*Rev. cient. cienc. salud. Diciembre 2022; 4(2):27-37*
*Doi: 10.53732/rccsalud/04.02.2022.27*

Artículo Original/ Original Article

# Relevant laboratory parameters in patients at hospital admission between July 2020 and October 2021 due to covid-19 at the Tesãi Foundation Hospital

**Dennise María Villanueva González, Eliana Romina Meza Miranda***

Universidad Nacional de Asunción. Centro Multidisciplinario de Investigaciones Tecnológicas. San Lorenzo, Paraguay

**How to reference this article/ Cómo referenciar este artículo**

**Villanueva González DM, Meza Miranda ER.** Relevant laboratory parameters in patients at hospital admission between july 2020 and october 2021 due to covid 19 at the Tesãi Foundation Hospital. Rev. cient. cienc. salud 2022; 4(2):27-37

## A B S T R A C T

**Background:** in the fight against COVID-19, the identification of laboratory predictors in the progression of severe and fatal forms is urgently needed. **Aims:** to describe the alterations of laboratory parameters of patients diagnosed with COVID-19 at admission to Tesãi Foundation Hospital in Ciudad del Este-Paraguay between July 2020 to October 2021. **Methods:** A retrospective study using the medical charts of 103 patients admitted to the hospital due to a diagnosis of COVID-19 was carried out. Demographic, clinical, and laboratory data were collected at hospital admission. **Results:** 53.4% of the patients were male, mean age of 62.3±15.4 years, and 43.6% were admitted due to pneumonia. According to the complete blood count, 54.3% had lymphopenia, 26% thrombocytopenia, and 27% anemia. In the liver and kidney profiles, 37.9% had elevated urea levels, 56.3% elevated GOT levels, 26% elevated GPT, and 61% GGT levels. Regarding biomarkers, 80% had elevated LDH levels, 34% elevated D-dimer levels, 100% elevated C-reactive protein, 43.7% elevated procalcitonin, and 89.3% elevated ferritin. Significant differences ($p<0.05$) were found according to sex for the parameters of hemoglobin, hematocrit, creatinine, and the LMR ratio. **Conclusion:** patients presented several alterations in hematological, renal, hepatic, and inflammatory marker parameters, which offer a general overview of the state of health with which the patient with COVID-19 is admitted to the hospital.

**Keywords:** biomarkers; laboratory critical values; COVID-19

# Parámetros de laboratorio relevantes en pacientes al ingreso hospitalario entre julio 2020 y octubre 2021 por covid 19 en el Hospital Fundación Tesãi

## R E S U M E N

**Introducción:** en la lucha contra el COVID-19 es urgente la identificación de predictores de laboratorio en la progresión de formas graves y fatales. **Objetivo:** describir las alteraciones de los parámetros de laboratorio de pacientes con COVID 19 ingresados al Hospital Fundación Tesãi de Ciudad del Este-Paraguay en el período de julio de 2020 a octubre de 2021. **Métodos:** estudio retrospectivo, utilizando los registros de 103 pacientes ingresados al hospital por diagnóstico de COVID 19. Se recolectaron datos demográficos, clínicos y de laboratorio al ingreso hospitalario. **Resultados:** el 53,4% de los pacientes era del sexo masculino, edad media de 62,3±15,4 años y el 43,6% ingresó por neumonía. El 54,3% presentaba linfopenia, el 26% trombocitopenia y el 27% anemia. En el perfil hepático y renal, el 37,9% tenían niveles elevados de urea, el 56,3% niveles elevados de GOT, 26% y 61% niveles elevados de GPT y GGT, respectivamente. En cuanto a los biomarcadores, el 80 % tenía niveles elevados de LDH, el 34 % niveles elevados de dímero D, el 100 % proteína C reactiva elevada, el 43,7 % procalcitonina elevada y el 89,3 % ferritina elevada. Se encontraron diferencias significativas ($p<0,05$) según el sexo en los parámetros de hemoglobina, hematocrito, creatinina y el índice LMR. **Conclusión:** los pacientes presentaron diversas alteraciones en casi todos los parámetros evaluados, resultados que ofrecen un panorama general del estado de salud con el que ingresa el paciente con COVID 19 al hospital.

**Palabras clave:** biomarcadores; valores críticos de laboratorio; COVID-19

Fecha de recepción: 17 julio 2022 Fecha de aceptación: 20 de setiembre 2022

***Autor correspondiente:** Eliana Romina Meza Miranda
Email: eliana.romina59@gmail.com

## INTRODUCTION

In December 2019 in the city of Wuhan, China, a series of cases of severe pneumonia of unknown origin were recorded[1]. Later, the etiological agent was identified as a new beta coronavirus RNA, different from the severe acute respiratory syndrome coronavirus "SARS-CoV" of 2002-2003 and the Middle East respiratory syndrome coronavirus "MERS-CoV"[2,3]. This new viral agent, known today as COVID-19, is the cause of atypical viral pneumonia and acute respiratory distress syndrome that affects all the world population[4]. When the number of cases had risen to more than 1.7 million and confirmed in more than 210 countries, the World Health Organization (WHO) declared COVID-19 a pandemic on 10 April 2020[5]. Up to date, more than 516 million cases have been reported globally, with approximately 6.25 million deaths[6].

