Association of biomarkers and severity of COVID-19: A cross-sectional study

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Abstract

Introduction

COVID-19 is a disease that has claimed the lives of many people. However, alterations in laboratory profiles in the city of Tacna have not been accurately established in association with its severity to support diagnosis and treatment.

Objective

To determine biomarkers related to the severity of COVID-19 in patients treated at the social security hospital in Tacna during 2020.

Methods

We performed an observational, cross-sectional, and analytical study that included 308 patients with COVID-19 from the social security hospital in Tacna, Peru, during the "first wave" of the pandemic (from July to August 2020). Immunological, hematological, arterial gas, hemostasis, and biochemical markers were collected. Patients were categorized into mild, moderate, and severe based on the clinical criteria found on clinical records. Correlation strength was performed according to Spearman's Rho coefficient. The performance of the biomarkers associated with severity was analyzed with the Receiver Operating Characteristic curve.

Results

Regarding hematological markers there was a positive correlation with monocyte count (correlation coefficient: 0.841; area under the curve 97.0%; $p < 0.05$) and a negative correlation with lymphocyte count (correlation coefficient: -0.622; area under the curve 82.7%; $p < 0.05$). Regarding biochemical markers, arterial gases and hemostasis, no significant correlations were found. In immunological markers, we found positive correlation with ferritin (correlation coefficient: 0.805; area under the curve 94.0%; $p < 0.05$), and C-reactive protein (correlation coefficient: 0.587; area under the curve 87.4%; $p < 0.05$).

Conclusions

The biomarkers that can be considered as parameters associated with the severity of COVID-19 are the absolute blood count of monocytes and serum ferritin concentration.

MAIN MESSAGES

- ♦ Biomarkers may help prevent complications in patients with COVID-19 disease. So far, laboratory biomarkers correlating with the severity of COVID-19 have not been accurately established in Peru.
- ♦ Limitations of this study are the high proportion of moderate and severe COVID-19 stages, the shortage of reagents, and the lack of standardized laboratory test profiles for COVID-19.
- ♦ This study may allow standardizing critical values of COVID-19 biomarkers that alert cardiac, renal, and hypercoagulability complications, significantly elevated in multiple organ failure.
- ♦ This work presents biomarkers as tools associated with COVID-19 severity to allow timely diagnosis and treatment of severe or critical states of the disease.

INTRODUCTION

To the World Health Organization (WHO), COVID-19 is the infectious disease caused by the SARS-CoV-2 virus that first broke out in Wuhan (China) in late 2019. This infection generates various complications, including severe acute respiratory syndrome (SARS) [1].

From the pandemic onset until October 2021, more than 249 million people have been infected with this new virus, and 2.07% have died worldwide [2]. In addition, it has been observed that older people and those with comorbidities are more likely to develop a severe disease characterized by severe pneumonia or multiple organ failure, which are the leading causes of death in these patients [3]. The disease burden in Peru is high since more than 2 million confirmed cases of COVID-19 and more than 200 000 deaths have been reported until October 2021 [2].

Several countries have widely described the clinical characteristics of COVID-19, clearly defining its signs and symptoms. However, laboratory profiles have not been accurately established as biomarkers with prognostic value, nor have there been defined alterations that can help prevent patient complications [4].

However, several investigations have shown that biomarkers such as C-reactive protein, lactate dehydrogenase, T-troponin, ferritin, hematological parameters, and D-dimer are useful in clinical practice because they improve the categorization of patients according to severity [5]. Research by Sirvent J. et al. in Spain [6], Pujani M. et al. in India [7], and Galicia C. et al. in Mexico [8], have shown that these biomarkers are significantly altered in the multiple organ failure produced by COVID-19, due to a sustained dysregulation of inflammatory response and organ hypoxia [9].

At the time of writing, there are more than 30 000 confirmed cases and 2 000 deaths due to COVID-19 in Tacna, Peru [10]. Thus, there is an urgent need to standardize the laboratory biomarkers that account for Tacna's epidemiology and identify patients who progress to severe stages [11].

This study aims to determine biomarkers related to the severity of COVID-19 patients treated at the Tacna social security hospital. Also, it aims to establish criteria that allow risk stratification to perform timely interventions aimed at patients with a higher probability of developing severe complications.

