

Meta-Analysis

Role of Inflammatory Markers in Severity, ICU Admission, and Mortality in COVID-19: A Systematic Review and Metaanalysis of 79,934 Patients

Hiwa O. Abdullah¹, Sadraldin A. Braim², Maria A. Rasool², Dashne M. Abdalla², Dyari Q. Hamad², Daban K. Ahmad², Ayman M. Mustafa¹, Fakher Abdullah³, Yousif M. Mahmood¹, Dilan S. Hiwa¹, Sasan M. Ahmed⁴, Karokh K. Mohammed², Berun A. Abdalla^{5*}, Shvan H. Mohammed⁶, Fahmi H. Kakamad⁷

- 1. Smart Health Tower, Madam Mitterrand Street, Sulaymaniyah, Kurdistan, Iraq
- 2. Smart Health Tower (Raparin Branch), Karukh Street, Ranya, Sulaymaniyah, Kurdistan, Iraq
- 3. Kscien Organization for Scientific Research (Europe office), Rotterdam, Netherlands
- 4. Kscien Organization for Scientific Research (Middle East office), Hamid Street, Azadi mol, Sulaymaniyah, Kurdistan, Iraq
- 5. Department of Biology, College of Education, University of Sulaimani, Madam Mitterrand Street, Sulaymaniyah, Kurdistan, Iraq
- 6. Xzmat Polyclinic, Rizgari, Kalar, Sulaymaniyah, Kurdistan, Iraq
- 7. College of Medicine, University of Sulaimani, Madam Mitterrand Street, Sulaymaniyah, Kurdistan, Iraq

* Corresponding author: <u>berun.anwer95@gmail.com</u> (B.A. Abdalla). Zargatay Taza, House number 54, Zip code: 46001, Sulaymaniyah, Kurdistan, Iraq

Check for updates

Keywords: SARS CoV-2 Coronavirus 2019 2019-nCoV Biomarkers Acute phase reactants

Received: April 29, 2024 Revised: May 31, 2024 Accepted: June 28, 2024 First Published: June 30, 2024

Copyright: © 2024 Abdullah et al. This is an open access article distributed under the terms of the Creative Commons Attribution License (https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Citation: Abdullah HO, Braim SA, Rasool MA, Abdalla DM, Hamad DQ, Ahmed DK, et al. Role of Inflammatory Markers in Severity, ICU Admission, and Mortality in COVID-19: A Systematic Review and Meta-analysis of 79,934 Patients. Barw Medical Journal. 2024;2(3):65-83.

https://doi.org/10.58742/bmj.v2i2.96

Abstract

Introduction

Despite extensive investigations into the roles of inflammatory biomarkers in the prognosis of COVID-19 through systematic reviews and meta-analyses, they are limited by small sample sizes and focus on a specific marker. This meta-analysis investigated the role of 11 inflammatory biomarkers in severity, intensive care unit (ICU) admission, and mortality among COVID-19 patients.

Methods

Studies up to October 25, 2023, were identified through a search of Google Scholar, limited to human studies published in English. Inclusion criteria required confirmed COVID-19 cases diagnosed via reliable laboratory methods, original articles from eligible journals, proper grouping of severity status, ICU admission, or mortality outcomes, and presentation of continuous data in mean and standard deviation, median with range, or interquartile range.

Results

A total of 241 studies, comprising 79,934 cases of COVID-19, were included in this study. Albumin levels significantly declined in severe, ICU, and dead cases compared to mild, moderate, non-ICU, and survived cases (p<0.001). C-reactive protein (CRP), D-dimer, erythrocyte sedimentation rate (ESR), ferritin, fibrinogen, Interleukin-6 (IL-6), lactate dehydrogenase (LDH), neutrophil-to-lymphocyte ratio (NLR), procalcitonin, and white blood cell (WBC) were all significantly (p<0.001) increased and correlated with the severity of COVID-19. CRP, D-dimer, ferritin, fibrinogen, IL-6, LDH, NLR, procalcitonin, and WBC were all significantly (p<0.05) elevated and correlated with the risk of ICU admission (except fibrinogen) and mortality in COVID-19 in both fixed and random effects.

Conclusion

Inflammatory biomarkers like albumin, CRP, D-dimer, ferritin, IL-6, LDH, NLR, procalcitonin, and WBC all significantly impact severity status, ICU admission, and mortality in COVID-19.

1. Introduction

The coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has emerged as a global pandemic with significant morbidity and mortality [1]. As of March 17, 2024, there were over 774 million confirmed COVID-19 cases, with seven million deaths. In February 2024 alone, 252,585 new cases were reported, with 5,272 reported deaths [2]. This infectious disease presents a spectrum of clinical manifestations, ranging from asymptomatic or mild symptoms to severe respiratory distress and multi-organ failure [3]. Approximately 70-80% of patients are expected to experience a variety of short- or long-term post-infection complications, particularly in cases of severe COVID-19 [3,4]. Inflammatory biomarkers (IBs) have garnered significant attention in understanding the pathogenesis and prognosis of COVID-19 [5]. Biomarkers such as C-reactive protein (CRP), interleukin-6 (IL-6), and ferritin play crucial roles in reflecting the inflammatory response and disease severity [6]. Other markers like D-dimer, neutrophil-to-lymphocyte ratio (NLR), and procalcitonin have shown promise in predicting disease progression and outcomes [7]. The prognosis of COVID-19 is influenced by various factors, including patient demographics, comorbidities, and disease severity [8]. Identifying risk factors associated with disease severity and mortality is essential for guiding clinical management and resource allocation [9]. Investigating IBs in COVID-19 patients can be vital for early risk stratification, informing treatment decisions, and improving patient outcomes [10]. Increasing evidence suggests that systemic inflammation contributes to COVID-19 progression by triggering the release of pro-inflammatory cytokines. Consequently, interventions aimed at suppressing inflammatory responses may hold promise in the management of severe cases of COVID-19. Despite extensive investigations into the roles of IBs in the prognosis of COVID-19 through systematic reviews and meta-analyses, they are limited by small sample sizes and focus on a specific marker [11-15]. This meta-analysis investigated the role of 11 IBs in severity, intensive care unit (ICU) admission, and mortality among COVID-19 patients.

2. Methods

2.1 Data sources and search strategy

The systematic review and meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Metaanalyses (PRISMA) guidelines. Studies published until October 25, 2023, were identified via a comprehensive search of Google Scholar. The studies should have investigated the correlation between levels of IBs and COVID-19 severity, ICU admission, and mortality. The strategy included the following keywords: search ("Inflammatory biomarker" OR "Inflammatory biomarkers" OR "Inflammatory marker" OR "Inflammatory markers" OR "C reactive protein" OR "C reactive proteins" OR CRP OR "Erythrocyte sedimentation rate" OR ESR OR Procalcitonin OR PCT OR "Serum amyloid" OR "Serum amyloids" OR Cytokines OR Cytokine OR "Alpha 1 acid glycoprotein" OR "Plasma viscosity" OR Ceruloplasmin OR Hepcidin OR Haptoglobin OR "Tumor Necrosis Factor" OR "Tumor Necrosis Factors" OR TNFa OR Interleukin OR Interleukins OR IL OR "Interferon gamma" OR "IFN γ" OR Fibrinogen OR Immunoglobulin OR Immunoglobulins OR IgM OR Albumin OR "White blood cell" OR "White blood cells" OR WBC OR Eosinophils OR Eosinophil OR Basophils OR Basophil OR Neutrophil OR Neutrophils OR "complete blood count" OR "complete blood counts" OR CBC OR "lactate dehydrogenase" OR LDH OR "D dimer" OR "D dimers" OR Ferritin OR Ferritins OR Calprotectin OR Interferon OR Interferons) AND ("SARS CoV 2" OR "COVID-19" OR "Coronavirus 2019" OR "2019-nCoV") AND (mortality OR morbidity OR outcome OR survival OR survive OR analysis OR evaluation OR severity OR complication OR complications OR hospitalization OR ICU OR "intensive care unit" OR death OR fatality OR comorbidity OR comorbidities OR risk OR risks). The search was restricted to human studies published in the English language.

2.2 Eligibility criteria

The inclusion criteria of the study encompassed: 1) Confirmed COVID-19 cases diagnosed via reverse transcriptasepolymerase chain reaction (RT-PCR) or other reliable laboratory methods, 2) Original articles published in eligible journals, 3) Assessment of IBs such as albumin, CRP, D-dimer, erythrocyte sedimentation rate (ESR), ferritin, fibrinogen, IL-6, lactate dehydrogenase (LDH), NLR, procalcitonin, serum amyloid, and white blood cell (WBC), 4) Identification and proper grouping of severity status, ICU admission, or mortality outcomes, 5) Presentation of quantitative or continuous data in mean and standard deviation, median with range, or interquartile range. Excluded studies involved pediatric populations, investigating other diseases besides COVID-19, review articles, studies deriving sample sizes from datasets or popular databases, and those published in warning journal lists.

2.3 Study selection process

Three researchers initially reviewed the titles and abstracts of the identified studies, followed by full-text screening based on predetermined eligibility criteria. Subsequently, eligible studies were chosen for inclusion. In cases of disagreement, a fourth

author intervened to facilitate resolution through deliberation and discourse.

2.4 Data extraction

Two authors extracted data, which was blindly reviewed by a third author for accuracy. The extracted data from each study encompassed various parameters, including the first author's surname, publication year, study country, design, sample size, demographic characteristics (such as mean age and gender distribution), prevalent comorbidities, extent of clinical severity, ICU admission status, outcomes, and levels of IBs presented as mean with standard deviation, median with range, or interquartile ranges for different groups (mild, moderate, severe, ICU, non-ICU, survived, and deceased). Median with range or interquartile ranges were transformed into means and standard deviation according to the calculation method proposed by Lou et al. and Wan et al. [16,17]. The IBs were extracted in standard measurement units as follows: albumin (g/L), CRP (mg/L), NLR (ratio), D-Dimer (µg/ml), ESR (mm/hr), ferritin (ng/mL), fibrinogen (g/L), IL-6 (pg/mL), LDH (UL), procalcitonin (ng/mL), WBC $(10^9/L)$.

2.5 Statistical Analysis

All statistical analyses were performed using MedCalc Statistical Software (version 22.021, MedCalc Software Ltd, Belgium). Meta-analysis (continuous measure) was utilized to analyze continuous data, and the Chi-squared test was used to measure categorical data. A p-value < 0.05 was considered statistically significant. Forest plots were generated to depict binary data of included markers for mild vs severe cases, moderate vs severe cases, ICU vs non-ICU cases, and survived vs deceased cases of COVID-19, utilizing standardized mean difference (SMD) and 95% confidence intervals (95% CI). A random-effects model was applied to calculate the SMD for the severity, ICU admission, and mortality risks of COVID-19. Heterogeneity among studies was assessed by the O test (p < p0.1), with I² values of 50% and 70% indicating moderate and high heterogeneity, respectively. Publication bias was evaluated using Begg's rank correlation test and Egger's regression asymmetry test via funnel plots. In cases of significant publication bias, studies with substantial standard errors (SE) and SMD were excluded iteratively to make the bias insignificant.

3. Results

3.1 Study search and selection

The systematic search initially yielded a total of 2,770 articles. Following the removal of duplicates (311), abstracts (143), and non-English articles (39), the titles and abstracts of 2,277 articles were screened. Of these, 1,485 were excluded due to irrelevance. Full-text screening was then conducted for 792 articles, resulting in the exclusion of 469. The remaining 323 articles were assessed against the full eligibility criteria, with 82 excluded due to their publication in predatory journals as identified by the Kscien list [18]. Finally, 241 eligible articles were included in



Figure 1. Prisma Flow Chart

the systematic review and meta-analysis [19-259]. A detailed PRISMA flow chart of the process is presented in (Figure 1).

3.2 Characteristics of the Studies

A total of 241 studies, comprising 79,934 cases of COVID-19, were included in this study. The majority of the studies were conducted in Turkey (25.3%), followed by Indonesia (10%), India (8.7%), and China (7.9%). Almost all of the studies were observational, with 73% being cohort studies, 21.2% cross-sectional studies, 4.6% case-control studies, and 0.8% case series. Additionally, one study was identified as a randomized controlled trial (0.4%) (Table 1). The raw data for each included study can be found in the supplementary material (Table 1 supplementary).

3.3 Main findings

Males accounted for 55.1% of the cases, while females represented 38.7%, with gender unspecified in 6.2% of cases. The mean age (means of mean) of patients was 58.2 ± 8.5 years, ranging from 41.2 to 86.6 years. Commonly reported comorbidities included hypertension (18.3%), diabetes mellitus (13.1%), and respiratory diseases (4.2%). Disease severity was reported in 29,490 cases (36.9%), categorized as mild in 10,551 cases (13.2%), moderate in 9,903 cases (12.4%), and severe in 9,036 cases (11.3%). ICU admission status was defined for 38,940 cases (48.7%), with 9,234 cases (11.5%) admitted to the ICU. In total, 43,051 cases (53.9%) survived the disease, while 11,937 cases (14.9%) died. Survival status was not defined in 31.2% of cases (Table 1).

Variables	Frequency / Percentage
Country of studies	
Turkey	61 (25.3%)
Indonesia	24 (10.0%)
India	21 (8.7%)
China	19 (7.9%)
Iran	16 (6.6%)
Pakistan	16 (6.6%)
Egypt	15 (6.2%)
Romania	8 (3.3%)
Iraq	7 (2.9%)
Mexico	6 (2.5%)
Italy	5 (2.1%)
Republic of Korea	5 (2.1%)
Snain	5 (2.1%)
Brazil	4(1.7%)
Others	-7(1.770) 29(12.0%)
Study design	29 (12:070)
Cohort	176 (72 0%)
Cross sostional	51 (21 294)
Closs-sectional	31(21.270) 11(4.697)
Case-control	2(0.89/)
Day daysing days the line days	2(0.870)
Randomized controlled trial	1 (0.4%)
Gender	11012 (55.10/)
Male	44043 (55.1%)
Female	30944 (38.7%)
N/R	4947 (6.2%)
Age* (year), mean of means \pm SD,	$58.2 \pm 8.5 (41.2 - 86.6)$
(min-max)	
Covid-19 severity	
Mild	10551 (13.2%)
Moderate	9903 (12.4%)
Severe	9036 (11.3%)
N/R	50444 (63.1%)
Comorbidities#	
Diabetes mellitus	10459 (13.1%)
Hypertension	14635 (18.3%)
Respiratory diseases	3336 (4.2%)
ICU admission	
Yes	9234 (11.5%)
No	29706 (37.2%)
N/R	40994 (51.3%)
Survival status	
Survived	43051 (53.9%)
Died	11937 (14.9%)
N/R	24946 (31.2%)

SD: Standard deviation, ICU: Intensive care unit, UAE: United Arab Emirates, N/R: not-reported

*The age belongs to 53196 cases.

#Other comorbidities might be present but only the most common have been included.

3.4 Meta-analysis of COVID-19 severity with age and gender

A total of 37 studies, comprising 5,029 patients for mild vs severe cases and 64 studies with 9,849 cases for moderate vs severe cases, were included in the analysis of disease severity based on age. Severity demonstrated a significant correlation with age in both groups—mild vs severe and moderate vs severe (SMD = 0.884; 95% CI, 0.667-1.101; p < 0.001; I² = 88.79%; P heterogeneity < 0.0001 and SMD = 0.497; 95% CI, 0.349-0.645; p < 0.001; I² = 89.86%; P heterogeneity < 0.0001, respectively). Statistically significant heterogeneity across the selected studies was observed, as evidenced by the I² statistics for age and severity of COVID-19. Begg's test (p = 0.0797 for mild vs severe, p = 0.5409 for moderate vs severe) and Egger's test (p = 0.0886 for mild vs severe, p = 0.0588 for moderate vs severe) for age were not significant (Table 2-A and B supplementary,

Figure 2). Funnel plots for the mild vs severe and moderate vs severe cases according to age suggested no potential publication bias (Figure 2). Disease severity was significantly associated with male gender in the analysis of 20,793 patients (p < 0.05) (Table 2).



Figure 2. Forest plots depict standardized mean differences (SMD) and 95% confidence intervals, indicating the association between age and severity (A and B), ICU admission (C), and mortality in COVID-19 (D). Random-effects funnel plots illustrate publication bias in studies examining the relationship between age and severity (A1 and B1), ICU admission (C1), and mortality in COVID-19 (D1).