COVID-19 is diagnosed through laboratory tests and radiological examinations, in those patients with an epidemiological history and clinical symptoms[7,8]. The evidence of alterations in routine laboratory tests is very nonspecific, but there are numerous studies that show that some hematological and hemochemical parameters were altered and that made it possible to assess the severity of the disease, the prognosis, and to monitor treatments[9,10].

An earlier study found that higher levels of C-reactive proteins (CRP), D-dimer, and procalcitonin (PCT) were associated with severe compared with non-severe patients[11]. Leukocytosis, high D-dimer levels, lactate dehydratase (LDH), and low platelet counts are risk factors associated with hospital death in critically ill patients[12-15]. Inflammatory and hematological markers are a good guide to predict disease severity and outcome, but changes in these parameters in the hospital alone are not predictive of overall mortality or therapeutic benefit. Other hematological markers that are known to be elevated in the current pandemic are the NLR (Neutrophil/lymphocyte), PLR (Platelet/lymphocyte) and LMR (Lymphocyte/monocyte) ratios, which directly correlate with the severity of the disease[16].

On the other hand, one of the emerging markers in coronavirus disease is serum procalcitonin, since it determines the severity of the infected patient, therefore, serial measurements of this parameter are important to establish the prognosis. It has been shown that procalcitonin level in COVID-19 patients with severe disease is higher compared with the patients with moderate disease[17]. Another important parameter is ferritin because, in patients with COVID-19, it has been shown that they have increased ferritin levels, a longer time period for viral clearance, and longer hospital stays[18]. The same implications were reported in the correlation between elevated ferritin levels and in-hospital mortality and invasive ventilator dependence[19]. The measurements of these biochemical parameters will help not only in early diagnosis, detection, and prevention of virus transmission, but will also ensure prompt treatment and herald impending complications[20].

In this complex context arises an obvious questioning by laboratory medicine, and is how it can contribute to counteracting possible future complications in these patients[21]. The identification of laboratory tests capable of discriminating between severe cases and those that are not, as well as patients with a high or low degree of mortality, will allow better risk stratification and an adequate allocation of resources. For all the aforementioned, the objective of this study was to describe the alterations of laboratory parameters of patients with diagnostics of COVID-19 at Tesãi Foundation Hospital in Ciudad del Este, Paraguay admission during the period of July 2020 to October 2021.

## METHODS

A retrospective, observational, descriptive cross-sectional study was carried out. 103 adult patients admitted for diagnosis of COVID-19 to the Hospital of the Tesãi Foundation in Ciudad del Este, Paraguay, were included in the period from July 2020 to October 2021, whose medical files contained all the study variables.

Demographic variables such as sex and age, clinical characteristics that correspond to the reason for hospital admission, were studied, as well as the hematological profile (red blood cells, hematocrit, hemoglobin, white blood cells, neutrophils, eosinophils, basophils, lymphocytes, platelets), renal (urea, creatinine), hepatic: Aspartate Aminotransferase, Alanine transaminase and Gamma-glutamyl Transferase (GOT, GPT, GGT, respectively)

and relevant monitoring, surveillance and mortality biomarkers in this type of patients (LDH, D-dimer, PCR, procalcitonin, ferritin). The laboratory reference ranges used were those of the Hospital itself.

As this is a retrospective study, there was no direct contact with the patients; however, the ethical principles of the Declaration of Helsinki were taken into account[22]. The confidentiality of the data was protected at all times.

After checking the consistency of the database and identifying the distribution of the quantitative variables, we proceeded to analyze the data, expressing them as averages and standard deviations. In the case of qualitative variables, these were expressed as frequency (n) and percentage (%). The statistical package used was SPSS© version 21.0 for Windows.

## RESULTS

Of the total population (n=103), 53.4% were male with an average age of 62.3±15.4 years, the most frequent range was 60 to 79 years (51.5%). Regarding clinical characteristics, 43.6% were admitted due to pneumonia, followed by 27% due to fever. (Table 1)

**Table 1.** Demographic and clinical characteristics at hospital admission of patients with COVID-19

| Variable | n (%) |
|---|---|
| **Gender** | |
| Male | 55 (53.4) |
| Female | 48 (46.6) |
| **Age in years (Average ±SD)** | 62.3±15.4 |
| **Age ranges** | |
| 20-39 | 9 (8.8) |
| 49-59 | 30 (29.1) |
| 60-79 | 53 (51.5) |
| ≥80 | 11 (10.6) |
| **Signs and symptoms** | |
| Pneumonia | 45 (43.6) |
| Fever | 28 (27) |
| Dry cough | 20 (19.4) |
| Dyspnoea | 21 (20.3) |
| Abdominal pain | 2 (2) |
| General discomfort | 1 (1) |
| Headache | 1 (1) |
| Asthenia | 4 (3) |
| Sore throat | 4 (1) |
| Anosmia | 3 (1) |
| Diarrhea | 3 (3) |
| Vomit | 2 (2) |
| Ageusia | 2 (1) |
| Myalgia | 1 (1) |

