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Agile laboratory scoring: Validating the precision and accuracy of Laboratory Markers in predicting hospital-based outcomes in COVID-19 patients

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Abstract:

This study aimed to identify laboratory predictors of mortality in individuals hospitalized with COVID-19, to establish a tool for identifying high-risk patients. The research included all patients admitted to the hospital due to COVID-19, totalling 201 individuals with a median age of 54.36 ± 13.51 years. Clinical outcomes revealed that 11.2% of patients were admitted to the Intensive Care Unit (ICU), 9.1% required mechanical ventilation support, and the overall mortality rate was <10%. Laboratory biomarkers deemed significant for mortality prediction were incorporated into a risk score calculation. Multivariate logistic regression model, considering parameters such as haemoglobin, erythrocytes, leukocytes, neutrophils, lymphocytes, creatinine, and other parameters along with demographic determinants have been used. A retrospective cohort study was conducted. Data were presented using frequency tables. Predictors of COVID-19 severity were identified using a multiple regression model, with adjusted relative risk (ARR), *p*-value, and 95% confidence interval (CI), to assess the significance. The presence of a statistically significant association between explanatory variables and COVID-19 outcomes was analyzed using a Binary Logistic regression model, with adjusted odds ratio (AOR), *p*-value, and 95% CI for AOR utilized for significance testing.

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Introduction:

The global impact of the COVID-19 pandemic has resulted in substantial losses worldwide.[1,2] Given the absence of targeted therapies and widespread vaccine distribution, identifying crucial laboratory biomarkers for early-stage disease severity becomes paramount for monitoring and preventing the progression of COVID-19 towards a severe form.[3] Various studies have been conducted to pinpoint important clinical and laboratory biomarkers that can predict disease severity and outcomes.[4,5,6] These investigations have revealed diverse clinical, laboratory, and radiologic markers with varying results, considering the evolving nature of the disease and geographical differences. Understanding these predictors is particularly vital in the Indian subcontinent about the population, demand and availability of healthcare-related resources. Laboratory markers play a significant role in indicating disease severity, progression, and outcomes. Abnormal cell counts, such as anaemia, polycythaemia, leukopenia, and leukocytosis with neutrophil predominance, along with decreased platelet counts, have been associated with severe disease and poorer outcomes in hospitalised patients.[7] Elevated liver enzymes and total bilirubin levels were also identified in severe and critical cases. An escalated inflammatory response, as reflected in increased levels of various interleukins and C-reactive proteins, has been reported.[8] Likewise, elevated coagulation markers, including fibrinogen and prothrombin time, are identified in severe and critical patients. Electrolyte imbalances in both hypo and hyper levels have been observed in sodium, potassium, and calcium levels among patients with severe disease, potentially attributed to the disease's impact on the body system or medication side effects.[9]

This study was designed to identify laboratory biomarkers predicting disease severity and outcomes among COVID-19 patients.

Study setting:

This retrospective cohort study was conducted at ESIC Medical College and Hospital, Bihta, Patna, Bihar, India between the period from February 2021 to July 2021, with the institutional approval 1/273593/2023(A-12016/59.2022-MED-VI).

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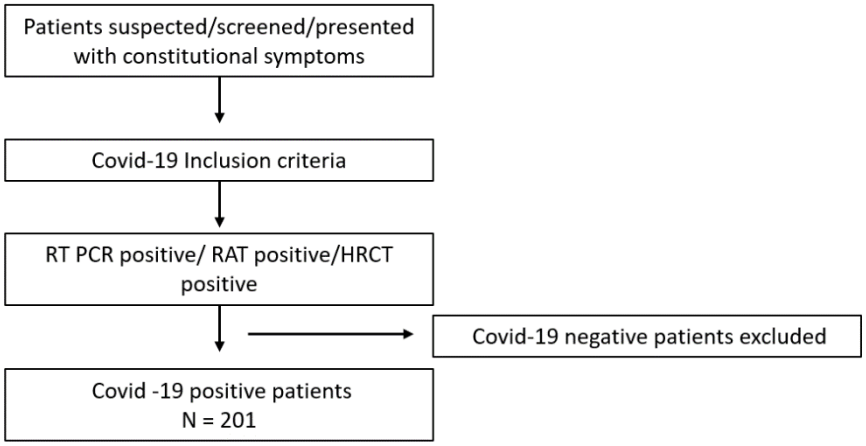
Recruitment of patients:

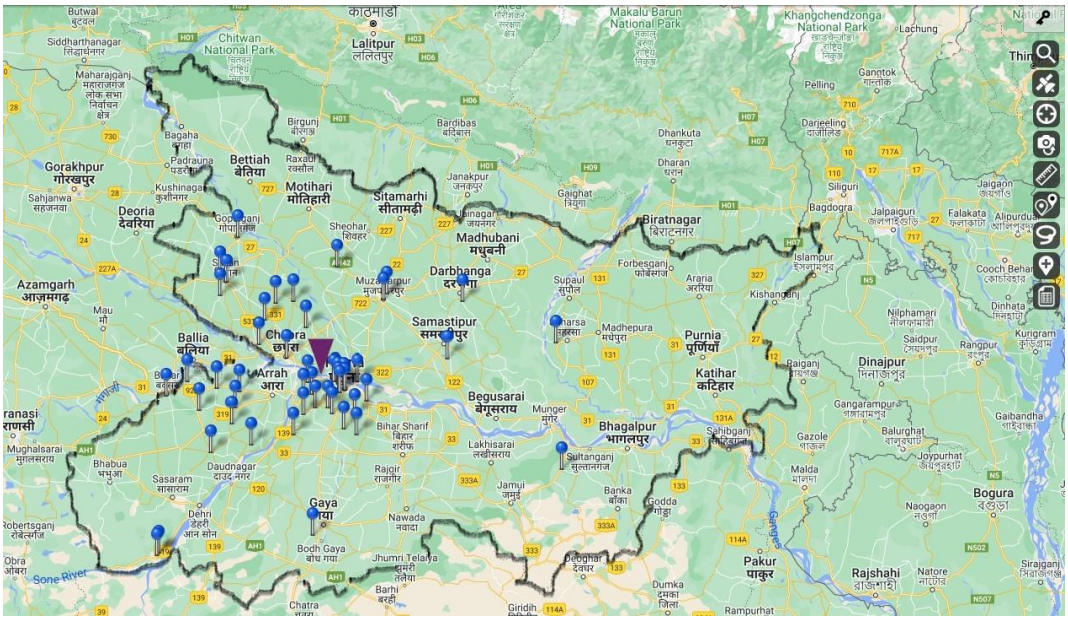
Figure 1.



The cohort of the population was COVID-19-positive patients mostly within a 30 km radius of the study centre. The study included all COVID-19 patients consecutively admitted over six months, followed by a four-month follow-up with comprehensive baseline clinical and laboratory data as well as outcome information.

Coordinate map tagging of the patients:

Figure 2.



The round blue head pins represent the cluster of patients, one head represents about 3 to 4 persons. The inverted triangle represents the study centre, ESIC Medical College and Hospital, Bihta, Patna, Bihar.

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Establishing COVID-19 severity:

COVID-19 severity score: was determined based on the WHO classification as follows.[16]

I. Mild Disease: Characterized by fever, malaise, cough, upper respiratory symptoms, and/or less common features of COVID-19 (headache, loss of taste or smell etc.).
II. Moderate Disease: Patients with lower respiratory symptom/s. They may have infiltrates on chest X-ray. These patients were able to maintain oxygen saturation on room air.
III. Severe Disease: These patients have developed complications. The following features can define severe illness:
i. Hypoxia: SpO_2 (oxygen saturation): 93% on atmospheric air or PaO_2(partial pressure of oxygen): FiO_2 (fraction of inspired oxygen) < 300mmHg (SF^* ratio < 315).
ii. Tachypnoea: in respiratory distress or RR>30 breaths/minutes.
iii. More than 50% involvement was seen on chest imaging.
*SF: Spo2/Fio2 ratio

