



RESEARCH ARTICLE

**REVISED** Altitude and its inverse association with abdominal obesity in an Andean country: a cross-sectional study [version 2; peer review: 2 approved, 1 not approved]

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**Abstract**

**Background:** Abdominal obesity represents an accurate predictor of overall morbidity and mortality, which is worrisome because it is also continuously increasing across Andean countries. However, its relationship with altitude remains unclear. The objective of this study was to assess the association between altitude and abdominal obesity in Peru, and how sociodemographic variables impact this association.

**Methods:** We estimated the prevalence of abdominal obesity in Peru and analyzed its association with altitude using the data from the 2012-2013 National Household Survey (ENAH). During this survey, a representative sample of Peruvians was screened for abdominal obesity, using waist circumference as a proxy, and the Adult Treatment Panel III guidelines cutoffs.

**Results:** Data were analyzed from a sample of 20 489 Peruvians (51% male). The prevalence of abdominal obesity was estimated at 33.6% (95% CI: 32.5 to 34.6%). In Peru, altitude was significantly and inversely associated with abdominal obesity, decreasing with higher altitudes: 1500-2999 meters above mean sea level (MAMSL) vs <1500 MAMSL, adjusted prevalence rate [aPR]= 0.90 (95% CI: 0.84 to 0.96); ≥3000 MAMSL vs <1500 MAMSL, aPR= 0.78 (95% CI: 0.72 to 0.84), when adjusting by age, gender and residence area (rural/urban). However, this association was significantly modified by age and gender ( $p < 0.001$ ).

**Conclusion:** Abdominal obesity is highly prevalent in Peru and decreases significantly with altitude, but age and gender modify this association. Thus, abdominal obesity appears to affect older women from low altitudes more than younger men from high altitudes.

**Keywords**

Abdominal obesity, Altitude, Obesity, Waist Circumference, Peru

**Open Peer Review**

Reviewer Status

	Invited Reviewers		
	1	2	3
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	↑		
version 1 published 10 Oct 2019	 report	 report	 report

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**REVISED Amendments from Version 1**

We modified the abstract reporting the PR obtained by the adjusted model without interaction terms.

In the introduction, we include more indicators of abdominal obesity. Likewise, we took into account other suggestions.

We included more information about sampling, how we estimated variables and interaction analysis.

In the result section, we corrected the paragraph related to the residence area associated with obesity. In Table 5, we incorporated a column with the adjusted prevalence rate without interaction terms.

Finally, we included the references suggested by reviewers.

**Any further responses from the reviewers can be found at the end of the article**

**Introduction**

The increasing prevalence of obesity represents a significant public health problem across low- to high-income countries<sup>1</sup>. The main reason is that obesity is strongly associated with morbidity and mortality, mostly due to type 2 diabetes, cancer and cardiovascular diseases<sup>2</sup>. However, body fat distribution, particularly that of abdominal obesity, has been reported as a better predictor of overall morbidity and mortality than total adiposity or obesity defined by body mass index (BMI)<sup>3,4</sup>. Furthermore, abdominal obesity is difficult to diagnose in routine clinical care because it requires access to computed tomography<sup>5</sup> or magnetic resonance imaging<sup>6</sup> for precise quantification. Anthropometric measures of abdominal obesity include waist circumference, waist-to-height ratio, waist-to-hip ratio, and the conicity index<sup>7,8</sup>. Thus, the most commonly used surrogate to diagnose abdominal obesity in clinical care and research examinations is waist circumference<sup>9,10</sup>.

In Peru, as in most Latin-American countries, the prevalence of obesity among children, adolescents and adults have grown consistently in recent decades. Among Peruvian adults, estimates of the national prevalence of obesity have grown from approximately 9% in 1975 to 21% in 2017<sup>11</sup>. However, this prevalence seems to vary substantially by altitude<sup>12</sup>.

Epidemiological studies carried out in the United States<sup>13</sup> and Peru<sup>12</sup> among adults and children<sup>14</sup> have described an inverse association between altitude and obesity. A previous study reported that the prevalence of obesity in Peru decreases by approximately 26% at between 1500–2999 meters above mean sea level (MAMSL), and by 46% at over 3000 MAMSL, as compared to at 0–499 MAMSL<sup>12</sup>.

Consequently, this study further assesses the association between altitude and abdominal obesity, when adjusted by standard sociodemographic variables. Additionally, we plan to estimate the prevalence of abdominal obesity by different cutoffs.

**Methods****Study design**

The study employed a cross-sectional multistage study design. Data were accessed from the **Peruvian National Household Survey (ENAHO)**, undertaken annually by the Peruvian National Institute of Statistics and Information (INEI) and the National Center for Food and Nutrition (CENAN) to assess social living conditions. For this purpose, the INEI and CENAN surveyed a representative sample of the Peruvian population using a probabilistic, stratified, multi-stage design, independent for each region, to collect data on participants of  $\geq 2$  months of age<sup>15</sup>. Briefly, the ENAHO sample household residents from all regions of Peru (third sampling level), sampling clusters of one or more blocks of ~120 houses (second sampling level) and sampling cities with 2000 or more inhabitants in the urban area or 500–2000 inhabitants in the rural area (first sampling level). ENAHO survey eligibility criteria were Peruvian households inhabitants, including family members, non-family members and domestic workers (with or without payment) that cohabitated during the 30 days prior to the survey, excluding pensions of 10 or more inhabitants<sup>15</sup>. In this study, we used ENAHO 2013 data to assess the prevalence of abdominal obesity and its association with altitude, while adjusting for their primary demographics and design effect. Out of 45 164 observations, people aged 20 years or older were included. We excluded pregnant women, and those observations with unreliable data.

