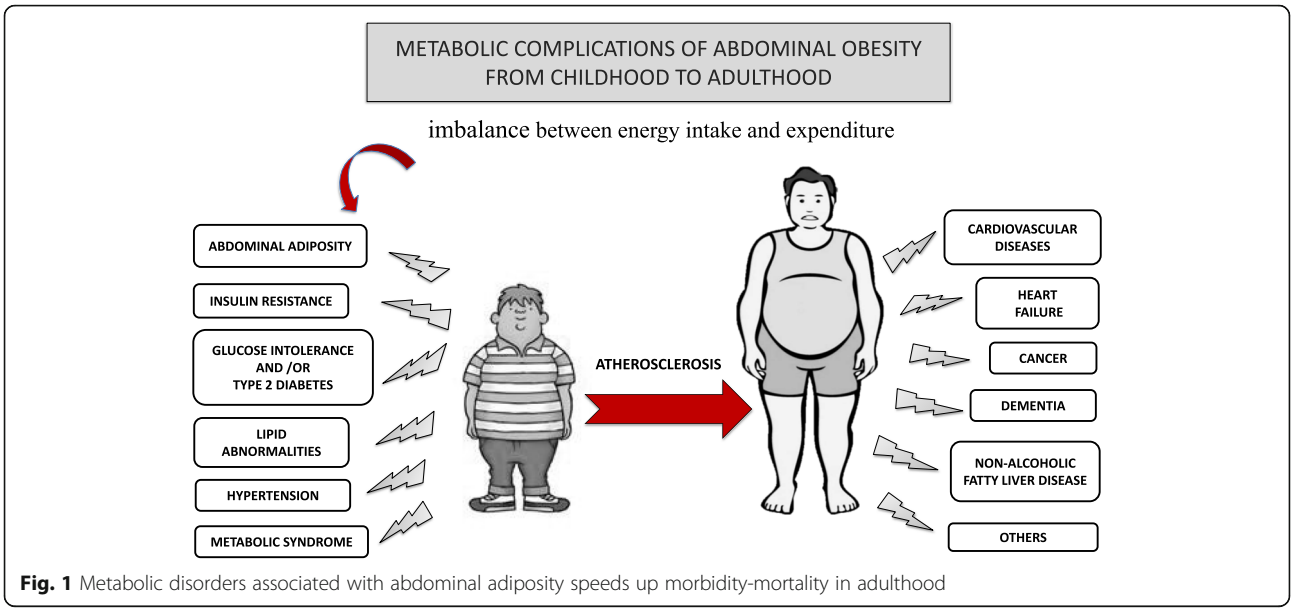

Fig. 1 Metabolic disorders associated with abdominal adiposity speeds up morbidity-mortality in adulthood

Hence, the association between general obesity and AO with cardiometabolic risk factors is different [35]. The excessive amount of visceral adipose tissue plays a role in the development of several metabolic disorders in pediatric population [36]. The importance of examining AO using low-cost anthropometric indices may contribute to identify cardiometabolic risk factors from adolescence through adulthood [34]. Thereby, simple anthropometric measures of AO, such as waist circumference (considering ethnicity, sex, and age) [37, 38], waist to hip ratio, and waist to height ratio (independent of age, gender or race/ethnicity), could be considered as predictors of AO [11, 39]. In this sense, a number of studies have shown that surrogate markers of AO are independent risk factors for type 2 diabetes mellitus, dyslipidemia, hypertension, and coronary artery disease [28, 40].

Disorders of glucose metabolism

Studies have shown that a high degree of obesity, especially AO, in children and adolescents is detrimental to glucose metabolism, regardless of the ethnic background, leading to a high prevalence of impaired glucose tolerance [41].

Considering glucose metabolism, it is important to clarify some definitions. *Insulin resistance* is a condition in which there is a low uptake of glucose by the tissues in response to insulin action. *Glucose intolerance* is a risk factor for future diabetes and/or adverse outcomes [42] in which an individual has higher than normal levels of glucose in the blood upon fasting or following a carbohydrate-rich meal, being an inability to properly metabolize glucose. T*ype 2 diabetes* is an array of dysfunctions characterized by hyperglycemia, resulting from the combination of varying degrees of resistance to insulin action, inadequate insulin secretion, and excessive or inappropriate glucagon secretion [43]. These metabolic abnormalities result in an inflammatory state, triggering cardiovascular risks to the individual.

In obese individuals, mainly with AO, hypertrophy of adipose tissue releases high quantities of preinflammatory markers (cytokines) as tumor necrosis factor alpha (TNF-alpha) and interleukin-6 (IL-6), producing lipotoxicity and triggering a resistance to the action of insulin by damaging the insulin receptor substrate (IRS-1). Thus, there will be a reduced capacity to transport and uptake glucose into the intracellular space. In case of a high fat diet, there is a widening in adipocyte size (hypertrophy), enhancing lipolysis, and releasing free fatty acids (FFA) to the circulation [44]. These particles will be deposited on the insulin-sensitive organs (lean tissues): muscle, liver, and heart, leading to an inflammatory state [45]. The described inflammatory state may produce other undesirable effects such as endothelial-vasomotor dysfunction [46].

Summing up, in obese people, initially, IR appears in adipose tissue and then in other tissues, leading to glucose intolerance. As a consequence, pancreatic β cells try to produce more and more insulin to reverse this situation, which does not occur, following up the resistance to them. The persistence of long-term hyperglycemia leads to the onset of type 2 diabetes [47].

In children and adolescents, epidemiological studies show an association between AO with such disorders, driving important and premature cardiometabolic risk in adulthood. The homeostatic model assessment (HOMA) index is a method to quantify IR, calculated as the product of fasting plasma insulin level (microU/ml) and fasting plasma glucose level (mmol/L), divided by 22.5 [48]. There is no widely agreed cutoff to define IR in children and adolescents; however, some values have been

proposed [49] that should be specific for age, sex, and pubertal development [50].

