

Original article

Evaluation of the Clinical and Biochemical Parameters of Hospitalized COVID-19 Patients: A Retrospective, Single-Center Study from Bosnia and Herzegovina

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SUMMARY

Background/Aim. For the first time, we evaluated and presented the socio-demographic characteristics, clinical manifestations and laboratory findings of hospitalized coronavirus disease 2019 (COVID-19) patients from Canton Sarajevo, Bosnia and Herzegovina.

Methods. This retrospective, single-centre study included 159 RT-PCR verified COVID-19 patients (92 mild/moderate; 67 severe/critical) consecutively hospitalized at the General Hospital "Prim. dr Abdulah Nakaš" in Sarajevo, Bosnia and Herzegovina. Socio-demographic, clinical, and laboratory data on admission were retrospectively obtained from each patient's electronic medical record and patient files by two experienced physicians.

Results. 43.4% of the patients belonged to the age range of 46-65 years; 71.1% were men, and 68.6% had comorbidities; hypertension was the most prevalent comorbidity (100%), followed by diabetes (91.7%) and ischemic heart disease (35.8%). The leading clinical symptoms were fever (87.44%), tiredness (77.8%), and body/muscle aches (70.3%). There was significant reduction of blood oxygen saturation ($p = 0.005$), and significant elevation of D-dimer ($p = 0.003$), CRP ($p = 0.044$), and fasting plasma glucose ($p = 0.047$) in the severe/critical patients group compared to mild/moderate group.

Conclusion. Older age, the male gender, confirmed comorbidities, decreased blood oxygen saturation, increased levels of CRP, D-dimer, and fasting plasma glucose, together with symptoms of chest pain/shortness of breath and/or diarrhea occurred more frequently in severe/critical than mild/moderate COVID-19 patients.

Keywords: COVID-19; SARS-CoV-2; Bosnia and Herzegovina

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INTRODUCTION

The coronavirus disease 2019 (COVID-19), a major health problem worldwide, with patient-zero confirmed in Wuhan (Hubei Province, China) in December 2019, is caused by a single-stranded, positive-sense RNA virus (1). The World Health Organization (WHO) and the International Committee on Taxonomy of Viruses named the novel virus "Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The origin of the virus is still unclear, although a bat-to-human transmission is suspected (2, 3). The clinical manifestations in COVID-19 patients may vary from mild illness, with very little or no symptoms, to severe illness with a prolonged hospital stay, intensive care unit (ICU) admission, specific medical supportive care, and poor prognosis. Cough, shortness of breath, fever, myalgia, headache, and diarrhea are the most frequent presenting symptoms of a SARS-CoV-2 infection (4). A high proportion of patients with different accompanying comorbidities show more severe disease outcomes, from respiratory failure, due to the development of an acute respiratory distress syndrome (ARDS), to multisystem organ failure and death (5).

Due to the variety of clinical and paraclinical symptoms reported in COVID-19 patients, this disease is a challenge for healthcare professionals, scientists, and governmental institutions. The patients follow diverse disease patterns, and the case fatality rate (CFR) of COVID-19 is constantly changing, thereby varying between countries. It seems that understanding the demographic characteristics of the patients as well as their clinical features is crucial in tackling the pandemic. Guidelines for effective clinical decision-making and disease control need to be continuously updated. Therefore, each country needs to contribute to the broadening of our collective knowledge regarding the various aspects of this disease.

However, limited information is available describing the differences in the clinical characteristics and outcomes of COVID-19 patients in most countries, including Bosnia and Herzegovina (BA). The SARS-CoV-2 virus was confirmed to have reached BA on the 5th of March 2020, when a patient who had traveled to Italy tested positive (6). The first positive confirmed cases of COVID-19 in Sarajevo, the capital city of BA, were reported on March 20th, 2020 (7). Shortly afterward, the SARS-CoV-2 infection was spreading rapidly throughout the country and the

number of cases rose exponentially and reached pandemic proportions. According to WHO, until the 31st of March 2021, BA had 169,626 confirmed cases of COVID-19 with 6,599 death outcomes (8). Because of the growing number of COVID-19 patients in our country, and since no previous similar studies from BA could be found in literature, we aim to evaluate the socio-demographic characteristics, clinical manifestations, and laboratory findings of COVID-19 patients at hospital admission in a single medical centre in Sarajevo and to present their outcomes and our observations.

