

Development of new scoring system to predict mortality of COVID-19 patients

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ABSTRACT

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that triggered the COVID-19 pandemic resulted in a major worldwide health disaster with high rates of morbidity and death. Proper prediction of disease severity and mortality is important not only for management of the patients but also for providing efficient patient treatment and resource use. This is the case even after finding different treatments such as Remdesivir and Dexamethasone, to address COVID-19 mortality, there is a need to develop a unique scoring system (Shang et al., 2020). In this study, we established a novel scoring system for COVID-19 mortality prediction. 455 hospitalized COVID-19 patients were identified during our retrospective cohort studies; 345 patients were assigned to the development group and 110 to the validation group. We obtained detailed data regarding attributes of the patient, various health issues, medical background, test results, and x-ray results. We analysed 16 factors, identifying 8 independent predictors (with p-values <0.05) associated with COVID-19 mortality using univariate and Cox proportional hazards regression analyses including need for oxygen supply during admission, fever, comorbidities such as hypertension and diabetes, and laboratory markers such as D-dimer, ferritin interleukin-6 levels and Infection detected in initial chest X-rays. Based on these factors, we constructed a scoring system ranging from 0 to 19 points.

Based on these factors, we constructed a scoring system with a maximum possible score of 19 points. The mortality risk score is calculated by adding up assigned points for each predictor such as fever (3 points), D-dimer ≥ 500 ng/mL (3 points), chest X-ray infiltration (3 points), hypertension (2 points), need of oxygen supply during admission (2 points), IL-6 ≥ 10 pg/mL (2 points), ferritin ≥ 400 ng/mL (2 points), and diabetes mellitus (2 points). We assessed the effectiveness of our scoring system using performance analysis with a receiver operating characteristic (ROC) curve. After calculating the Area Under the Curve (AUC) for the development group (AUC-0.960) and validation group (AUC-0.922), the ideal cut off value of score was found to be 8.5 points. At this threshold, the sensitivity and specificity of the scoring system were 88.24% and 97.62% in development group and 81.25% and 97.87% in validation group, respectively. Based on their scores, we divided the patients into four groups like low-risk (Score 0 to 4, mortality = 3.85%), intermediate-risk (Score 5 to 8, mortality = 9.62%), high-risk (Score 9 to 12, mortality = 42.31%), and very high-risk (Score >13, mortality = 44.23%) groups. The results of our work clearly indicate the possibility and utility of applying the presented scoring model to estimate the outcomes of COVID-19 infected patients. Therefore, this scoring system could assist clinicians in the early identification of high risk patients that could enhance the triage decision and the allocation of resources during the pandemic surges. To ensure that it is generalizable, external validation is warranted.

Keywords: SARS-CoV-2, mortality, scoring system, D-dimer, receiver operating characteristic (ROC), area under the curve (AUC).

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INTRODUCTION

Since the identification of the first SARS-CoV2 pneumonia in December 2019, the COVID-19 pandemic that is unique in many ways, has spread to other countries globally, coupled with the increase in severe diseases and deaths (Huang et al., 2020; Haque et al., 2025). This further worsened the scarcity of critical commodities such as the protective wear and isolation infrastructure.

Another treatment regimen endorsed for the management of COVID-19 includes the combination of Remdesivir plus Dexamethasone while new therapies being developed include monoclonal antibodies and Baricitinib (Beigel et al., 2020; Cohen, 2021; Horby et al., 2021; Kalil et al., 2021). Although there is indication on the right therapeutic strategy, the best therapy is still a factor of some controversy. Although COVID-19 symptoms vary and are mild for most patients, some individuals are at a higher risk of developing severe health complications that can lead to critical illness or death. Therefore, prediction of disease severity and mortality rate is essential in order to make appropriate management strategies. Many studies have also described the higher mortality rates in elderly patients and patients with acute cardiovascular diseases, diabetes, dementia and Malignancy. Further, certain biomarkers from laboratory include D-dimer, IL-6, C-reactive protein, ferritin, and lactate dehydrogenase have been identified to contribute to poor outcomes in COVID-19 patients (Shang et al., 2020). Despite several studies that utilize various existed scoring system, such as, the score for community-acquired pneumonia or sepsis, to assess severity of COVID-19, the development of new scoring system to predicts mortality associated with COVID-19 has not yet been achieved. Prognostication of COVID-19 outcomes has continued even to this day (Altschul et al., 2020).

