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ORIGINAL ARTICLE

Arterial blood gases and ventilation at rest by age and sex in an adult Andean population resident at high altitude

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Abstract

Purpose Arterial blood gases (ABG) are influenced by the altitude above sea level, age and sex. Most studies have been conducted at sea level and in small populations ascending to or residents at very high altitudes. Our objective was to evaluate the ventilation and ABG by age and sex in an Andean population resident at high altitude (2640 m).

Methods Analytical cross-sectional study was done in healthy volunteers. ABG and minute ventilation (VE) were measured. *T* test and ANOVA for differences by sex and age, and Pearson test for correlations between age, VE and ABG were performed.

Results We included 374 adults, 55% women from 18 to 83 years and hemoglobin of 15.7 ± 1.6 g/dl. There was a significant decrease in PaO_2 and SaO_2 and an increase in $P(A-a)O_2$ with age ($p < 0.001$). Unlike men, with age women had a significant increase in $PaCO_2$ and a higher decrease in PaO_2. The correlations between age, the decrease in PaO_2 and the increase in $PaCO_2$ were greater in women than in men. The VE adjusted to body surface area decreased with age, but this correlation was significantly higher in women.

Conclusions In this study, with a considerable number of healthy adults living at high altitude (2640 m), we established the physiological impact of altitude, aging and gender in ABG. The PaO_2 and $PaCO_2$ were significantly lower and the hemoglobin values slightly higher than described at sea level. In addition to PaO_2 decline with age, there was an age-related increase in $PaCO_2$ in women, associated with a greater reduction of VE.

Keywords Blood gas analysis · Altitude · Pulmonary ventilation · Women · Andean population

Abbreviations

ABG	Arterial blood gases
BP	Barometric pressure
BSA	Body surface area
$PaCO_2$	Arterial carbon dioxide pressure
PaO_2	Arterial oxygen pressure
$P(A-a)O_2$	Alveolar − arterial difference for oxygen pressure
RER	Respiratory gas exchange ratio
VE	Minute ventilation
ANOVA	Analysis of variance

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Introduction

Arterial blood gases (ABG) are the result of the integrity of the cardiorespiratory system and a proper balance between the cellular metabolism, renal adjustment and the alveolar ventilation, and influenced by altitude above sea level, sex, age, body mass index and race. There is more information about the effect of the altitude and age on the ABG and about the ventilatory adaptation depending on the race (Crapo et al. 1999; Beall 2007), but there is less information around gender differences in ventilation and the ABG in the altitude.

Although there is not a consensus, high altitude is usually defined as an elevation over 2500 m (~ 8200 feet). Although the physiological responses to hypobaric hypoxia start at lower elevations, they are more pronounced above this altitude and the risk of developing altitude illness also increases substantially (Luks et al. 2014). Between 2000 and 2012, the population living at altitudes higher than 1500 m above sea level increased from 220 to 271 million and those at altitudes higher than 2500 m increased from 65 to 76 million (Romeo et al. 2015).

With the altitude, the barometric pressure (BP) decreases and, therefore, the inspired oxygen pressure and arterial oxygen pressure (PaO_2) also decrease. The increase in ventilation with the decrease of the arterial carbon dioxide pressure ($PaCO_2$) is the main compensating mechanism that attenuates the drop in the PaO_2 (West 2004). Studies performed in residents in the Andes and Tibet document differences in the ventilatory adaptation depending on the race (Beall 2007), with higher levels of ventilation at rest and increased ventilatory response to hypoxia in Tibetans and higher hemoglobin concentrations in the Andeans at the same altitude.

Most of the studies evaluating ventilation and ABG values have been made at sea level and in small populations of people ascending to or residents at very high altitudes. The objective of this study was to evaluate the differences in ventilation and ABG by sex and age in adult Andean residents in Bogotá, a city located at high altitude (2640 m, BP 560 mmHg).

Methods

Design and participants

We conducted an analytical cross-sectional study in healthy volunteers of both sexes over 18 years of age residents in Bogotá, non-smokers, unexposed to biomass smoke and with normal spirometry. We excluded subjects with respiratory symptoms (cough, expectoration or shortness of breath), obesity, deformity of the rib cage and use of anticoagulants or medications that may modify alveolar ventilation, pH, bicarbonate or potassium metabolism (stimulants or depressants of the nervous system, corticosteroids, diuretics, beta blockers and beta agonists). This study was approved by the Committee of Ethics in Research of the Fundacion Neumológica Colombiana (approval number 200708-12103) and the participants signed an informed consent.