**Variables of interest**

The study outcome was abdominal obesity: we used waist circumference (WC) as a proxy for its diagnosis. During the ENAHO survey, trained personnel measured the subject's WC at the vertical position of the midpoint between the lowest rib and the border of the iliac crest<sup>10</sup>. We interpreted this measurement by using the cutoffs proposed by Adult Treatment Panel III guidelines (ATP III) for abdominal obesity: WC >102 cm for men and >88 cm for women<sup>16,17</sup>. Additionally, for comparison, we assessed the cutoffs proposed by the Latin-American Diabetes Association (ALAD): WC  $\geq 94$  cm for men and  $\geq 88$  cm for women<sup>18</sup> and that of the International Diabetes Federation (IDF): WC >90 cm for men and >80 cm for women<sup>19</sup>. Furthermore, we define abdominal obesity as a weight to height ratio (WtHR)  $\geq 0.5$ <sup>20</sup> and obesity as a BMI  $\geq 30$  kg/m<sup>2</sup>. For this purpose, WtHR was defined as subject's waist circumference divided by their height, both measured in cms.; and BMI was defined as the body weight (kg) divided by the square of the body height (m<sup>2</sup>).

To facilitate comparisons and interpretability, we categorized altitude (measured by GPS) as low (<1500 MAMSL), moderate (1500–2999 MAMSL), and high ( $\geq 3000$  MAMSL). Likewise, individuals were categorized by age as young adults (20–39 years), adults (40–59 years) and elders ( $\geq 60$  years). We classified the area of residence as rural using ENAHO/INEI standard definition, which define an area as rural or rural town, if has no more than

100 contiguous households grouped or have more than 100 households scattered or disseminated without forming blocks or cores<sup>15</sup>. Nutritional status was assessed by BMI and categorized using WHO standard cutoffs as underweight (<18.5 kg/m<sup>2</sup>), normal (18.5–24.9 kg/m<sup>2</sup>), overweight (25–29.9 kg/m<sup>2</sup>), and obese (≥30 kg/m<sup>2</sup>)<sup>21</sup>.

### Statistical analysis

We estimated the prevalence of abdominal obesity by considering survey sampling weights by using STATA survey (svy) commands and excluding registers with missing study outcomes. We assessed bivariate correlation by estimating the Spearman's rank-order correlation coefficient. Considering that the prevalence of abdominal obesity in Peru is not rare<sup>11</sup>, we estimated the adjusted prevalence ratio as a measure of association instead of the odds ratio<sup>22</sup>. Thus, we used a log-binomial regression model that has robust variance, rather than a Poisson regression model, to adjust our prevalence ratio estimates by gender, age group and area of residence<sup>23</sup>. Finally, we tested for interaction between gender and altitude, and between age and altitude using the Wald test because of the consensus that obesity prevalence vary by gender and age<sup>3</sup>. All statistical analyses were performed using STATA/MP 14.0 for Mac (StataCorp LP, College Station, TX), and the results of statistical tests were interpreted and summarized with 95% confidence intervals.

### Ethical statement

According to the Regulation of Ethics in Research of the Peruvian National Institute of Health, this study did not require approval or exemption from an ethics committee because the database is publicly available. Study dataset was published using Figshare, which requested to hide subjects' age and to strictly limit the data availability to only the variables analyzed in this study.

## Results

### Characteristics of the study population

We analyzed a population sample of 20 489 subjects from 703 different locations across 25 administrative regions of Peru. To summarize population demographics, most subjects were either female (51.6%), adults between 20 to 39 years of age (39.8%), or inhabitants from urban areas (79.6%)<sup>24</sup>. Of these three demographic measures, both age groups ( $p=0.0006$ ) and area of residence ( $p<0.0001$ ) distribution varied significantly by altitude (Table 1).

### Prevalence of obesity and abdominal obesity in Peru

The prevalence of abdominal obesity in Peru was 33.6% (95% CI: 32.5% - 34.6%) when using WC and the ATP III cutoff, 44.4% (95% CI: 43.2% - 45.6%) using the ALAD cutoff and 64.1% (95% CI: 63.0% - 65.2%) using the IDF cutoff

**Table 1. Peru's demographics by altitude level.**

Characteristics	Number of participants (%)			Total
	<1500 MAMSL	1500–2999 MAMSL	≥3000 MAMSL	
<b>Age (years)</b>				
20 to 39	5092 (40.7)	1262 (40.0)	1649 (36.4)	8003 (39.8)
40 to 59	4804 (37.8)	1226 (36.8)	1795 (38.0)	7825 (37.7)
≥60	2555 (21.5)	818 (23.2)	1288 (25.6)	4661 (22.5)
<b>Gender</b>				
Female	6796 (51.4)	1848 (52.0)	2703 (52.4)	11347 (51.6)
Male	5655 (48.6)	1458 (47.6)	2029 (47.6)	9142 (48.4)
<b>Residence area</b>				
Urban	9861 (89.4)	1744 (61.7)	2354 (57.3)	13959 (79.6)
Rural	2590 (10.6)	1562 (38.3)	2378 (42.7)	6530 (20.4)
<b>Body Mass Index</b>				
Underweight	139 (1.2)	46 (1.4)	93 (1.8)	278 (1.3)
Normal	4257 (33.1)	1614 (46.4)	2560 (52.1)	8430 (38.5)
Overweight	5317 (42.8)	1173 (37.2)	1578 (34.3)	8068 (40.5)
Obesity	2738 (22.9)	473 (15.0)	501 (11.8)	3712 (19.7)
<b>Abdominal obesity</b>				
By Waist ATP III	4402 (37.1)	893 (28.7)	1098 (24.3)	6393 (33.6)
By Waist ALAD	5683 (49.4)	1107 (37.0)	1394 (31.9)	8184 (44.4)
By Waist IDF	8330 (69.1)	1804 (57.2)	2342 (51.0)	12476 (64.1)
By WtHR >0.5	10632 (86.1)	2629 (80.8)	3666 (77.9)	16903 (83.9)

Parameters estimated considering the design effect and the complexities of the survey; WtHR, waist-to-height ratio; MAMSL, meters above mean sea level; ATP III, Adult Treatment Panel III guidelines; ALAD, Latin-American Diabetes Association; IDF, International Diabetes Federation.

