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Coronavirus Pandemic

The COVEG score to predict severity and mortality among hospitalized patients with COVID-19

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Abstract

Introduction: COVID-19 severity and mortality predictors could determine admission criteria and reduce mortality. We aimed to evaluate the clinical-laboratory features of hospitalized patients with COVID-19 to develop a novel score of severity and mortality.

Methodology: This retrospective cohort study was conducted using data from patients with COVID-19 who were admitted to five Egyptian university hospitals. Demographics, comorbidities, clinical manifestations, laboratory parameters, the duration of hospitalization, and disease outcome were analyzed, and a score to predict severity and mortality was developed.

Results: A total of 1308 patients with COVID-19, with 996 (76.1%) being moderate and 312 (23.9%) being severe cases, were included. The mean age was 46.5 ± 17.1 years, and 61.6% were males. The overall mortality was 12.6%. Regression analysis determined significant predictors, and a ROC curve defined cut-off values. The COVEG severity score was defined by age ≥ 54, D-dimer ≥ 0.795, serum ferritin ≥ 406, C-reactive protein ≥ 30.1, and neutrophil: lymphocyte ratio ≥ 2.88. The COVEG mortality score was based on COVEG severity and the presence of cardiac diseases. Both COVEG scores had high predictive values (area under the curve 0.882 and 0.883, respectively).

Conclusions: COVEG score predicts the severity and mortality of patients with COVID-19 accurately.

Key words: COVID-19; COVEG; predictors; score; severity; mortality.

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Introduction

The current COVID-19 pandemic, caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), was declared by the beginning of 2020. After approximately one year, the World Health Organization (WHO) declared more than 97 million confirmed cases globally, with more than 2 million deaths by the end of January 2021 [1]. Respiratory droplet and contact transmission are the main routes of transmission of SARS-CoV-2. Other potential transmission routes include aerosol, fecal-oral, or vertical transmissions [2].

Patients with COVID-19 can present clinically with a wide diversity of symptoms. The majority of patients have mild disease, but nearly 20% develop severe disease with pneumonia, respiratory failure, and even mortality [3]. Laboratory features of COVID-19 include lymphopenia, extended prothrombin time, high lactate dehydrogenase [4], elevated D-dimer, alanine transaminase, and C-reactive protein (CRP). However, patients admitted to the intensive care unit (ICU) develop numerous laboratory abnormalities suggesting that COVID-19 might be associated with a deficiency of cellular immunity, coagulation activation, and myocardial, hepatic, or renal injuries [5].

The mortality of critically ill patients is reported to range from 11% to 61% and increases markedly by 65

years of age and above [5-8]. Reducing the mortality of critically ill patients needs early identification and medical intervention. Determining patients at a high risk of severe disease or mortality is a critical step in managing COVID-19. Prior reports from Wuhan, where the pandemic started, identified that patients with specific comorbidities, such as diabetes, hypertension, and heart disease, are more likely to present to hospitals [9]. Other predictors of poor prognosis have been proposed, like renal affection or liver injuries, the requirement for mechanical ventilation, high CRP, elevated interleukin-6 (IL-6), lymphopenia, and elevated procalcitonin levels [8,10-12]. However, there are no apparent predictive factors for disease severity or mortality. These predictors could determine hospital-admission criteria and assess a risk estimation of ICU referral. Therefore, we evaluated the clinical and laboratory features of hospitalized Egyptian patients with COVID-19 to develop a novel score for predicting in-hospital severity and mortality.

Methodology

Patients

The records of patients with COVID-19 have been analyzed retrospectively from the medical records of 5 university hospitals: Ain-Shams University Hospital, Assiut University Hospitals, Fayuom University Hospital, Helwan University Hospital, and Zagazig University Hospital.

Inclusion criteria were COVID-19 positive diagnosis and complete medical records. The diagnosis of COVID-19 was based on positive reverse-transcriptase polymerase chain reaction (RT-PCR) testing for SARS-CoV-2 on nasopharyngeal swabs. Diagnosis and severity classification were in accordance with the management protocols of COVID-19, released by the Egyptian Ministry of Health and Population (MOHP) (March 2020) and its updated versions, in which COVID 19 patients were classified to:

Mild Cases: Those with mild clinical symptoms and no manifestations of pneumonia can be seen in imaging.