PATIENTS AND METHODS

Patients

This single-center observational retrospective study enrolled 159 confirmed COVID-19 patients who were consecutively hospitalized at the Covid-19 Department of the General Hospital "Prim. dr Abdulah Nakaš", in Sarajevo, BA, from November 1st, 2020 until March 15th, 2021. A positive reverse-transcriptase polymerase chain reaction (RT-PCR) assay for SARS-CoV-2 performed on nasopharyngeal samples confirmed the diagnosis of COVID-19. The samples were collected according to WHO interim guidance (9). Subjects who had a negative RT-PCR, asymptomatic subjects, subjects with missing data, and those who were younger than 18 were excluded from the study.

A modified version of the National Early Warning Score (NEWS) for use in COVID-19 patients was utilized to assess the clinical risk of the patients on hospital admission. The scoring system is based on seven variables: respiration rate, oxygen saturation, supplemental oxygen, systolic blood pressure, pulse rate, level of consciousness, and temperature, with age ≥ 65 years added as an independent risk factor. Every patient was clinically evaluated and grouped into one of the four risk categories based on the calculated score: low, medium, high, and exceptional (10).

According to the severity of COVID-19, every patient was classified into one of four disease severity groups: mild, moderate, severe, and critical. Patients having mild disease presented only with mild clinical symptoms (e.g., sore throat, cough, rhinorrhea, diarrhea, vomiting, arthralgia), with no imaging findings of pneumonia. Patients in the moderate severity group presented with fever (body

temperature (T) > 37.3°C) and respiratory symptoms, and radiological findings of pneumonia, but without the features of severe or critical disease.

Patients meeting any of the following criteria: (1) severe respiratory distress (respiratory rate (RR) \geq 30 breaths/min), (2) oxygen blood saturation (SpO₂) \leq 93% at rest on room air, or (3) arterial partial pressure of oxygen (PaO₂) or fraction of inspired oxygen (FiO₂) \leq 300 mmHg (\leq 39.9 kPa) were considered to have severe disease. Critical COVID-19 patients needed to meet one of the following criteria: (1) respiratory failure requiring mechanical ventilation, (2) septic shock, or (3) other organ dysfunction syndrome requiring admission to the ICU. For further analysis, patients with mild and moderate diseases were grouped together (mild/moderate patient group), and so were patients with the severe and critical disease (severe/critical patient group).

Demographics and comorbidities

The socio-demographic, clinical, and laboratory data were retrospectively obtained from electronic medical records and patient files by two experienced physicians. The baseline socio-demographic data included age and sex. Clinical parameters at hospital admission included: SpO₂, T, diastolic blood pressure (DBP), systolic blood pressure (SBP), pulse pressure (PP), mean arterial pressure (MAP), heart rate (HR), the NEWS score, clinical symptoms and signs (fever, headache, body/muscle aches, cough, loss of smell, loss of taste, tiredness, chest pain/shortness of breath, diarrhea), days from symptom onset to admission, comorbidities (diabetes mellitus (DM), hypertension (HTA), ischemic heart disease), COVID-19 therapy before hospitalization, duration of hospital stay, and disease outcome (recovery and discharge/transfer to tertiary medical care center/fatal outcome).

Laboratory parameters

Blood samples were collected in the first hours after admission and routine hematological and biochemical laboratory parameters were determined for each COVID-19 patient in the hospital central laboratory: red blood cell (RBC) count, white blood cell (WBC) count, platelet (PLT) count, hemoglobin (Hb), hematocrit (Hct), sodium (Na), potassium (K), chlorine (Cl), calcium (Ca), fasting plasma glucose (FPG), C-reactive protein (CRP), D-dimer, liver function

tests: alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatine kinase (CK), gamma-glutamyl transferase (GGT); kidney function tests: creatinine (CRE) and blood urea nitrogen (BUN).

Ethical approval

The study protocol was approved by the General Hospital "Prim. dr. Abdulah Nakaš" Ethics Committee (Ethical approval date and number: 01.02.2021; 555-14/21). Additionally, all participants or their relatives gave informed consent for the use and analysis of clinical data. The study was performed following the principles of the Declaration of Helsinki and its later amendments.

Statistical analysis

Continuous variables were presented as the means \pm standard deviation (SD) or medians and interquartile ranges (IQRs), while numbers (n) and percentages (%) were used for categorical variables. Kolmogorov-Smirnov test was performed to check the normality of distributions of the continuous variables. We used the independent samples Student's t-test (normal distribution) or the Mann-Whitney U test (abnormal distribution) to analyze the differences between two continuous variables. Categorical variables were compared using Pearson's chi-square (χ^2) test or Fisher's exact probability test. Statistical analyses were performed using SPSS software version 16.0 (SPSS, Inc., Chicago, IL). A value of $p < 0.05$ was considered statistically significant.

