Open Access

OBM Genetics

Research Article

Relationship between the Severity of Chest CT Scan Lesions, Arterial Oxygenation and Inflammatory Markers in High – Altitude Patients with Covid-19

Walter Calderón-Gerstein [1, ‡], Gabriela Torres-Samaniego [2], Kevin Pazos-Sovero [3], Mirella Calderón-Anyosa [4], Merly Quisurco-Cárdenas [1, *], Viviana Dorregaray-Lizárraga [1]

1. Universidad Continental. Huancayo, Perú; E-Mails: wcalderon@continental.edu.pe; 75963696@continental.edu.pe; 73384406@continental.edu.pe
2. San Pedro de Cajas Health Post, EsSalud. Tarma, Perú; E-Mail: gabrielaktorress@gmail.com
3. Juan Parra del Riego Clinic, Huancayo, Perú; E-Mail: pazossoverokevinantony@gmail.com
4. Arzobispo Loayza National Hospital. Lima, Perú; E-Mail: mirestephanie@gmail.com

‡ Current Affiliation: Internal Medicine Service, Ramiro Prialé Prialé National Hospital, EsSalud. Huancayo, Peru

* **Correspondence:** Merly Quisurco-Cárdenas; E-Mail: 75963696@continental.edu.pe

Academic Editors: Gustavo Zubieta-Calleja and Natalia Zubieta-DeUrioste

Special Issue: Oxygen Transport Physiology and COVID at High Altitude

OBM Genetics
2023, volume 7, issue 2
doi:10.21926/obm.genet.2302180

Received: December 01, 2022
Accepted: April 12, 2023
Published: April 19, 2023

Abstract

This study aims to determine the relationship between the severity of lung tomographic compromise with arterial oxygenation and inflammatory markers in patients with COVID-19, and to evaluate the relationship between the CTSS tomographic severity score and the mortality risk in a high-altitude population. A retrospective, longitudinal study reviewed medical records between January and July of 2021 at the Daniel Alcides Carrión Regional Teaching Clinical Surgical Hospital in Huancayo. Categorical variables were analyzed with the chi-square test, continuous variables with the ANOVA test, and correlations between continuous variables were calculated by calculating Spearman's coefficient. The predictive capacity of the CTSS score was evaluated by determining the ROC curve. Two hundred-three medical records were reviewed; 65% of patients (n = 132) were male and 84.7% came from Huancayo (n = 172). The average age was 55.86 years. 58.6% of the CT scans were in the peak phase and 14.3% in the progressive phase. The average value of the PaO2/FiO2 ratio in deceased patients was 107.4; in survivors it was 196.10. Mortality was 12% in those with mild lesions, 28.8% in those with moderate involvement, and 79.2% in those with severe pulmonary lesions. PO2/FiO2, SatO2/FiO2, DHL, CRP, D-dimer, and lymphopenia correlated with the severity of pulmonary tomographic patterns. Tomographic lesions and inflammatory marker values were more severe than in most international studies.

Keywords

Chest CT scan severity score; COVID-19; oxygen saturation; high-altitude; inflammatory markers

1. Introduction

SARS-CoV-2 has caused the COVID-19 pandemic, severely affecting Peru and Latin American countries [1]. SARS-CoV-2 enters the lung and causes damage to the alveolar and interstitial tissue, affecting other body organs such as the heart, kidney, and brain, among others [2, 3]. The damage produced in the lungs is especially important since, depending on the extent of respiratory compromise, the patient may develop severe respiratory failure requiring mechanical ventilation [4].

Altered gas exchange at the alveolar level is produced not only by injury to the capillary alveolar membrane but also by vascular obstruction due to the tendency to form microthrombi, which is characteristic of the disease [5], leading to a state of tissue hypoxia. From the physiological point of view, hypoxia in the patient affected by COVID-19 is an important characteristic of its pathophysiology [4]. During the first months of the pandemic, what some researchers called “happy hypoxemia” could be seen. The patient sought medical attention without manifesting severe dyspnea, presenting very low oxygen saturation levels and blood pressure [6]. This form of symptomatic oligo hypoxia presentation is similar to that described in high-altitude populations, especially in older adults [7].

Patients living at high altitudes are exposed to the hypoxia typical of an environment with a lower barometric pressure of oxygen, to which the hypoxia typical of pulmonary and vascular lesions from COVID-19 [8]. From a theoretical point of view, mortality from COVID-19 in high-altitude residents should be higher than that observed at sea level. On the contrary, however, there are controversial results in this regard. Publications from high-altitude populations in Latin America such as Peru [9], Bolivia [10], Ecuador [11] and the United States [12, 13] have shown that mortality may be lower than at sea level. In contrast, some Peruvian studies had not shown a difference between one population and another [14, 15].

The question persists as to whether the Andean population, due to the cardiovascular adaptations they have undergone in order to acclimatize to the altitude, would be able to tolerate hypoxia better than a sea-level population, or whether there could be a decrease in the aggressiveness of the virus which would decrease lung damage at high altitude. High-altitude residents have developed a rib cage with a diameter greater than 20% of normal, with a greater number of alveoli, bronchi and bronchioles [16], as well as a greater number of coronary arteries that supply the myocardium, and a higher pressure in the pulmonary artery that allows better irrigation of the upper pulmonary lobes [17]. These anatomical adaptations may have conferred an advantage to the high-altitude dweller over those not accustomed to experiencing low levels of barometric oxygen pressure. One way to decipher the behavior of SARS-CoV-2 at high altitudes is by comparing the severity and type of lung lesions with their effect on oxygenation values at altitude.