The blood count performed on hospital admission to patients with COVID-19, revealed that 27% had anemia according to hemoglobin, 41.8% had a low percentage of hematocrit, 23.3% had high levels of white blood cells, 54.3% low levels of lymphocytes and 26% low levels of platelets. Analysis of the renal and hepatic profile through serum biochemistry at hospital admission revealed that 37.9% had elevated urea levels, 19.4% elevated creatinine levels, 56.3% elevated GOT levels, 25.2 % elevated levels of GPT and 60.2 elevated levels of GGT. When evaluating the relevant prognostic and monitoring biomarkers in COVID-19 infection, it was found that 80% had elevated LDH levels, 34% elevated D-dimer levels, 100% elevated C-reactive protein, 43.7 % of elevated procalcitonin and 89.3% of elevated ferritin. (Table 2)

**Table 2.** Laboratory parameters at hospital admission of patients with COVID-19

| **Blood components** | **Normal levels (n-%)** | **Low levels (n-%)** | **Elevated levels (n-%)** |
|---|---|---|---|
| Red blood cells (/uL) | 94 (90,.3) | 9 (9.7) | 0 |
| Hemoglobin (g/dL) | 76 (73) | 27 (27) | 0 |
| Hematocrit (%) | 61 (58.2) | 42 (41.8) | 0 |
| White blood cells (/uL) | 63 (61.2) | 14 (15.5) | 25 (23.3) |
| Neutrophils (%) | 54 (52.4) | 0 | 49 (47.6) |
| Basophils (%) | 103 (100) | 0 | 0 |
| Eosinophils (%) | 103 (100) | 0 | 0 |
| Lymphocytes (%) | 45 (45.7) | 56 (54.3) | 0 |
| Monocytes (%) | 92 (90) | 2 (3) | 7 (7) |
| Platelets (/uL) | 76 (74) | 27 (26) | 0 |
| **Renal and hepatic profile** | **Normal levels (n-%)** | **Low levels (n-%)** | **Elevated levels (n-%)** |
| Urea (mg/dL) | 64 (62.1) | 0 | 38 (37.9) |
| Creatinine (mg/dL) | 81 (79) | 2 (1,6) | 20 (19.4) |
| GOT (UI/L) | 45 (43.7) | 0 | 58 (56.3) |
| GPT (UI/L) | 76 (74) | 0 | 7 (26) |
| GGT (U/L) | 40 (39) | 0 | 63 (61) |
| **Biomarkers of relevance in COVID-19** | **Normal levels (n-%)** | | **Elevated levels (n-%)** |
| LDH (U/L) | 21 (20) | | 82 (80) |
| D-dimer (ng/mL) | 68 (66) | | 35 (34) |
| CRP (mg/L) | 0 | | 103 (100) |
| Procalcitonin (ng/mL) | 58 (56.3) | | 45 (43.7) |
| Ferritin (ng/mL) | 11 (10.7) | | 92 (89.3) |

When evaluating the NLR, LMR and PLR ratios, the following values were observed: 7,7±7,3; 3,2±1,8 and 185,9±108,0 respectively. (Table 3).

**Table 3.** Hematologic markers of inflammation at hospital admission of patients with COVID-19

| ***Hematological index*** | ***Mean±DE*** |
|---|---|
| **NLR** | 7,7±7,3 |
| **LMR** | 3,2±1,8 |
| **PLR** | 185,9±108,0 |

When analyzing whether there are differences between the biochemical parameters studied, statistically significant values were found for hemoglobin, hematocrit, and creatinine according to sex, noting that women were the ones who mostly presented anemia and low hematocrit values. Creatinine, on the other hand, was found to be elevated in more men than women. In the rest of the parameters, no significant differences were found according to sex. (Table 4)

**Table 4.** Biochemical parameters according to sex at hospital admission of patients with COVID-19

| Biochemical parameters | Sex (n-%) | | | *p |
|---|---|---|---|---|
| **Hemoglobin** | **Female** | **Male** | **Total** | ***0.001*** |
| Normal levels | 28 (58.3) | 48 (87.3) | 76 (74) | |
| Low levels | 20 (41.7) | 7 (12.7) | 27 (26) | |
| **Hematocrit** | | | | |
| Normal levels | 22 (46) | 39 (71) | 61 (59.2) | ***0.010*** |
| Low levels | 26 (54) | 16 (29) | 42 (40.8) | |
| **Creatinine** | | | | |
| Normal levels | 37 (77.1) | 39 (71) | 76 (74) | |
| Low levels | 6 (12.5) | 2 (3.6) | 8 (7.6) | ***0.050*** |
| High levels | 5 (10.4) | 14 (25.4) | 19 (18.4) | |

**Chi square p<0.05*

Regarding the inflammation indices according to sex, significant differences were observed in the LMR ratio, it being possible to notice that women had the highest LMR ratio compared to men. (Table 5).

