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COVID-19: Hematological and laboratory parameters in patients hospitalized during the second and third epidemic wave (2021-2022) at a private hospital in Caracas, Venezuela

COVID-19: Estudio hematológico y de parámetros de laboratorio de los pacientes hospitalizados durante la segunda y tercera ola epidémica (2021-2022) en una clínica privada de Caracas, Venezuela

Aixa Müller[1,a,b], Andrés Soyano[2c], Luis Chirinos[3a], Alberto Ochoa A[4a], Guillermo Perez[5a], William Vidal[6a], Iraima Ramírez[7a], Alexandro Galea[8a], Grecia Molina[9a], Mario Comegna[10a], Maximiliano Ravard[11a], Karim Otero[12a], Maritza Durán[13a], Francisca Ruiz[14a], Judith Piña[15a], Héctor Marcano[16a], Jorge Domínguez[17a]

SUMMARY

The first wave of COVID-19 in Venezuela began in March 2020 and had a maximum of cases in August 2020. New outbreaks occurred in 2021 and 2022, during which we studied 603 hospitalized cases at the Clinica El Avila de Caracas: 370 (61.35 %) male and 233 (38.14 %) female. The average age was 65 years (range: 18-99 years). The hematological and laboratory studies were similar to those reported in other studies outside of Venezuela. One hundred two (102) patients were transferred to the Intensive Care Unit (ICU). 80 % of these patients had not been vaccinated or did not receive the full vaccination schedule against COVID-19. The overall mortality of the 603 patients was 11.27 %. Comorbidities were present in most severe patients with COVID-19 admitted to the ICU: overweight in 51 patients, hypertension in 28 patients, and diabetes mellitus in 20 patients. Sixty-eight (68) patients died, with mortality in the ICU being 66.66 %. There was a reduction in mortality compared to the first wave (74.5 %), but it was not statistically significant.

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ORCID: 0000-0001-8421-4441[1]
ORCID: 0000-0002-0728-9295[2]

[a]Clínica El Ávila, Caracas, Venezuela.
[b]Escuela de Medicina Luis Razetti, Facultad de Medicina, UCV.
[c]Centro de Medicina Experimental, Instituto Venezolano de Investigaciones Científicas (IVIC), Caracas.

Corresponding author: Dr. Aixa Müller; E-mail: asoyano@gmail.com

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RESUMEN

La primera ola de COVID-19 en Venezuela se inició en marzo de 2020 y tuvo un máximo de casos en agosto de 2020. Nuevos brotes ocurrieron en los años 2021 y 2022 durante los cuales estudiamos 603 casos hospitalizados en la Clínica El Ávila de Caracas: 370 (61,35 %) masculinos y 233 (38,14 %) femeninos. La edad promedio fue de 65 años (rango: 18-99 años). Los estudios hematológicos y de laboratorio fueron similares a los reportados en otros estudios fuera de Venezuela. Ciento dos (102) pacientes fueron trasladados a la Unidad de Cuidados Intensivos (UCI).

El 80 % de estos pacientes no había sido vacunado o no recibió el esquema de vacunación completo contra la COVID-19. La mortalidad general de los 603 pacientes fue de 11,27 %. Las comorbilidades estuvieron presentes en la mayoría de los pacientes graves con COVID-19 que ingresaron a la UCI: sobrepeso en 51 pacientes, hipertensión en 28 pacientes y diabetes mellitus en 20 pacientes. Fallecieron 68 pacientes, siendo la mortalidad en la UCI de 66,66 %. Hubo una reducción en la mortalidad con respecto a la primera ola (74,5 %), pero no fue estadísticamente significativa.

INTRODUCTION

The coronavirus disease-19 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), became a global pandemic that has been characterized by multiple waves, that occur at different times around the world. After the first outbreak in the first months of 2020, there was an increase in COVID-19 cases in many places where the epidemic first emerged. Among the most affected countries in Europe, Italy, France, the United Kingdom, Germany, and Spain experienced an initial outbreak around March 2020, followed by a decline in the number of cases after May 2020, peaking again in November 2020 (1).

