



The Role of Critical Laboratory Parameters to Determine the Severity and Prognosis of COVID-19: Systematic Review

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ABSTRACT

Introduction: Few studies have addressed the diagnostic and prognostic value of abnormal laboratory findings in COVID-19 patients. Objective: To identify and assess published studies on the role of laboratory parameters to determine the severity of COVID-19 patients. **Method:** Systematic review of articles identified from NCBI, Pubmed, BMC, and Elsevier from 2020-2022. **Results:** Laboratory parameters: complete blood count, serum electrolyte, renal function, liver function, pancreatic enzymes, D-dimer, inflammatory cytokines, and C-reactive protein have a diagnostic and prognostic value in determining the severity of COVID-19. **Conclusion:** Laboratory parameters have functional prognostic value in determining COVID-19 severity.

Keywords: COVID-19, prognostic value

ABSTRAK

Pendahuluan: Beberapa penelitian telah membahas nilai diagnostik dan prognostik dari temuan laboratorium abnormal pada pasien COVID-19. **Tujuan:** Mengidentifikasi peranan parameter laboratorium dalam menentukan keparahan pasien COVID-19. **Metode:** Review sistematis atas artikel berasal dari NCBI, Pubmed, BMC, Elsevier tahun 2020-2022. **Hasil:** Parameter laboratorium darah lengkap, elektrolit serum, fungsi ginjal, hati, pankreas, *D-dimer*, sitokin inflamasi, dan *C-reactive protein* memiliki nilai diagnosis dan prognosis pasien COVID-19. **Simpulan:** Parameter laboratorium berperan dalam menentukan keparahan pasien COVID-19. **Amanda Yuanita Kusdjianto. Peran Nilai Laboratorium dalam Penentuan Prognosis COVID-19: Tinjauan Sistematis**

Kata kunci: COVID-19, nilai prognosis



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INTRODUCTION

COVID-19 disease has become an international pandemic since its first report in 2019 in Wuhan, China.¹ COVID-19 patient presents clinical symptoms such as dry cough, difficulty breathing, and fever.² Some cases progress to a severe condition requiring specialized management at intensive care units (ICU).² According to the WHO's data, COVID-19 has already spread worldwide, with over 544,324,069 diagnosed cases in more than 210 different countries, causing 6,332,963

deaths as of July 1, 2022.³

The main routine examination usually requested for COVID-19 patients are complete blood count (CBC), coagulation and fibrinolysis cascades (PT, aPTT, and D-dimers), and inflammation-related parameters (ESR, CRP, ferritin, and procalcitonin).⁵ Laboratory studies have found some hematological and other abnormalities.¹ Some studies included laboratory parameters in scoring the risk factors for severe COVID-19.²

Few studies have addressed the diagnostic and prognostic value of abnormal laboratory findings in COVID-19 patients.⁴

OBJECTIVE

To identify and assess the results of published studies on the role of laboratory parameters in determining the severity of COVID-19.

METHOD

This systematic review study used PRISMA (*Preferred Reporting Items for Systematic reviews*

Table 1. PRISMA table

P (Patient)	I (Intervention)	C (Comparison)	O (Outcome)
COVID-19 patients, man or woman in all age	Laboratory parameters are used to determine severity of COVID-19.	The role of laboratory parameters in determining prognosis and severity of COVID-19 are compared to other findings such as clinical and imaging findings.	Laboratory parameters as one of the criteria for prognosis and for determining the severity of COVID-19 in routine practice.

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and Meta-Analyses) protocol. A systematic survey was done from May 2022 - June 2022 through some credible databases: NCBI, Pubmed, Elsevier, and BMC, using search terms: COVID-19, severe COVID-19, laboratory, criteria, prognostic, and diagnostic.

INCLUSION CRITERIA

Journals related to the role of laboratory parameters in prognosis and determining severity of COVID-19 patients

EXCLUSION CRITERIA

Articles reviews, meta-analyses, dan editorial journals are excluded from this study because those studies do not have results to be analyzed.

DATA EXTRACTION

Data extractions related to several journals or studies are made by using the standardized table that the author creates. The tables are made to be filled out in this order: (1) Main

author's name and year of publication; (2) Objective; (3) Methods; (4) Results; and (5) Conclusion.