**Table 5.** Hematological inflammation index according to sex at hospital admission of patients with COVID-19

| Inflammation index | Sex (mean range) | | *p |
|---|---|---|---|
| | **Female** | **Male** | |
| **NLR** | 47.78 | 55.68 | *0,181* |
| **PLR** | 50.15 | 53.62 | *0,556* |
| **LMR** | 61.41 | 43.79 | ***0,003*** |

**U de Mann-Whitney p<0,05*

## DISCUSSION

Currently, many hematological parameters are used to predict outcomes and mortality in patients infected with COVID-19. The objective of this study was to evaluate the clinical laboratory profile of patients hospitalized for COVID-19 to describe which ones are altered at the time of hospital admission.

A total of 103 patients diagnosed with COVID-19 were evaluated, of which 53.4% were male, an amount similar to that found by Álvarez-Arroyo and Montiel et al., who found in their studies 54.9% and 59% of women and men respectively in their population of patients hospitalized for COVID-19[23,24]. Regarding age, in the present study was an average of 62.3±15.4, an amount lower than that found by Álvarez-Arroyo et al., who observed an average of 70 years, but higher than that found by Vera and collaborators who observed an average of 55.6 years[23,25]. The predominant age range in this research work was 60 to 79 years in a proportion of 51.5%, in contrast to what was found by Montiel et al, in whose study it was observed that the predominant age range was 50 to 59 years in 24.7%[24]. Additionally, comparing our results with a study conducted by Bonnet et al.[26], in a population of 2,878 patients hospitalized by COVID-19 in April 2020, the patients were predominantly male and aged over 60 years, consistent with previous studies showing a greater percentage of male versus female patients[27-29]. Reports show that the proportion of men is even higher among those hospitalized directly to the intensive care unit for COVID-19 [30,31]. These results show that the most vulnerable group is older adults, probably due to present comorbidities or age itself, and that men are probably more vulnerable to being infected by COVID-19.

Regarding the clinical characteristics at hospital admission, it was found that 43.6% were admitted for diagnosed pneumonia, followed by 27% for presenting fever, the latter amounts below what was found by Álvarez-Arroyo and Montiel, in whose studies observed 74.5% and 69.9% admissions for pneumonia and fever, respectively[23,24]. Another study conducted by Sarhan et al., found that patients hospitalized for COVID-19, in most cases experienced influenza-like symptoms such as fever, cough, and mild myalgia from

admission and during their time at the hospital[32]. Fever is the most common symptom in the early stages of coronavirus disease. On the other hand, pneumonia is a complication derived from the coronavirus, which if not treated in time in the first few days, can be a cause of death in these patients.

The hemogram of the patients at hospital admission in this study revealed 54.3% with lymphopenia, an amount higher than that found by Vera and Montiel et al., who in their studies found 47.4% and 43.6%, respectively[24,25]. In another study carried out on 117 patients hospitalized for COVID-19 by Yuan et al., they found that at the time of admission, most of them have reduced lymphocyte counts, which was much more pronounced in critically ill patients[33]. Most viruses cause lymphocytosis when they infect humans because lymphocytes are virus-fighting effector cells[34]. The coronavirus family SARS-CoV, MERS-CoV, and SARS-CoV-2 all cause lymphocytic depletion in infected patients[35,36], and the mechanism may be caused by direct attack of coronavirus on lymphocytes or by immune-mediated apoptosis of lymphocytes[37].

In addition, 26% of thrombocytopenia was observed, an amount lower than that found by Álvarez-Arroyo et al., in whose study 29.2% were observed with platelet values below normal levels[23]. Thrombocytopenia is a well-known complication of many viral infections, with many underlying mechanisms causing the drop in platelet count. Immune-mediated thrombocytopenia is one of these mechanisms[38]. With the current SARS-CoV-2 pandemic, thrombocytopenia was reported in up to 36% of patients[27,39,40].

A proportion of 27% and 41.8% of patients presented low hemoglobin and hematocrit levels, respectively. In a retrospective cohort study among COVID-19 patients with anemia that investigated the association of anemia with severe pneumonia, anemic patients had elevated levels of inflammatory markers compared to their non-anemic counterparts. COVID-19 patients with anemia have an 8.2 times higher chance of developing severe pneumonia compared to COVID-19 patients without anemia, therefore, they need timely intervention and more care[41].