Once IR appears the foremost to development of MetS [51] in the pediatric population, associated with the other manifestations of the MetS. Although, the impact by which AO affects MetS risk in children and adolescents is unclear, studies have shown that the strongest metabolic impact of AO is IR [52].Moreover, the prevalence of glucose intolerance among children and adolescents was higher among girls (4.2 %) as compared with boys (3.2 %) and was even higher when AO was present in girls (12.7 %) [53].

Lipid abnormalities

Several chronic conditions such as obesity and diabetes may exacerbate the development of atherosclerosis [54], a process that begins as early as the first years of life [6, 55–57]. Atherogenesis has been associated with dyslipidemia, being an important risk factor for atherosclerosis and cardiovascular diseases, also in the pediatric population [58].

Atherogenic dyslipidemia is one of the metabolic abnormalities that define the MetS and is characterized by hypertriglyceridemia, increased levels of very-low-density lipoprotein (VLDL) and small dense low-density lipoprotein (LDL) particles, and reduced levels of high-density lipoprotein (HDL) [59]. General obesity is strongly associated with atherogenic dyslipidemia in youth [60]. Several studies show an association between AO and abnormal lipid profile in children and adolescents [11, 35, 58, 61–66], especially associated with high low-density lipoprotein cholesterol (LDL-C), low high-density lipoprotein cholesterol (HDL-C), and hypertriglyceridemia at all ages [67–70].

Moreover, AO promote a cluster of atherogenic risk factors [71, 72].

During the last decade, the atherogenic dyslipidemia prevalence is increasing in children and adolescents with obesity [73, 74]. Data from the Third National Health and Nutrition Examination Survey (NHANES III) indicate that 25 % of adolescents are characterized by high triglyceride (TG) concentrations and 40 % by low HDL cholesterol concentrations [60, 75]. The AVENA (*Alimentación y Valoración del Estado Nutricional en Adolescentes*) study, in Spanish adolescents, found a deleterious effect of both abdominal and truncal obesity on the lipid profile [76]. In the Bogalusa Heart Study, overweight schoolchildren were 2.4 to 7.1 times more likely to have elevated total cholesterol (TC), LDL cholesterol, and TG than their lean counterparts [60, 77].

The "portal free fatty acid" theory [78] was the first hypothesis explaining the close relationship between AO and metabolic complications. Due to its close proximity to the liver and drained by the portal circulation, excess visceral adipose tissue could alter lipoprotein metabolism mainly by inducing an overproduction of large triglyceride-rich lipoproteins, VLDLs [23]. Non-esterified FFAs released from the visceral adipose tissue are transformed into VLDLs enriched with TGs which leads to the formation of TG-rich LDL particles, which become remodeled into small and dense LDL particles, the most atherogenic form of dyslipidemia [79]. Thus, a high proportion of small and dense LDL has been associated with an increased risk of coronary heart disease.

Atherogenic dyslipidemia is associated with other components of the MetS and is an important risk factor for cardiovascular diseases [59, 73, 80]. Accordingly, AO represent one of the most important factors of its progression in children with obesity [81]. Currently, the literature shows novel merged dyslipidemic patterns in children and adolescents associated with obesity that consist in a moderate-to-severe elevation in TGs and non-HDL-C, mild elevation in LDL-C, and reduced HDL-C, showing a high atherogenic pattern [74]. This pattern of combined dyslipidemia is represented as both an increase in small, dense LDL and in overall LDL particle number and a reduction in total HDL-C and in large HDL particles [82–84].

In adults, children, and also in adolescents, AO may be associated with compositional changes in HDL particles, making them less efficient regarding their protective action on cholesterol efflux [85]. It is well known that low levels of HDL are associated with an increased risk of developing cardiovascular diseases [86]; however, high levels of HDL may not always be protective, since in a context of chronic inflammation, HDL particles may be less functional [87].

The association between AO and dyslipidemia is a complex trait that is associated with several metabolic diseases (e.g., insulin resistance, non-alcoholic fatty liver disease, chronic inflammation) during life [74], suggesting an integrated pathophysiological response to excessive weight gain.

Hypertension

Blood pressure (BP) is an easy and common measurement in health surveys, and it is well established that high BP can be identified in children and adolescents [88, 89]. In several epidemiological studies, hypertension prevalence has significantly increased among this young population over the recent years [90–96]. Numerous studies show that both overweight and obesity were associated with elevated BP in children and adolescents [91, 94, 97]. Moreover, data from clinical studies on high BP in childhood show that primary hypertension is commonly associated with other cardiovascular risk factors as well as obesity [98].

Regarding AO, a previous study assessing the association between fat distribution and cardiovascular risk in children showed that visceral fat (as well as total fat) is

associated to high BP in Italian children [99]. This association has also been established by several researchers [28, 61, 94, 100–106]. Some of these studies showed that this association was stronger in boys than in girls [104–106], and the association of AO with systolic hypertension have been seen more frequently than with diastolic hypertension [107, 108]. In a recent systematic review by Kelishadi et al., they found only one study showing that total body fat is a stronger predictor of elevated BP than AO in children and adolescents [28, 109].

Abdominal obesity plays a more important role in the occurrence of hypertension than subcutaneous adiposity [110]. The anatomical location may be the answer about functional differences between visceral and subcutaneous adipocytes. The accumulation of visceral fat promotes a greater activation of sympathetic nervous system (SNS) than subcutaneous fat [111], producing more proinflammatory cytokines (TNF-alpha and IL-6) and less adiponectin, resulting in insulin resistance. Further, hyperinsulinemia may result in the raise of sodium reabsorption (hypervolemia) and an increase of SNS (vasoconstriction) activity, contributing to hypertension [110, 112].

Metabolic syndrome

In 2005, the International Diabetes Federation (IDF) defined MetS in adults "as a cluster of risk factors for cardiovascular diseases and type 2 diabetes mellitus, including AO, atherogenic dyslipidemia (high TGs and low HDL-cholesterol, elevated apolipoproteina B (Apo B), small-dense LDL particles, and small HDL particles; all of these abnormalities are individually atherogenic) [113], impaired glucose tolerance and hypertension" [114]. MetS could be also defined as a grouping of abnormalities resulting from IR and the excess of AO [113]. Thus, two potential causative factors in the pathogenesis of MetS stand out: IR and AO.