In this study, we have incorporated observational studies that documented clinical laboratory parameters in individuals diagnosed with confirmed COVID-19. Diagnoses adhered to the guidelines established by either the World Health Organization or the data based on reviews from different studies. The primary focus of this study was on severe or critical cases of COVID-19, with a reference group representing non-severe cases. As per the criteria outlined by the WHO, severe COVID-19 was defined by the presence of dyspnoea, a respiratory rate exceeding 30 breaths per minute, blood oxygen saturation ≤93%, a PaO_2/FiO_2 ratio <300, and/or lung infiltrates exceeding 50% within 24-48 hours. Critical COVID-19 was characterized by respiratory failure, septic shock, and/or multiple organ failure. Non-severe COVID-19, on the other hand, was identified by the absence or mild presentation of pneumonia. Additionally, cases necessitating oxygen therapy and those admitted to intensive care units were also considered severe or critical. For the analysis, various clinical laboratory parameters, were broadly categorized into hematologic indices (White blood cells, neutrophils, lymphocytes, monocytes, platelets, hemoglobin), biochemical indices (total bilirubin, alanine aminotransferase, aspartate aminotransferase, total protein, albumin, globulin, urea, creatinine, glucose, Troponin I, lactate dehydrogenase etc.), infection/inflammation-related indices, C-reactive protein, Interleukin-6, erythrocyte sedimentation rate, procalcitonin, serum ferritin), coagulation indices (prothrombin time, activated partial thromboplastin time, D-dimer), and electrolytes (sodium, potassium, calcium, chloride).

In this study, we have excluded non-relevant parameters depending on the frequency and occurrence of symptoms, and overall sample size.

Relevant criteria for COVID-19 severity grading and review citations have been provided in the supplementary table 1.[15-19]

Data collection and processing:

Information was collected from the admission section, follow-up, and discharge records utilizing a pretested manual as well as an electronic data abstraction tool adapted from the

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various clinical and demographic platforms. Trained data extractors adhered to appropriate infection prevention and control measures. Before data entry and analysis, thorough checks were conducted to ensure data consistency and completeness.

Data analysis:

The study employed chi-square tests/Fisher's exact tests to discern statistically significant differences between COVID-19 severity and the history of pre-existing co-morbid illnesses, as well as baseline laboratory biomarkers. Variables demonstrating a *p*-value ≤ 0.05 were deemed to have a significant difference.

To identify predictors of COVID-19 disease severity, a regression model was utilized. Variables significantly associated with disease severity at a 25% significance level in the univariate analysis were incorporated into the multivariable model. The final model utilized adjusted relative risk (RR), *p*-value, and a 95% confidence interval for RR to assess significance and interpret results. Variables with a *p*-value ≤ 0.05 were considered significant predictors of disease severity.

For assessing the statistically significant association between COVID-19 disease outcome (death) and explanatory variables, a Binary Logistic regression model was applied. Univariate analysis screened independent variables for use in the multivariable Binary Logistic regression model at a 25% significance level. The adequacy of the final model was evaluated using goodness-of-fit. For Binary Logistic regression, a 95% confidence interval for the adjusted odds ratio (AOR) was calculated, and variables with a *p*-value ≤ 0.05 were deemed statistically associated with disease outcome.

All analyses were conducted using SPSS software version 25.0 (IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.).[10]

Results:

Disease progression and outcome:

Among the 201 patients included in the study, 86 individuals (42.8%) presented with severe disease, while the remaining 115 (57.2%) exhibited non-severe disease, comprising 15.6% with mild symptoms and 41.6% with moderate symptoms upon admission. In terms of disease outcome, 21 patients (10.4%) succumbed, while 180 individuals (89.6%) were discharged alive.

Demographical factors:

More than half of the participants were older than 50 years (52.3%) and males (76%). The majority (90%) were from the 30-kilometre radius of the study centre. Among the 201, 4 participants were from a distance of more than 100 km, and with a positive emporiatric history.

Eighty-five (42%) had a history of one or more preexisting co-morbid illnesses. The majority had diabetes (TIIDM) (39%), hypertension (22%), Asthma (20%), and cardiac disease (11%). Other co-morbid illnesses, including chronic diseases of the lung, kidney, liver, and neurology, constituted less than 1% of the total cases. The commonest symptoms were cough (70%), followed by fever (52%), sore throat (39%), shortness of breath (34.5%), and fatigue (30%) (Table 1).

