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Basic biochemical and hematological parameters in COVID-19 deceased: Analysis of potential mortality predictors

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ABSTRACT

Introduction: As a result of research conducted globally, experts continue to extensively study the long-term consequences that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections can have on patients, as well as the factors contributing to severe outcomes. The aim of this study was to investigate the values of basic biochemical and hematological parameters in patients with fatal outcomes of SARS-CoV-2 infection, as well as to determine the combination of hematological and biochemical parameters that contribute to the progression of SARS-CoV-2 infection. The examined parameters were correlated with the age and gender distribution of patients with fatal outcomes from the SARS-CoV-2 infection.

Methods: The study represents a retrospective study of patients hospitalized at the Cantonal Hospital Zenica from February to April 2021, focusing on the biochemical and hematological parameters of subjects with confirmed presence of the SARS-CoV-2 virus using the reverse transcription-polymerase chain reaction methods who were hospitalized at the Cantonal Hospital Zenica.

Results: Of the 250 deceased subjects in the sample, females comprised the relative majority at 53.6%. Among the examined parameters, hemoglobin, mean corpuscular hemoglobin (MCH), and MCH were significantly lower in females compared to males, while males had significantly higher values of urea, creatinine, and troponin. The average age of the patients was 74 years, and with aging, the values of erythrocytes, hemoglobin, and troponin increased. Troponin showed a statistically significant positive correlation with age, as well as with urea and creatinine.

Conclusion: We can conclude that hemoglobin, urea, creatinine, and troponin are parameters that can be considered to contribute to the progression of SARS-CoV-2 infection. These parameters can be useful for assessing disease severity and prognosis in patients infected with the SARS-CoV-2 virus.

Keywords: COVID-19; biochemical parameters; hematological parameters; age; gender; mortality

INTRODUCTION

Since December 2019, the issue with the newly discovered severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viruses and the disease called Coronavirus Disease 2019 has been ongoing (1). From sporadic cases of infection development and spread, it rapidly evolved into a pandemic with global consequences worldwide (2). In Bosnia and Herzegovina, the first case of SARS-CoV-2 infection was confirmed on March 5, 2020. As of August 2022, there have been 9.056 deaths associated with the virus and 248,742 recoveries in the Federation of Bosnia and Herzegovina. The clinical presentation varies in severity from asymptomatic to mild forms of the disease to more severe cases and fatal outcomes (3,4). Mild cases present with a slight fever and mild myalgia without pneumonia, while severe cases present with dyspnea and/or hypoxia (usually in the 1st week), leading to the development of acute respiratory distress syndrome, septic shock, metabolic acidosis, coagulopathy, and multiple organ dysfunction syndrome (5). Previous studies suggest that certain inflammatory biomarkers (procalcitonin, C-reactive protein), hematological markers (lymphocytes, platelets), and biochemical markers (D-dimer, aspartate aminotransferase [AST], alanine-aminotransferase [ALT], and lactate dehydrogenase [LDH]) are significantly associated with severe COVID-19 disease and are good predictors of poor outcomes; thus, they may be useful in assessing the risk of

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fatal outcomes in patients with confirmed COVID-19 disease (6-8). By analyzing the biochemical and hematological parameters routinely tested in a laboratory panel, it is possible to stratify patients. Our aim is to assess the basic routine tests performed in COVID-19 deceased patients during the peak of the pandemic and determine any potential correlation between the values of the examined markers, age, and gender.

METHODS

This study is a retrospective cohort study that focuses on the biochemical, hematological, and inflammatory parameters of patients with confirmed presence of the SARS-CoV-2 virus who experienced a fatal outcome. The research was conducted over a period of 3 months (February, March, and April) in 2021, specifically during the third wave of the pandemic in BiH. The examined biochemical, hematological, and inflammatory markers are part of the standard routine control panel for COVID-19 patients at the COVID department of the Cantonal Hospital Zenica. The data were presented with the consent of the Ethical Committee of the Cantonal Hospital Zenica, with the approval number: 00-03-35-2286-6/20. The source of data for this research is the medical records of the participants included in the study. The collected data were entered into the Microsoft Excel program, where appropriate mathematical and statistical functions and tools for data visualization were applied for data analysis. Descriptive statistical measures were used to describe the phenomena, and correlation techniques were used to examine the associations. The association between the indicated phenomena was tested using the Statistical Package for the Social Sciences program.