The renal and hepatic profile through serum biochemistry revealed 37.9% of patients with elevated urea levels. The elevated levels of this parameter in patients with COVID-19 indicate by itself that they are severe, as indicated in the study by Huang et al.[42]. Also, it was observed that the levels of GOT and GGT were elevated in 56.3% and 60.2% of the patients, respectively. A systematic review and meta-analysis conducted by Kumar-M et al. that included 128 studies about coronavirus disease and the liver, concluded that the pooled prevalence of GOT elevation was 23.41% and the pooled prevalence of GGT elevation overall was 27.94%[42]. Based on scientific evidence, GGT is recognized as a surrogate marker for increased oxidative stress and chronic inflammation. It is not known whether these elevations are related to acute inflammatory stress or are a marker of biliary injury, and this finding needs further evaluation[43].

When analyzing the biomarkers currently used as predictors of severity and mortality in patients with COVID-19, in the present study it was observed that the entire population presented elevated levels of C-reactive protein, an amount that exceeds the 92.1% found in the study by Montiel et al.[24]. Ferritin levels were found to be elevated in 89.3% of the patients, in contrast to the 91% and 75% found by Montiel and Álvarez-Arroyo et al., respectively[23,24]. These elevations point to the development of a systemic inflammatory response syndrome in patients with a severe form of the disease[44]. In addition, 80% of the patients had elevated levels of LDH (lactate dehydrogenase), an amount higher than the 66.1% found by Montiel et al.[24]. Regarding procalcitonin levels, 43.7% of patients presented elevated levels, compared to 46.7% and 33% found by Álvarez-Arroyo and Montiel[23,24]. The increase in these markers of inflammation is the critical point underlying systemic vasculitic processes and defects in coagulation processes that cause most parenchymal injuries in vital organs[45]. The CRP marker is significantly increased in the early stages of infection for patients with severe COVID-19. Importantly, CRP has been associated with disease development and is an early predictor of severe COVID-19[46].

D-dimer levels in the patients in this study were elevated in a proportion of 34%, in contrast to the 62.4% and 82% found by Álvarez-Arroyo and Montiel[23,24]. Abnormal coagulation parameters are associated with a poor prognosis. Specifically, markedly elevated D-dimer is common in patients who do not survive COVID-19[47]. D-dimer is frequently increased in patients with COVID-19 and may be related to serious complications and death[48]. For this reason, this is one of the monitoring and follow-up

parameters in patients with COVID-19 and should be measured with at least moderate frequency. If the patient in the first analysis presents levels in the upper limit, he should be admitted and the other parameters should be monitored.

When we evaluated the ratios corresponding to markers of inflammation, the NLR ratio was 7.7±7.3, in contrast to what was found by Asghar et al., who in their study on Hematological parameters predicting severity and mortality in COVID-19 patients, observed an NLR ratio of 4.56±4.84. Normally, this ratio should be less than 3, but a ratio greater than 3 means acute stress, and a ratio greater than 9 means sepsis. But due to variability in populations regarding the cut-off value of NLR, some studies suggest a cut-off value of 4[49]. The LMR ratio observed in this study was 3.2±1.8, in contrast to the study by Asghar et al., who showed an MRL ratio of 3.67±1.65. The normal range for this ratio is 3–9 with variability amongst populations[50]. The PLR ratio in this study was 185.9 ± 108.0, in contrast to the 152.60 ± 74.16 found by Asghar et al.[51] Normal values are usually in the range of 50 and 150 but are subject to differences between populations[50].

Finally, when we analyze if there are differences according to sex, of all the parameters studied, we have shown that there are more women with low hemoglobin and hematocrit levels compared to men. In this sense, a study carried out by Bergamaschi et al., showed that there was a significant inverse correlation of hemoglobin with the length of hospital stay in women who were discharged, but not in men, that is, that those women who did not have anemia established by hemoglobin levels had a shorter hospitalization time for COVID-19 than those who did have anemia by these values, which could not be confirmed in men[52]. These data show that women are more susceptible to anemia than men, therefore, hemoglobin should be a parameter that must be constantly evaluated during hospitalization to avoid other complications.

According to sex, women presented a significantly higher mean range of the LMR ratio than men, showing that it is possibly men who are patients with greater severity since it has been seen that this proportion decreases as an indicator of disease. Prognosis and higher chances of mortality in some prospective cohort studies[53].

This study has several limitations. Since this is a cross-sectional study, independent variables could not be evaluated for cause-and-effect associations. In addition, the presence of associated comorbidities was not evaluated.

As strengths, the epidemiological value of the results presented for the country can be highlighted, in addition to providing essential data for decision-making in terms of monitoring and consensus on the treatment that patients admitted to the hospital diagnosed with COVID-19 should receive, according to the parameters studied here.

With the results obtained in this study, we have been able to verify that hematological and ratios analyzes and, renal and hepatic parameters, are of the utmost importance in patients with COVID-19 at hospital admission, since they can offer a general overview of the state of health with which they are hospitalized. In addition, it is considered that the emerging biomarkers of the inflammatory response are CRP, ferritin, and lactate dehydrogenase and, on the other hand, D-dimer, an important indicator of the state of blood coagulation, for which it is recommended to continue with conducting longitudinal cohort studies to determine if these parameters are determinants of the severity and outcome of COVID-19 disease.