METHODS

The present observational, cross-sectional, analytical study was conducted at the social security hospital in Tacna, Peru, from June 1 to August 30, 2020. This work was approved by the Research Ethics Committee (CEI) of the *Universidad Privada de Tacna*, with Registration Code CEI-001.

The research consisted of 308 patients with clinical findings of lower respiratory tract infection who tested positive for COVID-19 through a rapid antigen test for detecting SARS-CoV-2 or by the real-time reverse transcription-polymerase chain reaction assay (RT-PCR test).

Exclusion criteria included patients under 18 years of age and patients with a history of disorders that basally affect the count or dosage of the analytes tested as biomarkers of COVID-19 severity (e.g., thrombocytopenic purpura, allergies, leukemia).

Data were collected from the laboratory management system, which considered the collection of serum, plasma, and whole blood samples from patients on admission. Ferritin, troponin I, and procalcitonin were tested using the electrochemilumines-cence method on the COBAS E411 automated analyzer from Roche Diagnostics. Hematological biomarkers (absolute counts of leukocytes, eosinophils, basophils, neutrophils, lymphocytes, and platelets) were measured with the Sysmex XS-1000*i* five-strain automated device from Roche Diagnostics. Biomarkers obtained from arterial gases (pH, partial oxygen and partial carbon dioxide pressure, arterial oxygen saturation, fractional percentage of inspired oxygen, and bicarbonate, sodium, potassium, chloride, ionized calcium, and lactate concentration) were measured with automated ABL800 FLEX from Radiometer. Coagulation biomarkers (prothrombin time, fibrin-ogen, and D-dimer) were measured with the Coatron A6 Plus

automated equipment from TECO Medical Instruments. Biochemical biomarkers (lactate dehydrogenase, aspartate aminotransferase, alanine aminotransferase, total creatine phosphokinase, myocardial creatine phosphokinase, glucose, urea, and creatinine) were estimated with the Bio System BA400 automated equipment, in addition to C-reactive protein, which is an immunological marker. The analytical methods were performed according to the manufacturer's indications, considering internal and external quality controls.

Patients were categorized into mild, moderate, and severe based on the clinical criteria found on medical records. Mild disease was defined as patients with mild symptoms that showed no changes in pulmonary imaging. Moderate disease was defined as having one of the following symptoms: oxygen saturation at room air less than or equal to 93%, respiratory rate greater than or equal to 30 breaths per minute, alveolar partial pressure of oxygen/fractional percentage of inspired oxygen ratio less than 300 millimeters of mercury, and pulmonary infiltrates greater than 50% within 24 to 48 hours of symptom onset [12]. Critical disease was defined as patients presenting respiratory failure with mechanical ventilation and requiring follow-up in the intensive care unit.

For statistical analysis, the Kolmogorov-Smirnov test was applied to corroborate the normality of the sample. Correlation strength between variables was performed according to Spearman's Rho coefficient. The hematological, biochemical, immunological, arterial gas, and hemostasis biomarker analytes were expressed according to mild, moderate, and severe categories in mean plus or minus one standard deviation (SD). Differences between means of biomarker values were analyzed using the Wilcoxon signed-rank test for independent samples.

The biomarkers associated with COVID-19 severity were performed with the Receiver Operating Characteristic (ROC) curve and the area under the curve (AUC). The performance of the aforementioned statistical tests was assessed using SPSS Statistics Data software version 25, with $p < 0.05$ considered statistically significant.

The information was collected between July and August 2020, when the "peak" of the pandemic wave hit the city of Tacna in Peru, which is why most of the population has a moderate to severe stage of COVID-19.

The shortage of reagents and the lack of a standardized laboratory testing protocol for COVID-19 were limiting factors to studying a larger population.

RESULTS

We evaluated 308 participants with a diagnosis of COVID-19. We identified 36 laboratory analytes in the following areas: hematology, biochemistry, immunology, hemostasis, arterial gases, and electrolytes.

Of the total population, 69% were male, with a mean age of 61.2 ± 13.7 years, and 37% showed some comorbidity.

