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REVIEW ARTICLE

The importance of laboratory parameters in predicting the severity of coronavirus disease-19 cases

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ABSTRACT

This literature review is aimed at exploring the significance of laboratory parameters in the follow-up of the coronavirus disease-19, which is the latest global biohazard for humanity. Laboratory parameters were classified under three main headings. These headings were hematological tests, inflammatory parameters and coagulation parameters. It has been determined that low lymphocyte count, which is one of the hematological tests, is a condition seen at every stage of the disease. High neutrophil counts are evident in worsening the course of the disease. The neutrophil/lymphocyte ratio increases with increasing disease severity. Low platelet levels may also be observed. It has been determined that high C-reactive protein (CRP) levels can be seen at every stage of the disease. In addition, as the prognosis of the illness worsened, C-reactive protein levels were found to increase more. Increased prothrombin time and high D-dimer values are evident in coagulation tests in patients with severe coronavirus disease-19. In addition, increased ferritin and procalcitonin levels are observed as the illness course worsens. As a result, lymphocytopenia and increased CRP levels come to the fore in the illness course. When the illness becomes more aggressive, prothrombin time, neutrophil/lymphocyte ratio, neutrophil count, D-dimer, ferritin and procalcitonin levels draw attention.

Keywords coagulation parameters, coronavirus, hematological tests, inflammatory parameters

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INTRODUCTION

World Health Organization (WHO) held an emergency meeting against coronaviruses due to the outbreaks of Severe Acute Respiratory Syndrome (SARS) that appeared in 2002 and Middle East respiratory syndrome (MERS) that appeared in 2012. A pneumonia epidemic of mysterious was declared in Wuhan, one of the most populated cities in China, at the last quarter of 2019.[1] The virus that caused this pneumonia epidemic is an newly

emerged virus belonging to the family Coronaviridae, possibly derived from a coronavirus such as SARS that can be found in bats and infects humans after mutations in the nucleocapsid N protein and spike glycoprotein (protein S).[2] The disease created by this virus was named coronavirus disease-2019 (COVID-19) by WHO. This zoonotic pathogen is considered the latest global biohazard to humans. The mortality rate of this virus is lower than that of MERS and SARS. However, the risk of transmission and spread of this virus is facilitated by a long incubation period of up to fourteen days.[3] According to the data of the WHO, as of August 1, 2022, 572239451 confirmed cases and 6390401 deaths due to coronavirus disease-2019 have been reported.[4]

COVID-2019 is a mysterious systemic and respiratory syndrome with clinical findings such as fever, shortness of breath and cough.[5] Real-time polymerase chain reaction (RT-PCR) is the most widely used method to diagnose COVID-19 disease and to determine the genetic information of the virus that causes this disease. This process include reverse transcription of the RNA genetic information of the virus into complementary DNA (cDNA) then by amplification of specific zone of the cDNA.[6] Based on clinical data, confirmed cases can be classified as severe, moderate, mild and critical cases. While approximately 5% of the cases are considered as critical cases, 14% are considered as severe cases.[7] The clinical status of COVID-19 patients, especially their peripheral oxygen saturation levels and accompanying comorbidities, largely determine the need for hospitalization in intensive care departments.[8]

Some of the coronavirus disease-2019 patients experience a very severe illness in the intensive care departments that requires ventilation and extracorporeal membrane oxygenation therapy.[9] Cases, who are at high risk of transmitting the virus and spreading the disease, increase occupancy rates in intensive care units. This situation poses a great difficulty in the hospitalization and treatment of patients in intensive care units.[8] Therefore, early recognition of serious cases is unconditionally necessary for timely triage of cases. Although peripheral oxygen saturation values and their concomitant comorbidities largely determine admission to intensive care units, various laboratory tests may facilitate assessment of illness severity. Considering this situation, the aim of our study is to investigate the importance of abnormal laboratory parameters observed in Coronavirus disease-19 patients in the course of the disease.

IMPORTANCE OF LABORATORY PARAMETERS

It is estimated that the efficiency of laboratory parameters in making whole clinical judgments is approximately 70%. These laboratory parameters constitute almost 40% to 94% of whole objective medical records. Un questionably, the correctness of laboratory parameters is necessary for the classification, identification, monitoring and cure of a disease.[10] The RT-PCR test, which is accepted as the most basic standard in the diagnostic of COVID-19 patients, is estimated to have a sensitivity of approximately 70% and a specificity of 95%.[6] In addition, the number of laboratory parameters requested per patient has increased dur-

ing the COVID-19 epidemic period. On the other hand, the rate of pre-analytical errors detected in the laboratory increased during this period.[11] However, pre-analytical error rates were found to be lower in studies conducted before this period.[12–14] In terms of laboratory parameters, some hematological, coagulation and inflammatory parameters are used for the classification, treatment and monitoring of COVID-19 cases according to the severity of the illness.