**Conflict of interest disclosure.** The authors have no conflicts of interest to report, and no financial interests related to the material in the manuscript.

**Authors' contribution:** Dennise Villanueva; development of research protocol and data collection. Eliana Meza; data processing and statistical analysis. Manuscript writing and review.

**Funding.** This research was self-financed by the authors themselves.

**BIBLIOGRAPHIC REFERENCES**

1. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497–506. https://doi.org/10.1016/S0140-6736(20)30183-5
2. De Wit E, van Doremalen N, Falzarano D, Munster VJ. SARS and

MERS: recent insights into emerging coronaviruses. Nat Rev Microbiol. 2016;14:523–34. https://doi.org/10.1038/nrmicro.2016.81
3. Hilgenfeld R, Peiris M. From SARS to MERS: 10 years of research on highly pathogenic human coronaviruses. Antiviral Research 2013; 100(1): 286–95. https://doi.org/10.1016/j.antiviral.2013.08.015
4. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with pneumonia in China. N Engl J Med 2019;382:727-33. https://doi.org/10.1056/nejmoa2001017
5. World Health Organization. Coronavirus Disease 2019 (COVID-19) Situation Report—81. https://apps.who.int/iris/handle/10665/331779
6. BMJ Best Practice. Coronavirus Disease 2019 (COVID-19). https://bestpractice.bmj.com/topics/en-gb/3000201
7. Ahn DG, Shin HJ, Kim MH, Lee S, Kim HS, Myoung J, et al. Current Status of Epidemiology, Diagnosis, Therapeutics, and Vaccines for Novel Coronavirus Disease 2019 (COVID-19). J Microbiol Biotechnol 2020;30(3):313–24. https://doi.org/10.4014/jmb.2003.03011
8. Chan JF, Yip CC, To KK, Tang TH, Wong SC, Leung KH, et al. Improved Molecular Diagnosis of COVID-19 by the Novel, Highly Sensitive and Specific COVID-19-RdRp/Hel Real-Time Reverse Transcription-PCR Assay Validated In Vitro and with Clinical Specimens. J Clin Microbiol 2020; 58(5):e00310-20. https://pubmed.ncbi.nlm.nih.gov/32132196/
9. Ferrari D, Motta A, Strollo M, Banfi G, Locatelli M. Routine blood tests as a potential diagnostic tool for COVID-19. Clin Chem Lab Med. 2020;58(7):1095-1099. https://doi.org/10.1515/cclm-2020-0398
10. 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(7):834-847. https://pubmed.ncbi.nlm.nih.gov/32282949/
11. Zhang JJ, Cao YY, Dong X, Wang BC, Liao MY, Lin J, et al. Distinct characteristics of COVID-19 patients with initial rRT-PCR-positive and rRT-PCR-negative results for SARS-CoV-2. Allergy. 2020;75(7):1809-1812. https://pubmed.ncbi.nlm.nih.gov/32281110/
12. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk Factors Associated with Acute Respiratory Distress Syndrome and Death in Patients with Coronavirus Disease 2019 Pneumonia in Wuhan, China. JAMA Intern Med. 2020;180(7):934-943. https://doi.org/10.1001/jamainternmed.2020.0994
13. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med. 2020;8(5):475-481. https://doi.org/10.1016/s2213-2600(20)30079-5
14. Li X, Xu S, Yu M, Wang K, Tao Y, Zhou Y, et al. Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan. J Allergy Clin Immunol. 2020;146(1):110-118. https://doi.org/10.1016/j.jaci.2020.04.006
15. Wang K, Zhang Z, Yu M, Tao Y, Xie M. 15-day mortality and associated risk factors for hospitalized patients with COVID-19 in Wuhan, China: an ambispective observational cohort study. Intensive Care Med. 2020;46(7):1472-1474. https://doi.org/10.1007/s00134-020-06047-w
16. Asghar MS, Khan NA, Haider Kazmi SJ, Ahmed A, Hassan M, Jawed R, et al. Hematological parameters predicting severity and mortality in COVID-19 patients of Pakistan: a

retrospective comparative analysis. J Community Hosp Intern Med Perspect. 2020;10(6):514-520. https://doi.org/10.1080/20009666.2020.1816276