Many countries have experienced multiple waves or outbreaks of COVID-19, and disease characteristics varied between waves (2-5). The third wave of COVID-19 infection was experienced by some countries (6,7). The aim of this study was to present the hematological and laboratory studies of patients with COVID-19 who required intensive care therapy at Clínica El Ávila in Caracas, Venezuela, during the second and third wave of COVID-19 in Venezuela.

MATERIALS AND METHODS

Patients. Six hundred three (603) patients were hospitalized at Clínica El Ávila in 2021 and 2022 with clinical manifestations of moderate to severe COVID-19 or in critical condition with a positive IgG and IgM COVID-19 test (497 patients in 2021 and 106 patients in 2022). Of the 603 admitted patients, 370 (61.35 %) patients were male and 233 (38.14 %) were female (*P< 0.05). The average age of all admitted COVID-19 patients was 65 years, with a range of 18-99 years. When the patients were subdivided by age group, we had 125 patients between 18 and 50 years (20.7 3 %), 242 patients between 51 and 70 years (42.1 3 %), and 236 patients over 70 years (39.1 3 %) (*P< 0.05) (Table 1). Of the 603 admitted patients, 102 were admitted to the Intensive Care Unit (ICU).

Table 1. Demographic characteristics of 603 hospitalized patients with COVID-19

NUMBER OF PATIENTS		603 (100 %)
Age (years)	65± 16	
Range (years)	18.99	
	18-50	125 (20.73 %)
	51-70	242 (42.13 %)*
	>70	236 (39.13 %)*
Male		370 (61.35 %)*
Female		233 (38.14 %)

*P< 0.05

Laboratory tests. All admitted patients underwent a real-time reverse transcription polymerase chain reaction (RT-PCR) test for SARS-CoV-2. Throat swab samples were collected to extract viral RNA. The RT-PCR assay was performed using a SARS-CoV-2 nucleic acid detection kit according to the manufacturer's protocol Solis BioDyne.

Initial clinical laboratory tests performed included complete hematology with platelet count, serum biochemical tests, including liver and kidney function, creatine kinase, lactate dehydrogenase, a coagulation profile with prothrombin time, Partial Thromboplastin Time (PTT), fibrinogen, and D-dimer test.

Coagulopathy was defined when the difference in seconds of the prothrombin time between the control and the patient was 3 seconds or

more, the prothrombin time or the PTT was more than 6 seconds of the activated partial thromboplastin time of the patient relative to the control. Hypoproteinemia was defined as a value of blood albumin of less than 25 g/L. In addition, the concentration of ferritin in the blood was measured. Respiratory specimens, including nasal and throat swabs, or sputum were tested to exclude evidence of other viral infections, including influenza, respiratory syncytial virus, avian influenza, parainfluenza virus, and adenovirus.

The study was authorized by the Ethical Committee of the Institution. The data were expressed as means ± S.E.M. and in percentage. The data were analyzed by the Student t test and a p-value<0.05 was considered statistically significant.

RESULTS

The most frequent symptoms upon admission to hospitalization were fever and cough, followed by sputum production and fatigue. The diagnosis was confirmed with real-time reverse transcriptase polymerase chain reaction (RT-PCR) test on nasal and pharyngeal swabs. Of 603 patients admitted to hospitalization, 102 patients required transfer to the ICU (16.91 %) due to acute respiratory distress syndrome with decreased oxygen saturation to <90 %. Of these 102 patients, 67 were male (65.68 %), and 35 female (34.32 %) (*P< 0.05). 80 % of the patients admitted to the ICU had not been vaccinated or did not receive the full vaccination schedule against COVID-19. Epidemiological, clinical, and laboratory data and radiological characteristics were obtained from these patients. Secondary infection was diagnosed when patients showed clinical symptoms or signs of pneumonia or bacteremia and a positive culture for pathogenic bacteria was obtained from lower respiratory tract samples (sputum, bronchoalveolar lavage fluid, or endotracheal aspirate) or blood samples obtained after admission to the Clinic. The symptoms presented by the 102 patients admitted to the ICU were shortness of breath (60 %), malaise (48 %), fever (42 %), cough (36 %), diarrhea (10 %), rhinorrhea (3 %), asthenia (13 %), myalgias (11 %), arthralgia (10 %), headache (7 %), hyporexia (6 %), anosmia (2 %), sore throat (2 %). Of the 34 ICU survivors, 21 were male (61.76 %) and 13 female (38.2 3 %) (*P< 0.05), and of the 68 deceased patients, 47 patients were male (69.11 %) and 21 were female s (30.88 %) (*P< 0.05). The average age of the 102 patients admitted to the ICU was 86 ± 9.1 years and the age of the deceased was 88 ± 4 years and that of the survivors was 87 ± 3 years (Table 2). When analyzing the comorbidities of these 102 patients admitted to the ICU, we observed overweight in 51 patients (50 %). The second comorbidity was hypertension in 28 patients (27.5 %) and the third, was diabetes mellitus in 20 patients (19.6 %). In the group of deceased patients, overweight was observed in 45 (66.2 %), arterial hypertension in 29 (42.6 %), and diabetes in 18 (26.5 %). The third comorbidity present in these 102 ICU patients was Diabetes Mellitus, which was present in 18 deceased patients (17.64 %). As can be seen, obesity and arterial hypertension were more frequent in the patients who died.

