ORIGINAL ARTICLE

Laboratory Biomarkers in Assessing the Severity of COVID-19 at Referral Hospital in Indonesia

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ABSTRACT

INTRODUCTION: The COVID-19 pandemic is challenging due to its high transmissibility and mortality rates. COVID-19 patients can rapidly deteriorate, underscoring the need to identify lab biomarkers for high-risk categorization. This study aims to explore the role and correlation of various laboratory parameters, including Neutrophil-to-Lymphocyte Ratio (NLR), Ferritin, Prothrombin (PT), D-Dimer, C-reactive protein (CRP), and Procalcitonin (PCT), in distinguishing between severe and non-severe cases of COVID-19. **MATERIALS AND METHODS**: This retrospective cross-sectional study was carried out at Sulianti Saroso Infectious Disease Hospital in Jakarta with approval from the ethics committee. The inclusion criteria for subjects consist of patients confirmed with COVID-19 through PCR test results, adults aged over 18 years, and those with relevant laboratory parameter results. The exclusion criteria include pregnant patients, patients who arrive in a state of death on arrival (DOA), and patients with incomplete data. A sample of 1,598 adult COVID-19 patients was analysed. Laboratory data were extracted from electronic medical records (SIMINTRO) from March 2020 to December 2022. The significance of the means was assessed through the independent Mann-Whitney test, with a p-value <0.05 regarded as statistically significant. After constructing the ROC (receiver-operating characteristic) curve, threshold values were identified based on Youden's index (J). **RESULT**: There are differences in the severe and non-severe groups based on age, gender, transmission risk factors, symptoms, and comorbidities ($p<0.05$). Severe COVID-19 patients show markedly elevated levels of (NLR, Ferritin, Prothrombin, D-Dimer, CRP, and Procalcitonin) compared to non-severe ones, and the statistical cut-off values between severe and non-severe groups according to parameters (NLR, Ferritin, PT, D-Dimer, CRP, and PCT) are significant ($p<0.001$). **CONCLUSION**: Besides clinical findings, biochemical parameters are valuable predictors for assessing COVID-19 severity.

Keywords:
COVID-19, C-reactive protein, ferritin, procalcitonin, severity

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INTRODUCTION

The initial recorded instance of Coronavirus Disease 2019 (COVID-19), attributed to the newly discovered virus Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), was reported in December 2019.[1-3] Since that time, the virus has swiftly spread across almost every country, affecting millions of people worldwide.[3] Because of its rapid spread and a mortality rate exceeding 2%, in March 2020, COVID-19 was officially classified as a pandemic by the World Health Organization (WHO).[4,5] Although most coronavirus infections are generally mild and self-limiting, two specific coronaviruses have previously led to global pandemics: The Middle East Respiratory Syndrome (MERS) emerged in 2012 following the emergence of Severe Acute Respiratory Syndrome (SARS) in 2002.[5,6] As indicated by its name, this virus primarily targets the respiratory tract, potentially causing lung infections such as pneumonia and, in severe cases, Acute Respiratory Distress Syndrome (ARDS).[3]

The disease burden of COVID-19 is significant, with far-reaching impacts on public health and the global health system. According to reports from the World Health Organisation (WHO), COVID-19 has caused more than 6 million deaths worldwide and infected more

than 600 million people to date. This demonstrates the urgency to understand and effectively address this disease burden.[7] However, studies indicate that mortality rates are notably higher among individuals with underlying conditions, including hypertension, diabetes mellitus, pre-existing heart or kidney conditions, and obesity.[8,9] In addition to respiratory issues, conditions such as myositis, kidney failure, and disseminated intravascular coagulation (DIC) have also played a role in the mortality of COVID-19 patients.[10-12] Thus, the early detection and identification of COVID-19 patients who are severely affected is crucial for timely intervention and lowering mortality rates. At present, the severity of COVID-19 is assessed by the existence of lung infiltrates, declining oxygen saturation, and examining clinical symptoms since there are no validated biomarkers available to forecast the disease's severity.[13,14] However, reports indicate sudden exacerbation of symptoms and rapid deterioration in approximately 6.5% of COVID-19 patients, leading to death in about half of these cases.[15,16] Therefore, it is essential to identify serum biomarkers that can act as early indicators for predicting and managing potentially severe cases of COVID-19.