The normal values of oxygenation by age group are known, as well as the arterial oxygen pressure about the inspiratory fraction of oxygen (PaO2/FiO2), the average PaO2 at altitude, and the impact that lung lesions would have, because they have already been described in populations at sea level [18]. This study aims to answer the question about the correlation between the severity of lung lesions and the variation in oxygenation in a high-altitude population in the second wave of the South American pandemic, in order to determine if the same severity of lesions can cause a deeper depression in the patient's oxygenation levels or if the oxygenation impairment is not as severe as the observed at sea level.

2. Materials and Methods

2.1 Study Design and Population

This is a retrospective, longitudinal study, performed by reviewing the medical records of a population of patients hospitalized for COVID-19 who were admitted to the intensive care unit and the internal medicine wards of Daniel Alcides Carrión Regional Clinical Surgical Teaching Hospital in the city of Huancayo, between January to July of 2021. Huancayo is 3,250 meters above sea level and is the capital of the Junin department. Seven hundred medical records were reviewed, of which 500 had chest CT scan image reports with their corresponding radiological report. Of the 500 charts with existing tomographic files, 203 cases were selected, in which complete data on oxygenation levels, laboratory tests, and detailed evaluation of chest CT scan patterns and lung involvement were available.

2.2 Determination of the Tomographic Severity Score

In order to make the chest CT scan evaluation, the 25-point tomographic severity score (CTSS) [19] was used. All five lung lobes were evaluated: the two left lung lobes and the three right lung lobes. Scoring for each lobar involvement was as follows: 1 point if there was the involvement of 5% or less of the lung parenchyma, 2 points for those with 5%-25% involvement, and 3 points for those with 26%-49% involvement. If the lung compromise was between 50%-75%, 4 points were given and for those with a compromise greater than 75%, 5 points were assigned.

To assess the total severity of lung compromise, the involvement of all the affected lobes was added, in such a way that the minimum value was 0 for five lobes with less than 5% involvement, and the maximum value was 25 when the five lobes were affected, with a compromise greater than 75%. If the lobar score was less than or equal to 7, it was considered mild tomographic involvement. The moderate degree was considered when the lobar score was between 8 and 17; if the score was 18 or more, it was considered severe [19].

According to the Peruvian legislation regarding observational studies in humans, the study was approved by the Ethic Committee of Carrión's hospital on October 19, 2022, with registration number 6126711. The study complies with the principles of the Declaration of Helsinki for medical research involving human subjects. The confidentiality and anonymity of the patients were secured.

3. Results

3.1 Epidemiological Data

Seven hundred clinical histories were revised, of which 500 had tomographic data, and finally reviewing, 203 medical charts with complete laboratory data, anamnesis, arterial blood gases and chest CT scans.

65% of the patients (n = 132) were male and 35% (n = 71) were female. The average age of the patients was 55.86 years, with a maximum value of 94 years and a minimum of 21 years.

Regarding the place of origin, 84.7% of the patients came from the city of Huancayo (n = 172), with 9.3% coming from various locations in the Mantaro Valley, an intermountain valley with altitudes between 3210 and 3300 meters above sea level (m.a.sl); 1.9% came from Pasco (4,300 m.a.s.l) and the same amount from other towns in the highlands.

All cases were confirmed by rapid antigen test (77.3%) and 18 cases (18.7%), with molecular (RT-PCR) test. The most frequent pathological history was obesity, which was observed in 37.4% (n = 76), followed by type 2 diabetes mellitus (18.7%) and arterial hypertension (16.7%). Chronic renal failure and pulmonary fibrosis were only found in 2% of cases each.

3.2 Complications Observed

Mortality in this population was 39.9% (n = 81). 96.1% of the patients developed adult respiratory distress syndrome; all patients had acute respiratory failure and required oxygen placement. 30% developed acute heart failure as a complication, 26.1% coagulation disorder, 17.7% multi-organ failure and 10.8% renal failure. 16.3% (n = 33) were placed on mechanical ventilation and two patients underwent dialysis.

The mean hospital stay was 10.33 days, with a maximum of 48 and a minimum of 3 days. Most patients had an average duration of symptoms of 8.85 days, with a minimum of 1 and a maximum of 30 days.

3.3 Chest CT Patterns of Lung Injury

The most common lesion observed was ground glass pattern, which was present in 99% of cases, followed by consolidations in 90.6%, bilateral ground-glass (70%), thickened septa (60.1%), reticular infiltrates (51.2%) vascular dilation (47.8%), and paratracheal nodes enlargement (47.3%).

3.4 Location and Distribution of Lung Lesions

Bilateral consolidation was observed in 79.3% of the cases. The most frequent pulmonary location was the left posterior basal segment (32%), followed by the right posterior basal segment (29.1%). The least frequent location was the right apical segment (20.7%). In 29.1% of the cases the involvement was multilobar.