(Table 1). Regardless of the cutoff used (i.e. ATP III, ALAD, or IDF), the prevalence of abdominal obesity decreased significantly ( $p < 0.001$ ) with altitude: abdominal obesity was more prevalent at low elevations (<1500 MAMSL), less prevalent at moderate elevations (1500–2999 MAMSL), and lowest at high elevations ( $\geq 3000$  MAMSL) (Table 1 and Figure 1).

Similarly, we estimated the prevalence of abdominal obesity in Peru using waist to height ratio (WtHR) to be 83.9% (95% CI: 83.1%-84.6%). Like the previous model that employed WC as a surrogate measure of abdominal obesity, the present model also demonstrated an inverse association between abdominal obesity and altitude category. In this model, the prevalence of abdominal obesity (as defined by WtHR) was 86.1% (95% CI: 85.1%-87.1%) for those at low altitudes, 80.7% (95% CI: 78.9%-82.7%) at moderate altitudes, and 77.9% (95% CI: 76.1% to 79.6%) at high altitudes ( $p < 0.001$ ) (Table 1).

We estimated the total prevalence of obesity in Peru by BMI to be 19.7% (95% CI: 18.9%-20.6%). Like that of abdominal obesity, the prevalence of obesity was inversely related to the categories of altitude that we defined. Obesity prevalence was 22.9% (95% CI: 21.7%-24.1%) at low elevations, 15.0% (95% CI: 13.5%-16.6%) at moderate elevations, and 11.8% (95% CI: 10.6%-13.1%) at high elevations for those living at or over 3000 MAMSL, respectively ( $p < 0.001$ ) (Table 1).

#### Variability of abdominal obesity by different cutoffs in Peru

Estimates of abdominal obesity prevalence vary significantly with altitude and in models that use different standard diagnostic cutoffs. When comparing the estimated prevalence of abdominal obesity using ATP III, ALAD and IDF cutoffs (Table 1 and Figure 1), there were significant differences between them

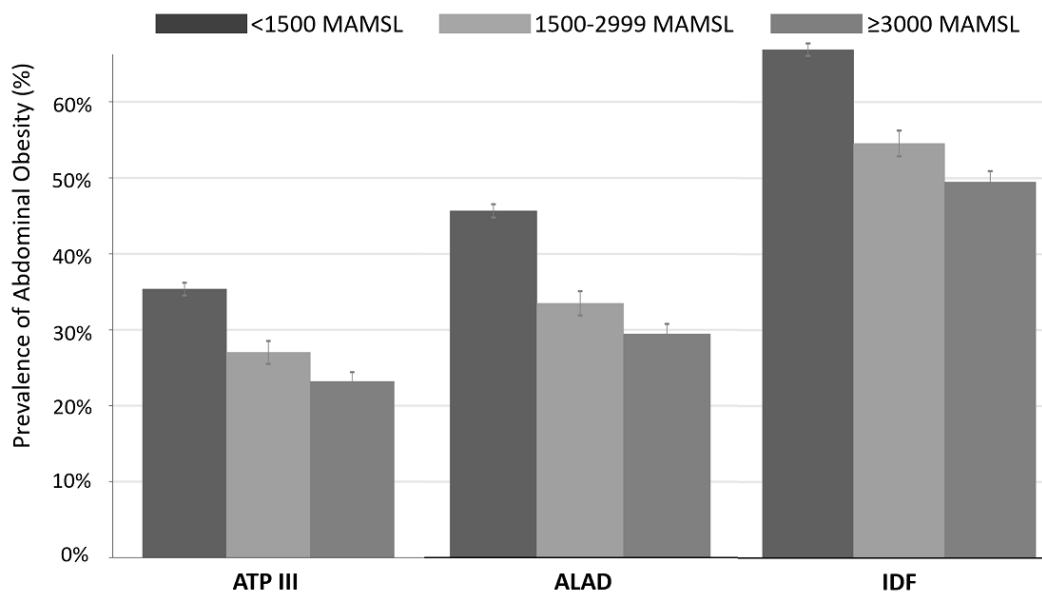
( $p < 0.001$  at each paired comparison). The same variability was observed regardless of age group, gender, and residence area (Table 2). Furthermore, in the correlation analysis (Table 3), we found that using the ATP III cutoff resulted in a stronger correlation with obesity by BMI (Spearman's  $\rho = 0.55$ ;  $p < 0.001$ ), as compared with the ALAD (Spearman's  $\rho = 0.53$ ;  $p < 0.001$ ) and IDF cutoffs (Spearman's  $\rho = 0.37$ ;  $p < 0.001$ ). However, the ATP III cutoff also has a weaker correlation with altitude (Spearman's  $\rho = 0.12$ ;  $p < 0.001$ ). Additionally, we found that the prevalence of abdominal obesity, as defined by WtHR  $> 0.5$ , has only a moderate correlation with the prevalence of obesity by BMI (Spearman's  $\rho = 0.43$ ;  $p < 0.001$ ) and a weak correlation with altitude (Table 3).

#### Variability of abdominal obesity by altitude in Peru

The prevalence of abdominal obesity and obesity vary significantly by altitude in Peru and are inversely associated with altitude category (trend analysis  $p < 0.001$  for both), regardless of age group, gender and residence area (Table 4). Both abdominal obesity and obesity prevalence were significantly higher among females than males ( $p < 0.001$  for both) and across urban areas than in rural areas ( $p < 0.001$  for both). The prevalence of obesity and abdominal obesity were significantly lower among young adults (20–39 years) than among adults (40–59 years); however, both obesity and abdominal obesity prevalence were significantly higher in young adults than elders ( $\geq 60$  years old).

#### Abdominal obesity and its association with altitude in Peru

Regression analyses demonstrated that the prevalence of abdominal obesity was significantly associated with altitude when either unadjusted and adjusted by age groups, gender, and residence. Additionally, we observed significant effect modification



**Figure 1. Prevalence of abdominal obesity by altitude and by different cutoffs.** ATP III, Adult Treatment Panel III guidelines; ALAD, Latin-American Diabetes Association; IDF, International Diabetes Federation; MAMSL, meters above mean sea level.