Moderate Cases: Patients have clinical symptoms, e.g., fever, respiratory tract symptoms, etc., and manifestations of pneumonia can be found in imaging.

Severe Cases: who have any of the following:

- Respiratory rate; 30 breaths/min.
- Oxygen saturations < 93% at a rest state.
- Oxygen arterial partial pressure (PaO_2), Inspired oxygen fraction (FiO_2) < 300 mm Hg.
- In lung imaging, those with lesions progress more than 50% within 24 to 48 hours.

Critical Cases: who have any of the following:

- Respiratory failure that requires mechanical ventilation.
- Occurrence of shock; organ failure requires treatment and monitoring in the ICU [13,14].

The requirement of written informed consent was waived because the study was retrospective. The study was approved by the Institutional Review Board of the Faculty of Medicine, Helwan University.

A total of 1,308 confirmed COVID-19 cases diagnosed between May and September 2020 were included. Data collected at hospital admission, either ward or ICU, included demographic data (age, gender, residence, and occupation), comorbidities (diabetes mellitus, hypertension, other systemic diseases, and malignancies), clinical manifestations (cough, fever, dyspnea, sore throat, anosmia, diarrhea, and vomiting), laboratory parameters (differential blood count, neutrophil: lymphocyte ratio [NLR], coagulation profile, liver enzymes, lactate dehydrogenase [LDH], kidney function, D-dimer, serum ferritin, and CRP), chest imaging by computed tomography (CT), complications (hypoxemia, ICU admission, and organ failure), duration of hospital stay, and disease outcome (cure or death). The used standard of care treatment consisted of azithromycin for three days and vitamin C and zinc supplements for 14 days, according to a standardized protocol provided by the Egyptian Supreme Council of University Hospitals. Hydroxychloroquine was given in 63% (N = 824) of cases. Oxygen therapy, anticoagulants, and corticosteroids were used in indicated hospitalized patients.

Data were analyzed, and a score to predict mortality or severity was developed.

Statistical analysis

Data entry and analysis were done using SPSS software version 20 (SPSS Inc, Chicago, IL, USA). Data were described as the mean and standard deviation in numerical data or frequency and percentage in the case of categorical data. The student's t-test was used for testing significant differences between the means after testing for equality of variance using the Levene test. A chi-square test was used to test associations between proportions.

A binary logistic regression analysis was conducted to determine the independent effects of different variables and their predictive ability. Hosmer and Lemeshow were used to estimate the model's fitness, and the likelihood ratio was used to differentiate between different models, with the highest likelihood

value being selected. The enter method was selected in conducting the regression analysis. Adding or removing variables were based on their contribution to the model in terms of the Wald test of significance, regression coefficient, and 95% confidence interval, which express the accuracy of the calculated odds ratio. The overall classification table percentages are presented to illustrate the fitting of the model or internal validity.

ROC curve and area under the curve (AUC) discriminate the ability of different predictors of either COVID-19 severity or mortality; they were calculated, and their 95% confidence interval was estimated. ROC curve analysis was performed to select the cut-off point of the total score with the highest specificity and considerable sensitivity in discrimination between moderate and severe cases and between deceased and surviving cases.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards [15]. The study was approved by the Research Ethics Committee (REC) for human subject research at the Faculty of Medicine, Helwan University (Serial: 59-2020), with a waiver of the need for the informed consent form.

Table 1. Demographic data, clinical features, outcomes, and mortality among the included patients.