3.5 Meta-analysis of COVID-19 ICU admission with age and gender

Twenty-four studies, with a sample size of 19,216, were analyzed to reveal the role of age and gender in ICU admission among COVID-19 patients. Age demonstrated a significant correlation in increasing the risk of ICU admission (SMD = 0.685; 95% CI, 0.274 to 1.096; p < 0.001; I² = 98.75%; P heterogeneity < 0.0001). Begg's test (p = 0.44) and Egger's test (p = 0.68) for age in the ICU and non-ICU groups were not significant (<u>Table 2-C supplementary</u>, Figure 2). The funnel plot revealed no potential publication bias (Figure 2). Gender showed no impact on admission to the ICU in the analysis of 25,489 patients (p = 0.26) (Table 2).

Gender	Severity			ICU status		Outcome	
	Mild	Moderate	Severe	ICU	Non-ICU	Dead	Survived
Female	3051 (38.8%)	2954 (41.4%)	2296 (39.7%)	2129 (36%)	7210 (36.8%)	3401 (39.6%)	12889 (45.8%)
Male	4816 (61.2%)	4188 (58.6%)	3488 (60.3%)	3781 (64%)	12369 (63.2%)	5188(60.4%)	15280 (54.2%)
Total	7867 (37.8%)	7142 (34.3%)	5784 (27.8%)	5910 (23.2%)	19579 (76.8%)	8589 (23.4%)	28169 (76.6%)
P-value	0.005		0.262		<0.001		





Figure 3. Forest plots illustrate the standardized mean difference (SMD) and 95% confidence intervals regarding the association between Albumin levels and severity (A and B), ICU admission (C), and mortality in COVID-19 (D). Random-effects funnel plots delineate publication bias in studies examining the relationship between Albumin levels and severity (A1 and B1), ICU admission (C1), and mortality in COVID-19 (D1).

3.6 Meta-analysis of COVID-19 mortality with age and gender

Across 41,320 patients in 115 studies, age again showed a significant correlation with mortality (SMD = 0.741; 95% CI, 0.626 to 0.857; p < 0.001; I² = 94.49%; P ^{heterogeneity} < 0.0001). Begg's test (p = 0.87) and Egger's test (p = 0.89) for age in the survived and dead groups were not significant (<u>Table 2-D</u> supplementary, Figure 2). The funnel plot also showed no significant publication bias (Figure 2). The male gender was highly vulnerable to mortality when analyzing 36,758 cases (p <0.0001) (Table 2).



Figure 4. Forest plots display the standardized mean difference (SMD) and 95% confidence intervals for the association between CRP levels and severity (A and B), ICU admission (C), and mortality in COVID-19 (D). Random-effects funnel plots delineate publication bias in the studies examining the association between CRP levels and severity (A1 and B1), ICU admission (C1), and mortality in COVID-19 (D1).

3.7 Meta-analysis of inflammatory markers and COVID-19 severity

Among both the mild vs severe groups and moderate vs severe groups, all studied IBs were significantly varied. Albumin level was significantly decreased in severe cases compared to mild and moderate cases (SMD = -0.959; 95% CI, (-1.399) – (-0.520); p < 0.001; $I^2 = 78.90\%$; P heterogeneity = 0.0002 and SMD = -0.798; 95% CI, (-1.033) – (-0.563); p < 0.001; $I^2 = 73.48\%$; P heterogeneity < 0.0001, respectively) (Table 2-E, F supplementary, Figure 3). Begg's test (p = 0.188 for mild vs severe, p = 0.68 for moderate vs severe) and Egger's test (p = 0.0959 for mild vs severe, p = 0.749 for moderate vs severe) for albumin were not significant and there was no publication bias (Figure 3). CRP



Figure 5. Forest plots depict the standardized mean difference (SMD) and 95% confidence intervals for the association between D-dimer levels and severity (A and B), ICU admission (C), and mortality in COVID-19 (D). Random-effects funnel plots detail publication bias in the studies investigating the association between D-dimer levels and severity (A1 and B1), ICU admission (C1), and mortality in COVID-19 (D1).

(SMD=1.118; 95% CI, 0.913 - 1.323; p<0.001; I² = 87.56%; P heterogeneity < 0.0001; Begg's test p =0.34; Egger's test p =0.87 for mild vs severe groups, SMD=0.630;95% CI, 0.520 - 0.740; p < 0.001; $I^2 = 78.29\%$; P heterogeneity < 0.0001; Begg's test p =0.943; Egger's test p =0.519 for moderate vs severe groups) (Table 2-G,H supplementary, Figure 4), D-dimer (SMD=1.086; 95% CI, 0.740 -1.432; p<0.001; $I^2 = 95.49\%$; P heterogeneity < 0.0001; Begg's test p = 0.178; Egger's test p = 0.834 for mild vs severe groups, SMD=0.665; 95% CI, 0.506 -0.824; p<0.001; I² = 83.26%; P heterogeneity < 0.0001; Begg's test p =0.659; Egger's test p =0.059 for moderate vs severe groups) (Table 2-I,J supplementary, Figure 5), ESR (SMD=0.713; 95% CI, 0.424 -1.001; p<0.001; $I^2 = 0.0\%$; P heterogeneity = 0.392; Begg's test p =0.174; Egger's test p =0.131 for mild vs severe groups, SMD=0.806; 95% CI, 0.434 - 1.178; p<0.001; I² = 71.86%; P heterogeneity = 0.0016; Begg's test p = 0.293; Egger's test p = 0.109for moderate vs severe groups) (Table 2-K,L supplementary, Figure 6), Ferritin (SMD=1.221; 95% CI, 0.961 - 1.481; p < 0.001; $I^2 = 87.84\%$; P heterogeneity < 0.0001; Begg's test p = 0.812; Egger's test p =0.248 for mild vs severe groups, SMD=0.563; 95% CI, 0.404 - 0.721; p<0.001; I² = 83.62%; P heterogeneity <0.0001; Begg's test p =0.345; Egger's test p =0.199



Figure 6. Forest plots present the standardized mean difference (SMD) and 95% confidence intervals for the association between ESR and severity (A and B) and mortality in COVID-19 (C). Random-effects funnel plots provide details on publication bias in studies examining the association between ESR and severity (A1 and B1) and mortality in COVID-19 (C1).

for moderate vs severe groups) (Table 2-M,N supplementary, Figure 7) Fibrinogen (SMD=0.750; 95% CI, 0.333 - 1.167; p < 0.001; $I^2 = 74.36\%$; P _{heterogeneity} = 0.0036; Begg's test p = 0.327; Egger's test p =0.464 for mild vs severe groups, SMD=0.387; 95% CI, (-0.0569) – (0.831); p=0.087; $I^2 =$ 84.17%; P heterogeneity <0.0001; Begg's test p =0.347; Egger's test p =0.50 for moderate vs severe groups) (Table 2-O,P supplementary, Figure 8), IL-6 (SMD=1.185; 95% CI, 0.774 -1.595; p<0.001; I² = 90.02%; P heterogeneity < 0.0001; Begg's test p = 0.564; Egger's test p = 0.0834 for mild vs severe groups, SMD=0.877; 95% CI, 0.633 – 1.122; p<0.001; I² = 87.45%; P heterogeneity <0.0001; Begg's test p =0.404; Egger's test p =0.545 for moderate vs severe groups) (Table 2-Q,R supplementary, Figure 9), LDH (SMD=1.186; 95% CI, 0.894 - 1.478; p<0.001; $I^2 = 90.87\%$; P heterogeneity < 0.0001; Begg's test p = 0.506; Egger's test p =0.332 for mild vs severe groups, SMD=0.735; 95% CI, 0.560 - 0.910; p<0.001; I² = 77.90%; P heterogeneity <0.0001; Begg's test p =0.119; Egger's test p =0.695 for moderate vs severe groups) (Table 2-S,T supplementary, Figure 10), NLR (SMD=1.188; 95% CI, 0.305 - 2.070; p<0.001; I² = 98.56%; P heterogeneity < 0.0001; Begg's test p = 0.471; Egger's test p =0.450 for mild vs severe groups, SMD=0.858; 95% CI, $0.679\ -\ 1.037;\ p{<}0.001;\ I^2\ =\ 88.29\%;\ P\ ^{heterogeneity}\ {<}0.0001;$ Begg's test p =0.870; Egger's test p =0.871 for moderate vs severe groups) (Table 2-U,V supplementary, Figure 11), procalcitonin (SMD=0.606; 95% CI, 0.333 - 0.880; p<0.001; I² = 60.86%; P heterogeneity = 0.0369; Begg's test p = 0.624; Egger's test p =0.244 for mild vs severe groups, SMD=0.441; 95% CI, 0.225 - 0.657; p<0.001; I² = 84.55%; P heterogeneity <0.0001; Begg's test p = 0.741; Egger's test p = 0.345 for moderate vs severe groups) (Table 2-W,X supplementary, Figure 12), and WBC (SMD=0.693; 95% CI, 0.400 - 0.985; p<0.001; I² =



Figure 7. Forest plots illustrate the standardized mean difference (SMD) and 95% confidence intervals for the association between Ferritin levels and severity (A and B), ICU admission (C), and mortality in COVID-19 (D). Random-effects funnel plots detail publication bias in the studies investigating the association between Ferritin levels and severity (A1 and B1), ICU admission (C1), and mortality in COVID-19 (D1).

88.66%; P heterogeneity < 0.0001; Begg's test p = 0.397; Egger's test p =0.240 for mild vs severe groups, SMD=0.438; 95% CI, 0.316 – 0.560; p<0.001; I² = 71.57%; P heterogeneity <0.0001; Begg's test p = 0.142; Egger's test p =0.104 for moderate vs severe groups) (Table 2-Y,Z supplementary, Figure 13), were all significantly increased and correlated with the severity of COVID-19 in both fixed and random effects except for fibrinogen in which reached significant level only in fixed effects.

3.8 Meta-analysis of inflammatory markers and ICU admission and Mortality in COVID-19

All IBs were significantly different between the non-ICU vs ICU groups and survived vs dead groups. Albumin level significantly declined in ICU and dead cases compared to non-ICU and survived cases (SMD = -0.674; 95% CI, (-1.072) – (-0.276); p < 0.001; I² = 96.51%; P ^{heterogeneity} < 0.0001 and SMD = -0.902; 95% CI, (-1.112) – (-0.692); p < 0.001; I² = 95.58%; P ^{heterogeneity} < 0.0001, respectively) (Table 3-A, B supplementary, Figure 3).



Figure 8. Forest plots depict the standardized mean difference (SMD) and 95% confidence intervals for the association between Fibrinogen levels and severity (A and B), ICU admission (C), and mortality in COVID-19 (D). Random-effects funnel plots delineate publication bias in the studies investigating the association between Fibrinogen levels and severity (A1 and B1), ICU admission (C1), and mortality in COVID-19 (D1).

Begg's test (p = 0.585 for non-ICU vs ICU groups, p = 0.441 for survived vs dead groups) and Egger's test (p = 0.389 for non-ICU vs ICU groups, p = 0.897 for survived vs dead groups) for albumin were not significant and there was no publication bias (Figure 3). CRP (SMD=0.708; 95% CI, 0.534 - 0.881; p<0.001; $I^2 = 90.37\%$; P_{heterogeneity} < 0.0001; Begg's test p = 0.436; Egger's test p =0.505 for non-ICU vs ICU groups, SMD=0.815;95% CI, 0.670 - 0.959; p<0.001; I² = 94.86%; P_{heterogeneity} < 0.0001; Begg's test p =0.648; Egger's test p =0.324 for survived vs dead groups) (Table 3-C,D supplementary, Figure 4), D-dimer (SMD=0.677; 95% CI, 0.453 - 0.900; p<0.001; I² = 82.96%; P heterogeneity < 0.0001; Begg's test p =0.583; Egger's test p =0.166 for non-ICU vs ICU groups, SMD=0.833; 95% CI, 0.686 -0.981; p<0.001; I² = 94.21%; P heterogeneity < 0.0001; Begg's test p =0.286; Egger's test p =0.759 for survived vs dead groups) (Table 3-E,F supplementary, Figure 5), ESR (SMD= 0.342; 95% CI, (-0.352) – (1.037); p

=0.334; I^2 = 97.38%; P heterogeneity < 0.0001; Begg's test p =0.573; Egger's test p =0.301 for survived vs dead groups (<u>Table 3-G</u> supplementary, Figure 6), Ferritin (SMD=0.745; 95% CI, 0.251 - 1.238; p=0.003; I^2 = 97.90%; P heterogeneity < 0.0001; Begg's test





Figure 9. Forest plots display the standardized mean difference (SMD) and 95% confidence intervals for the association between IL-6 levels and severity (A and B), ICU admission (C), and mortality in COVID-19 (D). Random-effects funnel plots outline publication bias in the studies investigating the association between IL-6 levels and severity (A1 and B1), ICU admission (C1), and mortality in COVID-19 (D1).

p = 0.697; Egger's test p = 0.718 for non-ICU vs ICU groups, SMD=0.956; 95% CI, 0.759 - 1.154; p<0.001; I² = 95.06%; P heterogeneity <0.0001; Begg's test p =0.330; Egger's test p =0.824 for survived vs dead groups) (Table 3-H,I supplementary, Figure 7) Fibrinogen (SMD=0.333; 95% CI, (-0.0242) -(0.691); p=0.068; I² = 73.85%; P_{heterogeneity} = 0.0041; Begg's test p = 0.624; Egger's test p =0.158 for non-ICU vs ICU groups, SMD=0.357; 95% CI, 0.147 – 0.566; p=0.001; I² = 84.70%; P heterogeneity <0.0001; Begg's test p =0.569; Egger's test p =0.530 for survived vs dead groups) (Table 3-J,K supplementary, Figure 8), IL-6 (SMD=0.928; 95% CI, 0.702 - 1.155; p<0.001; I² = 0.0%; P heterogeneity = 0.421; Begg's test p = 0.496; Egger's test p =0.460 for non-ICU vs ICU groups, SMD=0.823; 95% CI, 0.625 -1.022; p<0.001; I² = 92.63%; P heterogeneity <0.0001; Begg's test p =0.150; Egger's test p =0.918 for survived vs dead groups) (Table 3-L,M supplementary, Figure 9), LDH (SMD=1.057; 95% CI, 0.775 - 1.340; p<0.001; $I^2 = 91.23\%$; P heterogeneity < 0.0001; Begg's test p = 0.179; Egger's test p = 0.204 for non ICU vs ICU groups, SMD=0.978; 95% CI, 0.806 - 1.151; p<0.001; $I^2 = 91.75\%$; P heterogeneity <0.0001; Begg's test p =0.373; Egger's test p =0.438 for survived vs dead groups) (Table 3-N,O supplementary, Figure 10), NLR (SMD=1.231; 95% CI, 0.967 -



Figure 10. Forest plots illustrate the standardized mean difference (SMD) and 95% confidence intervals for the association between LDH levels and severity (A and B), ICU admission (C), and mortality in COVID-19 (D). Random-effects funnel plots provide insights into publication bias in the studies investigating the association between LDH levels and severity (A1 and B1), ICU admission (C1), and mortality in COVID-19 (D1).

1.496; p<0.001; $I^2 = 89.69\%$; P heterogeneity < 0.0001; Begg's test p = 0.654; Egger's test p = 0.970 for non-ICU vs ICU groups, SMD=1.013; 95% CI, 0.828 – 1.197; p<0.001; I² = 95.96%; P heterogeneity <0.0001; Begg's test p =0.499; Egger's test p =0.587 for non-ICU vs ICU groups) (Table 3-P,Q supplementary, Figure 11), procalcitonin (SMD=0.348; 95% CI, 0.055 - 0.640; $p = 0.020; I^2 = 53.53\%; P_{heterogeneity} = 0.116; Begg's test p =$ 0.601; Egger's test p =0.893 for non-ICU vs ICU groups, SMD=0.826; 95% CI, 0.627 - 1.025; p<0.001; I² = 93.28%; P heterogeneity <0.0001; Begg's test p = 0.753; Egger's test p = 0.609 for survived vs dead groups) (Table 3-R.S supplementary, Figure 12), and WBC (SMD=0.598; 95% CI, 0.324 - 0.872; p < 0.001; $I^2 = 91.23\%$; P heterogeneity < 0.0001; Begg's test p = 0.902; Egger's test p =0.356 for non-ICU vs ICU groups, SMD=0.676; 95% CI, 0.568 - 0.784; p<0.001; I² = 89.10%; P heterogeneity <0.0001; Begg's test p = 0.289; Egger's test p = 0.556 for survived vs dead groups) (Table 3-T,U supplementary, Figure 13), were all significantly elevated and correlated with the risk of ICU admission and mortality in COVID-19 in both fixed and random effects except for fibrinogen in which reached significant level only in fixed effects for ICU admission (p=0.014). In addition, ESR only correlated with mortality in



Figure 11. Forest plots display the standardized mean difference (SMD) and 95% confidence intervals for the association between NLR (Neutrophil-to-Lymphocyte Ratio) and severity (A and B), ICU admission (C), and mortality in COVID-19 (D). Random-effects funnel plots provide insights into publication bias in the studies investigating the association between NLR and severity (A1 and B1), ICU admission (C1), and mortality in COVID-19 (D1)..

fixed effects (p<0.001), and no effect on ICU admission was generated due to a lack of proper data.