Measurements

Spirometry was performed fulfilling the recommendations of the American Thoracic Society (Miller et al. 2005) using a V-MAX Spectra 229 (Sensormedics®). It was considered normal if the values of forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1) were higher than 80% of the predicted value and the FEV_1/FVC ratio higher than the lower limit of normality. The Hankinson spirometric reference values were used (Hankinson et al. 1999).

The ABG sample was carried out with simultaneous measurement of exhaled gases and minute ventilation (V-Max Spectra 229, Sensormedics®) with the patient in a sitting position, using a mouthpiece and nose clip. Participants breathed in the circuit before arterial puncture until they had ventilatory stability and a respiratory gas exchange ratio (RER) < 1.0 to rule out acute hyperventilation. Radial arterial puncture was performed with a syringe containing electrolyte-balanced heparin with a needle 23G 1in. The samples were processed immediately in an Analyzer ABL 800 (Radiometer®) calibrated previously according to the quality control protocols established by the manufacturer. PaO_2, $PaCO_2$ and pH were measured by the equipment and the values of bicarbonate, arterial saturation of oxygen and the alveolar–arterial difference for oxygen pressure $[P(A-a)O_2]$ were calculated. $P(A-a)O_2 = FIO_2 \times (BP\text{-}47) - PaCO_2 \times [FIO_2 + (1 - FIO_2/RER)] - PaO_2$, where FIO_2 (inspired fraction of oxygen) = 0.2093, mean BP = 560 mmHg and assuming $PaCO_2 = PAO_2$.

Data analysis

The normality of variables was tested using the Kolmogorov–Smirnov test. The ABG variables were expressed as mean ± standard deviation (SD), and the upper limits (UL) and lower limits (LL) were calculated as mean ± 1.645 × ED. We used the unpaired Student's *t* test to evaluate differences in the arterial blood gases values by sex in each age group and the one-way ANOVA test to assess differences by age groups in men and in women. We calculated the correlation between age and PaO_2 and $PaCO_2$ in the total group and by sex and used a specified approach to interpreting the correlation coefficient (Hinkle et al. 2003). Minute ventilation (VE) was compared between men and women, adjusting by body surface area (BSA). To compare the correlations between VE/BSA and age by sex, we used the Fisher's r to z transformation (Diedenhofen and Musch 2015). For data analysis, the statistical package SPSS 11.0 was used and deemed significant a p value < 0.05.

Results

We included 374 non-obese adults, 207 women and 167 men from 18 to 83 years of age. The mean hemoglobin value was 15.5 ± 1.5 gr/dL with a lower value in women ($p < 0.001$) (Table 1).

Table 1 Subject characteristics

	Total group $N=374$	Men $N=167$	Women $N=207$	p
Age, years	46.9 ± 17.3	46.2 ± 16.3	47.4 ± 18.1	0.487
BMI, kg/m^2	24.8 ± 2.9	25.1 ± 2.7	24.6 ± 3.0	0.089
FVC, L	3.74 ± 1.00	4.48 ± .81	3.15 ± .71	< 0.001
FVC, %	103.3 ± 12.8	103.1 ± 13.3	103.4 ± 12.4	0.803
FEV_1, L	3.05 ± .84	3.62 ± .69	2.58 ± .63	< 0.001
FEV_1, %	104.6 ± 14.4	104.8 ± 15.2	104.4 ± 13.8	0.785
FEV_1/FVC	81.4 ± 5.0	80.8 ± 4.7	81.8 ± 5.2	0.043
VE, L	10.2 ± 2.6	10.9 ± 2.8	9.5 ± 2.2	< 0.001
VE/BSA	6.1 ± 1.5	6.1 ± 1.6	6.1 ± 1.4	0.926
VCO_2/VO_2	0.94 ± 0.04	0.94 ± 0.04	0.94 ± 0.04	0.525
Hb, gr/dl	15.7 ± 1.6	17.0 ± 1.0	14.6 ± 1.2	< 0.001