In severe cases of COVID-19, a condition called a cytokine storm, also known as cytokine release syndrome (CRS), often occurs.[17] This syndrome is mainly mediated by interleukin-6 (IL-6), which plays a role in increasing the morbidity and mortality of COVID-19 patients. The characteristics of CRS are high IL-6 levels, high fever, and hypoxic pneumonitis, which often requires mechanical ventilation. Therefore, an increase in the number of inflammatory cells is always accompanied by an increase in IL-6 levels. However, IL-6 testing is relatively expensive, and not all hospitals can do it, especially regional hospitals, so substitute markers are needed. Some haematological parameters are reported to be associated with disease severity.[18]

Therefore, this study aimed to delineate the epidemiology, laboratory findings, radiological manifestations in confirmed COVID-19 patients, clinical features, and explore the correlation of laboratory parameters (such as Neutrophil-to-Lymphocyte Ratio (NLR), Ferritin, Prothrombin Time (PT), D-Dimer, C-reactive protein (CRP), Procalcitonin (PCT)) between severe and non-severe COVID-19 patients. This study represents the first publication concerning biomarkers and COVID-19 severity from the Sulianti Saroso Infectious Disease Hospital. Because there's a lack of reliable treatments for COVID-19, it's crucial to pinpoint precise biomarkers that can identify, early on and before the condition worsens, those individuals most prone to severe or critical illness. This identification can pave the way for early interventions to prevent disease progression.

MATERIALS AND METHODS

Study design

This retrospective cross-sectional research was carried out at Sulianti Saroso Infectious Disease Hospital (SSIDH), a tertiary care facility for infectious diseases in Indonesia that was designated as a COVID-19 management center during the ongoing pandemic.

Sample/Participants

Selection of patients and sample size

In this study, the inclusion criteria for subjects consist of patients confirmed with COVID-19 through PCR test results, adults aged over 18 years, and those with relevant laboratory parameter results, including Ferritin, C-Reactive Protein (CRP), D-Dimer, Prothrombin Time (PT), Procalcitonin (PCT), and Neutrophil-to-Lymphocyte Ratio (NLR). The exclusion criteria include pregnant patients, patients who arrive in a state of death on arrival (DOA), and patients with incomplete data. This study did not apply a sample size based on statistical calculations because all COVID-19 patients fulfilling the inclusion and exclusion criteria were selected as the study sample (consecutive sampling). However, the sample in this study has met ensuring the number of events per parameter (EPP) of ≥10.[19] Data from 1,598 adult COVID-19 patients were examined using the Hospital's electronic medical records (SIMINTRO) database covering the period from March 2020 to December 2022.

Classification of COVID-19 patients

Based on the symptoms and criteria set by the Ministry of Health of the Republic of Indonesia, patients were divided into two categories. The first group included those with non-severe illness, encompassing mild cases (symptomatic but without signs of viral pneumonia or hypoxia) and moderate cases (pneumonia with SpO2 ≥94% on room air). The second group consisted of patients with severe illness, defined by SpO2 levels below 94% on room air, a PaO2/FiO2 ratio of less than 300 mmHg, a respiratory rate exceeding 30 breaths per minute, or lung infiltrates covering more than 50% of the lungs. Patients classified as having critical illness included those experiencing Acute Respiratory Distress Syndrome (ARDS), sepsis, septic shock, or multiple organ failure.

Sample and Data Collection

Patient records were reviewed to gather COVID-19 related data, including comorbid conditions, modes of infection, symptoms, complications, and patient outcomes (discharge or death). Hematological assessments, such as the Neutrophil-to-Lymphocyte Ratio (NLR), were performed on whole blood samples collected in EDTA tubes using the fully automated Beckman DXS Coulter-800 analyser.