RESULTS

The baseline demographic and clinical characteristics of patients with COVID-19 at hospital admission are shown in Table 1. A total of 159 hospitalized COVID-19 patients were included in this study, of whom 46 (28.9%) were female and 113 (71.1%) were male. The median age was 63 years (IQR, 53 - 71 years), with an age range from 25 to 94 years. Most of the patients, 69 (43.4%), belonged to the aged range of 46 - 64 years, while 66 (41.5%) were 65 or over, and 24 (15.1%) were 45 or younger.

Mild/moderate disease was present in 92 (57.9%) patients, while 67 (42.1%) patients had severe/critical disease. The severe/critical patients' median age was 68 years (IQR, 62 - 75 years), which was

significantly higher than the median age of mild/moderate patients [59 years (IQR, 50.5 - 66.8 years)]. There was a significant difference ($p < 0.001$) in the proportion of mild/moderate and severe/critical patients among different age groups. Of patients with mild/moderate disease, 52 (56.5%) belonged to the age range of 46 - 65 years, while most of the severe/critical patients, 42 or 62.7%, belonged to the age group 65 and older. Among mild/moderate patients 67 (72.8%), and among severe/critical patients 46 (68.7%) were men, and there was no significant dif-

ference ($p = 0.567$) in the distribution of gender between the two groups. The median duration from initial symptom onset to hospital admission was 8 days (IQR, 6 - 11 days). Mild/moderate patients attended the hospital earlier than severe/critical patients [8 days (IQR, 6 - 10 days) vs 9 days (IQR, 6 - 11 days); $p = 0.229$, respectively]. When comparing mild/moderate patients with severe/critical patients, no significant difference was found between their SBP ($p = 0.414$), DBP ($p = 0.328$), PP ($p = 0.152$), MAP ($p = 0.885$) and HR ($p = 0.139$). Blood gas anal-

Table 1. Demographic and baseline clinical characteristics of mild/moderate and severe/critical patients with COVID-19

| | Total (n = 159) | Mild/Moderate (n = 92) | Severe/Critical (n = 67) | p- value |
|---|-----------------------|---------------------------|-----------------------------|-------------|
| Age (years) | 63.0 (53.0 - 1.0) | 59.0 (50.5 - 66.8) | 68.0 (62.0 - 75.0) | 0.000* |
| Age groups, n (%) | | | | |
| ≤ 45 years | 24 (15.1) | 16 (17.4) | 8 (11.9) | 0.000* |
| 46 - 65 years | 69 (43.4) | 52 (56.5) | 17 (25.4) | |
| > 65 years | 66 (41.5) | 24 (26.1) | 42 (62.7) | |
| Gender groups, n (%) | | | | |
| Female | 46 (28.9) | 25 (27.2) | 21 (31.3) | 0.567 |
| Male | 113 (71.1) | 67 (72.8) | 46 (68.7) | |
| Baseline clinical characteristics on admission | | | | |
| Symptoms onset to hospital admission (days) | 8.0 (6.0 - 11.0) | 8.0 (6.0 - 10.0) | 9.0 (7.0 - 12.0) | 0.229 |
| Oxygen blood saturation (%) | 92.0 (89.8 - 95.0) | 94.0 (92.0 - 96.0) | 90.0 (87.0 - 92.0) | 0.005 |
| Systolic blood pressure (mmHg) | 138.7 ± 22.0 | 137.4 ± 19.4 | 140.3 ± 25.2 | 0.414 |
| Diastolic blood pressure (mmHg) | 81.7 ± 12.3 | 82.5 ± 10.6 | 80.6 ± 14.4 | 0.328 |
| Pulse pressure (mmHg) | 55.0 (44.0 - 67.0) | 55.0 (42.0 - 65.0) | 60.0 (45.0 - 70.0) | 0.152 |
| Mean arterial pressure (mmHg) | 100.7 ± 14.1 | 100.8 ± 12.3 | 100.5 ± 16.3 | 0.885 |
| Heart rate (bpm) | 93.9 ± 15.5 | 92.3 ± 14.9 | 96.0 ± 16.3 | 0.139 |
| Body temperature (°C) | 36.8 (36.1 - 37.5) | 36.7 (36.0 - 37.4) | 37.0 (36.3 - 7.5) | 0.034 |
| NEWS | 4.0 (3.0 - 6.0) | 3.0 (2.0 - 4.0) | 6.0 (5.0 - 7.0) | 0.005 |

