



Original articles

CHARACTERISTIC CHANGES IN SOME CLINICAL LABORATORY PARAMETERS OF THE SARS-COV-2 INFECTION IN THE COURSE OF THE DISEASE

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ABSTRACT:

Global coronavirus disease 2019 (COVID-19) has posed major challenges to clinical laboratories, from initial diagnosis to patient monitoring and treatment. Some routine laboratory markers reveal a range of changes in patients with COVID-19. Among the most frequently observed are: increased levels of C-Reactive Protein (CRP), Lactate dehydrogenase (LDH), D-Dimer neutrophilia with lymphopenia and decreased platelet count.

The aim of our study is to present the changes in the values of CRP, LDH, D-Dimer, number of Thrombocytes (PLT), Lymphocytes (Ly) and Neutrophils (Neu) during hospitalization and at the discharge of patients with Sars-Cov-2.

Materials and methods: The object of the study are clinical laboratory results of 106 patients who underwent hospital treatment for Covid -19 in the "St. Ivan Rilski" St. Zagora, divided into two groups. The first group (Group I) is in the period November-December 2020, the second group (Group II) patients were hospitalized in April 2021. The values of CRP, LDH, D-Dimer, number of platelets, Ly, Neu from the day of the patient's admission to the hospital and from his discharge were examined.

Results and discussion: In 100% of the examined patients in the first group CRP with values at the time of admission to the hospital (TAH) 88.70 ± 63.132 mg/L. LDH was increased in three of the groups in more than 90% of the patients, with the highest values of the enzyme being recorded in Group II at the end of hospitalization, 802.33 U/L (± 557.836). In the studied groups, we found significantly more patients with elevated values in both groups at discharge (Group I 49.12% and Group II 46.94%). The highest number of patients with thrombocytopenia was observed in Group II at the time of admission to the hospital, 26.53% (n=13).

Conclusion: Quantification of these and other laboratory parameters could significantly aid the detection of at-risk patients and reveal disease severity. They represent objective and standardized criteria guiding therapy.

Keywords: Sars-Cov-2, CRP, LDH, D-dimer, PLT,

INTRODUCTION:

The COVID-19 disease is relatively new to the world, but in a short time, it has caused significant damage to both the health of the population and the economy worldwide. Global coronavirus disease 2019 (COVID-19) has posed major challenges to clinical laboratories, from initial diagnosis to patient monitoring and treatment.

For the accurate diagnosis and effective follow-up of the course of the disease in this huge number of patients, laboratory test biomarkers play a crucial role. Some routine laboratory markers reveal a range of changes in patients with COVID-19, among the most frequently observed are: increased levels of CRP, LDH, D-dimer neutrophilia with lymphopenia and decreased platelet count [2, 3, 4, 5]. Quantification of these and other laboratory parameters could significantly aid the detection of at-risk patients and reveal disease severity. Recently, some studies have reported that CRP levels can be used in the early diagnosis of pneumonia and that higher CRP values are associated with severe pneumonia [6, 7]. In a number of studies related to changes in clinical laboratory parameters in patients with COVID-19, it has been described that platelet counts are much lower in severe, critical and non-surviving patients compared to those with milder illness [8, 9, 10, 11].

There is evidence that neutrophilia, which is an expression of the cytokine storm and hyperinflammatory state, has a key role in the pathogenesis of COVID-19.

The cause of neutrophilia in patients with severe and advanced disease is a secondary bacterial infection. There is growing evidence that severe infection caused by the novel coronavirus that emerged in 2019 causes lymphopenia. In their study, Yang et al. [12] demonstrated lymphopenia in 80% of patients with severe COVID-19, while Chen et al. [13] demonstrated lymphopenia in 25% of patients with mild infection. Lymphopenia in severe cases of COVID-19 and non-survivors was also observed in the study by Henry et al. [14]. These data were also confirmed by Qin et al. [15]. Elevated neutrophil counts and decreased lymphocyte values in the differential blood count reflect an imbalance of the inflammatory response and may be considered a likely indicator of the severity of infectious diseases, such as sepsis and bacteremia [16].

Zeng F, et al. described that in severe cases of COVID-19 compared to milder cases, neutrophil values were significantly higher, and lymphocyte counts were low [17]. These studies show the association of neutrophilia in patients with a severe form of COVID-19.