17. Abadi MSS, Taheri E, Raesi A, Arjmand MH, Kheirii S, Shahinfard N, et al. Procalcitonin as a prognostic factor in patients with COVID-19 in southwestern Iran. Infect Disord Drug Targets. 2022; 22(3):e070122200097. https://doi.org/10.2174/1871526522666220107141109
18. Cao P, Wu Y, Wu S, Wu T, Zhang Q, Zhang R, et al. Elevated serum ferritin level effectively discriminates severity illness and liver injury of coronavirus disease 2019 pneumonia. Biomarkers. 202;26(3):207-212. https://doi.org/10.1080/1354750x.2020.1861098
19. Qeadan F, Tingey B, Gu LY, Packard AH, Erdei E, Saeed AI. Prognostic Values of Serum Ferritin and D-Dimer Trajectory in Patients with COVID-19. Viruses. 2021;13(3):419. https://doi.org/10.3390/v13030419
20. Gao Y, Li T, Han M, Li X, Wu D, Xu Y, et al. Diagnostic utility of clinical laboratory data determinations for patients with the severe COVID-19. J Med Virol. 2020;92(7):791–6 https://pubmed.ncbi.nlm.nih.gov/32181911/
21. Lippi G, Plebani M. Laboratory abnormalities in patients with COVID-2019 infection. Clin Chem Lab Med. 2020;58(7):1131-1134. https://doi.org/10.1515/cclm-2020-0198
22. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA. 2013;310(20):2191-4 https://doi.org/10.1001/jama.2013.281053
23. Álvarez-Arroyo Laura, Carrera-Hueso Francisco J., El-Qutob David, Robustillo-Villarino Montserrat, Girona-Sanz Ana M., Pin-Godos María T. et al. Estudio descriptivo de una cohorte de pacientes con COVID-19 hospitalizados en España. Gac Méd Méx. 2021;157(1):80-87. https://doi.org/10.24875/gmm.20000605
24. Montiel D, Torres E, Acosta A, Sobarzo P, Pérez H, Ávalos D, Ramos Y. Características clínicas, laboratoriales y predictores de mortalidad de pacientes con COVID-19 internados en el Hospital Nacional. Rev Cient Cienc Salud. 2021;3(1):26-37. https://doi.org/10.53732/rccsalud/03.01.2021.26
25. Vera N, Saavedra-Hernández D, Hidalgo-Mesa C, Aguila-López M, Abreu-Gutiérrez G, Herrera-González V, et al. Parámetros de laboratorio clínico en pacientes con la COVID-19. Rev Cub Med Mil. 2021;50(2): e02101171. http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S0138-65572021000200018
26. Bonnet G, Weizman O, Trimaille A, Pommier T, Cellier J, Geneste L, et al. Critical COVID-19 France Investigators. Characteristics and outcomes of patients hospitalized for COVID-19 in France: The Critical COVID-19 France (CCF) study. Arch Cardiovasc Dis. 2021;114(5):352-363. https://doi.org/10.1016/j.acvd.2021.01.003
27. Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020;382(18):1708-1720. 10.1056/NEJMoa2002032
28. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. JAMA. 2020; 323(20):2052-2059. https://doi.org/10.1001/jama.2020.6775
29. Docherty AB, Harrison EM, Green CA, Hardwick HE, Pius R, Norman L, et al. Features of 20,133 UK patients in hospital with covid-19

using the ISARIC WHO clinical characterization protocol: prospective observational cohort study. BMJ. 2020; 369:m1985. https://doi.org/10.1136/bmj.m1985

30. Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, et al. Baseline characteristics and outcomes of 1,591 patients infected with SARS CoV-2 admitted to ICUs of the Lombardy Region, Italy. JAMA. 2020; 323(16):1574-1581. https://doi.org/10.1001/jama.2020.5394
31. Yang J, Zheng Y, Gou X, Pu K, Chen Z, Guo Q, et al. Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis. Int J Infect Dis. 2020; 94:91-5. https://doi.org/10.1016/j.ijid.2020.03.017
32. Sarhan AR, Hussein TA, Flaih MH, Hussein KR. A Biochemical Analysis of Patients with COVID-19 Infection. Biochem Res Int. 2021; 1383830. https://doi.org/10.1155/2021/1383830
33. Yuan X, Huang W, Ye B, Chen C, Huang R, Wu F, et al. Changes of hematological and immunological parameters in COVID-19 patients. Int J Hematol. 2020;112(4):553-559. https://doi.org/10.1007/s12185-020-02930-w
34. Zhu Y, Cao X, Tao G, Xie W, Hu Z, Xu D. The lymph index: a potential hematological parameter for viral infection. Int J Infect Dis. 2013;17(7): e490–e493493. https://doi.org/10.1016/j.ijid.2012.12.002
35. Rabaan AA, Al-Ahmed SH, Haque S, Sah R, Tiwari R, Malik YS, et al. SARS-CoV-2, SARS-CoV, and MERS-COV: a comparative overview. Le infezioni in medicina. 2020;28(2):174–84. https://pubmed.ncbi.nlm.nih.gov/32275259/
36. Al-Tawfq JA, Hinedi K, Abbasi S, Babiker M, Sunji A, Eltigani M. Hematologic, hepatic, and renal function changes in hospitalized patients with Middle East respiratory syndrome coronavirus. Int J Lab Hematol. 2017;39(3):272–8. https://pubmed.ncbi.nlm.nih.gov/28444873/
37. Chu H, Zhou J, Wong BH, Li C, Chan JF, Cheng ZS, et al. Middle East respiratory syndrome coronavirus efciently infects human primary T lymphocytes and activates the extrinsic and intrinsic apoptosis pathways. J Infect Dis. 2016;213(6):904–14. https://doi.org/10.1093/infdis/jiv380
38. Gonze A, Hannesse C, Coppens N, Vellemans H, Maury G. SARS-CoV-2-Induced Severe Immune Thrombocytopenic Purpura. J Med Cases. 2020;11(6):166-168. https://doi.org/10.14740/jmc3481
39. Chen W, Li Z, Yang B, Wang P, Zhou Q, Zhang Z, et al. Delayed-phase thrombocytopenia in patients with coronavirus disease 2019 (COVID-19). Br J Haematol. 2020;190(2):179-184. https://pubmed.ncbi.nlm.nih.gov/32453877/
40. Sahu KK, Siddiqui AD, Rezaei N, Cerny J. Challenges for management of immune thrombocytopenia during COVID-19 pandemic. J Med Virol. 2020;92(11):2277-2282. https://pubmed.ncbi.nlm.nih.gov/32619062/
41. Chen C, Zhou W, Fan W, Ning X, Yang S, Lei Z, Zheng C. Association of anemia and COVID-19 in hospitalized patients. Future Virol. 2021:10.2217/fvl-2021-0044. 10.2217/fvl-2021-0044
42. Huang D, Yang H, Yu H, Wang T, Chen Z, Zongan L, Rong Y. Blood Urea Nitrogen to Serum Albumin Ratio (BAR) Predicts Critical Illness in Patients with Coronavirus Disease 2019 (COVID-19). Int J Gen Med. 2021;14:4711–21. https://doi.org/10.2147/ijgm.s326204
43. Kumar-M P, Mishra S, Jha DK, Shukla J, Choudhury A, Mohindra R, et al. Coronavirus disease (COVID-19) and the liver: a

