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Association between cytokine levels and anthropometric measurements: a population-based study

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Abstract

Obesity is currently considered a public health problem with pandemic proportions and is associated with chronic low-grade inflammation, which can predispose to the development of several chronic diseases and metabolic complications. This cross-sectional population-based study, conducted with 743 Brazilian adults, aimed to evaluate the association between inflammatory cytokines with anthropometric measurements. Socio-demographic, anthropometric, behavioural and biochemical variables were collected. Multiple linear regression stratified by sex and adjusted for confounding factors was performed. In men, waist circumference (WC) was associated with IL-1β (3·52 pg/ml; 95 % CI 0·60, 6·45), IL-6 (6·35 pg/ml; 95 % CI 0·35, 12·34), IL-8 (8·77 pg/ml; 95 % CI 2·37, 15·17), IL-10 (3·09 pg/ml; 95 % CI 0·56, 5·61), IL12p70 (8·31 pg/ml; 95 % CI 3·11, 13·52) and TNF-α (4·22 pg/ml; 95 % CI 0·20, 10·48). Waist:height ratio was associated with IL-6 (3·21 pg/ml; 95 % CI 0·02, 6·39). BMI was associated with IL-1β (1·50 pg/ml; 95 % CI 0·46, 2·34), IL-6 (2·97 pg/ml; 95 % CI 0·78, 5·16), IL-8 (4·48 pg/ml; 95 % CI 2·21, 6·75), IL-10 (1·31 pg/ml; 95 % CI 0·30, 2·31), IL-12p70 (3·59 pg/ml; 95 % CI 1·24, 5·95) and TNF-α (2·00 pg/ml; 95 % CI 0·81, 3·19). In women, WC was associated with IL-6 (5·10 pg/ml; 95 % CI 0·68, 9·51) and IL-10 (4·16 pg/ml; 95 % CI 1·26, 7·06). BMI was associated with IL-6 (2·67 pg/ml; 95 % CI 0·34, 4·99), and WHR was associated with TNF-α (2·84 pg/ml; 95 % IC 0·86–6·54). The results highlight the importance of anthropometric assessment in clinical practice and the need to develop public policies and interventions to reduce the prevalence of obesity and, consequently, of inflammation and possible metabolic complications.

Keywords: **Adipose tissue: Anthropometry: Inflammation: Cytokines: IL**

Obesity is currently considered a public health problem, affecting a large part of the world population[1]. It is characterised by the excess accumulation of adipose tissue, which can promote health risks[2] and is considered a chronic disease with complex control, with a multifactorial aetiology in which biological, social, environmental and emotional aspects are involved[3].There are several methods used to establish the diagnosis and classification of obesity. Anthropometry is one of them, being widely used due to several advantages: it provides a portable, universally applicable, low-cost and non-invasive technique that allows the assessment of size, proportions and body composition[4].

For a long time, obesity was considered a public health problem only in developed countries. However, this scenario has changed, and, nowadays, the prevalence of overweight and obesity is increasing in low- and middle-income countries, especially in urban regions[2], highlighting the relevance of studying this theme.

This condition is marked by a chronic low-grade inflammation process, which is associated with the development of comorbidities[5], such as coagulation disorders, atherosclerosis, metabolic syndrome, insulin resistance and type 2 diabetes mellitus[6]. The excess of adipose tissue plays a fundamental role in obesity-related inflammation, since with its expansion, several metabolic adaptations occur, stimulating inflammatory pathways and culminating in the increase of systemic markers of inflammation, such as cytokines[5]. It is noteworthy that the obesity-related inflammation is not restricted to adipose tissue, as it is considered a systemic inflammation that affects several organs and tissues, such as pancreas, liver, intestine and muscle tissue[7].

In view of the lack of knowledge on the association of inflammatory status with different anthropometric and body

Abbreviations: BF, body fat; WC, waist circumference; WHR, waist:hip ratio; WHtR, waist:height ratio.

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composition measures in Brazilian population-based studies and considering the importance for public health and clinical practice of knowing this association in a study with a representative sample, the aim of the present study was to investigate the association between serum levels of inflammatory cytokines with anthropometric and body composition measurements in adults. Our hypothesis is that individuals with obesity have higher serum levels of inflammatory cytokines when compared with individuals with anthropometric measurements in the normal range.