Values as mean ± SD

BMI body mass index, *FVC* forced vital capacity, FEV_1 forced expiratory volume in 1 s, V_E minute ventilation at rest, *BSA* body surface area, VO_2 oxygen uptake, VCO_2 carbon dioxide production, *Hb* hemoglobin

Arterial blood gases

Mean PaO_2 in the whole group was 65.2 ± 5.6 mmHg, SpO_2 92.4 ± 2.3%, $PaCO_2$ 33.0 ± 2.9 mmHg and bicarbonate 21.7 ± 1.6 mEq/L with significant differences by age and sex (Tables 2 and 3). The pH of all age groups was 7.43 ± 0.02 (LL: 7.40 and UL: 7.47) and the base excess − 1.3 ± 1.4 mEq/L without gender differences.

Differences by sex and age

As age increased, in both men and women, there was a significant decrease in PaO_2 and SaO_2, as well as a significant increase in the $P(A-a)O_2$ ($p<0.001$); the decrease in the PaO_2 with age was higher in women than in men (Table 2). Furthermore, with age, the $PaCO_2$ and HCO_3^- increased significantly in women ($p<0.001$), unlike men, in whom these values were similar in all age groups ($PaCO_2$: 33.5 ± 2.6 and HCO_3^- 21.9 ± 1.4). In the group between 18 and 39 years, women had a lower $PaCO_2$ and bicarbonate than men (Table 3). In women, the $PaCO_2$ was 3.5 mmHg higher in the group older than 50 years than in the younger (34.6 ± 2.6 vs. 31.1 ± 2.4, $p<0.001$).

Correlations between age and PaO_2, $PaCO_2$ and ventilation

There was a significant moderate correlation between the age increase and the decrease in the PaO_2 in the whole group ($r=-0.507$, $p<0.001$), but this correlation was greater in women ($r=-0.616$, $p<0.001$) than in men ($r=-0.319$, $p<0.001$) (Fig. 1). There was also

Table 2 PaO_2, SaO_2 and $P(A-a)O_2$ values by age and sex

N		Age, years	PaO_2, mmHg				SaO_2, %				$P(A-a)O_2$, mmHg			
Men	Women		Men**		Women**		Men**		Women**		Men**		Women**	
			Mean ± SD	LL–UL	Mean ± SD	LL–UL	Mean ± SD	LL–UL	Mean ± SD	LL–UL	Mean ± SD	UL	Mean ± SD	UL
29	41	18–30	68.1 ± 4.0	61.6–74.6	70.1 ± 4.6	62.6–77.6	93.5 ± 1.4*	91.3–95.8	94.3 ± 1.4	92.0–96.6	5.4 ± 2.8	10.1	6.0 ± 3.3	11.4
33	44	30–39	66.7 ± 4.5	59.3–74.1	66.9 ± 4.2	60.0–73.9	93.1 ± 1.3	91.1–95.2	93.1 ± 1.3	90.9–95.3	5.8 ± 3.0*	10.6	8.0 ± 3.0	12.8
36	27	40–49	66.4 ± 5.5	57.3–75.6	66.7 ± 4.8	58.7–74.6	92.9 ± 1.8	89.9–96.0	92.8 ± 1.7	90.1–95.6	6.6 ± 3.7	12.7	7.7 ± 3.7	13.8
29	25	50–59	65.9 ± 4.0*	59.4–72.4	62.4 ± 3.8	56.1–68.6	93.0 ± 1.4*	90.7–95.2	91.9 ± 1.8	89.0–94.9	6.7 ± 2.8*	11.3	9.4 ± 2.6	13.6
19	42	60–69	64.1 ± 4.4*	56.8–71.4	59.8 ± 6.1	49.8–69.8	91.9 ± 2.1*	88.4–95.4	89.8 ± 3.2	84.5–95.1	7.6 ± 2.7*	12.1	10.7 ± 3.7	16.8
21	28	≥ 70	62.5 ± 4.9	54.5–70.6	60.5 ± 4.4	53.2–67.7	91.4 ± 1.8	88.5–94.4	90.6 ± 2.1	87.1–94.2	10.1 ± 4.0	16.6	11.5 ± 3.2	16.8

