Insulin Resistance and its Association with Metabolic Syndrome Components

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Abstract

Background: Individuals with insulin resistance are more prone to the development of metabolic syndrome (MS), Type 2 Diabetes Mellitus and Cardiovascular Disease (CVD)

Objetive: To evaluate the association between insulin resistance (IR) and metabolic syndrome components.

Methods: Cross-sectional study of 196 individuals between 2 and 18 years, treated at the Brazilian Public Healthcare system. The association of IR with the MS components was evaluated by Chi-square test, adopting the Homeostasis model assessment–insulin resistance (HOMA-IR) value ≥ 2.5, and by analysis of variance (ANOVA) and Tukey's test, by comparing the means of the components in the HOMA-IR quartiles. Statistical analysis was performed using SPSS 17.0 software and significance level was set at 5%.

Results: IR was observed in 41.3% of the studied population and was associated with age between 10 and 18 years (p = 0.002 PR = 3.2), to MS in both sexes [Male (p = 0.022 PR = 3.7) and female (p = 0.007 PR = 2.7)] and altered triglycerides (p = 0.005 PR = 2.9) in females. The mean values of the MS components differed significantly between HOMA-IR quartiles (p <0.01), except for HDL-cholesterol.

Conclusions: Insulin resistance can be considered a marker of cardiovascular risk. (Arq Bras Cardiol 2011;97(5):380-389)

Keywords: Insulin ressitance/physiology; metabolic syndrome/diagnosis; obesity; body mass index.

Introduction

Obesity is recognized by the World Health Organization (WHO) as a public health problem in childhood and adolescence. Changes in lifestyle triggered by technical and scientific progress have been identified as one of the determining factors of this condition[1].

Obesity is associated with several chronic diseases, among which the metabolic syndrome (MS) is highlighted, already present in the early stages of life. This has resulted in the development of cardiovascular disease at younger ages[2].

In Brazil, the prevalence of MS varies from 1.1%[3] in the population of adolescent students in public schools, 6% in adolescents with a family history of type 2 diabetes and 26.1% in obese children and adolescents[4].

Among the alterations associated with obesity that contribute to the increased prevalence of MS, insulin resistance (IR) has been emphasized[5]. Studies have verified that individuals with insulin resistance are more prone to later developing MS, diabetes type 2 (DM2) and cardiovascular disease (CVD)[6,7].

Insulin resistance is defined as the inefficiency of plasma insulin, at normal concentrations, to properly promote peripheral glucose uptake, suppress hepatic gluconeogenesis and inhibit the production of very low density lipoprotein[8].

The American College of Endocrinology[9] considers the presence of elevated triglycerides, low HDL-C, high blood pressure and fasting glycemia or high postprandial glycemia as "identifying abnormalities" of possible carriers of IR. Sinakio et al[10] found a strong correlation between insulin resistance, HDL cholesterol (HDL-C), triglycerides (TG) and systolic blood pressure in individuals aged 13 to 23 years.

In children, obesity seems to be an important insulin resistance trigger[11], which makes obese children a risk group. Notwithstanding, there is no consensus for the definition of metabolic syndrome in children. A recent review on the subject found 40 different definitions adapted from those proposed for adults[12].

Therefore, the present study aims at determining the association between insulin resistance and the other components of MS in children and adolescents with a diagnosis of overweight or obesity.

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Methodological procedures

This cross-sectional study was carried out between April/2009 and April/2010 as part of a larger project entitled "Prevalence of cardiometabolic risk factors in obese or overweight children and adolescents".

The study included children and adolescents between 2 and 18 years, treated at the Brazilian Public Health System (SUS), in Campina Grande, state of Paraíba, Brazil. The study participants were invited by disseminating the research in the Basic Health Units, by the Health Secretariat of the municipality. Individuals were referred by healthcare staff to the Center for Childhood Obesity (COI), established at Instituto de Saúde Elpídio de Almeida (ISEA), in Campina Grande, PB, specifically to meet the demands of this study. The COI consists of researchers and a multidisciplinary team, including an endocrinologist, a nutritionist, a psychologist, a nurse, a social worker and a physical trainer.