Regarding the distribution of the lesions, they had a central and peripheral distribution in 93.1% of the cases and an exclusively central distribution in 6.9% of the cases. There were no pulmonary lesions of exclusively peripheral distribution.

The most frequent phase of disease progression was the peak phase at 58.6%, followed by the progressive phase at 14.3%.

3.5 Vital Signs, Oxygen Saturation and Arterial Oxygenation

The average body mass index was 28,438; the mean respiratory rate was 24.49 breaths per minute, with a minimum of 18 and a maximum of 50 per minute. The average heart rate was 96.44 beats per minute, while the average temperature was 37.3°C. Mean systolic blood pressure was 113.8 mmHg and diastolic was 73.6 mmHg.

About arterial gases, the average oxygen pressure was 61.87 mmHg, with an average FiO2 of 0.5241. The average oxygen saturation was 89.3%, with a minimum of 43% and a maximum of 98.7%. The relationship between oxygen saturation and average FiO2 (SatO2/FiO2) was 230.45, with a minimum value of 48 and a maximum of 457.14. The average PaO2 and FiO2 (PaFi) ratio was 160.72 with a minimum value of 24.4 and a maximum of 414.29. The average saturation with the oximeter was 78.75% with a minimum value of 44% and a maximum of 93% (Table 1).

Table 1 Blood gas values and pulse oximetry.

	No.	Minimum	Maximum	Half	Dev. Deviation
PaO2	203	22.0	111.0	61,87	15.91
FiO2	203	21	90	52.41	26,80
SatO2	203	43.2	98.7	89,348	9.02
SatO2/FiO2	203	48.00	457.14	230.45	125.66
PaO2/FiO2	203	24.44	414.29	160.72	96.76
Oximeter saturation	203	44.00	93.00	78.75	8.64

PaO2: arterial oxygen pressure, FiO2: fraction of inspired oxygen, SatO2: oxygen saturation, SatO2/FiO2: peripheral oxyhemoglobin saturation/fraction of inspired oxygen and PaO2/FiO2(PaFi): Arterial pressure of oxygen/fraction of inspired oxygen.

3.6 Inflammatory and Biochemical Markers

The average lymphocyte count was 917 cells per cubic millimeter, the average value of leukocytes was 10,741 per cubic millimeter, and platelets were 262,879 per cubic millimeter. Mean hemoglobin was 16.45 gr/dL and hematocrit was 49.85%. The average percentage of lymphocytes was 10.8%, with the minimum being 0.23%. The average number of neutrophils was 9338 and the number was 8%.

The average value of lactic dehydrogenase was 584 U/L, with a maximum value of 2406 U/L. The mean C-reactive protein was 135.43 gr/dL, while glucose remained at an average of 152 mg/dL and ferritin at 623.16 mg/dL. The mean D-dimer value was 2015 ug/L and creatinine was 0.9 mg/dL.

3.7 Pulmonary Compromise on Chest CT Scan and Mortality

The most frequently involved lung lobe was the right lower lobe in 44.31% of the cases, followed by the left lower lobe in 42.17%. Most patients had a CORADS score of 5, with an average value of 4.97. The minimum percentage of lung involvement was 5%, and the maximum was 95%, averaging 51.58%. The average diameter of the trunk of the pulmonary artery was 27.7 mm, with a maximum value of 38 mm.

A statistically significant association (p = 0.00) was found between the involvement of the right lower lobe and mortality (53.3%), as well as an increased risk of mortality when the left lower lobe was involved (51.11%). The lobes least associated with mortality were the left upper lobe (39%) and the right upper lobe (41%).

The diameter of the trunk of the pulmonary artery was higher among the deceased with an average value of 29.3 mm, than in the survivors who had an average value of 25.9 mm.

3.8 Laboratory Tests and Mortality

Mortality was higher in patients with lymphopenia: the deceased had an average of 791 lymphocytes per cubic millimeter and the survivors hadan average of 1000 lymphocytes per cubic millimeter. Similarly, hemoglobin was higher in deceased patients (16.8 gr/dL) than in those who survived (16.18 gr/dL) (p = 0.025). The average hematocrit in the deceased patients was 51% and in the survivors it was 49% (p = 0.027).

3.9 Oxygenation Values and Mortality

The average value of the PaO2/FiO2 ratio in deceased patients was only 107.4 while in survivors it was 196.10. The relationship between oxygen saturation and FiO2 (SatO2/FiO2) was 153.55 in the deceased and 281.5 in the survivors. The average age was higher in the deceased patients (62.48 years) than in those who survived (51.47 years) (Table 2).

Table 2 Oxygenation values, age, and diameter in the pulmonary artery in survivors and deceased.

Mortality		PaO2/FiO2	SatO2/FiO2	Age	Pulmonary artery diameter
Survivors	Mean	196,10	281.51	51.47	25.93
	No.	122	122	122	55
	St. Deviation	87.74	114.13	13,239	3,167
Non survivors	Mean	107.43	153.55	62.48	29.33
	No.	81	81	81	36
	St. Deviation	84.94	101.0	12,889	3,505
Total	Mean	160.75	230.45	55.86	27.27
	No.	203	203	203	91
	St. Deviation	96.76	125.66	14,143	3,68
P value		0.000	0.000	0.000	0.000

3.10 CTSS Score and Mortality

Using the CT severity score, 12.3% (n = 25) of the patient cases were classified as mild, 61.6% (n = 125) as moderate, and 26.1% (n = 53) as severe pulmonary disease.