In the South region of Brazil, a high prevalence of MetS among adolescents with AO and IR was observed [115]. Weiss et al. stated that, in children and adolescents, MetS is far more common than formerly reported and its prevalence increases directly with the degree of obesity [116]. In a systematic review, Friend et al. [117] found that the prevalence of MetS in the general population of children and adolescents worldwide was 3.3 % (range 0–19.2 %); in overweight, 11.9 % (2.8–29.3 %) and it was 29.2 % (10.0–66.0 %) in the obese population. For non-obese, non-overweight children and adolescents was lower than 1 %.

Waist circumference is an independent predictor of cardiovascular risk in adults and children and an indicator of IR, dyslipidemia, and hypertension. Waist circumference measurement is easy and cheap, and it is considered a clinical parameter to infer the degree of abdominal adiposity [118] but it may vary depending on the ethnic group. In addition, there is no consensus in the literature on the standard cutoff points, for classification of AO in children and adolescents [119].

Subjects with MetS usually manifest a proinflammatory state (elevated high sensitive C-reactive protein (CRP), elevated unhealthy cytokines (TNF-alpha, IL-6), decrease adiponectin plasma concentrations) and a prothrombotic state (fibrinolytic factors—plasminogen activator inhibitor-1 (PAI-1)) [114]. Individuals with MetS in which diabetes is not already present have five times more risk of developing type 2 diabetes [120]. Nevertheless, the identification of MetS in children and adolescents through clinical and metabolic factors should be done earlier to allow risk stratification on the onset of type 2 diabetes and cardiovascular diseases in this population [118].

Concerning the pediatric population, based on previous studies [75, 116, 121–123], the IDF suggested modified adult criteria to be applied in children and adolescents. In addition, MetS should not be diagnosed in children younger than 10 years, but in those with AO (90th percentile as a cutoff for waist circumference), they should "work on weight reduction," with healthy changes on lifestyle. For children aged 10 years till 16 years old, MetS can be determined by the presence of AO and two or more clinical risk factors such as high triglycerides (≥150 mg/dl), low HDL-cholesterol(<40 mg/dl), high blood pressure(95th percentile), or high fasting plasma glucose(>100 mg/dl). For adolescents aged 16 years or more, the IDF adult criteria can be used [124]. However, considering children and adolescents, some studies have proposed scientific evidence's items to evaluate and characterize this population with metabolic risk factors, since there is not an updated and precise definition. These items include personal and family history, pubertal status, metabolic abnormalities, and clinical feature [125, 126].

Defining body composition or metabolic abnormalities in children through single cutoff points is difficult because they change with age, sex, and pubertal development, but this is not been taken into account duly, once current definitions have considered the age rather than the pubertal status. In accordance, studies have shown a high prevalence of MetS, not only in pubertal but also in prepubertal obese children [127, 128].

Prepubertal obese children [129] showed an elevation of proinflammatory factors (TNF-alpha, IL-6, CPR, PAI-1), and markers of endothelial dysfunction which contribute to early increase of cardiovascular diseases later in life. Likewise, serum myeloperoxidase (MPO) level was elevated in prepubertal obese children [129]. MPO is an enzyme which has bactericidal action and plays an important role in the onset and progression of acute and chronic inflammatory diseases.

Conclusions

According to the literature, children and adolescents with obesity are more likely to develop cardiovascular risk factor and MetS. Abdominal obesity plays an important role on the pathophysiological process, linking obesity to atherosclerosis and cardiovascular diseases, clearly involving a chronic inflammatory state. Abdominal obesity leads to insulin resistance and the development of type 2 diabetes.

The goal should be to focus on the prevention and treatment of obesity in childhood and young adulthood, since its complications are harmful to health, leading to serious outcomes in later life. Hence, it becomes of great importance the awareness on individuals at high risk of overweight and obesity, mainly children and adolescents. The attention on their lifestyle is urgent, considering the quality of dietary habits and avoiding "obesogenic" environments, encouraging and increasing physical activity in groups, and adequate sedentary behavior to reduce it mostly during leisure time. Understand and build up an early behavior of healthy habits would be the basis for a future life with more health and wellness.

Abbreviations

AO: Abdominal obesity; Apo B: Apolipoproteina B; BP: Blood pressure; CRP: C-reactive protein; FFAs: Free fatty acids; HDL-C: High-density lipoprotein cholesterol; HOMA: Homeostatic model assessment; IDF: International Diabetes Federation; IL-6: Interleukin-6; IR: Insulin resistance; IRS-1: Insulin receptor substrate; LDL-C: Low-density lipoprotein cholesterol; MetS: Metabolic syndrome; MPO: Myeloperoxidase; PAI-1: Plasminogen activator inhibitor-1; SNS: Sympathetic nervous system; TG: Triglycerides; TNF-alpha: Tumor necrosis factor alpha; VLDL: Very-low-density lipoprotein

Acknowledgements

Not applicable.

Funding

The author Tara Rendo-Urteaga was given post-doctoral scholarship from *São Paulo Research Foundation*—FAPESP(proc. 2014/25233-0). Full Prof. Luis A. Moreno was given scholarship of visiting professor from *São Paulo Research Foundation—FAPESP* (proc. 2015/11406-3). Augusto César F. de Moraes is in receipt of a post-doctoral scholarship from *National Counsel of Technological and Scientific Development* (CNPq: proc. 313772/2014-2) and *São Paulo Research Foundation—FAPESP* (proc. 2014/13367-2 and 2015/14319-4). The GENUD Research Group co-financed by the European Regional Development Fund (MICINN-FEDER).

Authors' contributions

EF participated in the design the work and drafted and revised the manuscript. TU helped to draft the manuscript and revised the manuscript. MF and AM revised the manuscript. LM conceived, designed, and revised the work that led to the submission of the manuscript. HC designed and revised the work that led to the submission of the manuscript. All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

Author details

[1]Department of Preventive Medicine, School of Medicine of the University of SãoPaulo, YCARE (Youth/Child and cArdiovascular Risk and Environmental) Research Group, Avenida Dr. Arnaldo, 455, Cerqueira Cesar, São Paulo, SP CEP 01246-903, Brazil. [2]Faculty of Health Sciences of the University of Zaragoza, GENUD (Growth, Exercise, Nutritionand Development) Research Group, Instituto Agroalimentário de Aragón (IA2), Zaragoza, Spain. [3]Department of Preventive Medicine, Visiting professor School of Medicine of the University of São Paulo, São Paulo, Brazil. [4]Department of Epidemiology, Johns Hopkins University, Bloomberg School of Public Health, Baltimore, USA.