Blood samples for D-dimer measurement were drawn into tubes containing 3.2% sodium citrate and analysed with a Stago-Compact Max automated analyser. Biochemical assessments were conducted on serum samples obtained from blood collected in clot activator tubes. C-reactive protein (CRP) and serum procalcitonin levels were measured using the COBAS-6000 automated system, while serum ferritin levels were determined with the Abbott Architect I-2000. Before testing, all analysers underwent calibration, and quality control checks were performed at two levels to ensure accuracy.

Instrument

In this study, we used a case report form for collecting secondary data.

Statistical analysis

All collected data were carefully verified for completeness and accuracy. Pre-coded data were entered into a computer and analysed using Statistical Package for Social Sciences (SPSS) version 25.0 (SPSS/PC; SPSS-25.0, Chicago, USA). Quantitative variables were summarized using medians and interquartile ranges (IQR), while qualitative variables were expressed as numbers and percentages. To compare qualitative variables, the chi-square test was utilized. The normality of quantitative data was assessed, and for non-normally distributed variables, comparisons were conducted using the nonparametric Mann-Whitney test. The receiver operating characteristic (ROC) curve was employed to assess the discriminatory power of clinical biomarkers in predicting disease severity. Additionally, Spearman's correlation test was performed to analyze the relationship between NLR, CRP, D-dimer, and serum ferritin levels. A p-value of ≤ 0.05 was considered statistically significant.

INSTITUTIONAL REVIEW BOARD (ETHIC COMMITTEE)

This study was carried out in compliance with the guidelines outlined in the Declaration of Helsinki and received approval from the Health Research Ethics Committee of Sulianti Saroso Infectious Disease Hospital (No. 26/XXXVIII.10/V/2023).

RESULT

Of the 315 COVID-19 patients with severe degrees. Both severe and non-severe COVID-19 patients were predominantly aged 18-59 years and male. In both groups, the majority had no history of travel-related risk factors or close contact exposure. Sociodemographic and transmission risk factors were significantly associated with severity ($p<0.05$). The most commonly occurring symptom is cough. Shortness of breath is mostly experienced by patients with severe illness. All of these symptoms were significantly associated ($p<0.05$) with severity, except fever, diarrhea, and nausea/vomiting ($p>0.05$). Hypertension and Diabetes mellitus comorbidities were significantly to the degree of COVID-19 pain ($p<0.001$). (Table 1).

Table I: Characteristics of the Study Patients (n=1598), According to Disease Severity