A linear correlation was found between the tomography severity score and mortality: mortality was 12% among those patients with mild lesions, 28.8% in patients with moderate lung involvement, and 79.2% in those who had severe lung injury ($p < 0.05$) (Table 3).

Table 3 Degree of tomographic severity and mortality from COVID-19.

			Chest CT Severity Score		
			Mild degree	Moderate degree	Severe degree
Mortality	NO	Count	22	89	11
		% within CT Severity Score	88.0%	71.2%	20.8%
	YES	Count	3	36	42
		% within CT Severity Score	12.0%	28.8%	79.2%
Total		Count	25	125	53
		% within CT Severity Score	100.0%	100.0%	100.0%

Patients with the mild disease had a mean PaFi of 240, while those with moderate lesions had a PaFi of 180.7 and those with severe disease had a mean PaO2/FiO2 of 75.86. The SatO2/FiO2 ratio increased according to the severity of the CT scan lesions, 323.18 in those with mild pulmonary lesions, 258.5 in those with moderate lesions, and 120.57 in people with severe lesions. The average amount of oxygen received by patients with mild injuries was 32.32%. In comparison, those with a moderate injury received a mean of 45.47% and those with severe lung injury received an average of 78.26% (Table 4).

Table 4 Oxygenation, pulmonary artery diameter and tomographic severity.

CTSS Severity Score		**PaO2/FiO2**	**SatO2/FiO2**	**Pulmonary Artery (mm)**	**Oximeter saturation**	**FiO2**
Mild degree	Mean	240.41	323.18	25.25	84,20	32.32
Moderate degree	Mean	180.76	258.50	26.98	80.52	45.47
Severe degree	Mean	75.86	120.57	28.82	72,00	78.26
Total	Mean	160.72	230.45	27.27	78.75	52.41
P value		0.000	0.000	0.034	0.000	0.000

The average age of the patients who had mild injuries was 54.12 years, in those with moderate injuries it was 53.7 years and in those with severe injuries it had an average age of 61.77 years. C-reactive protein, D-dimer, and lactic dehydrogenase values were associated with a more severe tomography. In the same way, decreased values of lymphocytes are associated with lower survival (Table 5).

Table 5 Inflammatory markers and severity of tomographic lesions.

TEM Severity Score		Age	DHL	CRP	Lymphocytes	D-dimer	Ferritin
Mild degree	Mean	54.12	332.33	69,81	991.60	1295,78	530,96
Moderate degree	Mean	53.70	538.53	130,54	967.52	995,37	624,75
Severe degree	Mean	61.77	783.26	176,08	763.96	5183,57	655,90
Total	Mean	55.86	584.13	10.81	917.34	2015,66	623,16
P value		0.02	0.000	0.000	0.039	0.000	0.067

Surviving patients had a mean CTSS score of 11.48, as opposed to 18.62 among deceased patients. The difference was statistically significant (p = 0.00) (Table 6).

Table 6 CTSS score and mortality.

Mortality	Mean Score	No.	St.Deviation
Survived	11.48	122	4,55
Deceased	18.62	81	5,92
Total	14.33	203	6,21

A clear association was found between the risk of death and high CTSS score values. This was confirmed by evaluating the area under the receiver-operator curve (COR curve) of the CTSS score for mortality, finding an area under the curve of 0.820 with a 95% confidence interval between 0.756 and 0.883. The predictive capacity of the pulmonary tomographic compromise severity score using the CTSS instrument was adequately correlated with the mortality risk (Figure 1).

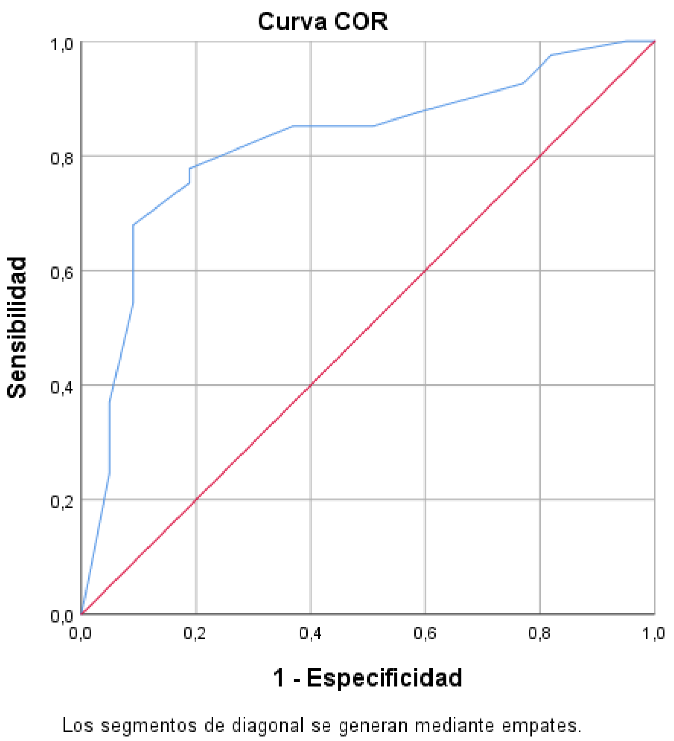

Figure 1 CTSS score and mortality. ROC curve.