Table 1 shows that out of 308 eligible patients with COVID-19, the mean age was 61.2 years (confidence interval: 59.6 to 62.7 years), the female population represented 31% (mean age: 64.5 years), and the male population represented 69% (mean age: 59.7 years). Thirty-six percent of the study population reported some comorbidity, the most frequent being diabetes (17%) and arterial hypertension (8%). When correlating the degree of severity of COVID-19 with laboratory analytes, we observed positive and negative correlations with various parameters.

Concerning the positive correlation, we found that this was:

a) Of high degree with absolute monocyte count and serum ferritin concentration.
b) Of moderate degree with the absolute leukocyte count, neutrophils, troponin I, and C-reactive protein.
c) Of low degree with lactate dehydrogenase, urea, procalcitonin, and lactate.
d) Of very low degree with blood potassium, chloride, ionized calcium, D-dimer, glucose, and creatinine.

Likewise, the absolute lymphocyte count was highly and negatively correlated with COVID-19 severity. Moreover, the absolute eosinophil and platelet count (moderate degree) and partial pressure of oxygen and arterial oxygen saturation (low degree) negatively correlated with COVID-19 severity.

Absolute monocyte count and serum ferritin concentration showed the strongest correlation with the degree of severity of COVID-19.

The degrees of clinical severity of mild, moderate, and severe COVID-19 were tested for normality and compared using the Kruskal Wallis test.

Table 2 shows a statistically significant difference ($p < 0.05$), where the absolute count of leukocytes, monocytes, neutrophils, serum concentration of lactate dehydrogenase, alanine aminotransferase, creatine kinase myocardium isoenzyme, glucose, urea, creatinine, percentage of inspired oxygen, sodium, potassium, lactate, ferritin, troponin I, procalcitonin and C-reactive protein, and D-dimer were higher in patients with severe COVID-19 than in those with mild and moderate COVID-19. Meanwhile, the absolute count of eosinophils, lymphocytes, platelets, and partial pressure of oxygen and arterial oxygen saturation was lower in patients with severe COVID-19 than in those with mild and moderate COVID-19.

ROC curves (shown in Table 3 and Figure 1) were constructed to evaluate the association of the severity of COVID-19 patients at admission with laboratory biomarkers. The results showed that the area under the curve (AUC) with the highest performance in hematological biomarkers were monocytes (AUC: 97%) and eosinophils (AUC: 84.3%); in biochemical biomarkers, were lactate dehydrogenase (AUC: 67.4%) and urea (AUC: 66.9%); in arterial gas biomarkers were arterial oxygen saturation (AUC: 66.3%) and partial oxygen saturation (AUC: 63.1%); while in immunological biomarkers were ferritin (AUC: 94%) and C-reactive protein (AUC: 87.4%).

Table 1. Correlation between COVID-19 severity with laboratory biomarkers.

	r*	P value
Hematological biomarkers		
Hemoglobin (g/dL)	0.065	0.258
Hematocrit (%)	0.061	0.283
Leukocytes (x10¹/µL)	0.502	0.000
Eosinophils (x10¹/µL)	-0.487	0.000
Basophils (x10¹/µL)	-0.037	0.515
Monocytes (x10¹/µL)	0.841	0.000
Lymphocytes (x10¹/µL)	-0.622	0.000
Neutrophils (x10¹/µL)	0.596	0.000
Platelets (x10¹/µL)	-0.587	0.000
Biochemical biomarkers		
LDH (U/L)	0.309	0.000
TGO (U/L)	0.004	0.943
TGP (U/L)	-0.073	0.223
CPK-total (U/L)	0.056	0.407
CPK-mb (U/L)	0.112	0.097
Glucose (mg/dL)	0.198	0.001
Urea (mg/dL)	0.296	0.000
Creatinine (mg/dL)	0.149	0.009
Arterial gas and electrolyte biomarkers		
pH	-0.063	0.270
PO2 (mmHg)	-0.246	0.000
PCO2 (mmHg)	0.021	0.713
SaO2 (%)	-0.311	0.000
FiO2	0.221	0.000
HCO3- (mmol/L)	-0.018	0.758
Sodium (mmol/L)	-0.038	0.503
Potassium (mmol/L)	0.174	0.002
Chloride (mmol/L)	0.119	0.037
Ionized calcium (mmol/L)	0.120	0.035
Lactate (mmol/L)	0.201	0.000
Immunological biomarkers		
Ferritin (ng/mL)	0.805	0.000
Troponin I (ng/mL)	0.436	0.000
Procalcitonin (ng/mL)	0.363	0.000
C-reactive protein (mgL)	0.587	0.000
Hemostasis biomarkers		
Prothrombin Time (s)	0.052	0.663
INR	0.056	0.643
Fibrinogen (mg/dL)	0.024	0.742
D-dimer (ng/mL)	0.173	0.005