LDH is a ubiquitous enzyme located on the cell membrane, which increases its plasma concentration during any type of cell destruction. Akdođan D, et al. found that in the early stages of COVID-19, LDH values were strongly associated with lung lesions, possibly reflecting disease severity [18]. In their study, Han Y, Zhang et al. summarized that LDH could be considered a powerful predictive factor for early recognition of lung injury of COVID-19 and correlates with disease severity [19]. One of the earliest tests to prove fibrin formation in the body is D-dimer (fibrinolysis in vivo starts at the same time as fibrin formation), its increase is an indicator of the formation and accumulation of fibrin, which speaks of thrombosis or risk of thrombosis. It increases in venous thrombosis, in pulmonary embolism, damage to the endothelium in diabetes and atherosclerosis.

Elevation of D-dimer has been reported to be one of the most common laboratory findings seen in COVID-19 patients requiring hospitalization [5, 20]. A major finding in the study by Zhang L et al. is that D-dimer values above 2.0 µg/mL in hospitalized patients with COVID-19 are an independent predictor of in-hospital death. This finding provides a well-established cut-off value for identifying patients with COVID-19 who have a poor prognosis [21].

PURPOSE:

The aim of our study is to present the changes in the values of CRP, LDH, D-Dimer, number of PLT, Ly and Neu at the time of admission to the hospital and at the end of hospitalization of patients with Sars-Cov-2.

MATERIALS AND METHODS:

Clinical laboratory results of 106 patients who underwent hospital treatment for COVID-19 at the “St. Ivan Rilski” St. Zagora, divided into two groups: The first group (Group I) is in the period November-December 2020, the second group (Group II) patients were hospitalized in April 2021.

The values of the following laboratory parameters were examined: CRP, LDH, D-Dimer, number of platelets, lymphocytes, granulocytes from the day of the patient’s admission to the hospital and from his discharge. Their de-

termination was performed with a Mindray biochemical analyzer BS 300 and 3- Diff hematology analyzer BC 3600. CRP was determined photometrically by measuring the change in optical density corresponding to the antigen-antibody reaction by the endpoint method at 340 nm. Reference limits up to 6 mg/l. D-Dimer was studied by an immunoenzymatic method with the participation of a fluorogenic substrate and enzyme-labeled monoclonal antibodies. Reference values - up to 0.5 mg/L. The catalytic activity of LDH was determined by measuring the decreasing absorbance at 340 nm – a kinetic test with the participation of NAD. Reference values of the method – 200-400 U/L.

For the statistical presentation of the results, the following were used: Descriptive evaluation methods and methods - descriptive analysis, quantitative analysis and graphical representations. Parametric and non-parametric tests for testing hypotheses - Student’s t-test for comparison of mean values, Chi-square test, Kolmogorov-Smirnov and Shapiro-Wilk methods for checking the normality of the distribution. A significance level of p<0.05 was adopted for all statistical analyses. SPSS version - SPSS for Windows 19.0 was used to process the survey data.

RESULTS AND DISCUSSION:

The first group of persons (**Group I**) covers the period November-December 2020, n= 57 Second group (**Group II**) patients were hospitalized in April 2021, n=49. Roughly, these were patients from the second and third waves of the pandemic, with the second wave being reported to be caused by the so-called “British” strain of COVID-19. The age of the individuals varies widely from 23 to 90 years, on average 60.62 ±12.797 years. The average age of men is 58.28 ±14.129 years, and for women, 64.64 ±8.919 years.

In 100% of the examined patients in the first group, CRP had high values during hospitalization, 14.8 times above the upper reference limit of 88.7 ± 63.132 mg/L. The data in the second group shows lower values, as 85.71% (n=42) of patients were admitted with elevated CRP levels - 65.0 mg/L ± 54.963, 10.8 times above the upper limit reference limit. Two times lower values were observed at the end of the hospital stay, with the CRP concentration in group I reaching average values of 42.8 mg/L ± 84.987 and in Group I 25.6 ± 36.390 mg/L. The relatively high proportion of patients with elevated CRP concentration was preserved. (Table 1.)

Table 1. Mean CRP values, SD and proportion of patients with elevated levels.