The child and adolescent population of Campina Grande, registered in December 2008 in the primary healthcare information system (SIAB), consisted of 65,890 children and adolescents between 1 and 19 years[13]. To calculate the sample size, we initially considered the prevalence of overweight and obesity of 25%[4] and later, the prevalence of MS of 42% among Brazilian children and adolescents with this condition[14], totaling 194 children and adolescents after adding 20% for eventual losses.

Following ethical guidelines, after explaining the objectives and methods to be followed, the parents or tutors of the children and adolescents who agreed to participate in the study signed the free and informed consent form.

A screening was carried out at the first meeting to assess whether the referred individuals met the inclusion criteria of the study. Of the total 200 cases, we excluded those who, at the time of data collection, had any disease or were taking any medication that interfered with lipid or glucose metabolism. We recorded two losses that did not attend the blood collection and two exclusions due to corticosteroid use, resulting in a total of 196 subjects that were followed. At that time, the first questionnaire was applied, which addressed socioeconomic, personal and family history issues, anthropometric measurements were assessed and laboratory tests were scheduled to determine the lipid profile, which were performed within 15 days after the interview.

Anthropometric data (weight, height and waist circumference) were collected in duplicate, considering the mean value of two measurements. To measure the weight, a Welmy® digital platform scale was used, with a capacity of 150 kg and precision of 0.1 kg. Height was measured using a Tonelli® stadiometer with a precision of 0.1 cm. During the measurement, the individuals were wearing light clothing and the procedures recommended by the WHO were followed[15].

For the classification of nutritional status, the body mass index (BMI) was calculated as recommended by the Centers for Disease Control and Prevention (CDC)[16], working with the following categories: overweight (BMI ≥ 85 <95) obesity (BMI ≥ 95th percentile <97) and severe obesity (BMI ≥ 97th percentile).

Waist circumference (WC) was measured using an inelastic Cardiomed ® tape, with a precision of 0.1 cm, midway between the upper border of the iliac crest and the last costal margin, with the patient standing, without clothes covering the region, with arms positioned along the body and at the expiratory phase of respiration. Values above the 90th percentile were considered increased, but with a maximum of 88 cm for girls and 102 cm for boys[17,18].

Blood collection was carried out after a fasting period of 10 to 12 hours at the Clinical Analysis Laboratory of Universidade Estadual da Paraíba (LAC/UEPB).

Total cholesterol, HDL-cholesterol, triglycerides and glycemia were assessed by the enzymatic colorimetric method in automatic equipment (BioSystems Model 310), according to the Labtest® kit manufacturer's recommendations at LAC/UEPB, and insulin was measured by the INSULIN-CT radioimmunoassay method by CIS Bio International®, using an Abbott ® gamma counter (intra-assay coefficient of variation 2.6%) in a third-party laboratory that has a quality control label.

Insulin resistance was assessed by HOMA-IR, as described by Matthews et al[19] and validated by several authors for epidemiological studies, which is the product of fasting insulin (μUI/mL) and fasting plasma glucose (mmol/L) divided by 22.5[20]. As the cutoff, we used HOMA-IR ≥ 2.5[8,21].

The diagnosis of MS was attained using the criteria recommended by the National Cholesterol Education Program/Adult Treatment Panel III (NCEP / ATPIII), adapted for the age group that considers the presence of at least three of the following items: WC above or at the 90th percentile for sex, age and race; Triglycerides ≥ 100 mg/dL and/or HDL-C < 45 mg/dL, fasting glucose ≥ 100mg/dL, systolic and/or diastolic blood pressure > 90th percentile for sex, height and age. The cutoffs for TG, HDL-C and fasting glucose followed the recommended values in the I Guideline of Atherosclerosis in Childhood[22,23].

The data were presented as proportions, means ± standard deviations (SD). Comparison of insulin resistance between groups was performed using the chi-square test or Fisher's test. To assess the degree of resistance and its relationship with MS components, HOMA-IR was distributed in quartiles, in four categories according to the percentiles: <25, 25 to 49.9, 50 to 74.9 and ≥ 75 and the mean value of each MS component was compared according to the quartiles by analysis of variance (ANOVA) and Tukey's Post Hoc test.

The analyses were performed using SPSS software version 17.0 (SPSS Inc, Chicago, USA) and the significance level was set at 5%.

The study was approved by the Ethics Committee in Research of Universidade Estadual da Paraíba, process number 0040.0.133.000-08.

