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CONNECTION BETWEEN THROMBOCYTES VALUES AND ELEVATED D-DIMER AND LDH LEVELS IN PATIENTS WITH Sars-Cov-2

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Abstract: COVID-19 is an infection caused by the new coronavirus Sars-Cov-2. For the specific treatment of patients, it is important to determine the severity of the disease with the help of biomarkers when they are hospitalized. Many of them reveal a range of changes in patients with COVID-19. Among the most commonly observed changes are decreased thrombocytes count, increased D-dimer and LDH values. The aim of the present study is to present the changes in Thrombocytes (Thr), Lactatedehydrogenase (LDH) and D-Dimer values in hospitalized patients with Sars-Cov-2 and the relationship between them. For our research, we took the values from the clinical laboratory results of 106 hospitalized patients for the treatment of Covid-19 in the "St. Ivan Rilski" town of Zagora. Patients were divided into two subgroups depending on the period of their hospitalization. In both groups, the laboratory values of LDH, Thre, D-Dimer on the first day of admission to the hospital are presented. In the two groups of patients studied by us, we found a positive correlation between thrombocytes values and LDH values at admission: r=0.234, p<0.05. A greater number of patients developed thrombocytopenia during hospitalization in Group II 26.53% (n=13). A number of authors have reported that in COVID-19, LDH correlates with disease severity and can be considered a major predictor of lung injury in these patients. Elevation of LDH was observed in over 96% of patients in both groups. Thrombocyte count monitoring during hospitalization is important in the prognosis of patients with coronavirus disease. Thrombocytopenia, elevation of D-dimer, and the following complications in patients with COVID-19 are among the most common laboratory findings requiring hospitalization.

Keywords: *Sars-Cov-2, LDH, D-dimer, Thrombocytes.*
Field: Medical Sciences and Health

1. INTRODUCTION

COVID-19 is a disease caused by the novel coronavirus Sars-Cov-2 and causes severe acute respiratory syndrome in some patients and, not infrequently, death. A number of studies prove that in 80% of cases the disease is asymptomatic or mild, about 15% of those infected are patients with a severe form of COVID-19 requiring hospitalization. The proportion of critical patients requiring ventilation and life support procedures is 5% (Mollova, Valeva, Bekir & Uzunova, 2021); (Lippi & Plebani, 2020). For the specific treatment of patients, it is important to determine the severity of the disease using biomarkers that reveal many changes in patients with COVID-19, even at the time of their hospitalization. Clinical studies in this area have identified thrombocytopenia as an important feature of Sars-Cov-2 (Liu Y et al. 2020); (Wool & Miller 2021). Patients with mild symptoms have a slightly elevated platelet count (Thr), while thrombocytopenia is characteristic of more severe forms of COVID -19. The decreased platelet count is due to the onset of hypercoagulability, in which microthrombi are found in the lung parenchyma and the microcirculation of other parenchymal organs, a syndrome similar to the microvascular thromboses associated with DIC. The resulting complications are also due to these microthrombi. (Rohlfing, Rath, Geisler & Gawaz, 2021); (Thachil, 2020). Thrombocytopenia is found in over 50% of patients with severe Sars-Cov-2 and is an important indicator of poor prognosis (Kermali, Khalsa, Pillai, Ismail, & Harky, 2020); (Yang et al. 2020). Therefore, platelet monitoring during hospitalization may be important for the prognosis of Sars-Cov-2 patients (Liu Y et al. 2020).

During anaerobic glycolysis, the intracellular enzyme lactate dehydrogenase (LDH) catalyzes the oxidation of pyruvate to lactate (Komolafe, Pereira, Davidson, & Gurusamy, 2017). In the human body, the highest concentrations are in the lungs, muscles, kidneys and blood cells, heart and the liver. In a clinical setting, LDH is tested in a number of diseases. Elevated serum LDH values are associated with poor prognosis in inflammatory diseases and tumors.