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Table 1. Baseline demographic determinants and parameter-based characteristics:

Determinant	Number (n)/%	Determinant	Number (n)/%
Age (years)		**Sore throat**	
< 20	6 (2.9)	Absent	123 (61.0)
21-30	20 (10.0)	Present	78 (39.0)
31-40	32 (16.0)	**Nasal symptoms**	
41-50	38 (18.8)	Absent	181 (90.0)
> 50	105 (52.3)	Present	20 (10.0)
Gender		**Chest pain**	
Female	48 (24.0)	Absent	141 (70.2)
Male	153 (76.0)	Present	60 (29.5)
Co-morbidity		**Myalgia**	
Absent	116 (58.0)	Absent	161 (80.0)
Present	85 (42.0)	Present	40 (20.0)
Cardiac history		**Arthralgia**	
Absent	179 (89.0)	Absent	165 (82.0)
Present	22 (11.0)	Present	36 (18.0)
Hypertension		**Fatigue**	
Absent	157 (78.0)	Absent	141 (70.0)
Present	44 (22.0)	Present	60 (30.0)
DM		**Dyspnea**	
Absent	122 (60.2)	Absent	131 (65.5)
Present	79 (39.0)	Present	70 (34.5)
Asthma		**Headache**	
Absent	161 (80.0)	Absent	338 (78.8)
Present	40 (20.0)	Present	53 (26.2)
Fever		**Pain abdomen**	
Absent	96 (48.0)	Absent	148 (74.0)
Present	105 (52.0)	Present	53 (26.0)
Cough		**Nausea/ vomiting**	
Absent	60 (30.0)	Absent	183 (91.0)
Present	141 (70.0)	Present	18 (9.0)
Diarrhea			
Absent	195 (97.0)		
Present	6 (3.0)		

DM: Diabetes mellitus

The comprehensive blood count analysis of the study participants revealed a notable prevalence of polycythemia, while a smaller proportion exhibited anaemia. Around one-third of individuals showed deviations in their white blood cell count (WBC), with some classified as leukopenic and some with leukocytosis. The majority demonstrated a neutrophil-predominant and lymphopenic cell count profile. Approximately 41.2% of patients had a high neutrophil-to-lymphocyte ratio (NLR) of >3. The majority had a normal platelet count.

Concerning biochemical markers, the majority of patients displayed an elevated urea level, while normal to elevated creatinine levels. Elevated liver enzyme levels, including Serum

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Glutamic Pyruvic Transaminase (SGPT), Serum Glutamic Oxaloacetic Transaminase (SGOT), and Alkaline Phosphatase (ALP), were observed (Table 2).

Table 2. Laboratory parameters and severity:

Variable	COVID-19 Severity		*p*-value	Variable	COVID-19 Severity		*p*-value
	Non-severe	Severe			Non-severe	Severe	
Cardiac history				**WBC**			
Absent	60	40	**0.001**	4.5-11 xl0^3/ul	85	55	0.06
Present	25	76		< 4.5/> 11/ul	31	30	
Hypertension				**NLR**			
Absent	84	51	**0.001**	<3	50	3	< **0.0001**
Present	21	45		>3	65	83	
DM				**Platelet count**			
Absent	99	62	< **0.0001**	150-450 x 10^3/ul	104	67	**0.001**
Present	16	24		< 150/>450 x 10^3/ul	12	18	
Asthma				**Urea**			
Absent	109	78	0.224	<20mg/dl	91	71	0.234
Present	5	9		>20mg/dl	24	15	
Hematocrit				**Creatinine**			
<36%	6	5	0.992	0.6-1.1 mg/dl	90	59	0.062
36-45%	68	50		<0.6/>11 mg/dl	26	26	
>45%	42	30		**SGPT**			
ALP				<41 **IU/L**	74	39	< **0.0001**
<I00 IU/L	102	63	< **0.0001**	>41 **IU/L**	42	46	
>100 IU/L	14	22		**SGOT**			
Na				<40 **IU/L**	104	48	< **0.0001**
135-145 mequ/1	106	57	< **0.0001**	>40 **IU/L**	12	37	
<135/>145mequ/1	10	28					
K							
3.5-4.5 mequ/1	85	48	< **0.0001**				
<3.5/>4.5 mequ/1	30	38					

DM: Diabetes mellitus, ALP: Alkaline phosphatase, Na: Sodium, K: Potassium, WBC: White blood cell, NLR: Neutrophil lymphocyte ratio, SGPT: Serum Glutamic Pyruvic Transaminase, SGOT: Serum glutamic-oxaloacetic transaminase.

COVID-19 disease severity:

Univariate analysis with cut-off significance level identified several factors as potential predictors of COVID-19 disease severity, including age group, sex, hypertension, Type II diabetes mellitus, fever, sore throat, myalgia, arthralgia, fatigue, headache, haematocrit, white blood cell count (WBC), platelet count, neutrophil-to-lymphocyte ratio (NLR), urea, creatinine, Serum Glutamic Pyruvic Transaminase (SGPT), Serum Glutamic Oxaloacetic Transaminase (SGOT), Alkaline Phosphatase (ALP), sodium (Na), and potassium (K).