**Table 2. Abdominal obesity prevalence by demographic and nutritional factors at different altitude levels.**

	ATP III				ALAD				IDF			
	<1500 MAMSL % (95% CI)	1500–2999 MAMSL % (95% CI)	≥3000 MAMSL % (95% CI)	Total % (95% CI)	< 1500 MAMSL % (95% CI)	1500–2999 MAMSL % (95% CI)	≥3000 MAMSL % (95% CI)	Total % (95% CI)	<1500 MAMSL % (95% CI)	1500–2999 MAMSL % (95% CI)	≥3000 MAMSL % (95% CI)	Total % (95% CI)
<b>All</b>	37 (36-38)	29 (27-30)	24 (22-26)	34 (33-35)	49 (48-51)	37 (35-40)	32 (30-34)	44 (43-46)	69 (68-71)	57 (55-60)	51 (49-53)	64 (63-65)
<b>Age groups</b>												
20 to 39 years	25 (24-27)	19 (16-22)	20 (17-22)	24 (22-25)	35 (33-37)	25 (22-28)	24 (22-27)	32 (30-33)	56 (54-58)	46 (42-49)	45 (42-48)	53 (51-54)
40 to 59 years	44 (42-47)	38 (34-41)	31 (27-34)	41 (39-42)	58 (56-61)	48 (44-52)	40 (37-44)	54 (52-55)	78 (76-80)	68 (64-71)	58 (54-62)	73 (71-74)
≥60 years	47 (44-50)	31 (27-36)	22 (19-25)	39 (37-41)	61 (59-64)	41 (35-46)	30 (27-34)	52 (50-54)	79 (77-81)	60 (55-64)	49 (45-52)	70 (68-71)
<b>Gender</b>												
Female	56 (54-58)	44 (41-47)	40 (38-43)	51 (50-53)	56 (54-58)	44 (41-47)	40 (38-43)	51 (50-52)	80 (79-82)	71 (69-74)	66 (63-68)	76 (75-77)
Male	18 (16-19)	12 (10-15)	7 (5-8)	15 (14-16)	43 (40-45)	29 (26-32)	23 (26-38)	37 (35-39)	57 (55-59)	42 (38-45)	36 (31-38)	51 (49-53)
<b>Residence area</b>												
Urban	39 (37-40)	35 (32-37)	31 (29-34)	37 (36-39)	51 (50-53)	45 (43-48)	42 (39-45)	49 (48-51)	71 (70-72)	66 (63-68)	61 (58-64)	69 (68-70)
Rural	23 (20-25)	19 (16-22)	15 (13-17)	18 (17-20)	32 (29-36)	23 (21-26)	19 (16-21)	25 (23-27)	53 (40-56)	43 (40-47)	37 (34-41)	44 (42-47)

Estimates considering the design effect and the complexities of the survey; abdominal obesity estimated using the cutoffs proposed by Adult Treatment Panel III guidelines (ATP III); MAMSL, meters above mean sea level; ALAD, Latin-American Diabetes Association; IDF, International Diabetes Federation.

**Table 3. Correlation between altitude and each of our parameters of interest.**

	Altitude	BMI	Waist	WtHR	AO-ATP III	AO-ALAD	AO-IDF	AO-WtHR >0.5
BMI	-0.1872							
Waist	-0.2049	0.8406						
WtHR	-0.1437	0.8375	0.8997					
AO-ATP III	-0.1241	0.6396	0.6573	0.7264				
AO-ALAD	-0.1559	0.6823	0.7680	0.7539	0.8258			
AO-IDF	-0.1608	0.6175	0.6861	0.7067	0.5397	0.6536		
AO-WtHR >0.5	-0.1218	0.6349	0.7462	0.7552	0.5613	0.7007	0.6132	
Obesity	-0.1350	0.7438	0.6137	0.6271	0.5546	0.5330	0.3679	0.4340

All the correlations estimated in the table resulted in a p-value <0.001 when tested as equal to zero. BMI, body mass index; AO, abdominal obesity; WtHR, waist to height ratio; ATP III, Adult Treatment Panel III guidelines; ALAD, Latin-American Diabetes Association; IDF, International Diabetes Federation.

**Table 4. Obesity and abdominal obesity prevalence by demographic at different altitudes.**

Characteristics	Abdominal obesity **				Obesity by BMI*			
	Prevalence (95% CI)				Prevalence (95% CI)			
	<1500 MAMSL	1500–2999 MAMSL	≥3000 MAMSL	Total	<1500 MAMSL	1500–2999 MAMSL	≥3000 MAMSL	Total
<b>All</b>	37 (36-39)	29 (26-31)	24 (22-26)	36 (33-35)	23 (21-24)	15 (14-17)	12 (11-13)	20 (19-21)
<b>Age groups</b>								
20 to 39 years	25 (24-27)	19 (16-22)	20 (17-22)	24 (22-25)	18 (16-19)	10 (9-12)	8 (6-10)	15 (14-16)
40 to 59 years	44 (42-47)	38 (34-41)	30 (27-34)	41 (39-42)	27 (25-29)	20 (18-23)	17 (14-19)	24 (23-26)
≥60 years	47 (44-50)	31 (27-36)	22 (19-25)	39 (37-41)	25 (22-27)	15 (12-19)	10 (8-12)	20 (19-22)
<b>Gender</b>								
Female	56 (54-58)	44 (41-47)	40 (38-43)	51 (50-53)	26 (24-28)	20 (18-22)	18 (16-20)	23 (22-25)
Male	18 (16-19)	12 (10-15)	7 (5-8)	15 (14-16)	20 (18-22)	10 (8-12)	5 (4-7)	16 (14-17)
<b>Residence area</b>								
Urban	39 (37-40)	35 (32-37)	31 (29-34)	37 (36-39)	24 (23-25)	20 (17-21)	16 (15-17)	22 (21-23)
Rural	23 (20-25)	19 (16-22)	15 (13-17)	18 (17-20)	13 (11-15)	8 (7-10)	6 (5-7)	9 (8-10)