Variable	Severity			p-value	RR (95%CI)
	Severe (n=315; 19.7%)	Non-Severe (n=1283; 80.3%)	Total		
Age, mean (SD)	54.9 (12.9)	45.4 (15.2)			
≥ 60 years	123 (39.0%)	245 (19.1%)		0.000	2.71 (2.08-3.54)
18-59 years	192 (61.0%)	1038 (80.9%)			
Sex					
Male	194 (61.6%)	653 (50.9%)	847 (53.0%)	0.001	1.55 (1.20-1.99)
Female	121 (38.4%)	630 (49.1%)	751 (47.0%)		
Risk Factor					
Contact History					
Yes	42 (13.3%)	457 (35.6%)	499 (31.2%)	0.000	0.28 (0.19-0.39)
Travel History					
Yes	10 (3.2%)	109 (8.5%)		0.002	0.41 (0.22-0.74)
Symptoms					
Fever					
Yes	147 (46.7%)	572 (44.6%)	719 (45.0%)	0.547	1.07 (0.88-1.30)
Cough					
Yes	240 (76.2%)	1064 (82.9%)	1304 (81.6%)	0.007	0.72 (0.58-0.91)
Runny Nose					
Yes	17 (5.4%)	291 (22.7%)	308 (19.3%)	0.000	0.24 (0.15-0.38)
Sore Throat					
Yes	22 (7.0%)	158 (12.3%)	180 (11.3)	0.010	0.59 (0.40-0.89)
Headache					
Yes	34 (10.8%)	297 (23.1%)		0.000	0.46 (0.33-0.65)
Myalgia					
Yes	8 (2.5%)	78 (6.1%)		0.019	0.46 (0.24-0.89)
Diarrhoea					
Yes	11 (3.5%)	62 (4.8%)		0.384	0.76 (0.43-1.32)
Nausea&/or Vomiting					
Yes	71 (22.5%)	275 (21.4%)		0.726	1.05 (0.83-1.33)
Shortness of breath					
Yes	263 (83.5%)	417 (32.5%)		0.000	6.83 (5.16-9.04)
Underlying Illnesses					
Heart Disease					
Yes	1 (0.3%)	1 (0.1%)		0.355*	4.08 (0.26-65.45)
Hypertension					
Yes	18 (5.7%)	16 (1.2%)		0.000	4.80 (2.42-9.52)
Diabetes					
Yes	18 (5.7%)	14 (1.1%)		0.000	5.49 (2.70-11.17)
Asthma					
Yes	0 (0%)	1 (0,1%)		1.000	-
HIV/AIDS					
Yes	2 (0.6%)	2 (0.2%)		0.176*	4.09 (0.57-29.17)
Tuberculosis					
Yes	2 (0.6%)	1 (0.1%)		0.101	8.19 (0.74-90.63)
Obesity					
Yes	1 (0.3%)	0 (0%)		0.197*	-
Stroke					
Yes	2 (0.6%)	2 (0.2%)		0.176*	4.09 (0.57-29.17)

There was a statistically significant difference ($p<0.001$) between the two groups in terms of NLR, Ferritin, PT, D-Dimer, CRP, and PCT levels when compared according to the severity of the infection. Patients with severe infection had elevated values for these markers compared to those with non-severe infection (Table II).

Table II: Concentration of Haematological Markers in Study Patients (n=1598) Based on Disease Severity

Haematological markers (unit)	Severity of COVID-19		p-value
	Severe (n=315) (Median/Q1-Q3)	Non-severe (n=1283) (Median/Q1-Q3)	
NLR	9.44 (4.63-15.00)	2.75 (1.81-4.41)	0.000
Ferritin (ng/ml)	1494 (841.00-2001.00)	273 (103.00-733.00)	0.000
PT (seconds)	11.00 (10.40-12.00)	10.60 (10.00-11.20)	0.000
D-Dimer (ng/mL)	1.20 (0.70-3.40)	0.50 (0.30-0.90)	0.000
CRP (mg/L)	89.77 (41.77-155.77)	10.59 (4.00-41.47)	0.000
PCT (ng/mL)	0.20 (0.09-0.92)	0.04 (0.02-0.08)	0.000

Cut-off values for diagnosing COVID-19 were determined using Youden's index (J) and a Receiver-Operating Characteristic Curve (ROC). The area under the curve (AUC) was calculated. ROC analysis was used to further evaluate the statistically significant differences between the severe and non-severe groups for measures such NLR, Ferritin, PT, D-Dimer, CRP, and PCT. In connection with the findings from the ROC analyses, Table III and Figure 1 demonstrated the observations that have been made about patients with severe COVID-19 infection in this study.

Table III: Suggested threshold values for key markers in predicting severe cases of Coronavirus infection

Parameters	AUC*	95% CI	p-value	Recommended cut off	Sensitivity	Specificity
NLR	0.834	0.81-0.86	<0.001	4.62	0.756	0.776
Ferritin	0.825	0.80-0.85	<0.001	582.50	0.857	0.698
PT	0.613	0.58-0.65	<0.001	10.85	0.610	0.604
D-Dimer	0.755	0.73-0.79	<0.001	0.750	0.717	0.680
CRP	0.824	0.80-0.85	<0.001	37.22	0.806	0.732
PCT	0.816	0.79-0.84	<0.001	0.085	0.759	0.755

