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Disorder Of laboratory parameters in hospitalized patients during Covid-19 infection

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Abstract

Background. The coronavirus disease (COVID-19) is an infectious disease caused by the SARS-CoV-2 virus. A disturbance in the number of white blood cells results from direct damage to cells, primarily lymphocytes, by the SARS-CoV-2 virus.

Aim. The work aims to examine the impact of the SARS-CoV-2 virus on the laboratory parameter values in bedridden patients during hospitalization.

Results. To determine the impact of COVID-19 infection on laboratory parameter values , the study included 80 respondents hospitalized at the UCC Tuzla Infectious Diseases Clinic from 1.1.2021. - 31.12.2021. year. Among the respondents, 58.75% were men and 41.25% were women. A review of laboratory findings shows that there is a statistically significant difference between erythrocyte values and the time of measurement (P=0.028). At admission, 93.75% of subjects had high C-reactive protein (CRP) values, 87.50% of subjects on day 5 of measurement, and 67.50% of subjects had high values at discharge from the hospital. There was a statistically significant increase in CRP values compared to reference values (P=0.000). There was a statistically significant increase in platelets in subjects measured on admission (11.25% of subjects), on the 5th day of hospital stay (28.75% of subjects), and at discharge (33.75% of subjects) (P=0.000).

Conclusion. Given the results obtained, we can conclude about the impact of the SARS-CoV-2 virus on the disruption of laboratory parameter values, especially the decrease in the number of erythrocytes and the increase in ferritin and C-reactive protein.

Keywords: SARS-Cov-2; Laboratory Parameters; C-Reactive Protein; Erythrocytes; Platelets

1. Introduction

The coronavirus disease (COVID-19) is an infectious disease caused by the SARS-CoV-2 virus [1]. The first coronaviruses were discovered in the 1930s of the last centuries, when the contagious bronchitis virus caused an acute respiratory infection. The first human coronaviruses were identified in the 1960s. In 2003, SARS-CoV (severe acute respiratory

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syndrome) caused a lung infection, and the mortality rate reached approximately 10%. Therefore, the World Health Organisation (WHO) reported that SARS-CoV could cause a severe acute infectious disease worldwide. In 2012, another severe coronavirus infection was discovered in the Middle East. The discovery process was similar to SARS. The patient had severe unexplained pneumonia, and it was later determined that a new type of coronavirus caused it. A new virus, Middle East Respiratory Syndrome MERS-CoV (MERS), was first found in a patient from Saudi Arabia with severe unexplained pneumonia [2]. The common feature of all three well-known β-CoVs, namely SARS-CoV-1 (the causative agent of SARS), MERS-CoV, and SARS-CoV-2, is that they can replicate in the lower respiratory tract and cause fatal pneumonia [3]. 80% of SARS-CoV-2 infections in outpatients manifest as mild respiratory disease. About 15% of patients with moderate-to-severe pneumonia require hospitalisation [4]. A disturbance in the number of white blood cells results from the SARS-CoV-2 virus directly damaging cells, primarily lymphocytes. Numerous morphological changes can be seen on the peripheral blood smears of infected individuals [5]. Lymphopenia is the main marker of infection and is present in a wide range of values in all symptomatic COVID-19 patients. Research has indicated a correlation between the severity of the disease and the reduction in lymphocyte levels [6]. Certain clinical studies suggest that, like its predecessors SARS-CoV and HCoV-229E, the SARS-CoV-2 virus inhibits the process of haematopoiesis in the bone marrow via certain receptors. It is evident that the SARS-CoV-2 virus has the capacity to diminish platelet production within the bone marrow, consequently resulting in thrombocytopenia [7]. Thrombocytopenia is one of the laboratory findings that indicate an unfavourable course of COVID-19 [8]. The most widely accepted theory regarding the development of thrombocytopenia in clinical studies is the so-called consumptive thrombocytopenia, which occurs as a result of lung damage and an inadequate response of macrophage system cells, leading to the formation of microthrombi within the pulmonary capillary vessels [8]. Decreased haemoglobin levels have been observed in some patients with severe COVID-19. A meta-analysis of four studies showed that haemoglobin concentrations are lower in severe forms of the disease than in mild infections [9]. Several studies have found no significant changes in haemoglobin levels in patients with COVID-19 [10]. No significant effects were observed on the number of red blood cells (RBCs), although structural alterations were detected [9]. From 20% to 40% of patients with COVID-19 have leukopenia, and 3% to 24% have leukocytosis. Lymphopenia (lymphocyte count ≤ 1100 cells/μL) has been observed in 30% to 75% of patients with COVID-19. A meta-analysis by Huan and Pranata revealed a strong association between lymphopenia and severe disease of COVID-19 [11]. Neutrophilia has been reported in patients with severe COVID-19. An elevated neutrophil-to-lymphocyte ratio has been identified as a marker of in-hospital mortality and severe disease of COVID-19 [9]. The current explanation for lymphopenia is viral invasion of lymphocytes, as ACE2 receptors are found on these cells [12]. The virus can directly attack lymphocytes, inducing apoptosis, infect bone marrow cells, or destroy the spleen and lymph nodes. Elevated lactic acid levels in COVID-19 may lead to reduced lymphocyte proliferation [13]. Cytokine storm can adversely affect the number and function of T-cells [14]. Recent research has revealed a strong correlation between C-reactive protein (CRP) levels and the severity of various infections. Hepatocytes in the liver synthesise CRP, a plasma protein whose production can be stimulated by various inflammatory mediators, including interleukin-6 (IL-6). CRP levels are markedly elevated in patients with severe SARS-CoV-2 infection [15]. Recent studies have shown that patients with COVID-19 have elevated CRP levels, and high CRP levels are closely associated with more severe forms of COVID-19, where age was considered a major risk factor for poor outcome [16]. In addition to serum C-reactive protein (CRP), other inflammatory indicators may also be associated with the severity of SARS-CoV-2 infection in individuals. These include serum ferritin, hypocalcaemia, procalcitonin and erythrocyte sedimentation rate [17]. Several retrospective studies comparing survivors and non-survivors have shown an increasing trend in acute-phase proteins, including CRP, procalcitonin (PCT), and IL-6, in non-survivors, and a stable or decreasing trend in survivors [16]. In a multicenter retrospective study, higher CRP levels were reported in patients who developed thrombotic complications following COVID-19 infection [16].