Received: 21 June 2016 Accepted: 13 September 2016
Published online: 05 October 2016

References

1. ORGANIZATION. WH. Childhood overweight and obesity [Available from: www.who.int/dietphysicalactivity/childhood/en/. Accessed 23 May 2016.
2. Seidell JC, Halberstadt J. The global burden of obesity and the challenges of prevention. Ann Nutr Metab. 2015;66 Suppl 2:7–12.
3. Van Putte-Katier N, Rooman RP, Haas L, Verhulst SL, Desager KN, Ramet J, et al. Early cardiac abnormalities in obese children: importance of obesity per se versus associated cardiovascular risk factors. Pediatr Res. 2008;64(2):205–9.
4. Freedman DS, Dietz WH, Tang R, Mensah GA, Bond MG, Urbina EM, et al. The relation of obesity throughout life to carotid intima-media thickness in adulthood: the Bogalusa Heart Study. Int J Obes Relat Metab Disord. 2004;28(1):159–66.
5. Hubert HB, Feinleib M, McNamara PM, Castelli WP. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. Circulation. 1983;67(5):968–77.
6. Berenson GS, Srinivasan SR, Bao W, Newman 3rd WP, Tracy RE, Wattigney WA. Association between multiple cardiovascular risk factors and atherosclerosis in children and young adults. The Bogalusa Heart Study. N Engl J Med. 1998;338(23):1650–6.
7. Daniels SR. Complications of obesity in children and adolescents. Int J Obes (Lond). 33 Suppl 1. England2009. p. S60-5.
8. Ramos TD, Dantas TM, Simoes MO, Carvalho DF, Medeiros CC. Assessment of the carotid artery intima-media complex through ultrasonography and the relationship with Pathobiological Determinants of Atherosclerosis in Youth. Cardiol Young 2015. p. 1-10.
9. Must A, Jacques PF, Dallal GE, Bajema CJ, Dietz WH. Long-term morbidity and mortality of overweight adolescents. A follow-up of the Harvard Growth Study of 1922 to 1935. N Engl J Med. 1992;327(19):1350–5.
10. Singla P, Bardoloi A, Parkash AA. Metabolic effects of obesity: a review. World J Diabetes. 2010;1(3):76–88.
11. Mokha JS, Srinivasan SR, Dasmahapatra P, Fernandez C, Chen W, Xu J, et al. Utility of waist-to-height ratio in assessing the status of central obesity and related cardiometabolic risk profile among normal weight and overweight/obese children: the Bogalusa Heart Study. BMC Pediatr. 2010;10:73.
12. Mathieu P, Poirier P, Pibarot P, Lemieux I, Despres JP. Visceral obesity: the link among inflammation, hypertension, and cardiovascular disease. Hypertension. 2009;53(4):577–84.
13. de Onis M, Blossner M, Borghi E. Global prevalence and trends of overweight and obesity among preschool children. Am J Clin Nutr. 2010;92(5):1257–64.
14. Rome ES. Obesity prevention and treatment. Pediatr Rev. 2011;32(9):363–72. quiz 73.
15. Lobstein T, Jackson-Leach R, Moodie ML, Hall KD, Gortmaker SL, Swinburn BA, et al. Child and adolescent obesity: part of a bigger picture. Lancet. 2015;385(9986):2510–20.
16. ORGANIZATION WH. Obesity and overweight [Available from: www.who.int/mediacentre/factsheets/fs311/en/. Accessed 30 May 2016.
17. Lobstein T. Prevalence and trends across the world [Available from: www.ebook.ecog-obesity.eu/chapter-epidemiology-prevention-across-europe/prevalence-trends-across-world. Accessed 23 May 2016.
18. Kain J, Hernandez Cordero S, Pineda D, de Moraes AF, Antiporta D, Collese T, et al. Obesity prevention in Latin America. Curr Obes Rep. 2014;3(2):150–5.
19. Aiello AM, Marques de Mello L, Souza Nunes M, Soares da Silva A, Nunes A. Prevalence of obesity in children and adolescents in Brazil: a meta-analysis of cross-sectional studies. Curr Pediatr Rev. 2015;11(1):36–42.
20. Zhang YX, Wang ZX, Zhao JS, Chu ZH. Prevalence of overweight and obesity among children and adolescents in Shandong, China: urban-rural disparity. J Trop Pediatr. 2016; 62(4):293–300.
21. Dinsa GD, Goryakin Y, Fumagalli E, Suhrcke M. Obesity and socioeconomic status in developing countries: a systematic review. Obes Rev. 2012;13(11):1067–79.