When correlating the severity score of the chest CT scan with the inflammatory values, it was observed that the greater severity of lung lesions was related to lower lymphocyte counts, and higher levels of ferritin, C-reactive protein, D-dimer, and lactic dehydrogenase.

An inverse relationship was noticed between oxygen saturation, PO2/FiO2 and SatO2/FiO2 and the severity of the tomographic score. The correlation was maximum between SatO2/FiO2 with an R coefficient of -0.582 and PO2/FiO2 with a coefficient of -0.572. The correlation was weaker with the lymphocytes count (R = -0.158) and with the ferritin levels (R = -0.183) (Table 7).

Table 7 Correlation between tomographic severity point and values of inflammatory and oxygenation markers.

CT severity score		
Association variables	p-value	R*
Lymphocytes	0.024	-0.158
Ferritin	0.020	0.183
PCR	0.000	0.367
D-dimer	0.000	0.410
DHL	0.000	0.422
SatO2	0.000	-0.461
PaO2/FiO2	0.000	-0.572
SatO2/FiO2	0.000	-0.582

R* Pearson correlation values

The correlation most strongly associated with the severity of the tomography was that of the satO2/FiO2 with a coefficient of minus -0.582 followed by PaO2/FiO2 with an R value of -0.572.

4. Discussion

The present study revealed the presence of an inverse relationship between the severity of pulmonary tomographic patterns and arterial oxygenation levels at altitude. On the other hand, a direct relationship between inflammatory markers and indicators of lung destruction was also observed, as in previous studies at sea level. Lung compromise was more severe in this population of Huancayo than in most studies worldwide. Mortality was high (39.9%) because this was a very high-risk population, in which all hospitalized patients had respiratory failure and received oxygen therapy or mechanical ventilation. This high mortality rate was similar to that found by Ito et al. in La Paz, Bolivia [20], where they found an Odds ratio (OR) of 29.67 for mortality in patients with Covid-19 pneumonia, compared to an OR of 5.26 for those who developed only upper respiratory symptoms.

Most studies of tomographic correlation and oxygenation levels come from Egypt and the Middle East. Qaasenya et al. carried out a tomographic study with 173 patients with COVID-19 in March 2022 [21], and found that 87.6% of their patients had ground glass lesions and 83.8% of lesions were bilateral. As in the present study, it was found that pleural effusion was infrequent (2.3%). In the study above, carried out at the Baqiyatallah University Hospitals in Iran, the CTSS tomographic classification was used, finding no differences in oxygenation among patients aged 28 to 40 the degree of lesions. The researchers found a correlation of -0.587 with oxygen saturation; the lower the oxygen saturation, the greater the severity of the lung lesions. In that study, a chest CT scan was ordered when the patient's oxygen saturation was below 93%. The mean age of their population was 63 years, higher than that of the present study, which was 55.86 years. Regarding the involvement of the pulmonary lobes, the most affected lobe was the right lower lobe with 87.3% and the left lower lobe with 88.4%. This pattern of lower lobes compromise is consistent with the results reported by Malbuisson et al. of the CT Scan ARDS Study Group [22], which found that the lower lobes received the greater pressure exerted by the heart and that that increased pressure was even greater in patients with ARDS as compared with normal controls. It is important to note that according to Coudert et al. [23], in a study performed in La Paz, Bolivia, at high altitude, in healthy volunteers placed in the recumbent position, pulmonary artery flow was higher in the right lower lobe while lower in the right upper lobe.

Abd El Megid et al. conducted a study at the Zagazig University Hospital [24]. They evaluated the severity of chest CT scan lesions in a population with 36% of mild lung involvement, 53.4% of moderate compromise and only 10.5%of severe lung involvement. The average oxygen saturation level was 95.6% in those with mild to moderate involvement and 85.4% in those with severe lung involvement. As can be seen, it is extremely difficult to make an adequate comparison between the severity of this study with a high-altitude population. The average saturation in Huancayo is 94% for a person under 40, reaching 89% in patients over 80 years of age [18]. For this reason, an oxygen saturation of 95.6% as described by the researchers is usually found at sea level or below 3000 meters of altitude. In our population, those with mild compromise had an average oxygen saturation of 84.2%, those with moderate compromise 80.5%, and those with severe lesions had an average saturation of 72%; patients with severe compromise in the study by Abd El Megid et al. corresponded to the mild cases of the patients from Huancayo. As in our study, these authors found lung involvement was more severe in male patients; mild pulmonary lesions were observed more in women, while in the case of moderate lesions, these were observed in 60% of men and 50.8% of women.