Results

Of the 196 children and adolescents studied, most (64.8%) were females. The mean age was 11.1 ± 3.8 years. According to age group, 9.7% were preschoolers, 26.5% were schoolchildren and 63.8% were adolescents. As for the

nutritional status, 15.8% were overweight, 18.9% were obese and 65.3% were severely obese.

Metabolic syndrome was diagnosed in 59.7% of the individuals; of these, 39.8% had three components, 19.4% four and 0.5%, five. The most common alterations were low HDL-c, 80.6%; altered WC, 79.6%; hypertension, 69.4%; hypertriglyceridemia, 36.7%, and high blood glucose, 1% (Table 1).

Insulin resistance was observed in 41.3% of the studied population and its presence was associated with age between 10-18 years ($p = 0.000$) (Table 1).

Table 2 shows a significant association between altered TG ($p = 0.005$) and diagnosis of MS ($p = 0.007$) with IR in the female sex; and MS and the presence of IR ($p = 0.022$) in the male sex. The chance of a female individual, in the presence of IR, to have altered triglycerides is 2.9 (1.3 to 6.1) and MS, 2.7 (1.3 to 5.7). The male sex has a 3.7 (1.2-11.5) higher chance to have MS together with IR.

There was no association between the presence of IR with MS or its components at the age range of 2 to 5 years. Among the adolescents (10 to 18 years), the presence of IR was associated with alterations in TG, HDL-C and MS (Table 3). The chance of an adolescent, in the presence of IR, to have altered triglycerides is 3.4 (1.6 to 7.4); HDL, 3.0 (1.1 to 7.5) and MS, 3.2 (1 0.5 to 6.7).

The mean values of MS components behave differently according to the quartile of HOMA-IR. It was observed that virtually all components of MS increased their means as the values or percentile of HOMA-IR increased (Table 4). There was no significant variation in HDL-C according to the quartile.

There was a statistically significant difference between the number of components and the mean values of HOMA-IR ($p = 0.008$), and this difference was observed in the group with one and two components when compared to that with four components ($p < 0.05$).

The mean HOMA-IR in this population was 2.4 (± 1.55). In those who had three components, with a diagnosis of MS, the mean value was 2.5 (± 1.71) (Figure 1).

There was variation in the mean HOMA-IR value according to the number of MS components. There was a statistically significant difference between the mean value of those with one or two components and those with four components ($p < 0.05$).

Discussion

The early identification of children and adolescents with MS is important for the stratification of the overall risk of an individual in relation to future cardiovascular events. Therefore, it is important to know the risk factors that indicate their presence or increased likelihood of its occurrence, such as the presence of IR, as this is a strong predictor for the development of MS and, consequently, of CVD[23].

The present study showed that most overweight or obese children and adolescents evaluated here already had MS (59.7%) and that 41.3% also had IR.

Studies that associated IR with the presence of MS and its components in childhood, such as the study by Ferreira et al[2] with 52 obese children between 7 and 10 years, found a prevalence of metabolic syndrome of 17.3%. When analyzing the HOMA-IR mean by tertiles, they also found that the simultaneous occurrence of risk factors determining the MS is strongly associated with insulin resistance, measured by HOMA-IR.

The prevalence of MS and IR observed in this study was higher than that found by Cáceres et al[15], who evaluated 61 obese Bolivian children and adolescents between 5 and 18 years, and found that 36% had MS and 39.4% had IR, and that by Souza et al[24] in a study involving 84 obese or overweight adolescents between 10 and 19 years in Sao Paulo, who found a prevalence of MS of 40% and 57% of IR; also, Lopez et al[25], evaluating 466 obese Mexican adolescents, found a similar prevalence of IR (51%), but a lower prevalence of MS (20%).

There is no consensus in the pediatric population for the diagnosis of MS, or a cutoff for its components. Moreover, the behavior of each component and their relationship vary according to ethnicity. In African-Americans, although the increase in waist circumference is related to a faster increase of cardiovascular factors than in Hispanics and Caucasians, the relationship between triglycerides and insulin resistance is reversed, i.e., as insulin resistance increases, triglycerides decrease[26].

The difference observed between the prevalence of IR in the aforementioned studies is due to the assessed age group, as adolescents are more insulin-resistant when compared to children. When stratifying by age group, it was observed that the group of adolescents had 53.6% of IR, whereas the children had 19.7%. Moreover, it is important to observe that different diagnostic criteria for MS make it difficult to compare prevalence rates and despite that, the observed results were already high in children and adolescents.