*Area Under the ROC (full term) curve

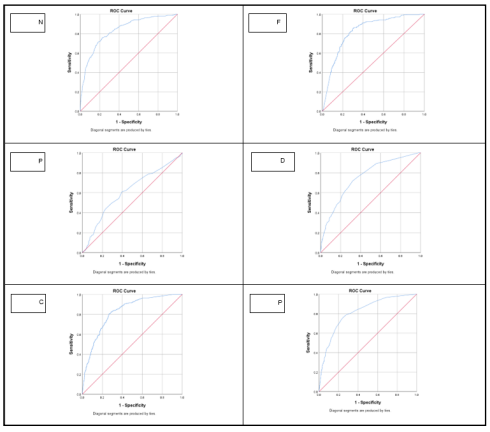

Figure 1: ROC (full term) for key markers in predicting severe cases of COVID-19

DISCUSSION

Male patients and individuals aged 50 years or older are at a greater risk of experiencing severe COVID-19. Additionally, comorbidities and clinical symptoms play

a crucial role in determining disease severity and prognosis. Our study found that men are more susceptible to COVID-19 infection and are more likely to develop severe conditions compared to women (OR=2.41, p<0.00001). Similar results have been reported in previous studies.[20,21] Research from Spain suggests that men may be more vulnerable due to a lack of caution regarding the risks of the pandemic. Another study from Spain also indicated that severity and case fatality rates (CFR) are higher among men and older individuals.[22] Furthermore, women appear to have greater resistance to the virus, which may be linked to female sex hormones, whereas men exhibit lower resistance due to the higher expression of ACE2 receptors, which facilitate viral entry.[23]

The main clinical symptoms are fever (temperature >38℃), cough, and difficulty breathing. ARDS, septic shock, metabolic acidosis, and haemorrhage are found in severe cases with rapid and progressive worsening.[24] More than 40% of fevers in COVID-19 patients have peak temperatures between 38.1-39°C, while 34% have fevers over 39°C.[17] The main clinical symptoms described by the Indonesian Lung Doctors Association (PDPI) are in line with the research journal report of Huang et al. (2020), by defines mild symptoms. According to the journal, mild symptoms in patients with Coronavirus Disease 2019 (COVID-19) are defined as patients with uncomplicated acute upper respiratory tract infections, which can be accompanied by fever, fatigue, cough (with or without sputum, anorexia, malaise, throat pain, nasal congestion, or headache.[25]

Comorbid diseases are health conditions that already exist before a person is infected with COVID-19, such as diabetes, hypertension, heart disease, obesity, chronic lung disease, and cancer.[26,27] The relationship between comorbid diseases and COVID-19 severity is significant, as comorbidities can worsen the body's immune response[27,28] and increase the risk of complications.[26,29] Comorbid diseases worsen COVID-19 infection by various mechanisms, such as weakening the immune system, increasing inflammation, and aggravating the work of vital organs. Therefore, people with comorbid diseases are advised to be more vigilant, implement strict health protocols, and get complete vaccinations to reduce the risk of severity.

Ferritin is a protein in the body that binds iron. According to Zhou et al. (2020), patients with severe COVID-19 exhibited elevated levels of hepcidin and serum ferritin compared to other groups [30]. Iron homeostasis is closely linked to the development of severe COVID-19. Its assessment is both specific and sensitive in predicting disease severity at an early stage in COVID-19 patients. In these patients, cytokine storm syndrome is driven by pro-inflammatory cytokines, leading to acute lung injury and multiorgan failure [31,32]. Increased serum ferritin needs to be observed in COVID-19 patients. Patients with COVID-19 may experience increased ferritin levels due to the inflammatory process. Hyperferritinaemia serves as a parameter for acute phase reactions, aiding clinicians in evaluating therapeutic responses. Meanwhile, recent studies indicate that elevated ferritin levels are not only observed during acute phase reactions but may also contribute significantly to inflammation, particularly in the progression of cytokine storms.[33]