22. Rokholm B, Baker JL, Sørensen TI. The levelling off of the obesity epidemic since the year 1999—a review of evidence and perspectives. Obes Rev. 2010;11(12):835–46.
23. Bastien M, Poirier P, Lemieux I, Després JP. Overview of epidemiology and contribution of obesity to cardiovascular disease. Prog Cardiovasc Dis. 2014; 56(4):369–81.
24. de Jonge LL, van Osch-Gevers L, Willemsen SP, Steegers EA, Hofman A, Helbing WA, et al. Growth, obesity, and cardiac structures in early childhood: the Generation R Study. Hypertension. 2011;57(5):934–40.
25. Tounian P, Aggoun Y, Dubern B, Varille V, Guy-Grand B, Sidi D, et al. Presence of increased stiffness of the common carotid artery and endothelial dysfunction in severely obese children: a prospective study. Lancet. 2001;358(9291):1400–4.
26. Reilly JJ, Kelly J. Long-term impact of overweight and obesity in childhood and adolescence on morbidity and premature mortality in adulthood: systematic review. Int J Obes (Lond). 2011;35(7):891–8.
27. Sturm W, Sandhofer A, Engl J, Laimer M, Molnar C, Kaser S, et al. Influence of visceral obesity and liver fat on vascular structure and function in obese subjects. Obesity (Silver Spring). 17. United States 2009. p. 1783-8.
28. Kelishadi R, Mirmoghtadaee P, Najafi H, Keikha M. Systematic review on the association of abdominal obesity in children and adolescents with cardio-metabolic risk factors. J Res Med Sci. 2015;20(3):294–307.
29. Benmohammed K, Nguyen MT, Khensal S, Valensi P, Lezzar A. Arterial hypertension in overweight and obese Algerian adolescents: role of abdominal adiposity. Diabetes Metab. 2011;37(4):291–7.
30. Chen B, Li HF. Waist circumference as an indicator of high blood pressure in preschool obese children. Asia Pac J Clin Nutr. 2011;20(4):557–62.
31. Plourde G. Impact of obesity on glucose and lipid profiles in adolescents at different age groups in relation to adulthood. BMC Fam Pract. 2002;3:18.
32. Xu S, Xue Y. Pediatric obesity: causes, symptoms, prevention and treatment. Exp Ther Med. 2016;11(1):15–20.
33. de Moraes ACF, Fadoni RP, Ricardi LM, Souza TC, Rosaneli CF, Nakashima ATA, et al. Prevalence of abdominal obesity in adolescents: a systematic review. Obes Rev. 2011;12(2):69–77.
34. Costa de Oliveira Forkert E, de Moraes AC, Carvalho HB, Kafatos A, Manios Y, Sjostrom M, et al. Abdominal obesity and its association with socioeconomic factors among adolescents from different living environments. Pediatr Obes. 2016. doi:10.1111/ijpo.12116.
35. Ataie-Jafari A, Heshmat R, Kelishadi R, Ardalan G, Mahmoudarabi M, Rezapoor A, et al. Generalized or abdominal obesity: which one better identifies cardiometabolic risk factors among children and adolescents? The CASPIAN III study. J Trop Pediatr. 2014;60(5):377–85.
36. Ruminska M, Majcher A, Pyrzak B, Czerwonogrodzka-Senczyna A, Brzewski M, Demkow U. Cardiovascular risk factors in obese children and adolescents. Adv Exp Med Biol. 2016;878:39–47.
37. Moreno LA, Pineda I, Rodriguez G, Fleta J, Sarria A, Bueno M. Waist circumference for the screening of the metabolic syndrome in children. Acta Paediatr. 2002; 91(12):1307–12.
38. Brambilla P, Bedogni G, Moreno LA, Goran MI, Gutin B, Fox KR, et al. Crossvalidation of anthropometry against magnetic resonance imaging for the assessment of visceral and subcutaneous adipose tissue in children. Int J Obes (Lond). 2006;30(1):23–30.
39. Ashwell M, Gibson S. Waist-to-height ratio as an indicator of 'early health risk': simpler and more predictive than using a 'matrix' based on BMI and waist circumference. BMJ Open. 2016;6(3):e010159.
40. Freedman DS, Kahn HS, Mei Z, Grummer-Strawn LM, Dietz WH, Srinivasan SR, et al. Relation of body mass index and waist-to-height ratio to cardiovascular disease risk factors in children and adolescents: the Bogalusa Heart Study. Am J Clin Nutr. 2007;86(1):33–40.
41. Sinha R, Fisch G, Teague B, Tamborlane WV, Banyas B, Allen K, et al. Prevalence of impaired glucose tolerance among children and adolescents with marked obesity. N Engl J Med. 2002;346(11):802–10.
42. WHO. Definition and diagnosis of diabetes mellitus and intermediate hyperglycaemia 2006 [Available from: http://who.int/diabetes/publications/en/. Accessed 30 May 2016.
43. VERSION MMP. DIABETES IN CHILDREN AND ADOLESCENTS [Available from: http://www.merckmanuals.com/professional/pediatrics/endocrine-disorders-in-children/diabetes-in-children-and-adolescents. Accessed 30 May 2016.
44. Fernandez-Quintela A, Churruca I, Portillo MP. The role of dietary fat in adipose tissue metabolism. Public Health Nutr. 10. England2007. p. 1126-31.
