



## Original Article

## Relationship between body fat percentage and insulin resistance in adults with Bmi values below 25 Kg/M2 in a private clinic



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## ABSTRACT

**Aim:** To evaluate the association between elevated body fat percent (BF%) and the prevalence of insulin resistance (IR) in the adult population with body mass index (BMI) in the normal values.

**Methods:** We carry out an analytical cross-sectional study. The participants attended outpatient from 2012 to 2016 in a private clinic in Lima-Peru between 18 and 60 years with a BMI between 19 and 24.9/Kg/m<sup>2</sup>. We defined elevated BF% if the values were greater than 25% in men and 30% in women and IR with a cut-off point of HOMA-IR based in the 75th percentile. We performed a generalized linear model from family Poisson (crude and adjusted) with robust standard errors to evaluate the association between BF% and the IR. We reported as association measure the prevalence ratio (PR) with their respective 95% confidence intervals (CI).

**Results:** We included 284 participants, the average age was 33.77 ± 10.86 (SD) years and the percentage of women was 88.1%. The prevalence of elevated BF% was 71.13% and the prevalence of IR was 25%. We found an association between the elevated BF% and IR, PR = 3.17; 95% CI: 1.46–6.91.

**Conclusions:** Body fat percentage seems to be a good indicator of IR in patients with normal BMI and without endocrine comorbidities. Longitudinal prospective studies are recommended to corroborate our findings.

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## 1. Introduction

In the last years, the rate of obesity increased the global mortality and morbidity, and one of the possible reasons behind this is the insulin resistance (IR), a state where the body cannot respond properly to the insulin in the blood [1]. This condition has been associated with obstructive sleep apnea [2], polycystic ovary

syndrome (PCOS) [3], fatty tissue deposits [4], contrast-induced nephropathy during the percutaneous coronary intervention (PCI) [5], the severity of pancreatic ductal carcinoma [6], breast cancer in postmenopausal women [7] and endometrial cancer [8]. The prevalence of IR varies according to the study populations; the Afro-Americans, Hispanic and American Mexicans represent the majority of cases [9,10]. A recent group of the population on investigations are the normal-weight obese (NWO), which are people who have body mass index (BMI) in normal values but the body fat percentage (BF%) is increased [11]; the risk of them is similar as the obese category by BMI. Nowadays, tools like the bioimpedance analysis (BIA) allows fast and easy measurement of the BF%, which enables early diagnosis of them in the outpatient clinic [12].

In Peru, the prevalence of obesity is not different from the rest of the world which encourages the physicians to establish prevention measures in their daily activities, which includes early diagnosis in

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high-risk groups. Possibly, the NWO are a high-risk group with a small research focus in the country. The relationship of them with IR, a condition that worsens the obesity outcomes and can also be the trigger of it, is not known and may require prompt intervention. Therefore, the purpose of this investigation is to evaluate the association between elevated BF% and the presence of IR in a Peruvian population with BMI in normal values.

## 2. Methods

### 2.1. Design and population

We conducted an analysis from a previous database with an analytic cross-sectional design. Benites-Zapata et al. [13] used the received data in a study which found an association between thyroid hormones and IR in a healthy population group. The primary recompilation included outpatient adults between 2012 and 2014 that attended a private clinic in Lima-Peru. They excluded, pregnant, participants who consumed corticoids in the last three months or participants with duplicated, absent or aberrant data. There were a total of 600 people included with these selection criteria.

In this study, we review the clinical records from 2014 to 2016 with the same eligibility criteria of the primary study, which lead to a total of 2047 participants. We included adults between 18 and 60 years with a BMI between 19 kg/m<sup>2</sup> and 24.9 kg/m<sup>2</sup>. We excluded people with history of endocrine disease, fasting glucose greater than 126 mg/dl and thyroid hormone levels out of this normal ranges for triiodothyronine (FT3): 2.3–4.2 pg/mL; thyroxine (FT4): 0.89–1.76 ng/dL; and stimulant thyroid hormone (TSH): 0.40–5.0 uU/mL.

### 2.2. Sample and statistical power

After we applied the eligibility criteria we were left with 284 participants for the analysis (Fig. 1). For the calculation of statistical power, we will assume a ratio of exposed/unexposed of 0.5, a prevalence of 30% of IR in those with elevated BF%. Then, with the number of participants reached and a confidence level of 95%, we have an 80% statistical power to calculate prevalence ratios above 2.