RESULTS

During the observed period of 3 months, the results of laboratory tests conducted on 250 patients with a fatal outcome were analyzed. In terms of the total number of patients, as shown in Table 1, the number of female participants was 134, accounting for 53.6%, while the male participants accounted for approximately 46.4%, with 116 patients.

Table 1 show that the majority of participants belong to the age group of 65 years and older, and there is no statistically significant difference between genders in terms of illness in this age group. In addition, female participants were the majority in the sample, but the Pearson Chi-square test did not show a statistically significant difference in illness between genders (0.534, $p > 0.05$).

A descriptive analysis of the observed parameters presented in Table 2 in 250 COVID-19 patients who died indicates that the youngest patient was 45 years old, while the oldest was 97 years old. The mean age was 74.8 years, with a standard deviation of 8.8 years. In addition, there is no statistically significant difference in age between males and females, as the analysis of variance test showed $p > 0.05$. Among all the observed parameters, statistically significant differences between male and female genders were found for hemoglobin, mean corpuscular hemoglobin (MCH), and MCHC ($p < 0.05$). The concentration of hemoglobin was measured in 230 patients with fatal outcomes, with the lowest concentration being 65 g/L and the highest being 235 g/L. Females had lower hemoglobin levels, which was statistically significant ($p < 0.05$). Although there is a statistically significant difference in hemoglobin levels between males and females, it should be interpreted from a physiological perspective, considering natural differences and biological characteristics of gender. MCH was measured in 212 patients, with the lowest value of 18.9 and the highest of 40.7 pg. MCHC was measured in 212 patients, with the lowest value of 29.2 and the highest of 36.7 g/dL. Both parameters show statistical significance ($p < 0.05$).

TABLE 1. Representation of patients by gender and age groups

Gender	Age		Total	*p*-values*
	41-64 years	65 years and older		
Male	17	99	116	0,534
n=116	14.6%	85.4%	100.0%	
Female	15	119	134	
n=134	11.2%	88.8%	100.0%	
Total	32	218	250	
	12.8%	87.2%		

*p-values were calculated using the Pearson Chi-square test

Based on the analysis of laboratory findings presented in Table 3, statistically significant differences were observed between males and females in several measured parameters. Significant differences were found in the values of urea, creatinine, AST, LDH, and troponin between the genders. Males tended to have higher values for urea, creatinine, and troponin compared to females. The average value of urea in males was 15.1 mmol, while in females, it was 12.0 mmol. Despite physiological differences in creatinine values between males and females, statistical analysis was performed for creatinine as the average value exceeded the reference level. The average value of creatinine in males was 157.5 μmol/L, while in females, it was 118.4 μmol/L, and this difference was found to be statistically significant. The average value of AST in males was 109.1 U/L, while in females, it was 118.96 U/L. In addition, the average value of LDH in males was 531.3 U/L, while in females, it was 665.8 U/L. Finally, the average value of troponin in males was 77.5 ng/L, while in females, it was 64.1 ng/L.

The analysis of laboratory findings presented in Table 4 between two age groups, 41-64 years and 65 years and above revealed several statistically significant differences in parameters. In the older age group (65+), a statistically significant higher value of erythrocytes ($p = 0.036$) and hemoglobin ($p = 0.037$) was observed compared to the younger age group. In addition, a statistically significant lower value of MCHC was observed in the older age group ($p = 0.034$). There were no statistically significant differences in the values of leukocytes, hematocrit, mean corpuscular volume (MCV), MCH, red cell distribution width, platelets, and mean platelet volume between the two age groups.