Komurcuoglu et al. performed a retrospective study in Turkey with 277 adult patients [25], using the CTSS score. This group of researchers found that the cut-off point for this severity score was 15 and that patients with scores higher than this value had higher mortality. Most of our hospitalized patients, except 6 patients with a score between 5 and 6, had 7 or more severity points. Although the Turkish group found a cut-off point of 15 for mortality, in our population the deceased patients had an average severity of 18.62, unlike the surviving patients whose average severity score was 11.48.

Mohamed's research group studied 120 patients at the Rozham Emergency Hospital in Erbil in Iraq [26]. They found, as in our study and all existing studies, that the greater the lung involvement, the lower the oxygen saturation. In patients with 40 to 60% lung involvement they found an oxygen saturation of 90% but in those with severe lung involvement the saturation was on average 80%. As can be seen, these values are higher than those found in our patients, since those with mild involvement in the Huancayo group had a saturation of 84% and the severe ones had an average saturation of 72%.

Qadir et al. evaluated 105 patients [27], among whom 92.9% had ground glass lesions on the chest CT scan and 27.6% had diabetes mellitus. They defined hypoxemia as an oxygen saturation lower than 95%; In this sense, all the patients from Huancayo before having any respiratory pathology would fit the hypoxemia criteria proposed by this research group. When evaluating the patients with severe pulmonary involvement, they found that only 1 of every 23 patients did not have hypoxemia, unlike the group with mild pulmonary involvement, in which 14 of 40 patients who did not present hypoxemia were identified. The correlation of oxygen saturation with the CTSS score had a coefficient of -0.336, lower than that found in our study, which was -0.461. Because the population of Huancayo is a high-altitude population in which all patients received supplemental oxygen when hospitalized, a better correlation was found using PO2/FiO2 and using SatO2/FiO2, in which in both cases a higher correlation – of -0.57 - was obtained. SatO2/FiO2 is currently used to evaluate patients with Covid-19 pneumonia before the arterial blood gases results are available. According to Roozeman et al. [28], the correlation of those measurements in patients on mechanical ventilation reaches 0.79.

Aalinezhad's research group reviewed the chest CT scans of 270 patients hospitalized at the medical centers of the University of Isfahan in Iran [29]. The average oxygen saturation in these groups was 89.65% and the average CTSS score was 15.16. The relationship between oxygen saturation and the severity of the tomographic CTSSS score was very similar to ours with a correlation coefficient of -0.44 very close to the correlation of -0.461 found in our study.

Yanamandra evaluated 298 patients, 61.4% male [30]. CT scans were performed on all patients with an oxygen saturation of 94% or higher using the CTSS score. The researchers correlated tomographic severity and certain inflammatory variables such as C-reactive protein, ferritin, D-dimer, and lactic dehydrogenase. These variables were also evaluated in the study by Abd El Megid, which determined the relationship between lymphocytes and lung involvement. All the variables above were evaluated in our study, and relevant comparisons could be made.

In the study conducted in Zagazig, Egypt [24], patients with mild involvement had an average of 1500 lymphocytes per cubic millimeter, a higher figure than our patients with mild involvement with an average of 990 lymphocytes per cubic millimeter. In this study, those with severe compromise had 1120 lymphocytes per cubic millimeter. In the present study this average was 773 per cubic millimeter, much lower than that found in the work above.

Concerning D dimer, an average of 320 ug/L was obtained in the Egyptian study [23] and 434 ug/L in the Indian study by Yanamandra [30], values well below those found in Huancayo where the average D dimer was 1295 ug/L in mild cases. The Egyptian study's patients with severe tomographic pulmonary compromise had an average D-dimer of 1210 ug/L. In the Indian study it was 1004 ug/L, values well below 5183 ug/L, the average D-dimer value in our severe cases.

In the Egyptian study, patients with mild or moderate compromise had an average of 12.6 mg/dlof C reactive protein (CRP). In contrast, in the Indian study its average value was 29 mg/dL, values much lower than those found in our population, in which patients with mild compromise had an average of 69.8 mg/dL of C-reactive protein. The moderate cases of the study from India [30] had an average CRP of 66.6, which was even below the values of the mild cases from Huancayo, where the patients with moderate involvement had an average C-reactive protein of 130.5. mg/dL.

Regarding the correlation between certain inflammatory markers, as well as the value of lymphocytes in our population, a significant relationship was observed between the progressive elevation of inflammatory values and the degree of lung injury, clearly appreciating that the levels of inflammation observed in our population were much higher than those observed in other populations, especially from India and Egypt. At similar severity levels, our patients had higher values of C-reactive protein, lactic dehydrogenase, and D-dimer, as well as lower levels of lymphocyte count. Among these markers, ferritin showed a more moderate elevation than the other laboratory values.

A special comment deserves the high rate of heart failure observed as a complication of respiratory failure secondary to Covid-19 infection. Right ventricular function is impaired at altitude, leading the left ventricle, even though cardiac output can be preserved through increase heart rate secondary to sympathetic activation [30]. Furthermore, hypoxia produces pulmonary hypertension and vasoconstriction [31, 32], reducing end-diastolic volume without decreasing the ejection fraction. This altered response of the heart to hypoxic conditions may be responsible for the high number of patients who developed heart failure, even though less than 5% of our patients had the cardiac disease previously. This result is consistent with the low prevalence of preexisting heart disease in Bolivians with Covid-19 in La Paz; only 1.7%.