\*Estimates considering the design effect and the complexities of the survey; +, abdominal obesity estimated using the cutoffs proposed by Adult Treatment Panel III guidelines (ATP III); MAMSL, meters above mean sea level; BMI, body mass index; 95% CI, confidence intervals of 95%.

of this association by age group and gender, which seems to be particularly high at altitudes over 3000 MAMSL. Once adjusted by the interaction terms, the association between abdominal obesity and altitude varies significantly by gender, age group and residence area, with different patterns of distribution at different altitudes. At lower altitudes (<1500 MAMSL), the prevalence of abdominal obesity exhibits a positive trend increasing by age group, while above 1500 MAMSL, it exhibits an inverted-u shaped relationship (Figure 2).

#### Abdominal obesity and its associated factors in Peru

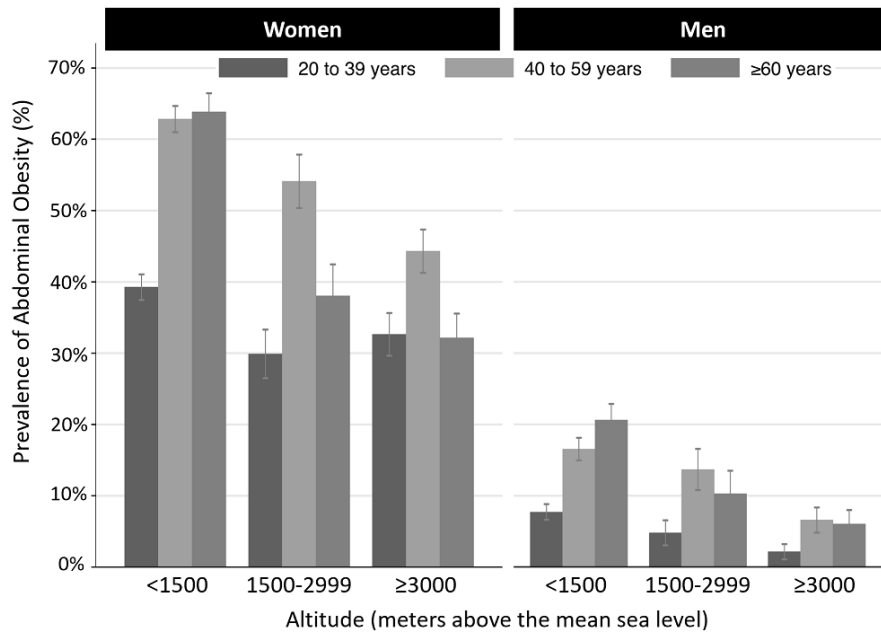
In the regression analysis, we found that altitude, age groups, gender, and residential area were significantly associated with the prevalence of abdominal obesity in Peru (Table 5). Based on our multivariate regression analysis outputs, we observed that the prevalence of abdominal obesity decreased with altitude, increased with age, and is lower among male and rural populations. However, contrary to what was observed for the prevalence of abdominal obesity by altitude in the case of gender and residence area, both of which decrease with altitude, the variability of the prevalence of abdominal obesity by age group exhibits different patterns of distribution at different altitudes.

Overall, the prevalence of abdominal obesity in Peru is higher among women ≥60 years living at <1500 MAMSL (68.4%; 95% CI, 64.6 to 71.9), and lower among men between 20 to 39 years of age living at ≥3000 MAMSL (2.8%; 95% CI, 1.6 to 4.8), exhibiting an inverted-u shaped relationship (Figure 2).

#### Discussion

The prevalence of abdominal obesity in Peru is high and decreases with altitude, an association that is modified by age and gender. This prevalence was higher among women over 60 years of age below 1500 MAMSL, and lowermost among men 20 to 39 years of age over 3000 MAMSL, exhibiting an inverted-u shaped relationship. Understanding the intricacies of this association is critical in countries with high elevation such as Peru, where approximately 20% of the Peruvian population lives at or above 3000 MAMSL<sup>25</sup>.

The usefulness of WC as an indicator of abdominal obesity is quite clear; however, there is a permanent discussion regarding the cutoffs for its diagnosis. WC varies by ethnic groups, which has generated the recommendation that each country or



**Figure 2. Prevalence of abdominal obesity (by Adult Treatment Panel III guidelines cutoffs) by age group and altitude.** The association between abdominal obesity and altitude vary greatly by gender and age group, which behave as effect modifiers.

**Table 5. Factors associated with abdominal obesity (by ATP III) in Peru.**

Factors	Unadjusted PR	CI 95%	Adjusted PR* w/o IT	CI 95%	Adjusted PR** w/ IT	CI 95%
<b>Altitude (MAMSL)</b>						
<1500	Ref.		Ref.		Ref.	
1500 to 2999	0.77	0.71 to 0.84 <sup>‡</sup>	0.90	0.84 to 0.96 <sup>‡</sup>	0.86	0.75 to 0.97 <sup>‡</sup>
≥ 3000	0.65	0.60 to 0.71 <sup>‡</sup>	0.78	0.72 to 0.84 <sup>‡</sup>	0.98	0.87 to 1.11 <sup>°</sup>
<b>Age group (years)</b>						
20–39	Ref.		Ref.		Ref.	
40–59	1.73	1.62 to 1.85 <sup>‡</sup>	1.67	1.57 to 1.77 <sup>‡</sup>	1.66	1.54 to 1.79 <sup>‡</sup>
≥60	1.66	1.55 to 1.79 <sup>‡</sup>	1.68	1.57 to 1.80 <sup>‡</sup>	1.77	1.64 to 1.91 <sup>‡</sup>
<b>Gender</b>						
Female	Ref.		Ref.		Ref.	
Male	0.29	0.26 to 0.32 <sup>‡</sup>	0.30	0.27 to 0.33 <sup>‡</sup>	0.33	0.30 to 0.36 <sup>‡</sup>
<b>Residence area</b>						
Urban	Ref.		Ref.		Ref.	
Rural	0.49	0.45 to 0.53 <sup>‡</sup>	0.57	0.52 to 0.62 <sup>‡</sup>	0.58	0.53 to 0.63 <sup>‡</sup>
<b>Altitude x gender</b>						
1500 to 2999 x Male					0.85	0.67 to 1.08 <sup>°</sup>
≥3000 x Male					0.5	0.38 to 0.66 <sup>‡</sup>
<b>Altitude x age group</b>						
1500 to 2999 x 40–59					1.17	1.01 to 1.36 <sup>‡</sup>
(1500 to 2999 x ≥60) or (≥3000 x 40 to 59)					0.95	0.83 to 1.08 <sup>°</sup>
≥3000 x ≥60					0.63	0.53 to 0.75 <sup>‡</sup>