Even though there are many existing prognostic scores, most of them are complex and require advanced calculations or depends on biomarkers, which are not available in every setting at admission (Durie et al., 2023). There remains a need to have an easy and quick first hour early warning tool based on parameters that are accessible during the first hours of hospitalization to enable triage and allocation of resources is still present. To address this gap, we aimed to develop and validate a pragmatic scoring system using parameters that can be reliably gathered within the first hours of hospitalization to predict in-hospital mortality

MATERIALS AND METHODS

Study design, patient selection and data collection

A retrospective cohort study of COVID-19 patients admitted to Jagannath Gupta Institute of Medical Sciences and Hospital, Budge Budge, Kolkata-700137, West Bengal, India, from 4th August, 2020

to 11th January 2022. Confirmation of COVID-19 patients were based on real-time Reverse-Transcriptase Polymerase Chain Reaction (qRT-PCR) testing of Viral Transport Media (VTM) containing nasopharyngeal and oropharyngeal swab samples.

To determine the possibility of the selection bias, we conducted a comparative study of the main demographic and clinical features (age, sex, and in-hospital mortality) of the 455 patients who were considered in the end analysis and 201 patients who were omitted because of missing laboratory or radiology data. Follow-up of admitted patients continued until their discharge or death. We collected data from the electronic health records of the patients including epidemiological traits, existing comorbidities, clinical manifestations, laboratory outcomes, and radiographic assessments. Initial chest X-ray findings were categorized into two groups such as absence of active lesions and presence of unilateral or bilateral infiltration. The main endpoint under scrutiny was COVID-19 related mortality observed throughout the follow-up duration.

Flow chart for the study design. (Haque et al., 2024)

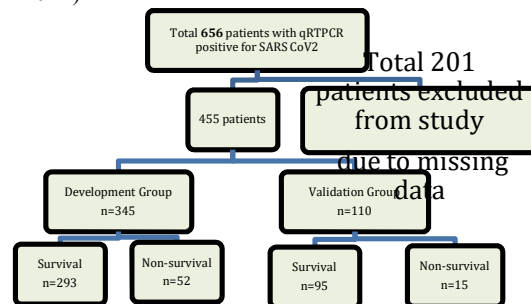


Figure 1: Flowchart of the Study Population

Ethics approval

This study was approved by the Institutional Ethics Committee of Jagannath Gupta Institute of Medical Sciences and Hospital (JIMSH), Budge budge, Kolkata (Approval no-JIMSH-IEC-11-2021 dated 22-11-2021).

Statistical analyses

We analyzed all statistical data using the IBM SPSS ver-22, and randomized and assigned the patients to the development and validation groups in a 345 and 110 patients respectively. Categorical variables were presented as numerical values and proportions, and their comparison was conducted utilizing either the chi-squared test.

univariate logistic regression was performed to determine factors that were associated with mortality in the form of odds ratios (OR) with 95% confidence intervals (CI). Univariate analysis was thereafter used to show variables with p value <0.05 to a multivariate Cox proportional hazards regression model to determine the independent predictors while considering time to event. The Cox model provides the results in the form of hazard

ratios (HR) with 95% CI. As a result, we could verify the match of the risk score to possible attributes by regulating parameters in the development cohort according to the Cox proportional hazards model. Data from both the development and validation cohorts were used to evaluate the performance of the scoring system with sensitivity and specificity assessed through receiver operating characteristic (ROC) curve analysis. Using Youden's J statistic, the ROC curve was used to determine the optimum cut off score, which balanced sensitivity and specificity (Rao et al., 2020). We assessed the prediction value of the new scoring system by calculating the area under the curve (AUC) of the ROC analysis. For statistical investigations, including ROC curve analysis and criterion value determination, MedCalc statistical software (https://www.medcalc.org/calc/diagnostic_test.php) (Version 22.023; accessed April 24, 2024) was used. A p-value of <0.05 was considered statistically significant.

RESULT

COVID-19 mortality is impacted by patient samples and clinical observations

This study enrolled a total of 656 patients hospitalized with COVID-19. The total case fatality rate was 10.21%, and 67 patients died during hospitalization. Of the total patients, 201 were excluded due to incomplete laboratory data; 455 patients were ultimately included and analysed in the study. Among them, 345 patients were randomly designated to the development group, and 110 patients were assigned to the validation group. The mortality rates of the development group and validation group were 15.07% and 13.63%, respectively.