LDH has been accepted as a marker of inflammation, which usually occurs in acute or chronic tissue damage. In their study, Poggialia et al found that during acute and severe lung injury and interstitial

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lung infections, LDH levels are increased, even though it is an enzyme found in many other organs and tissues (Poggialia et al. 2020). Despite the fact that LDH is an enzyme that originates in many organs, it is significantly increased in patients with lung damage. In their study, Akdogan D et al. (2021) found that LDH levels were strongly associated with lung lesions in early stage COVID-19, which the authors suggest likely reflects disease severity. In their study, Ferrari D et al. (2020) reported that LDH values are significantly higher in cases of tissue damage and that higher levels of the enzyme depend on the degree of inflammation (Ferrari, Motta, Strollo, Banfi & Locatelli 2020).

There is a lot of evidence that LDH is one of the biomarkers for assessing the severity of COVID-19. In 2020, in a study by Zhang et al. (2020) stated that high CRP and LDH values were found to be characteristic of severely ill patients with COVID-19.

A valuable laboratory indicator for diagnosing and monitoring a wide range of clinical conditions associated with the risk of thrombosis is the D-dimer (Tripodi, 2011). As the most common laboratory finding observed in hospitalized patients with Covid-19 is the elevation of D-Dimer. (Keykavousi et al, 2022); (Tripodi, 2011); (Wool & Miller, 2021).

D-Dimer is considered one of the earliest tests related to fibrin formation in the human organism (fibrinolysis in vivo starts simultaneously with fibrin formation). Its increased values signal the formation and deposition of fibrin, which leads to the risk of thrombosis. Venous thrombosis, pulmonary embolism, endothelial damage in diabetes and atherosclerosis are always associated with elevated D-dimer (Esmailian, Vakili, Nasr-Esfahani, Heydari, & Masoumi 2022).

In the studies of Wu C et al. (2020) and Naymagon et al. (2020) described that elevated D-dimer levels above 2.0 g/mL reliably predicted in-hospital mortality in patients with the infection. It is identified as a useful marker in establishing the diagnosis. These studies show that mortality in patients with COVID-19 is always accompanied by significantly elevated D-dimer values. Therefore, its determination can be one of the most valuable options for initial assessment.

Other authors found that D-dimer levels were significantly higher in a group of 94 patients infected with Sars-Co v-2 compared to a healthy control group (Han et al, 2020).

In their report, Naymagon et al. (2020) summarized that higher D-dimer levels at admission and trends toward elevation were associated with a significantly higher risk of mortality. They emphasize the need for further research to clarify whether the high D-dimers that are so common among patients with COVID-19 are the result of a propensity for thrombus formation and how D-dimers can be incorporated into diagnostic models in clinical decision making.

2. PURPOSE

In our study, we set out to analyze the changes in the values of Thr, LDH and D-Dimer, during hospitalization of patients with proven Sars-Cov-2 and establish the correlation between them.

3. MATERIALS AND METHODS

For our study, we used the clinical and laboratory results of 106 patients who underwent hospital treatment for Covid-9 at the St. Ivan Rilski Hospital in Zagora., divided into two groups. The first group (I group) includes patients admitted for hospital treatment in the months of November and December 2020. The second group (II group) was formed by patients with proven Sars-Cov-2 in 2021. April.

LDH, D-Dimer and Thr count levels were analyzed from the day the patient was admitted to the hospital.

Quantification of LDH, D-Dimer, Thr along with other laboratory parameters was performed in the clinical laboratory of the hospital. The 3-Diff BC 3600 hematology analyzer was used to determine Thr.

An immunoenzymatic method with enzyme labeled monoclonal antibodies and the participation of a fluorogenic substrate was used for the determination of D-Dimer. The reference interval when using the method - up to 0.5 mg/l. To determine the catalytic activity of LDH, the laboratory used a kinetic test, measuring the decrease in absorbance under optimal conditions and 340 nm in the presence of NAD. The permissible values of the method are in the range of 200 - 400 U/L.

The obtained data from the laboratory indicators were statistically processed using SPSS - SPSS for Windows 19.0.