Design effect was considered according to complex survey data; ATP III, Adult Treatment Panel III guidelines; PR, prevalence rates; IT, interaction terms; CI 95%, confidence intervals of 95%, MAMSL: meters above mean sea level; \*, Adjusted prevalence rate without interaction terms; \*\*, Adjusted prevalence rate with interaction terms; °, non-significant p-value; †, p-value <0.05; ‡, p-value <0.001.



region produces its cutoffs<sup>26</sup>. Worldwide, the most used cutoffs for WC are the ones proposed by the ATP III, which are primarily specific for adult European Caucasian populations<sup>16,17</sup>.

There are some efforts in Latin America to propose WC cutoffs for their population. A recent study carried out in five Latin American countries recommended using cutoffs of 90–92 cm for women and 94 cm for men<sup>27</sup>. In Peru, the PREVENTION study proposed WC cutoffs at high altitude (~2600 MAMSL) of 87 cm for women and 97 cm for men based on abnormalities of intima-media thickness and cardiovascular manifestations<sup>28</sup>. Similarly, different countries have proposed their cutoffs for WC, including Portugal (91 and 97 cm)<sup>29</sup>, China (80 and 84 cm)<sup>30</sup>, and South Asian countries (84 and 88 cm)<sup>31</sup>. In our study, different cutoffs produced a wide range of estimates for the prevalence of abdominal obesity. We observed that when using ATP III cutoffs, the estimated prevalence of abdominal obesity was over three times higher among women than in men (51% vs 15%).

Furthermore, regardless of altitude, these differences seem to be even larger  $\geq 3000$  MAMSL (40% vs 7%). These differences are similar to those reported previously<sup>32</sup>, so we believe they can be explained by both the altitude effect and the cutoffs itself, which are gender-differentiated. Further studies are needed to assess the necessity of specific cutoffs corrected by altitude, gender, and age.

Another important finding of our study is that the prevalence of abdominal obesity varies significantly between urban and rural areas, a difference that remains consistent at different altitudes. As reported elsewhere, the prevalence of abdominal obesity in Peru is higher in urban areas than in rural areas<sup>33</sup>, but also shows a slower increase in time in WC compared to rural areas<sup>34</sup>. However, such a difference between urban and rural areas seems to increase with higher altitudes, ranging from 1.7:1 at <1500 MAMSL to 2.1:1 at  $\geq 3000$  MAMSL. This finding is relevant in countries with large populations living over 3000 MAMSL, due to the cardiovascular risk that this could imply.

Regardless of WC cutoffs utilized, the mean WC in the Peruvian population living at high altitudes is high. In our study, at >3000 MAMSL the mean WC among men was 87.1 cm and among women 86.0 cm, which are lower than those reported at ~3600 MAMSL in La Paz-Bolivia (93 cm in women and 93 cm in men)<sup>35</sup> and close to those reported at ~3660 MAMSL in Tibet (84.5 cm overall)<sup>36</sup>.

According to our results, by both WC and WtHR, Peruvians who live at higher altitudes have a lower prevalence of abdominal obesity than those living a lower altitude. This finding concurs with previous reports<sup>12,37</sup>; moreover, a higher percentage

of overweight (36.3% vs 25.3%), obesity (17.5% vs 8.5%), hypercholesterolemia (18.9% vs 14.6%), low HDL (45.7% vs 40.3%), hypertension (9.8% vs 3.9%) and glycemia >126 mg/dL (2.9% vs 0.9%) were observed in people living above 3000 MAMSL vs below 1000 MAMSL<sup>37</sup>. Overall, the lower cardiovascular risk observed at higher altitudes could be explained in part by the lower levels of urbanization and income, commonly reported in developing countries<sup>38</sup>. Also, it might be explained by the variability in the progress of the epidemiological transition in Peru observed at different altitudes<sup>39</sup>. It is important to highlight that a WtHR >0.5 seems to overestimate Peruvian abdominal obesity. Regardless of the evidence<sup>20</sup>, if we use a cutoff of 0.5, over 80% of the Peruvian population is classified as having abdominal obesity. Further studies are needed to assess the usefulness of such an indicator in Latin-American countries such as Peru.

We should mention as a limitation that the ENAHO is a cross-sectional survey that was meant to represent Peru's nutritional status, and the sample might not represent all altitudes of the country. Likewise, it is essential to emphasize that Peru is one of the few countries with many large populations over 3000 MAMSL. Therefore, the association between altitude and obesity could remain unnoticed at low altitude countries. Another limitation is the absence of variables such as socioeconomic status, education level, physical activity and diet. However, the area of residence (urban and rural) is a variable that encompasses socioeconomic and educational aspects in our country.