There was no difference in the distribution of MS components in relation to age and sex, but the presence of insulin resistance was associated with adolescents, possibly because the hormonal changes of puberty contribute to the exacerbation of the disease[27].

There is evidence that insulin resistance varies according to pubertal stage: it increases significantly between stages 1 and 2 of Tanner, remains stable in stages 2, 3 and 4, and decreases significantly in stage 5[28]. Thus, the differences observed in relation to sex and age can be justified by the influence of sexual maturation on IR values and the development of MS components[29,30].

Hyperinsulinemia is considered an independent risk factor for cardiovascular disease, as it plays an important role in the development of other components of metabolic syndrome such as dyslipidemia, hypertension and hiperuricemia. Bao et al[31], evaluating the long-term levels of plasma insulin in children (5 to 9 years) and young adults (17 to 23 years) of the population of the Bogalusa Heart Study, found that after eight years, cases of hypertension and dyslipidemia were 2.5 to 3-fold higher, respectively, in individuals who had persistently elevated insulin levels.

When assessing the presence of MS components in accordance with the presence of insulin resistance, sex or

age, it was observed that in the presence of IR, girls had a 2.9-fold higher risk than boys to have elevated TG and adolescents had 3 and 3.4-fold higher risk than children to have altered levels of TG and HDL-C. Insulin has several effects on lipid metabolism regulation, for instance, regulating the synthesis of triglycerides by adipocytes and participation

Table 1 – Distribution of IR and MS and their components according to sex and age range of 196 overweight and obese children and adolescents, Campina Grande-PB, 2009-2010

	Sex		p	Age Range (yrs)		p	
	Female	Male		2 to 9	10 to 18		Total
	n (%)	n (%)		n (%)	n (%)		n (%)
WC (cm) Altered	94 (74)	62 (89.9)	0.009	60 (84.5)	96 (76.8)	0.198	156 (79.6)
Normal	33 (26)	7 (10.1)		11 (15.5)	29 (23.2)		40 (20.4)
SBP (mmHg) ≥90	49 (38.6)	27 (39.1)	0.940	22 (31)	54 (43.2)	0.092	76 (38.8)
< 90	78 (61.4)	42 (60.9)		49 (69)	71 (56.8)		120 (61.2)
DBP (mmHg) ≥ 90	76 (59.8)	49 (71)	0.120	45 (63.4)	80 (64)	0.931	12 (63.8)5
< 90	51 (40.2)	20 (29)		26 (36.6)	45 (36)		71 (36.2)
Glycemia (mg/dL) ≥ 100	1 (0.8)	1 (1.4)	0.580*	0 (0)	2 (1.6)	–	2 (1)
< 100	126 (99.2)	68 (98.6)		71 (100)	123 (98.4)		194 (99)
TG (mg/dL) ≥ 100	47 (37)	25 (36.2)	0.914	23 (32.4)	49 (39.2)	0.342	72 (36.7)
< 100	80 (63)	44 (63.8)		48 (67.6)	76 (60.8)		124 (63.3)
HDL (mg/dL) < 45	101 (79.5)	57 (82.6)	0.602	55 (77.5)	103 (82.4)	0.401	158 (80.6)
≥ 45	26 (20.5)	12 (17.4)		16 (22.5)	22 (17.6)		38 (19.4)
MS Present	73 (57.5)	44 (63.8)	0.391	39 (54.9)	78 (62.4)	0.305	117 (59.7)
Absent	54 (42.5)	25 (36.2)		32 (45.1)	47 (37.6)		79 (40.3)
IR (HOMA) Present	55 (43.3)	26 (37.7)	0.445	14 (19.7)	67 (53.6)	0.000	81 (41.3)
Absent	72 (56.7)	43 (62.3)		57 (80.3)	58 (46.4)		115 (58.7)
Number of components 0	3 (2.4)	0(0)	–	2 (2.7)	1 (0.8)	–	3 (1.5)
1	17 (13.4)	3 (4.3)		6 (8)	14 (11.6)		20 (10.2)
2	34 (26.8)	22 (31.9)		24 (32)	32 (26.4)		56 (28.6)
3	49 (38.6)	29 (42)		30 (40)	48 (39.7)		78 (39.8)
4	24 (18.9)	14 (20.3)		13 (17.3)	25 (20.7)		38 (19.4)
5	0 (0)	1 (1.4)		0 (0)	1 (0.8)		1 (0.5)