4. RESULTS AND DISCUSSION

The data from clinical laboratory values of 106 hospitalized persons (men n = 67, women n = 39) were processed for two periods - November-December 2020, first group (Group I, n = 57), and patients hospitalized in April 2021 second group (Group II, n = 49). The mean age of the subjects in the study was 60.62 ±12.797.

In both groups, we found approximately the same proportion of persons with high LDH, and in Group I I the mean values were lower (560.71 U/L) compared to Group I (648.84 U/L). In the study we found that thrombocytopenia was characteristic of Group II 26.53% (n=13) than in Group I where they were 19.30% (n=11). Table 1. We found that patients requiring hospitalization showed D-dimer values >0.5 mg/l. Our study confirmed the findings of a number of other studies, finding significantly high levels of D-dimer related to promotion.

The findings in a number of other studies were also confirmed for a significantly high percentage of patients with elevated D-dimer values in both groups - Group I 36.84% (n=21) and Group II 28.57% (n=14).

Table 1. Laboratory biomarkers mean, SD, and percentage of patients with elevated levels

Group	LDH U/L (SD)	LDH > 250 U/L	Thr (10^9/l) (SD)	Thr <140x10 ^{9}/l	D-dimer	D-dimer >0.5 mg/l
Group I	648.84 (± 260.133)	96.49% (n=55)	222 . 12 (± 85.578)	19.30% (n=11)	1.18 25 (±2.142)	36.84% (n=21)
Group II	560.71 (± 251.405)	97.96% (n=48)	174.14 (± 56.360)	26.53% (n=13)	1.66 41 (±4.57)	28.57% (n=14)

As a breakdown product of anafibrin, D-dimer is one of the most commonly investigated coagulation tests in patients with COVID-19. It is very often used to determine the severity of infectious diseases and assess the risk of sepsis. In a retrospective study by Zhou et al. (2020), which included 191 patients, D-dimer values > 1 μg/ml at hospitalization was accepted as an independent risk factor for in-hospital death.

In a retrospective study, Liao et al. (2020), reported that dynamic monitoring of hematologic and coagulation parameters (Neu to Ly ratio, Thr count, D-dimer, and prothrombin time may provide a reliable and convenient method to classify and predict severity and outcomes in patients with COVID -19.

In their study, Durmus Kocak et al, summarized that laboratory findings during admission, such as Ly and Thr count was lower in patients who were admitted to the intensive care unit, while a marker of inflammation, such as D-dimer, was significantly higher.

Using Pearson's correlation coefficient, the relationship between Thr values was measured and D-dimer at admission in both groups studied by us. The linear correlation between the two variables is moderately positive (Group I) r =0. 107, p < 0.01, N=106. The effect size was large or larger than typical (Cohen, 1998) Figure 1.

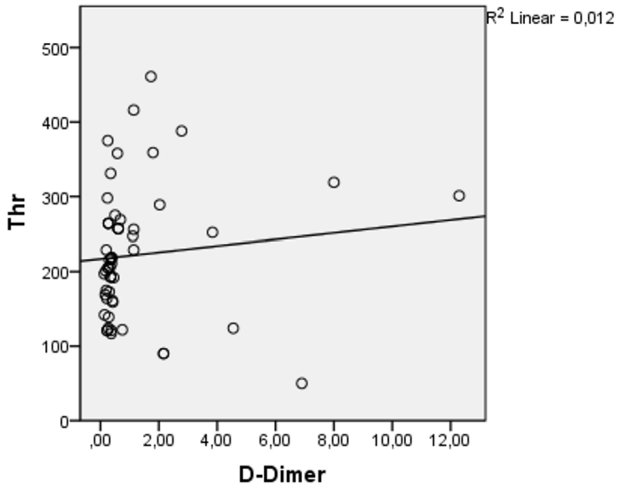

Fig.1. Correlation between Thr and D-dimer in hospitalization Group I

The linear correlation between the two variables Thr and D-dimer in Group II is positive r =0.380, p <0.01, N=106. The effect size was large or larger than typical (Cohen, 1998). Figure 2.