4. Discussion

While the majority of COVID-19 cases manifest with mild or moderate symptoms, prompt identification of critical cases is crucial to mitigate prolonged hospitalization and higher mortality rates. Hematological and biochemical indicators play a significant role in early detection and prognosis assessment. Severe COVID-19 patients frequently exhibit systemic inflammation [92]. Treatment approaches diverge significantly between mild and severe COVID-19 cases. Mild cases often require minimal intervention, with some patients recovering without any treatment. In contrast, severe cases may necessitate various measures, including mechanical ventilation, extracorporeal membrane oxygenation, and continuous renal replacement therapy [8]. It has been indicated that heightened levels of inflammatory cytokines in the bloodstream are associated with liver and pulmonary damage in COVID-19



Figure 12. Forest plots depict the standardized mean difference (SMD) and 95% confidence intervals for the association between Procalcitonin levels and severity (A and B), ICU admission (C), and mortality in COVID-19 (D). Random-effects funnel plots provide insights into publication bias in the studies investigating the association between Procalcitonin levels and severity (A1 and B1), ICU admission (C1), and mortality in COVID-19 (D1).

infection [13]. An expedient and early COVID-19 diagnostic test is imperative as a biomarker to aid in predicting and mitigating associated morbidity and mortality. Additionally, routine blood tests have been proposed as a more acceptable method for screening asymptomatic or mildly symptomatic individuals and could be utilized for screening purposes in outbreak areas [12]. This study represents the most extensive and comprehensive systematic review and meta-analysis, at least to the best of our knowledge, elucidating the roles of several common IBs in determining severity, ICU admission, and mortality among COVID-19 patients.

Regarding gender in COVID-19 patients, Ahmed et al. observed a male predominance of 69%. Similarly, a retrospective cohort study of 239 hospitalized COVID-19 cases in Lombardy, Italy, reported 71% of cases being male, while another report from Wuhan, China, noted a rate of 75% male cases [30, 260,261]. However, a meta-analysis conducted by Zavalaga-Zegarra et al. found that among 12,245 cases, the male population constituted 56.5% [15]. In the current meta-analysis, disease severity among 20,793 patients and mortality among 36,758 cases were significantly associated with the male gender (p < 0.05 and p <

0.0001, respectively). However, gender had no impact on ICU admission in the analysis of 25,489 patients (p = 0.26).

Increasing patient age independently predicted mortality, alongside significant associations with severity, with median ages of 65.5 years and 56 years observed in non-survivors and severe cases, respectively [30]. Luo Xiaomin et al.'s study on 298 COVID-19 cases from China also found a higher mortality proportion among those aged above 60, indicating age-related disease progression [262]. This can be attributed to impaired innate and adaptive immunity in elderly individuals. In healthy individuals, innate immunity typically neutralizes the virus early in the disease process, preventing it from reaching the alveoli. However, in elderly patients, innate immunity may fail to do so, allowing the virus to reach and replicate in the alveoli extensively. This triggers a robust response from macrophages and lymphocytes to eliminate virally infected cells, leading to elevated levels of cytokines [11]. In the present study, severity showed a significant correlation with age in both groups, mild vs severe and moderate vs severe (SMD = 0.884; 95% CI, 0.667-1.101; p < 0.001 and SMD = 0.497; 95% CI, 0.349-0.645; p < 0.001, respectively). Age also demonstrated a significant correlation with an increased risk of ICU admission (SMD = 0.685; 95% CI, 0.274 to 1.096; p < 0.001) and mortality (SMD = 0.741; 95% CI, 0.626 to 0.857; p < 0.001).

Hypoalbuminemia indicates malnutrition, hepatic and renal impairment, and diminished survival among critically ill patients. Furthermore, it has been identified as an independent risk factor linked to unfavorable outcomes in COVID-19 patients [92]. Reduced albumin levels may heighten mortality risk in COVID-19 patients. Yet, besides its anti-inflammatory role, albumin is suggested to have antioxidative, antithrombotic properties, and potential antiviral effects by binding to the SARSCoV-2 spike protein S1 subunit [263]. Baig et al. observed ICU patients initially with normal albumin levels, which rapidly decreased within 24 hours alongside increased oxygen needs. These patients lacked typical causes (proteinuria or chronic liver disease) for low albumin. The decline correlated with rising CRP, suggested as a hallmark of COVID-19 pneumonia. Furthermore, discharged ICU patients showed improved serum albumin levels, while those who succumbed to COVID-19 pneumonia had persistently low serum albumin levels [264]. Huang et al. suggested hypoalbuminemia in COVID-19 may arise from systemic inflammation. Serum albumin levels below 35 g/L were associated with a six-fold increase in COVID-19related mortality risk (Odds ratio: 6.394, 95% CI: 1.316-31.092) [265]. Albumin levels, in this meta-analysis, were significantly decreased in severe cases compared to mild and moderate cases (SMD = -0.959; 95% CI, -1.399 to -0.520; p < 0.001 and SMD = -0.798; 95% CI, -1.033 to -0.563; p < 0.001, respectively). They also significantly declined in ICU and deceased cases compared to non-ICU and survived cases (SMD = -0.674; 95% CI, -1.072 to -0.276; p < 0.001 and SMD = -0.902; 95% CI, -1.112 to -0.692; p < 0.001, respectively).

In severe cases of COVID-19, elevated levels of CRP and other IBs including IL-6, IL-8, IL-2R, and IL-10 were observed compared to non-severe cases. The heightened levels of cytokines, chemokines, and NLR in severe cases indicate a potential role of hyperinflammatory response in the



Figure 13. Forest plots illustrate the standardized mean difference (SMD) and 95% confidence intervals for the association between WBC (White Blood Cell count) and severity (A and B), ICU admission (C), and mortality in COVID-19 (D). Random-effects funnel plots provide insights into publication bias in the studies investigating the association between WBC and severity (A1 and B1), ICU admission (C1), and mortality in COVID-19 (D1).

pathogenesis of COVID-19 [11,13]. In a meta-analysis of 38 articles involving 5,699 patients with severity outcomes and 6,033 patients with mortality outcomes, it was found that severe cases and non-survivors of COVID-19 had higher NLR levels upon admission compared to non-severe cases and survivors (SMD 0.88; 95%CI 0.72-1.04; I²=75.52% and 1.87; 95%CI 1.25-2.49; I²=97.81%, respectively) [10]. Ali et al.'s metaanalysis, comprising 11 studies and 2,437 COVID-19 patients, found significantly elevated serum levels of CRP (SMD = 3.363, P value<.001), D-Dimer (SMD = 1.073, P value <.001), and LDH (SMD = 3.345, P value <.001) in severe cases of COVID-19 [11]. Another study revealed a positive correlation between CRP levels and the diameter of lung lesions, suggesting CRP is a potential indicator of disease severity [266]. Furthermore, other scholars observed that common markers, including WBC count, neutrophil count, lymphocyte count, CRP, and D-dimer levels, showed trends in predicting disease severity and mortality outcomes [218,257]. Nugroho et al.'s meta-analysis of 29 studies (4,328 patients) revealed higher D-dimer levels on admission in severe cases compared to non-severe cases (MD = 0.95, 95% CI: 0.61-1.28, P < .05; $I^2 = 90\%$). Non-survivors showed significantly higher D-dimer values (MD = 5.54, 95%

CI: 3.40-7.67, P < .05; $I^2 = 90\%$), while ICU admission did not significantly affect D-dimer levels (MD = 0.29, 95% CI: -0.05 to 0.63, P = 0.10; $I^2 = 71\%$) [9].

IL-6 plays a key role in maintaining immunocompetence, defined as the host's ability to respond to infections [267]. However, elevated levels have been linked to increased disease severity. These findings suggest high IL-6 levels during viral infections may promote virus survival and worsen the disease [268]. Amiri-Dashatan et al. found in 23 studies that elevated CRP, TNF-a, and IL-6 levels were linked to severe COVID-19 and potential liver damage [13]. Aziz et al. analyzed nine studies, showing significantly higher IL-6 levels in severe cases, also associated with increased mortality risk [269]. Ahmed et al. reviewed 157 COVID-19 cases and found ferritin levels significantly associated with disease severity and mortality [30]. In another study, hyperferritinemia (> 400 µg/L) was observed in severe cases, 1.5 to 5.3 times higher than non-severe cases. Non-survivors had ferritin levels around 1400 ng/mL, 3 to 4 times higher than survivors [270]. A pooled analysis showed that patients with elevated LDH faced a 16-fold higher mortality rate and over 6-fold increased risk of severe COVID-19 illness. Additionally, in all included studies reporting mortality, elevated LDH levels were observed in 95% of non-survivors compared to 60% of survivors [6]. Henry et al. analyzed 21 studies involving 2,984 patients and found that markers such as D-dimer, CRP, ferritin, and procalcitonin were significantly elevated in patients with severe COVID-19. Furthermore, in the mortality cohort comprising three studies, these markers were significantly higher in non-survivors compared to survivors [271]. Other scholars, in a multivariate analysis of 271 patients, reported that elevated levels of procalcitonin and CRP were significantly associated with mortality, even after adjusting for age, sex, and race or ethnicity [97]. In this meta-analysis, all IBs, such as CRP, D-dimer, ferritin, IL-6, LDH, NLR, procalcitonin, and WBC, were significantly associated with severity, ICU admission, and mortality in COVID-19 patients. However, ESR only showed a correlation with the severity of COVID-19 and had no impact on mortality (p = 0.334). Fibrinogen was significantly associated with severe cases compared to mild cases (p < 0.001); however, it did not significantly differ between moderate and severe cases (p = 0.087). It showed a significant increase in deceased cases (p = 0.001) but did not affect ICU admission (p = 0.068).

Although this study boasts the largest sample size and includes the largest number of IBs, it encounters several limitations. Firstly, the search was exclusively conducted on Google Scholar, potentially overlooking studies not indexed in the search. Additionally, most of the included studies were observational, contributing to the high statistical heterogeneity observed post-meta-analysis. This heterogeneity stems from clinical and methodological variations among the included studies but could also be influenced by geographical differences and risk of bias. Moreover, estimated effect measures were calculated as mean differences without adjusting for potential confounders such as age, sex, or comorbidities, which may influence inflammatory processes. Therefore, we could not definitively claim that any marker is superior to others in assessing the prognosis of patients with COVID-19.

5. Conclusion

The IBs can play a pivotal role in determining the clinical course and outcomes among patients with COVID-19. Albumin, CRP, D-dimer, ferritin, IL-6, LDH, NLR, procalcitonin, and WBC all significantly impact severity status, ICU admission, and mortality. However, ESR and fibrinogen cannot reliably reflect all three situations among COVID-19 patients.

Declarations

Conflicts of interest: The author(s) have no conflicts of interest to disclose.

Ethical approval: Not applicable.

Patient consent (participation and publication): Not applicable.

Source of Funding: None.

Acknowledgements: None to be declared.

Authors' contributions: FHK and HOA were major contributors to the conception of the study and the literature search for related studies. AMM, DSH, BAA, HOA, and SHM were involved in the literature review, manuscript writing, and data analysis and interpretation. SAB, MAR, DMA, DQH and SMA Literature review, final manuscript approval, and the Figures' processing. FA, DKA, YMM and KKM were involved in the literature review, the study's design, and the manuscript's critical revision. HOA and FHK Confirmation of the authenticity of all the raw data All authors approved the final version of the manuscript.

Use of AI: AI was not used in the drafting of the manuscript, the production of graphical elements, or the collection and analysis of data.

Data availability statement: Not applicable.

References

- Amin AA, Awakhti AH, Hussein LA, Fattah FH, Baba HO, Kakamad FH, et al. Survived COVID-19 patient presented with death on arrival: a case report. International Journal of Surgery Case Reports. 2021;81:105826. doi:10.1016/j.ijscr.2021.105826
- World Health Organization. WHO COVID-19 dashboard (2024). Accessed on: April 1, 2024. <u>https://data.who.int/dashboards/covid19/cases?m49=001&n=c.</u>
- Amin BJ, Kakamad FH, Ahmed GS, Ahmed SF, Abdulla BA, Mikael TM, et al. Post COVID-19 pulmonary fibrosis; a meta-analysis study. Annals of Medicine and Surgery. 2022; 77:103590. doi:10.1016/j.amsu.2022.103590
- Kakamad FH, Mahmood SO, Rahim HM, Abdulla BA, Abdullah HO, Othman S, et al. Post covid-19 invasive pulmonary Aspergillosis: a case report. International journal of surgery case reports. 2021 May 1; 82:105865. doi:10.1016/j.ijscr.2021.105865
- Ulloque-Badaracco JR, Ivan Salas-Tello W, Al-kassab-Córdova A, Alarcón-Braga EA, Benites-Zapata VA, Maguiña JL, et al. Prognostic value of neutrophil-to-lymphocyte ratio in COVID-19 patients: a systematic review and meta-analysis. International Journal of Clinical Practice. 2021 ;75(11):e14596. doi:10.1111/jicp.14596
- Henry BM, Aggarwal G, Wong J, Benoit S, Vikse J, Plebani M, et al. Lactate dehydrogenase levels predict coronavirus disease 2019 (COVID-19) severity and mortality: A pooled analysis. The American journal of emergency medicine. 2020;38(9):1722-6. <u>doi:10.1016/j.ajem.2020.05.073</u>

- Sarkar S, Khanna P, Singh AK. The impact of neutrophil-lymphocyte count ratio in COVID-19: a systematic review and meta-analysis. Journal of intensive care medicine. 2022;37(7):857-69. doi:10.1177/08850666211045626
- Li X, Liu C, Mao Z, Xiao M, Wang L, Qi S, et al. Predictive values of neutrophil-to-lymphocyte ratio on disease severity and mortality in COVID-19 patients: a systematic review and meta-analysis. Critical Care. 2020;24(1):1-10. doi:10.1186/s13054-020-03374-8
- Nugroho J, Wardhana A, Maghfirah I, Mulia EP, Rachmi DA, A'yun MQ, et al. Relationship of D-dimer with severity and mortality in SARS-CoV-2 patients: A meta-analysis. International journal of laboratory hematology. 2021;43(1):110-5. <u>doi:10.1111/ijlh.13336</u>
- Simadibrata DM, Calvin J, Wijaya AD, Ibrahim NA. Neutrophil-tolymphocyte ratio on admission to predict the severity and mortality of COVID-19 patients: A meta-analysis. The American journal of emergency medicine. 2021; 42:60-9. *doi:10.1016/j.ajem.2021.01.006*
- Ali AH, Mohamed SO, Elkhidir IH, Elbathani ME, Ibrahim AA, Elhassan AB, et al. The association of lymphocyte count, crp, d-dimer, and ldh with severe coronavirus disease 2019 (COVID-19): a meta-analysis. Sudan Journal of Medical Sciences. 2020;15(2):9-23. <u>doi:10.18502/sjms.v15i5.7146</u>
- Alkhatip AA, Kamel MG, Hamza MK, Farag EM, Yassin HM, Elayashy M, Naguib AA, Wagih M, Abd-Elhay FA, Algameel HZ, Yousef MA. The diagnostic and prognostic role of neutrophil-to-lymphocyte ratio in COVID-19: a systematic review and meta-analysis. Expert review of molecular diagnostics. 2021;21(5):505-14. <u>doi:10.1080/14737159.2021.1915773</u>
- Amiri-Dashatan N, Koushki M, Ghorbani F, Naderi N. Increased inflammatory markers correlate with liver damage and predict severe COVID-19: a systematic review and meta-analysis. Gastroenterology and hepatology from bed to bench. 2020;13(4):282. DOI: N/A
- He Z, Yan R, Liu J, Dai H, Zhu Y, Zhang F, et al. Lactate dehydrogenase and aspartate aminotransferase levels associated with the severity of COVID-19: A systematic review and meta-analysis. Experimental and Therapeutic Medicine. 2023;25(5):1-9. <u>doi:10.3892/etm.2023.11920</u>
- Zavalaga-Zegarra HJ, Palomino-Gutierrez JJ, Ulloque-Badaracco JR, Mosquera-Rojas MD, Hernandez-Bustamante EA, Alarcon-Braga EA, et al. C-reactive protein-to-albumin ratio and clinical outcomes in COVID-19 patients: a systematic review and meta-analysis. Tropical Medicine and Infectious Disease. 2022;7(8):186. <u>doi:10.3390/tropicalmed7080186</u>
- Luo D, Wan X, Liu J, Tong T. Optimally estimating the sample mean from the sample size, median, mid-range, and/or mid-quartile range. Statistical methods in medical research. 2018 Jun;27(6):1785-805. doi:10.1177/0962280216669183
- Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. BMC medical research methodology. 2014;14:1-3. <u>doi:10.1186/1471-2288-14-135</u>
- Muhialdeen AS, Ahmed JO, Baba HO, Abdullah IY, Hassan HA, Najar KA, et al: Kscien's List; A New Strategy to Discourage Predatory Journals and Publishers (Second Version). Barw Med J.2023; 1 (1): 24-26. doi:10.58742/bmj.v1i1.14
- Abbas AA, Alghamdi A, Mezghani S, Ben Ayed M, Alamori AM, Alghamdi GA, et al. Role of Serum Amyloid A as a Biomarker for Predicting the Severity and Prognosis of COVID-19. Journal of Immunology Research. 2022;2022. <u>doi:10.1155/2022/6336556</u>
- Abbas S, Hayat A, Majeed N, Jaffar SR, Asghar J, Ali S. Comparison of inflammatory markers with different levels of severity of COVID-19 disease. Pakistan Armed Forces Medical Journal. 2020;70(2):S455-58. DOI: N/A
- AbdelFattah EB, Madkour AM, Amer SM, Ahmed NO. Correlation between the serum level of ferritin and D-dimer and the severity of COVID-19 infection. The Egyptian Journal of Bronchology. 2023;17(1):1-11. doi:10.1186/s43168-023-00218-1
- Abdelhakam DA, Badr FM, El Monem Teama MA, Bahig Elmihi NM, El-Mohamdy MA. Serum amyloid A, ferritin and carcinoembryonic antigen as biomarkers of severity in patients with COVID-19. Biomedical Reports. 2022;16(2):1-3. <u>doi:10.3892/br.2021.1496</u>
- Abeid ST, Mezedawee AA, Alam YS. Exploring the influence of neutrophillymphocyte ratio on outcome prediction of severely-ill patients with covid-19. Wiad Lek. 2022;75(12):2926-32. *doi:10.36740/WLek202212106*
- Abrishami A, Eslami V, Arab-Ahmadi M, Alahyari S, Azhideh A, Sanei-Taheri M. Prognostic value of inflammatory biomarkers for predicting the extent of lung involvement and final clinical outcome in patients with COVID-19. Journal of Research in Medical Sciences. 2021;26(1):115. <u>doi:10.4103/jrms.JRMS_1160_20</u>
- Acar E, Demir A, Yıldırım B, Kaya MG, Gökçek K. The role of hemogram parameters and C-reactive protein in predicting mortality in COVID-19 infection. International journal of clinical practice. 2021;75(7):e14256. <u>doi:10.1111/ijcp.14256</u>