5. Conclusions

By correlating the tomographic findings of our population with inflammatory markers and oxygenation levels, an inverse linear relationship could be found in which oxygenation levels decreased with greater lung involvement. The PO2/FiO2 and SatO2/FiO2 ratio correlated better with the severity of the tomographic patterns than oxygen saturation. Lactic dehydrogenase uniformly accompanied the increase in the severity of the lesions, as did C-reactive protein and D-dimer, as well as a drop in lymphocyte count, and to a lesser extent ferritin values.

Most cases in the population evaluated were moderate with a small percentage of mild cases. The risk of mortality from COVID-19 could be evaluated very precisely by applying the CTSS score, in which it was possible to see that those patients who survived the disease had an average of 11.48 points, unlike the deceased who had an average of 18.62. The CTSS tomographic severity score proved to be a good predictor of mortality with an area under the curve of 0.820, having a score of 8.5 or more, a sensitivity of 82.6% with a specificity of 77% for predicting mortality.

It is concluded that this high-altitude population had a severity of tomographic lesions and inflammatory markers much higher than most international studies, with the possibility that COVID-19 produces a more severe inflammatory and destructive pulmonary process than at sea level. But that, due to the chronic adaptation of the high-altitude inhabitant to hypoxic conditions, the severity of the lesions and the inflammatory process would be compensated in their effects by the cardiopulmonary adaptations the Andean inhabitant has. Tolerance to severe levels of hypoxia in the evaluated population would have contributed to lower-than-expected mortality. New studies are required to evaluate the CTSS score in combination with existing scores.

Limitations: Being a retrospective study, there is the possibility of some registration bias in the medical charts. Even though the sampling of arterial blood gases was concurrent with oxygen saturation determination, some clinical data are lacking because they were not registered.

Future Directions: More research is needed regarding severe respiratory infections in high altitude populations. The information obtained in these settings can be valuable to evaluate the hypoxic response in several medical conditions.

Acknowledgments

The authors wish to thank the authorities of the Regional Surgical Medical “Daniel A. Carrión” Hospital, who gave us the facilities to carry out the study.

Author Contributions

The idea of manuscript was planned by MCA and WCG. The basic literature was brought together and first draft was prepared by APS, MCA, GTS, WCG, MQC and VDL. APS, GTS, MQC and VDL collected and compiled the information. WCG edited the final draft and MCA and GTS approved the final version of the manuscript. All the authors have read and approved the submission of manuscript.

Funding

Self-financed study.

Competing Interests

The authors have declared that no competing interests exist.

References

1. Arreaza A, López O, Toledo M. The COVID-19 pandemic in Latin America: Impacts and perspectives [Internet]. Caracas: CAF; 2021. Available from: http://scioteca.caf.com/handle/123456789/1788.
2. Chua F, Armstrong-James D, Desai SR, Barnett J, Kouranos V, Kon OM, et al. The role of CT in case ascertainment and management of COVID-19 pneumonia in the UK: Insights from high-incidence regions. Lancet Respir Med. 2020; 8: 438-440.
3. Behzad S, Aghaghazvini L, Radmard AR, Gholamrezanezhad A. Extrapulmonary manifestations of COVID-19: Radiologic and clinical overview. Clin Imaging. 2020; 66: 35-41.
4. Xie J, Covassin N, Fan Z, Singh P, Gao W, Li G, et al. Association between hypoxemia and mortality in patients with COVID-19. Mayo Clin Proc. 2020; 95: 1138-1147.
5. Terpos E, Ntanasis-Stathopoulos I, Elalamy I, Kastritis E, Sergentanis TN, Politou M, et al. Hematological findings and complications of COVID-19. Am J Hematol. 2020; 95: 834-847.
6. Akoumianaki E, Vaporidi K, Bolaki M, Georgopoulos D. Happy or silent hypoxia in COVID-19–A misnomer born in the pandemic era. Front Physiol. 2021; 12: 745634.
7. Pham K, Parikh K, Heinrich EC. Hypoxia and inflammation: Insights from high-altitude physiology. Front Physiol. 2021; 12: 676782.
8. Zubieta-Calleja G, Zubieta-DeUrioste N. Pneumolysis and "silent hypoxemia" in COVID-19. Indian J Clin Biochem. 2021; 36: 112-116.
9. Seclén SN, Nunez-Robles E, Yovera-Aldana M, Arias-Chumpitaz A. Incidence of COVID-19 infection and prevalence of diabetes, obesity and hypertension according to altitude in Peruvian population. Diabetes Res Clin Pract. 2020; 169: 108463.
10. Arias-Reyes C, Carvajal-Rodriguez F, Poma-Machicao L, Aliaga-Raduán F, Marques DA, Zubieta-DeUrioste N, et al. Decreased incidence, virus transmission capacity, and severity of COVID-19 at altitude on the American continent. PLoS One. 2021; 16: e0237294.
11. Ortiz-Prado E, Fernandez Naranjo RP, Vasconez E, Simbaña-Rivera K, Correa-Sancho T, Lister A, et al. Analysis of excess mortality data at different altitudes during the COVID-19 outbreak in Ecuador. High Alt Med Biol. 2021; 22: 406-416.