Table 2. Characteristics of COVID-19 patients admitted to the Intensive Care Unit (ICU)

	Total	Survivors	Deceased
Number	102	34(33,34 %)	68(66,66 %)
Age (years)	86 ± 9,1*	87 ± 3	88 ± 4
Male	67(65.68 %)	20(58.82 %)	47(69,11 %)
Female	35(34,3 %)	14(41,18 %)	21(30,88 %)
Mortality General			(68/603)11,28 %
Mortality IUC			(68/102)66,66 %

Age 82-99 years **P< 0.05

Among patients who died in the ICU, the median time from symptom onset to hospital admission was 10 days (interquartile range 7.0-13.0).

The hematological results obtained on the admission of the 603 patients with COVID-19 admitted to the hospital from January 1, 2021 to December 31, 2022, was a leukocyte count

of 10.25 ± 8.4 x 10^9/L, presenting 49 (8.12 %) patients of the 603 leukopenia less than 4.5 x 10^9/L, and 22 (8.12 %) of these patient's leukopenia less than 3.5 x 10^9/L. The differential count of these 603 patients showed neutrophils 7.5 ± 1.8 x 10^9/L, lymphocytes 1.4 ± 0.7 x 10^9/L, monocytes 7.6 ± 0.9 x 10^9 /L. Neutrophil/lymphocyte ratio 5.35.

Of the 102 patients with COVID-19 who were admitted to the ICU, the leukocyte count was: 13.2 ± 8.7 × 10^9/L, of these 5 (4.9 %) patients had leukopenia with a white count < 3.7 ×10^9/L and 38 (37.25 %) patients had leukocytosis of 10.6 to 19.99 ×10^9/L and 19 (18.62 %) patients had marked leukocytosis of ≥20 × 10^9/L to 50 x10^9/ L. The differential leukocyte count of these patients showed neutrophils: 8.1 ± 1.7 x 10^9 /L, lymphocytes: 0.83 ± 0.6 x 10^9 /L, monocytes: 0.6 ±0.6 x 10^9 / L. Neutrophil / lymphocyte ratio 9.75.

Of the 68 patients with COVID-19 who died in the ICU, the leukocyte count was: 8.04 ± 6.2 × 10^9/L, of these 27 (39.70 %) patients had leukocytosis with a white count ≥ 10-19.79 × 10^9/L and 14 (20.59 %) patients with marked leukocytosis ≥ 20-53 x 10^9/L and only 4 patients with leukopenia 2.09 - 3.77 × 10^9/L. The differential leukocyte count of these deceased patients showed Neutrophils: 8.2 ± 1.6 × 10^9/L, Lymphocytes: 0.8 ± 0.6 × 10^9/L, Monocytes: 0.8 ± 0.1 × 10^9 /L. The neutrophil/lymphocyte ratio was 10.25 (Table 3). Observation of the blood under a light microscope showed morphological abnormalities in the blood of 70 % of the patients, such as hyposegmentation of neutrophils, toxic granulations in neutrophils, Howell-Jolly bodies, nuclei in pseudo-Peger Huet and Dohle bodies in neutrophils. In the lymphoid series, the presence of large granular lymphocytes, plasmacytoid and atypical lymphocytes was observed. In monocytes the presence of one or several large coalescing vacuoles in their cytoplasm. In eosinophils the presence of vacuoles in their cytoplasm.