WC - Waist circumference; SBP - Systolic blood pressure; DBP - Diastolic blood pressure; TG – triglycerides; MS - Metabolic syndrome; HDL – High Density Lipoprotein; IR - Insulin resistance.

in fatty acid uptake from circulating lipoproteins, a fact not observed in obese individuals caused by frequent changes that occur in the performance of certain enzymes and in lipid metabolism due to IR[17].

IR enhances the oxidation of free fatty acids (FFA) in serum, provides substrate for the synthesis of TG in the liver and increases the hepatic release of TG-rich very low density lipoprotein (VLDL-c), to the serum, thereby increasing its levels[32].

Under normal conditions, insulin has several effects on the regulation of lipid metabolism; however, in obese individuals this situation is not observed, due to the frequent changes that occur in the performance of certain enzymes and in the lipid metabolism due to insulin resistance. The main alterations in the lipid profile are: increased levels of VLDL-c, due to increased production of triglycerides by the liver and lower catabolism; decrease in the levels and size of HDL-c related to the decrease in HDL-C sub-fraction and higher catabolism due to a higher concentration of triglycerides in these particles and smaller and denser LDL-c particles, richer in apolipoprotein B[33].

In the present study, it was observed that IR was associated with MS in both sexes and at the age range between 10 and 18 years. The association of IR with age may be due to a physiological reduction in insulin sensitivity, which is compensated by the increase in its secretion, a fact observed in adolescents[34].

The mean HOMA-IR value was 2.4, lower than that found by Ferrreira et al[2] (3.2 ±1.9) in 52 obese children aged 7 to 10 years. On the other hand, a study carried out in Argentina found a HOMA-IR among obese children of 2.76 and, in the United States, it ranged from 3.12 in overweight children to 8.69 among the severely obese ones. This fact might be due to the interaction between nutritional factors, ethnicity and time of obesity[7].

Schmidt et al[35] observed that the values observed in the highest quintile of IR had higher OR values for metabolic syndrome (MS) when there was a cluster of two, three and especially four or more of these metabolic abnormalities (hypertension, diabetes, hypertriglyceridemia, low HDL-cholesterol and elevated TG).

The results of this study also show that the highest values of HOMA-IR were associated with the presence of greater numbers of MS components and that the mean values of each component increased as the percentile of HOMA-IR increased, a fact confirmed by Oliveira et al[36], whose study showed that the HOMA-IR values increased from zero to five components of MS and with greater significance among individuals with two and three isolated components. This fact can be explained by the production and secretion of several factors that intensify with obesity, for instance, tumor necrosis factor α (TNF-α), resistin, plasminogen activator inhibitor 1 (PAI-1), Interleukin-6 and macrophage chemoattractant protein 1 (MCP-1), and are directly associated with insulin resistance induction, hypercoagulability and atherogenesis, which in turn cause hypertension and intensify the pro-inflammatory states, representing some of the criteria of MS and leading to an increased risk of cardiovascular and thromboembolic events[37].