- Acehan S, Gülen M, ISİKBER C, Adem KA, Nurdan UN, Cagdas IN, et al. C-reactive protein to albumin ratio is associated with increased risk of mortality in COVID-19 pneumonia patients. Cukurova Medical Journal. 2021;46(4):1449-58. <u>doi:10.17826/cumj.977050</u>
- Adil M, Baig ZF, Amir M, Chatha SS, Habib A, Majid M. NEUTROPHIL TO LYMPHOCYTE RATIO VS PLATELETS TO LYMPHOCYTE RATIO: BIOMARKERS TO PREDICT SEVERITY OF DISEASE AND THEIR COMPARISON IN PATIENTS OF COVID-19. Pakistan Armed Forces Medical Journal. 2020;70(6):1609-5. doi:10.51253/pafmi.v70i6.5010
- Aditianingsih D, Soenarto RF, Puiantana AM, Pranata R, Lim MA, Raharja PA, et al. Dose response relationship between D-dimer level and mortality in critically ill COVID-19 patients: a retrospective observational study. F1000Research. 2023; 11:269. doi:10.12688%2Ff1000research.108972.2
- Ahmad Z, Zhetira R, Liana P, Bahar E. Correlation of Interleukin 6 Levels with C-Reactive Protein in Various Severity of Covid-19 Patients in Rsup Dr. Mohammad Hoesin Palembang. Journal of Medical and Health Studies. 2022;3(4):94-7. <u>doi:10.32996/jmhs.2022.3.4.14</u>
- Ahmed S, Ahmed ZA, Siddiqui I, Rashid NH, Mansoor M, Jafri L. Evaluation of serum ferritin for prediction of severity and mortality in COVID-19-A cross sectional study. Annals of medicine and Surgery. 2021;63:102163. doi:10.1016/j.amsu.2021.02.009
- Ayub Z, Ahmed A, Afzal F, Bashir S, Iqbal H, Nawaz KH. ROLE OF INTERLEUKIN-6 AND PROCALCITONIN AS INFLAMMATORY BIOMARKERS IN EVALUATING COVID-19 DISEASE SEVERITY ON HRCT CHESTAN EXPERIENCE AT CMH QUETTA. Pakistan Armed Forces Medical Journal. 2021;71(6):2131-34. doi:10.51253/pafmj.v71i6.6977
- Ahmed S, Ahmed ZA, Rashid NH, Mansoor M, Siddiqui I, Jafri L. Procalcitonin as a predictor of severity and mortality in a cohort of patients hospitalised with COVID-19. The Malaysian journal of pathology. 2021;43(3):375-80. DOI: N/A
- Ahmed AO, Rashed HA, Solyman AF, El-Kareem A, Doaa M. Inetrleukin-6 and C-reactive protein as predictors of mortality among critically ill COVID-19 patients in Assiut university hospitals (ICUs). Egypt J Immunol. 2022:29 (3):44-53. DOI: N/A
- Ahnach M, Zbiri S, Nejjari S, Ousti F, Elkettani C. C-reactive protein as an early predictor of COVID-19 severity. Journal of medical biochemistry. 2020;39(4):500-7. <u>doi:10.5937%2Fjomb0-27554</u>
- Akan OY, Bilgir O. Effects of neutrophil/monocyte, neutrophil/lymphocyte, neutrophil/platelet ratios and c-reactive protein levels on the mortality and intensive care need of the patients diagnosed with Covid-19. Eurasian Journal of Medicine and Investigation. 2021; 5 (1):21-6. doi:10.14744/ejmi.2021.14888
- Aksakal A, Kılıç AF, Tanülkü U, Tavacı T, Baygutalp NK. Interleukin-28 as a Promising Marker for Predicting Invasive Mechanical Ventilation Requirement and Mortality in COVID-19 Patients. Thoracic Research and Practice. 2023;24(2):61-65. doi:10.5152%2FThoracResPract.2023.22146
- Aksit M, Aksit MZ, Kazar M, Caliskan T, Senger SS, Akar H, et al. The relationship between ischemia-modified albumin/albumin ratio levels and disease severity in COVID-19 patients. International Journal of Medical Biochemistry. 2023;6(3): 143-149. doi:10.14744/ijmb.2023.74436
- Alaaluah RH, Al-Ani A, Lafi SA. Association of white blood cell counts, procalcitonin, C-reactive protein, interleukin-6, troponin, and ferritin with mortality in severe COVID-19. Journal of Emergency Medicine, Trauma & Acute Care. 2022;2022(6):9. <u>doi:10.5339/jemtac.2022.aimco.9</u>
- Al-Aghbari N, Maldar A, Angolkar M, Khurseed R, Shrestha S, Saikam P. Inflammatory Markers for Prognosis of COVID-19 Mortality in Hospitalized Indian Patients: A Single-Center Retrospective Study. University of Science and Technology Journal for Medical Sciences. 2023;1(1). <u>doi:10.59222/ustjms.1.1.A1</u>
- ALICI G, HARBALIOĞLU H, Omer GE, Allahverdiyev S, YILDIRIM A, Fahri ER, et al. High-sensitivity cardiac troponin I and D-dimer are risk factors for in-hospital mortality of adult patients with COVID-19: A retrospective cohort study. Ege Tıp Dergisi. 2021;60(2):113-20. doi:10.19161/etd.950576
- Allahverdiyev S, Quisi A, Harbahoğlu H, Alıcı G, Genç Ö, Yıldırım A, et al. The neutrophil to lymphocyte ratio and in-hospital all-cause mortality in patients with COVID-19. European Journal of Therapeutics. 2020;26(3):251-6. <u>doi:10.5152/eurjther.2020.20067</u>
- Almasaud AS, Chalabi J, Arfaj AA, Qarni AA, Alkroud A, Nagoor Z, et al. Association of serum zinc and inflammatory markers with the severity of covid-19 infection in adult patients. Nutrients. 2023;15(2):340. <u>doi:10.3390/nu15020340</u>
- Aminy RZ, Mudjanarko SW, Novida H. Correlation of Dynamic D-dimer Levels with Mortality in COVID-19 Patients with Type 2 Diabetes Mellitus. Gaceta Medica de Caracas. 2023;131:S121-S129. doi:10.47307/GMC.2023.131.s2.5

- Andriani I, Utariani A, Hanindito E, Airlangga PS. Correlation Between CRP II-6 Level, Severity and Mortality in Patients with Covid-19 Infection in Indonesia.2021;2 (4):618-27. <u>doi:10.51542/ijscia.v2i4.27</u>
- Antariksa B, Burhan E, Susanto AD, Alatas MF, Taufik FF, Sari DY, et al. Inflammatory Markers upon Admission as Predictors of Outcome in COVID-19 Patients. Jurnal Respirologi Indonesia. 2021;41(4):252-9. doi:10.36497/jri.v41i4.185
- Apriningsih H, Prabowo NA, Reviono R, Anindita BD, Myrtha R, Putri DP, et al. Correlation of Interleukin-6 Level with Neutrophil to Lymphocyte Ratio and Disease Severity in COVID-19 Patients. Global Medical & Health Communication (GMHC). 2023;11(1):51-6. <u>doi:10.29313/gmhc.v11i1.9643</u>
- Arbănaşi EM, Halmaciu I, Kaller R, Mureşan AV, Arbănaşi EM, Suciu BA, et al. Systemic inflammatory biomarkers and chest CT findings as predictors of acute limb ischemia risk, intensive care unit admission, and mortality in COVID-19 patients. Diagnostics. 2022;12(10):2379. doi:10.3390/diagnostics12102379
- Aripova TU, Askarov TA, Usarov AM, Ruzimurodov NF. Assessment of the Cytokine Profile in Patients with Covid-19 Depending on the Severity of the Disease. Central Asian Journal of Medical and Natural Science. 2022;3(6):217-22. <u>doi:10.17605/cajmns.v3i6.1198</u>
- Arsentieva NA, Liubimova NE, Batsunov OK, Korobova ZR, Kuznetsova RN, Rubinstein AA, et al. Predictive value of specific cytokines for lethal COVID-19 outcome. Инфекция и иммунитет. 2022;12(5):859-68. doi:10.15789/2220-7619-PVQ-2043
- Arshad AR, Khan I, Shahzad K, Arshad M, Haider SJ, Aslam MJ. Association of inflammatory markers with mortality in COVID-19 infection. Journal of the College of Physicians and Surgeons Pakistan. 2020;41(16.74):10-29271. doi:10.29271/jcpsp.2025.01.158
- Khadija AS, ABBAS F. Role of Neutrophil Lymphocyte Ratio (NLR) in Predicting Disease Severity in Covid-19. Turkish Journal of Internal Medicine.2022;4(1):6-12. <u>doi:10.46310/tjim.1011041</u>
- Astagimath M, Aryapu R, Patil V, Doddamani S. C-reactive protein and lactate dehydrogenase in intensive care unit and nonintensive care unit COVID-19 patients–A retrospective study. APIK Journal of Internal Medicine. 2023;11(1):33-6. doi:10.4103/ajim.ajim_18_22
- Atlas A, Altay N, Karahan MA, PEHLİVAN VF, Pehlivan B, Duran E, et al. Neutrophil-to-lymphocyte and fibrinogen-to-albumin ratios may be indicators of worse outcomes in ICU patients with COVID-19. Journal of Surgery and Medicine. 2021;5(6):623-7. <u>doi:10.28982/josam.930254</u>
- Awasthi S, Mittal A, Singh V, Kumar A, Ahmad F, Sharma N. Role of hematological and inflammatory markers in early diagnosis and severity of COVID-19 disease. Acta Medica International. 2022;9(1):73-7. doi:10.4103/amit.amit 39 22
- Ayalew G, Mulugeta B, Haimanot Y, Adane T, Bayleyegn B, Abere A. Neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio can predict the severity in COVID-19 patients from Ethiopia: a retrospective study. International Journal of General Medicine. 2022;15:7701. doi:10.2147%2fjgm.s383558
- BAHADIRLI S, Erdem KU. Predictive value of C-reactive protein/albumin ratio in predicting poor outcome of hospitalized patients with COVID-19. Journal of Health Sciences and Medicine. 2021;4(4):505-10. doi:10.32322/jhsm.945522
- Bal T, Dogan S, Cabalak M, Dirican E. Lymphocyte-to-C-reactive protein ratio may serve as an effective biomarker to determine COVID-19 disease severity. Turkish Journal of Biochemistry. 2021;46(1):23-8. <u>doi:10.1515/tjb-2020-0410</u>
- Balci U, Önder KD, Keskin AS. Evaluation of the relationship between lactate dehydrogenase/lymphocyte ratio with interleukin-6 levels in hospitalized patients with COVID-19. Mediterr J Infect Microb Antimicrob. 2021;10 (62). doi:10.4274/mjima.galenos.2021.2021.62
- Batool H, Khan MD, Chughtai OR, Chughtai AS, Ashraf S, Amir S. Correlation of inflammatory biomarkers with disease severity in hospitalised patients of COVID-19 at presentation. J Fatima Jinnah Med Univ.2021; 15:171-6. <u>doi:10.37018/SELQ5005</u>
- Bayram M, Yildirim O, S Ozmen R, Soylu B, Dundar AS, Koksal AR, et al. Prognostic Nutritional Index and CRP, age, platelet count, albumin level score in predicting mortality and intensive care unit admission for COVID-19. Biomarkers in Medicine. 2021;15(18):1733-40. <u>doi:10.2217/bmm-2021-</u> 0337
- Belaid B, Lamara Mahammad L, Mihi B, Rahali SY, Djidjeli A, Larab Z, et al. T cell counts and IL-6 concentration in blood of North African COVID-19 patients are two independent prognostic factors for severe disease and death. Journal of leukocyte biology. 2022;111(1):269-81. doi:10.1002/JLB.4COV.A1020-703R
- Bellan M, Azzolina D, Hayden E, Gaidano G, Pirisi M, Acquaviva A, et al. Simple parameters from complete blood count predict in-hospital mortality in COVID-19. Disease Markers. 2021; 2021:1-7. <u>doi:10.1155/2021/8863053</u>