comprehensive systematic review and meta-analysis. Hepatol Int. 2020;14(5):711–22. https://doi.org/10.1007/s12072-020-10071-9

44. Henry BM, de Oliveira MHS, Benoit S, Plebani M, Lippi G. Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a meta-analysis. Clin Chem Lab Med. 2020;58(7):1021-1028. https://doi.org/10.1515/cclm-2020-0369
45. Ponti G, Maccaferri M, Ruini C, Tomasi A, Ozben T. Biomarkers associated with COVID-19 disease progression. Crit Rev Clin Lab Sci. 2020;57(6):389–99. https://doi.org/10.1080/10408363.2020.1770685
46. Tan C, Huang Y, Shi F, Tan K, Ma Q, Chen Y, et al. C-reactive protein correlates with computed tomographic findings and predicts severe COVID-19 early. J Med Virol. 2020;92(7):856-862. https://pubmed.ncbi.nlm.nih.gov/32281668/
47. Tang N, Li D, Wang X. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost. 2020;18(4):844–847. https://pubmed.ncbi.nlm.nih.gov/32073213/
48. Lippi G, Favaloro EJ. D-dimer is Associated with Severity of Coronavirus Disease 2019: A Pooled Analysis. Thromb Haemost. 2020;120(5):876-878. https://doi.org/10.1055/s-0040-1709650
49. Martins EC, Silveira LDF, Viegas K, Beck AD, Fioravantti Júnior G, Cremonese RV, et al. Neutrophil-lymphocyte ratio in the early diagnosis of sepsis in an intensive care unit: a case-control study. Rev Bras Ter Intensiva. 2019;31(1):64-70. https://doi.org/10.5935/0103-507x.20190010
50. Lee JS, Kim NY, Na SH, Youn YH, Shin CS. Reference values of neutrophil-lymphocyte ratio, lymphocyte-monocyte ratio, platelet-lymphocyte ratio, and mean platelet volume in healthy adults in South Korea. Medicine (Baltimore). 2018;97(26): e11138. https://journals.lww.com/md-journal/Fulltext/2018/06290/Reference_values_of_neutrophil_lymphocyte_ratio,.21.aspx
51. Asghar MS, Khan NA, Haider Kazmi SJ, Ahmed A, Hassan M, Jawed R, et al. Hematological parameters predicting severity and mortality in COVID-19 patients of Pakistan: a retrospective comparative analysis. J Community Hosp Intern Med Perspect. 2020;10(6):514-520. https://doi.org/10.1080/20009666.2020.1816276
52. Bergamaschi G, Borrelli de Andreis F, Aronico N, Lenti MV, Barteselli C, Merli S. Internal Medicine Covid-19 Collaborators. Anemia in patients with Covid-19: pathogenesis and clinical significance. Clin Exp Med. 2021;21(2):239-246. https://doi.org/10.1007/s10238-020-00679-4
53. Lissoni P, Rovelli F, Monzon A, Privitera C, Messina G, Porro G et al. Evidence of Abnormally Low Lymphocyte-To-Monocyte Ratio In Covid-19-Induced Severe Acute Respiratory Syndrome. J Immuno Allerg. 2020;1(2):1-6. http://dx.doi.org/10.37191/Mapsci-2582-6549-1(2)-011