N: 308; r: correlation coefficient; mmHg; millimeters of mercury; Hb: hemoglobin; Hto: hematocrit; LDH: lactate dehydrogenase; TGO: aspartate aminotransferase; TGP: alanine aminotransferase; CPK: creatine phosphokinase; CPK-mb: creatine phosphokinase of the myocardium; PO2: partial pressure of oxygen; PCO2: partial pressure of carbon dioxide; SaO2: arterial oxygen saturation; FiO2: fractional percentage of inspired oxygen; HCO_3: bicarbonate concentration; INR: international normalized ratio.

A p value < 0.5 was considered statistically significant.

Spearman's correlation coefficient was used to study the relationship between laboratory biomarkers and the severity of COVID-19.

Source: Prepared by the authors of this study.

The laboratory analytes that showed the highest correlation with severe disease in COVID-19 patients were absolute monocyte blood count, serum ferritin concentration, and C-reactive protein.

DISCUSSION

This study showed a high percentage (36%) of comorbidity among eligible participants. These results resemble those found

Table 2. Differences in laboratory biomarkers according to the severity of COVID-19.

	COVID-19 severity			
	Mild **(N = 48)**	**Moderate** **(N = 103)**	**Severe** **(N = 157)**	**P value**
Hematological biomarkers				
Hemoglobin (g/dL)	13.2 ± 2.3	13.9 ± 2.0	13.8 ± 2.3	0.123
Hematocrit (%)	39.1 ± 6.3	40.5 ± 6.0	40.3 ± 6.4	0.196
Leukocytes (x101/µL)	9517.3 ± 2075.2	11175.0 ± 3835.7	14020.9 ± 3753.6	0.000
Eosinophils (x101/µL)	118.0 ± 142.3	92.1 ± 31.2	36.4 ± 10.9	0.000
Basophils (x101/µL)	27.2 ± 57.5	49.2 ± 81.7	30.7 ± 60.7	0.138
Monocytes (x101/µL)	400.5 ± 128.6	662.0 ± 286.1	1452.9 ± 440.5	0.000
Lymphocytes (x101/µL)	2423.8 ± 498.2	1781.6 ± 716.2	1204.2 ± 442.7	0.000
Neutrophils (x101/µL)	6547.7 ± 1649.4	8590.1 ± 2985.4	11296.8 ± 3074.5	0.000
Platelets (x101/µL)	343646 ± 68004	339612 ± 111688	236459 ± 47509	0.000
Biochemical biomarkers				
LDH (U/L)	652.5 ± 309.3	711.1 ± 236.7	870.0 ± 322.7	0.000
TGO (U/L)	68.9 ± 56.6	63.0 ± 47.1	66.1 ± 61.3	0.980
TGP (U/L)	71.3 ± 65.9	89.4 ± 75.1	71.8 ± 67.9	0.031
CPK-total (U/L)	134.8 ± 131.0	134.2 ± 232.5	220.5 ± 594.8	0.605
CPK-mb (U/L)	56.7 ± 85.9	25.3 ± 15.3	37.6 ± 51.6	0.019
Glucose (mg/dL)	143.0 ± 80.4	163.8 ± 103.5	182.6 ± 114.0	0.002
Urea (mg/dL)	38.6 ± 35.7	38.8 ± 36.3	57.2 ± 46.8	0.000
Creatinine (mg/dL)	1.2 ± 1.3	1.2 ± 1.2	1.6 ± 1.7	0.033
Arterial gas and electrolyte biomarkers				
pH	7.4 ± 0.1	7.4 ± 0.1	7.4 ± 0.1	0.516
PO2 (mmHg)	74.5 ± 34.7	64.6 ± 17.8	60.8 ± 27.8	0.000
PCO2 (mmHg)	33.1 ± 6.0	33.1 ± 6.3	35.6 ± 14.1	0.919
SaO2 (%)	91.6 ± 9.5	89.3 ± 7.9	83.3 ± 13.4	0.000
FiO2	25.9 ± 11.6	28.1 ± 14.3	37.6 ± 24.3	0.001
HCO3- (mmol/L)	21.4 ± 3.7	20.8 ± 3.7	21.1 ± 4.6	0.938
Sodium (mmol/L)	139.2 ± 5.8	134.9 ± 6.3	152.0 ± 135.0	0.000
Potassium (mmol/L)	3.8 ± 0.5	3.9 ± 0.5	4.1 ± 0.7	0.008
Chloride (mmol/L)	106.0 ± 5.3	106.8 ± 5.6	107.7 ± 7.7	0.101
Ionized calcium (mmol/L)	1.1 ± 0.1	1.1 ± 0.1	1.1 ± 0.1	0.110
Lactate (mmol/L)	1.8 ± 1.0	2.0 ± 0.7	2.4 ± 1.3	0.001
Immunological biomarkers				
Ferritin (ng/mL)	401.4 ± 128.6	637.5 ± 308.5	1733.3 ± 4080.9	0.000
Troponin I (ng/mL)	0.012 ± 0.017	0.014 ± 0.028	0.063 ± 0.146	0.000
Procalcitonin (ng/mL)	0.21 ± 0.34	0.27 ± 0.60	0.58 ± 0.85	0.001
C-reactive protein (mg/L)	6.22 ± 4.62	6.84 ± 5.22	15.27 ± 7.72	0.000
Prothrombin time (s)	14.7 ± 2.0	13.9 ± 4.7	14.5 ± 1.6	0.002
Hemostasis biomarkers				
INR	1.07 ± 0.17	1.01 ± 0.41	1.06 ± 0.14	0.002
Fibrinogen (mg/dL)	490.6 ± 247.5	580.2 ± 227.8	599.1 ± 460.3	0.171
D-dimer (ng/mL)	1038.2 ± 2637.0	748.5 ± 2066.2	1719.3 ± 4050.6	0.002