Patients that were excluded because of missing data (n=201) comprised a median age of 56 years (IQR 50-62) and in-hospital mortality rate of 8.46% (17/201), not significantly different as compared to the included cohort (mortality 14.73%, p=0.12). The ratio of sex was comparable (42.3% female in the excluded and 38.2% in the included group, p=0.41). The demographic and clinical characteristics (Table-1) of both survival and non-survival subgroups within the development and validation cohorts reveal that male gender predominated in both groups (60.58% and 65.45% respectively) and that the median of ages were near similar between the groups [55.0 (53.0–57.0) and 56.0 (52.0–59.0) respectively].

The median age was significantly higher in non-survivors compared to survivors in both groups (p<0.001). [Development group: 54(52-55) vs. 62(57-66), p<0.001; validation group: 55(50-58) vs. 62(51-72), p<0.001].

Other clinical signs, including heart rate (HR), fever, cough, loss of smell and taste, sore throat, diabetes, hypertension, chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD),

heart failure (HF), and need for oxygen supply, were significant determinants of non-survival in both groups (all p < 0.001). Additionally, other variables such as D-dimer, lactate dehydrogenase (LDH), ferritin, interleukin-6 (IL-6), creatinine, hemoglobin (Hb), total white blood cell count (WBC), RT-PCR positivity at admission, and initial chest X-ray findings were also statistically related to non-survival (all p-values < 0.001).

Table-1: Clinical Features and Results of COVID-19 patients admitted to JIMSH, Kolkata-137.

Variable	Development Group				Validation Group			
	Total n=345	Survival n=293	Non-survival n=52	P-value	Total n=110	Survival n=95	Non-survival n=15	P-value
Sex	136 (39.42%)	117 (40.27%)	17 (32.7%)	0.353	35 (31.82%)	36 (37.89%)	3 (20%)	<0.001
Female	42 (12.46%)	75 (25.59%)	8 (15.4%)	0.003	5 (4.55%)	8 (8.42%)	2 (13.33%)	0.001
Age, year	55 (53-57)	54 (52-57)	62 (57-66)	<0.001	56 (52-59)	55 (52-58)	62 (51-72)	<0.001
HR/min (>100 beats/min)	24 (9.26%)	22 (7.51%)	21 (40.4%)	<0.001	28 (25.45%)	18 (18.95%)	10 (66.6%)	<0.001
YES	96 (27.83%)	65 (22.18%)	5 (9.6%)	0.001	82 (74.55%)	77 (81.05%)	5 (33.33%)	<0.001
Fever	24 (6.96%)	22 (7.51%)	20 (38.5%)	<0.001	70 (63.64%)	65 (68.42%)	6 (40%)	<0.001
No	51 (14.73%)	5 (1.69%)	3 (5.8%)	0.001	6 (5.45%)	6 (6.32%)	5 (33.33%)	<0.001

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YES	38 (1.0)	32 (0.9)	6 (.5)	5 (4.5)	4 (4.2)	1 (6.7)	0 (1)	0 (1)
Hypertension			<0.001			<0.001		
No	25 (72.4)	23 (30.5)	17 (2.7)	77 (70)	73 (68)	4 (26.7)		
YES	95 (7.5)	60 (0.5)	35 (7.3)	33 (30)	22 (20)	11 (73)		
Need oxygen supply during admission (<84%)			<0.001			<0.001		
No	29 (84.3)	26 (33.7)	31 (5.6)	90 (81.8)	82 (76.3)	8 (53)		
YES	54 (5.6)	33 (1.3)	21 (0.38)	20 (18.2)	13 (12)	7 (46.7)		
D-dimer (>500 ng/mL)			0.001			<0.001		
No	23 (67.5)	22 (28.1)	8 (1.4)	72 (65.5)	67 (62)	5 (33)		
YES	11 (32.4)	68 (3.2)	44 (62)	38 (35)	28 (25)	10 (67)		
LDH (>400 U/L)			<0.001			<0.001		
0 units/L			0.001			0.001		
No	81 (23.4)	73 (28)	15 (.3)	24 (22)	21 (19)	3 (20)		
YES	4 (76.5)	22 (0.75)	8 (4.62)	86 (81.8)	74 (68)	12 (80)		
Ferritin (>400 ng/mL)			<0.001			<0.001		
No	25 (72.4)	22 (28.1)	25 (3.9)	71 (64.5)	62 (57)	9 (60)		
YES	94 (7.2)	67 (2.8)	27 (3.9)	39 (35.5)	33 (30)	6 (40)		
IL-6 (10 pg/mL)			<0.001			<0.001		
No	24 (71.5)	23 (29.2)	15 (2.8)	73 (66.3)	65 (60)	8 (53)		
YES	98 (8.4)	61 (0.8)	37 (5.2)	37 (33.6)	30 (27.6)	7 (46.7)		
Creatinine (>1 mg/dL)			<0.001			<0.001		
No	28 (82.6)	27 (34.9)	10 (1.4)	94 (85.5)	85 (78)	9 (60)		
YES	60 (7.3)	18 (6.1)	0 (.77)	16 (14.5)	10 (9)	6 (40)		
CRP			0.002			0.006		