- Bendardaf R, Bhamidimarri PM, Al-Abadla Z, Zein D, Alkhayal N, Georgy RR, Al Ali F, et al. Ferritin, blood urea nitrogen, and high chest CT score determines ICU admission in COVID-19 positive UAE patients: A single center retrospective study. PLoS One. 2022;17(7):e0269185. doi:10.1371/journal.pone.0269185
- Bergantini L, d'Alessandro M, Gangi S, Bianchi F, Cameli P, Perea B, et al. Predictive role of cytokine and adipokine panel in hospitalized COVID-19 patients: evaluation of disease severity, survival and lung sequelae. International Journal of Molecular Sciences. 2023;24(16):12994. doi:10.3390/ijms241612994
- Birben B, Birben OD, Akın T, Akkurt G, Surel AA, Yakısık E, et al. Efficacy of the delta neutrophil index in predicting 30-day mortality in COVID-19 patients requiring intensive care. International Journal of Clinical Practice. 2021;75(5):e13970. doi:10.1111/jjcp.13970
- BOMBACI E, SARAÇOĞLU K, ÇİYİLTEPE F, SARAÇOĞLU A, DEMİRHAN R. The Role of Inflammatory Markers in Predicting Mortality in Critical COVID-19 Patients: A Single-Center, Retrospective, Observational Study. Flora İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Dergisi. 2023;28(1):37-47. doi:10.5578/flora.20239903
- Le Borgne P, Abensur Vuillaume L, Alame K, Lefebvre F, Chabrier S, Berard L, et al. Do blood eosinophils predict in-hospital mortality or severity of disease in SARS-CoV-2 infection? A retrospective multicenter study. Microorganisms. 2021;9(2):334. <u>doi:10.3390/microorganisms9020334</u>
- Bozan O, Çekmen B, Atiş SE, Kocer MT, Senturk M, Karaaslan EB, et al. Prognostic value of neutrophil to lymphocyte ratio and platelet to lymphocyte ratio for mortality in patients infected with SARS-CoV-2. Ukrainian Journal of Nephrology and Dialysis. 2021;2 (70):13-18. <u>doi:10.31450/ukrjnd.2(70).2021.03</u>
- Çakırca TD, Çakırca G, Torun A, Bindal A, Üstünel M, Kaya A. Comparing the predictive values of procalcitonin/albumin ratio and other inflammatory markers in determining COVID-19 severity. Pakistan Journal of Medical Sciences. 2023;39(2):450-55. <u>doi:10.12669%2Fpjms.39.2.6856</u>
- Kesmez Can F, Özkurt Z, Öztürk N, Sezen S. Effect of IL-6, IL-8/CXCL8, IP-10/CXCL 10 levels on the severity in COVID 19 infection. International Journal of Clinical Practice. 2021;75(12):e14970. <u>doi:10.1111/ijcp.14970</u>
- Cardiero G, Palma D, Vano M, Anastasio C, Pinchera B, Ferrandino M, et al. Calprotectin levels and neutrophil count are prognostic markers of mortality in COVID-19 patients. Diagnostics. 2022 ;12(10):2554. doi:10.3390/diagnostics12102554
- Çelikkol A, Doğan M, Güzel C, Erdal B, Yılmaz A. A novel combined index of D-Dimer, Fibrinogen, Albumin, and Platelet (FDAPR) as mortality predictor of COVID-19. Nigerian Journal of Clinical Practice. 2022;25(9):1418-23. <u>doi:10.4103/njcp.njcp_1633_21</u>
- Vidal-Cevallos P, Higuera-De-La-Tijera F, Chavez-Tapia NC, Sanchez-Giron F, Cerda-Reyes E, Rosales-Salyano VH, Servin-Caamano A, Vazquez-Medina MU, Mendez-Sanchez N. Lactate-dehydrogenase associated with mortality in hospitalized patients with COVID-19 in Mexico: a multi-centre retrospective cohort study. Annals of hepatology. 2021;24:100338. doi:10.1016/j.aohep.2021.100338
- Chen PK, Yeo KJ, Chang SH, Liao TL, Chou CH, Lan JL, et al. The detectable anti-interferon-γ autoantibodies in COVID-19 patients may be associated with disease severity. Virology Journal. 2023;20(1):33. dio:10.1186/s12985-023-01989-1
- Chen Y, Han P, Gao Y, Jiang R, Tao M, Li X. The value of the neutrophil to lymphocyte ratio and PLT count for the diagnosis and prediction of COVID-19 severity. Plos one. 2023;18(10):e0293432. doi:10.1371/journal.pone.0293432
- Cheng A, Hu L, Wang Y, Huang L, Zhao L, Zhang C, et al. Diagnostic performance of initial blood urea nitrogen combined with D-dimer levels for predicting in-hospital mortality in COVID-19 patients. International journal of antimicrobial agents. 2020;56(3):106110. doi:10.1016/j.ijantimicag.2020.106110
- 77. Chiu KH, Yip CC, Poon RW, Leung KH, Li X, Hung IF, et al. Correlations of Myeloperoxidase (MPO), Adenosine deaminase (ADA), C–C motif chemokine 22 (CCL22), Tumour necrosis factor alpha (TNFa) and Interleukin-6 (IL-6) mRNA expression in the nasopharyngeal specimens with the diagnosis and severity of SARS-CoV-2 infections. Emerging microbes & infections. 2023;12(1):2157338. doi:10.1080/22221751.2022.2157338
- Chopra P, Sehgal T, Yadav R, Meena S, Maitra S, Soni KD, et al. A combination of inflammatory and hematological markers is strongly associated with the risk of death in both mild and severe initial disease in unvaccinated individuals with COVID-19 infection. EJIFCC. 2023;34(1):42-56. DOI: N/A
- Cinar C, Vural DG, Birinci A. EVALUATION OF INTERLEUKIN-18 AND INDUCTIVE PROTEIN-10 LEVELS AS BIOLOGICAL MARKERS RELATED TO THE SEVERITY OF COVID-19 DISEASE. Acta Medica. 2023; 39:545. doi:10.19193/0393-6384_2023_2_78

- Çölkesen F, Kurt EK, Vatansev H, Korkmaz C, Çölkesen F, Yücel F, Yıldız E, Evcen R, Aykan FS, Kılınç M, Aytekin G. Memory B cells and serum immunoglobulins are associated with disease severity and mortality in patients with COVID-19. Postgraduate medical journal. 2022;98(1164):765-71. doi:10.1136/postgradmedj-2021-140540
- Datta S, Maity B, Pradhan AK, Mozzaffar M, Chatterjee D, Roy S, et al. Role of Neutrophil Lymphocyte Ratio as a cheap prognostic marker in predicting disease Severity in COVID-19 patients in a resource constraint setting. European Journal of Cardiovascular Medicine. 2023;13(3). DOI: N/A
- Sanchez-de Prada L, Gorgojo-Galindo O, Fierro I, Martínez-García AM, de Quintana GS, Gutiérrez-Bustillo R, et al. Time evolution of cytokine profiles associated with mortality in COVID-19 hospitalized patients. Frontiers in immunology. 2022; 13:946730. <u>doi:10.3389/fimmu.2022.946730</u>
- Deng F, Zhang L, Lyu L, Lu Z, Gao D, Ma X, et al. Increased levels of ferritin on admission predicts intensive care unit mortality in patients with COVID-19. Medicina Clínica (English Edition). 2021;156(7):324-31. doi:10.1016/j.medcle.2020.11.015
- Deniz CD, Baran N, Ugur AR, Guneyk A, Ozcan M, Tuncez IH, et al. Evaluation of the relationship between C-reactive protein/albumin ratio and hospitalization in novel coronavirus disease 2019. International Journal of Medical Biochemistry. 2022;5(1)8-14. doi:10.14744/ijmb.2021.57070
- Devang N, Sreelatha S, BV M. Assessment of inflammatory markers and their association with disease mortality in severe COVID-19 patients of tertiary care hospital in South India. The Egyptian Journal of Bronchology. 2022;16(1):55. <u>doi:10.1186/s43168-022-00159-1</u>
- Haroon H, Acharya V, Unnikrishnan B, Mithra P, Mascarenhas C, Dhillon NS, et al. Predictive accuracy of neutrophil-to-lymphocyte ratio on severity and outcomes in COVID-19 patients: A retrospective study. Journal of Datta Meghe Institute of Medical Sciences University. 2022;17(Suppl 1):S15-20. doi:10.4103/jdmimsu.jdmimsu_154_22
- El-Desoky MM, Tharwat S, Mostafa N, Hewidy AA, Elmorsey RA, Abdelhafez MS, et al. Association of interleukin-17F polymorphism and mortality predictors with the risk of COVID-19. International journal of clinical practice. 2022;2022. <u>doi:10.1155/2022/4761631</u>
- El-Khattab SO, Abdelhamid AE, Abdalla Ibrahim W, Yousef Elsherif AI, Khalil GM. C-reactive protein as an early marker of severity and outcome in patients with SARS-CoV-2 infection. Egyptian Journal of Anaesthesia. 2023;39(1):95-9. <u>doi:10.1080/11101849.2023.2171545</u>
- Ergenç H, Ergenç Z, Usanmaz M, Gozdas HT. C-reactive protein and neutrophil–lymphocyte ratio as predictors of mortality in coronavirus disease 2019. Revista da Associação Médica Brasileira. 2021;67:1498-502. doi:10.1590/1806-9282.20210679
- Ergenç Z, Ergenç H, Araç S, Usanmaz M, Alkılınç E, Kaya G, et al. Novel biochemical prognostic indicators in COVID-19: Can CRP/albumin, urea/albumin, and LDH/albumin ratios be used to predict mortality and length of hospitalization? Novel biochemical prognostic indicators for COVID-19. Medical Science and Discovery. 2022;9(6):310-8. doi:10.36472/msd.v9i6.741
- Ergenc I, Capar E, Erturk SB, Bahramzade G, Atalah F, Kocakaya D, et al. Diagnostic performance of lactate dehydrogenase (LDH) isoenzymes levels for the severity of COVID-19. Journal of Medical Biochemistry. 2023;42(1):16-26. doi:10.5937%2fjomb0-37234
- Ertekin B, Acar T. The relationship between albumin and its proportion to other markers in predicting mortality in severe COVID-19 patients. European Review for Medical & Pharmacological Sciences. 2023;27(13): 6429-6436. doi: N/A
- Esa T, Budu B, Mulyono B, Soraya GV, Usman AN, Intansari US. Correlation of serum interleukin-6 levels and neutrophil-lymphocyte ratio in the severity of COVID-19. F1000Research. 2023;12: 1189. doi:10.12688%2ff1000research.132157.1
- 94. EvlíCe O, Fatiĥ KU, BEKTAŞ M. PREDICTIVE RELEVANCE OF DIFFERENT CLINICAL AND LABORATORY FINDINGS FOR HIGHER MORTALITY IN PATIENTS WITH COVID-19 IN A SINGLE CENTER COHORT: NEUTROPHIL/LYMPHOCYTE RATIO, HIGH CRP, GGT AND CREATININE LEVELS ARE ASSOCIATED WITH HIGH MORTALITY. Journal of Istanbul Faculty of Medicine. 2022;85(2):139-46. doi:10.26650/UUTFD.896789
- Făgărăşan I, Rusu A, Comşa H, Simu TD, Vulturar DM, Todea DA. IL-6 and neutrophil/lymphocyte ratio as markers of ICU admittance in SARS-CoV-2 patients with diabetes. International Journal of Molecular Sciences. 2023;24(19):14908. doi:10.3390/ijms241914908
- Falih ES, Obaid SH. Diagnostic utility of IL-6 and some biomarker correlated with the diseases severity of COVID-19 patients. Al-Nisour Journal for Medical Sciences.2022;4(2):24-35. DOI: N/A
- Feng T, James A, Doumlele K, White S, Twardzik W, Zahid K, et al. Procalcitonin levels in COVID-19 patients are strongly associated with mortality and ICU acceptance in an underserved, inner city population. Medicina. 2021;57(10):1070. <u>doi:10.3390/medicina57101070</u>

- Gadotti AC, de Castro Deus M, Telles JP, Wind R, Goes M, Ossoski RG, et al. IFN-γ is an independent risk factor associated with mortality in patients with moderate and severe COVID-19 infection. Virus research. 2020; 289:198171. doi:10.1016/j.virusres.2020.198171
- Gatselis NK, Lygoura V, Lyberopoulou A, Giannoulis G, Samakidou A, Vaiou A, et al. Soluble IL-2R levels at baseline predict the development of severe respiratory failure and mortality in COVID-19 patients. Viruses. 2022;14(4):787. <u>doi:10.3390/v14040787</u>
- Geraili Z, Hajian-Tilaki K, Bayani M, Hosseini SR, Khafri S, Ebrahimpour S, et al. Prognostic accuracy of inflammatory markers in predicting risk of ICU admission for COVID-19: application of time-dependent receiver operating characteristic curves. Journal of International Medical Research. 2022;50(6):03000605221102217. <u>doi:10.1177/03000605221102217</u>
- 101. Ghorbaninezhad F, Bakhshivand M, Saeedi H, Alizadeh N. The Association of Elevated Levels of LDH and CK-MB with Cardiac Injury and Mortality in COVID-19 Patients. ImmunoAnalysis. 2022;2(1):8. <u>doi:i10.34172/ia.2022.08</u>
- 102. Gjuzelova AA, Nakova VV, Nanovic Z, Metodieva M, Stojkoska AJ, Camurovski N, et al. Association of Inflammatory Markers with Disease Severity and Outcome in Covid-19 Patients. Prilozi. 2023;44(1):89-95. DOI: N/A
- 103. Gohda T, Murakoshi M, Suzuki Y, Hiki M, Naito T, Takahashi K, et al. Circulating tumor necrosis factor receptors are associated with mortality and disease severity in COVID-19 patients. Plos one. 2022;17(10):e0275745. doi:10.1371/journal.pone.0275745
- 104. Gopalakrishnan S, Krishnan B, Krishnan MS, Kandasamy S, Hameed PM, Karunakaran V. The prognostic role of inflammatory markers in COVID-19 patients: A retrospective analysis in a tertiary care hospital of southern India. Journal of Current Research in Scientific Medicine. 2022;8(2):108-15. doi:10.4103/jcrsm.jcrsm 4_22
- 105. Gormez S, Ekicibasi E, Degirmencioglu A, Paudel A, Erdim R, Gumusel HK, et al. Association between renin-angiotensin-aldosterone system inhibitor treatment, neutrophil-lymphocyte ratio, D-Dimer and clinical severity of COVID-19 in hospitalized patients: a multicenter, observational study. Journal of Human Hypertension. 2021;35(7):588-97. <u>doi:10.1038/s41371-020-00405-3</u>
- 106. Hachim IY, Hachim MY, Hannawi H, Naeem KB, Salah A, Hannawi S. The inflammatory biomarkers profile of hospitalized patients with COVID-19 and its association with patient's outcome: A single centered study. PLoS One. 2021;16(12):e0260537. doi:10.1371/journal.pone.0260537
- 107. Hafeez MM, Khan MT, Shakoori TA, Mahmood W, Khalid MS, Rana MA, et al. Assessment of Inflammatory Biomarkers as Predictor of Mortality in COVID-19 Patients. Pakistan Journal of Medical & Health Sciences. 2022;16(04):343-45. <u>doi:10.53350/pjmhs22164343</u>
- 108. Halmaciu I, Arbănaşi EM, Kaller R, Mureşan AV, Arbănaşi EM, Bacalbasa N, et al. Chest CT Severity Score and Systemic Inflammatory Biomarkers as Predictors of the Need for Invasive Mechanical Ventilation and of COVID-19 Patients' Mortality. Diagnostics. 2022;12(9):2089. doi:10.3390/diagnostics12092089
- Hammad R, Eldosoky MA, Fouad SH, Elgendy A, Tawfeik AM, Alboraie M et al. Circulating cell-free DNA, peripheral lymphocyte subsets alterations and neutrophil lymphocyte ratio in assessment of COVID-19 severity. Innate Immunity. 2021;27(3):240-50. <u>doi:10.1177/1753425921995577</u>
- 110. Yu HH, Qin C, Chen M, Wang W, Tian DS. D-dimer level is associated with the severity of COVID-19. Thrombosis research. 2020;195:219-25. <u>doi:10.1016/j.thromres.2020.07.047</u>
- 111. Haroun RA, Osman WH, Eessa AM. Interferon-γ-induced protein 10 (IP-10) and serum amyloid A (SAA) are excellent biomarkers for the prediction of COVID-19 progression and severity. Life Sciences. 2021; 269:119019. doi:10.1016/j.lfs.2021.119019
- 112. Harsini Harsini, Jatu Aphridasari, Artrien Adhiputri, Agung Prasetyo, Hie Sukiyanto, Aditya Sri Listyoko. Interleukin-6 and Neutrophil–Lymphocyte Ratio in Predicting Outcome of Confirmed COVID-19 Patients. J Respi May;9(2):108-116. <u>doi:10.20473/jr.v9-1.2.2023.108-116</u>
- 113. Hasanah U, Kartini A, Abd Kadir N, Abdullah AA. Lactate Dehydrogenase Levels as A Marker of COVID-19 Severity. INDONESIAN JOURNAL OF CLINICAL PATHOLOGY AND MEDICAL LABORATORY. 2022;29(1):81-5. doi:10.24293/ijcpml.v29i1.1910
- 114. Hasegawa T, Hato T, Okayama T, Ikeo K, Miyamoto Y, Iwanaga N, et al. Th1 cytokine endotype discriminates and predicts severe complications in COVID-19. European Cytokine Network. 2022 Jun;33(2):1-2. doi:10.1684/ecn.2022.0477
- 115. Hassan AE, Nosair NA, Ahmed MH, Sherif DE, Habib EM, Farahat N. Relation Between Interleukin-6, Interleukin-10 And Interleukin-2 Receptor and Mortality In Severely III COVID-19 Patients. JPMA. The Journal of the Pakistan Medical Association. 2023;73(4):S179-83. <u>doi:10.47391/jpma.egvs4-36</u>