In conclusion, our study found that abdominal obesity is highly prevalent in Peru and that abdominal obesity varies substantially by altitude, age, gender, and urbanization. Overall, the prevalence of abdominal obesity decreases with altitude, but age and gender modify such association; abdominal obesity seems to affect older women from low altitudes more than younger men from high altitudes. These findings should help to guide interventions to reduce Peruvian's cardiovascular risk, which should be a matter of more significant concern in future years.

## Data availability

### Underlying data

Figshare: Altitude and its inverse association with abdominal obesity in an Andean country. <https://doi.org/10.6084/m9.figshare.9920234.v1><sup>24</sup>

This project contains the following underlying data:

- altitude\_abdominal\_obesity\_dataset.xls (demographic and abdominal obesity data for participants)

Data are available under the terms of the [Creative Commons Attribution 4.0 International license](#) (CC-BY 4.0).

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# Open Peer Review

Current Peer Review Status:   

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## Version 2

Reviewer Report 07 January 2020

<https://doi.org/10.5256/f1000research.24140.r58020>

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**Antonio Bernabe-Ortiz** 

CRONICAS Center of Excellence in Chronic Diseases, Cayetano Heredia University, Lima, Peru

Although authors have improved the manuscript, they have not addressed all the comments submitted in the first review.

### MAJOR CONCERNS:

#### Methods:

- If the ENAHO is conducted yearly, why to use the 2013 ENAHO? Why not to use the last one available? This needs to be explained or at least considered as a limitation.
- Was any criterion related to time living in high altitude (e.g. at least 6 months living in the city/area)? Are 30 days enough to see the potential impact of altitude on health? If not, please, add as limitation.
- How altitude was measured? Was GPS used for this? Only a simple calculation of the altitude of the city was used? Please explain. Usually, 2500 meters is used as the cutoff and not 3000... Since this variable is the main exposure, details should be given to understand if any misclassification could be introduced...
- Only those aged 20 years and more were included in the analysis? How about those between 18 to 20 years or those younger... why they were not included?
- Why education level and socioeconomic status were not confounders? As they are associated with obesity and people in high altitude settings, mainly rural, tend to have low SES and low education... should be they confounders? These variables are available in the ENAHO survey and must be included in analysis or demonstrate why not to include them?

#### Results:

- What do you mean for "703 different locations"? This part is not explained in the Methods section. Were they the areas with altitude information?

- Obesity prevalence must be standardized by age. Authors always said that the prevalence of obesity was lower in high altitude, but that is only the crude estimate... at least age standardization (if possible by sex also) must be conducted to say something like that.
- Please use appropriate graphs to see the inverted-u shape relationship... three points are not enough... use appropriate linear regression models? Or used more categories in the exposure variable... for example, an increase every 500 meters...

**Discussion:**

- What is the relevance of the findings? This is not clear as apparently the discussion is used only to compare results with other studies. A paragraph is needed to show the public health relevance of this association.
- I would also suggest to tone down some of the sentences as this is only a cross sectional study and not better analysis has been done to improve the understanding of the association between altitude and obesity prevalence.

**MINOR CONCERNS:**

- Change “Peruvian National Institute of Statistics and Information” for “Peruvian National Institute of Statistics and Informatics”.
- Please in Methods explain how what unreliable data defined.
- Usually there are no references in the Results section (verify #24).

**Competing Interests:** I know one of the authors, but we never worked together.

**Reviewer Expertise:** Noncommunicable diseases (type 2 diabetes, hypertension and obesity).

**I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.**

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**Version 1**

Reviewer Report 05 December 2019

<https://doi.org/10.5256/f1000research.22774.r56783>

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**Yuri Arnold Dominguez**

National Institute of Endocrinology (INEN), Havana, Cuba

In the topic number 1 and referring specifically to what was written in paragraph number one of the Introduction, I consider that not only the abdominal waist is the only predictor of abdominal obesity, there are other indicators as important as that, such as the Waist Index- size (taking into account that the

Peruvian population prevails people with short stature), the waist waist index, the conicity index, which are usually more accurate than mere measurement than the abdominal circumference. I recommend that this investigation be continued in a larger sample , that it is even necessary to evaluate risk factors such as physical activity and diet, which are major confounders.

Otherwise I catalogue the article as excellent.

**Is the work clearly and accurately presented and does it cite the current literature?**

Partly

**Is the study design appropriate and is the work technically sound?**

Yes

**Are sufficient details of methods and analysis provided to allow replication by others?**

Yes

**If applicable, is the statistical analysis and its interpretation appropriate?**

Yes

**Are all the source data underlying the results available to ensure full reproducibility?**

Yes

**Are the conclusions drawn adequately supported by the results?**

Yes

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Epidemiology of diabetes.

**I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.**

Reviewer Report 25 November 2019

<https://doi.org/10.5256/f1000research.22774.r56784>

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**Ugo Fedeli**

Regional Epidemiology Service, Padua, Italy

The paper is interesting and well written. I have few suggestions:

Methods, statistical analysis: please add some detail on interaction terms introduced in the log-binomial regression models; also in Results some interpretation about estimates obtained for the altitude x gender and altitude x age group would be useful for the reader.

Page 6, second paragraph: it is stated that abdominal obesity and obesity prevalence were higher across rural areas than in urban areas; possibly the contrary should be reported.

Table 5: my advice is to report in three separate columns estimates for unadjusted PR, adjusted PR without interaction terms, and adjusted PR with interaction terms (full model). It is not clear if PR reported in the Abstract are obtained from the full model; my advice is to report in the Abstract PR obtained by the adjusted model without interaction terms.

In Discussion it is reported that differences in socio-economic status might be captured by the urban/rural variable. Are there also differences in ethnic background by altitude?

Page 9, findings are summarized of a previous study reporting a higher percentage of overweight and other cardiovascular risk factors in people living above 3000 m vs. those living below 1000 m. However, these results seem to be in contrast with the present study; please explain.