Data are expressed as number (n), mean ± standard deviation (SD), or median (interquartile range; IQR); NEWS - National Early Warning Score (modified version for the use in COVID-19 patients); p - values indicate differences between mild/moderate and severe/critical groups
* statistically significant at 0.001 ($p < 0.001$)

Table 2. Symptoms, treatment, and comorbidities before admission of mild/moderate and severe/critical patients with COVID-19

| | Total (n = 159) | Mild/Moderate (n = 92) | Severe/Critical (n = 67) | p-value |
|--|--------------------|---------------------------|-----------------------------|---------|
| Symptoms before admission n (%) | | | | |
| Fever (T > 37.3 °C) | 139 (87.4) | 79 (85.9) | 60 (89.6) | 0.489 |
| Headache | 79 (49.7) | 54 (58.7) | 25 (37.3) | 0.008 |
| Body/Muscle aches | 116 (73.0) | 62 (67.4) | 54 (80.6) | 0.06 |
| Cough | 84 (52.8) | 45 (48.9) | 39 (58.2) | 0.246 |
| Loss of smell | 12 (7.5) | 10 (10.9) | 2 (3.0) | 0.06 |
| Loss of taste | 11 (6.9) | 8 (8.7) | 3 (4.5) | 0.312 |
| Tiredness | 123 (77.8) | 66 (72.5) | 57 (85.1) | 0.06 |
| Chest pain/Shortness of breath | 72 (45.3) | 35 (38.0) | 37 (55.2) | 0.032 |
| Diarrhea | 87 (54.7) | 44 (47.8) | 43 (64.2) | 0.04 |
| COVID-19 treatment before admission n (%) | | | | |
| Any COVID-19 treatment | 159 (100) | 92 (100) | 67 (100) | 1.00 |
| Antiviral drugs | 11 (6.9) | 7 (7.6) | 4 (6.0) | 0.687 |
| Antibiotics | 115 (72.3) | 68 (59.1) | 47 (40.9) | 0.601 |
| Corticosteroids | 20 (12.6) | 13 (14.1) | 7 (10.4) | 0.489 |
| Antithrombotic drugs | 45 (28.3) | 26 (28.3) | 19 (28.4) | 0.989 |
| Comorbidities n (%) | | | | |
| Any comorbidity | 109 (68.6) | 55 (59.8) | 54 (80.6) | 0.005 |
| Diabetes mellitus | 100 (91.7) | 51 (92.7) | 49 (90.7) | 0.706 |
| Hypertension | 109 (100) | 55 (59.8) | 54 (80.6) | 0.005 |
| Ischemic heart disease | 39 (35.8) | 16 (29.1) | 23 (42.6) | 0.141 |

Data are expressed as number (n) and percentage (%); p - values indicate differences between mild/moderate and severe/critical groups

ysis showed that compared to the patients in mild/moderate group, patients from the severe/critical group had significantly lower ($p = 0.005$) SpO₂ [90.0% (IQR, 87.0 - 92.0%) vs 94.0% (IQR, 92.0 - 96.0%)]. Further, severe/critical patients also had significantly higher T [37.0°C (IQR, 36.3 - 37.5°C) vs 36.7°C (IQR, 36.0 - 37.4°C); ($p = 0.034$)] and a higher NEWS score [6 (IQR, 5 - 7) vs 3 (IQR, 2 - 4); ($p = 0.005$)].

The main symptoms, treatment, and comorbidities before admission of the COVID-19 patients are presented in Table 2. The most common symptoms were fever - 139 (87.4%), tiredness - 123 (77.8%), body/muscle aches - 116 (73.0%), diarrhea - 87 (54.7%), cough - 84 (52.8%), headache - 79 (49.7%), chest pain/shortness of breath - 72 (45.3%). Less common symptoms were loss of smell - 12 (7.5%) and loss of taste - 11 (6.9%) patients. Compared with the