### 2.3. Variables and measures

Our main outcome was IR, we considered IR present if the calculated value of Homeostatic Model Assessment (HOMA) - IR [Fasting glucose x Fasting insulin/405] was greater than the 75th percentile of the population [14]. In this study, the cut off value was 2.32. Our principal exposure variable was body fat percent (BF %), which was considered elevated if the value was equal or greater than 25% or 30%, in male and female, respectively [15]. The BF% values were measured with the portable device InBody 270 Body Composition Analyzer.

Other variables included in the analysis were sex, age (years), BMI (kg/m<sup>2</sup>) and the FT3/FT4 ratio, in order to avoid the collinearity between FT3 and FT4.

### 2.4. Statistical analysis

We performed statistical analysis with the software STATA v14.0. For the description, the proportions summarized the qualitative variables; while the mean and standard deviation (SD) represented the quantitative variables. In the comparison of two categorical variables, the chi-square test was done, and for the comparison of the numeric variables the T student and Wilcoxon test were chosen according to the symmetric distribution of the

variables. A descriptive linear regression between BF% and the numeric value of HOMA-IR was evaluated with a Pearson correlation and scatter plot. Also, we carry out a multivariate generalized linear model from the Poisson family (crude and adjusted) with robust variance. The variables included a priori in the multivariate model were age, sex, and FT4/FT3 ratio and were chosen by the review of literature [13,16]. The association measure was prevalence ratio (PR) with its respective 95% confidence interval (CI).

### 2.5. Ethical issues

The database was provided without identification codes to maintain the confidentiality of the participants and was approved by the Institutional Review Board of the Universidad Peruana de Ciencias Aplicadas (UPC).

## 3. Results

From a total of 2047 patients retrieved in the study period (2012–2016), we excluded 1763 participants because they showed BMI, age, FT3, FT4, TSH and fasting glucose levels outside of the ranges described in the selection criteria. In addition, we excluded two patients who did not have fasting insulin data. Thus, we analyzed 284 participants (Fig. 1).

The mean age of the participants was 33.77 ± 10.86 years, 254 (88.1%) were women and the mean BMI was 22.48 ± 1.58 kg/m<sup>2</sup>. In the population with elevated BF%, it is observed a higher proportion of women (97.5%,  $p < 0.001$ ) and a higher mean BMI (22.8 kg/m<sup>2</sup>,  $p < 0.001$ ) than those with normal BF%. Thyroid hormone tests obtained averages of 2.33 μU/mL for TSH and 2.61 for the T3L/T4L ratio and there were no statistically significant differences between the study groups (Table 1).

The prevalence of IR was 25% ( $n = 71$ ) and the prevalence de elevated BF% was 71.1% ( $n = 202$ ). There was a higher prevalence of IR in women than in men (25.3% vs 23.1%), and the average BMI was higher in the group with IR, both characteristics were statistically different in both study groups ( $p < 0.01$ ) (Table 2). The correlation between BF% and the logarithm of HOMA-IR was positive and weak ( $r = 0.28$ ,  $p < 0.001$ ) (Fig. 2).

The prevalence of IR was 31.68% and 8.5% in those with elevated and normal BF%, respectively. In the crude analysis, we observed that participants with elevated BF% increases by 3.71 times the prevalence of IR in comparison of participants with normal BF% (PR = 3.711, 95% CI 1.774–7.765). In the adjusted analysis for age (years) and sex, the association remains their statistical significance (PR = 3.172; 95% CI: 1.456–6.907). In adjusted analysis, when we added the variable FT3/FT3 ratio in the previous adjusted model, participants with elevated BF% increases the prevalence of IR by 3.6 times (PR = 3.558, 95% CI: 1.674–7.559). Finally, in the adjusted analysis for age, sex, FT3/FT4 ratio and BMI; participants with the elevated BF% increased by 2.73 times the prevalence of IR compared to those with normal BF% (PR = 2.732, 95% CI: 1.201–6.212). Table 3 shows the crude and adjusted Poisson regression models.

## 4. Discussion

We found an association between body fat percentage and insulin resistance in adults with a BMI in normal values. Thus, in this group, the prevalence of IR increased in those who have elevated body fat percentage compared with those in normal values. This relationship remained statistically significant despite adjusting for confounding variables such as BMI, thyroid hormones, age, and sex.