Table 3. Hematological parameters of patients with COVID-19

	HOSPITALIZED	ICU SURVIVORS	ICU DECEASED
Number of patients	603	34	68
Leukocyte	10.25 ± 8.4	13.2 ± 8.7	8.04 ± 6.2
Neutrophils	7.50 ± 1.8	8.1 ± 1.7	8.2 ± 1.6
Lymphocyte	1.40 ± 0.7	0.83 ± 0.6	0.81 ± 6.2
Monocytes	7.60± 0.9	0.6 ± 0.6	0.82 ± 13.6
Hemoglobin (g/dL)	13.8 ± 9.2	11.10 ± 2.12	14.4 ± 6.8
Hematocrit (%)	40.15 ± 5.17	40.01 ± 5.41	40.2 ± 4.98
Platelets (10^9/L)	235 ± 89.4	250 ± 102.56	219 ± 74.3

ICU: Intensive Care Unit, *P< 0.05

The most consistent morphologic finding was cytoplasmic vacuolation with large coalescing vacuoles in monocytes and smaller vacuoles in neutrophils, lymphocytes, and eosinophils.

The hemoglobin of the 603 patients admitted with COVID-19 was: 13.8 ± 9.2 g/dL, (117 patients had anemia with Hb 10.4 - 11.8 g/dL). The hematocrit of the 603 patients was: 35 ± 2.9 % The hemoglobin of the 68 deceased patients was 14.4 ± 6.8 g/dL (10 patients of the 68 deceased presented anemia on admission with hemoglobin less than 11.8 g/dL).

The platelet count in the 603 admitted patients was: 247 × 10^9/L ± 230.4) (57 of the patients had thrombocytopenia on admission, with values from 23 to 139 × 10^9/L) and 30 patients presented thrombocytosis out of 453 -1 253×10^9/L. Only 6 patients of the 68 deceased presented thrombocytopenia of 42 -118 × 10^9/L on admission.

The 603 patients had serum ferritin values of 898.1 ± 115.8 (VN: 20-140 ng/mL) on admission. The patients who died on admission presented serum ferritin values of 746.8 ± 197.7 ng/mL.

In relation to the coagulation tests performed, the Prothrombin Time (PT) of the 603 admitted patients was 14.1 ± 2.5 seconds (control 12.4 ± 0.04 sec.), 4 (0.66 %) patients of the 603 patients admitted with COVID-19 had increased PT with a range of 2.02-3.02 sec. The PTT was 37.1 ± 7.9 sec. (control 32.5 ± 0), 61 (10.11 sec.) patients had increased PTT on admission, with a PTT difference of 6.2- 26 sec. Of the 68 deceased patients, 11 (16.18 %) patients presented increased PTT with a PTT difference of 6.2-21.1 seconds. The D-dimer of the 603 patients was 2.53 ± 2.1 ng/mL (normal value <0.5 ng/mL). In the deceased 13.09 ± 5.02 ng/mL.

Plasma creatinine levels on admission were 1.2 ± 0.88 mg% (VN 0.84-1.21 mg/dL). High creatinine values were observed in 73 (12.10 %) patients, 37 (50.68 %) of them with high values but less than 1.75 mg% and 36 (49.32 %) with high values between 1,88 to 8.16 mg% due to pre-COVID-19 renal failure. Six deceased patients presented an increase in creatinine of 1.46-3.54 mg% on admission.

C-reactive protein was at plasma levels of 8.5 ± 10.1 mg% in the 603 admitted patients, and the 68 deceased patients had higher values (9.8 ± 7.2 mg%), while 14 patients presented very high values of 10-33, 6 mg%.