Items	N (%)
Age (mean ± SD)	46.5 ± 17.1
Sex	
Males	806 (61.6)
Females	502 (38.4)
Comorbidities:	
Symptoms	
Dry cough	794 (61.4)
Fever	772 (59.7)
Dyspnea	489 (37.8)
Sore throat	382 (33.1)
Anosmia	129 (18.0)
Diarrhoea	154 (11.9)
Vomiting	50 (3.9)
Severity classification	
Moderate	996 (76.1)
Severe	312 (23.9)
ICU admission	248 (24.0)
Relevant CT for COVID 19	762 (69.3)
Outcome	
Cure	1126 (87.4)
Death	162 (12.6)
Mortality among ICU patients	152 (61.3)

Results

Demographics and clinical features

Data of 1,308 patients with COVID-19 have been recovered retrospectively from the medical records of 5 university hospitals. The average age of all patients was 46.5 ± 17.1 years with an age range from 1 to 93 years; 1.6% of them (N = 27) were children, and 61.6% (N = 783) were males. A similar frequency of females and males, 13% and 12.3%, respectively, died of COVID-19 among the hospitalized patients. Cough, fever, and dyspnea were the main presenting symptoms (61.4%, 59.7%, and 37.8%, respectively), whereas anosmia, vomiting, and diarrhea were the least (18%, 11.9%, and 3.9%, respectively). Regarding disease severity, 23.9% of patients were classified as severe (N = 312) and 76.1% (N = 996) as moderate. Of these, 19% (N = 248) were critically ill and were admitted to the ICU. According to MOHP protocol, mild cases of COVID-19 are treated at home and were therefore excluded from this study. In 63% (N = 762) of patients, CT findings were compatible with COVID-19. The overall mortality rate was 12.6% (N = 162), whereas it reached 61.3% (N = 152) among the ICU-admitted patients (Table 1). We noticed an increase in mortality from ≥ 35-year-old patients, reaching 38.7% among those ≥ 70 years old. Our study revealed that 20.6% (N = 57/277) of patients with diabetes, 27.7% (N = 26/94) of patients with coronary heart diseases, 23.8% (N = 64/269) of hypertensive patients, 33.3% (N = 8/24) of patients with liver diseases, 37.8% (N = 14/37) of patients with renal disease, 10.3% (N = 104/1010) of patients without diabetes, 11.3% (N = 134/1190) of patients with no coronary heart diseases, 9.5% (N = 97/1017) with normal blood pressure, 12.2% (N = 154//1261) with no liver diseases, and 11.7% (N = 145/1236) without renal diseases, died of COVID-19 with significant association *p* values of 0.001, 0.001, 0.04, 0.001, 0.001, 0.008, and 0.001, respectively. Moreover, patients with severe COVID-19 carried a 50% risk of death compared with 0.5% in moderate cases. Detailed demographic, clinical, and outcome-related data for patients with or without comorbidities are listed in Table 2.

Laboratory data of the included patients

The laboratory parameters and duration of hospital stay in relation to the disease outcome among the enrolled patients are summarized in Table 3. Hemoglobin, lymphocyte count, and oxygen saturation were significantly lower in severe and deceased patients than in moderate cases and survivors. Other blood parameters, kidney functions, aspartate aminotransferase (AST), lactate dehydrogenase (LDH),

Table 2. Comparison between patients with and without comorbidities in the study.

Variables	Comorbidities		*p* value
	Absent N (%)	Present N (%)	
Death Rate	63 (7.8)	99 (20.5)	< 0.001*
Age ≥ 65	72 (8.9)	138 (28.5)	< 0.001*
Gender §			
Male	462 (59.0)	321 (41.0)	< 0.001*
Female	339 (69.5)	149 (30.5)	
Fever	473 (58.3)	299 (61.9)	0.226
Cough	447 (55.1)	347 (71.8)	< 0.001*
Dyspnea	230 (28.4)	259 (53.7)	< 0.001*
CRP (> 6)	333 (52.7)	315 (77.2)	< 0.001*
Lymphopenia (< 1.5 mil/mL)	263 (41.3)	194 (59.1)	< 0.001*
Ferritin (> 283)	177 (38.7)	152 (68.2)	< 0.001*
NLR (≥ 3.1)	133 (24.1)	111 (48.1)	< 0.001*
D-Dimer (> 500)	100 (20.5)	88 (30.9)	< 0.001*
Platelets (< 150)	76 (11.1)	59 (14.9)	0.029*
O_2 Saturation (< 92)	58 (12.9)	82 (40.2)	< 0.001*
Need for O_2 Support	218 (26.7)	248 (51.6)	< 0.001*
Need for ICU admission	98 (16.3)	150 (34.6)	< 0.001*
Need for High Steroid Dose	74 (10.7)	99 (21.7)	< 0.001*
Need for Actemra	31 (6.9)	68 (20.8)	<0.001*
Need for Convalescent Plasma	20 (4.5)	41 (12.7)	< 0.001*

§ % are calculated from rows.

ferritin, and CRP were significantly higher in the severe and deceased cases. The duration of hospitalization was significantly longer in the moderate cases and survivors than in the severe or deceased cases.