45. Schenk S, Saberi M, Olefsky JM. Insulin sensitivity: modulation by nutrients and inflammation. J Clin Invest. 2008;118(9):2992–3002.
46. Arcaro G, Zamboni M, Rossi L, Turcato E, Covi G, Armellini F, et al. Body fat distribution predicts the degree of endothelial dysfunction in uncomplicated obesity. Int J Obes Relat Metab Disord. 1999;23(9):936–42.
47. Esposito K, Nappo F, Marfella R, Giugliano G, Giugliano F, Ciotola M, et al. Inflammatory cytokine concentrations are acutely increased by hyperglycemia in humans: role of oxidative stress. Circulation. 2002;106(16):2067–72.
48. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia. 1985; 28(7):412–9.
49. Tresaco B, Bueno G, Pineda I, Moreno LA, Garagorri JM, Bueno M. Homeostatic model assessment (HOMA) index cut-off values to identify the metabolic syndrome in children. J Physiol Biochem. 2005;61(2):381–8.
50. Peplies J, Jimenez-Pavon D, Savva SC, Buck C, Gunther K, Fraterman A, et al. Percentiles of fasting serum insulin, glucose, HbA1c and HOMA-IR in pre-pubertal normal weight European children from the IDEFICS cohort. Int J Obes (Lond). 2014;38 Suppl 2:S39–47.
51. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. Jama. 2002;287(3):356–9.
52. He F, Rodriguez-Colon S, Fernandez-Mendoza J, Vgontzas AN, Bixler EO, Berg A, et al. Abdominal obesity and metabolic syndrome burden in adolescents—Penn State Children Cohort Study. J Clin Densitom. 2015;18(1):30–6.
53. Ranjani H, Sonya J, Anjana RM, Mohan V. Prevalence of glucose intolerance among children and adolescents in urban South India (ORANGE-2). Diabetes Technol Ther. 2013;15(1):13–9.
54. Lusis AJ. Atherosclerosis. Nature. 2000;407(6801):233–41.
55. McGill HC, McMahan CA, Zieske AW, Sloop GD, Walcott JV, Troxclair DA, et al. Associations of coronary heart disease risk factors with the intermediate lesion of atherosclerosis in youth. The Pathobiological Determinants of Atherosclerosis in Youth (PDAY) Research Group. Arterioscler Thromb Vasc Biol. 2000;20(8):1998–2004.
56. Giannini C, de Giorgis T, Scarinci A, Ciampani M, Marcovecchio ML, Chiarelli F, et al. Obese related effects of inflammatory markers and insulin resistance on increased carotid intima media thickness in pre-pubertal children. Atherosclerosis. 2008;197(1):448–56.
57. Herouvi D, Karanasios E, Karayianni C, Karavanaki K. Cardiovascular disease in childhood: the role of obesity. Eur J Pediatr. 2013;172(6):721–32.
58. Sarni RS, de Souza FI, Schoeps Dde O, Catherino P, de Oliveira MC, Pessotti CF, et al. Relationship between waist circumference and nutritional status, lipid profile and blood pressure in low socioeconomic level pre-school children. Arq Bras Cardiol. 2006;87(2):153–8.
59. Grundy SM. Atherogenic dyslipidemia associated with metabolic syndrome and insulin resistance. Clin Cornerstone. 2006;8 Suppl 1:S21–7.
60. Steinberger J, Daniels SR, American Heart Association Atherosclerosis Hp, and Obesity in the Young Committee (Council on Cardiovascular Disease in the Young), American Heart Association Diabetes Committee (Council on Nutrition PyA, and Metabolism). Obesity, insulin resistance, diabetes, and cardiovascular risk in children: an American Heart Association scientific statement from the Atherosclerosis, Hypertension, and Obesity in the Young Committee (Council on Cardiovascular Disease in the Young) and the Diabetes Committee (Council on Nutrition, Physical Activity, and Metabolism). Circulation. 2003;107(10):1448–53.
61. Hu YH, Reilly KH, Liang YJ, Xi B, Liu JT, Xu DJ, et al. Increase in body mass index, waist circumference and waist-to-height ratio is associated with high blood pressure in children and adolescents in China. J Int Med Res. 2011; 39(1):23–32.
62. da Silva AC, Rosa AA. Blood pressure and obesity of children and adolescents association with body mass index and waist circumference. Arch Latinoam Nutr. 2006;56(3):244–50.
63. Adegboye AR, Andersen LB, Froberg K, Sardinha LB, Heitmann BL. Linking definition of childhood and adolescent obesity to current health outcomes. Int J Pediatr Obes. 2010;5(2):130–42.
64. Li C, Ford ES, Mokdad AH, Cook S. Recent trends in waist circumference and waist-height ratio among US children and adolescents. Pediatrics. 2006; 118(5):E1390–8.
65. Kelishadi R, Gheiratmand R, Ardalan G, Adeli K, Mehdi Gouya M, Mohammad Razaghi E, et al. Association of anthropometric indices with cardiovascular disease risk factors among children and adolescents: CASPIAN Study. Int J Cardiol. 2007;117(3):340–8.
66. Kavey RE, Daniels SR, Lauer RM, Atkins DL, Hayman LL, Taubert K, et al. American Heart Association guidelines for primary prevention of