mild/moderate patients, patients with severe/critical disease were more likely to report chest pain/shortness of breath ($p = 0.032$) and diarrhea ($p = 0.04$), while headache was a more frequent symptom in mild/moderate compared to severe/critical patients ($p = 0.008$). Before admission, most patients received antibiotic therapy (115/72.3%). Antithrombotic drugs were used in 45 (28.3%) patients, corticosteroids in 20 (12.6%), and antiviral therapy in 11 or 6.9% of patients. There was no significant difference between the mild/moderate and severe/critical patient groups in terms of COVID-19 treatment before admission. Of the 159 patients, 109 (68.6%) had at least one comorbidity. Among them, HTA was found in all patients (109/100%) and was the most common comorbidity present, followed by DM (100/91.7%) and ischemic heart disease (39/35.8%). Compared with the mild/moderate disease

patient group, severe/critical patients were significantly ($p = 0.005$) more likely to have comorbidities [54 (80.6%) vs 55 (59.8%)]. Severe/critical patients showed an increased prevalence of HTA (80.6% vs 59.8%; $p = 0.005$), but no significant difference was

observed in other comorbidities between the two groups.

Amid the analyzed laboratory parameters at admission, the values of CRP, D-dimer, ALT, AST, GGT, and FPG were increased in COVID-19 patients

Table 3. Laboratory characteristics at hospital admission of mild/moderate and severe/critical patients with COVID-19

| | Normal range | Total (n = 159) | Mild/Moderate (n = 92) | Severe/Critical (n = 67) | p- value |
|----------------------------------|--------------|---------------------------|---------------------------|----------------------------|----------|
| CRP (mg/L) | 0.0 - 5.0 | 81.1 ± 74.2 | 71.2 ± 64.4 | 94.6 ± 84.5 | 0.044 |
| D-dimer (µg/L) | 0 - 804 | 880.0 (570.0 - 1675.0) | 710.0 (500.0 - 1420.0) | 1110.0 (710.0 - 2950.0) | 0.003 |
| ALT (U/L) | 10 - 36 | 62.0 (40.5 - 89.5) | 60.0 (41.0 - 88.0) | 65.0 (40.0 - 95.0) | 0.591 |
| AST (U/L) | 8 - 30 | 46.0 (35.0 - 70.0) | 45.0 (34.0 - 69.0) | 51.0 (36.8 - 74.0) | 0.135 |
| CK(U/L) | 40 - 153 | 133.0 (63.0 - 305.25) | 126.5 (77.3 - 305.3) | 136.0 (53.0 - 333.0) | 0.501 |
| GGT (U/L) | 9 - 35 | 62.5 (34.0 - 118.5) | 53.0 (33.0 - 113.5) | 78.0 (40.0 - 122.0) | 0.217 |
| Creatinine (µmol/L) | 63 - 107 | 86.5 (76.0 - 101.75) | 84.0 (76.0 - 97.0) | 92.0 (75.5 - 110.0) | 0.08 |
| BUN (mmol/L) | 2.8 - 8.3 | 6.1 (4.7 - 8.4) | 5.8 (4.3 - 7.4) | 7.1 (5.4 - 9.7) | 0.001 |
| FPG (mmol/L) | 4.4 - 6.4 | 7.1 (6.0 - 9.2) | 6.9 (5.8 - 8.2) | 7.3 (6.2 - 10.8) | 0.047 |
| RBC (x 10¹²/L) | 3.86 - 5.08 | 4.6 ± 0.7 | 4.6 ± 0.6 | 4.6 ± 0.7 | 0.823 |
| WBC (x 10⁹/L) | 3.4 - 9.7 | 6.6 (5.0 - 8.6) | 6.2 (4.8 - 8.2) | 7.1 (5.4 - 9.2) | 0.08 |
| PLT (x 10⁹/L) | 158 - 424 | 222.0 (159.3 - 292.0) | 214.5 (150.0 - 280.5) | 238.0 (170.5 - 314.3) | 0.109 |
| Hemoglobin (g/L) | 119 - 157 | 137 ± 17.6 | 137.6 ± 16.7 | 136.0 ± 18.9 | 0.573 |
| Hematocrit | 0.35 - 0.47 | 0.40 ± 0.05 | 0.40 ± 0.04 | 0.40 ± 0.05 | 0.809 |
| Sodium (mmol/L) | 137 - 146 | 139.3 ± 4.2 | 140.2 ± 3.8 | 138.2 ± 4.4 | 0.004 |
| Potassium (mmol/L) | 3.6 - 5.1 | 4.3 ± 0.5 | 4.2 ± 0.5 | 4.3 ± 0.5 | 0.147 |
| Chlorine (mmol/L) | 97 - 108 | 99.0 (96.0 - 102.0) | 99.5 (97.8 - 102.0) | 99.0 (95.0 - 102.0) | 0.08 |
| Calcium (mmol/L) | 2.14 - 2.53 | 2.22 ± 0.13 | 2.21 ± 0.13 | 2.23 ± 0.13 | 0.487 |