The association between BF% and RI has been reported in some previous studies. In a study developed in Brazil, Madeira et al., considered elevated the value of BF% > 23.1 in men and > 33.3 in

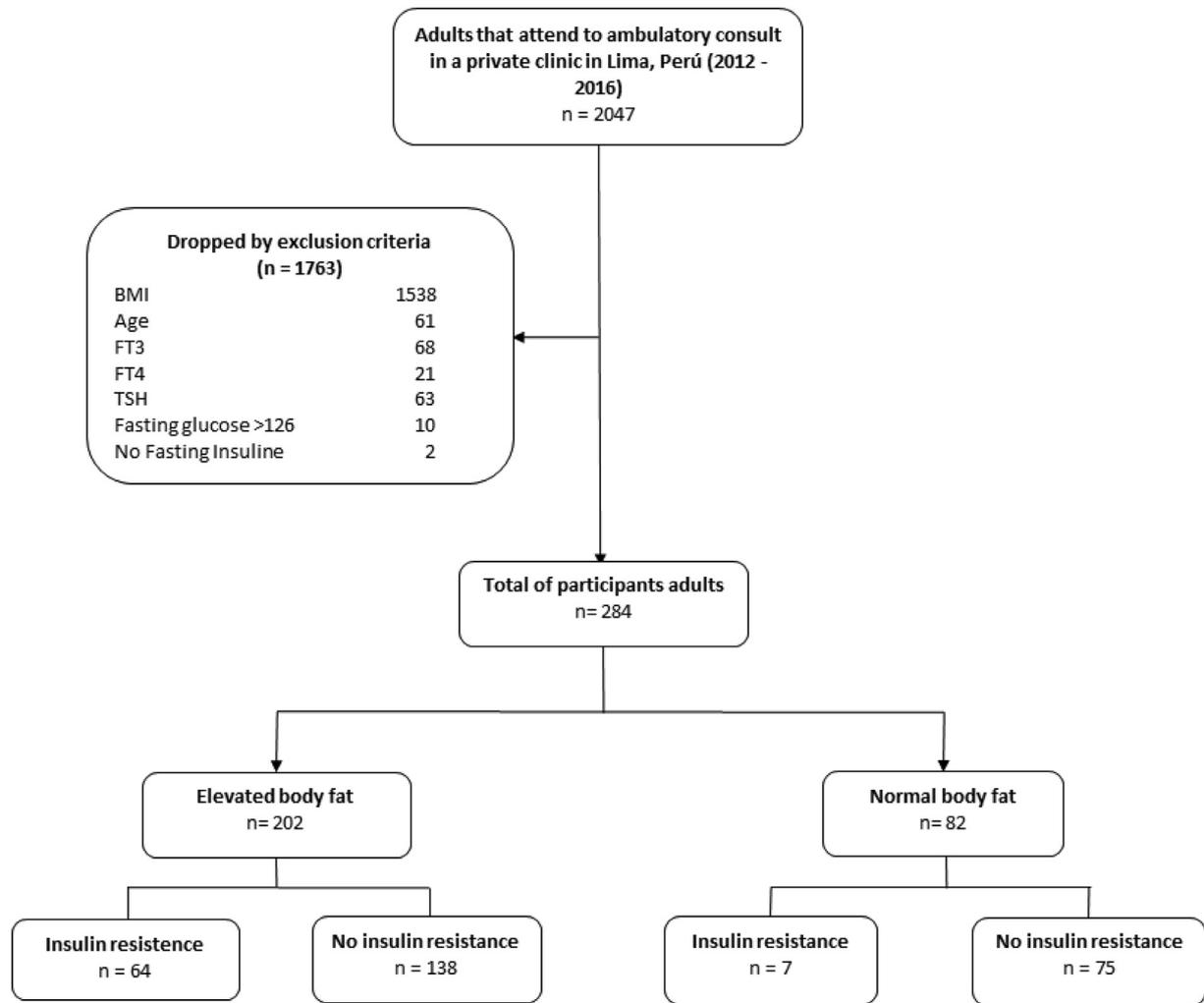


Fig. 1. Flow chart of adult's admission to the database 2012–2016 for the analysis.