RESULTS

Below are the results of several journals:

DISCUSSION

Petersen and Jhala used laboratory parameters such as D-Dimer (>1 mg/L), C-reactive protein (>10 mg/dL), lactate dehydrogenase (>245

Table 2. The role of several laboratory markings in determining the severity and prognosis of COVID-19 patients

Reference	Objective	Method	Results	Conclusion
Petersen and Jhalla, 2022	To analyse a proposed new scoring system JRSS (Jhalla Risk Scoring System) which include laboratory parameters to assess the severity of COVID-19 risk.	Patients were chosen from a retrospective review of all SARS-CoV-2 reverse transcriptase-polymerase chain reaction (RT-PCR) tests collected and performed at the regional Veterans Administration Medical Center (VAMC) serving the Philadelphia and surrounding areas from March 17th, 2020 to May 20th, 2020. As this study was for prognosis after infection with SARS-CoV-2, only positive test results were considered. They were assessed based on clinical characteristic and laboratory findings, including D-Dimer (>1 mg/L), C-reactive protein (>10 mg/dL), lactate dehydrogenase (>245 U/L), troponin (>2 times the upper limit of normal), ferritin (>500 ng/mL), creatine phosphokinase (>2x the upper limit of normal), and the absolute lymphocyte count (<800/microliter). Laboratory addendum of additional points based on the laboratory parameters would be added for those with a score less than 7. Points to be added would range from 1 point (1 laboratory parameter exceeded set limit), 2 points (2 or 3 laboratory parameters exceeded set limits), or 3 points (4 or more laboratory parameters exceeded set limits).	The JRSS identified a subset of patients who may be at higher risk of requiring hospitalization. Considering both the initial scoring and the laboratory addendum, 74 potentially higher risk patients (with a score >7) had been identified. The odds ratio for an elevated score, calculated from the above data, is 7.15 with a 95% confidence interval ranging from 3.63 to 14.08; this indicates a statistically significant association between a score of >7 and requirement for hospitalization or continued medical monitoring. The JRSS with laboratory addendum was also successful in predicting death, requirement for intubation, and requirement to be admitted to an ICU (statistically significant).	This study found that the JRSS, which assessed points based on age, ethnicity, pre-existing conditions, smoking habit, predictive value in determining which patients may be at elevated risk of hospitalization. The addendum of laboratory findings strengthen the predictive value of this scoring system.
Karimi, et al. 2021	To investigate the importance of clinical symptoms, initial vital signs, laboratory findings, and chest CT-Scan findings among patients with negative and positive rRT-PCR results.	This research was a case-control study that was performed in two hospitals in Alborz Province of Iran. A total of 164 patients participated in this study from March 5 to April 5, 2020. The study divided the patients into two groups: 111 rRT-PCR positive (67.6%) and 53 rRT-PCR negative patients (32.4%). The patients were evaluated for symptoms, initial vital signs, comorbidity, clinical and laboratory findings (CBC, biochemistry parameters, inflammation markers) and date of symptoms' onset before admission and CT-Scan was also performed at the day of submission.	Statistical analysis of initial vital signs showed that clinical presentation which are R.R., Temp, SBP, and DBP were similar between positive and negative rRT-PCR groups. The two groups (RT-PCR positive and negative) had significant similarities concerning comorbidities, and only hyperlipidemia was significantly higher in the positive rRT-PCR group. In the multivariate model, all variables with a p-value less than 0.1 in the univariate model were included in the model. In the MLR model, among all clinical characteristics and laboratory findings only presence of cough symptom (OR: 2.74; 95% CI: 1.11–6.8; p-value: 0.02) and increasing Hb (OR: 1.26; 95% CI: 1.02–1.57; p-value:0.03) was associated with rRT-PCR positivity.	This study concluded that the decision on COVID-19 patients should not exclusively depend on rRT-PCR positivity during the pandemic. Clinical manifestations, laboratory findings, and positive C.T. results play a critical role in clinicians' decisions, especially in countries with a high prevalence of COVID-19 with lower medical facilities.
Darmadi, et al. 2022	To explore the clinical and inflammatory parameters of severe and critically ill COVID-19 patients in the intensive care unit (ICU).	This study is a cross-sectional study was conducted in all COVID-19 cases (confirmed by the RT-PCR test) admitted to the ICU of Mitra Medica General Hospital Medan, Indonesia, between May and June 2021. Inclusion criteria were all subjects classified as severe COVID-19 according to the World Health Organisation guidelines. Demographic data, clinical history, and vaccination status of patients were collected from their medical records, including COVID-19 vaccination status. BMI data were calculated from the patient's weight and height. Laboratory parameters included in this study were haematologic parameters (haemoglobin, leukocytes, thrombocytes, neutrophils, lymphocytes, monocytes), serum electrolyte (sodium, potassium, chloride, calcium), renal function (urea, creatinine), liver function [aspartate transaminase (AST); alanine transaminase (ALT)], pancreatic enzymes (amylase, lipase), D-dimer, inflammatory cytokines (IFN-gamma, TNF-alpha, IL-6, IL-10, MCP-1), and C-reactive protein (CRP).	The most frequent comorbidities found among the subjects (80 subjects was included in this study) were obesity (36.35%) and diabetes (22.5%). Only 13.75% of subjects were vaccinated. Laboratory results indicated leucocytosis and neutrophilia. The mean inflammatory findings (IL-6, IL-10, TNF-alpha, IFN-gamma, MCP-1), D-dimer, CRP, and lipase increased. Lipase, IL-6, and MCP-1 levels were significantly higher (p=0.019, <0.0001, and 0.03, respectively) in the non-vaccinated group.	This study concluded that most patients with severe COVID-19 have comorbidities, non-vaccinated, and had elevated inflammatory markers.