Methods

Study design and participants

This study used data from a population-based cross-sectional research, conducted from 2012 to 2014 in the urban area of Viçosa, Minas Gerais, Brazil, which aimed to assess the health conditions of the adult population. The study included adults aged between 20 and 59 years, of both sexes, living in the urban area of Viçosa. Pregnant women, puerperal women, bedridden individuals and/or unable to remain in the prone position for measuring anthropometric measurements, individuals who have undergone orthopedic surgery or who use a prosthesis at the site to be evaluated and individuals without the ability to answer the questionnaire were excluded.

Theoretical and practical training for data collection was carried out, in addition to a pilot study with eighty-four individuals, aiming to identify possible errors in the elaboration and application of the questionnaire, as well as in the protocols for anthropometric measurements and biochemical tests. Further details about the study protocol were previously described[8].

The sampling process was by conglomerates in double-stage clusters (census tract as the first-stage units and households as the second-stage units), without replacement. At the end of the survey, 1229 individuals were interviewed, of which 486 did not undergo laboratory tests. The final sample size for cytokine evaluation was 743 individuals (Fig. 1).

Study variables

Socio-demographic and behavioural variables. Socio-demographic variables were collected through a structured form, applied by pairs of previously trained interviewers. The socio-demographic variables were age (completed years and categorised into 20 to 39 years and 40 to 59 years), schooling (completed years) and menopause (yes or no). The behavioural variables were smoking (non-smoker, smoker and ex-smoker), alcohol consumption (the number of drinks consumed per drinking occasion: zero doses, one to seven doses, eight to fourteen doses and more than fifteen doses), sedentary time (screen time was evaluated, obtained by adding up the time individuals spent sitting watching television and/or using the computer on weekdays and weekends) and physical activity level, measured using the long version of the International Physical Activity Questionnaire, validated for the Brazilian population in young adults[9]. The physical activity level was estimated from the time of physical activity (in minutes) performed in one week, considering the domain of 'leisure'.

To assess the presence of comorbidities, participants were asked if they had a medical diagnostic of type 2 diabetes mellitus or systemic arterial hypertension and if they were using any medication to treat these comorbidities. Subsequently, a variable was created to assess the presence or absence of these comorbidities, grouping the affirmative answers to the questions mentioned above. Individuals were classified as having 'presence' of comorbidities when at least one of the answers was affirmative and with 'absence' of comorbidities when all answers were negative.

Anthropometric and body composition variables

Weight and height were measured based on the recommendations of Lohman, Roche, Martorell, 1988[10], using calibrated equipment. Weight was measured using a digital scale (Tanita®), and height was measured using a fixed-rod stadiometer, attached to the wall (Welmy®). BMI was calculated by the ratio between weight in kilograms and height in metres squared (kg/m^2). BMI categorisation was performed based on cut-off points established by the WHO[2], grouping individuals into three categories: (1) eutrophy; (2) overweight and (3) obesity.

Waist circumference (WC) was measured in triplicate, adopting the mean of the three measurements. The measurement occurred during the participant's expiration, at the midpoint between the last rib and the iliac crest, using a flexible and inelastic tape (Sanny®). WC was classified as high when ≥ 102 cm for men and ≥ 88 cm for women[11]. The hip circumference was measured under the largest bulge in the gluteal region, also in triplicate, at the end obtaining the average of the three measurements. The waist:hip ratio (WHR) was obtained by the ratio between WC and hip circumference and was considered high when ≥ 0·90 for men and ≥ 0·85 for women[11]. The waist:height ratio (WHtR) was calculated by the ratio between WC and height and categorised as normal when WHtR < 0·5 and altered when WHtR ≥ 0·5, for both sexes[3]. All measurements were performed by previously calibrated evaluators.