CPK-mb: creatine phosphokinase myocardium isoenzyme; CPK: creatine phosphokinase; FiO2: fractional percentage of inspired oxygen; HCO3: bicarbonate concentration; Hb: hemoglobin; Hto: hematocrit; INR: international normalized ratio; LDH: lactate dehydrogenase; PCO2: partial pressure of carbon dioxide; PO2: partial pressure of oxygen; SaO2: arterial oxygen saturation; TGO: aspartate aminotransferase; TGO: aspartate aminotransferase; TGP: alanine aminotransferase; TGP: alanine aminotransferase.
A p value < 0.5 was considered statistically significant.
The degrees of clinical severity of COVID-19 – mild, moderate, and severe – were tested for normality and compared using the Kruskal Wallis test.
Source: Prepared by the authors of this study.

in a study in Peru in 2020, where existing comorbidities were present in almost 40% of patients [13]. We found a positive correlation between the severity of COVID-19 and the absolute monocyte count and serum ferritin concentration. These

Table 3. Performance of laboratory biomarkers (AUC) on COVID-19 severity prognosis.

	Area under de curve (AUC)			
	Area	95% CI lower limit	95% CI upper limit	P value
Hematological biomarkers				
Leukocytes (x101/µL)	0.776	0.725	0.828	0.000
Eosinophils (x101/µL)	0.843	0.788	0.899	0.000
Basophils (x101/µL)	0.970	0.951	0.989	0.000
Monocytes (x101/µL)	0.827	0.780	0.873	0.000
Lymphocytes (x101/µL)	0.819	0.773	0.866	0.000
Neutrophils (x101/µL)	0.836	0.792	0l881	0.000
Biochemical biomarkers				
LDH (U/L)	0.674	0.603	0.745	0.000
CPK-mb (U/L)	0.582	0.506	0.658	0.037
Urea (mg/dL)	0.669	0.597	0.741	0.000
Creatinine (mg/dL)	0.575	0.499	0.651	0.057
Arterial gas and electrolyte biomarkers				
PO2 (mmHg)	0.631	0.568	0.694	0.000
SaO2 (%)	0.663	0.602	0.724	0.000
FiO2	0.611	0.548	0.674	0.001
Potassium (mmol/L)	0.601	0.538	0.665	0.002
Ionized calcium (mmol/L)	0.567	0.503	0.631	0.043
Lactate (mmol/L)	0.602	0.539	0.666	0.002
Immunological biomarkers				
Ferritin (ng/mL)	0.940	0.880	1.000	0.000
Troponin I (ng/mL)	0.705	0.561	0.850	0.011
Procalcitonine (ng/mL)	0.732	0.595	0.869	0.004
C-reactive protein (mgL)	0.874	0.783	0.965	0.000