Values as mean ± SD

LL lower limit, *UL* upper limit

*$p<0.05$ differences between men and women by age groups

**$p<0.01$ differences by age in men and women (one-way ANOVA)

Table 3 $PaCO_2$ and HCO_3 values by age and sex

Age, years	$PaCO_2$, mmHg				HCO_3, mEq/L			
	Men		Women**		Men		Women**	
	Mean ± SD	LL–UL	Mean ± SD	LL–UL	Mean ± SD	LL–UL	Mean ± SD	LL–UL
18–30	33.3 ± 2.4*	29.4–37.2	30.3 ± 2.1	26.9–33.8	21.9 ± 1.2*	19.9–23.9	20.2 ± 1.0	18.6–21.9
30–39	33.4 ± 2.7*	29.0–37.8	31.4 ± 2.2	27.8–35.0	22.1 ± 1.6*	19.5–24.7	20.6 ± 1.3	18.5–22.6
40–49	33.2 ± 2.8	28.6–37.8	31.8 ± 3.0	26.8–36.8	21.7 ± 1.4	19.3–24.0	21.1 ± 1.6	18.5–23.7
50–59	33.3 ± 1.8*	30.3–36.3	34.3 ± 1.7	31.5–37.1	21.9 ± 1.1*	20.0–23.7	22.8 ± 1.4	20.5–25.2
60–69	34.5 ± 2.7	30.1–38.9	35.3 ± 3.3	29.9–40.6	22.3 ± 1.3	20.2–24.3	22.8 ± 1.6	20.2–25.4
≥ 70	33.5 ± 3.0	28.5–38.5	33.9 ± 2.0	30.5–37.2	21.6 ± 1.6	18.9–24.3	22.3 ± 1.6	19.7–24.8

Values as mean ± SD

LL lower limit, *UL* upper limit

*$p < 0.05$ differences between men and women by age groups

**$p < 0.01$ differences by age in men and women (one-way ANOVA)

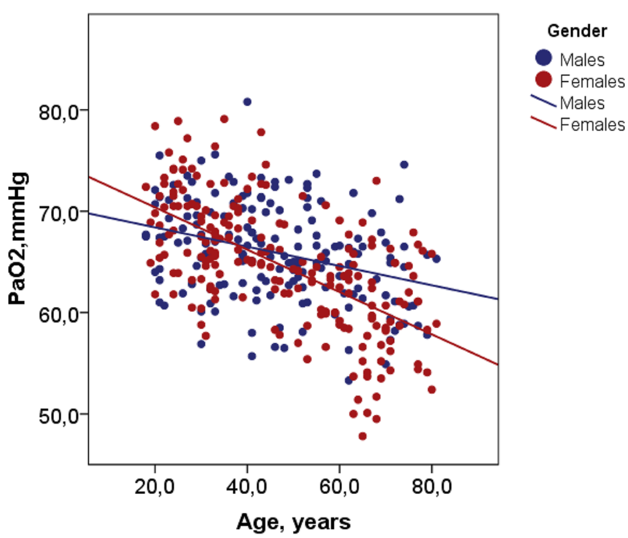

Fig. 1 Correlation between PaO_2 and age by sex. The correlation between PaO_2 and age in the whole group was − 0.507 ($p < 0.001$), higher in women ($r = -0.616$, $p < 0.001$) than in men (r = − 0.319, $p < 0.001$) ($Z = -3.70$, $p < 0.001$)