Data are expressed as number (n), mean ± standard deviation (SD), or median (interquartile range; IQR); CRP - C reactive protein; ALT - Alanine aminotransferase; AST - Aspartate aminotransferase; CK - Creatinine kinase; GGT - Gamma-glutamyl transferase; BUN - Blood urea nitrogen; FPG - Fasting plasma glucose; RBC - red blood cell count; WBC - white blood cell count; PLT - platelet count; p - values indicate differences between Mild/Moderate and Severe/Critical groups

compared to the normal range. The patients in the severe/critical group had significantly higher values of CRP ($p = 0.044$), D-dimer ($p = 0.003$), and FPG ($p = 0.047$) compared to patients in the mild/moderate group. Additionally, although concentrations of Na and BUN in COVID-19 were within the normal range, the severe/critical patients had significantly higher values of BUN ($p = 0.001$), and significantly lower values of Na ($p = 0.004$) compared to mild/moderate patients. No remarkable differences were noted concerning ALT, AST, CK, GGT, CRE, RBCs, WBCs, PLTs, Hb, Hct, K, Cl, and Ca between the two groups (Table 3).

The duration of hospital stay and the outcomes of COVID-19 patients are presented in Table 4. The median duration of hospital stay was 11 days

(IQR, 9 - 14 days). Among mild/moderate patients, the median duration of hospital stay was 11 days (IQR, 8 - 14 days), while among those in the severe/critical group the median duration of hospital stay was longer, but the difference between the two groups was insignificant [11 days (IQR, 10 - 17 days); ($p = 0.067$)]. At the end of March 15th, 2021, 154 (96.9%) patients recovered and were discharged, 3 (1.9%) patients were transferred to a tertiary medical care center, 3 (1.3%) had a fatal outcome while being hospitalized. Additionally, severe/critical patients were less likely to recover and be discharged [62/92.5% vs 92/100%; $p = 0.008$], but more likely to be transferred to a tertiary medical care center [3/4.5% vs 0/0.0%], and have a fatal outcome [2/1.3% vs 0/0.0%] compared to mild/moderate patients.

Table 4. Duration of hospital stay and outcomes at end of hospitalization of mild/moderate and severe/critical patients with COVID-19

| | Total (n = 159) | Mild/Moderate (n = 92) | Severe/Critical (n = 67) | <i>p</i> -value |
|---|--------------------|---------------------------|-----------------------------|-----------------|
| Duration of hospital stay (days) | 11 (9 - 14) | 11 (8 - 14) | 11 (10 - 17) | 0.067 |
| Outcomes n (%) | | | | |
| Recovery and discharge | 154 (96.9) | 92 (100) | 62 (92.5) | 0.008 |
| Transfer to a tertiary medical care center | 3 (1.9) | 0 (0) | 3 (4.5) | 0.000* |
| Death | 2 (1.3) | 0 (0) | 2 (1.3) | 0.000* |

Data are expressed as number (n) and percentage (%) or median (interquartile range); *p* - values indicate differences between mild/moderate and severe/critical groups (* $p < 0.001$)

DISCUSSION

To the best of our knowledge, this is the first single-center report of the socio-demographic, clinical, and laboratory findings of hospitalized RT-PCR confirmed COVID-19 patients from Sarajevo, BA, at the time of admission, along with their disease outcomes. Because reports in literature from this geographic region are scarce, it is necessary to present data on this topic and provide trustworthy references that can help create proper health interventions.

Our results indicate no differences in gender ratios between patients with mild/moderate and severe/critical disease, although in both patient groups there was a higher proportion of men. Our results are consistent with the results of Popov et al. (11) who reported that greater proportions (63.0%) of hospitalized patients in their retrospective study were men. Women appear to be less likely to get infected with SARS-CoV-2 because of the presence of immune regulatory genes encoded by two X chromosomes which cause lower viral loads, and less inflammation than in men, and also their CD4+T cell