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In the multivariable regression analysis, after adjusting for other covariates, age group, fever, fatigue, NLR, SGOT, Na, and K emerged as significant predictors of COVID-19 disease severity at a 5% significance level. Being 50 years and older increased the risk of developing severe disease, and presenting symptoms such as fever and fatigue were associated with an increased risk of severity. An NLR greater than 3, raised SGOT, and deranged levels of Na and K were also linked to an elevated risk of severe disease.

For instance, having an NLR of greater than 3 was associated with a 5 times increased risk of developing severe disease. Similarly, having a raised SGOT of 41 and above increased the risk of severe disease by 2%. Patients with deranged values of Na and K levels had 1.5 and 1.3 times the risk, respectively, compared to those with normal values (Table 2,3).

Agile predictors of COVID-19 outcome:

An initial analysis of each independent variable with disease outcome was conducted at a significant cut-off level. The univariate analysis revealed that age group, sex, hypertension, Type II diabetes mellitus (TIIDM), sore throat, chest pain, myalgia, arthralgia, fatigue, respiratory rate, haematocrit (Hct), white blood cell count (WBC), platelet count, urea, creatinine, Serum Glutamic Pyruvic Transaminase (SGPT), Serum Glutamic Oxaloacetic Transaminase (SGOT), Alkaline Phosphatase (ALP), sodium (Na), and potassium (K) were significantly associated with COVID-19 disease outcome (Table 4).

Table 4. Significant parameters on multivariable regression model:

Parameter	CRR (95% CI)	ARR (95% CI)	*p*-value
Age	1.438 (1.144, 1.808)	1.007 (0.796, 1.278)	0.0001*
Fever	1.258 (1.016, 1.558)	1.000 (0.814, 1.229)	0.025*
Fatigue	1.656 (1.404, 2.098)	1.000 (0.815, 1.224)	0.0007*
NLR	1.671 (0.849, 3.282)	1.000 (0.507, 1.971)	0.0001*
SGOT	1.775 (1.459, 2.164)	1.000 (0.816, 1.221)	0.002*
Na	1.580 (1.303, 1.923)	1.000 (0.824, 1.217)	0.003*
K	1.192 (0.963, 1.477)	1.000 (0.834, 1.198)	0.008*

CRR: Crude Risk ratio, ARR: Adjusted Risk ratio, CI: Confidence interval, NLR: Neutrophil lymphocyte ratio, Na: Sodium, K: Potassium, SGOT: Serum glutamic-oxaloacetic transaminase.

After adjusting for other covariates, patients aged 50 years and older had higher odds of mortality compared to those under 50 years of age Adjusted Odds Ratio, AOR = 1.000 (0.396, 2.520) with 95% CI (confidence interval).

Laboratory markers that were identified as significant determinants of disease outcome included white blood cell (WBC) count and sodium (Na) level. Following adjustments for other factors, having deranged laboratory markers (both lower and raised values) of WBC count and Na level were associated with higher odds of mortality compared to those with normal values for these markers (Table 5).

Table 5. Significant parameters on binary multivariable regression model:

Parameter	COR (95% CI)	AOR (95% CI)	*p*-value
Age	1.826 (0.911, 3.656)	1.000 (0.396, 2.520)	0.014*
WBC	1.067 (0.560, 2.031)	1.000 (0.451, 2.218)	0.0001*
Na	2.170 (1.129, 4.180)	1.000 (0.418, 2.393)	0.003*

COR: Crude Odds ratio; AOR: Adjusted Odds ratio; Cl: Confidence interval, Na: Sodium.

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Discussion:

In this study, we investigated the impact of clinical and laboratory markers on the severity and outcome of COVID-19 in 201 patients admitted to the ESIC Medical College and Hospital, Bihta, Patna, India from February to July 2021. Identifying biomarkers early in the course of COVID-19 could aid in targeted interventions and patient management. Among the studied patients, 36.2% had severe disease, and <10.0% died, while 20.6% had non-severe disease, with 10.6% classified as mild and 30.0% as moderate upon admission.