Table 1

Characteristics of study population based on body fat.

Variables	General (n = 284)	Elevated (n = 202)	Normal (n = 82)	P value
Age (years)	33.77 ± 10.86	34.48 ± 10.93	32.04 ± 10.56	0.104
Sex				<0.001
Male sex	32(11.27)	5(2.58)	27(32.93)	
Female sex	254(88.81)	197(97.5)	55(67.1)	
BMI (kg/m <sup>2</sup> )	22.48 ± 1.58	22.82 ± 1.42	21.62 ± 1.63	<0.001
TSH (μU/mL)	2.33 ± 1.06	2.34 ± 1.02	2.32 ± 1.14	0.901
T3F/T4F ratio	2.61 ± 0.42	2.58 ± 0.42	2.69 ± 0.41	0.06

Data presented as average ± standard deviation or frequency (percentage). BMI: Body mass index; TSH: Thyroid stimulating hormone; T4F: Free thyroxine; T3F: Free triiodothyronine.

women, and in a population of adults between 23 and 25 years with normal BMI. They found that those who meet this definition have more HOMA-IR points than those who do not [17]. Likewise, Martínez et al. found a positive relationship between BMI levels increased and the HOMA-IR levels increased. The prevalence of IR was 45% higher in the group of adults with normal BMI and elevated BF% compared with those with normal BMI with normal BF%, adjusted for confounding variables such as age, sex, race, and physical activity [18]. Therefore, the classification of people based on the increased levels of BF% appears to be a better indicator of adiposity within this apparently "normal" group according to BMI. In the same way, in other populations, such as women with

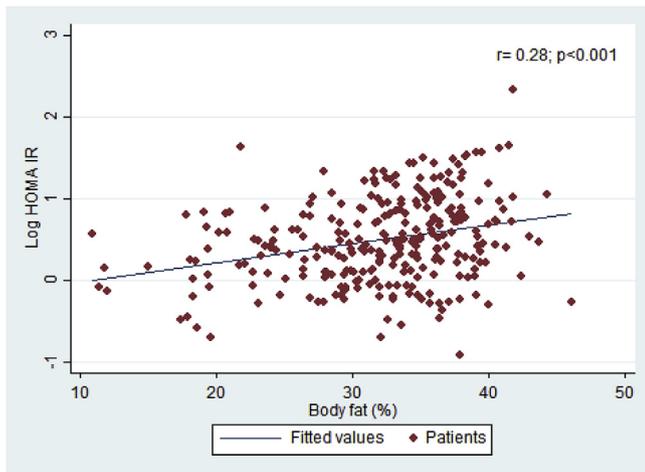
polycystic ovary syndrome, geriatric patients the results were like this study [19,20].

Our study preferred to use the percentage of body fat percentage since several studies endorse the importance to facilitate its use in clinical practice. There is still controversy because several studies have suggested that the intra-abdominal adipose tissue (visceral) might be more useful to assess the development of IR. However, we consider that only a small proportion of total BF% is represented by the visceral fat (approximately 15%). The relationship between deposits of fat and IR could be explained by the decrease in the activity of GLUT4 transporters and, in turn, the reduction in the consumption of glucose [21].

**Table 2**  
Characteristics of study population based on insulin resistance.

Variables	Yes (n = 71)	No (n = 213)	P value
Body fat			p < 0.001
Elevated	64(31.68)	138(68.32)	
Normal	7(8.54)	75(91.46)	
Age (years)	32.97 ± 11.83	34 ± 10.54	0.473
Sex			0.009
Male	2(6.25)	30(93.75)	
Female	69(27.38)	183(72.62)	
BMI (kg/m <sup>2</sup> )	22.99 ± 1.60	22.30 ± 1.53	0.001
TSH (μU/mL)	2.42 ± 0.95	2.30 ± 1.09	0.429
T3F/T4F ratio	2.75 ± 0.42	2.57 ± 0.41	0.001

Data presented as average ± standard deviation or frequency (percentage). BMI: Body mass index; TSH: Thyroid stimulating hormone; T4F: Free thyroxine; T3L: Free triiodothyronine.