Body composition was determined by dual energy X-ray absorptiometry in a DPX-IQ#5781 device (Lunar Radiation®) and usingEnCORE® software version 13·3. The evaluation was performed by a technician specialised in radiological evaluations, with the individual being evaluated in the supine position. To classify the percentage of body fat (%BF), the cut-off points determined by Lohman[12]were adopted, considering high %BF when ≥ 25 % for males and ≥ 32 % for females.

Individuals who had WC, WHR, WHtR and %BF values lower than the cut-off points used were considered reference individuals in the multiple analyses. In the case of BMI, which has been classified into three categories, individuals with obesity were compared with individuals classified as eutrophic (reference individuals for BMI).

Inflammatory cytokines

Blood samples were collected by peripheral intravenous puncture after 12 h of fasting. The samples were centrifuged for 15 min at 3000 rpm, and the serum was subsequently frozen

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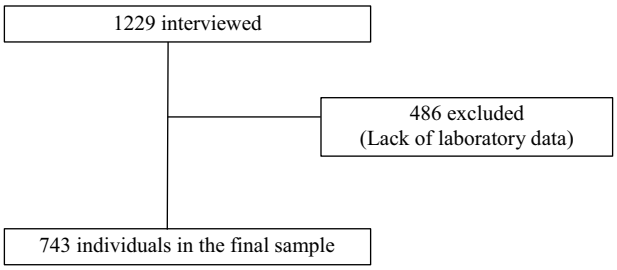

Fig. 1. Flowchart of selection of study participants. Viçosa, MG, Brazil, 2012–2014.

in an ultrafreezer at −80°C. Thawing was performed only on the day the analyses were performed. For the analysis of cytokines (IL-1β, IL-6, IL-8, IL-10 and IL-12p70 TNF-α), the human inflammatory cytokines Cytometric Bead Array Kit (Becton Dikinson) was used according to the manufacturer's instructions, and a feasibility test was also carried out. Results were expressed in picograms per milliliter (pg/ml).

Statistical analysis

Statistical analyses were performed using the STATA® statistical program, version 14·0 for Windows. Data normality was assessed using the asymmetry coefficient (considering normal distribution when Skewness < 0·5 and Kurtosis < 3·0). Descriptive analyses were presented through tables as means, SE and 95 % CI for continuous variables and proportion, SE and 95 % CI for categorical variables. All analyses were adjusted for the effect of study design and weighted by sex, age and schooling (using the 'svy' command in STATA®). The weights were determined by the ratio between the proportions of the study sample and the census carried out by the Brazilian Institute of Geography and Statistics[13].

Multiple linear regression was conducted to determine the association between cytokines (dependent variables) and anthropometric and body composition indicators (independent variables). The analysis was stratified by sex, with categorised anthropometric indicators, allowing the assessment of individuals classified with high measures compared with reference individuals. The model was adjusted for confounding variables, which were determined by biological and epidemiological relevance (age, smoking, alcohol consumption, sedentary time, physical activity level, presence of comorbidities and menopause). Adjusted β coefficients were used as a measure of association. It was used to indicate the difference, for more or less, of the cytokine concentrations of individuals classified with high anthropometric parameters compared with reference individuals (which had normal anthropometric measurements, below the cut-off points used). The multicollinearity between the variables was also evaluated by the variance inflation factor. Residuals were normally distributed for the final model.

The sample size was calculated using the OpenEpi software by difference of means, based on a previous study with a similar design. The only outcome with a significant difference in means between the groups was TNF-α, which showed a higher concentration in the group of individuals with obesity and was considered for our calculation[14]. A study power of 80 % and a confidence interval of 95 % were considered, and a calculation of 286 individuals was obtained. Including a design effect of 2·0, an additional 10 % for confounding factors and 10 % for possible losses, a final sample calculation of 692 individuals was obtained.

Ethical aspects

This study was conducted in accordance with the guidelines established in the Declaration of Helsinki, and all procedures involving human beings were approved by the Ethics Committee of the Federal University of Viçosa (protocol 1 104 521). Written informed consent was obtained from all participants.

