


Research Article

Relationship between Waist Girth, Insulinemia and Metabolic Parameters in Brazilian Adults

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Abstract

Purpose: Waist girth, an indirect measure of central fat, is significantly associated with a higher risk of all-cause mortality. The aim of this study was to evaluate the relationship between waist circumference measures with insulinemia, hepatic steatosis and criteria used for diagnosing metabolic syndrome (MS).

Methods: This is a cross-sectional, retrospective, single-center study in patients who underwent annual check-up appointment at our institution between from October/2020 to March/2021. A total of 1017 adult individuals (74% male), with mean age of 46 years were selected for the study which included Body Mass Index (BMI), waist girth (WG), total fat index (TFI), blood pressure (BP), abdominal ultrasound, fasting insulinemia, in addition to triglyceride, fasting glycemia and High-Density Lipoprotein - Cholesterol (HDL-C) dosages.

Results: The cut-off for fast hyperinsulinemia diagnosis considered in this analysis was 8 mU/L and 10 mU/L, respectively, for men and women, defined by the mean +2 Standard Deviation (SD) of values found in individuals with two normal (WG + BMI), three normal anthropometric parameters (BMI, TFI and WG), three normal anthropometric parameters (BMI, TFI and WG) and/or without any of the following five criteria for diagnosing metabolic syndrome - BP \geq 130/85 mm/Hg or drug treatment for hypertension, HDL-C <40 mg/dL (men), <50 mg/dL (women), glycemia \geq 100 mg/dL or hypoglycaemic agents, triglycerides \geq 150 mg/dL or drug treatment for hypertriglyceridemia, WG \geq 90 cm (men), WG \geq 80 cm (women).

Conclusion: The analysis led to the conclusion that insulinemia, frequency of hepatic steatosis, and all other parameters considered—including BP, HDL-C, triglycerides, and blood glucose—progressively and significantly change with the increase in abdominal circumference. Early reduction of insulinemia in those patients with levels above the cut-off defined in this study, regardless of high adiposity, may provide subsequent clinical benefits.

Keywords: waist girth; hyperinsulinemia; metabolic syndrome; anthropometric parameters; hepatic steatosis

Abbreviations: **MS:** Metabolic Syndrome; **BMI:** Body Mass Index; **WG:** Waist Girth; **TFI:** Total Fat Index; **BP:** Blood Pressure; **HDL-C:** High-Density Lipoprotein – Cholesterol; **IDF:** International Diabetes Federation;

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SD: Standard Deviation; **HOMA-IR:** Homeostatic Model Assessment for Insulin Resistance; **ANOVA:** Analysis of Variance; **LDL-C:** Low-Density Lipoprotein - Cholesterol; **HbA1C:** Glycated Hemoglobin

Introduction

The association of general adiposity as defined by body mass index (BMI) as a risk factor for metabolic syndrome (MS) and its consequences, is well-known [1,2]. However, BMI has some limitations, by not differentiating tissues or the distribution of body fat [3], which can induce a delay in medical intervention.

Central fat indices such as waist girth (WG) and others, regardless of overall adiposity, are significantly associated with a higher risk of all-cause mortality, more evidently than BMI, which is why it should be preferred for measuring adiposity risks [4-10].

MS, the epicenter of obesity-related clinical complications, is associated with insulin resistance and hyperinsulinemia due to a prolonged and subclinical inflammatory process which can be evidenced by a series of biomarkers such as pro-inflammatory cytokines, pro-oxidant and prothrombotic factors [11-17].

In this study, we analyzed the relationship between varying ranges of WG with insulinemia and the following International Diabetes Federation (IDF) criteria used for diagnosing MS (i.e., triglycerides ≥ 150 mg/dL or patient receiving fibrate; high density lipoprotein-cholesterol (HDL-C) < 40 mg/dL in men and < 50 mg/dL in women; blood glucose ≥ 100 mg/dL; increased WG (variable with ethnicity); and hypertension ≥ 130 and/or/85 mm Hg or patient receiving antihypertensive treatment.