AUC: area under the curve; CI: confidence interval; CPK-mb: creatine phosphokinase myocardium isoenzyme; FiO2: fractional percentage of inspired oxygen; LDH: lactate dehydrogenase; PO2: partial pressure of oxygen; SaO2: arterial oxygen saturation; µL: microliters.

Receiver operating characteristic curves show the relative diagnostic performance of laboratory parameters associated with disease severity in patients with SARS-CoV-2 infection.

Source: Prepared by the authors of this study.

results align with Lippi G. et al. and Zeng et al. findings [4,9], who found hematological counts and serum ferritin as markers of disease severity progression. However, it should be taken into account that these studies were performed in other settings and that our work presented certain methodological limitations, including incomplete data on clinical records, which negatively impacted the sample size of this study.

We found that a severe COVID-19 disease was significantly associated ($p < 0.05$) with absolute leukocyte, monocytes, neutrophils count, and serum concentration of lactate dehydrogenase, alanine aminotransferase, creatine kinase myocardium isoenzyme, glucose, urea, creatinine, ferritin, troponin I, procalcitonin, C-reactive protein, and plasma D-dimer concentration. Regarding biomarker performance, absolute blood counts, ferritin, and C-reactive protein were strongly associated with severe disease.

Regarding hematological biomarkers, we found a positive correlation between the total leukocyte, monocyte, and neutrophil counts and the severity of COVID-19. These results agree with Michael B. et al. study [14], where a positive correlation was found in both leukocyte and neutrophil counts. On the other hand, a meta-analysis performed by Ghahramani S. et al. [15] found a negative correlation with lymphocyte, eosinophil, and platelet counts, which also aligns with our results.

Several studies conducted in different settings, such as Mardani R. et al. in Iran, Dong X. et al. in China, Bennouar S. et al. in Algeria, and Aloisio E. et al. in Italy [16–19], indicate that there is a significant correlation between lactate dehydrogenase and the degree of severity of patients diagnosed with COVID-19. These results support our findings. In addition to these biomarkers, we found a significant correlation with glucose, creatinine, and urea.

Concerning arterial gas and electrolyte biomarkers, we found a low positive correlation of oxygen partial pressure, fractional percentage of inspired oxygen, potassium, chloride, ionized calcium, and lactate with disease severity. Moreover, we found a negative correlation between arterial oxygen saturation and disease severity.

Gutiérrez J. et al. [20] found that troponin I and procalcitonin correlate with the severity of patients with COVID-19. On the other hand, Huang I. et al. [21] found that C-reactive protein,