- 116. Hassan A, Ali ZU, Iftikhar HI, GRADED A, HAIDER Z, REHMAN HU. An emerging marker predicting the severity of Covid-19: neutrophil-lymphocyte count ratio. PJMHS. 2021;15:3398-9. <u>doi:10.53350/pjmhs2115113398</u>
- 117. Yavuz OT, AVCIOĞLU G. Comparison of amylase, lipase and d-dimer levels in the etiopathogenesis of mortality in Covid 19 pneumonia. Cumhuriyet Medical Journal. 2022;44(1):117-24. <u>doi:10.7197/cmj.1053522</u>
- 118. Hilda F, Liana P, Nurtjahyo A, Hudari H, Sari NP, Umar TP, et al. D-dimer as a sensitive biomarker of survival rate in patients with COVID-19. The Eurasian Journal of Medicine. 2022;54(3):219. <u>doi:10.5152%2Feurasianjmed.2022.21145</u>
- 119. Hosseinzadeh M, Pouladzadeh M, Eftekhar A, Choghakabodi PM, Sokooti A. Evaluation of D-dimer as a predictor of severity, degree of pulmonary involvement and mortality in patients with COVID-19. Scientia Medica. 2022;32(1):e43281. doi:N/A
- 120. Huang Y, Lyu X, Li D, Wang L, Wang Y, Zou W, et al. A cohort study of 676 patients indicates D-dimer is a critical risk factor for the mortality of COVID-19. PloS one. 2020;15(11):e0242045. doi:10.1371/journal.pone.0242045
- 121. Huyut MT, Huyut Z. Effect of ferritin, INR, and D-dimer immunological parameters levels as predictors of COVID-19 mortality: A strong prediction with the decision trees. Heliyon. 2023;9(3):e14015. doi:10.1016/j.heliyon.2023.e14015
- 122. Isbaniah F, Juliani T, Damayanti T, Yenita D, Yunus F, Antariksa B, et al. The Role of Neutrophil-Lymphocyte Ratio (NLR), Platelet-Lymphocyte Ratio (PLR), and D-Dimer in Predicting the Outcome of Confirmed COVID-19 patients. Jurnal Respirologi Indonesia. 2021;41(4):236-44. doi:10.36497/jri.v41i4.215
- 123. Islam MM, Islam S, Ahmed R, Majumder M, Sarkar B, Himu MER, et al. Reduced IFN-y levels along with changes in hematologic and immunologic parameters are key to COVID-19 severity in Bangladeshi patients. Exp Hematol. 2023; 118:53-64.e1. <u>doi:10.1016/j.exphem.2022.11.006</u>
- 124. Jang HJ, Leem AY, Chung KS, Ahn JY, Jung JY, Kang YA, et al. Soluble IL-2R levels predict in-hospital mortality in COVID-19 patients with respiratory failure. Journal of Clinical Medicine. 2021;10(18):4242. <u>doi:10.3390/jcm10184242</u>
- 125. Javed MW, Anwar M, Bangash TM, Satti RU, Rehman M, Malik UI. C-REACTIVE PROTEIN LEVELS AND THE SEVERITY OF COVID-19. Pakistan Armed Forces Medical Journal. 2020;70(2): S603-07. DOI: N/A
- 126. Marcos-Jiménez A, Sánchez-Alonso S, Alcaraz-Serna A, Esparcia L, López-Sanz C, Sampedro-Núñez M, et al. Deregulated cellular circuits driving immunoglobulins and complement consumption associate with the severity of COVID-19 patients. European Journal of Immunology. 2021;51(3):634-47. doi:10.1002/eji.202048858
- 127. Jin Z, Zheng M, Shi J, Ye X, Cheng F, Chen QL, et al. Correlation analysis between serum uric acid, prealbumin level, lactate dehydrogenase, and severity of COVID-19. Frontiers in Molecular Biosciences. 2021; 8:615837. <u>doi:10.3389/fmolb.2021.615837</u>
- 128. Fu J, Huang PP, Zhang S, Yao QD, Han R, Liu HF, et al. The value of serum amyloid A for predicting the severity and recovery of COVID-19. Experimental and therapeutic medicine. 2020;20(4):3571-7. <u>doi:10.3892/etm.2020.9114</u>
- 129. Kalyon S, Gültop F, Şimşek F, Adaş M. Relationships of the neutrophillymphocyte and CRP-albumin ratios with the duration of hospitalization and fatality in geriatric patients with COVID-19. Journal of International Medical Research. 2021;49(9):03000605211046112. doi:10.1177/03000605211046112
- 130. Katkat F, Kalyoncuoglu M, Karahan S, Ozcan S, Tasdemir ZA, Kucuk SH, et al. The Predictive Ability of the C-reactive Protein to Albumin Ratio As A Mortality Predictor in Hospitalized Severe SARS-CoV-2 Infected Patients with Cardiovascular Diseases. Medical Bulletin of Haseki/Haseki Tip Bulteni. 2022;60(2): 152-160. doi:N/A
- 131. Kaya T, Yaylaci S, Nalbant A, Yıldırım İ, Kocayiğit H, Çokluk E, et al. Serum calprotectin as a novel biomarker for severity of COVID-19 disease. Irish Journal of Medical Science (1971-). 2021;191:1-6. <u>doi:10.1007/s11845-021-02565-8</u>
- 132. Khan H, Khan S, Riaz H, Khattak AR. Prognostic Factors and Association of Inflammatory Biomarkers with Severity and Mortality in COVID-19. Journal of Bahria University Medical and Dental College. 2022;12(01):25-30. <u>doi:10.51985/JBUMDC054</u>
- 133. Khurshid F, Mumtaz M, Iqbal S. Evaluation of Liver Function Tests (LFT) and C-reactive protein in COVID-19 (SARS Cov-2) positive patients diagnosed by Real-time PCR. Pakistan Journal of Medical & Health Sciences. 2022;16(12):170. <u>doi:10.53350/pimhs20221612170</u>
- Kilic M, Hokenek UD. Association between D-dimer and mortality in COVID-19 patients: a single center study from a Turkish hospital. Disaster and Emergency Medicine Journal. 2022;7(4):225-30. doi:10.5603/DEMJ.a2022.0039

- 135. Kılıç M, Ak R, Alışkan H. The utility of hemoglobin, albumin, lymphocyte and platelet (HALP) score in predicting mortality among COVID-19 patients: a preliminary study. Signa Vitae. 2023;19(1):143-7. doi:10.22514/sv.2022.080
- Kim SY, Hong DY, Kim JW, Park SO, Lee KR, Baek KJ. Predictive values of procalcitonin and presepsin for acute kidney injury and 30-day hospital mortality in patients with COVID-19. Medicina. 2022;58(6):727. doi:10.3390/medicina58060727
- 137. Kocyigit A, Sogut O, Durmus E, Kanimdan E, Guler EM, Kaplan O, et al. Circulating furin, IL-6, and presepsin levels and disease severity in SARS-CoV-2–infected patients. Science progress. 2021;104(2_suppl):00368504211026119. doi:10.1177/00368504211026119
- 138. Küçük B, Kocabeyoğlu GM, ÖZEN SB, KOSOVALI BD, Mutlu NM, ÇAKIR EY, et al. Prognostic marker for mortality of COVID-19 patients in the intensive care unit: the delta neutrophil index. Kastamonu Medical Journal. 2022;2(3):63-7. <u>doi:10.51271/KMJ-0057</u>
- Küçükceran K, Ayranci MK, Girişgin AS, Koçak S. Predictive value of Ddimer/albumin ratio and fibrinogen/albumin ratio for in-hospital mortality in patients with COVID-19. International Journal of Clinical Practice. 2021;75(7):e14263. doi:10.1111/jjcp.14263
- 140. Kuizon BA, Damian K, Villanueva III E. Baseline Complete Blood Count and Cell Population Data as Prognostic Markers for In-Hospital Mortality among COVID-19 Patients admitted at the Philippine General Hospital from March 2020 to January 2022. PJP. 2023;8(1):13-20. doi:10.21141/PJP.2023.04
- 141. Kumari S, Nayak S, Tripathy S, Bhuniya S, Mangaraj M, Ramadass B, et al. Analysis of biochemical and inflammatory markers for predicting COVID-19 severity: insights from a tertiary healthcare institution of eastern India. Cureus. 2023;15(1): 33893. <u>doi:10.7759/cureus.33893</u>
- 142. Kurri N, Tyagi B, Singhal E, Gupta N, Agarwal AK, Gupta V, et al. Assessing the impact of inflammatory markers and CT severity score on disease severity of COVID-19 patients admitted to ICU at a tertiary hospital. Journal of the Association of Physicians of India. 2021; 69:41-9. DOI: N/A
- 143. Kwon JS, Kim JY, Kim MC, Park SY, Kim BN, Bae S, et al. Factors of severity in patients with COVID-19: cytokine/chemokine concentrations, viral load, and antibody responses. The American journal of tropical medicine and hygiene. 2020;103(6):2412. <u>doi:10.4269%2Fajtmh.20-1110</u>
- 144. Lashin AH, El-Ghafar A, Osama A, Mahmoud AM, Shewi E, El Sayed M. Value of Interleukin 6 in Assessment of the Disease Severity in Patients with COVID-19 Infection without Preexisting Comorbidities. Benha Medical Journal. 2023;40(Annual conference issue):74-86. doi:10.21608/bmfj.2023.185224.1738
- 145. Lee GH, Park M, Hur M, Kim H, Lee S, Moon HW, et al. Utility of Presepsin and Interferon-λ3 for Predicting Disease Severity and Clinical Outcomes in COVID-19 Patients. Diagnostics. 2023;13(14):2372. doi:10.3390/diagnostics13142372
- 146. Lee S, Lee JM, Choi T, Park K, Lee KY, young Jang J. Procalcitonin as a Predictive Factor for the Clinical Outcome of Patients with Coronavirus Disease 2019. Journal of Acute Care Surgery. 2022;12(2):53-62. doi:10.17479/jacs.2022.12.2.53
- 147. Li J, Li M, Zheng S, Li M, Zhang M, Sun M, et al. Plasma albumin levels predict risk for nonsurvivors in critically ill patients with COVID-19. Biomarkers in Medicine. 2020;14(10):827-37. <u>doi:10.2217/bmm-2020-0254</u>
- Lino K, Guimarães GM, Alves LS, Oliveira AC, Faustino R, Fernandes CS, et al. Serum ferritin at admission in hospitalized COVID-19 patients as a predictor of mortality. Brazilian Journal of Infectious Diseases. 2021;25:101569. doi:10.1016/j.bjid.2021.101569
- 149. Liu QQ, Cheng A, Wang Y, Li H, Hu L, Zhao X, et al. Cytokines and their relationship with the severity and prognosis of coronavirus disease 2019 (COVID-19): a retrospective cohort study. BMJ open. 2020;10(11):e041471. <u>doi:10.1136/bmjopen-2020-041471</u>
- 150. Liu L, Zheng Y, Cai L, Wu W, Tang S, Ding Y, et al. Neutrophil-tolymphocyte ratio, a critical predictor for assessment of disease severity in patients with COVID-19. International journal of laboratory hematology. 2021;43(2):329-35. <u>doi:10.1111/jjlh.13374</u>
- 151. Luo M, Liu J, Jiang W, Yue S, Liu H, Wei S. IL-6 and CD8+ T cell counts combined are an early predictor of in-hospital mortality of patients with COVID-19. JCI insight. 2020;5(13): e139024. doi:10.1172%2Fjci.insight.139024
- Mahmood N, Riaz Z, Tariq H, Altaf F, Sattar A, Ijaz S, et al. White blood count and inflammatory markers in the patients with COVID-19 infection and severity of illness. The Professional Medical Journal. 2022;29(12):1755-9. doi:10.29309/TPMJ/2022.29.12.7226
- 153. Merza MY, Hwaiz RA, Hamad BK, Mohammad KA, Hama HA, Karim AY. Analysis of cytokines in SARS-CoV-2 or COVID-19 patients in Erbil city, Kurdistan Region of Iraq. Plos one. 2021;16(4):e0250330. doi:10.1371/journal.pone.0250330

- 154. Martinez Mesa A, Cabrera César E, Martín-Montañez E, Sanchez Alvarez E, Lopez PM, Romero-Zerbo Y, et al. Acute lung injury biomarkers in the prediction of COVID-19 severity: Total thiol, ferritin and lactate dehydrogenase. Antioxidants. 2021;10(8):1221. doi:10.3390/antiox10081221
- Adnan Mezher M, Bahjat Alrifai S, Mahmood Raoof W. Analysis of proinflammatory cytokines in COVID-19 patients in Baghdad, Iraq. Archives of Razi Institute. 2023;78(1):305-13. doi:10.22092/ari.2022.359356.2411
- 156. Milenkovic M, Hadzibegovic A, Kovac M, Jovanovic B, Stanisavljevic J, Djikic M, et al. D-dimer, CRP, PCT, and IL-6 levels at admission to ICU can predict in-hospital mortality in patients with COVID-19 pneumonia. Oxidative medicine and cellular longevity. 2022;2022. doi:10.1155/2022/8997709
- 157. Mizrak S, Ozdemir A, Aladag E, Tayyar N. The roles of bun/d-dimer and bun/lactate ratios in indicating mortality in intensive care patients with COVID-19. Annals of Clinical and Analytical Medicine. 2022:1224-8. <u>doi:10.4328/ACAM.21260</u>
- Fathy MM, Aljarallah AN, Doudar NA, Ryad HR, Senosy SA, Ahmed DM, et al. Neutrophil-and platelet-lymphocyte ratios as valuable prognostic biomarkers in ICU COVID-19 patients. Egyptian Journal of Medical Research. 2023;4(4):78-93. doi:10.21608/ejmr.2022.138155.1229
- 159. Mohammadshahi J, Ghobadi H, Matinfar G, Boskabady MH, Aslani MR. Role of lipid profile and its relative ratios (cholesterol/HDL-C, triglyceride/HDL-C, LDL-C/HDL-C, WBC/HDL-C, and FBG/HDL-C) on admission predicts in-hospital mortality COVID-19. Journal of Lipids. 2023;2023. <u>doi:10.1155/2023/6329873</u>
- 160. Moisa E, Corneci D, Negoita S, Filimon CR, Serbu A, Negutu MI, et al. Dynamic changes of the neutrophil-to-lymphocyte ratio, systemic inflammation index, and derived neutrophil-to-lymphocyte ratio independently predict invasive mechanical ventilation need and death in critically ill COVID-19 patients. Biomedicines. 2021;9(11):1656. doi:10.3390/biomedicines9111656
- 161. Monserrat J, Gómez-Lahoz A, Ortega MA, Sanz J, Muñoz B, Arévalo-Serrano J, et al. Role of innate and adaptive cytokines in the survival of COVID-19 patients. International journal of molecular sciences. 2022;23(18):10344. doi:10.3390/ijms231810344
- Morfi CW, Sabri YS, Mizarti D. Differences in IL-6 Levels Based on Clinical Severity and Outcome of COVID-19 Patients at Dr. M. Djamil Hospital. Respiratory Science. 2023;4(1):1-4. <u>doi:10.36497/respirsci.v4i1.94</u>
- 163. Mortaz E, Jamaati H, Roofchayee ND, Sheikhzade H, Mirenayat M, Sadeghi M, et al. Decreased serum levels of angiotensin converting enzyme (ACE) 2 and enhanced cytokine levels with severity of COVID-19: normalisation upon disease recovery. Heliyon. 2022;8(2): e08957. doi:10.1016/j.heliyon.2022.e08957
- 164. Mureşan AV, Hălmaciu I, Arbănaşi EM, Kaller R, Arbănaşi EM, Budişcă OA, et al. Prognostic nutritional index, controlling nutritional status (CONUT) score, and inflammatory biomarkers as predictors of deep vein thrombosis, acute pulmonary embolism, and mortality in COVID-19 patients. Diagnostics. 2022;12(11):2757. <u>doi:10.3390/diagnostics12112757</u>
- 165. Naqvi SS, Phulpoto AH, Memon AQ, Channo MA, Mangi MR, Maher A. Association of mortality and raised inflammatory markers such as serum LDH, serum ferritin and CRP in hospitalized patient with COVID-19 infection. P J M H S. 2021; 42:17-84. doi: N/A
- 166. Avila-Nava A, Cortes-Telles A, Torres-Erazo D, López-Romero S, Aké RC, Solis AL. Serum IL-6: A potential biomarker of mortality among SARS-CoV-2 infected patients in Mexico. Cytokine. 2021;143:155543. doi:10.1016/j.cyto.2021.155543
- 167. NAZNIN L, GITI S, KHAN A, AKTER Y, PARVIN M, SULTANA S. Evaluation of Serum Ferritin in Hospitalized Patients with COVID-19 as A Potential Biomarker for Assessing COVID-19 Severity. Journal of Bangladesh College of Physicians and Surgeons. 2021;39(4):220-24. <u>doi:10.3329/jbcps.v39i4.55942</u>
- Nazri NA, Azman WN, Musa N, Ismail TS, Harun A, Yaacob NM, et al. Creactive Protein, Albumin, Urea, CRP/Albumin Ratio, and Urea/Albumin Ratio: A Retrospective Evaluation in COVID-19 Patients. Malaysian Journal of Medicine & Health Sciences. 2023;19(6):164-70. doi:10.47836/mjmhs.19.6.22
- 169. Marzieh N, Khojasteh SS, Majid NA. Evaluation of serum levels of IL-6 and adiponectin in COVID-19 patients and their relationship with disease severity. Инфекция и иммунитет. 2022;12(3):511-8. <u>doi:10.15789/2220-7619-eos-1783</u>
- 170. Nurhayatun E, Prabowo NA, Harioputro DR, Putranto W, Indarto D, Purvanto B. Neutrophil to lymphocyte ratio and Hs-CRP predict mortality in COVID-19 patients. Advances in Health Sciences Research; Proceedings of the 4th International Conference on Sustainable Innovation 2020–Health Science and Nursing (ICoSIHSN 2020). 2021;33: 80-82. doi:10.2991/ahsr.k.210115.016