Hematological tests

Coronavirus disease-19 is a disease that has important effects on the hemostasis and hematopoietic system. Lymphopenia can be well evaluated as an important hematological parameter and is potentially predictic. The ratios of lymphocyte to neutrophil and platelet can help to evaluate the severity of the illness.[15]

Lymphocyte count

Data obtained from 15 published articles evaluating the hematological tests of COVID-19 cases consisting of severe and mild cases by publishing Pourbagheri-Sigaroodi et al. (2020) are summarized as follows. While lymphopenia is an obvious symptom in most patients, an increase in neutrophil count has been reported in some studies. In particular, the whole leukocyte count may differ among cases, which may mirror the predominance of neutrophilia or lymphopenia. Reduced lymphocyte count with mild thrombocytopenia are among the most widespread abnormal parameters in the complete blood count of Coronavirus disease-19 cases.[16] The lymphocyte count is a significant finding to straight distinguish between cases without and with severe case with COVID-19.[17,18] Given that most Coronavirus disease-19 deaths experience lymphopenia, it is legitimate to presume that lymphocyte count is a widely and rapid present hematological finding that can prognosticate illness severity in Coronavirus disease-19.[17,19]

Neutrophil count

In a study consisting of 94 cases by Yang et al. (2020), neutrophil and leukocyte count were also important higher in severe cases.[20] Consistent with these studies, Huang et al. (2020) stated that cases in the intensive care department experience neutrophilia, leukocytosis, and lymphopenia more frequently than patients not in the intensive care department.[21] Wang et al. (2020) also stated that intensive care department cases had more leukocyte and neutrophil count and fewer lymphocyte count than patients not in the intensive care unit.[22] Thrombocytopenia is incorporated with a worse course of illness and a higher risk of myocardial injury. Lymphopenia findings include a multi-factor mechanism including the cytopathic impact of the virus, interleukin 1-mediated pyro ptosis, induction of apoptosis, and putting pressure on the bone marrow with inflammatory cytokines.[6]

Neutrophil lymphocyte ratio

Liu et al. (2020) stated that severe patients with COVID-19 tend to have a higher neutrophil lymphocyte ratio.[23] In a study by Yang et al., they stated that a high neutrophil lymphocyte ratio can predict the prognosis of COVID-19.[20] The conclusion of a systematic review evaluating six studies showed that an increased neutrophil lymphocyte ratio may suggest a poor course of illness in Coronavirus disease-19 cases.[24] In addition, the incidence of serious disease was found to be 9.1% in cases with a neutrophil-lymphocyte ratio below 3.13, and 50% in cases with a neutrophil-lymphocyte ratio above 3.13 in cases of coronavirus disease-19 over the age of 50.[25]

In summary, in the hematological tests of COVID-19 patients, it is seen that the lymphocyte count decreases, the neutrophil count increases, and the neutrophil/lymphocyte ratio increases in parallel.

Inflammatory parameters

The main ordinary laboratory parameters demanted for Coronavirus disease-19 cases contain complete blood count, tests analyzing fibrinolysis and coagulation steps, and parameters related to inflammation.[16] It has been previously determined that signs of inflammation are extremely elevated in the acute stage. This rule also applies to the Coronavirus disease-19. Because the C-reactive protein (CRP), procalcitonin, ferritin and erythrocyte sedimentation rate increase in the blood serum samples of Coronavirus disease-19 patients, albeit at different levels.[16]

C-reactive protein

It has been found that changes in CRP levels in patients with Coronavirus disease-19 occur before computed tomography parameters. More significantly, CRP values have been related with illness development and have been shown to well perform in predictic illness severity at an early phase of Coronavirus disease-19.[26]

Procalcitonin

Although the diagnosis level of C-reactive protein is excellent to procalcitonin, procalcitonin may potentially have a greater level than CRP for predicting illness progression.[16] In a study conducted by grouping the Coronavirus disease-19 patients according to the severity of the illness, it was found that the median procalcitonin values were 4 times higher in severe cases compared to mild cases, and 8 times higher in critical cases compared to mild cases.[27]