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(>6 mg/dL)	3 6	3 4		
No	16 14 19 1(2(3 46. 48. 6. 67 46 54))) 18 15 33	58 50 (5 (5 8(2.7 2. 53 3) 6) .3)		
YES	4(1(6 53. 51. 3. 33 54 46)))	52 45 (4 (4 7(7.2 7. 46 7) 4) .7)		
HB (<9 g/dL)	< 0 0 1	< 0 0 1		
No	32 27 3(5(48 93. 93. (9 62 86 2.)) 3)	89 (6 (9 3. 67 0) 7))	10 (5 (6 (8 (5	
YES	22 18 (6. (6. 4(38 14 7.)) 7)	11 6(33 (1 6. .3 0) 3) 3)		
WBC (<4000/ μ L)	< 0 0 1	< 0 0 1		
No	27 7(24 37 80. 0(7 29 81. 1.) 9) 2)	75 63 (6 (6 12 8.1 6. (8 8) 3) 0)		
YES	68 53 15 (1 (1 (2 9.7 8.1 8.)) 8)	35 32 (3 (3 3(1.8 3. 20 2) 7))		
qRTP CR Ct value (\leq 27)	< 0 0 1	< 0 4 5		
No	23 4(20 28 67. 6(5 83 70. 3.) 3) 8)	44 38 6((4 (4 40 0) 0))		
YES	11 1(87 24 32. (2 (4 17 9.7 6.)) 2)	66 57 9((6 (6 60 0) 0))		
Infection	< 0.	< 0.		

n detected in initial chest X-rays	0 0 1	0 0 1		
No	17 5(16 10 50. 5(1 72 56. 9.) 3) 2)	50 (5 (55 2. 5((5 63 33 0)) .3)		
YES	17 0(12 42 49. 8(8 28 43. 0.) 7) 8)	45 (4 10 (55 7. (6 (5 37 6. 0)) 7)		

Legends to Table 1: Data are presented as n (%), COPD=chronic obstructive pulmonary disease, HR/min=heart rate per minute, CKD= chronic kidney disease, IL-6= Interleukin-6, HB=haemoglobin, WBC=white blood cell count, qRTPCR= quantitative Real-Time Reverse-Transcriptase Polymerase Chain Reaction, CRP= C-reactive protein, LDH= Lactate dehydrogenase.

Severe risk factors predict mortality

In the development cohort, we performed a univariate logistic regression analysis to explore various factors and employed Cox proportional hazards regression to evaluate overall mortality during the observation period (Table 2). To predict mortality, we established cut off values, including age \geq 70 years and CRP levels >6 mg/dL. For the Cox hazards regression analyses, we considered factors such as need of oxygen supply during admission (HR 2.310; 95% CI 1.250–4.268; p<0.001), fever (HR 3.067 95% CI 1.478–6.366; p<0.001), hypertension (HR 2.457 95% CI 1.228–4.914; p=0.011), diabetes mellitus (HR 2.121; 95% CI 1.050–4.282; p=0.036), D-dimer (HR 2.891; 95% CI 1.139–7.339; p=0.025), ferritin (HR 2.25; 95% CI 1.14–4.44; p=0.019), Interleukin 6 (IL-6) (HR 2.270; 95% CI 1.077–4.781; p=0.031), and Infection detected in initial chest X-rays (HR 2.693; 95% CI 1.235–5.872; p=0.013).