12. Woolcott OO, Bergman RN. Mortality attributed to COVID-19 in high-altitude populations. High Alt Med Biol. 2020; 21: 409-416.
13. Pun M, Turner R, Strapazzon G, Brugger H, Swenson ER. Lower incidence of COVID-19 at high altitude: Facts and confounders. High Alt Med Biol. 2020; 21: 217-222.
14. Nicolaou L, Steinberg A, Carrillo-Larco RM, Hartinger S, Lescano AG, Checkley W. Living at high altitude and COVID-19 mortality in Peru. High Alt Med Biol. 2022; 23: 146-158.
15. Segovia-Juarez J, Castagnetto JM, Gonzales GF. High altitude reduces infection rate of COVID-19 but not case-fatality rate. Respir Physiol Neurobiol. 2020; 281: 103494.
16. Weinstein KJ. Thoracic skeletal morphology and high-altitude hypoxia in Andean prehistory. Am J Phys Anthropol. 2007; 134: 36-49.
17. Fakhri S, Hannon K, Moulden K, Peterson R, Hountras P, Bull T, et al. Residence at moderately high altitude and its relationship with WHO Group 1 pulmonary arterial hypertension symptom severity and clinical characteristics: The Pulmonary Hypertension Association Registry. Pulm Circ. 2022; 12: e12112.
18. Calderón Gerstein W, López Martínez O. Valores gasométricos en población adulta y adulta mayor residente de gran altitud. An Fac Med. 2020; 81: 154-160.
19. Sharma S, Aggarwal A, Sharma RK, Patras E, Singhal A. Correlation of chest CT severity score with clinical parameters in COVID-19 pulmonary disease in a tertiary care hospital in Delhi during the pandemic period. Egypt J Radiol Nucl Med. 2022; 53: 166. doi:10.1186/s43055-022-00832-x.
20. Ito R, Maeda M, Takehara Y, Komori GD, Nishi Y, Kondo K, et al. An epidemiological evaluation of COVID-19 in La paz, Bolivia. J Infect Chemother. 2023; 29: 333-338.
21. Qaasemya A, Khajehpoura H, Galehb HE, Dorostkarb R, Assadollahic E, Alidadid S. Chest CT-scan findings in COVID-19 patients: The relationship between the duration of symptoms and correlation with the oxygen saturation level. Rom J Mil Med. 2021; 124: 29-36.
22. Malbouisson LM, Busch CJ, Puybasset L, Lu QI, Cluzel P, Rouby JJ, et al. Role of the heart in the loss of aeration characterizing lower lobes in acute respiratory distress syndrome. Am J Respir Crit Care Med. 2000; 161: 2005-2012.
23. Coudert J, Paz-Zamora M, Barragan L, Briancon L, Spielvogel H, Cudkowicz L. Regional distribution of pulmonary blood flow in normal high-altitude dwellers at 3,650 m (12,200 ft). Respiration. 1975; 32: 189-209.
24. Abd El Megid AG, El Shabrawy M, Abdalla AA. Correlation between chest CT severity scoring system with oxygen saturation and laboratory inflammatory markers in adult patients with COVID-19 infection. Egypt J Radiol Nucl Med. 2022; 53: 72.
25. Komurcuoglu B, Susam S, Batum Ö, Turk MA, Salik B, Karadeniz G, et al. Correlation between chest CT severity scores and clinical and biochemical parameters of COVID-19 pneumonia. Clin Respir J. 2022; 16: 497-503.
26. Mohammad ZJ, Khoshnaw ZS. Correlation between chest CT severity score and the oxygen saturation of patients with COVID-19 pneumonia. Int J Appl Sci. 2022; 13: 117-125.
27. Qadir FI, Kakamad FH, Abdullah IY, Abdulla BA, Mohammed SH, Salih RQ, et al. The relationship between CT severity infections and oxygen saturation in patients infected with COVID-19, a cohort study. Ann Med Surg. 2022; 76: 103439.

28. Roozeman JP, Mazzinari G, Neto AS, Hollmann MW, Paulus F, Schultz MJ, et al. Prognostication using SpO2/FiO2 in invasively ventilated ICU patients with ARDS due to COVID-19–insights from the PRoVENT-COVID study. J Crit Care. 2022; 68: 31-37.
29. Aalinezhad M, Alikhani F, Akbari P, Rezaei MH, Soleimani S, Hakamifard A. Relationship between CT severity score and capillary blood oxygen saturation in patients with COVID-19 infection. Indian J Crit Care Med. 2021; 25: 279-283.
30. Yanamandra U, Shobhit S, Paul D, Aggarwal B, Kaur P, Duhan G, et al. Relationship of computed tomography severity score with patient characteristics and survival in hypoxemic COVID-19 patients. Cureus. 2022; 14: e22847.
31. Mallet RT, Burtscher J, Richalet JP, Millet GP, Burtscher M. Impact of high altitude on cardiovascular health: Current perspectives. Vasc Health Risk Manag. 2021; 17: 317-335.
32. Sime F, Penaloza D, Ruiz L. Bradycardia, increased cardiac output, and reversal of pulmonary hypertension in altitude natives living at sea level. Br J Cardiol. 1971; 33: 647-567.