Group	CRP mg/L	SD	CRP > 6 mg/L
Group I at the TAH	88.7 mg/L	± 63.132	100.00% (n=57)
Group I at the end of hospitalization	42.8 mg / L	± 84.987	77.19% (n =44)
Group II at the TAH	65.0 mg/L	± 54.963	85.71 % (n=42)
Group II at the end of hospitalization	25.6 mg/L	± 36.390	61.22% (n=30)

LDH was increased in three of the groups in over 90% of patients (Group I and Group II at the TAH, Group I at the end of hospitalization). Group II at the end of hospitalization shows a slightly lower proportion of exam-

ined persons with increased values of LDH, 85.71% (n=42), but this group showed the highest levels of the enzyme, 802.33 ± 557.836 U/L. (Table 2.)

Table 2. Mean LDH values, SD and proportion of patients with elevated levels.

Group	LDH U/L	SD	LDH > 250 U/L
Group I at the TAH	648.84	± 260.133	96.49% (n=55)
Group I at the end of hospitalization	500.60	± 276.654	91.23% (n=52)
Group II at the TAH	560.71	± 251.405	97.96% (n=48)
Group II at the end of hospitalization	802.33	± 557.836	85.71% (n=42)

In their study, Poggiali E, et al. described that CRP and LDH could be considered a predictor of respiratory failure and be useful guide in patients who need respiratory monitoring and more intensive supportive therapies to avoid a poor prognosis [4].

Mei H, et al. conclude that thrombocytopenia and subsequent complications in patients with COVID-19 are common. The high mortality rate is also due to them. Cases of significant bleeding have been rarely reported in COVID-19 (22).

In our study, we found that the highest percentage of patients who developed thrombocytopenia were in Group II at the TAH, 26.53% (n=13). In the first wave in

Group I at the TAH, they were 19.30% (n=11). In both waves of the pandemic, at discharge, the percentage of individuals with low PLT values <140x10⁹/L was slightly lower in Group I at the end of hospitalization 14.04% (n=8), Group II at the end of hospitalization 20.41% (n=10). The average values of PLT are presented in Table.3.

Elevation of D-dimer is one of the most common laboratory findings observed in patients with COVID-19 requiring hospitalization. In the studied groups, we found significantly more patients with elevated values in both groups at discharge (Group I 49.12% and Group II 46.94%) Table 3. This points to the need for longer follow-up of D-dimer and PLT values after discharge of the patients.

Table 3. Mean D-dimer and PLT values, SD and proportion of patients with elevated levels.

Group	D-dimer	SD	D-dimer >0.5 mg/L	PLT (10 ⁹ /L)	SD	Thrombocytopenia PLT<140x10 ⁹ /L
Group I at the TAH	1,18	±2.142	36.84% (n=21)	222.12	± 85.578	19.30% (n=11)
Group I at the end of hospitalization	1,57	±2.469	49.12% (n=28)	303.16	± 144.420	14.04% (n=8)
Group II at the TAH	1,66	±4.571	28.57% (n=14)	174.14	± 56.360	26.53% (n=13)
Group II at the end of hospitalization	2,12	±4.612	46.94% (n=23)	269, 86	±149.781	20.41% (n=10)

Lymphopenia at admission has been demonstrated in numerous studies, with values varying widely. In our study, we found mean values of lymphocytes at hospitalization of Group I at 14.451% (±7.279) and slightly higher

in Group II in hospitalization at 17,880 (±7,407). A pronounced neutrophilia was observed during the hospitalization of both groups. Lymphopenia and neutrophilia persisted after the patients were discharged. (Table 4.)

Table 4. Ly and Neu values and SD in the different patient groups.

Group	Ly %	SD	Neu %	SD
Group I at the TAH	14.451	±7.279	77,793	±13.741
Group I at the end of hospitalization	17.044	±12.408	72,925	±17.686
Group II at the TAH	17,88	±7.407	73.280	±12.557
Group II at the end of hospitalization	16.137	±9.308	74.269	±14.966

CONCLUSIONS:

The findings in the present study, in accordance with data published by various authors, confirmed:

- Laboratory results provide guidance on disease severity and prognosis.
- When platelet and lymphocyte counts are lowest, LDH, CRP and D-Dimer values are highest.
- These and other laboratory biomarkers represent objective and standardized criteria to guide therapy.

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