Table-2: Mortality Risk Factor Admitted with COVID-19 in the Development group

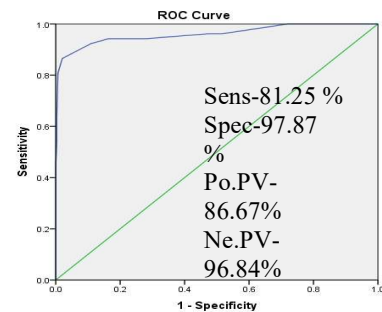
Variable	Univariate Analysis		Multivariable Cox Analysis		Score
	OR (95% CI)	p-value	HR (95% CI)	p-value	

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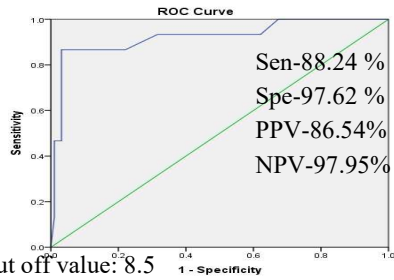
Age ≥70 years	0.93 (0.18-4.87)	0.931	0.68 (0.31-1.51)	0.343	-
Sex, female	1.04 (0.27-4.09)	0.955	0.89 (0.44-1.82)	0.759	-
Need for O ₂ supply on admission	8.15 (1.57-42.47)	0.013	2.31 (1.25-4.27)	<0.001	2
Fever	9.98 (4.50-117.32)	<0.001	3.07 (1.48-6.37)	<0.001	3
Hypertension	14.14 (3.42-58.42)	<0.001	2.46 (1.23-4.91)	0.011	2
Breathlessness	2.203 (0.351-13.834)	0.400	1.693 (0.735-3.901)	0.216	-
COPD	0.43 (0.034-5.478)	0.515	1.013 (0.281-3.651)	0.984	-
Heart failure	8.987 (1.004-80.432)	0.05	0.386 (0.088-1.7)	0.208	-
Chronic Kidney Disease	2.813 (0.462-17.111)	0.262	0.592 (0.204-1.721)	0.336	-
Diabetes mellitus	10.49 (2.46-44.84)	<0.001	2.12 (1.05-4.28)	0.036	2

D-dimer >500 ng/mL	12.93 (4.97-135.20)	<0.001	2.89 (1.14-7.34)	0.025	3
Ferritin >400 ng/mL	3.90 (1.00-15.25)	0.049	2.25 (1.14-4.44)	0.019	2
CRP >6 mg/dl	1.261 (0.294-5.415)	0.755	1.102 (0.516-2.353)	0.802	-
LDH	1.516 (0.282-8.159)	0.628	0.921 (0.326-2.607)	0.877	-
Interleukin-6 (IL-6) >10 pg/mL	13.71 (3.05-61.59)	<0.001	2.27 (1.08-4.78)	0.031	2
Infection detected in initial chest X-ray	6.49 (1.48-28.50)	0.013	2.69 (1.24-5.87)	0.013	3

Legends to Table 2: OR, odds ratio; CI, confidence interval; HR, hazard ratio. The mortality score was developed using independent predictors (p<0.05) from the multivariable Cox model. Total score range: 0–19 points.



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Optimal cut off value: 8.5
AUC: 0.960 (0.925–0.996),
p=0.018

Figure-2:
ROC
curve of

development group

Figure-3: ROC curve

of validation group

AUC, area under the curve; Sens, sensitivity; Spec, specificity; Po.PV, positive predictive value; Ne.PV, negative predictive value.

New scoring system to predict mortality in COVID-19

We developed a new scale that includes 8 risk factors (p<0.05) linked to mortality in COVID-19 cases such as need of oxygen supply during admission, fever, hypertension, diabetes mellitus, D-dimer, ferritin, Interleukin 6 (IL-6), and Infection detected in initial chest X-rays (Table 2). This scale was created based on the coefficients from Cox regression analyses. Risk scores range from 0 to 19, reflecting increasing levels of risk in the development cohort. Among the patients, 194 (42.64%) had scores between 0 and 4. As the scores increased, the number of patients decreased and the mortality rates rose correspondingly.

Predictive value of the newly established COVID-19 mortality scale

The table of Youden's index presents the threshold scores along with their respective sensitivity and specificity values for the development cohort. Using a cut off score exceeding 8.5 points, the ROC curve demonstrated a substantial AUC of 0.960 (95% CI: 0.925–0.996, p < 0.018). At this threshold, the sensitivity and specificity of the scale were 88.24% and 97.62%, respectively. Additionally, the positive predictive value was 86.54%, while the negative predictive value was 97.95%.

We categorized the scores as follows: 0 to 4 points as low-risk, 5 to 8 points as intermediate-risk, 9 to 12 points as high-risk, and scores of 13 points or more as very high-risk (Table 7). The mortality rates for the low-risk group were 3.85% in the development cohort and 6.67% in the validation cohort. In contrast, the mortality rates for the very high-risk group were 44.23% in the development cohort and 46.67% in the validation cohort (Table 7).