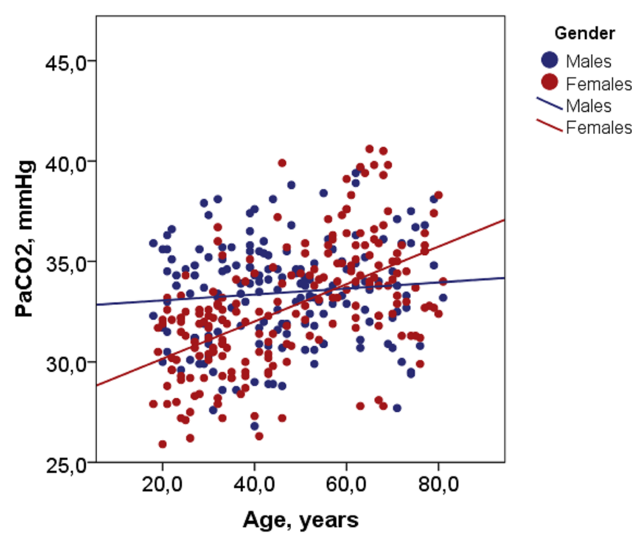

Fig. 2 Correlation between $PaCO_2$ and age by sex. The correlation between $PaCO_2$ and age in the whole group was 0.369 ($p < 0.001$), higher in women ($r = 0.548$, $p < 0.001$) than in men ($r = 0.094$, $p = 0.225$) ($Z = 4.97$, $p < 0.001$)

a significant moderate correlation between age and the increase of $PaCO_2$ in women ($r = 0.548$, $p < 0.001$) but not in men ($r = 0.094$, $p = 0.225$) (Fig. 2).

In the total group, the absolute values of V_E at rest were lower in women, but when the V_E was adjusted to BSA, there were no differences by sex. The VE/BSA decreased by age in both men and women. The correlation between VE/BSA was low in men ($r = -0.252$, $p < 0.001$) and in women ($r = -0.435$, $p < 0.001$), but significantly higher in women ($p = 0.047$) (Fig. 3).

Discussion

In this study with a considerable number of healthy adults living at high altitude (2640 m), we established the physiological impact of altitude, aging and gender in ABG. The PaO_2 and $PaCO_2$ were significantly lower and the hemoglobin slightly higher than at sea level. There was a significant decline with age in PaO_2 and SaO_2, with a progressive age-related widening of the $P(A - a)O_2$. As a significant finding of this study, there was an increase in the $PaCO_2$ with age in women, associated with a greater reduction of ventilation and PaO_2 compared to men. These significant

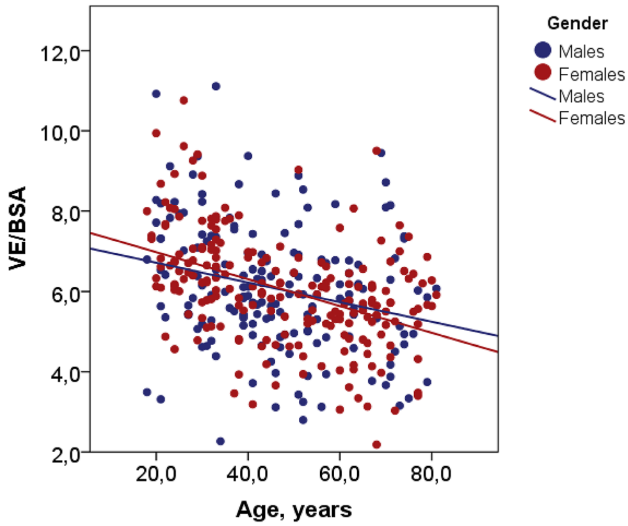

Fig. 3 Correlation between minute ventilation and age by sex. VE/BSA: minute ventilation corrected by body surface area. The decreases in the VE/BSA was higher in women ($r = -$ 0.435, $p < 0.001$) than in men ($r = -$ 0.252, $p = 0.001$) ($Z = -$ 1.99, $p = 0.047$)

physiological differences allow us to propose reference values by gender and age for our population and probably for other Andean populations at similar altitude, which will surely improve the clinical interpretation of ABG.

Previous studies have shown a decrease in PaO_2 with age or altitude (Cerveri et al. 1995; Crapo et al. 1999; Klaestrup et al. 2011). However, in our population, the slope of decrease of PaO_2 with age (− 0.17 mmHg/year) was lower than the one described at 1440 m (− 0.25 mmHg/year) and at sea level (− 0.23 mmHg/year) (Crapo et al. 1999) suggesting that some physiological compensation could decrease the falling of PaO_2 before reaching harmful low levels. The decrease in PaO_2 was parallel to an increase in $P(A-a)O_2$ and could be related to an increase in pulmonary ventilation–perfusion imbalance (Cardus et al. 1997) and a diffusion limitation in elderly subjects (Guenard and Marthan 1996). Some studies that have not confirmed changes with age, included only subjects over 70 years, which limits the demonstration of a progressive fall of PaO_2 seen when younger subjects are included (Guenard and Marthan 1996; Hardie et al. 2004).