Based on the analysis of laboratory findings presented in Table 5 between two age groups (41-64 years and 65 years and above), several statistically significant differences in parameters were observed. In the 65+ age group, significantly lower values of creatinine ($p < 0.049$) were recorded. The mean value of creatinine in the older group (133.03 μmol/L) was lower compared to the younger group (163.41 μmol/L). In addition, statistically significant higher values of AST ($p < 0.027$) and troponin ($p < 0.034$) were found in older individuals. The mean AST

TABLE 2. Values of hematological parameters in relation to gender

Parameter	Gender	n=250	Mean/SD	Minimum	Maximum	*p*-values*
Age of participants	Male	116	75.2±8.7	46	93	0.536
	Female	134	74.4±8.9	45	97	
	Total	250	74.8±8.8	45	97	
Leukocytes 3.4-10×10^9/L	Male	106	9.5±5.1	1.27	36.0	0.509
	Female	122	10.0±5.6	2.77	39.1	
	Total	228	9.8±5.4	1.27	39.1	
Erythrocytes 3.89-5.08×10^{12}/L	Male	108	4.4±0.6	2.93	6.6	0.437
	Female	122	4.3±0.6	2.08	6.2	
	Total	230	4.4±0.69	2.08	6.6	
Hemoglobin 119-157 g/L	Male	108	134.4±22.8	74	235	0.013
	Female	122	127.3±20.7	65	178	
	Total	230	130.6±21.9	65	235	
Hematocrit 0.36-0.47L/L	Male	108	0.39±0.06	0.24	0.56	0.101
	Female	122	0.38±0.06	0.19	0.59	
	Total	230	0.39±0.06	0.19	0.59	
MCV 81-99fL	Male	99	87.7±5.7	69.9	111.7	0.223
	Female	113	86.7±6.3	63.7	106.2	
	Total	212	87.1±6.1	63.7	111.7	
MCH 26-32 pg	Male	99	29.9±2.4	22.0	40.7	0.035
	Female	113	29.2±2.6	18.9	35.3	
	Total	212	29.5±2.5	18.9	40.7	
MCHC 31-35 g/dL	Male	99	34.1±1.2	30.8	36.7	0.007
	Female	113	33.6±1.6	29.2	36.4	
	Total	212	33.8±1.4	29.2	36.7	
RDW 11.6-16.8%CV	Male	97	14.2±1.5	12.0	22.0	0.409
	Female	113	14.4±1.8	11.2	23.7	
	Total	210	14.3±1.7	11.2	23.7	
Platelets 150-400×10^9/L	Male	108	209.1±100.4	18	508	0.510
	Female	122	216.9±79.4	72	555	
	Total	230	213.2±89.8	18	555	
MPV 7.4-10.4fL	Male	98	10.6±1.0	7.6	14.2	0.067
	Female	114	10.9±0.9	9.0	13.9	
	Total	212	10.8±1.0	7.6	14.2	

MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; RDW: Red cell distribution width; MPV: Mean platelet volume; **p*-values were calculated using the t-test

value in the older group (120.66 U/L) was significantly higher compared to the younger group (76.12 U/L), and the mean troponin value in the older group (76.285 ng/L) was significantly higher compared to the younger group (26.353 ng/L). There were no statistically significant differences in the values of urea, ALT, LDH, pO2, and glucose between these two age groups.

The results of the correlation analysis presented in Table 6 suggest a positive correlation (r = 0.163, $p < 0.05$) between age and troponin, which is statistically significant ($p < 0.05$), as well as a negative correlation with MCHC (r = –0.141, $p < 0.05$). In addition, a statistically significant correlation was found between hemoglobin and erythrocytes (r = 0.818, $p < 0.01$), as well as creatinine (r = –0.167, $p < 0.05$). The correlation coefficient between hemoglobin and erythrocytes (r = 0.818, $p < 0.01$) and MCHC showed a statistically significant positive correlation (r = 0.314, $p < 0.05$), indicating a connection between high MCHC values and an increased concentration of hemoglobin in erythrocytes, and a negative correlation with creatinine (r = –0.186, $p < 0.01$). The correlation coefficient between urea and creatinine (r = 0.832, $p < 0.01$), as well as troponin (r = 0.236, $p < 0.01$), showed a statistically significant positive correlation, implying a connection between elevated urea values and increased creatinine and troponin values, while the correlation coefficients between creatinine and urea (r = 0.832, $p < 0.01$) and troponin (r = 0.175, $p < 0.05$) showed a statistically significant positive correlation, suggesting that higher creatinine values may be associated with elevated urea and troponin levels. The correlation coefficients between creatinine and erythrocytes (r = –167, $p < 0.05$), MCHC (r = –167, $p < 0.05$), and hemoglobin (r = –186, $p < 0.01$) showed a statistically significant negative correlation, indicating that lower creatinine values may be associated with lower erythrocyte, MCHC, and hemoglobin values. The correlation coefficients between troponin and age (r = 0.163, $p < 0.05$), urea (r = 0.206, $p < 0.01$), and creatinine (r = 0.175, $p < 0.05$) showed a statistically significant positive correlation. These results imply a possible association between older age, elevated creatinine values, and high troponin levels.