Calculation of cut off value by Youden's index

An evaluation of the cut of value calculated through Youden's index methodology. Youden's J statistics represents a single measure of how well a binary diagnostic test works which goes by names such as Youden's index and Youden's

statistics. Youden's J statistic is J=Max (sensitivity + specificity-1). The best cut off value based on Youden's index derives from maximum J value at 8.5 points in both the development and validation groups.

Table- (3 & 4) Youden's index

Optimal cutoff value: 8.5
AUC: 0.922 (0.835–1.000),
p<0.001

Table-3:

calculation of cut off value in development group

Positive if Greater Than or Equal 8.5	Sensitivity	1 - Specificity	J
-1.0000	1.000	1.000	0.000
1.0000	1.000	.860	0.140
2.5000	1.000	.720	0.280
3.5000	.962	.515	0.446
4.5000	.962	.471	0.491
5.5000	.942	.280	0.662
6.5000	.942	.164	0.778
7.5000	.923	.109	0.814
8.5000	.865	.020	0.845
9.5000	.808	.007	0.801
10.5000	.635	.003	0.631
11.5000	.538	.003	0.535
12.5000	.442	0.000	0.442
13.5000	.308	0.000	0.308
14.5000	.212	0.000	0.212
16.0000	.038	0.000	0.038
18.0000	0.000	0.000	0.000
Development group			

Table-4: calculation of cut off value in validation group

Positive if Greater Than or Equal 8.5	Sensitivity	1 - Specificity	J
-1.0000	1.000	1.000	0.000
1.0000	1.000	.937	0.063
2.5000	1.000	.842	0.158
3.5000	1.000	.674	0.326
4.5000	.933	.621	0.312
5.5000	.933	.316	0.618
6.5000	.867	.221	0.646
7.5000	.867	.168	0.698
8.5000	.867	.032	0.835
9.5000	.667	.032	0.635
10.5000	.467	.032	0.435
12.0000	.467	.011	0.456
13.5000	.333	.011	0.323
15.5000	.133	.011	0.123
18.0000	0.000	0.000	0.000
Validation Group			

Sensitivity and specificity of ROC curve by MedCalc

Table-5: Sensitivity and specificity of ROC curve by Medcalc

Statistic	Value	95% CI
Sensitivity	88.24%	76.13% to 95.56%
Specificity	97.62%	95.16% to 99.04%
Positive Likelihood Ratio	37.06	17.70 to 77.58
Negative Likelihood Ratio	0.12	0.06 to 0.26
Disease prevalence (*)	14.78%	11.21% to 18.97%
Positive Predictive Value (*)	86.54%	75.44% to 93.08%
Negative Predictive Value (*)	97.95%	95.75% to 99.02%
Accuracy (*)	96.23%	93.64% to 97.98%
Development Group		

Table-6: Sensitivity and specificity of ROC curve by Medcalc

Statistic	Value	95% CI
Sensitivity	81.25%	54.35% to 95.95%
Specificity	97.87%	92.52% to 99.74%
Positive Likelihood Ratio	38.19	9.50 to 153.50
Negative Likelihood Ratio	0.19	0.07 to 0.53
Disease prevalence (*)	14.55%	8.55% to 22.54%
Positive Predictive Value (*)	86.67%	61.79% to 96.31%
Negative Predictive Value (*)	96.84%	91.70% to 98.84%
Accuracy (*)	95.45%	89.71% to 98.51%
Validation Group		

DISCUSSION

In our study of 455 hospitalized COVID-19 patients, we found 14.73% of them unfortunately did not survive. To better predict which patients might be at higher risk, we created a new scoring system that takes into account 8 important factors: whether the patient needed oxygen during admission, their fever status, hypertension, diabetes, D-dimer levels, ferritin, interleukin-6 (IL-6) levels, and any infections seen in their initial chest X-rays (Bae et al., 2021). Based on the scores assigned to the patients, we

divided the patients into four risk groups and found out that there was high risk of mortality among the patients in the higher risk group. Our findings, confirmed by ROC curves, showed excellent discrimination with an AUC of 0.960 (p=0.018). This underscores the accuracy of our novel scale in estimating mortality in COVID-19 cases, which uses parameters such as demographics, comorbidities, D-dimer levels, Interleukin-6 (IL-6) levels, and chest X-ray results.