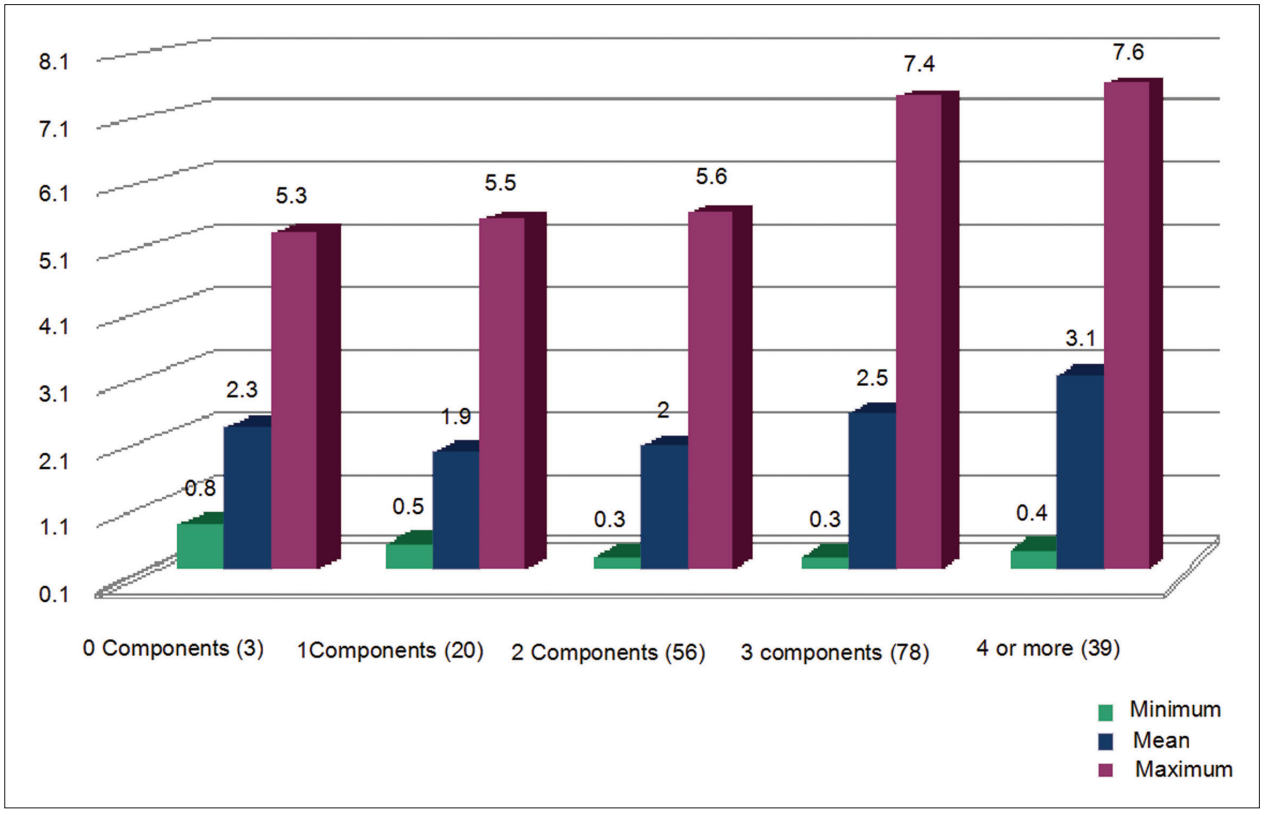

Figure 1 - *Homeostasis model assessment–insulin resistance (HOMA-IR) values according to the number of components of MS in 196 overweight or obese children and adolescents, Campina Grande-PB, 2009-2010.*

Table 2 – Distribution and prevalence ratio (PR) of MS and its components according to the presence of insulin resistance and sex of 196 overweight and obese children and adolescents, Campina Grande-PB, 2009-2010

	IR				PR (95%CI)	p
	Present		Absent			
Female	**n**	**(%)**	**n**	**(%)**		
WC (cm) Alterad	44	46.8	50	53.2	1.2 (0.9-1.7)	0.179
Normal	11	33.3	22	66.7		
SBP (mmHg) ≥ 90	23	46.9	26	53.1	1.5 (0.6-2.6)	0.513
< 90	32	41	46	59		
DBP (mmHg) ≥ 90	31	40.8	45	59.2	0.8 (0.4-1.6)	0.485
< 90	24	47.1	27	52.9		
Glycemia (mg/dL) ≥ 100	1	100	L0	0	-	-
< 100	54	42.9	72	57.1		
TG (mg/dL) ≥ 100	28	59.6	19	40.4	2.9 (1.3-6.1)	0.005
< 100	27	33.8	53	66.2		
HDL (mg/dL) < 45	48	47.5	53	52.5	2.4 (0.9-6.4)	0.059
≥ 45	7	26.9	19	73.1		
MS Present	39	53.4	34	46.6	2.7 (1.3-5.7)	0.007
Absent	16	29.6	38	70.4		
Male						
WC (cm) Alterad	26	41.9	36	58.1	-	-
Normal	0	0	7	100		
SBP (mmHg) ≥ 90	13	48.1	14	51.9	2.1 (0.8-5.6)	0.150
< 90	13	31	29	69		
DBP (mmHg) ≥ 90	21	42.9	28	57.1	2.0 (0.6-6.5)	0.165
< 90	5	25	15	75		
Glycemia (mg/dL) ≥ 100	1	100	0	0	-	-
< 100	25	36.8	43	63.2		
TG (mg/dL) ≥ 100	13	52	12	48	2.6 (0.9-7.1)	0.064
< 100	13	29.5	31	70.5		
HDL (mg/dL) < 45	23	40.4	34	59.6	2.0 (0.5-8.3)	0.256*
≥ 45	3	25	9	75		
MS Present	21	47.7	23	52.3	3.7 (1.2-11.5)	0.022
Absent	5	20	20	80		