1.1. Aim

This study examines the impact of SARS-CoV-2 on laboratory parameters in bedridden patients during hospitalization.

2. Material And Methods

This retrospective study included data from 80 patients admitted to the Clinic for Infectious Diseases at UKC Tuzla between January 1 and December 31, 2021. Data were collected for the following laboratory parameters: erythrocytes, leukocytes, platelets, hemoglobin, hematocrit, lymphocytes, C-reactive protein and ferritin. Data were collected using Excel spreadsheets. Standard statistical parameters (mean values and chi-squared tests) were used for the analysis using the SPSS software package, and a p-value of <0.05 was considered significant. For the collection and processing of data, we received consent from the Ethics Committee of the University of Applied Sciences Tuzla.

3. Results

To determine the impact of COVID-19 infection on laboratory parameter values, the study included 80 subjects hospitalized at the JZU UKC Tuzla Clinic for Infectious Diseases from January 1, 2021, to December 31, 2021. year. Among the respondents, 58.75% were men and 41.25% were women. It can be seen that respondents from both groups are predominantly in the 18- to 64-year-old age range (Figure 1).

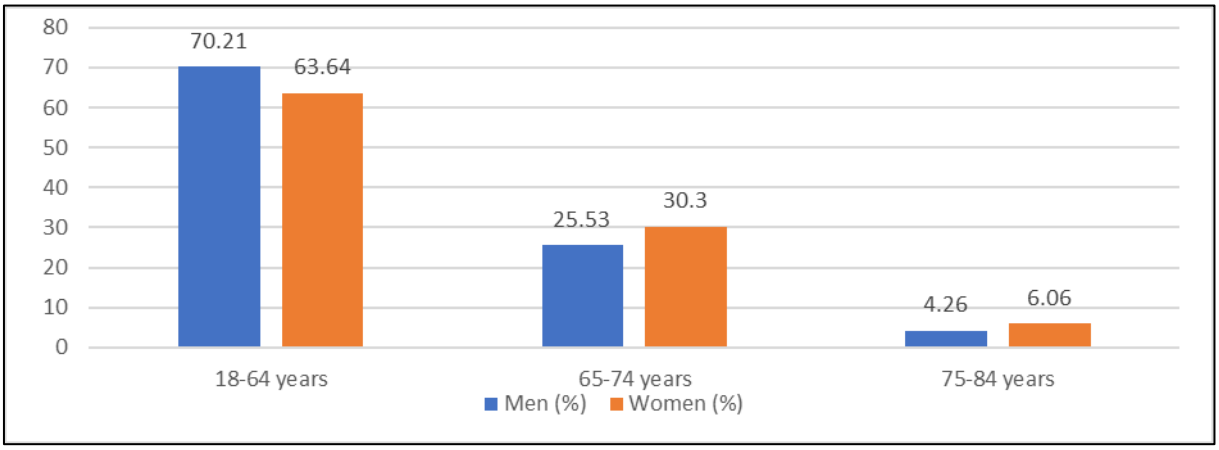

Figure 1 Number and structure of respondents in terms of age and gender

Respondents with a secondary vocational education predominate among men (59.57%), while respondents with primary vocational education predominate among women (45.45%) (Figure 2).