Results

The sample was composed of 743 adults, being 55·84 % female and 44·16 % male, with mean age of 38·80 and 35·46 years, respectively. Other socio-demographic, behavioural, anthropometric characteristics and the means of inflammatory cytokines are shown in Table 1. Among the characterisation variables, there was a difference in age between the sexes, with women having a higher mean than men. Women in the sample also had lower physical activity level, lower consumption of alcohol and higher prevalence of comorbidities than men. Among the anthropometric indicators evaluated, there is a significant difference between the sexes for WC, WHR and %BF, with female individuals presenting a higher prevalence of inadequacy when compared with males, as shown in Table 1.

Tables 2 and 3 present crude and adjusted β values, as well the 95 % CI of the multiple analyses stratified by sex. It was observed that WC, BMI and WHtR are positively associated with the levels of some of the evaluated cytokines in males. In women, some cytokines were associated with WC, WHR and BMI.

Men in the sample categorised with high WC have, on average, greater serum concentrations of IL-1β (3·52 pg/ml; 95 % CI 0·60, 6·45), IL-6 (6·35 pg/ml; 95 % CI 0·35, 12·34), IL-8 (8·77 pg/ml; 95 % CI 2·37, 15·17), IL-10 (3·09 pg/ml; 95 % CI 0·56, 5·61), IL12p70 (8·31 pg/ml; 95 % CI 3·11, 13·52) and TNF-α (4·22 pg/ml; 95 % CI 0·20, 10·48). A positive association was also observed between WHtR and concentrations of IL-6 demonstrating that men categorised with high WHtR have, on average, greater serum concentrations of IL-6 (3·21 pg/ml; 95 % CI 0·02, 6·39). BMI was positively associated with all cytokines, showing that men categorised with obesity by BMI have greater levels of IL-1 β (1·50 pg/ml; 95 % CI 0·46, 2·34), IL-6 (2·97 pg/ml; 95 % CI 0·78, 5·16), IL-8 (4·48 pg/ml; 95 % CI 2·21, 6·75), IL-10 (1·31 pg/ml; 95 % CI 0·30, 2·31), IL-12p70 (3·59 pg/ml; 95 % CI 1·24, 5·95) and TNF-α (2·00 pg/ml; 95 % CI 0·81, 3·19).

Women in the sample categorised with high WC have, on average, greater serum concentrations of IL-6 (5·10 pg/ml; 95 % CI 0·68, 9·51) and IL-10 (4·16 pg/ml; 95 % CI 1·26, 7·06). BMI was also positively associated with IL-6, showing that female categorised with obesity by BMI have greater levels of this cytokine (2·67 pg/ml; 95 % CI 0·34, 4·99). WHR was associated with TNF-α, demonstrating that woman categorised with

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Table 1. Distribution of volunteers according to socio-demographic, behavioural, anthropometric and inflammatory biomarkers variables. Viçosa, MG, Brazil, 2012–2014
(Mean values with their standard errors; 95 % confidence intervals)