Fisher's Test.; WC - Waist circumference; SBP - Systolic blood pressure; DBP - Diastolic blood pressure; TG – triglycerides; MS - Metabolic syndrome; HDL – High Density Lipoprotein; IR - Insulin resistance.

Table 3 – Distribution and prevalence ratio of MS and its components according to the presence of IR and age range of 196 overweight and obese children and adolescents, Campina Grande-PB, 2009-2010

	IR				PR (95%CI)	p
	Present		Absent			
2 to 9 years	**n**	**(%)**	**n**	**(%)**		
WC (cm) Alterad	14	23.3	46	76.7	-	-
Normal	0	0	11	100		
SBP (mmHg) ≥ 90	5	22.7	17	77.3	1.3 (0.4-4.5)	0.669
< 90	9	18.4	40	81.6		
DBP (mmHg) ≥ 90	10	22.2	35	77.8	1.6 (0.4-5.6)	0.355*
< 90	4	15.4	22	84.6		
Glycemia (mg/dL) ≥ 100	0	0	0	0	-	-
< 100	14	19.7	57	80.3		
TG (mg/dL) ≥ 100	6	26.1	17	73.9	1.8 (0.5-5.9)	0.350
< 100	8	16.7	40	83.3		
HDL (mg/dL) < 45	11	20	44	80	1.1 (0.3-4.5)	0.612*
≥ 45	3	18.8	13	81.2		
MS Present	10	25.6	29	74.4	2.4 (0.7-8.6)	0.139*
Absent	4	12.5	28	87.5		
10 to 18 years						
WC (cm) Alterad	53	57.6	39	42.4	1.5 (1.0-2.1)	0.064
Normal	11	37.9	18	62.1		
SBP (mmHg) ≥90	31	57.4	23	42.6	1.3 (0.6-2.7)	0.457
< 90	36	50.7	35	49.3		
PAD (mmHg) ≥ 90	42	52.5	38	47.5	0.9 (0.4-1.8)	0.742
< 90	25	55.6	20	44.4		
Glycemia (mg/dL) ≥ 100	2	100	0	0	-	-
< 100	65	52.8	58	47.2		
TG (mg/dL) ≥ 100	35	71.4	14	28.6	3.4 (1.6-7.4)	0.001
< 100	32	42.1	44	57.9		
HDL (mg/dL) < 45	60	58.3	43	47.7	3.0 (1.1-7.9)	0.024
≥ 45	7	31.8	15	68.2		
MS Present	50	64.1	28	35.9	3.2 (1.5-6.7)	0.002
Absent	17	36.2	30	63.8		

Fisher's Test; WC - Waist circumference; SBP - Systolic blood pressure; DBP - Diastolic blood pressure; TG – triglycerides; MS - Metabolic syndrome; HDL – High Density Lipoprotein; IR - Insulin resistance.

Moreover, the excess of circulating FFA, resulting from the lipotoxicity process, is a strong inducer of peripheral resistance to insulin action, increasing the likelihood of developing type 2 DM and MS[37]. The disclosure of an increasing frequency of MS as the HOMA-IR values increase, especially MS associated with components more specifically related to IR, may be pointing to the possibility of using the index as an indicator of the presence of IR associated with MS, which would favor the definition of the therapeutic approach and, consequently, the prognosis of affected individuals, more specifically non-diabetic ones[36].

It was also verified that the mean value of HOMA-IR for those who had three components of MS was equal to 2.5 cutoff used in the study for the diagnosis of IR, and that the mean value observed in the group of individuals who did not have any MS component (2.3), higher than that in the group with one component, was due to the HOMA-IR equal to 5 shown by one of the individuals who fit into this group.