DISCUSSION

When we analyzed the sex of the 603 patients admitted to the Clínica El Ávila in the years 2021 and 2022, we found that the majority were male, as occurred in Wuhan, China, where Huang et al. reported the first outbreak of COVID-19, and also in the patients who were attended with COVID-19 at the Clínica El Ávila in the first epidemic outbreak of 2020, as previously reported (8,9). The predominance of the male sex has also been reported in the 4 other waves of COVID-19 in other parts of the world (10). Many global epidemiological data sources indicate that men account for a higher proportion of severe SARS-CoV-2 infections than women, despite roughly equivalent infection rates (11,12). The cause is multifactorial but various hypotheses have been put forward as underlying factors behind this trend, such as a higher prevalence of smoking among men, testosterone deficiency, which favors an inflammatory storm, the pathogenesis of SARS-Androgen-driven-CoV-2, a protective effect of estrogen in women, and inborn errors of cytokine immunity (13).

A study in Iran showed a significant difference between men and women infected with COVID-19, with men having higher rates of the disease early on. However, as the pandemic progressed, the proportion of women gradually increased, and ultimately more women were diagnosed with COVID-19 during the fifth wave (14). A meta-analysis of 3.1 million patients with confirmed SARS-CoV-2 infections reported that men were nearly three times as likely (OR = 2.84; 95 % confidence interval [CI]= 2.06-3.92) than women requiring ICU admission and had higher odds of death (OR = 1.39; 95 % CI = 1.31–1.47) despite a roughly equivalent incidence of SARS-CoV-2 infections among men and women (15).

The average age of the patients admitted during the years 2021 and 2022 was 65 years, with a range of 18-99 years, with a predominance of patients over 51 years of age, while those of the first outbreak of COVID-19 of the patients treated at the Clínica El Ávila were slightly younger than 62.7 years with a range of 31-91 years of age (9). In the first outbreak of COVID-19, Wang et al. reported a mean age of 56 years with a range of 22 to 92 years in 138 patients hospitalized for COVID-19 pneumonia in Wuhan (16). In 204 patients admitted to the University Hospital of Sant Joan in Reus, Spain, in the first wave and 264 in the second wave, it was found that those in the second wave were significantly younger (58 ± 26 vs. 67 ± 18 years; p <0.001) (17). Oda et al. reported in Japan in a study of patients with COVID-19 in the third wave that the mean age was 78 years with an age range between 62-83 years, being older than the patients with COVID-19 of the first and second waves (53 years) (7). There is evidence from around the world to suggest that age itself is the most important risk factor for severe disease from COVID-19. Early data from China show that the case fatality rate of COVID-19 increases with age, from 0.4 % or

less in patients 40 and younger, 1. 3 % in those 50-59, 3.6 % in those 60-69, 8 % in those 70-79 years, and 14.8 % in those 80 years or older; in general, the case fatality rate is 2. 3 % (18, 19). In a meta-analysis of 29 articles with 4,884 patients with COVID-19, a positive association was found between a group of symptoms and comorbidities with the age of the patient (19). Wu et al. reported that the elderly infected with COVID-19 older than 80 years had a higher case fatality rate (14.8 vs. 8.0 %) than those aged 70 to 80 years (18-21). Likewise, it was found that a group of symptoms such as fever, dyspnea/respiratory difficulty, nausea, vomiting, abdominal pain, dizziness, anorexia, and pharyngitis, and on the other hand comorbidities such as diabetes, hypertension, coronary disease, EBPOC/lung disease, and distress syndrome acute respiratory syndrome (ARDS) were associated with the age of patients infected with COVID-19 (21). These patients had respiratory distress with associated cough and fever as their main symptoms. The symptoms of the patients reported in the present study are the same as those already reported in the first outbreak in patients admitted to the Clínica Avila and by other authors internationally, being the most common symptoms of SARS-CoV-2 infection, fever, dry cough and fatigue and the less common symptoms, headache, sore throat, myalgia or arthralgia, shortness of breath, diarrhea, vomiting, dyspnea, chills and changes in smell (anosmia, hyposmia) and taste (ageusia, dysgeusia) (7-11, 22). In the first outbreak of COVID-19, the most frequent symptoms of patients admitted to the ICU at Clínica El Avila were fever, cough, dyspnea, and asthenia, and in the second and third waves, fever with respiratory symptoms continued to be the main reason of consultation. In Iran, Amin et al. observed in the first wave that the patients mainly presented respiratory symptoms as previously reported to which gastrointestinal complaints were added during the second wave, in the third wave neurological manifestations with peripheral involvement replaced gastrointestinal complaints and during the fourth and fifth waves wave manifestations of the central nervous system were added. A significant difference in the mean age of the patients was revealed between the five waves ($P< 0.001$) (23).