Methods

Case selection and study design

This is a cross-sectional, retrospective, single-center study with the aim to evaluate a relationship between waist circumference with the diagnostic parameters of MS and insulinemia in Brazilian adults of both genders. A cohort of 1017 adult study participants (743 men) with a mean age of 46.5 ± 8.91 years was recruited from participants who underwent elective screening consultations (check-ups) from October 2020 to March 2021. Patients were examined for comorbidities such as hypertension, diabetes, dyslipidemia, and obesity, due to their relevance to the proposed analyses. This study was approved by the Ethics and Research Committee of Hospital Alemão Oswaldo Cruz de São Paulo (CAAE: 46489021.6.0000.0070).

Clinical evaluation and sample collection for laboratory tests

Blood pressure (BP) was measured using the auscultatory

method with a manual sphygmomanometer. [18,19] Waist girth (WG, cm) was measured at the midpoint between the last rib and the iliac crest [20,21]; total fat index (TFI) was determined by bioimpedance using an InBody 270 body composition analyser (Seoul, South Korea), with normal TFI values being considered below 20 and 30 for men and women, respectively. Body mass index (BMI) was calculated after confirming weight and height. [21,22] Patients with previously diagnosed comorbidities that required specific treatment (such as hypertension and dyslipidemia) were on use of drug therapy appropriate to the underlying disease.

The five criteria used by the IDF [23,24] for the diagnosis of MS, as listed above, were: Blood glucose ≥ 100 mg/dL (≥ 5.6 mmol/L); HDL-C < 40 mg/dL (< 1.0 mmol/L) and < 50 mg/dL (< 1.5 mmol/L), respectively for men and women; waist girth ≥ 90 cm (men) or ≥ 80 cm (women); Triglycerides ≥ 150 mg/dL (≥ 1.7 mmol/L) or drug treatment for elevated triglycerides; and arterial hypertension, BP $\geq 130/85$ mmHg or drug treatment for arterial hypertension.

Each participant also authorized an additional blood sample to be used for the determination of fasting serum insulin. The samples were collected after 10–12 h fasting and were analyzed in addition to the standard tests pre-defined by the check-up program of Hospital Alemão Oswaldo Cruz (São Paulo), at no additional cost to customers, companies, or healthcare providers. The samples were collected after 10–12 h fasting and were analyzed in addition to the standard tests predefined by the check-up program of Hospital Alemão Oswaldo Cruz (São Paulo), at no additional cost to customers, companies, or healthcare providers.

The standard laboratory analyses were conducted on the day of the allocated appointment, with their respective evaluation methods and reference values considered by the analysis laboratory and included: Blood glucose: enzymatic method; Fasting insulin: electro chemiluminometric assay; HOMA-IR (Homeostatic Model Assessment for Insulin Resistance); HDL-C: homogeneous enzyme assay; Triglycerides: enzymatic assay. In addition, hepatic steatosis was assessed using abdominal ultrasound by the same team using the same equipment.

The cut-off values for fasting insulin in men and women were based on our previous study in Brazilian patients [25] and hyperinsulinemia diagnosis considered in this study were: 8 mU/L and 10 mU/L, respectively, for men and women. These levels were defined by the mean +2 SD insulin levels found in individuals with fulfilled all the following criteria: blood glucose ≥ 100 mg/dL (≥ 5.6 mmol/L), HDL-cholesterol < 40 mg/dL (< 1.0 mmol/L) or < 50 mg/dL (< 1.5 mmol/L), respectively men and women; waist girth ≥ 90 cm (men) or 80 cm women), Triglycerides ≥ 150 mg/dL (≥ 1.7 mmol/L) or drug treatment for elevated triglycerides, and arterial hypertension (BP $\geq 130/85$ mmHg or drug treatment for arterial hypertension).