Our analysis constructed a simple, 8-point scoring system which showed an excellent level of discriminatory power to in-hospital mortality in our group of hospitalized COVID-19 patients, and has an AUC that is better than the well-validated 4C Mortality Score in our particular population. The fact that our model works based on parameters that can be obtained within the initial hours of admission (a basic clinical assessment (fever, oxygen requirement), past medical history (high blood pressure, diabetes), routine blood tests (D-dimer, ferritin, IL-6), and a chest X-ray are the parameters of our model).

The discriminative power of our scoring system (AUC 0.960) appears high relative to other fully developed COVID-19 mortality scores, including the popular 4C Mortality Score, which typically reports an AUC of approximately 0.77 to 0.80. This implies that our model, which incorporates the outcomes of chest X-ray and interleukin-6 and other more common parameters, can provide the predictive power in the environs where the variables are measured. Nonetheless, no direct, head-to-head comparison on a similar patient population was carried out in the study and would be justified in future studies.

Table-7. Stratified Risk Group by Score and Mortality in the Development and Validation Groups

Risk Group	Score Range	Development Group			Validation Group		
		Total number of patients (%)	Number of healthy patients (%)	Number of Deaths (%)	Total number of patients (%)	Number of healthy patients (%)	Number of Deaths (%)
Low	0-4	157 (42.27%)	155 (90.0%)	2 (3.85%)	37 (33.64%)	36 (89.0%)	1 (6.67%)
	5-8	137 (30.03%)	132 (95.62%)	5 (9.62%)	57 (51.81%)	56 (95.0%)	1 (6.67%)

High	0-12	27(18.37)	5(1.71)	22(42.31)	8(7.27)	2(2.11)	6(40)
Very High	≥13	24(9.33)	1(0.34)	23(44.23)	8(7.27)	1(1.05)	7(46.67)
Total		345(100)	293(100)	52(100)	11(100)	95(100)	15(100)

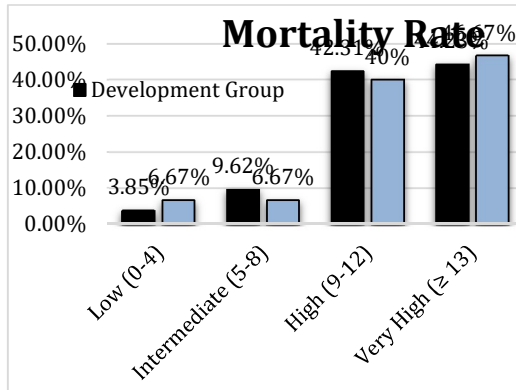


Figure-4: Mortality rate in development group & validation group

Recently, several studies have attempted to derive a simple prognostic score for COVID-19 in terms of the prognosis and the outcome of the disease (Zhang et al., 2020; Altschul et al., 2020). Oxygen supplementation on admission and fever have come out to be important clinical predictors of the severity and outcome of COVID-19 illness. All the patients who required oxygen upon admission exhibited severe manifestations, indicating either respiratory dysfunction or moderate to severe respiratory discomfort. This need for supplemental oxygen is helpful in determining the amount of pulmonary involvement and the severity of the viral pneumonia. Further, fever which is another sign of COVID-19 can also be used as a sign of disease severity. Fever has been related to the onset of systemic inflammation and immune system stimulation which affects the respiratory system and leads to advanced stages of the disease. Thus, associated with a need for oxygen supplementation upon admission and a large number of cases with fever, timely monitoring and comprehensive intensive therapy to achieve the best outcomes in the treatment of severe COVID-19 and reduce the risk of complications (area under the curve, 0.966) (Zou et al., 2020; Imanieh et al., 2023).

Each of IL-6 and d-dimer has been examined previously as a marker of inflammation and coagulation for the possibility to identify severity in COVID-19. The correlation established between IL-6 and the severity of COVID-19 involved prognosis,