	Male (44·16 %)			Female (55·84 %)		
Variable	Mean or proportion	SE	CI (95 %)	Mean or proportion	SE	CI (95 %)
Age (years)	35·46	0·72	34·05, 36·87	38·80	0·59	37·64, 39·96
Age (%)						
20–39	63·70	4·52	54·03, 72·36	52·32	3·62	44·89, 59·64
40–59	36·30	4·52	27·63, 45·96	47·68	3·62	40·35, 55·10
Schooling (Years)	11·98	3·58	11·28, 12·69	10·87	3·55	10·17, 11·56
Level of physical activity (minutes per week)	148·60	14·14	120·85, 176·94	85·93	8·90	68·44, 103·41
Sedentary time (%)						
Tertile 1	31·57	4·65	22·87, 41·78	41·70	3·75	34·27, 49·53
Tertile 2	33·21	2·72	27·87, 39·01	34·12	2·90	28·44, 40·29
Tertile 3	35·22	3·72	28·02, 43·16	24·18	2·94	18·66, 30·69
Smoking (%)						
Non smoker	64·74	2·90	58·84, 70·20	71·41	2·68	65·87, 76·37
Smoker	16·24	2·09	12·53, 20·78	11·57	2·09	8·51, 15·53
Ex-smoker	19·02	2·67	14·32, 24·82	17·02	2·67	12·80, 22·26
Alcohol consumption (%)						
0 doses	10·98	1·76	7·85, 15·14	23·68	2·87	18·30, 30·04
1–7 doses	57·85	3·73	50·07, 65·25	68·15	2·60	62·59, 73·23
8–14 doses	14·08	1·88	10·64, 18·39	6·15	1·53	3·67, 10·14
15 or more doses	17·09	3·15	11·55, 24·53	2·01	0·01	1·07, 3·73
Menopause (%)						
No				82·07	2·23	77·03, 86·19
Yes				17·93	2·23	13·80, 22·96
Comorbidities (%)						
Absence	75·33	2·55	69·72, 80·18	61·20	3·37	51·10, 67·85
Presence	24·67	2·55	19·81, 30·27	38·80	3·37	32·14, 45·90
BMI (%)						
Eutrophy	47·85	4·01	39·79, 56·04	51·75	3·91	43·75, 59·66
Overweight	39·65	3·61	32·52, 47·23	28·66	2·24	24·28, 33·47
Obesity	12·50	1·92	9·06, 17·02	19·59	2·53	14·90, 25·29
BMI (kg/m^2)	25·11	0·29	24·51, 25·71	24·82	0·34	24·07, 25·58
WC (%)						
Normal	90·90	1·57	87·30, 93·54	74·40	2·73	68·68, 79·40
High	09·10	1·57	6·45, 12·69	25·60	2·73	20·59, 31·31
WC (cm)	86·17	0·79	84·54, 87·80	80·67	1·04	78·52, 82·81
WHR (%)						
Normal	67·11	2·97	61·03, 72·65	69·12	2·95	63·05, 74·59
High	32·89	2·97	27·34, 74·59	30·88	2·95	25·41, 36·95
WHR (ratio)	0·87	0·01	0·86, 0·89	0·81	0·01	0·79, 0·82
WHtR (%)						
Normal	56·83	4·76	46·92, 66·21	49·77	4·80	40·05, 59·50
High	43·17	4·76	33·79, 53·07	50·23	4·80	40·49, 59·94
WHtR (ratio)	0·50	0·01	0·48, 0·50	0·50	0·01	0·48, 0·52
%BF (%)						
Below or above average	48·46	3·49	41·68, 55,29	22·46	2·43	18·04, 27·57
High	51·54	3·49	44·70, 58·31	77·54	2·43	72·42, 81·95
%BF (mean)	24·40	0·63	23·10, 25·70	37·16	0·51	36·11, 38·20
Cytokines (pg/ml)						
IL-1β	9·36	0·42	8·54, 10·17	10·18	0·46	9·27, 11·08
IL-6	12·24	0·55	11·16, 13·31	13·62	0·62	12·40, 14·84
IL-8	27·37	0·95	25·49, 29·24	26·81	0·72	25·37, 28·24
IL-10	9·38	0·28	8·80, 9·97	10·20	0·47	9·23, 11·16
IL-12p70	17·98	0·72	16·55, 19·39	19·51	0·93	17·68, 21·34
TNF-α	10·66	0·46	9·75, 11·56	11·43	0·51	10·42, 12·44

EP, standard error; WC, waist circumference; WHR, waist:ratio; WHtR, waist:ratio; %BF, percentage of body fat; cm, kg/m², kilos per square meter; centimeters; pg/ml, picograms per milliliter; IL-1β, interleukin-1 beta; IL-6, interleukin-6; IL-8, interleukin-8; IL-10, interleukin-10; IL-12p70, interleukin-12p70; TNF-α, tumor necrosis factor alpha.

high WHR have, on average, greater concentration of this cytokine (2·84 pg/ml; 95 %IC 0·86, 6·54).