Statistical analysis

The D'Agostino-Pearson omnibus and Shapiro-Wilk tests were used to assess the distribution of variables. Variables with parametric distribution were expressed as mean \pm standard deviation and compared using the Student's t-test when in two groups and using analysis of variance (ANOVA) when in three or more groups. Where data distributions were non-parametric, the variables were expressed as median and interquartile ranges, and compared using the Mann-Whitney U test for two groups or the Kruskal-Wallis test among three or more groups. Nominal variables were expressed as absolute and percentage counts and were analyzed using the Chi-squared or Fisher's exact test. Values of $p < 0.05$ were considered statistically significant. Statistical analyses were performed using GraphPad Prism version 8.00 (GraphPad Software, San Diego, CA, United States) and SPSS 25.0 (IBM Corp, Armonk, NY, United States) software programs.

Results

This is a cohort of 1,017 adult study participants (752 men, 265 women), with a mean age of 46.5 ± 8.9 years old. It is important to highlight that in both sexes the Low-Density Lipoprotein - Cholesterol (LDL-C) mean value was above 100mg/dl (124mg/dl in men and 109.6mg/dL in women), the mean waist girth in men was also above >90 cm and that about one third of patients showed evidence of hepatic steatosis on ultrasound analysis. Mean serum creatinine was 1.0 mg/dL (0.8-1.5) and 0.74 mg/dL (0.5-1.1), for men and

women, respectively. The baseline characteristics of patients are described on Table 1.

The relationship between ranges of two (BMI, WG) and three (WG + BMI + TFI) anthropometric parameters were compared with insulin and HOMA-IR and are described on Tables 2 and 3, respectively. It can be noted that the mean values of insulinemia and HOMA-IR are inversely proportional are inversely proportional to the number of normal anthropometric parameters, which ratifies the correlation between such parameters with biochemical markers associated with insulin resistance.

In the Table 4 we evaluated patients with three normal anthropometric parameters (WG + BMI + TFI), and without any diagnostic criteria for MS and in the Table 5 patients only without any diagnostic criteria for MS. It is very relevant to observe that patients without any criteria for MS and normal anthropometric parameters had lower levels of fasting insulin and HOMA-IR than those without normal anthropometric parameters. This finding suggests that altered anthropometric parameters may reflect metabolic disturbances and insulin resistance even in the absence of the classic criteria of MS.

The Tables 6 and 7 tables reveal the relationship between waist girth and the different parameters used for the diagnosis of MS, as well as the frequency of hepatic steatosis and normal insulinemia. We must highlight the reduction in the proportion of patients with normal metabolic parameters as abdominal circumference increases in both men and women.

Table 1: Baseline characteristics of patients

Variables	Men (n = 751)	Women (n = 264)
Age (years)	47.3 \pm 9.7	44.8 \pm 7.1
Body Mass Index (kg/m ²)	28.2 \pm 3.8	25.4 \pm 4.17
Waist Girth (cm)	100.6 \pm 10.9	87.6 \pm 10.9
Systolic blood pressure (mmHg)	127.3 \pm 13.5	117.9 \pm 15.7
Diastolic blood pressure (mmHg)	85.1 \pm 9.9	75.2 \pm 11.1
Total Cholesterol (mg/dL)	187.8 \pm 35.9	186.1 \pm 36.2
LDL (mg/dL)	124.0 \pm 72.9	109.6 \pm 32.6
HDL (mg/dL)	47.7 \pm 12.9	60.4 \pm 15.9
Triglycerides (mg/dL)	124.5 \pm 70.4	92.2 \pm 50.2
Fasting glucose (mg/dL)	96.2 \pm 13.7	91.2 \pm 8.4
Insulin (mU/L)	12.1 \pm 8.4	9.9 \pm 6.2
HOMA-IR	2.9 \pm 2.3	2.3 \pm 1.53
HbA1C (%)	5.3 \pm 0.5	5.2 \pm 0.5
Hepatic Steatosis (n / %)	299 / 743 (40.2)	43 / 255 (16.9)
Serum creatinine (mg/dl)	1.0 (0.8-1.5)	0.74 (0.5-1.1)

Table 2: Fasting insulinemia and Homa-IR values in individuals with two normal anthropometric parameters (WG + BMI)*