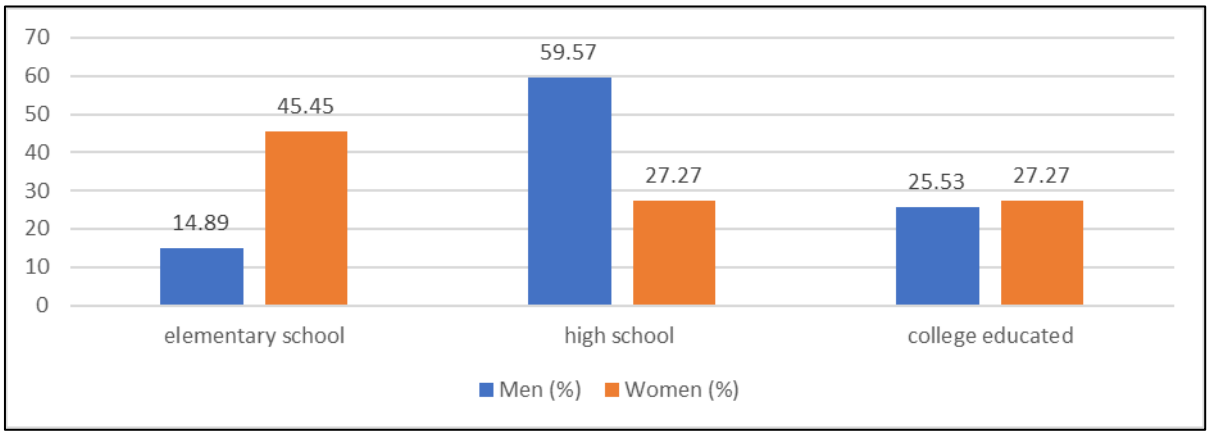

Figure 2 Number and structure of respondents about gender and education

Table 1 Laboratory values in subjects

R/b	Parameters	Value	Day of measurement						Chi-square test	df	P
			On admission		5th after admission		Upon discharge				
			f	%	f	%	f	%			
1	Erythrocytes	Below reference values	19	23.75	30	37.50	34	42.50	10.84	4	0.028
		Reference values	61	76.25	47	58.75	45	56.25			
		Above reference values	0	0.00	3	3.75	1	1.25			
2	Leukocytes	Below reference values	3	3.75	1	1.25	0	0.00	14.90	4	0.005
		Reference values	55	68.75	40	50.00	37	46.25			
		Above reference values	22	27.50	39	48.75	43	53.75			
3	Hemoglobin	Below reference values	27	33.75	35	43.75	41	51.25	7.09	4	0.131
		Reference values	53	66.25	44	55.00	39	48.75			
		Above reference values	0	0.00	1	1.25	0	0.00			
4	Hematocrit	Below reference values	36	45.00	44	55.00	48	60.00	3.96	4	0.411
		Reference values	42	52.50	34	42.50	31	38.75			
		Above reference values	2	2.50	2	2.50	1	1.25			

Legend: f-number of subjects, df-degree of freedom; P-value of the Chi-square test

An analysis of the laboratory findings presented in Table 1 shows a statistically significant difference between erythrocyte values and the time of measurement ($p = 0.028$). During each measurement, subjects with reference values of erythrocytes predominate (23.75% of subjects at admission).