and computed tomography grading also helped differentiate patients based on severity among those with comorbidities (Chen et al., 2020). In the same way, D-dimer has been identified as independent predictors of the severity of the disease from COVID-19 with higher levels to be associated with worsened prognosis. Nevertheless, the utility of IL-6 and D-dimer in this respect to predict the mortality in patients is still questionable. Some of the previous research works have shown strong relationships between either IL-6 or D-dimer and mortality, and there are others that have not demonstrated any such links. In disparity, our study supports the key findings of previous studies on IL-6 and D-dimer to be of high value in identifying COVID-19 patients at high risk of complications. The hypothesis is that patients with higher D-dimer level have higher coagulation activity while those with higher IL-6 level have higher inflammation (Matthews et al., 2018). These results are linked to increased periods of hospitalization with higher levels of adverse outcomes. Mainly, features of the longitudinal changes of IL-6 and D-dimer values during the early stay are needed to assess the prognostic value of both biomarkers in the management of COVID-19. Hypertension and diabetes mellitus which are among the complications frequently reported in COVID-19 patients, have also been established to be associated with the severity of the disease as well as mortality rate (Fang et al., 2020).. Research has indicated that people with hypertension or diabetes are most likely to have complications if they contract COVID-19. Some of the hypertensive patients with higher blood pressure levels than their usual baseline were reported to be severe cases and more deaths from COVID-19 illness than others. Likewise, the patients with diabetes have been more vulnerable to severe enshrinement, respiratory failure and death as compared to the normal populace (Zhang et al., 2020). The fact that hypertension and diabetes are comorbidities in patients who have contracted COVID19 shows that despite the global pandemic, efforts should be put in place to ensure that such conditions are well managed so as not to contribute to worse outcomes. Furthermore, individualised therapy on blood pressure and glucose might help in enhancing the prognosis and minimizing mortality among this fashionable populace.

Presence of infection in the initial chest X-rays can be used as major risk predictor of COVID-19 severity and its outcomes. Studies consistently show that abnormalities in chest X-rays at the onset of infection are early indicators of disease progression and potential complications. Such changes, particularly bilateral ground-glass opacities, consolidation or infiltrates indicate pulmonary involvement and inflammation. It has been found that both their presence and extent are closely related to worsening respiratory manifestations and oxygen demand, and the need for aggressive

measures such as ventilator support (Rousan et al., 2020). Indeed, identifying infection on chest X-ray at an early stage makes clinical management decisions easier, triage and treatment administration, and resource mobilisation, hence improving the patient's outcome and ultimately reducing COVID-19 mortality.

The present work supports the findings of other studies that depicted that the chest X-ray findings are critical determinants of the severity of COVID-19. As it has been found in other studies, cavity on chest X-ray Patients with infiltrations are in a higher risk of developing severe illness. For instance, the Brixia score, which measures the extent of lung lesion in Chest X-rays, has significant association with high risk severity in COVID-19 pneumonia (Gatti et al., 2020). However, an improvement of Brixia score has been identified to predict better outcome, while a worsening of the score and initial scores more than 3 points indicated poor outcome such as mortality (Wong et al., 2012).

Additionally, studies highlight different clinical factors, including patients' age, neutrophil-lymphocyte ratio, and chest computed tomography severity score in the prognosis of severe pneumonia in COVID-19 (Fang et al., 2020). Based on these parameters, they created a nomogram with which they can calculate the probability of serious pneumonia. Although the chest X-ray findings are rather non-specific, their availability, affordability and prognostic utility is beyond doubt. Prior work proposes incorporating chest X-rays to Prognostic scoring systems such as ours due to their utility, in enabling a prediction of COVID-19 severity and coverage of proper management approaches (Bae et al., 2021).

We use the results from chest X-rays and standard lab tests to determine points to each variable in our scoring system, which is renowned for its simplicity. Consequently, it is simple to apply in clinical environments.

To the best of our knowledge, there is no new scoring system that incorporates different comorbidities together with IL-6, D-dimer, as well as chest X-ray findings. This scale with its higher sensitivity, specificity, and accuracy classifies the patients into the low risk and high risk group and guide them to the appropriate health care facilities. As a result, such approach allows for using medical resources as effectively as possible while reducing the amount of patient transfers and transports as much as possible.

CONCLUSION

This work proposes a new risk model that aims at estimating COVID-19 mortality based on clinical variables, D-dimer, IL-6 and chest X-ray findings. Since measuring clinical outcomes would help in deciding on the severity of the condition in COVID19 patients, and where the patients should be admitted, the prediction would be helpful in developing the right solutions.

LIMITATION OF OUR STUDY

First and foremost, it is a retrospective, single-center investigation. Although we determined that internal validation was excellent, we cannot determine the performance of our system when used with other populations and in other healthcare settings. Therefore, external validation on a larger, multi-center and prospective cohort scale is the essential next step and must be completed before this tool can be suggested to be widely used in a clinical setting.

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