The study conducted by Bozkurt et al. l showed that ferritin levels were the only significant predictor of COVID-19 disease severity (p = 0.004), with the results of ROC curve analysis obtained an AUC of 88%. [34,35] The study of Ahmed et al. (2020) showed a statistically significant difference in ferritin in the two severity categories.[36] Binary logistic regression showed ferritin to be an independent predictor of all causes of death completed with an AUC value of 69% on the ROC chart analysis. Research by Rajanna et al. (2020) shows that ferritin correlates with clinical outcomes. Based on ROC analysis obtained an AUC value of 80.08% with a cut-off point of 352 ng/ml, with a specificity and sensitivity of 76.32% and 74.6% respectively.

Ferritin is a protein found within cells that functions as an iron storage unit and plays a crucial role in various inflammatory conditions, including infections, cancer, and neurodegenerative diseases. As a characteristic of "hyperferritinaemia syndrome," elevated circulating ferritin levels are associated with four severe conditions:

macrophage activation syndrome (MAS), adult-onset Still's disease (AOSD), catastrophic antiphospholipid syndrome (CAPS), and septic shock. Several studies have indicated that ferritin serves as an independent risk factor for disease severity in COVID-19 patients.[37]

C-reactive protein (CRP) is an acute protein synthesized in the liver in response to the cytokines IL-1 and IL-6 and inflamed damaged tissue. CRP can be detected in blood, CSF, synovial, amniotic, and pleural fluid; its level increases 12 hours after inflammation and will peak at 2-3 days. The greater the stimulus, the longer CRP will persist, and once the inflammatory stimulus is removed, CRP levels will fall rapidly.[38] CRP serves as a marker of systemic inflammatory response by directly attaching to microorganisms as an opsonin, aiding the complement system, stimulating neutrophil activity, preventing platelet aggregation, facilitating the removal of necrotic tissue, and activating natural killer cells.[39]

Elevated D-dimer levels in COVID-19 can rapidly identify disease severity, pulmonary complications, and the risk of venous thromboembolism in pro-thrombotic states. This can help risk stratification and therapy selection to reduce COVID-19 morbidity and mortality. COVID-19 patients admitted to the ICU showed significantly elevated D-dimer levels. Special attention should be given to venous thromboembolism (VTE), particularly in severe cases, as these patients are often bedridden and have impaired coagulation function. A rapid decline in their condition was observed, accompanied by a notable increase in D-dimer levels. Especially if the patient presents with clinical symptoms such as rapid hypotension, sudden exacerbation of oxygenation, dyspnoea, post-DVT pulmonary embolism should be considered and treated immediately. Besides being associated with thrombosis and pulmonary embolism, D-dimer levels can also indicate the progression of severe viral infections.[40]

Elevated D-dimer is often found in severe COVID-19 patients and is a predictor of ARDS, the need for intensive care unit treatment, and death. The study by Zhou et al. showed that elevated D-dimer >1.0 µl/mL was the strongest predictor of mortality in COVID-19 patients.[41] The study by Cui et al. found that a D-dimer level exceeding 1.5 µg/mL served as a predictor of venous thromboembolism in COVID-19 patients, demonstrating a sensitivity of 85% and a specificity of 88.5%.

Research 55 found that D-dimer levels exceeding the cutoff (>788.5 ng/mL) are strongly linked to the progression and severity of COVID-19 infection. The risk of severe COVID-19 infection was more than five times higher, both before and after taking into account the influential factors of age and comorbid DM. D-dimer levels above the cut-off can predict the severity of COVID-19 infection with moderate accuracy.[42]

Prothrombin time (PT) is one of the frequently used coagulation parameters. Several studies have reported associations between PT and the severity of COVID-19. Study 56 in its review systematics reported that PT was higher in the severe degree group compared to the mild degree ($p<0.05$).[43] In the ICU and non-ICU groups, PT was also found to be higher in the ICU group than in the non-ICU group. These results are also supported by research, which states that prolongation of PT is an early prognostic indicator of severe COVID-19 events that require ICU treatment.[44] The study also compared survival rates between groups of patients with normal PT and prolonged PT.[12]