Figure 1. ROC curve analysis, using hematological biomarkers, in diagnosing severe cases of COVID-19.
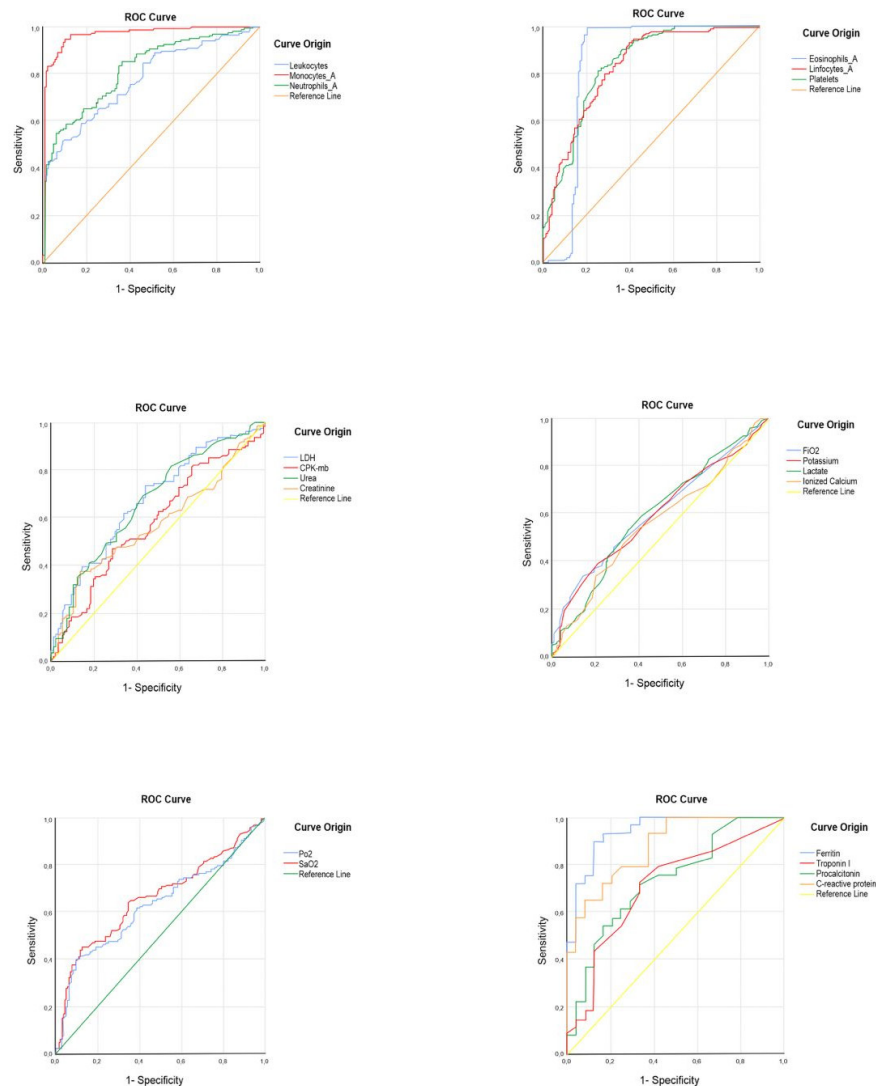
ROC: Receiver Operating Characteristic.
Source: Prepared by the authors of this study.

procalcitonin, and ferritin also correlate with disease severity. These findings align with our results.

Regarding coagulation biomarkers, we found no correlation between the degree of disease severity and the prothrombin time, international normalized ratio, and fibrinogen tests. In contrast, the D-dimer test showed a positive correlation. Despite epidemiological differences with our work, Long H. et al. [22], in their research conducted at the Tianyou Hospital of Wuhan University of Science and Technology, reported similar results concerning the D-dimer. However, they also found a positive correlation between the measurement of fibrinogen and the severity of COVID-19.

In our setting, we found results shared with other studies on the differences in hematological biomarkers according to the severity stratification of patients with COVID-19. Gallo B. et al. [23],

Tan L. et al. [24], and Henry B. et al. [25] reported decreased lymphocyte counts in patients diagnosed with severe COVID-19. Lippi G [26]. and Tjendra Y. et al. [27] found an association between low platelet count and the severe severity of COVID-19. On the other hand, Tuta E. et al. [28] and Dinevari M [29]. found low hemoglobin levels in severe cases of COVID-19, agreeing with our findings on lymphocytes and platelets, but not with hemoglobin levels. The differences in the results may be due to the nature of the studies or the type of population.

Moreover, we found that most of the biochemical and immunological tests increased with the severity of the disease, except for aspartate aminotransferase and total creatine phosphokinase. These results align with Gutiérrez et al. [20] and Ocampo C et al. [30] in their work on biomarkers.

In all, we found that hematological and immunological examinations had the highest correlation with disease severity. The parameters with the best performance were eosinophil count, monocytes, lymphocytes, neutrophils, platelets, C-reactive protein, and ferritin. These results share similarities with research conducted in other settings, such as those of Fang L. et al. [31], Gutiérrez C. et al. [20], and Ocampo C. et al. [30].

It should be emphasized that it is of utmost importance to establish risk and diagnostic profiles involving the measurement of biomarkers for the management or prognosis of patients with COVID-19.