DISCUSSION

The study, conducted on a sample of 250 deceased individuals, indicates that the majority of participants belonged to

TABLE 3. Values of biochemical parameters in relation to gender

Parameter	Gender	n=250	Mean/SD	Minimum	Maximum	*p*-values*
Urea 1,7-8,3 mmol	Male	101	15.1±11.1	2.3	57.2	0.021
	Female	113	12.0±8.3	1.7	44.7	
	Total	214	13.5±9.8	1.7	57.2	
Creatinine 44-84 μmol/L	Male	100	157.5±54.9	24	1044	0.032
	Female	112	118.4±60.2	28	786	
	Total	212	136.9±85.1	24	1044	
ALT 0-35 U/L	Male	87	60.7±22.5	9	1135	0.955
	Female	93	61.7±20.6	7	757	
	Total	180	61.2±21.2	7	1135	
AST 0-35 U/L	Male	71	109.1±44.1	12	3255	0.049
	Female	93	118.9±64.2	10	1798	
	Total	180	114.2±76,2	10	3255	
LDH 110-248 U/L	Male	41	531.3±113.2	157	1089	0.041
	Female	66	665.8±154.0	173	4522	
	Total	117	607.2±190,2	157	4522	
sO2	Male	89	78.6±14.8	17.2	98.1	0.674
	Female	102	77.7±14.6	31.2	97.8	
	Total	191	78.1±14.7	17.2	98.1	
Troponin <14 ng/L	Male	79	77.5±35.7	7.6	879.0	0.027
	Female	81	64.1±27.1	4.1	519.2	
	Total	170	70.4±44,7	4.1	879.0	
Glucose 3,3-6,1mmol/L	Male	107	10.4±5.9	2.8	35.3	0.332
	Female	120	11.2±5.9	2.9	35.8	
	Total	227	10.8±5.9	2.8	35.8	

ALT: Alanine-aminotransferase; AST: Aspartate aminotransferase; LDH: Lactate dehydrogenase; **p*-values were calculated using the t-test

TABLE 4. Values of hematological parameters in relation to age

Parameter	Age	n	Mean	*p*-values*
Leukocytes 3.4-10×10^9/L	41–64 years	31	8.9±4.7	0.311
	65 years and older	196	9.9±5.5	
Erythrocytes 3.89-5.08×10^{12}/L	41–64 years	31	4.1±0.6	0.036
	65 years and older	198	4.4±0.6	
Hemoglobin 119-157 g/L	41-64 years	31	125.5±20.5	0.037
	65 years and older	130	131.3±22.1	
Hematocrit 0.36-0.47 L/L	41–64 years	31	0.36±0.06	0.140
	65 years and older	198	0.38±0.05	
MCV 81-99fL	41–64 years	29	87.2±4.9	0.913
	65 years and older	182	87.1±6.3	
MCH 26-32 pg	41–64 years	29	30±2.0	0.300
	65 years and older	182	29.5±2.6	
MCHC 31-35 g/dL	41–64 years	29	34.4±1.1	0.034
	65 years and older	182	33.7±1.5	
RDW 11.6-16.8% CV	41–64 years	28	14.5±2.4	0.706
	65 years and older	181	14.3±1.5	
Platelets 150-400×109/L	41–64 years	31	208.2±108	0.744
	65 years and older	198	213.9±87	
MPV 7.4-10.4 fL	41–64 years	29	10.8±1.2	0.960
	65 years and older	182	10.8±0.9	

MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; RDW: Red cell distribution width; MPV: Mean platelet volume; **p*-values were calculated using the t-test

TABLE 5. Values of biochemical parameters in relation to age

Parameter	Age	n=250	Mean	*p*-values*
Urea a1.7–8.3 mmol	41-64 years	28	11.7±13	0.298
	65 years and older	186	13.8±9.3	
Creatinine 44–84 μmol/L	41-64 years	27	163.4±55	0.049
	65 years and older	140	133±43	
ALT 0–35 U/L	41-64 years	31	46.7±28	0.512
	65 years and older	120	63.6±31	
AST 0–35 U/L	41-64 years	31	76.1±18	0.027
	65 years and older	120	120.6±27.1	
LDH 110–248 U/L	41-64 years	15	736.9±105	0.297
	65 years and older	102	588.1±98.1	
pO2 %	41-64 years	21	46.8±7.3	0.579
	65 years and older	168	48.4±13.3	
Troponin<14 ng/L	41-64 years	19	26.3±11.3	0.034
	65 years and older	150	76.2±25.3	
Glucose 3.3–6.1 mmol/L	41-64 years	26	9.6±6.4	0.262
	65 years and older	201	11±5.9	

ALT: Alanine-aminotransferase; AST: Aspartate aminotransferase; LDH: Lactate dehydrogenase; **p*-values were calculated using the t-test

the age group of 65 and older, where there is no significant difference in disease occurrence between genders. Possible reasons for the higher presence of older participants in the sample include weakened immune systems, higher exposure to risk factors throughout life, and a greater likelihood of multiple chronic conditions that commonly affect older individuals (9). However, it is worth noting that the majority of participants in the sample were females, which contradicts findings from other studies where the incidence of mortality is higher among males (10,11). When examining the biochemical and hematological parameters, it can be observed that leukocytes, erythrocytes, MCV, and MCH were mostly within the reference ranges for both genders, while hemoglobin levels were lower in women. Hemoglobin showed statistical significance in our study, and as mentioned by Cavezzi et al., it remains unclear whether the underlying pathological process of the virus starts in the lungs with subsequent generalized anemic

TABLE 6. Correlation analysis of age and biochemical-hematological parameters

Correlations	Age	Erythrocytes 3.89-5.08×10^{12}/L	MCHC 31-35 g/dL	Hemoglobin 119-157 g/L	Urea 1.7-8.3 mmol	Creatinine 44-84 μmol/L	Troponin <14 ng/L
Age							
Pearson correlation	1	0.109	−0.141*	0.063	0.071	−0.077	0.163*
Sig. (2-tailed)		0.099	0.041	0.338	0.298	0.267	0.034
n	250	230	212	230	214	212	170
Erythrocytes 3,89-5.08×10^{12}/L							
Pearson correlation	0.109	1	0.024	0.818**	−0.113	−0.167*	0.013
Sig. (2-tailed)	0.099		0.726	0.000	0.108	0.017	0.872
n	230	230	212	230	205	203	162
MCHC 31-35 g/dL							
Pearson correlation	−0.141*	0.024	1	0.314**	−0.206**	−0.167*	−0.096
Sig. (2-tailed)	0.041	0.726		0.000	0.005	0.022	0.240
n	212	212	212	212	189	187	152
Hemoglobin 119-157 g/L							
Pearson correlation	0.063	0.818**	0.314**	1	−0.137	−0.186**	0.028
Sig. (2-tailed)	0.338	0.000	0.000		0.050	0.008	0.722
n	230	230	212	230	205	203	162
Urea 1,7-8,3 mmol							
Pearson correlation	0.071	−0.113	−0.206**	−0.137	1	0.832**	0.206**
Sig. (2-tailed)	0.298	0.108	0.005	0.050		0.000	0.008
n	214	205	189	205	214	212	165
Creatinine 44-84 μmol/L							
Pearson correlation	−0.077	−0.167*	−0.167*	−0.186**	0.832**	1	0.175*
Sig. (2-tailed)	0.267	0.017	0.022	0.008	0.000		0.025
n	212	203	187	203	212	212	163
Troponin <14 ng/L							
Pearson correlation	0.163*	0.013	−0.096	0.028	0.206**	0.175*	1
Sig. (2-tailed)	0.034	0.872	0.240	0.722	0.008	0.025	
n	170	162	152	162	165	163	170