The number of subjects with lower erythrocyte values (lower than reference) increases when measured on the 5th day after admission (37.5%) and after discharge (42.5% of subjects). The level of haemoglobin (Hb) was also monitored in the subjects. As shown in Table 1, at admission, 33.75% of respondents had Hb values below the reference range; 43.75% on the fifth day of measurement; and 51.25% at discharge. However, no statistically significant decrease in Hb

values was observed during the measurement period (p = 0.13; Table 1). Similar results were obtained by examining hematocrit (Hct) values. As illustrated in Table 1, the initial Hct values were lower in 45% of subjects at the time of hospital admission, with this figure increasing to 55% on day 5 and reaching 60% at the time of discharge. Statistically significant decreases in Hgb values have not been demonstrated (P=0.41). Among the laboratory values, we also assessed leukocytes. As shown in Table 1, subjects with leukocyte counts within the reference range predominated at admission. However, a higher percentage of subjects exhibited leukocyte values above the reference range on the fifth day after admission and at discharge. Elevated leukocyte levels were observed in 27.5% of subjects at admission, 48.75% on the fifth day, and 53.75% at discharge. A statistically significant difference in leukocyte values was found between the time points of measurement (fifth day and discharge) (p = 0.005) (Table 1).

Table 2 Laboratory values in subjects

R/b	**Parameters**	**Value**	**Day of measurement**						**Chi-square test**	**df**	**P**
			On admission		5th after admission		Upon discharge				
			f	%	f	%	f	%			
1	Ferritin	Below reference values	0	0.00	0	0.00	0	0.00	0.14	2	0.931
		Reference values	19	23.75	17	21.25	18	22.50			
		Above reference values	61	76.25	63	78.75	62	77.50			
2	CRP	Below reference values	0	0.00	0	0.00	0	0.00	21.23	2	0.000
		Reference values	5	6.25	10	12.50	26	32.50			
		Above reference values	75	93.75	70	87.50	54	67.50			
3	Platelets	Below reference values	16	20.00	4	5.00	3	3.75	22.98	4	0.000
		Reference values	55	68.75	53	66.25	50	62.50			
		Above reference values	9	11.25	23	28.75	27	33.75			
4	Lymphocytes	Below reference values	65	81.25	65	81.25	63	78.75	0.22	4	0.994
		Reference values	14	17.50	14	17.50	16	20.00			
		Above reference values	1	1.25	1	1.25	1	1.25			

Legend: f-number of subjects, CRP-C-reactive protein; df-degree of freedom; P-value of the Chi-square test

At admission, 93.75% of subjects had high C-reactive protein (CRP) values, 87.50% of subjects had high values on the 5th day of measurement, and 67.50% of subjects had high values upon discharge from the hospital. There is a statistically significant increase in CRP values compared to reference values (P=0.000) (Table 2).

There is a statistically significant increase in platelets in subjects measured at admission (11.25% of subjects), on the 5th day of hospital stay (28.75% of subjects), as well as at discharge (33.75% of subjects) (P=0.000) (Table 2).

4. Discussion

In 2021, a total of 403,615 COVID-19 cases were reported in Bosnia and Herzegovina, while during the same period, 704,753,890 cases of SARS-CoV-2 infection were recorded worldwide [18]. The SARS-CoV-2 virus infected and caused systemic changes in the infected subjects, which is why disturbances in laboratory parameters were examined. In a study in Wuhan, China, 51% of patients had decreased Hgb values [19]. Chen et al. reported reduced haemoglobin (Hb) levels in 51% of subjects [20]. Zhou et al. reported reduced Hgb in 15% of subjects [21]. In the study by Guan et al., 41% of subjects had lower Hgb [22]. During a study in Italy, 61% of subjects had anaemia during COVID-19 infection [23]. In our study, 23.75% of respondents had haemoglobin (Hb) values below the reference range at admission, 37.5% on the fifth day of hospitalisation, and 42.5% at discharge. In one study, lymphopenia was found in 87.9% of cases and neutrophilia in 90.9% of cases in Northeast India. This finding is consistent with the findings of a study conducted by Li et al. in China, which demonstrated a decrease in the number of lymphocytes and an increase in the number of neutrophils in cases of infection with SARS-CoV-2, compared to uninfected controls [24]. In a study conducted in Colombia, lymphopenia (69.6–100%) and thrombocytopenia (20–55%) were reported in patients with SARS-CoV-1 infections [25]. A study conducted in China revealed that 35% of subjects exhibited lymphopenia, while a subsequent study in Singapore reported a figure of 36.9% [26]. A study conducted in China revealed that 63% of subjects exhibited lymphopenia [27]. Several studies have reported varying degrees of lymphopenia among patients with COVID-19. In Wuhan, lymphocyte reduction was observed in 35% of patients [19], while another study from the same region reported lymphocytopenia in 64% of cases [25]. Studies from China demonstrated lymphopenia in 35.5% and 55% of patients, respectively [29,30], whereas Guan et al. found lymphopenia in 69% of cases [22]. In the United States, 72% of patients exhibited lymphopenia [28]. Cao et al. reported a lower incidence, with lymphopenia present in 8.9% of patients [31]. Similarly, Zhao et al. observed decreased lymphocyte counts in 40% of subjects, further supporting the association between SARS-CoV-2 infection and lymphocyte depletion [21]. In a study in Saudi Arabia, leukocytopenia was present in 48.6% of subjects [32]. In Suzhou, 45.3% of subjects had lymphopenia, 21.3% had leukopenia [33]. In Pakistan, 37.6% of respondents have lymphopenia, 2% leukopenia [34]. In our study, lymphopenia was proven in 81.2% of subjects at admission and 78.75% at discharge from the hospital.