The multivariable regression model revealed that age group, neutrophil-to-lymphocyte ratio (NLR), Serum Glutamic Oxaloacetic Transaminase (SGOT), sodium, and potassium were significant predictors of COVID-19 severity. After adjusting for other factors, being 50 years and older was associated with an increased risk of developing severe disease. Age has consistently shown an association with severe disease and adverse outcomes in various studies.[11-14]

Fever and fatigue symptoms were significant predictors of disease severity, increasing the risk of severe disease. Symptomatic disease, beyond those used in disease classification, tends to prolong recovery and is linked to a more severe disease category.

An NLR greater than three indicated a 5 times increased risk of developing severe disease. Elevated NLR is considered an indirect indicator of the body's stress level due to disease severity, aligning with findings from other studies.

A raised SGOT level of 41 and above increased the risk of severe disease by 2%. The SARS-CoV-2 virus may directly affect hepatocytes, or liver injury may result indirectly from an enhanced inflammatory response, leading to liver damage and elevated enzyme levels.

Patients with deranged sodium (Na) and potassium (K) levels, either low or high levels, had 1.5 to 1.3 times higher risks respectively of developing severe disease compared to those with normal values. Electrolyte imbalances can affect various organ systems, compromising the body's response to disease stress and leading to severe complications.

In assessing factors associated with disease outcome, age group, white blood cell (WBC) count, and Na level were significant predictors. After adjusting for other covariates, the odds of death were 2.5 times higher among patients aged 50 years and older compared to those under 50 years.

Deranged WBC count was associated with 4.5 times higher odds of mortality, indicating that both leukopenia and leukocytosis were linked to severe COVID-19. Similarly, deranged Na levels were associated with 3.0 times higher odds of death.

These findings emphasize the importance of timely identification of clinical and laboratory markers to predict COVID-19 severity and outcome, aiding in POCT (Point of care testing) interventions and patient care.

Conclusion:

This study focused on evaluating laboratory markers for predicting disease severity and outcomes. The findings indicated that age above 50 years, an NLR above three, elevated SGOT, and imbalances in Na and K levels were identified as significant predictors of developing severe COVID-19. Additionally, deranged values of WBC and Na levels were

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significantly associated with a worse outcome for the disease. Hence, the assessment and monitoring of these laboratory markers at the early stages of the disease could play a crucial role in preventing disease progression and fatalities.

Conflict of interest:

None declared.

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Supplementary table:

S 1. COVID-19 severity grading:

Patient	Description	Score	Severity Level
Uninfected	Uninfected; no viral RNA detected	0	Not applicable for inpatient
Ambulatory mild disease	Asymptomatic; viral RNA detected	1	
	Symptomatic; independent	2	
	Symptomatic; assistance needed	3	
Hospitalised: moderate disease	Hospitalised; no oxygen therapy	4	NEITHER
	Hospitalised; oxygen by mask, nasal prongs	5	O_2/NIV (supplemental oxygen) or non-invasive ventilation
Hospitalised: severe disease	Hospitalized; oxygen by NIV or high-flow	6	O_2/NIV (supplemental oxygen) or non-invasive ventilation
	Intubation and mechanical ventilation, $pO_2/FiO_2 \geq 150$ or $SpO_2/FiO_2 \geq 200$	7	IMV (invasive mechanical ventilation)
	Mechanical ventilation $pO2/FIO_2 < 150$ ($SpO_2/FiO_2 < 200$) or vasopressors	8	
	Mechanical ventilation $pO_2/FiO_2 <$ 150 and vasopressors, dialysis, or ECMO	9	
Dead	Dead	10	Not applicable for baseline severity

RNA: Ribonucleic acid, pO_2: Partial pressure of oxygen, ECMO: Extracorporeal membrane oxygenation.

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References:

1. Lenzen M, Li M, Malik A, Pomponi F, Sun YY, Wiedmann T, Faturay F, Fry J, Gallego B, Geschke A, Gómez-Paredes J. Global socio-economic losses and environmental gains from the Coronavirus pandemic. PloS one. 2020 Jul 9;15(7):e0235654.
2. Aburto JM, Schöley J, Kashnitsky I, Zhang L, Rahal C, Missov TI, Mills MC, Dowd JB, Kashyap R. Quantifying impacts of the COVID-19 pandemic through life-expectancy losses: a population-level study of 29 countries. International journal of epidemiology. 2022 Feb 1;51(1):63-74.
3. Tsilingiris D, Vallianou NG, Karampela I, Christodoulatos GS, Papavasileiou G, Petropoulou D, Magkos F, Dalamaga M. Laboratory Findings and Biomarkers in Long COVID: What Do We Know So Far? Insights into Epidemiology, Pathogenesis, Therapeutic Perspectives and Challenges. International Journal of Molecular Sciences. 2023 Jun 21;24(13):10458.
4. Malik P, Patel U, Mehta D, Patel N, Kelkar R, Akrmah M, Gabrilove JL, Sacks H. Biomarkers and outcomes of COVID-19 hospitalisations: systematic review and meta-analysis. BMJ evidence-based medicine. 2020 Sep 15.
5. Ng PC, Ma TP, Lam HS. The use of laboratory biomarkers for surveillance, diagnosis and prediction of clinical outcomes in neonatal sepsis and necrotising enterocolitis. Archives of Disease in Childhood-Fetal and Neonatal Edition. 2015 Jan 2.
6. Ponti G, Maccaferri M, Ruini C, Tomasi A, Ozben T. Biomarkers associated with COVID-19 disease progression. Critical reviews in clinical laboratory sciences. 2020 Aug 17;57(6):389-99.
7. Xue G, Gan X, Wu Z, Xie D, Xiong Y, Hua L, Zhou B, Zhou N, Xiang J, Li J. Novel serological biomarkers for inflammation in predicting disease severity in patients with COVID-19. International immunopharmacology. 2020 Dec 1;89:107065.
8. Sonawane MD, Nimse SB. C-Reactive protein: a major inflammatory biomarker. Analytical Methods. 2017;9(23):3400-13.
9. Lippi G, South AM, Henry BM. Electrolyte imbalances in patients with severe coronavirus disease 2019 (COVID-19). Annals of clinical biochemistry. 2020 May;57(3):262-5.
10. Corportation IB. IBM SPSS statistics for windows (version 25.0 armonk). IBM Corp.: Armonk, NY, USA. 2017.
11. Du R-H, Liang L-R, Yang C-Q, Wang W, Cao TZ, Li M, etal. Predictors of mortality for patients with COVI 0-19 pneumonia caused by SARSCoV-2: a prospective cohort study. Eur Respir J. 2020; 2020 (55: 2000524).
12. Gupta S, Hayek SS, Wang W, Chan L, Mathews KS, Melamed ML, et al. Factors Associated With Death in Critically Ill Patients With Coronavirus Disease 2019 in the US. JAMA Intern Med.2020; e203596. https://doi.org/10.1001/jamainternmed.2020.3596 PMID: 32667668
13. Williamson E.J., Walker A.J., Bhaskaran K, Bacon S, Bates C, Morton CE, et al. Factors associated with COVI 0-19-related death using OpenSAFEL Y. Nature. 584:430---{l (2020). https://doi.org/10.1038/ s41586-020-2521-4 PMI D: 32640463

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14. Li Xiaochen, Xu Shuyun, Yu Muqing, Ke W, Ying Z, Jing S, etal. Risk factors for severity and mortality in dull COVID-19 inpatients in Wuhan. J ALLERGY CLIN IMMUNOL. 2020; 146:11 Q----8. https://doi.org/ 10.1016/J.jaci.2020.04.006 PMI D: 32294485
15. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, Zhao X, Huang B, Shi W, Lu R, Niu P. A novel coronavirus from patients with pneumonia in China, 2019. New England journal of medicine. 2020 Feb 20;382(8):727-33.
16. World Health Organization. Clinical care for severe acute respiratory infection: toolkit: COVID-19 adaptation. World Health Organization; 2022.
17. Wei PF. Diagnosis and treatment protocol for novel coronavirus pneumonia (trial version 7). Chinese medical journal. 2020 May 5;133(9):1087-95.
18. Moutchia J, Pokharel P, Kerri A, McGaw K, Uchai S, Nji M, Goodman M. Clinical laboratory parameters associated with severe or critical novel coronavirus disease 2019 (COVID-19): A systematic review and meta-analysis. PloS one. 2020 Oct 1;15(10):e0239802.
19. Garry EM, Weckstein AR, Quinto K, Bradley MC, Lasky T, Chakravarty A, Leonard S, Vititoe SE, Easthausen IJ, Rassen JA, Gatto NM. Categorization of COVID-19 severity to determine mortality risk. Pharmacoepidemiology and Drug Safety. 2022 Jul;31(7):721-8.