*.Correlation is significant at the 0.05 level (2-tailed)
**.Correlation is significant at the 0.01 level (2-tailed)

hypoxia and disrupted iron metabolism or if hemoglobin-iron dysmetabolism is the leading process resulting in multi-organ disease and hypoxia. Early detection and treatment of this condition may prevent poor prognostic outcomes in patients with COVID-19 infection (11-13). Our results suggest that MCHC and the age of the participants are important parameters for assessing patient outcomes, which aligns with previous research findings. The data were separated by gender due to established differences in the hematological profile between males and females, in line with recent research. These differences are often associated with higher testosterone levels in males or periodic menstrual blood loss in females (8,14-17). Significant differences exist in the values of urea, creatinine, AST, LDH, and troponin between genders. Males tended to have higher values in these parameters compared to females. Increased levels of urea and creatinine in males may indicate a greater impact of COVID-19 on kidney function in males compared to females. This could be due to differences in hormonal status between genders, urinary system differences, or other biological variations. Additionally, higher values of AST and LDH may be a result of differences in metabolic or immune responses between genders (18-21). Higher troponin levels in men may imply a greater impact of COVID-19 on the cardiac muscle in men compared to women. These differences could be due to biological variations in cardiac function, cardiac muscle structure, or the infection itself. These results are consistent with previous research on patients with COVID-19 (11,12,22). Age is an important determinant of disease severity, and in our study, the average age of the affected individuals was 74.84 years. In our study, it was observed that older patients had significantly lower levels of creatinine and significantly higher levels of AST and troponin, which may indicate a higher risk of liver damage and cardiac complications in these patients. It is important to note that no statistically significant differences were observed in other analyzed parameters, suggesting that creatinine, AST, and troponin are more specific and reliable indicators for evaluating renal and cardiovascular function in older patients with COVID-19 infection. These results align with the findings of referenced studies concluding that elevated levels of cardiac troponin in geriatric patients, without the presence of acute coronary syndrome, have independent prognostic value in predicting morbidity and mortality from all causes. This finding is significant because it suggests that cardiac troponins can provide additional risk and prognostic information in these patients beyond traditional risk factors for cardiovascular disease (23,24). Considering that the results of the correlation analysis suggest a statistically significant positive correlation between age and elevated levels of cardiac troponin in our study, it may indicate a higher risk of cardiac issues with increasing

age. Additionally, a negative correlation between MCHC and troponin was observed, implying that elevated troponin levels may be associated with lower hemoglobin concentrations in erythrocytes. Moreover, troponin also showed a statistically significant positive correlation with urea and creatinine, suggesting that high troponin levels may be associated with elevated urea and creatinine levels, which may also indicate kidney problems. We note that correlation analysis allows for assessing the degree of relationship between variables but cannot provide absolute confirmation of causal relationships or the clinical significance of the results. Therefore, it is necessary to consider these results in the context of other clinical information and individual patient characteristics.

CONCLUSION

This research paper highlights mechanisms associated with the progression of SARS-CoV-2 infection, particularly in relation to hematological and biochemical parameters. The aim is to provide new information to the scientific community to improve therapeutic approaches for COVID-19. Our results support the importance of monitoring creatinine, AST, and troponin in assessing kidney function and cardiovascular system in elderly patients with COVID-19. However, further research is needed to better understand the cause-and-effect relationship between these parameters and clinical outcomes in these patients. It is also important to note that our results have certain limitations, such as the retrospective study design, small sample size, and lack of data on comorbidities and therapeutic treatments received by the patients. Further research should encompass these aspects to better understand the clinical significance of differences in laboratory parameters.

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DECLARATION OF INTERESTS

Authors declare no conflict of interests.

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