- 171. Oguz EG, Yeter HH, Akcay OF, Besli S, Selen T, Derici U, et al. Predictive value of neutrophil-to-lymphocyte ratio in terms of need for intensive care unit and mortality in maintenance hemodialysis patients with COVID-19. Hemodialysis International. 2022;26(3):377-85. <u>doi:10.1111/hdi.13001</u>
- 172. Oliveira DC, Spiri BS, Schluga YC, Justus JL, Lopes Neto FD, Azambuja AP. Evaluation of lymphocyte count, T-cell subsets and neutrophil-to-lymphocyte ratio as early predictors for severity and outcome of COVID-19 disease-a report from a highly complex hospital in Brazil. Hematology, Transfusion and Cell Therapy. 2023; 45:330-7. doi:10.1016/j.htct.2022.05.007
- 173. Olivieri F, Sabbatinelli J, Bonfigli AR, Sarzani R, Giordano P, Cherubini A, et al. Routine laboratory parameters, including complete blood count, predict COVID-19 in-hospital mortality in geriatric patients. Mechanisms of Ageing and Development. 2022; 204:111674. doi:10.1016/j.mad.2022.111674
- 174. Onuk S, Sipahioğlu H, Karahan S, Yeşiltepe A, Kuzugüden S, Karabulut A, et al. Cytokine levels and severity of illness scoring systems to predict mortality in COVID-19 infection. Healthcare .2023;11 (3):387. doi:10.3390/healthcare11030387
- 175. Tural Onur S, Altın S, Sokucu SN, Fikri BI, Barça T, Bolat E, et ak. Could ferritin level be an indicator of COVID-19 disease mortality?. Journal of medical virology. 2021;93(3):1672-7. <u>doi:10.1002/jnv.26543</u>
- 176. Özdemir S, Algin A. Evaluation of the ability of the C-reactive protein-toalbumin ratio to predict short-term mortality in patients with COVID-19. Journal of Clinical Medicine of Kazakhstan. 2021;18(6):35-9. <u>doi:10.23950/jcmk/11324</u>
- Özdemir S, Altunok İ. Comparison of the predictive ability of the blood urea nitrogen/albumin, C-reactive protein/albumin, and lactate/albumin ratios for short-term mortality in SARS-CoV-2-infected patients. Avicenna Journal of Medicine. 2023;13(01):043-8. doi:10.1055/s-0043-1761471
- Ozdin M, Kaya H, Gulacti U, Lok U, Kafadar H, Yucetas C. The diagnostic value of neutrophil to lymphocyte ratio in determining the severity of COVID-19. IMC J Med Sci. 2022;16(1):1-7. <u>doi:10.55010/imcjms.16.001</u>
- Ozger HS, Karakus R, Kuscu EN, Bagriacik UE, Oruklu N, Yaman M, et al. Serial measurement of cytokines strongly predict COVID-19 outcome. PloS one. 2021;16(12):e0260623. <u>doi:10.1371/journal.pone.0260623</u>
- 180. Ozsurekci Y, Aykac K, Er AG, Halacli B, Arasli M, Oygar PD, et al. Predictive value of cytokine/chemokine responses for the disease severity and management in children and adult cases with COVID-19. Journal of medical virology. 2021;93(5):2828-37. <u>doi:10.1002/jmv.26683</u>
- 181. Pál K, Molnar AA, Huţanu A, Szederjesi J, Branea I, Timár Á, et al. Inflammatory biomarkers associated with in-hospital mortality in critical COVID-19 patients. International Journal of Molecular Sciences. 2022;23(18):10423. doi:10.3390/ijms231810423
- Ergenç H, Ergenç Z, Usanmaz M, Gozdas HT. C-reactive protein and neutrophil–lymphocyte ratio as predictors of mortality in coronavirus disease 2019. Revista da Associação Médica Brasileira. 2021;67:1498-502. doi:10.1590/1806-9282.20210679
- 183. Paranga TG, Pavel-Tanasa M, Constantinescu D, Plesca CE, Petrovici C, Miftode IL, et al. Comparison of C-reactive protein with distinct hyperinflammatory biomarkers in association with COVID-19 severity, mortality and SARS-CoV-2 variants. Frontiers in immunology. 2023; 14:1213246. doi:10.3389/fimmu.2023.1213246
- Parimoo A, Biswas A, Baitha U, Gupta G, Pandey S, Ranjan P, et al. Dynamics of inflammatory markers in predicting mortality in COVID-19. Cureus. 2021;13(10):19080. <u>doi:10.7759%2fcureus.19080</u>
- Peng F, Yi Q, Zhang Q, Deng J, Li C, Xu M, et al. Performance of D-dimer to lymphocyte ratio in predicting the mortality of COVID-19 patients. Frontiers in Cellular and Infection Microbiology. 2022; 12:1053039. doi:10.3389/fcimb.2022.1053039
- 186. Phan F, Boussouar S, Lucidarme O, Zarai M, Salem JE, Kachenoura N, et al. Cardiac adipose tissue volume and IL-6 level at admission are complementary predictors of severity and short-term mortality in COVID-19 diabetic patients. Cardiovascular diabetology. 2021;20:1-10. <u>doi:10.1186/s12933-021-01327-1</u>
- 187. Pirsalehi A, Salari S, Baghestani A, Vahidi M, Khave LJ, Akbari ME, et al. Neutrophil-to-lymphocyte ratio (NLR) greater than 6.5 may reflect the progression of COVID-19 towards an unfavorable clinical outcome. Iranian Journal of Microbiology. 2020;12(5):466. doi:10.18502%2Fijm.v12i5.4609
- Pramana IM, Herawati S, Purnamasidhi CA, Mulyantari NK, Lestari AW, Wande IN. Eosinophil count, neutrophil-to-lymphocyte ratio, and pentraxin-3 level as predictors of clinical severity in SARS-CoV-2 patients. Bali Journal of Anesthesiology. 2022;6(1):21-5. <u>doi:10.4103/bjoa.bjoa.122_21</u>
- 189. Prebensen C, Lefol Y, Myhre PL, Lüders T, Jonassen C, Blomfeldt A, et al. Longitudinal whole blood transcriptomic analysis characterizes neutrophil activation and interferon signaling in moderate and severe COVID-19. Scientific reports. 2023;13(1):10368. <u>doi:10.1038/s41598-023-37606-y</u>
- Putra YA, Mutiara M. The Difference Coagulopathy Factor and Interleukin-6 between Survival and Non-survival Patients COVID-19. Open Access

Macedonian Journal of Medical Sciences. 2022;10(B):873-6. doi:10.3889/oamjms.2022.9112

- 191. Rahayu R, Winarto W, Nasihun T. Interleukin-6 and C-reactive Protein on Admission as Predictor of Mortality in Severe COVID-19 Patients: A Retrospective Cohort Study. Open Access Macedonian Journal of Medical Sciences. 2022;10(B):227-31. <u>doi:10.3889/oamjms.2022.7968</u>
- 192. Rai DK, Ranjan A, Pandey SK, Vardhan H. Association of inflammatory markers, neutrophil-lymphocyte ratio, and D-dimer with mortality in COVID-19 infection: A hospital-based retrospective analysis. Journal of Applied Sciences and Clinical Practice. 2023;4(2):79-85. doi:10.4103/jascp.jascp_4_22
- 193. Raman N, Kv P, Ashta KK, Vardhan V, Thareja S, Kumar A. Ferritin and hemoglobin as predictors of fatal outcome in COVID-19: two sides of the same coin. J Assoc Physicians India. 2021;69(8):11-2. doi: N/A
- 194. Rasyid H, Sangkereng A, Harjianti T, Soetjipto AS. Impact of age to ferritin and neutrophil-lymphocyte ratio as biomarkers for intensive care requirement and mortality risk in COVID-19 patients in Makassar, Indonesia. Physiological Reports. 2021;9(10):e14876. <u>doi:10.14814/phv2.14876</u>
- 195. Rehman HU, Nukrich RS, Ahmed MA, Dilawar SM, Shalim E. Evaluation of Neutrophil Percentage to Albumin Ratio as Predictor of Mortality in Patients with Covid-19. Pakistan Journal of Medical & Health Sciences. 2023;17(02):327. <u>doi:10.53350/pjmhs2023172327</u>
- 196. Rizo-Tellez SA, Mendez-Garcia LA, Rivera-Rugeles AC, Miranda-Garcia M, Manjarrez-Reyna AN, Viurcos-Sanabria R, et al. The combined use of cytokine serum values with laboratory parameters improves mortality prediction of COVID-19 patients: The interleukin-15-to-albumin ratio. Microorganisms. 2021;9(10):2159. <u>doi:10.3390/microorganisms9102159</u>
- 197. Ortega-Rojas S, Salazar-Talla L, Romero-Cerdán A, Soto-Becerra P, Díaz-Vélez C, Urrunaga-Pastor D, et al. The neutrophil-to-lymphocyte ratio and the platelet-to-lymphocyte ratio as predictors of mortality in older adults hospitalized with COVID-19 in Peru. Disease Markers. 2022;2022. doi:10.1155/2022/2497202
- 198. Moreira-Rosário A, Marques C, Pinheiro H, Araújo JR, Ribeiro P, Rocha R, Mota I, et al. Gut microbiota diversity and C-reactive protein are predictors of disease severity in COVID-19 patients. Frontiers in Microbiology. 2021; 12:705020. <u>doi:10.3389/[micb.2021.705020</u>
- 199. Sakthivadivel V, Bohra GK, Maithilikarpagaselvi N, Khichar S, Meena M, Palanisamy N, et al. Association of Inflammatory Markers with COVID-19 outcome among hospitalized patients: experience from a tertiary healthcare Center in Western India. Maedica. 2021;16(4):620. <u>doi:10.26574%2fmaedica.2021.16.4.620</u>
- Salehi H, Pakzad B, Salehi M, Abbasi S, Salehi MM, Naeini MK. C-reactive protein, D-dimer, erythrocyte sedimentation rate, and troponin in intensive care unit patients with COVID-19 in Iran. Journal of Research in Medical Sciences. 2023;28(1):56. <u>doi:10.4103/jrms.jrms_352_22</u>
- Saputra K, Tavianto D, Pison OM. Comparison Between C-Reactive Protein and D-Dimer Serum in Pneumonia Phase as the Predictors of COVID-19 Patients' Mortality. Malaysian Journal of Medicine & Health Sciences. 2023;19(5):102-7. <u>doi:10.47836/mjmhs19.5.15</u>
- 202. Sari ND, Serin I, Bakir A, Alacam S. Could serum thrombocyte/lymphocyte (TLR), neutrophil/lymphocyte (NLR) and neutrophil/albumin (NAR) ratios be indicators of hospitalization and mortality in COVID-19? Iran J Microbiol. 2022 Dec;14(6):913-20. <u>doi:10.18502%2Fijm.v14i6.11266</u>
- Sarraf S, Singapurwala M, Jain H, Singh R, Julka A. Role of Inflammatory Markers in Predicting Severity in COVID-19 Patients at Tertiary Care Hospital, Ujjain (MP). J. Pulmonol. Respir. Res. 2023; 7:4-9. doi:10.29328/journal.jprr.1001043
- 204. Satilmis D, Yildiz E, Cevik E. Prognostic values of urea/lymphocyte and LDH/lymphocyte ratios for predicting mortality in COVID-19 patients. Frontiers in Emergency Medicine. 2023;7(3):e24. doi:10.18502/fem.v7i3.13820
- Satış H, Özger HS, Yıldız PA, Hızel K, Gulbahar Ö, Erbaş G, et al. Prognostic value of interleukin-18 and its association with other inflammatory markers and disease severity in COVID-19. Cytokine. 2021; 137:155302. doi:10.1016/j.cyto.2020.155302
- Saylik F, Akbulut T, Kaya S. Can C-reactive protein to albumin ratio predict in-hospital death rate due to COVID-19 in patients with hypertension?. Angiology. 2021;72(10):947-52. *doi:10.1177/00033197211012145*
- 207. Selanno Y, Widaningsih Y, Esa T, Arif M. Analysis of neutrophil lymphocyte ratio and absolute lymphocyte count as predictors of severity of COVID-19 patients. Indonesian Journal of Clinical Pathology and Medical Laboratory. 2021;27(2):184-9. <u>doi:10.24293/ijcpml.v27i2.1738</u>
- Senol A. The ability of D-dimer, albumin, and D-Dimer/albumin ratio to predict in-hospital mortality and intensive care unit admission in COVID-19 patients admitted to the emergency department. Bratislava Medical Journal/Bratislavske Lekarske Listy. 2022;123(12):908. doi:10.4149/bll_2022_145

- 209. Serin I, Sari ND, Dogu MH, Acikel SD, Babur G, Ulusoy A, et al. A new parameter in COVID-19 pandemic: initial lactate dehydrogenase (LDH)/Lymphocyte ratio for diagnosis and mortality. Journal of infection and public health. 2020;13(11):1664-70. *doi:10.1016/j.jiph.2020.09.009*
- Sai SS, Vijeth KV, Hemalatha AS. Differential white blood cell count predicting severity and mortality in patients with COVID-19. The Journal of Association of Chest Physicians. 2021;9(2):59-64. doi:10.4103/jacp.jacp_3_21
- 211. Seyfi S, Azadmehr A, Ezoji K, Nabipour M, Babazadeh A, Saleki K, et al. Mortality in ICU COVID-19 Patients Is Associated with Neutrophil-to-Lymphocyte Ratio (NLR): Utility of NLR as a Promising Immunohematological Marker. Interdisciplinary Perspectives on Infectious Diseases. 2023;2023. doi:10.1155/2023/9048749
- 212. Shalaby HM, Abd ElMaksoud SS, Ezzelregal HG, Salem DD. Assessment of interleukin-6 role in detecting coronavirus disease 2019 severity, mortality, and its control: A cohort study. The Egyptian Journal of Chest Diseases and Tuberculosis. 2023;72(2):183-90. <u>doi:10.4103/ecdt.ecdt_75_22</u>
- 213. Shamseldeen AM, Fawzy A, Soliman S, Hegazy EA, Rashed L, Hosny H, et al. Inflammatory biomarkers and severity of COVID-19: Cross sectional study among Egyptian patients. Egyptian Journal of Immunology. 2022;29(2):96-105. doi: N/A
- Sharif-Askari FS, Sharif-Askari NS, Hafezi S, Mdkhana B, Alsayed HA, Ansari AW, et al. Interleukin-17, a salivary biomarker for COVID-19 severity. PloS one. 2022;17(9):e0274841. <u>doi:10.1371/journal.pone.0274841</u>
- Shetty BA, Shilpa TA, Rajanna AH, Ravi K, Rao M, Bhat B. Association of neutrophil-lymphocyte ratio with clinical outcome of COVID-19 patients: A prospective study. APIK Journal of Internal Medicine. 2021;9(4):215-20. <u>doi:10.4103/ajim.ajim_43_21</u>
- Shokri-Afra H, Moradi M, Musavi H, Moradi-Sardareh H, Moradi Poodeh B, Kazemi Veisari A, et al. Serum calprotectin can indicate current and future severity of COVID-19. Journal of Clinical Laboratory Analysis. 2023;37(1): e24809. <u>doi:10.1002/jcla.24809</u>
- 217. Shrivastava S, Chelluboina S, Jedge P, Doke P, Palkar S, Mishra AC, et al. Elevated levels of neutrophil activated proteins, alpha-defensins (DEFA1), calprotectin (S100A8/A9) and myeloperoxidase (MPO) are associated with disease severity in COVID-19 patients. Frontiers in Cellular and Infection Microbiology. 2021; 11:751232. doi:10.3389/fcimb.2021.751232
- 218. Singh Y, Singh A, Rudravaram S, Soni KD, Aggarwal R, Patel N, et al. Neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio as markers for predicting the severity in covid-19 patients: a prospective observational study. Indian Journal of Critical Care Medicine: Peer-reviewed, Official Publication of Indian Society of Critical Care Medicine. 2021;25(8):847. doi:10.5005%2Fjp-journals-10071-23906
- Smail SW, Babaei E, Amin K, Abdulahad WH. Serum IL-23, IL-10, and TNF-α predict in-hospital mortality in COVID-19 patients. Front Immunol. 2023; 14:1145840. <u>doi:10.3389/fimmu.2023.1145840</u>
- 220. Smail SW, Babaei E, Amin K. Hematological, inflammatory, coagulation, and oxidative/antioxidant biomarkers as predictors for severity and mortality in COVID-19: a prospective cohort-study. International Journal of General Medicine. 2023:565-80. doi:N/A
- 221. Solimando AG, Susca N, Borrelli P, Prete M, Lauletta G, Pappagallo F, et al. Short-term variations in neutrophil-to-lymphocyte and urea-to-creatinine ratios anticipate intensive care unit admission of COVID-19 patients in the emergency department. Frontiers in Medicine. 2021; 7:625176. <u>doi:10.3389/fmed.2020.625176</u>
- 222. Hernández-Solis A, Güemes-González AM, Ruiz-Gómez X, Álvarez-Maldonado P, Castañeda-Casimiro J, Flores-López A, et al. IL-6, IL-10, sFas, granulysin and indicators of intestinal permeability as early biomarkers for a fatal outcome in COVID-19. Immunobiology. 2022;227(6):152288. doi:10.1016/j.imbio.2022.152288
- Suastika NK, Suega K. Diagnostic value of neutrophil to lymphocyte ratio for assessing the disease severity in covid-19 patients. Eastern Journal of Medicine. 2021;26(2):199-203. <u>doi:10.5505/ejm.2021.35761</u>
- Suhartono S, Wijaya I, Dalimoenthe NZ. The correlation of neutrophil-tolymphocyte ratio (NLR) and monocytes-to-lymphocytes ratio (MLR) with disease severity in hospitalized patients with Coronavirus disease 2019 (COVID-19). Bali Medical Journal. 2021;10(2):653-8. doi:10.15562/bmj.v10i2.2434
- Sukrisman L, Sinto R. Coagulation profile and correlation between D-dimer, inflammatory markers, and COVID-19 severity in an Indonesian national referral hospital. Journal of International Medical Research. 2021;49(11):03000605211059939. <u>doi:10.1177/03000605211059939</u>
- 226. Suliman L, Elwasefy M, Farrag NS, Tawab HA, Abdelwahab HW. The platelet-to-lymphocyte ratio versus neutrophil-to-lymphocyte ratio in prediction of COVID-19 outcome. Pulmonologiya. 2022;32(6):849-53. doi:10.18093/0869-0189-2022-32-6-849-853
- 227. Szabo R, Petrisor C, Bodolea C, Simon R, Maries I, Tranca S, et al. Hyperferritinemia, low circulating iron and elevated hepcidin may negatively