U/L), troponin (>2 times the upper limit of normal), ferritin (>500 ng/mL), creatine phosphokinase (>2x the upper limit of normal), and the absolute lymphocyte count (<800/microliter) in a study to analyze risk scoring system for the severity of COVID-19 patients.² This scoring system, called JRSS, identified a subset of patients at higher risk of requiring hospitalization. Considering the initial scoring and the laboratory addenda, 74 potentially higher-risk patients (with a score > 7) were identified. The odds ratio for an elevated score, calculated from the above data, is 7.15, with a 95% confidence interval ranging from 3.63 to 14.08; this indicates a statistically significant association between a score of >7 and the requirement for hospitalization or continued medical monitoring. The JRSS with laboratory addendum also successfully predicted death, the requirement for intubation, and the requirement to be admitted to an ICU (statistically significant). Laboratory findings added a helpful criterion in determining severity and prognostic value.

Another study by Karimi, *et al*, showed that positive criteria for COVID-19 should not rely only on the RT-PCR test.⁴ The patients were also evaluated for symptoms, initial vital signs, comorbidity, and clinical and laboratory findings (CBC, biochemistry parameters, and inflammatory markers). Clinical manifestations and laboratory findings play a critical role in clinicians' decisions, especially in countries with a high prevalence of COVID-19 with lower medical facilities such as the use of CT-scan.

A study conducted by Darmadi, *et al*, stated that most severe COVID-19 patients have comorbidities, are non-vaccinated, and had elevated inflammatory markers.⁶ Laboratory parameters included in this study were haematologic parameters (hemoglobin, leukocytes, thrombocytes, neutrophils, lymphocytes, monocytes), serum electrolyte (sodium, potassium, chloride, calcium), renal function (urea, creatinine), liver function [aspartate transaminase (AST); alanine transaminase (ALT)], pancreatic enzymes (amylase, lipase), D-dimer, inflammatory cytokines (IFN-gamma, TNF-alpha, IL-6, IL-10, MCP-1), and C-reactive protein (CRP). Laboratory results indicated leucocytosis and neutrophilia. The mean inflammatory findings (IL-6, IL-10, TNF-alpha, IFN-gamma, MCP-1),