Sex	n (%)	Fasting Insulin (mU/L)				HOMA-IR			
		Mean	SD	Mean + 1 SD	Mean + 2 SD	Mean	SD	Mean + 1SD	Mean + 2SD
Male (n=752)	35 (4.7)	4.8	1.9	6.7	8.6**	1.1	0.4	1.5	1.9**
Female (n=255)	55 (21.5)	5.7	2.4	8.1	10.5**	1.2	0.5	1.7	2.2**

*BMI<23; WG<90 (Men), WG<80 (Women); **p<0.0005.

Table 3: Fasting insulinemia and Homa-IR values in individuals with three normal anthropometric parameters (WG + BMI + TFI)

Sex	n (%)	Fasting Insulin (mU/L)				HOMA-IR			
		Mean	SD	Mean + 1 SD	Mean + 2 SD	Mean	SD	Mean + 1SD	Mean + 2SD
Male (n=752)	18 (2.4)	4.3	1.4	5.7	7.1**	0.98	0.35	1.33	1.68**
Female (n = 265)	38 (14.3)	5.4	2.3	7.7	10**	1.17	0.51	1.68	2.19**

BMI < 23; WG < 90 (men), < 80 (women); TF < 20 (men), < 30 (women); ** p < 0.005

Table 4: Insulin and HOMA-IR values in individuals with three normal anthropometric parameters (WG + BMI + TFI), and without any diagnostic criteria for MS

Sex	n (%)	Fasting Insulin (mU/L)				HOMA-IR			
		Mean	SD	Mean + 1 SD	Mean + 2 SD	Mean	SD	Mean + 1SD	Mean + 2SD
Male (n=752)	11 (1.5)	4	1.64	5.64	7.28**	0.89	0.3	1.19	1.49**
Female (n = 265)	33 (12.5)	5.3	2.17	7.47	9.64**	1.1	0.5	1.6	2.10**

** p < 0.005

Table 5: Insulin and HOMA-IR values in individuals without any diagnostic criteria for MS

Sex	n (%)	Fasting Insulin (mU/L)				HOMA-IR			
		Mean	SD	Mean + 1 SD	Mean + 2 SD	Mean	SD	Mean + 1SD	Mean + 2SD
Male (n=752)	49 (6.5)	4.6	1.8	6.4	8.2**	1.01	0.43	1.44	1.87**
Female (n = 265)	48 (18.1)	5.6	2.3	7.9	10.2**	1.1	0.5	1.6	2.10**

** p < 0.0005

Table 6: Frequency of the five diagnostic criteria for MS, hepatic steatosis and normal insulinemia (less than the cut-off above defined) according to various WG ranges, in men

Parameters	Waist Girth (cm)					Linear trend test on proportions	
	< 90 (n=103)	90-99 (n=264)	100-109 (n=230)	≥ 110 (n=109)	> 120 (n=37)	χ^2_1	p-value
Normal* (%)	44	19	8	3	0	85.51	<0.0005
HDL-C ≥ 40mg/dl (%)	91	77	73	63	57	30.14	<0.0005
Triglycerides <150mg/dl (%)	89	78	71	63	68	23.05	<0.0005
Fasting glucosis <100mg/dl (%)	81	77	71	65	62	12.12	<0.0005
Blood pressure <130x85mmHg (%)	68	53	42	30	27	45.47	<0.0005
Fasting Insulina < 8mU/L (%)	76	43	26	10	3	139.13	<0.0005
Hepatic steatosis (%)	9	27	49	73	92	171.05	<0.0005

*Metabolically Normal: men without any diagnostic criteria for MS, and insulinemia <8 mU/L.

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Table 7: Frequency of the five diagnostic criteria for MS, hepatic steatosis and normal insulinemia (less than the cut-off above defined) according to various WG ranges, in women.