C-reactive protein (CRP) was one of the parameters that deviated from the reference values. In a study conducted in Iraq, 17.65% of the 88 subjects had CRP levels within the reference range at admission. During hospitalization, CRP levels increased in 64.7% of patients, with a gender distribution of 42% men and 22.7% women among those with elevated CRP [15]. In the research in Northeast India, 78% of the respondents had elevated CRP values. The mean value of CRP in milder cases was 8.57 mg/L, of which 90.9% of subjects with a moderately severe clinical picture and 100% of subjects with a severe form of COVID-19 infection had elevated CRP values [24]. In a study conducted in China, Chen et al. evaluated the use of C-reactive protein (CRP) as a marker for assessing the severity of COVID-19 and found a positive correlation between CRP levels and increasing disease severity. Moderate and severe infections have been shown to have higher CRP levels compared to mild infections (95% confidence interval) [24]. In a study in China, 86% of subjects had elevated CRP values [26]. In China, 53.8% of subjects had elevated CRP [35]. In the Wuhan study, 91.9% of patients had elevated CRP [36]. Yang et al. examined CRP changes in COVID-19 patients and found that CRP was increased in 55% of patients [37]. Given that the majority of research was conducted in China, an increase in CRP was visible in 78.4% of subjects in one of these studies [31]. As demonstrated by Wu et al., an increase in CRP was observed in 46% of patients [38]. In contrast, Guan et al. reported elevated CRP values in 93% of patients [22]. In Suzhou, 58.7% of respondents have elevated CRP [33]. In the present study, elevated CRP values were observed in 93.7% of respondents upon admission to the hospital, 87.5% on day 5, and 67.5% upon discharge.

In a study conducted in Novi Sad, the platelet count was observed in a group of subjects who exhibited a positive disease outcome. It was observed that 93.2% of subjects demonstrated a reduced or physiological level of platelets, while an elevated platelet count was observed in 6.8% of subjects [39]. In China, thrombocytopenia occurred in 12% of patients, while in Singapore it occurred in 20% of patients [25]. In the Wuhan study, 18.8% of patients had thrombocytopenia [40]. In another study in Wuhan, China, 4% of patients had elevated platelet counts and 12% of patients had decreased platelet counts [39]. In the trial conducted by Yang et al., 13.4% of subjects had decreased platelets [37], while in Liu et al., 8% of subjects had thrombocytopenia [30]. In one trial in China, 17.6% of subjects had thrombocytopenia [31]. Zhou et al. showed a reduced number of platelets in 7% of subjects [21], while in the study conducted by Guan et al., 17% of

subjects had thrombocytopenia [22]. In Suzhou, 12% of subjects have thrombocytopenia [33]. In Pakistan, 39% of respondents have thrombocytopenia [34]. In our study, 88.75% of patients had a reduced or physiological platelet count on the first day of admission to the hospital, 71.25% on the 5th day of hospitalization, 66.25% on discharge from the hospital, while elevated values were present in 11.25% of patients on admission, 28.75% on the 5th day of hospitalization and 33.75% on discharge from the hospital.

5. Conclusion

At hospital discharge, a significant number of patients exhibited abnormalities in laboratory parameters. Specifically, 42.5% of patients had decreased red blood cell counts, 53.75% had elevated white blood cell counts, and 78.75% had lymphopenia. Thrombocytopenia was observed in 62.5% of patients. Regarding inflammatory and organ function markers, 77.5% of patients had elevated ferritin and CRP. These results indicate a significant impact of SARS-CoV-2 infection on haematological and biochemical parameters, even at the time of hospital discharge, highlighting the need for ongoing monitoring of laboratory values in patients following acute infection, which could be used in the future for a better therapeutic approach to such patients.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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