counts are higher and show a better immune response. Further, the production of antibodies in women is higher than in men, and they generally remain longer in circulation (12). In our study, the severe/critical patients had an older median age compared to mild/moderate patients, and they mostly belonged to the age group of 65 and older. Ghweil *et al.* (13) reported that severe COVID-19 was more frequent in older patients, while mild to moderate disease was more frequent in younger patients. Also, results from a similar study showed that elderly COVID-19 patients are more likely to progress to severe COVID-19, in comparison with young and middle-aged COVID-19 patients (14). Zhou *et al.* (15) explained this with an age-dependent reduction in cell-mediated immune responses, and impairments of the humoral immune system. The current study results indicate that the median time from symptom onset to hospital admission was similar for both COVID-19 patient groups. Our findings are comparable to the findings of a recent study, where the median time from symptom onset to hospital admission in patients with 2019 novel CoV (2019-nCoV)-infected pneumonia was 7 days (IQR: 4 - 8) (16). We identified fever, tiredness, and body/muscle aches as the most frequent mild symptoms, while both losses of smell and taste were less commonly reported at admission. In recent studies, it was shown that headache, fever, dry cough, and muscle aches are often the first symptoms to appear, while smell and taste impairments are rarely the leading symptoms (17). In their systematic review and meta-analysis, Fu and *al.* (18) listed fever as one of the dominant clinical features of COVID-19. In our study, chest pain/shortness of breath and diarrhea were significantly more frequent in severe/critical patients than in mild/moderate patients, while the prevalence of headache was significantly higher in mild/moderate patients. Similarly, a retrospective cohort study by Trigo *et al.* (19) showed that headache is a frequent symptom in COVID-19 patients and its' association with lower mortality risk. A recently published meta-analysis showed no significant difference in the prevalence of headache between severe/critical and non-severe COVID-19 patients (20). The results of the present study showed that more than half of the patients (68.8%) had one or more comorbidity, among which HTA was the most prevalent, followed by DM and ischemic heart disease. These findings are consistent with a recent meta-analysis which reported that HTA, cardiovas-

cular diseases, and DM are the most prevalent underlying comorbidities in hospitalized patients with COVID-19 (21). In our study, the presence of comorbidities including HTA was significantly higher in severe/critical compared to mild/moderate patients. Present results are in accordance with the results of a study conducted in Serbia which showed that comorbidities were present in 66.7% of the patients with severe COVID-19 infection. These researchers also reported that HTA was present in 70.1% of the patients with a severe form and 16.4% of the patients with a moderate form of COVID-19 infection (22). CRP is a useful biochemical indicator of inflammation (23). Therefore, the measurements of CRP levels in COVID-19 patients are of great importance in evaluating the severity of infection. The significantly increased values of CRP and D-dimer in severe/critical patients in our study indicate that COVID-19 is a hyperinflammatory and hypercoagulable state. Our results are consistent with previous studies which also showed that CRP in severe disease is significantly higher than in non-severe disease and that CRP was an independent risk factor for severe COVID-19, with the optimal working point of 38.55 mg/L (24). Our results confirm the findings of Petrilli *et al.* (25) who reported particularly strong associations of higher initial levels of CRP and D-dimer with mortality risk and critical illness among hospitalized patients with COVID-19. A significantly higher level of FPG found in severe/critical patients in our study might be a stress reaction and can be interpreted as a result of increased cortisol secretion (26). In the present study, severe/critical COVID-19 patients showed significantly lower values of SpO₂ than mild/moderate patients with COVID-19. Based on a review published in October 2020, key indicators for differentiation of the severity level in COVID-19 are reported to be respiratory symptoms and SpO₂ (27).

A retrospective cohort of hospitalized patients with COVID-19 in Lima, Peru identified SpO₂ below 90% on admission as a strong predictor of in-hospital mortality in patients with COVID-19 (28). The patients enrolled in our study had elevated levels of ALT, AST, and GGT compared to the normal range, which indicates that SARS-CoV-2 may infect hepatocytes and bile duct cells and cause abnormal values of liver function tests as seen in these patients. Abnormal liver enzyme activities in patients with COVID-19 were reported for the first time by Chen *et al.* (29). Medetalibeyoglu *et al.* (30) suggested that

the systemic hyperinflammatory state may be the main liable mechanism for the elevation in liver enzymes. The median duration of hospital stay of our patients was 11 days (IQR, 9 - 14 days), with no significant difference in the duration of hospital stay between the groups. Data about the duration of hospital stay varied between studies. Wang et al. (16) reported that the median hospital stay among COVID-19 patients who were discharged alive was 10 days (IQR, 7 -14). Another retrospective study conducted in North Sardinia, Italy, found the median length of hospital stay was 18 days (IQR, 12 - 24 days) (31). Compared with the mild/moderate patients, severe/critical patients in our study were less likely to recover and get discharged, but more likely to be transferred to a tertiary medical care center and die. These results are consistent with the results of a previous study that reported that male patients, age ≥ 50 years with comorbidities (kidney disease, cerebrovascular disease, cardiovascular disease, respiratory disease, DM, HTA, and cancer) had a significantly increased mortality risk associated with COVID-19 (32).