Discussion

To the author's knowledge, this is the first population-based Brazilian study that evaluated the association between different anthropometric and body composition measures and inflammatory cytokines in the adult population. The results showed that, in the evaluated sample, the indicators that had a positive association with inflammatory cytokines were WC, WHtR and BMI in men and WC, WHR and BMI in women, which partially confirms our hypotheses, since %BF showed no statistically significant association with any cytokine in both sexes. The results can

Table 2. Crude and adjusted multiple linear regression models with inflammatory cytokines as dependent variables and anthropometric and body composition variables as independent variables in men. Viçosa, MG, Brazil, 2012–2014
(Coefficient values and 95 % confidence intervals)

.	%BF†			WC†			WHR†			WHtR†			BMI†		
	β^*	β^{**}	CI 95 %	β^*	β^{**}	CI 95 %	β^*	β^{**}	CI 95 %	β^*	β^{**}	CI 95 %	β^*	β^{**}	CI 95 %
IL-1β	–0·36	0·76	–1·97, 3·49	2·25	3·52	0·60, 6·45	0·12	1·22	–2·07, 4·52	0·61	1·50	0·22, 3·21	0·51	1·40	0·46, 2·34
IL-6	1·17	2·98	–1·83, 7·79	5·23	6·35	0·35, 12·34	2·00	3·27	–2·82, 9·37	2·57	3·21	0·02, 6·39	2·05	2·97	0·78, 5·16
IL-8	0·32	4·12	–1·56, 9·82	6·50	8·77	2·37, 15·17	0·04	4·42	–3·12, 11·95	3·29	4·90	0·58, 9·23	2·35	4·48	2·21, 6·75
IL-10	–0·58	0·47	–1·95, 3·90	2·33	3·09	0·56, 5·61	–0·56	–0·02	–2·89, 2·85	0·22	0·89	–0·54, 2·31	0·60	1·31	0·30, 2·31
IL12p70	–0·64	2·16	–3·95, 8·29	4·75	8·31	3·11, 13·52	–1·71	–0·63	–5·28, 4·02	2·16	4·71	–0·13;9·56	1·55	3·59	1·24, 5·95
TNF-α	–0·31	0·82	–2·24, 3·88	2·94	4·22	0·20, 10·48	0·17	0·66	–2·34, 3·67	0·54	1·00	–1·52, 3·54	0·95	2·00	0·81, 3·19

* Crude analysis.
** Adjusted analysis; %BF, percentage of body fat; WC, waist circumference; WHR, waist:hip ratio; WHtR, waist:height ratio.
† Model adjusted for age (categorical), level of physical activity (continuous), smoking (categorical), sedentary time (categorical), alcohol consumption (categorical) and presence of comorbidities (categorical).

Table 3. Crude and adjusted multiple linear regression models with inflammatory cytokines as dependent variables and anthropometric and body composition variables as independent variables in women. Viçosa, MG, Brazil, 2012–2014
(Coefficient values and 95 % CI)

	%BF†			WC†			WHR†			WHtR†			BMI†		
	β^*	β^{**}	CI 95 %	β^*	β^{**}	CI 95 %	β^*	β^{**}	CI 95 %	β^*	β^{**}	CI 95 %	β^*	β^{**}	CI 95 %
IL-1β	–0·53	0·44	–2·14, 3·02	1·78	2·71	–1·28, 6·72	0·91	2·08	–1·61, 5·78	0·86	2·36	–1·67, 6·39	0·33	1·59	–0·06, 3·24
IL-6	0·50	0·23	–3·36, 3·83	3·53	5·10	0·68, 9·51	5·01	2·20	–2·54, 6·95	2·56	2·57	–2·03, 7·18	1·25	2·67	0·34, 4·99
IL-8	0·84	1·32	–3·34, 6·00	2·56	4·37	–4·01, 12·75	4·85	–3·27	–11·69, 5·14	2·60	3·44	–2·51, 9·40	–0·28	0·14	–3·71, 3·99
IL-10	–0·28	0·99	–1·35, 3·33	2·24	4·16	1·26, 7·06	1·83	–0·89	–3·67, 1·89	0·37	1·47	–1·50, 4·44	0·30	0·96	–0·61, 2·54
IL12p70	–0·83	1·63	–4·06, 7·33	4·57	7·03	–0·31, 14·39	3·03	2·50	–4·15, 9·17	1·68	4·38	–3·03, 11·79	0·23	2·59	–0·50, 5·69
TNF-α	–0·26	0·81	–3·27, 3·44	2·48	5·14	–0·39, 6·70	1·78	2·84	0·86, 6·54	0·55	0·84	–3·01, 4·70	0·13	1·46	–0·60, 3·52

* Crude analysis.
** Adjusted analysis; %BF, percentage of body fat; WC, waist circumference; WHR, waist:hip ratio; WHtR, waist-to-height ratio.
† Model adjusted for age (categorical), level of physical activity (continuous), smoking (categorical), sedentary time (categorical), alcohol consumption (categorical), menopause (categorical) and presence of comorbidities (categorical).

be generalised to populations with similar characteristics to those of the present study: adults living in urban areas, mainly in university cities.