The presence of inflammatory indications in COVID-19 patients can be known using the PCT examination.[45] Patients with COVID-19 are always accompanied by a bacterial infection. In COVID-19 patients, PCT examination can help distinguish between severe bacterial pneumonia and mild viral pneumonia. However, the PCT parameter has several disadvantages, namely the high cost of the examination and the long examination time, so it is not widely available in health facilities in Indonesia[46]. High PCT levels suggest that COVID-19 patients with severe symptoms may develop bacterial superinfections that contribute to complications in the clinical picture.

While the initial PCT level can aid in assessing disease severity, it is not always a dependable prognostic marker.

Pre-existing comorbidities, such as CKD and congestive heart failure, can influence PCT levels, potentially causing them to be elevated from the start. However, when interpreted within the clinical context, PCT remains a highly valuable source of information.[47]

The neutrophil-lymphocyte ratio reflects the balance between distinct yet complementary immune pathways, combining the role of neutrophils in non-specific inflammatory responses with lymphopenia, which indicates severe physiological stress and weakened health. Therefore, this ratio represents two crucial immune mechanisms and serves as a predictive marker rather than just an isolated parameter.

In severe systemic inflammation, the immune system responds with an increased neutrophil-lymphocyte ratio. The rise in the neutrophil-lymphocyte ratio (NLR) results from direct or indirect stimulation of the bone marrow, leading to an increased number of neutrophils in the bloodstream.[48] The rise in neutrophil levels is driven by proinflammatory cytokines like IL-6, IL-1, and TNF-α, which are released by macrophages, while the reduction in lymphocyte count is due to elevated secretion of glucocorticoid hormones that inhibit lymphocyte production.[49]

COVID-19 is a pathological infection that attacks the respiratory tract, in some cases patients admitted to the ICU are accompanied by sepsis. An increase in NLR can be used as a warning sign for early signs of severe or worsening COVID-19 symptoms and as an independent prognosis in COVID-19 patients. Evaluating the neutrophil -lymphocyte ratio can enhance the assessment of COVID -19 patients. Therefore, incorporating this ratio along with age considerations is recommended for prognosis determination, assessing disease severity based on clinical symptoms, and guiding appropriate treatment for COVID-19 patients.[50]

The limitation of this study is that no analysis was performed on other biomarkers. For example, IL-6 testing is relatively expensive and not all hospitals, especially regional hospitals, can perform it, making the need for an alternative marker essential. Several haematological parameters have been reported to be associated with the severity of the disease.

CONCLUSION

This study highlights the significant role and correlation of various laboratory parameters, including Neutrophil-to -Lymphocyte Ratio (NLR), Ferritin, Prothrombin (PT), D -Dimer, C-Reactive Protein (CRP), and Procalcitonin (PCT), in distinguishing between severe and non-severe cases of COVID-19. Findings indicate that severe cases, particularly among elderly males, exhibit markedly elevated levels of these biomarkers, which are associated with a higher risk of cytokine storm and complications. Specifically, increased D-dimer levels serve as a critical indicator of lung tissue damage, reinforcing the importance of these biochemical parameters as valuable predictors for assessing the severity of COVID-19 and guiding clinical management.

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CONFLICT OF INTEREST

The author states that no conflicts of interest exist.

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AUTHOR CONTRIBUTIONS

Conceptualization was contributed by H, DWT, and FM; Design was carried out by ADW, SM, MLT, and DWT; Supervision was provided by MLT; Data collection was conducted by KW, R, and TZP; Data analysis was performed by SM; Literature search was conducted by ADW, FM, SM, and NM; Manuscript writing was carried out by H, DWT, ADW, and SM. All authors have read and agreed to the published version of the manuscript.

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