Ferritin

Ruan et al. (2020), who investigated the clinical determinants of Coronavirus disease-19 mortality, stated that Coronavirus disease-19 mortality may result from virus-activated cytokine storm syndrome. C-reactive protein levels were found to be 126.6 mg/L in fatal patients versus 34.1 mg/L in discharged patients. In the same study, serum ferritin values were stated to be 1297 ng/mL in fatal patients versus 614 ng/mL in discharged patients.[17] In a study by Zhou et al. (2020), ferritin values have been stated to increase as the disease worsened throughout the clinical course.[28] In particular, it has been stated that hyperferritinemia can prompt macrophages that increase the subsequent inflammation, and the secretion of proinflammatory cytokines is largely liable for organ harm.[29] Although serum ferritin level increases during inflammation and a positive acute phase reactant, dying cells can also secrete ferritin. Therefore, it is reasonable to assume that higher ferritin values in severely affected Coronavirus disease-19 cases may indicate a greater degree of organ harm.[16]

In a study on the relation between inflammatory parameters and the severity of coronavirus disease-19, it was stated that C-reactive protein, procalcitonin and ferritin values of coronavirus cases hospitalized in the intensive care department were higher than both coronavirus patients hospitalized in the service and healthy individuals. In addition, it was stated that the CRP values of coronavirus patients hospitalized in the ward were higher in healthy individuals.[30] In a study investigating the effect of laboratory parameters of coronavirus patients on the duration of hospitalization, it was found that ferritin, CRP and procalcitonin levels were positively related with the day of hospitalization.[31] In a study conducted with coronavirus cases with type 2 diabetes mellitus, high levels of procalcitonin, CRP and ferritin were found.[32] Similar results were obtained in studies with different variants.[33]

In summary, CRP, ferritin and procalcitonin values in the inflammatory parameters of COVID-19 cases seem to be important in predicting the course of the disease.

Coagulation parameters

The predictive importance of laboratory parameters is not restricted to the precious data symbolized by simple complete blood count analysis. Increased D-dimer and prothrombin time levels may be an indicator of a worse course of illness.[21,34] Tang et al. (2020) stated that there is a important difference in the incidence of coagulopathy in terms of disseminated intravascular coagulation among Coronavirus disease-19 cases who died from the illness compared to those who survived.[34] Hypercoagulability is widespread in cases hospitalized for Coronavirus disease-19. Emphasizing the progressive increase in high D-dimer values, it was stated that the illness status was shown to worsen. Other coagulation parameters, such as severe thrombocytopenia and prolongation of prothrombin time show the possibility of disseminated intravascular coagulation.[15] The D-dimer median level in severe cases was higher than in non-severe cases. It has been emphasized that an increase in D-dimer level can effectively contribute to reflecting the progression of the illness towards an negative clinical chart.[35] Huang et al. (2020) recommend 0.4 μg/mL as a threshold value for D-

dimer to predict poor course of illness in COVID-19 patients.[21] In a study comparing 2 case groups with mild and severe Coronavirus disease-19, it was reported that the severe cases had significantly abnormal coagulation tests compared to the mild cases. In this study, it was reported that the prothrombin time, INR, and D-dimer levels were stated to be higher in the severe group.[36] It has been determined that prothrombin time and D-Dimer values are important in the detection of coagulopathy and thrombocytopenia in patients with PCR-positive follow-up in COVID-19 services.[37] It has been reported that D-dimer levels are very high, especially in coronavirus cases hospitalized in the intensive care department.[38]

In summary, D-Dimer values and prothrombin time in coagulation tests of COVID-19 cases seem to be important in those with severe disease.

CONCLUSION

Laboratory parameters in coronavirus patients show changes that occur as a result of hyper-activation of the coagulation and immune system, hyper-inflammation, and cytokine storm development. Monitoring lymphocyte counts and CRP values throughout the course of the disease can help assess the illness. The neutrophil/lymphocyte ratio, neutrophil counts, prothrombin time, D-dimer, procalcitonin and ferritin levels are considered to be important factors indicating a worse prognosis in the disease becoming more aggressive.

As a result, the values of some laboratory parameters vary in cases of coronavirus disease-19. The severity of coronavirus disease-19 cases can be estimated using these parameters.

ABBREVIATION

cDNA: complementary DNA, COVID-19: coronavirus disease-2019, CRP: C-reactive protein, MERS: middle east respiratory syndrome, RT-PCR: real-time polymerase chain reaction, SARS: severe acute respiratory syndrome, WHO: world health organization.

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DECLARATIONS

Authors' contributions

Conceptualization and methodology: NA. Data curation, investigation, software, drafting, and reviewing the manuscript: NA, FB, ED. Methodology: NA. Resources: NA and FB.

Conflict of interest

The authors declare no conflict of interest.

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Not applicable.

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