**Fig. 2.** Correlation between body fat percentage and logarithm of HOMA-IR values.

About the relationship between BF% and IR in populations with normal BMI, Yaghootkar et al. found genes such as IRS1, GRB14, ARL15, FAM13A, LYPLAL1, PEPD, PDGFC, RSPO3, PPARG, TET2 and ANKRD55 that could be related to this condition in which the family inheritance and the "subtly lipodystrophic" phenotype could predispose the development of IR despite the BMI [22]. Besides the fact that more studies are needed to corroborate our research, there are several works that could explain our findings.

There are several non-invasive methods for assessing BF%. A study in children evaluated the correlation between these measures and found that BMI, the sum of folds, body circumferences and BIA can be adequately correlated with fat mass found with dual-energy X-ray absorptiometry (DEXA scan). At the same time, recommend that when it is not practical, BMI and folds can be used [23].

However, using BMI classification does not include people with elevated BF in the obesity group so it is recommended to base a categorization using BF% [24]. In a population of Colombia, the

correlation between BIA and DEXA was observed, though BF% cannot be adequately estimated with BIA [25]. In other measures comparisons, it was found that the BF% measured with BIA overestimated the value found with DEXA in BMI values above 30, while the measurement of folds with Caliper underestimated it in all BMI groups. Thus, in the non-obese group both DEXA and BIA measurements showed no difference [26]; for the reasons mentioned above, considering the advantages of BIA like being non-invasive, safe, fast, low cost, portable, easy to use, and good consistency in repeated measurements [27].

According to our findings and evidence reviewed in previous studies, it is recommended to evaluate the BF% in daily clinical practice, and their use in the IR screening in populations with hereditary risk factors or lifestyle that may predispose to the development of metabolic syndrome, diabetes and cardiovascular diseases. This public health service can be done with BIA during health campaigns. Therefore, we believe that the screening for IR can be carried out in more population groups to initiate preventive work at younger ages for the benefit of the country. However, the BF% should be complemented with other indicators that have also been shown to be related to IR in normal BMI population, such as hip waist ratio, triglyceride/HDL ratio, and triglyceride and glucose index [28–30].

The main strength of our study is that covers a research topic in progress that can contribute widely to further other investigations about this. Therefore, those with normal BMI but with elevated BF% would have the same risk of IR as those with high BMI [31]. This study has certain limitations, the IR was not measured with the gold standard (the hyperinsulinemic-euglycemic clamping). However, the HOMA-IR has a good correlation with the hyperinsulinemic-euglycemic clamping. For adiposity, BIA has a sensitivity between 34% and 48.7%; and a specificity between 93% and 100% [15]. This could have an impact on the measurement bias in the study as the number of false negatives increased and the true positives decreased. Also, the cut-off point for IR used was not from a Hispanic population. However, since we did not find in the reviewed literature an optimal value for the general population and we wanted to facilitate the interpretation for the physicians, we used the cut-off point from a Caucasian population. This cross-sectional study does not allow to identify causality between variables, and due to non-probabilistic sampling in a single location, the prevalence found cannot be extrapolated to the entire population with normal weight in Peru. However, the association found has internal validity, since the number of included participants allowed the modeling of a multivariate regression model. At this point, since this study was based on a secondary basis, no other variables were added in the analysis. Among them, there are other parameters to measure adiposities such as abdominal perimeter or skin folds, and variables like socioeconomic level and physical activity that can be considered in future research [32].

## 5. Conclusion

Our study shows an association between elevated BF% and IR in an apparently healthy adult population with BMI normal values and

**Table 3**  
Poisson regression model crude and adjusted to assess the association between elevated body fat and insulin resistance.

Variables	Crude PR [CI 95%]	Adjusted PR * [CI 95%]	Adjusted PR ** [CI 95%]	Adjusted PR *** [CI 95%]
Normal body fat	Reference	Reference	Reference	Reference
Elevated body fat	3.711 [1.774–7.765]	3.172 [1.456–6.907]	3.558 [1.674–7.559]	2.732 [1.201–6.212]

\* Adjusted by age (years) and sex.

\*\* Adjusted by age (years), sex and T3F/T4F ratio.

\*\*\* Adjusted by age (years), sex, T3F/T4F ratio and BMI (kg/m<sup>2</sup>).

without evidence of metabolic diseases. Long-term prospective studies are needed to assess the role of BF% measurement in the early detection of IR with more sensitive methods.

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## Conflicts of interest

The authors have no potential competing interests.

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