The patients in our study presented comorbidities. In general, older men (>60 years) with comorbidities are more likely to develop severe respiratory illness requiring hospitalization or even death, whereas most youth and children have only mild illness (no pneumonia or mild pneumonia) or are asymptomatic (24).

Our data show that the ICU mortality of this group of patients was 66.66 % and the mortality of ICU patients during the first outbreak of COVID-19 was 74.54 %. The mortality of the first outbreak of COVID-19 in the ICU was similar to the mortality of Mexican patients treated in an ICU from January 2020 to December 2021, which was 75 %; the highest percentages were observed in patients with mechanical ventilation admitted to the hospital (87 %) and to an ICU (75 %). The Mexican public sector had the highest percentage of mortality (25). Arentz et al. found 67 % mortality in patients with COVID-19 in the intensive care unit of the Evergreen Public Hospital in February 2020 (26). Mahendra et al., reported a mortality of 54.64 % among severe cases of COVID-19 in the ICU and only 5 % among cases with mild to moderate COVID-19 (27).

Regarding the hematological findings of the 102 patients admitted to the ICU, 55.9 % presented leukocytosis and of the deceased patients, leukocytosis occurred in 60.3 % of them. Chua et al. observed a significant count-response increase in white blood cell and neutrophil levels when the COVID-19 patient progressed from non-severe to severe cases with fatal outcomes (28). Our results demonstrate that, 71 patients from 603 admitted with COVID-19 had leukopenia, as occurs in most viral infections. Severe disease is often complicated by leukopenia, lymphopenia, thrombocytopenia, and coagulopathy, often leading to disseminated intravascular coagulopathy (29). Further, Kovalic et al. found that the most severe or critically ill cases were associated with leukocytosis, neutrophilia, lymphopenia, elevated creatinine kinase, elevated lactate dehydrogenase (LDH), and elevated prothrombin time (PT) (30). These patients that we are presenting had neutrophilia and lymphopenia and the neutrophils lymphocyte ratio (NLR) was higher in patients who required ICU and even higher in patients who died. According to systematic reviews with meta-analyses, higher values of the neutrophil-lymphocyte ratio were confirmed to be associated

with severity and mortality in hospitalized patients with COVID-19. Sarkar et al. found the prognosis value of NLR on admission for severity and mortality in patients with COVID-19 is good (31). Parthasarathi et al. did a meta-analysis with 15,683 patients that showed a difference in the NLR ratio of 3.93 between survivors and non-survivors of the disease (32). The neutrophil-lymphocyte ratio showed a sensitivity of 80.2 % and a specificity of 75.8 % for the prediction of severity and a specificity of 78.8 % sensitivity and 73.0 % for mortality and was not influenced by age, gender, or comorbid conditions. Other authors have confirmed the importance of the NLR relationship in COVID-19 (33-35).

In the present study, 117 (19.40 %) patients out of the 603 admitted with COVID-19 had anemia with hemoglobin (Hb) values of 10.4-11.8 g/dL and 10 patients out of the 68 who died in the ICU presented anemia on admission with hemoglobinemia less than 11.8 g/dL. A study of 67 COVID-19 patients in Singapore reported that during their course in an ICU, patients developed significantly lower deeper hemoglobin levels, compared with patients who were not admitted to the ICU (36). It has been reported that anemia on admission was independently associated with increased odds of all-cause mortality in hospitalized patients with COVID-19. Additionally, moderate-severe anemia (Hb <11 g/dL) was an independent risk factor for severe COVID-19 outcomes (37). These reported findings in relation to anemia in COVID-19 were not in line with our present data.