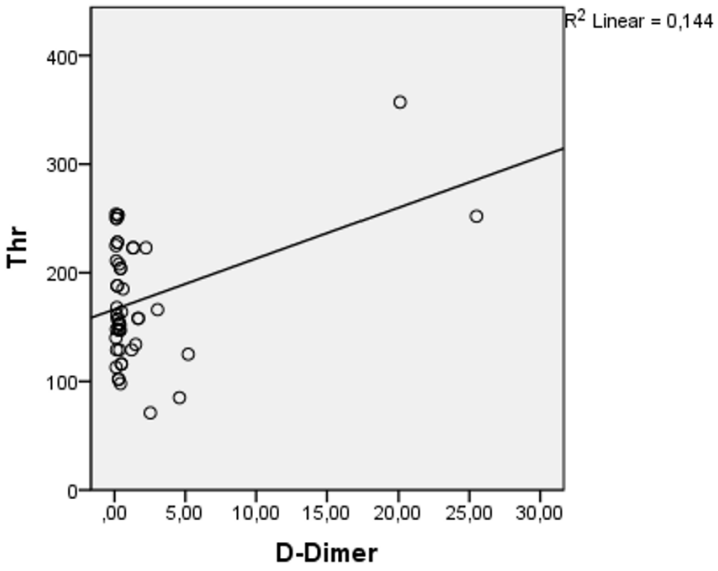

Fig. 2. Correlation between Thr and D-dimer in hospitalization Group II

In the study by Han et al. (2020) reported a strong correlation between LDH with lung injury and that LDH could be identified as a powerful predictor for early recognition of lung injury and severe cases of COVID-19. In our study, we found that LDH correlated positively with Thr values in hospitalization of patients with Sars-Cov-2 r =0.234, p <0.05, N =106. Figure 3.

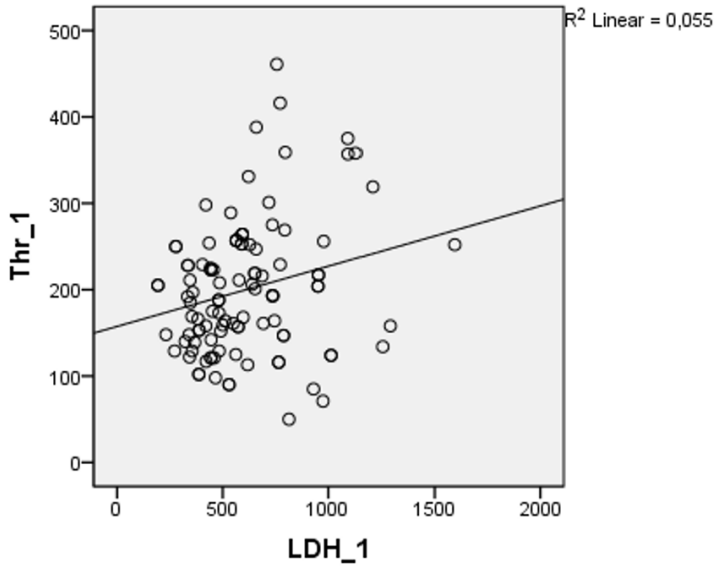

Fig.3. Relationship between LDH and Thr in Group I and Group II

All severe infectious diseases are associated with changes in the laboratory values of hemostasis, as well as with thrombosis and bleeding. There is a growing number of publications related to research on COVID-19 and its associated hemostatic changes. (Wool & Miller 2021).

5. CONCLUSIONS

Data published in various research studies on COVID-19 are consistent with our findings discussed in the study among 106 patients. Laboratory results can provide useful guidance on the severity of the test in patients with COVID-19 to help predict their response.

• The importance of platelet monitoring is explained by the fact that low values can be an indicator of the development of coagulopathy in patients with SARS-CoV-2.

• Thrombocytopenia in patients with COVID-19 may be associated with higher levels of LDH and D-Dimer. These associations between Thr, LDH, and D-Dimer have been observed in various clinical studies and may contribute to assessment of severity and prognosis.

• LDH, D-dimer, Thr and other laboratory biomarkers may be accepted as objective and standardized criteria to support treatment.

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