LIMITATIONS

Finally, it should be mentioned that our study has certain limitations. Among them is the pandemic setting in which the data collection was performed, which limited the available information. Moreover, the management of COVID-19 patients varied continuously as the scientific knowledge and guidelines changed over time. On the other hand, the sample size was relatively small for reasons unrelated to the study, limiting the extrapolation of results to other regions in Peru.

CONCLUSIONS

With the so-called "wave peak", the COVID-19 pandemic presented enormous challenges to the healthcare system. Amidst critical scenarios, it is necessary to ensure rational use of medical resources to treat patients with severe diseases effectively. However, management requires early diagnostic tools to reduce mortality in the affected population. In the present work, we investigated the strength of correlation between laboratory biomarkers and the degree of severity of COVID-19 disease. We found that the absolute monocyte count and serum ferritin concentration had the highest correlation with COVID-19 severity. These findings establish these laboratory biomarkers as valuable parameters to infer the prognosis of hospitalized COVID-19 patients.

This study proposes a mathematical approach that integrates monocytes and ferritin as an index of inflammation and, possibly, as a predictor of the dysregulation of the inflammatory response produced by COVID-19.

Considering that the data was collected at the "peak" of the first wave of the pandemic in the city of Tacna, further research with larger samples is recommended to confirm our findings.

IMPLICATIONS

With the results obtained in this work, it may be possible:

- To standardize critical values of COVID-19 biomarkers available in Tacna, Peru, according to population characteristics and logistic feasibility.
- To analyze laboratory markers that signal cardiac, muscular, renal, and thrombotic complications

– significantly elevated in multiple organ failure – and are associated with COVID-19 severity.
- To encourage further studies to develop clinical diagnostic tools that integrate, through a mathematical index, laboratory analytes that show high statistical correlation with the severity of COVID-19 to allow the diagnosis and timely treatment of the severe or critical disease states.

Notes

study. However, the data can be available upon reasonable request and with the institution's permission.

Provenance and peer review

Not commissioned. Externally peer-reviewed by three reviewers, double-blind.

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Spanish.

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Asociación de biomarcadores y severidad de COVID-19: estudio transversal

Resumen

Introducción

COVID-19, es una enfermedad que ha cobrado la vida de muchas personas. Sin embargo, las alteraciones en los perfiles de laboratorio en la ciudad de Tacna, no han sido establecidas de manera precisa en asociacion a su gravedad para apoyo en el diagnostico y tratamiento.

Objetivo

Determinar los biomarcadores que esten relacionados al grado de severidad de los pacientes COVID-19 atendidos en el hospital de la seguridad social, en Tacna durante 2020.

Métodos

Estudio observacional, transversal y analitico. Conformado por 308 pacientes con COVID-19
del hospital de la seguridad social de la ciudad de Tacna, Peru, durante el golpe de la "primera ola" (de julio a agosto de 2020). Se recolectaron resultados de marcadores inmunologicos, hematologicos, gases arteriales, hemostasia y bioquimicos. Los pacientes se categorizaron en leves, moderados y severos, basandonos en el criterio medico – clinico de la historia clinica. Las correlaciones y fuerza de correlacion fueron realizadas segun coeficiente Rho de Spearman. El rendimiento de los biomarcadores asociado a la gravedad, se realizo con curva Receiver Operating Characteristic.

Resultados

En marcadores hematologicos existe correlacion positiva con recuento de monocitos (coeficiente de correlacion: 0,841; area bajo la curva 97,0%; $p < 0,05$) y correlacion negativa con recuento de linfocitos (coeficiente de correlacion: -0,622; area bajo la curva 8.27%; $p < 0,05$). En marcadores bioquimicos, gases arteriales y hemostasia, no se hallaron correlaciones significativas. En marcadores inmunologicos, encontramos correlacion positiva con ferritina (coeficiente de correlacion: 0,805; area bajo la curva 94,0%; $p < 0,05$), y proteina C reactiva (coeficiente de correlacion: 0,587; area bajo la curva 87,4%; $p < 0,05$).

Conclusiones

Los biomarcadores que pueden considerarse como parametros asociados a la gravedad de
COVID-19, son el recuento sanguineo absoluto de monocitos y la concentracion serica de ferritina.