atherosclerotic cardiovascular disease beginning in childhood. Circulation. 2003;107(11):1562–6.
67. Freedman DS, Serdula MK, Srinivasan SR, Berenson GS. Relation of circumferences and skinfold thicknesses to lipid and insulin concentrations in children and adolescents: the Bogalusa Heart Study. Am J Clin Nutr. 1999;69(2):308-17 10p.
68. Crowther NJ, Ferris WF, Ojwang PJ, Rheeder P. The effect of abdominal obesity on insulin sensitivity and serum lipid and cytokine concentrations in African women. Clin Endocrinol (Oxf). 2006;64(5):535–41.
69. Hirschler V, Aranda C, Calcagno Mde L, Maccalini G, Jadzinsky M. Can waist circumference identify children with the metabolic syndrome? Arch Pediatr Adolesc Med. 2005;159(8):740–4.
70. Hashemipour M, Soghrati M, Malek AM. Anthropometric indices associated with dyslipidemia in obese children and adolescents: a retrospective study in isfahan. ARYA Atheroscler. 2011;7(1):31–9.
71. Kannel WB, Cupples LA, Ramaswami R, Stokes J, Kreger BE, Higgins M. Regional obesity and risk of cardiovascular disease; the Framingham Study. J Clin Epidemiol. 1991;44(2):183–90.
72. Després JP. Targeting abdominal obesity and the metabolic syndrome to manage cardiovascular disease risk. Heart. 2009;95(13):1118–24.
73. Daniels SR, Greer FR, Nutrition Co. Lipid screening and cardiovascular health in childhood. Pediatrics. 2008;122(1):198–208.
74. Kavey RE. Combined dyslipidemia in childhood. J Clin Lipidol. 2015;9(5 Suppl): S41–56.
75. de Ferranti SD, Gauvreau K, Ludwig DS, Neufeld EJ, Newburger JW, Rifai N. Prevalence of the metabolic syndrome in American adolescents: findings from the Third National Health and Nutrition Examination Survey. Circulation. 2004; 110(16):2494–7.
76. Tresaco B, Moreno LA, Ruiz JR, Ortega FB, Bueno G, Gonzalez-Gross M, et al. Truncal and abdominal fat as determinants of high triglycerides and low HDL-cholesterol in adolescents. Obesity (Silver Spring). 2009;17(5):1086–91.
77. Freedman DS, Dietz WH, Srinivasan SR, Berenson GS. The relation of overweight to cardiovascular risk factors among children and adolescents: the Bogalusa Heart Study. Pediatrics. 1999;103(6 Pt 1):1175–82.
78. Björntorp P. "Portal" adipose tissue as a generator of risk factors for cardiovascular disease and diabetes. Arteriosclerosis. 1990;10(4):493–6.
79. Jensen MD. Is visceral fat involved in the pathogenesis of the metabolic syndrome? Human model. Obesity (Silver Spring). 2006;14 Suppl 1:20S–4S.
80. Steinberger J, Daniels SR, Eckel RH, Hayman L, Lustig RH, McCrindle B, et al. Progress and challenges in metabolic syndrome in children and adolescents: a scientific statement from the American Heart Association Atherosclerosis, Hypertension, and Obesity in the Young Committee of the Council on Cardiovascular Disease in the Young; Council on Cardiovascular Nursing; and Council on Nutrition, Physical Activity, and Metabolism. Circulation. 2009;119(4):628–47.
81. D'Adamo E, Guardamagna O, Chiarelli F, Bartuli A, Liccardo D, Ferrari F, et al. Atherogenic dyslipidemia and cardiovascular risk factors in obese children. Int J Endocrinol. 2015;2015:912047.
82. Otvos J. Measurement of triglyceride-rich lipoproteins by nuclear magnetic resonance spectroscopy. Clin Cardiol. 1999;22(6 Suppl):II21–7.
83. Kuller L, Arnold A, Tracy R, Otvos J, Burke G, Psaty B, et al. Nuclear magnetic resonance spectroscopy of lipoproteins and risk of coronary heart disease in the cardiovascular health study. Arterioscler Thromb Vasc Biol. 2002;22(7): 1175–80.
84. Blake GJ, Otvos JD, Rifai N, Ridker PM. Low-density lipoprotein particle concentration and size as determined by nuclear magnetic resonance spectroscopy as predictors of cardiovascular disease in women. Circulation. 2002;106(15):1930–7.
85. Navab M, Anantharamaiah GM, Fogelman AM. The role of high-density lipoprotein in inflammation. Trends Cardiovasc Med. 2005;15(4):158–61.
86. Després JP, Lemieux I, Dagenais GR, Cantin B, Lamarche B. HDL-cholesterol as a marker of coronary heart disease risk: the Québec cardiovascular study. Atherosclerosis. 2000;153(2):263–72.
87. Ansell BJ, Navab M, Hama S, Kamranpour N, Fonarow G, Hough G, et al. Inflammatory/antiinflammatory properties of high-density lipoprotein distinguish patients from control subjects better than high-density lipoprotein cholesterol levels and are favorably affected by simvastatin treatment. Circulation. 2003;108(22):2751–6.
88. de Moraes AC, Lacerda MB, Moreno LA, Horta BL, Carvalho HB. Prevalence of high blood pressure in 122,053 adolescents: a systematic review and meta-regression. Medicine (Baltimore). 2014;93(27):e232.
89. Adolescents NHBPEPWGoHBPiCa. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics. 2004;114(2 Suppl 4th Report):555–76.
90. McNiece KL, Poffenbarger TS, Turner JL, Franco KD, Sorof JM, Portman RJ. Prevalence of hypertension and pre-hypertension among adolescents. J Pediatr. 2007;150(6):640–4. 4.e1.
91. Salvadori M, Sontrop JM, Garg AX, Truong J, Suri RS, Mahmud FH, et al. Elevated blood pressure in relation to overweight and obesity among children in a rural Canadian community. Pediatrics. 2008; 122(4):e821–7.
92. Kovacs VA, Gabor A, Fajcsak Z, Martos E. Role of waist circumference in predicting the risk of high blood pressure in children. Int J Pediatr Obes. 2010;5(2):143–50.
93. Mehdad S, Hamrani A, El Kari K, El Hamdouchi A, El Mzibri M, Barkat A, et al. Prevalence of elevated blood pressure and its relationship with fat mass, body mass index and waist circumference among a group of Moroccan overweight adolescents. Obes Res Clin Pract. 2013;7(4):e284–9.
94. Guo X, Zheng L, Li Y, Yu S, Zhou X, Wang R, et al. Gender-specific prevalence and associated risk factors of prehypertension among rural children and adolescents in Northeast China: a cross-sectional study. Eur J Pediatr. 2013; 172(2):223–30.
95. Muntner P, He J, Cutler JA, Wildman RP, Whelton PK. Trends in blood pressure among children and adolescents. JAMA. 2004;291(17):2107–13.
96. Din-Dzietham R, Liu Y, Bielo MV, Shamsa F. High blood pressure trends in children and adolescents in national surveys, 1963 to 2002. Circulation. 2007;116(13):1488–96.
97. Zhang CX, Shi JD, Huang HY, Feng LM, Ma J. Nutritional status and its relationship with blood pressure among children and adolescents in South China. Eur J Pediatr. 2012;171(7):1073–9.
98. Falkner B. Hypertension in children and adolescents: epidemiology and natural history. Pediatr Nephrol. 2010;25(7):1219–24.
99. Genovesi S, Antolini L, Giussani M, Pieruzzi F, Galbiati S, Valsecchi MG, et al. Usefulness of waist circumference for the identification of childhood hypertension. J Hypertens. 2008;26(8):1563–70.
100. Flores-Huerta S, Klünder-Klünder M, Reyes de la Cruz L, Santos JI. Increase in body mass index and waist circumference is associated with high blood pressure in children and adolescents in Mexico city. Arch Med Res. 2009; 40(3):208–15.
101. Abolfotouh MA, Sallam SA, Mohammed MS, Loutfy AA, Hasab AA. Prevalence of elevated blood pressure and association with obesity in egyptian school adolescents. Int J Hypertens. 2011;2011. doi:10.4061/2011/952537.
102. Lurbe E, Alvarez V, Liao Y, Tacons J, Cooper R, Cremades B, et al. The impact of obesity and body fat distribution on ambulatory blood pressure in children and adolescents. Am J Hypertens. 1998;11(4 Pt 1): 418–24.
103. Dulskiene V, Kuciene R, Medzioniene J, Benetis R. Association between obesity and high blood pressure among Lithuanian adolescents: a cross-sectional study. Ital J Pediatr. 2014;40:102.
104. Gopinath B, Baur LA, Garnett S, Pfund N, Burlutsky G, Mitchell P. Body mass index and waist circumference are associated with blood pressure in preschool-aged children. Ann Epidemiol. 2011;21(5):351–7.
105. Maffeis C, Banzato C, Brambilla P, Cerutti F, Corciulo N, Cuccarolo G, et al. Insulin resistance is a risk factor for high blood pressure regardless of body size and fat distribution in obese children. Nutr Metab Cardiovasc Dis. 2010; 20(4):266–73.
106. Valerio G, Iafusco D, Zucchini S, Maffeis C. (ISPED) S-GoDoISoPEaD. Abdominal adiposity and cardiovascular risk factors in adolescents with type 1 diabetes. Diabetes Res Clin Pract. 2012;97(1):99–104.
107. Griz LH, Viegas M, Barros M, Griz AL, Freese E, Bandeira F. Prevalence of central obesity in a large sample of adolescents from public schools in Recife, Brazil. Arq Bras Endocrinol Metabol. 2010;54(7):607–11.
108. Kromeyer-Hauschild K, Neuhauser H, Schaffrath Rosario A, Schienkiewitz A. Abdominal obesity in German adolescents defined by waist-to-height ratio and its association to elevated blood pressure: the KiGGS study. Obesity Facts. 2013;6(2):165–75.
109. Kouda K, Nakamura H, Fujita Y, Ohara K, Iki M. Increased ratio of trunk to appendicular fat and increased blood pressure: study of a general population of Hamamatsu children. Circ J. 2012;76(12):2848–54.
110. Esler M, Straznicky N, Eikelis N, Masuo K, Lambert G, Lambert E. Mechanisms of sympathetic activation in obesity-related hypertension. Hypertension. 2006;48(5):787–96.