Regarding the platelet count, 57 (9.45 %) of the 603 patients presented thrombocytopenia on admission, with values from 23 to 139 × 10^9/L and 6 (8.82 %) patients of the 68 deceased presented thrombocytopenia of 42-118 × 10^9/L on admission. The number of platelets was reported to be significantly reduced in patients with COVID-19 (38,39). In China, the incidence of thrombocytopenia (< 150 × 10^9/L) on admission in patients with COVID-19 was 36.2 %, although this population is different from that of the present study (40).

The mechanisms by which SARS-CoV-2 causes thrombocytopenia are currently believed to involve the following: 1. An impaired hematopoietic microenvironment caused by systemic inflammation or cytokine storm, e.g. elevated IL-6, which is a common phenomenon in SARS-CoV-2. Infection could suppress hematopoiesis (41,42). 2. SARS-CoV-2 could directly infect hematopoietic stem cells or megakaryocytes through angiotensin-converting enzyme 2 (ACE2), CD13 or CD66a, as in other coronavirus infections that cause thrombocytopenia (43). 3. Antiviral antibodies that cross-react with hematopoietic cells or platelets, such as anti-adenovirus antibodies, can cross-react with the platelet integrin GPIIb/IIIa (44). In fact, Chen et al. showed that late-phase thrombocytopenia in patients with COVID-19 was the result of impaired megakaryocyte maturation (45). 4. Some of the patients with COVID-19 may present thrombotic microangiopathy and disseminated intravascular coagulation that increases platelet consumption (45,46). Platelets from patients with COVID-19 are hyperactivated and can be cleared by splenic or hepatic macrophages (46-48).

In the present study, thrombocytosis was detected in 30 patients out of 603 admitted patients, which is in accordance with the data reported by Lucijanic et al., who found in their patients both normal platelets count as well as thrombocytopenia and thrombocytosis. Lucijanic et al. reported that 4.6 % of their patients had a platelet count ≥450×10^9/L (1.1 % with platelets ≥600×10^9/L (49).

We report that patients had hyperferritinemia. Taneri et al. conducted a systematic review with a meta-analysis in 57 000 patients diagnosed with COVID-19 and demonstrated that higher ferritin levels were detected in deceased patients compared to survivors (50). Similar findings were reported by other authors (51,52). No difference in ferritin levels between deceased and survival patients was observed in the present study.

With respect to coagulation tests, an increase in prothrombin time and especially PTT was found, and to a greater extent in the deceased; D-dimer was higher in the deceased, indicating the development of a coagulopathy. It has been described those elevated levels of coagulation markers, such as PT, fibrinogen, fibrin, and D-dimer, may suggest activation of coagulation pathways, development of thrombosis, and an alarm of progression of COVID-19 towards a potentially serious outcome (52-54).

Elevated D-dimer levels could be an indicator of the development of deep vein thrombosis in patients with COVID-19 (55,56). No patients with deep vein thrombosis were observed in this study of patients with COVID-19. Its constant increase during the course of the disease has been reported to be particularly associated with severe disease progression and mortality (57-61).

Of the total number of patients admitted with COVID-19, 12.10 % of them presented elevated creatinine levels and 8.82 % of the deceased patients. A systematic review and meta-analysis investigating the effects of COVID-19 on renal function in 4 528 patients demonstrated that the prevalence of acute renal failure in patients with COVID-19 was 4 % and was significantly lower among non-severe patients compared with the patients who did not survive, however, they concluded that COVID-19 does not extensively involve the renal system and other possible mechanisms must be ruled out (62). The differences in the percentages of elevation of creatinine in our patients *vs*. the aforementioned meta-analysis perhaps lie in the difference in sample size.

C-reactive protein (CRP) was elevated in most of the patients in this study and even more in the deceased. CRP was useful in this study in identifying super aggregated bacterial infections and guiding antibiotic therapy in these patients. CRP as a marker of systemic inflammation has been associated with venous thrombosis, renal failure, critical illness, and mortality from COVID-19 (63). Serum ferritin, D-dimer, and CRP accurately predict patients who develop severe COVID-19 infections, as well as those at risk of developing COVID-19 pneumonia (64,65).

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