There was a high prevalence of excess adiposity in the sample, as both sexes had a high %BF, being even more expressive among women. Among the anthropometric and body composition measurements evaluated, women had a higher prevalence of high %BF and WC, and men had a higher mean WHR. Although women in the sample had a higher prevalence of inadequacy in anthropometric parameters, cytokines were more associated with these indicators in males. This may be due to the difference in fat deposition between sexes, as women tend to store adipose tissue in the gynoid region and extremities, while men tend to store it mostly in the android region[15], and the literature suggests that visceral adipose tissue plays an important role in the inflammatory process[16]. Therefore, this difference in the location of fat deposition may have influenced the results of the multiple analyses.

Other factors may influence obesity-associated inflammation and were adjusted in our multiple analyses. About 17 % of the women in the sample had menopause, a factor that is associated with a greater deposit of visceral fat and higher concentrations of cytokines such as TNF-α and IL-6[17]. Alcohol consumption influences fat deposition, favouring lipodystrophy that contributes to the accumulation of fat in peripheral organs and the increase of inflammatory markers[18]. According to our results, men had a higher prevalence of consumption of high doses of alcohol, which may have influenced the observed associations. It was also observed that men evaluated were more physically active than women. The practice of physical activity can exert an immunoregulatory function and reduce the inflammation of adipose tissue[19]. On the other hand, sedentary behaviour can lead to several health damages, leading to a greater risk of developing obesity and its consequences[20]. Advancing age has also been shown to be associated with a remodelling in the pattern of cytokine expression, with a tendency to maintain a pro-inflammatory phenotype[21]. An expressive part of the sample was classified between 40 and 59 years old, mainly in females.

The relationship of chronic low-grade inflammation with the pathogenesis of comorbidities reinforces the importance of monitoring inflammatory markers[22]. Metabolic disorders, when accompanied by overweight, increase the risk of morbidity and mortality. A recent systematic review showed that individuals with obesity had high cardiometabolic risk factors and higher concentrations of inflammatory cytokines[23]. Additionally, the literature indicates that central obesity is the main cause of systemic inflammation[24,25], an association also evidenced by our results, especially in men. Evidence suggests that with the increase in WC, the risk of developing CVD and type 2 diabetes mellitus increases, in addition to a proportional increase in all-cause mortality[26]. Such consequences are associated with adipose tissue modifications and dysfunction due to adipocyte hypertrophy and hyperplasia, a situation that exacerbates the production of cytokines and increases the expression of several receptors, in addition to activating inflammatory signalling pathways[5,27].

Among the cytokines evaluated, IL-1β is a key cytokine in the developmentof DM2, as it plays an important role in the dysfunction and death ofpancreatic beta cells[28]. It also plays a role in the development of obesity-associated inflammation[29], and its concentrations are often greater in individuals with this condition[7], which we evidenced in males in our multiple analyses, since this cytokine was positively associated with BMI and WC.

IL-6 is considered a first-line cytokine that initiates subsequent inflammatory cascades in individuals with central obesity[30]. It also stimulates the production of C-reactive protein in the liver and is associated with the development of several diseases, such as CVD, cancer, pulmonary hypertension, type 2 diabetes mellitus and metabolic syndrome[31]. In our sample, this cytokine was associated with WC and BMI in both sexes and with WHtR in men. In a study carried out in Hong Kong with eighty-three individuals of both sexes, a higher mean concentration of IL-6 was found in individuals with central obesity when compared with individuals without obesity[30], a result that corroborates our study. Evaluating general obesity, a Brazilian cross-sectional study with adults evidenced higher means of IL-6 levels and BMI[32]. In our study, we found a positive association between these variables. Malshe and Udipi (2017)[33] evaluated the association between cytokine concentrations and WHtR in a sample of 1500 women and their study showed a positive correlation between WHtR and IL-6, but our findings evidenced this association only in men.