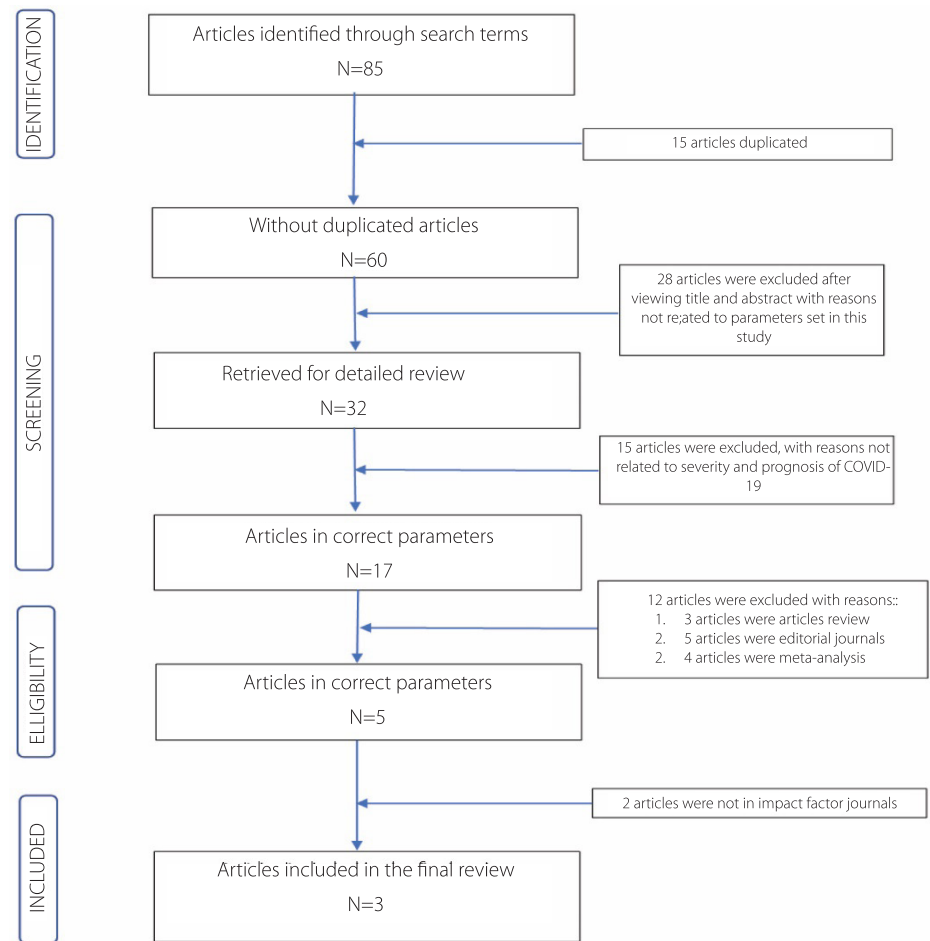


Figure. Flow chart of articles selection

D-dimer, CRP, and lipase increased. Lipase, IL-6, and MCP-1 levels were significantly higher.⁶

Clinicians can use laboratory parameters to evaluate the functional activity of the organs, which can be impaired by the virus' ability to damage several vital organs. These parameters can be the markers clinicians use to make crucial decisions. With so many laboratory parameters evaluated in many studies, it can be concluded that the worse the laboratory results, the worse the patients' conditions are. Those laboratory parameters, as stated in a study conducted by Darmadi, *et al*, are used in daily practice to stratify the risk of morbidity and mortality in COVID-19 patients at the time and during the time of hospitalization, especially to detect cytokine storms in patients with COVID-19.⁶

CONCLUSION

Severe COVID-19 cases were associated with the above cut-off value of laboratory parameters. Laboratory findings have

functional prognostic value to determine the severity, the need for hospitalization, and the need for ICU. They were haematologic parameters/complete blood count (hemoglobin, leukocytes, thrombocytes, neutrophils, lymphocytes, monocytes), serum electrolyte (sodium, potassium, chloride, calcium), renal function (urea, creatinine), liver function [aspartate transaminase (AST); alanine transaminase (ALT)], pancreatic enzymes (amylase, lipase), D-dimer, inflammatory cytokines (IFN-gamma, TNF-alpha, IL-6, IL-10, MCP-1), and C-reactive protein (CRP). It can be concluded that the worse the laboratory results, the worse the patients' conditions.



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