The increase in alveolar ventilation is a well-recognized compensating mechanism of adaptation to the altitude (Chiodi 1957; West 2004; Dempsey and Forster 1982). The studies comparing adaptation to hypoxia between Andean and Tibetan natives have been conducted at altitudes between 3500 and 4500 m and have demonstrated that both groups raise the ventilation and the hemoglobin, but the Tibetans have higher resting ventilation and lower hemoglobin compared to Andeans (Beall 2007; Moore 2017). The significantly lower $PaCO_2$ values in our study in contrast with the sea level values confirm that the increase in the alveolar ventilation is the main compensating mechanism of adaptation to the altitude in these subjects. In addition to the increased ventilation, we observed somewhat higher levels of hemoglobin in both men and women in comparison to studies at sea level and at a lower altitude than Bogota (Crapo et al. 1999; Gassmann et al. 2019). The hemoglobin levels in our population were slightly higher than in other populations in Africa and Asia at a similar altitude, a fact that supports the hypothesis of differences in the adaptation to high altitude between different races (Beall 2007; Gassmann et al. 2019).

Noticeably, in our study group of non-obese women, we found an increase in the $PaCO_2$ as age increases, more pronounced in the group older than 50 years. In young women, the $PaCO_2$ was significantly lower than in men, but this difference disappeared with age. This finding was related to the fact that the VE adjusted by BSA was higher in young women than in men, but with age the VE decreased more in women and became lower than in men. Previous studies have shown a slight increase in $PaCO_2$ in women compared to men, but without demonstrating an increase with age (Crapo et al. 1999; Klaestrup et al. 2011; Loeppky et al. 2001). In some of these studies, the majority of the population was less than 40 years which limits a confirmation of age-related changes (Klaestrup et al. 2011; Loeppky et al. 2001).

There are contradictory findings in the literature about differences by sex in the ventilation, the changes by age and the hormonal influence, probably due to methodological difficulties of this kind of studies. These limitations include a small number of subjects, the effect of BSA, the natural variability of circulating hormones and the inclusion of different kinds of subjects such as athletes, high-altitude natives or those who ascend from sea level (Behan and Wenninger 2008; Behan and Kinkead 2011; Duke 2017). Regardless of this, we considered that the higher ventilation and the low $PaCO_2$ in young women compared to men and the higher $PaCO_2$ in women older than 50 years can be explained by hormonal effects. Serum progesterone, a known respiratory stimulant, is higher in premenopausal women and its levels decline in the years previous to menopause with a nadir early in menopause (Burger et al. 2008; Loeppky et al. 2001; Behan and Wenninger 2008; Behan and Kinkead 2011; Duke 2017). As in other studies, to make comparisons by sex we corrected the minute ventilation by BSA, considering the effect of the BSA on the metabolic rate, i.e., carbon dioxide output which in turn has an effect on ventilation (Aitken et al. 1986; Macnutt et al. 2012; Duke 2017).

In our population, there were also differences in the bicarbonate levels by age and sex. It was lower in young women with a gradual increase with age and it remaining unchanged in men. Our bicarbonate values are slightly higher than shown in previous studies (Paulev and Zubieta-Calleja 2005; Zubieta-Calleja et al. 2011; Ramirez-Sandoval et al. 2016) based on theoretical estimates and without considering differences by sex. Despite the differences between men and women and the changes of the $PaCO_2$ with age in this study, the pH was the same in all age groups with no differences by sex. The average value of pH in our study was higher than 7.40, such as previous reports at sea level (Cerveri et al. 1995; Guenard and Marthan 1996; Crapo et al. 1999; Klaestrup et al. 2011), in the altitude (Vera 1991; Pereira-Victorio et al. 2014; Crapo et al. 1999) and reviews in the literature (Berend 2011; Berend and Duits 2019). We also compare our results with the acid–base charts modified for the altitude (Paulev and Zubieta-Calleja 2005). In addition to pH, the $PaCO_2$ and HCO_3^- values obtained in our work reliably fall within the normal nomogram area for altitudes between 2000 and 3000 m.