**Is the work clearly and accurately presented and does it cite the current literature?**

Yes

**Is the study design appropriate and is the work technically sound?**

Yes

**Are sufficient details of methods and analysis provided to allow replication by others?**

Yes

**If applicable, is the statistical analysis and its interpretation appropriate?**

Partly

**Are all the source data underlying the results available to ensure full reproducibility?**

Partly

**Are the conclusions drawn adequately supported by the results?**

Yes

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** epidemiology of non-communicable diseases

**I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.**

Reviewer Report 04 November 2019

<https://doi.org/10.5256/f1000research.22774.r55852>

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**Antonio Bernabe-Ortiz** 

CRONICAS Center of Excellence in Chronic Diseases, Cayetano Heredia University, Lima, Peru

***Overall comment:***

This paper looks for the association between altitude and abdominal obesity. Although the idea is not novel, extra reports using existing data can help to understand better this. I would expect more details regarding the variables (exposure and outcome) used in the analysis. Moreover, any other kind of models, not that using only three categories for altitude would be more relevant, or verifying if the association is similar for overweight and obesity. This analysis can be improved by looking extra ways to see the association more than the traditional form to check that, for example, using linear regression if possible or polynomial models (quadratic at least).

***Major concerns:***

Abstract:

Please change it accordingly to comments below.

Introduction:

- Obesity has different indicators and in the reference is used similarly for BMI (overall obesity), waist circumference (abdominal obesity), etc. Please be careful and consistent with words used.
- Some longitudinal studies have been published showing the association of interest and they have not been considered here (e.g. PMID: 29472520<sup>1</sup>).
- What is the novelty in this paper? Is it altitude? Apparently not as shown in the longitudinal paper... is it the rurality? Usually rural areas are in high altitudes. Is waist circumference an easy measure to do? Is it routinely done?
- How the usefulness of waist circumference in high altitudes is evaluated in this paper? I think that is no part of this study as pointed out in the last part of the first paragraph.
- Any reference for the last sentence of the second paragraph?
- Third paragraph: is the risk of obesity decreasing due to altitude? The reference is a cross sectional study, so is it possible to talk about risk?

Methods:

- Study design: why this study is multicentric? How many centers were included? Please explain.
- If the ENAHO is conducted yearly, why to use the 2013 ENAHO? Why not to use the last one available?
- Please explain how the sampling was done? Stratified by what? How many stages does the sampling have?
- Was any criterion related to time living in high altitude (e.g. at least 6 months living in the city/area)? Are 30 days enough to see the potential impact of altitude on health?
- Why households with 10 or more inhabitants were excluded? Any explanation? What proportion of households in Peru has 10 dwellers or more? Are these decisions biasing results?
- How altitude was measured? Was GPS used for this? Only a simple calculation of the altitude of the city was used? Please explain. Usually, 2500 meters is used as the cutoff and not 3000... Since this variable is the main exposure, details should be given to understand if any misclassification could be introduced...
- Only those aged 20 years and more were included in the analysis? How about those between 18 to 20 years or those younger?
- How the rural index was built? Explain please... Any reference helping to understand this? I am pretty sure the ENAHO stratifies the sample by urban/rural settings... was not the case this time?

- Categorization of BMI is presented in different way compared to how it was analyzed... please be consistent in definitions used
- “We assessed bivariate association using...” Association of what? Do you mean correlation between definitions of abdominal obesity? What was the gold standard?
- “Thus, we used a log-binomial...” Why education level or socioeconomic status were not confounders? As they are associated with obesity and people in high altitude settings, mainly rural, tend to have low SES and low education... should be they confounders? I know these variables are available in the ENAHO survey... why were they excluded?
- Ethic statement: where the dataset is available... add the link and how to get the data... I know a dataset has been added using Figshare, but that it not all the info available in the ENAHO dataset.

#### Results:

- What do you mean for “703 different locations”? This part is not explained in the Methods section. Were they the areas with altitude information?
- Education level and socioeconomic status should be included in the info as they are available in the ENAHO dataset.
- Waist to height ratio (definition) should be included since the methods section.
- Was obesity prevalence standardized by age? Authors always said that the prevalence of obesity was lower in high altitude, but that is only the crude estimate... at least age standardization (if possible by sex also) must be conducted to say something like that.
- “... we found that using the ATP III cutoff resulted in a stronger correlation with obesity”... what kind of obesity? Defined by BMI? By WC? By WtHr?
- Please use appropriate graphs to see the inverted-u shape relationship... three points are not enough... use appropriate linear regression models? Or used more categories in the exposure variable... for example, an increase every 500 meters...
- Would be good to know if stratification variables were effect modifiers? What was the test used for this? Although this was defined a priori, it would be good to have these estimates...

#### Discussion:

- I would suggest discussing about the relevance of this paper in the context of other papers (mainly those longitudinal).
- What is the relevance of the findings? This is not clear as apparently the discussion is used only to compare results with other studies. I would also suggest to tone down some of the sentences as this is only a cross sectional study and not better analysis has been done to improve the understanding of the association between altitude and obesity prevalence.

#### **Minor concerns:**

- Correct grammar spelling.
- Paper should be reviewed by an English native speaker.

#### **References**

1. Carrillo-Larco RM, Miranda JJ, Gilman RH, Checkley W, Smeeth L, Bernabé-Ortiz A: Trajectories of body mass index and waist circumference in four Peruvian settings at different level of urbanisation: the CRONICAS Cohort Study. *J Epidemiol Community Health*. **72** (5): 397-403 [PubMed Abstract](#) | [Publisher Full Text](#)

**Is the work clearly and accurately presented and does it cite the current literature?**

No

**Is the study design appropriate and is the work technically sound?**

No



**Are sufficient details of methods and analysis provided to allow replication by others?**

No

**If applicable, is the statistical analysis and its interpretation appropriate?**

Partly

**Are all the source data underlying the results available to ensure full reproducibility?**

No

**Are the conclusions drawn adequately supported by the results?**

Partly

**Competing Interests:** I know one of the authors, but we have never worked together.

**Reviewer Expertise:** Noncommunicable diseases (type 2 diabetes, hypertension and obesity).

**I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.**

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