Thus, it is evident that the prevalence of individual risk factors for MS increases together with increased values of insulin resistance[28,38,39].

Some studies point to the hypothesis that the negative impact of increased amount of adipose tissue in the body on insulin sensitivity can be clearly demonstrated in most individuals, as well as increased insulin sensitivity observed with body weight reduction and physical exercise[40].

Despite the lack of a unanimous hypothesis about the pathophysiological pathways that lead to the emergence of metabolic syndrome, it is suggested that plasma insulin levels, as well as the simple evaluation of BMI, are valuable indicators of clinical disorders compatible with MS in children[40] .

The fact that these are the results of a cross-sectional study, which does not allow the identification of a true causal relationship, as cause and effect are measured at the same time, is a limitation of the study. There is a possibility of reverse causality, as individuals with IR are more likely to develop MS, but we cannot affirm that this fact actually occurs in the studied population. A longitudinal study of this population, excluding individuals with MS, and dividing them into groups according to presence or absence of IR, would allow the evaluation of its effect on MS.

In spite of this limitation, the results indicate that one factor that should be monitored in obese children and adolescents is the level of insulin resistance, as the higher the level of IR, the greater the presence of cardiovascular risk factors, the higher the prevalence of MS, and consequently, the higher the risk of premature development of type 2 DM and CVD.

Conclusions

The results of the present study showed that MS is already a reality for many obese children and adolescents. It was also observed that the higher the level of insulin resistance, the greater the number of cardiometabolic factors present, which indicates a predisposition to the future development of type 2 DM and CVD. Thus, the high percentage of IR associated with the components of MS in this population point to the need of implementing programs of prevention, early detection and intervention of complications associated with obesity, particularly MS and IR, allowing the reduction of cardiovascular risk in this population, which makes up a significant part of the general population. This fact shows the need of reinforcing the new model of health, which calls for health protection and promotion and disease prevention,

Table 4 – Mean values and standard deviation of MS components according to quartiles of HOMA-IR of 196 overweight and obese children and adolescents, Campina Grande-PB, 2009-2010

Variables	HOMA				p
	< 1.139	1.14-2.154	2.155-3.189	> 3.19	
	Mean (SD) CI	Mean (SD) CI	Mean (SD) CI	Mean (SD) CI	
WC (cm)	76.33 (10.63)	82.51 (11.33)	89.75 (11.41)	93.86(11.70)	0.000*
	(73.27-79.38)	(79.26-82.45)	(86.47-93.03)	(90.56-97.22)	
SBP (mmHg)	103.88 (10.62)	106.88 (10.96)	109.74 (11.21)	112.49(13.01)	0.002†
	(100.83-106.93)	(110.73-110.03)	(106.52-112.96)	(108.75-116.23)	
DBP (mmHg)	69.99 (9.76)	70.47 (8.02)	75.80 (10.21)	73.88(11.00)	0.009‡
	(67.15-72.80)	(68.17-72.77)	(72.87-78.73)	(70.72-77.04)	
Glycemia (mg/dL)	76.73 (6.49)	80.55 (6.60)	82.80 (7.43)	84.69(6.95)	0.000*
	(74.87-78.60)	(78.65-82.45)	(80.66-84.93)	(82.70-86.69)	
TG (mg/dL)	98.00 (45.28)	126.78 (69.34)	128.39 (56.96)	154.57(76.48)	0.000§
	(84.99-111.01)	(106.86-146.69)	(112.03-144.75)	(132.60-176.54)	
HDL (mg/dL)	39.31 (8.50)	39.51 (7.26)	38.88 (11.14)	36.61(7.98)	0.344
	(36.86-41.75)	(37.42-41.60)	(35.68-42.08)	(34.32-38.91)	

(*) Significant difference (p < 0.01) between quartiles 1 and 3 and 4; (§) < 0.01 between quartiles 1 and 4; (†) p < 0.05 between quartiles 1 and 4; (‡) p < 0.05 between quartiles 1 and 2 and 3. WC - Waist circumference; SBP - Systolic blood pressure; DBP - Diastolic blood pressure; TG – triglycerides; CI -Confidence interval; SD - Standard deviations.

and stimulates the development of intersectoral policies capable of promoting adherence to a healthier lifestyle.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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