Although "adaptation" refers to any change in structure, function or behavior that allows to maintain the physical ability of the subjects and increase the ability to survive and reproduce in a given environment (West 2017; Moore 2017), aspects that go beyond the discussion of this article, there are several physiological measurements frequently used to evaluate and compare the altitude adaptation between populations. Some of these variables related to increased arterial content and oxygen delivery to tissues are the rise in ventilation, hemoglobin, changes in heart rate and redistribution of blood flow. In this study, the decrease $PaCO_2$ secondary to a rise in ventilation and the higher hemoglobin compared to sea level, are indicative of adaptation to altitude. In chronic exposure to hypoxia, the decrease in $PaCO_2$ and the increase in pH trigger a renal compensatory mechanism with acid retention and increased HCO_3 excretion that results in a decrease in arterial blood pH towards normal levels (Krapf et al. 1991; Swenson 2016). Considering this, the pH of 7.43 in these permanent residents at altitude could be interpreted as an incomplete metabolic adaptation to the altitude hypoxia (West 2006; Porcelli et al. 2017), although as already mentioned, this pH is similar to the reported values in several studies conducted at sea level (Cerveri et al. 1995; Crapo et al. 1999; Hardie et al. 2002; Klaestrup et al. 2011; Berend and Duits 2019).

Even though the previous ABG studies in Bogotá were mainly performed in small samples of subjects, usually under 30 years and without description of differences by sex, the values of PaO_2 and $PaCO_2$ in the age group between 20 and 30 years were similar to our results (Restrepo et al. 1982; Acevedo and Solarte 1984; Duran et al. 1993; Hurtado et al. 2007). Other studies in Latin America at similar or higher altitude than Bogota have shown the decrease of the PaO_2 and $PaCO_2$ in the altitude. However, some of these studies have limited sample sizes or did not include subjects of different age groups making it difficult to compare ABG by sex or age with our results (Vera 1991; Pereira-Victorio et al. 2014; Ramirez-Sandoval et al. 2016; Rico et al. 2001).

The main strengths of this study were the large sample size of healthy subjects resident at high altitude from both sexes; the simultaneous measurement of VE that allowed us to explain changes in $PaCO_2$ by age and sex; the use of the exhaled gas sample to rule out the presence of acute hyperventilation during arterial puncture and the use of the measured respiratory quotient for calculating $P(A-a)O_2$ instead of assuming a theoretical value.

We also had a strict definition of normal participants with a medical evaluation and spirometry that allowed us to excluded subjects with obesity, smokers, users of drugs that could alter the alveolar ventilation, pH, or the bicarbonate and those with abnormal spirometry. Although we did not perform chest X-rays or other tests to exclude asymptomatic diseases, we consider it unlikely that subjects with important respiratory or cardiovascular disease would have been included that would significantly change the ABG values. In the same way, it is possible that the volunteer subjects included in the study did not report some comorbidities, but the clinical evaluation, the use of spirometry and the exclusion of obesity allowed us to rule out participants with significant diseases to modify the results. Although we did not take into account the menstrual-cycle phase for the ABG sample, we consider that the small changes on resting ventilation and CO_2 that has been described in previous studies did not meaningfully affect our results (Slatkovska et al. 2006; Macnutt et al. 2012).

In summary, this study with a considerable number of healthy adults living at high altitude (2640 m), describes the physiological impact of altitude, aging and gender on ABG. As expected, PaO_2 and $PaCO_2$ were significantly lower and hemoglobin slightly higher than at sea level. In addition to a significant decrease in PaO_2 and SaO_2 with age, we observed an increase in $PaCO_2$ in women, related to a greater reduction in VE, likely associated with hormonal changes.

Author contributions MGG, DM, MB and CATD contributed to the research initiative and data acquisition; MGG, DM, and CATD contributed to the study design; MGG, DM, AC and CATD contributed to the data analysis; and MGG, DM, MB, AC, and CATD contributed to the article writing.

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Availability of data and material The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethics approval This study was approved by the Committee of Ethics in Research of the Fundacion Neumologica Colombiana (Approval number 200708-12103).

Consent to participate Informed consent was obtained from all individual participants included in the study.

Consent for publication The work has been seen and approved by all co-authors.

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