Our study has several limitations. Firstly, this is a single-center study that included data from one single geographic region and one hospital, without cooperation with other institutions. The possibility to apply the results of this study to other ethnic groups and geographic regions needs to be further explored. Secondly, our study has a retrospective design. A

prospective cohort study may give us more complete and detailed information about the COVID-19 patients from BA. Finally, the small sample size increases the probability of bias and confounding factors and restricts the applicability of the results and conclusions to a broader population. Further, multicenter, prospective studies with a larger sample size in BA are required to confirm our results.

CONCLUSION

In conclusion, this first retrospective BA study provides data about the socio-demographic and clinical manifestations, laboratory findings, and outcomes of confirmed hospitalized COVID-19 patients. It reveals that older, male Bosnian and Herzegovinian patients, with confirmed comorbidities, are more likely to develop severe/critical COVID-19 and have adverse outcomes. Additionally, decreased SpO₂, increased levels of CRP, D-dimer, and FPG, together with symptoms of chest pain/shortness of breath and/or diarrhea were observed more frequently in severe/critical than mild/moderate COVID-19. Although the patients with COVID-19 in our study have similar clinical manifestations, laboratory findings, and outcomes with other cohorts, and that study confirms recent trends observed at other centers, it is important to present these results in the context of a broader understanding of the ethical and geographical differences in COVID-19.

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Evalvacija kliničkih i biohemijskih parametara hospitalizovanih bolesnika sa infekcijom kovid 19 - retrospektivna studija iz Bosne i Hercegovine

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SAŽETAK

Uvod/Cilj. Po prvi put su evaluirane i predstavljene socio-demografske karakteristike kliničke manifestacije, kao i rezultati laboratorijskih analiza hospitalizovanih bolesnika zaraženih korona virusom, kovid 19, iz Kantona Sarajevo, Bosna i Hercegovina

Metode. Retrospektivnom, jednocentričnom studijom obuhvaćeno je 159 bolesnika zaraženih virusom kovid 19 (92 bolesnika sa lakim/umerenim stadijumom; 67 bolesnika sa teškim/kritičnim stadijumom bolesti), kod kojih je prisustvo virusa potvrđeno RT-PCR metodom, hospitalizovanih u Opštoj bolnici "Prim. dr Abdulah Nakaš" u Sarajevu, Bosna i Hercegovina. Socio-demografski, klinički i laboratorijski podaci na prijemu su retrospektivno korišteni iz elektronskog medicinskog kartona svakog bolesnika, od strane dva iskusna i nezavisna lekara.

Rezultati. Starosnom dobu od 46 do 65 godina pripadalo je 43,4% bolesnika; 71,1% bili su muškarci, dok je 68,6% imalo komorbiditete. Hipertenzija je bila najzastupljeniji komorbiditet (100%), zatim dijabetes (91,7%) i ishemijska bolest srca (35,8%). Vodeći klinički simptomi bili su: groznica (87,44%), umor (77,8%) i bolovi u telu/mišićima (70,3%). Dokazano je statistički značajno smanjenje zasićenosti krvi kiseonikom ($p = 0,005$), statistički značajno povećanje D-dimera ($p = 0,003$), CRP-a ($p = 0,044$) i serumske koncentracije glukoze natašte ($p = 0,047$) u grupi bolesnika koji su bili sa teškim/kritičnim stadijumom, u poređenju sa bolesnicima sa blagim/umerenim stadijumom.

Zaključak. Starije životno doba, muški pol, potvrđeni komorbiditeti, smanjena zasićenost krvi kiseonikom, povećane vrednosti CRP-a, D-dimera i serumske koncentracije glukoze natašte, zajedno sa simptomima, kao što su bol u grudima, kratkoća daha i/ili dijareja, češće su se javljali kod bolesnika sa teškim/kritičnim stadijumom izazvanim virusom kovid 19 u odnosu na bolesnike sa blagim/umerenim stadijumom bolesti.

Ključne reči: COVID-19; SARS-CoV-2; Bosna i Hercegovina