impact outcome in COVID-19 patients: A pilot study. Antioxidants. 2022;11(7):1364. <u>doi:10.3390/antiox11071364</u>

- Taghiloo S, Soltanshahi M, Aliyali M, Abedi S, Mehravaran H, Ajami A, et al. Cytokine profiling in Iranian patients with COVID-19; association with clinical severity. Iranian Journal of Immunology. 2021;18(1):54-64. doi:10.22034/iji.2021.87630.1810
- 229. SALEH MA, TAMIM HH, MARAWAN M, SAMEH A, SELIM M. TNF-a and IL-10 Serum Levels in COVID-19 Patients and their Relation to Disease Severity. The Medical Journal of Cairo University. 2022;90(9):1459-67. doi:10.21608/mjcu.2022.264601
- Tang Y, Sun J, Pan H, Yao F, Yuan Y, Zeng M, et al. Aberrant cytokine expression in COVID-19 patients: Associations between cytokines and disease severity. Cytokine. 2021; 143:155523. doi:10.1016/j.cyto.2021.155523
- Tanrıverdi M, Gündoğdu N, Benlier N, Yıldırım M, Çeliktürk H, Özkur HA, et al. Could ischemia-modified albumin levels predict the severity of disease in SARS-CoV-2 infection?. The Journal of Infection in Developing Countries. 2023;17(08):1055-62. <u>doi:10.3855/jidc.17456</u>
- Taşkin Ö, Yilmaz A, Soylu VG, Demir U, Inan FÇ. Ferritin/albumin ratio could be a new indicator of COVID-19 disease mortality. The Journal of Infection in Developing Countries. 2023;17(01):37-42. doi:10.3855/jidc.17409
- Tawfik H, AbdelKader R. The predictive role of red cell distribution width, neutrophil-lymphocyte ratio and platelet lymphocyte ratio on mortality in COVID-19 patients admitted to intensive care units. The Egyptian Journal of Geriatrics and Gerontology. 2022;9(1):56-67. doi:10.21608/ejgg.2022.237005
- 234. Rizo-Téllez SA, Méndez-García LA, Flores-Rebollo C, Alba-Flores F, Alcántara-Suárez R, Manjarrez-Reyna AN, et al. The neutrophil-to-monocyte ratio and lymphocyte-to-neutrophil ratio at admission predict in-hospital mortality in Mexican patients with severe SARS-CoV-2 infection (Covid-19). Microorganisms. 2020;8(10):1560. doi:10.3390/microorganisms8101560
- 235. Terra PO, Donadel CD, Oliveira LC, Menegueti MG, Auxiliadora-Martins M, Calado RT, et al. Neutrophil-to-lymphocyte ratio and D-dimer are biomarkers of death risk in severe COVID-19: a retrospective observational study. Health Science Reports. 2022;5(2):e514. <u>doi:10.1002/hsr2.514</u>
- 236. Thungthienthong M, Vattanavanit V. Platelet-to-White blood cell ratio as a predictor of mortality in patients with severe COVID-19 pneumonia: A retrospective cohort study. Infection and drug resistance. 2023:445-55. doi: N/A
- 237. Escamilla Tilch M, López Dawn LL, Balderrama A, Ramírez Bernal F, Aceves Poveda B, Díaz Quiroz G, et al. Inflammatory and Tissue Damage Biomarkers Progression as Mortality Prognosis in Patients with Covid-19 Disease. Journal of Cardio-Thoracic Medicine. 2021;9(4):878-83. doi: N/A
- Tjahyadi RM, Astuti T, Listyoko AS. COVID-19: Correlation between CRP and LDH to disease severity and mortality in hospitalized COVID-19 patients. Medica Hospitalia: Journal of Clinical Medicine. 2020;7(1A):144-9. doi:10.36408/mhjcm.v7i1A.467
- Topcu H, Arik YE. The importance of D-dimer, ferritin, CRP and lymphocyte values in determining mortality in COVID-19 disease in Turkey. Clin. lab. 2022;68:2274-80. <u>doi:10.7754/Clin.Lab.2021.210720</u>
- 240. Torun A, Çakırca TD, Çakırca G, Portakal RD. The value of C-reactive protein/albumin, fibrinogen/albumin, and neutrophil/lymphocyte ratios in predicting the severity of COVID-19. Revista da Associação Médica Brasileira. 2021;67:431-6. <u>doi:10.1590/1806-9282.20200883</u>
- 241. Turda Ü, Deligöz Ö, Ekinci O. The Effect of CRP/Albumin, Platelet/Lymphocyte, SOFA, and APACHE II in Predicting Mortality in Covid-19 Patients in Intensive Care Unit. Age. 2023; 30:69-9. <u>doi:10.14744/GKDAD.2023.63383</u>
- 242. Uzum Y, Turkkan E, UZUM Y, TURKKAN E. Predictivity of CRP, albumin, and CRP to albumin ratio on the development of intensive care requirement, mortality, and disease severity in COVID-19. Cureus. 2023;15(1):33600. doi:10.7759/cureus.33600
- 243. Vadi S, Pednekar A, Bajpe S, Sonawane S, Shinde S, Vaishnav Y, et al. Association of Dynamic Changes in Illness Severity Scores Biochemical and Inflammatory Markers with Outcomes in Invasively Ventilated COVID-19 in Resource-limited Settings: A Time-course Study. Indian Journal of Respiratory Care. 2023;12(3):222-9. <u>doi:10.5005/jp-journals-11010-1053</u>
- 244. Vaseie M, Amini M. Comparative Study of the Findings of the First Complete Blood Cell Count in Determining the Outcome of Patients with Covid-19: A Cross-Sectional Study. Journal of Police Medicine. 2022;11(1):1-10. doi:10.30505/11.1.32
- Vastani ZF, Ahmadi A, Abounoori M, Ardeshiri MR, Masoumi E, Ahmadi I, et al. Interleukin-29 profiles in COVID-19 patients: Survival is associated with IL-29 levels. Health Science Reports. 2022;5(2): e544. <u>doi:10.1002%2Fhsr2.544</u>
- 246. Tamayo-Velasco A, Martinez-Paz P, Penarrubia-Ponce MJ, De la Fuente I, Pérez-González S, Fernández I, et al. HGF, IL-1α, and IL-27 are robust

biomarkers in early severity stratification of COVID-19 patients. Journal of clinical medicine. 2021;10(9):2017. *doi:10.3390/jcm10092017*

- Visuddho V, Subagjo A, Setyoningrum RA, Rosyid AN. Predictive accuracy of blood inflammatory markers on COVID-19 mortality. Journal of Ideas in Health. 2021;4(Special4):623-9. *doi:10.47108/jidhealth.Vol4.Iss4.196*
- 248. Abensur Vuillaume L, Le Borgne P, Alamé K, Lefebvre F, Bérard L, Delmas N, et al. Neutrophil-to-lymphocyte ratio and early variation of NLR to predict in-hospital mortality and severity in ED patients with SARS-CoV-2 infection. Journal of Clinical Medicine. 2021;10(12):2563. <u>doi:10.3390/jcm10122563</u>
- 249. Wang X, Li X, Shang Y, Wang J, Zhang X, Su D, et al. Ratios of neutrophilto-lymphocyte and platelet-to-lymphocyte predict all-cause mortality in inpatients with coronavirus disease 2019 (COVID-19): a retrospective cohort study in a single medical centre. Epidemiology & Infection. 2020;148:e211. doi:10.1017/s0950268820002071
- 250. Yağcı S, Serin E, Acicbe Ö, Zeren MI, Odabaşı MS. The relationship between serum erythropoietin, hepcidin, and haptoglobin levels with disease severity and other biochemical values in patients with COVID-19. International Journal of Laboratory Hematology. 2021;43:142-51. doi:10.1111/jjlh.13479
- Yılmaz E, Ak R, Doğanay F. Usefulness of the neutrophil-to-lymphocyte ratio in predicting the severity of COVID-19 patients: a retrospective cohort study. São Paulo Medical Journal. 2021;140:81-6. <u>doi:10.1590/1516-3180.2021.0298.R1.27052021</u>
- Yurt NS, Metin OC. Ferritin/lymphocyte percentage ratio to predict the severity and mortality of COVID-19. Malawi Medical Journal. 2023;35(3):183-9. <u>doi:10.4314/mmj.v35i3.8</u>
- Zakeri A, Faraone A, Matin S. Does procalcitonin play a role as a predictor of in-hospital mortality among COVID-19 patients admitted to intensive care unit?. Journal of Parathyroid Disease. 2022;10(1):e9144. <u>doi:10.34172/jpd.2022.9144</u>
- 254. Soltani-Zangbar MS, Parhizkar F, Ghaedi E, Tarbiat A, Motavalli R, Alizadegan A, et al. A comprehensive evaluation of the immune system response and type-I Interferon signaling pathway in hospitalized COVID-19 patients. Cell Communication and Signaling. 2022;20(1):106. doi:10.1186/s12964-022-00903-6
- 255. Zhang JN, Gao Y, Wang XT, Li NN, Du X, Tang YJ, et al. Lymphocyte–C-reactive protein ratio can differentiate disease severity of COVID-19 patients and serve as an assistant screening tool for hospital and ICU admission. Frontiers in immunology. 2022; 13:957407. doi:10.3389/fimmu.2022.957407
- 256. Zhao K, Huang J, Dai D, Feng Y, Liu L, Nie S. Serum iron level as a potential predictor of coronavirus disease 2019 severity and mortality: a retrospective study. Open forum infectious diseases. 2020;7 (7): ofaa250). doi:10.1093/ofid/ofaa250
- 257. Zhou C, Chen Y, Ji Y, He X, Xue D. Increased serum levels of hepcidin and ferritin are associated with severity of COVID-19. Medical science monitor: international medical journal of experimental and clinical research. 2020;26:e926178-1. <u>doi:10.12659%2FMSM.926178</u>
- Zhu B, Feng X, Jiang C, Mi S, Yang L, Zhao Z, et al. Correlation between white blood cell count at admission and mortality in COVID-19 patients: a retrospective study. BMC infectious diseases. 2021;21:1-5. doi:10.1186/s12879-021-06277-3
- 259. Zope R, Kate P, Jaison J, Saraf S, Bhide S, Gupta D. Evaluation of WBC Parameters and Their Significance in COVID-19 Patients in Western Maharashtra, India. Medical Laboratory Journal. 2022;16(6):1-7. doi:N/A
- Cecconi M, Piovani D, Brunetta E, Aghemo A, Greco M, Ciccarelli M, et al. Early predictors of clinical deterioration in a cohort of 239 patients hospitalized for Covid-19 infection in Lombardy, Italy. Journal of clinical medicine. 2020;9(5):1548. <u>doi:10.3390/jcm9051548</u>
- 261. Wang F, Yang Y, Dong K, Yan Y, Zhang S, Ren H, et al. Clinical characteristics of 28 patients with diabetes and COVID-19 in Wuhan, China. Endocrine Practice. 2020;26(6):668-74. <u>doi:10.4158/EP-2020-0108</u>
- Luo X, Zhou W, Yan X, Guo T, Wang B, Xia H, et al. Prognostic value of Creactive protein in patients with coronavirus 2019. Clinical Infectious Diseases. 2020 Oct 15;71(16):2174-9. doi:10.1093/cid/ciaa641
- Wybranowski T, Napiórkowska M, Bosek M, Pyskir J, Ziomkowska B, Cyrankiewicz M, et al. Study of albumin oxidation in COVID-19 pneumonia patients: Possible mechanisms and consequences. International Journal of Molecular Sciences. 2022;23(17):10103. <u>doi:10.3390/ijms231710103</u>
- Baig MA, Raza MM, Baig M, Baig MU. Serum albumin levels monitoring in ICU in early days and mortality risk association in patients with moderate to severe COVID-19 pneumonia. Pakistan Journal of Medical Sciences. 2022;38(3Part-I):612. <u>doi:10.12669%2Fpjms.38.3.4154</u>
- 265. Huang J, Cheng A, Kumar R, Fang Y, Chen G, Zhu Y, et al. Hypoalbuminemia predicts the outcome of COVID-19 independent of age and co-morbidity. Journal of medical virology. 2020;92(10):2152-8. <u>doi:10.1002/jmv.26003</u>
- 266. Wang L. C-reactive protein levels in the early stage of COVID-19. Medecine et maladies infectieuses.
 2020;50(4):332-4. doi:10.1016/j.medmal.2020.03.007

- Rose-John S, Winthrop K, Calabrese L. The role of IL-6 in host defence against infections: immunobiology and clinical implications. Nature Reviews Rheumatology. 2017;13(7):399-409. <u>doi:10.1038/nrrheum.2017.83</u>
- Velazquez-Salinas L, Verdugo-Rodriguez A, Rodriguez LL, Borca MV. The role of interleukin 6 during viral infections. Frontiers in microbiology. 2019;10:445678. <u>doi:10.3389/fmicb.2019.01057</u>
- 269. Aziz M, Fatima R, Assaly R. Elevated interleukin-6 and severe COVID-19: a meta-analysis. Journal of medical virology. 2020;92(11):2283. doi:10.1002%2Fjmv.25948
- 270. Gómez-Pastora J, Weigand M, Kim J, Wu X, Strayer J, Palmer AF, et al. Hyperferritinemia in critically ill COVID-19 patients-is ferritin the product of inflammation or a pathogenic mediator?. Clinica Chimica Acta; International Journal of Clinical Chemistry. 2020; 509:249. doi:10.1016%2Fj.cca.2020.06.033
- 271. Henry BM, De Oliveira MH, Benoit S, Plebani M, Lippi G. Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a metaanalysis. Clinical Chemistry and Laboratory Medicine (CCLM). 2020;58(7):1021-8. <u>doi:10.1515/cclm-2020-0369</u>