111. Grassi G, Dell'Oro R, Facchini A, Quarti Trevano F, Bolla GB, Mancia G. Effect of central and peripheral body fat distribution on sympathetic and baroreflex function in obese normotensives. J Hypertens. 2004;22(12):2363–9.
112. da Silva AA, do Carmo J, Dubinion J, Hall JE. The role of the sympathetic nervous system in obesity-related hypertension. Curr Hypertens Rep. 2009; 11(3):206–11.
113. Carr DB, Utzschneider KM, Hull RL, Kodama K, Retzlaff BM, Brunzell JD, et al. Intra-abdominal fat is a major determinant of the National Cholesterol Education Program Adult Treatment Panel III criteria for the metabolic syndrome. Diabetes. 2004;53(8):2087–94.
114. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. Lancet. 2005; 365(9468):1415–28.
115. Rosini N, Moura SAZO, Rosini RD, Machado MJ, Da Silva EL. Metabolic syndrome and importance of associated variables in children and adolescents in Guabiruba - SC, Brazil. Arq Bras Cardiol. 2015;105(1):37–44.
116. Weiss R, Dziura J, Burgert TS, Tamborlane WV, Taksali SE, Yeckel CW, et al. Obesity and the metabolic syndrome in children and adolescents. N Engl J Med. 2004;350(23):2362–74.
117. Friend A, Craig L, Turner S. The prevalence of metabolic syndrome in children: a systematic review of the literature. Metab Syndr Relat Disord. 2013;11(2):71–80.
118. Damiani D, Kuba VM, Cominato L, Dichtchekenian V, Menezes Filho HC. Metabolic syndrome in children and adolescents: doubts about terminology but not about cardiometabolic risks. Arq Bras Endocrinol Metabol. 2011; 55(8):576–82.
119. Ferreira de Moraes AC, Fulaz CS, Netto-Oliveira ER, Reichert FF. Prevalence of metabolic syndrome in adolescents: a systematic review. Cadernos De Saude Publica. 2009;25(6):1195–202.
120. Stern MP, Williams K, Gonzalez-Villalpando C, Hunt KJ, Haffner SM. Does the metabolic syndrome improve identification of individuals at risk of type 2 diabetes and/or cardiovascular disease? Diabetes Care. 2004;27(11):2676–81.
121. Cook S, Weitzman M, Auinger P, Nguyen M, Dietz WH. Prevalence of a metabolic syndrome phenotype in adolescents—findings from the Third National Health and Nutrition Examination Survey, 1988-1994. Archives of Pediatrics & Adolescent Medicine. 2003;157(8):821–7.
122. Cruz ML, Weigensberg MJ, Huang TTK, Ball G, Shaibi GQ, Goran MI. The metabolic syndrome in overweight Hispanic youth and the role of insulin sensitivity. Journal of Clinical Endocrinology & Metabolism. 2004;89(1):108–13.
123. Ford ES, Ajani UA, Mokdad AH. The metabolic syndrome and concentrations of C-reactive protein among U.S. youth. Diabetes Care. 2005; 28(4):878–81.
124. Zimmet P, Alberti GKMM, Kaufman F, Tajima N, Silink M, Arslanian S, et al. The metabolic syndrome in children and adolescents—an IDF consensus report. Pediatr Diabetes. 2007;8(5):299–306.
125. Efstathiou SP, Skeva II, Zorbala E, Georgiou E, Mountokalakis TD. Metabolic syndrome in adolescence can it be predicted from natal and parental profile? The Prediction of Metabolic Syndrome in Adolescence (PREMA) study. Circulation. 2012;125(7):902–10.
126. Brambilla P, Lissau I, Flodmark CE, Moreno LA, Widhalm K, Wabitsch M, et al. Metabolic risk-factor clustering estimation in children: to draw a line across pediatric metabolic syndrome. Int J Obes. 2007;31(4):591–600.
127. Olza J, Gil-Campos M, Leis R, Bueno G, Aguilera CM, Valle M, et al. Presence of the metabolic syndrome in obese children at prepubertal age. Ann Nutr Metab. 2011;58(4):343–50.
128. Ahrens W, Moreno LA, Marild S, Molnar D, Siani A, De Henauw S, et al. Metabolic syndrome in young children: definitions and results of the IDEFICS study. Int J Obes. 2014;38:S4–S14.
129. Olza J, Aguilera CM, Gil-Campos M, Leis R, Bueno G, Martinez-Jimenez MD, et al. Myeloperoxidase is an early biomarker of inflammation and cardiovascular risk in prepubertal obese children. Diabetes Care. 2012;35(11):2373–6.