Our multiple analyses of males showed a positive association between IL-8 and IL-12p70 with WC and BMI. IL-8's main function is the chemotaxis of inflammatory cells, recruiting them to the inflamed site[34], and IL12-p70 is identified as a cytokine with a fundamental role in the development of atherosclerosis and metabolic syndrome[35]. Corroborating our results, Schmidt *et al.*[14] showed that individuals with central obesity had higher concentrations of IL-12. Straczkowski *et al.*[36] evaluated IL-8 concentrations in a sample of fifty-four adult individuals and observed that obese patients had greater concentrations of this cytokine when compared with non-obese individuals, which is also evidenced in our findings.

A result that deserves to be highlighted in our study is the positive association found between IL-10 and WC in both sexes, and with BMI in men, despite being considered an anti-inflammatory cytokine[37]. This cytokine has a protective effect on the development and progression of atherosclerosis[37]and on the preservation of insulin sensitivity[6]. Previous studies conducted with adults and children showed an inverse relationship between BMI and IL-10 level, indicating that obese individuals would have lower concentrations of this cytokine[38–40]. On the other hand, the findings by Schmidt *et al.* (2015)[14] corroborate ours, positively associating IL-10 with central obesity. There is evidence that the increase in visceral adipose tissue may be an alternative source of IL-10 secretion, which is commonly secreted by T cells and macrophages, which would explain the higher concentrations of this cytokine in individuals with a greater measure of WC[41].

TNF-α showed a positive association with WC and BMI in men and with WHR in women and its association with obesity is already well established in the literature[42]. TNF-α plays an important role in the development of obesity-related insulin resistance and atherosclerosis, in addition to increasing the

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secretion of other pro-inflammatory molecules, including IL-6[43]. Similarly to our study, a Mexican study with 147 healthy individuals showed higher concentrations of TNF-α in individuals with general obesity, but who also had a high WC measurement[44].

Among the anthropometric measurements analysed, we did not find an statistically significant association between inflammatory cytokines and %BF, even in the literature showing that the changes generated by excess adipose tissue are directly associated with inflammatory mechanisms[45]. It is noteworthy that the location of body fat is directly associated with inflammation, as the visceral adipose tissue demonstrates inflammatory characteristics and functions, mediating the chronic inflammatory process related to obesity[16]. Possibly, for this reason, the indicators related to central obesity (WC, WHR andWHtR) were associated with some of the evaluated cytokines in both sexes. This is a highly relevant finding for clinical practice since the pattern of fat distribution in adults is directly related to morbidity and mortality[11]and with the risk of developing CVD[16].

Based on the results presented, the importance of anthropometric assessment for public health is highlighted. The assessment of the presence obesity is of paramount importance to support strategies aimed at minimising the occurrence of possible metabolic complications resulting from chronic low-grade inflammation.

We highlight as strengths of our study, like the representativeness of the sample due to the population-based design, the methodological rigor and the training applied at all stages of data collection, as well as the carrying out of a pilot study. These aspects reinforce the quality and the validity of the results obtained. As a limitation, we point out that the primary study was not designed to assess inflammatory outcomes. However, we sought to minimise this limitation by adjusting our analyses for confounding factors.

Conclusion

In this cross-sectional population-based study, four of the five anthropometric indicators were associated with serum levels of inflammatory cytokines: WC, WHR,WHtR and BMI. A positive association was found in both sexes, but mainly in men. Our results reinforce the relevance of performing the anthropometric assessment, assessing general obesity and the distribution of body adiposity, for clinical practice and public health for the diagnosis and classification of obesity. Such assessment may help in decision making for health interventions aimed at reducing fat mass and, consequently, reducing the risk of developing metabolic complications associated with low-grade chronic inflammation.

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The authors declare no conflicts of interest

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