Parameters	Waist Girth (cm)				Linear trend test on proportions	
	< 80 (n=62)	80-89 (n=95)	90-99 (n=59)	≥ 100 (n=39)	χ^2_1	p-value
Normal* (%)	77	49	22	13	53.91	<0.0005
HDL-C ≥ 50mg/dl (%)	87	80	66	51	19.13	<0.0005
Triglycerides <150mg/dl (%)	97	95	86	79	11.1	<0.0005
Fasting glucosis <100mg/dl (%)	97	94	81	72	18.58	<0.0005
Blood pressure <130x85mmHg (%)	92	82	64	51	27.27	<0.0005
Fasting Insulina < 10mU/L (%)	90	76	49	21	60.87	<0.0005
Hepatic steatosis (%)	0	5	27	54	59.41	<0.0005

*Metabolically Normal: women without any diagnostic criteria for MS, and insulinemia <10 mU/L.

Discussion

Central obesity, regardless of general adiposity, is known to be associated with a higher risk of all-cause mortality, around 10% to 12% for every 10 cm increase in WG. On the other hand, larger hip and thigh girths are associated with lower risk [2].

The present analysis clearly demonstrated that insulinemia, frequency of hepatic steatosis and all the other parameters, including BP, HDL-C, triglycerides, and blood glucose, progressively and significantly change with increasing waist girth. Adiposity reduction, combined with correct diet and adequate and regular physical activity, are the best therapeutic option. However, in practice the results of these interventions remain disappointing as a result of the lack of information and encouragement from the State.

Insulin resistance, hyperinsulinemia and central adiposity are recognized as jointly occurring morbidities. Hyperinsulinemia has long been considered secondary to insulin resistance, resulting from an inflammatory process generated by adiposity, but more recently it has also become recognized as directly responsible for the inflammatory condition and obesity itself [26-31]. Insulin has a double action in the endothelium: it is protective by increasing the production of nitric oxide, which is an important vasodilator, anti-aggregant and limit to the growth of muscle cells, but insulin also interferes with the release of endothelin ET-1, a potent vasoconstrictor. These beneficial effects predominate under normal conditions but are reversed in the face of insulin resistance and hyperinsulinemia [16]. It is therefore an important predictor of complications.

However, despite its importance, the cut-off defined by clinical analysis laboratories for diagnosing hyperinsulinemia is very variable and often poorly justified. Some laboratories have established a 'normal' insulin limit of up to 25 (or more) mU/L, which is deleterious to the patient's health, as it can delay initiation of preventive therapeutic measures for

important (and prevalent) complications. Equally, there are laboratories that define normal fasting hyperinsulinemia levels up to or above 12 mU/L [27,32], while others below 10 mU/L [33]. We have defined insulin levels of 8 mU/L (men) and 10 mU/L (women) as the upper cut-off for hyperinsulinemia diagnosis, based on the mean +2 SD found in metabolically normal Brazilian individuals [25].

We conclude that the pharmacological and early reduction of insulinemia, especially in those who were not able to reduce adiposity with lifestyle and diet changes, is critical for the health of the population.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics and Research Committee of Hospital Alemão Oswaldo Cruz de São Paulo (CAAE: 46489021.6.0000.0070). In the scenario of a retrospective study based on medical records, informed consent was exempt.

Competing interests

All the authors declare that they have no competing interests.

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Authors' contributions

PRC: Conception and design, data acquisition, analysis and interpretation, drafting the article, critically revising the article, funding acquisition, supervision of the research group. PDMMN: Data analysis and interpretation, drafting the article, critically revising the article. VAHS: Data analysis and interpretation, drafting the article, critically revising the article. SM: Data analysis and interpretation, critically revising the article. ESO: Data analysis and interpretation, critically revising the article. LVBP: Data analysis and

interpretation, critically revising the article. AMB: Data analysis and interpretation, critically revising the article. FPS: Data analysis and interpretation, critically revising the article. FMO: Conception and design, data acquisition, critically revising the article. JAD: Data interpretation, drafting the article, critically revising the article. ALCN: Data analysis and interpretation, drafting the article, critically revising the article. All the authors approved the final version of the manuscript.

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