Development of COVEG severity and mortality scores

The regression analysis of the severity predictors showed that D-dimer, age, ferritin, CRP, and the neutrophil: lymphocyte ratio (NLR) were significant predictors. This number of included patients allowed the inclusion of at least 15 patients in each of the predictor variables (positive) for the conduction of multivariable analysis. The odds ratio generated from the regression analysis model was rounded to the nearest decimal to generate a total score of 14: D-dimer ≥ 0.795 of 2, age ≥ 54 of 3.5, ferritin ≥ 406 of 3.5, CRP ≥ 30.1 of 2, and NLR ≥ 2.88 of 3 (Table 4).

A ROC curve identified the cut-off point that discriminates between moderate and severe COVID-19 hospitalized cases. Age, CRP, serum ferritin, NLR, and D-dimer were used as possible discriminators, and a cut-off point giving 80% specificity was taken to

Table 3. The laboratory parameters and duration of hospitalization in cured versus deceased patients and patients with moderate versus severe COVID-19.

Variables	Cure Mean (SD)	Death Mean (SD)	*p* value	Moderate Mean (SD)	Severe Mean (SD)	*p* value
Hemoglobin (g/dl)	12.9 (1.8)	12.1 (2.0)	< 0.001	12.9 (1.8)	12.5 (2.0)	0.001
Platelets ($\times 10^3/\mu L$)	241.1 (87.6)	234.3 (102.7)	0.468 NS	241.1 (85.5)	236.1 (103.1)	0.492 NS
INR	1.42 (5.4)	1.22 (0.26)	0.731 NS	1.45 (5.7)	1.18 (0.3)	0.497 NS
D- dimer (mg/L)	0.981 (2.4)	1.133 (1.2)	0.571 NS	0.951 (2.5)	1.179 (1.5)	0.142 NS
WBC ($\times 10^3/\mu L$)	6.25 (3.3)	9.7 (5.3)	< 0.001	6.1 (3.3)	8.6 (4.8)	< 0.001
Absolute Lymphocytic Count ($\times 10^3/\mu L$)	1.8 (2.41)	1.3 (1.2)	0.006	1.9 (2.5)	1.3 (1.1)	< 0.001
PNL	4.0 (4.9)	7.3 (4.6)	< 0.001	3.8 (5.1)	6.5 (4.4)	< 0.001
NLR	2.8 (3.6)	8.6 (8.7)	< 0.001	2.62 (3.3)	7.2 (7.7)	< 0.001
Urea (mg/dL)	26.2 (20.8)	56.4 (48.5)	< 0.001	25.9 (17.3)	44.6 (45.9)	< 0.001
Creatinine (mg/dL)	10.7 (28.4)	17.2 (39.9)	0.068 NS	9.7 (26.8)	17.1 (38.3)	< 0.01
ALT (IU/L)	49.8 (69.1)	53.9 (54.8)	0.511 NS	45.5 (63.2)	66.1 (77.5)	< 0.001
AST (IU/L)	33.7 (29.7)	50.9 (44.9)	< 0.001	32.4 (29.3)	47.9 (39.2)	< 0.001
LDH (U/L)	278.0 (171.5)	635.7 (344.7)	< 0.001	269.3 (169.4)	460.5 (290.9)	< 0.001
Ferritin (ng/mL)	397.2 (489.9)	1061.2 (855.5)	< 0.001	332.9 (381.6)	944.9 (841.6)	< 0.001
CRP (mg/L)	41.7 (69.3)	116.9 (95.3)	<0.001	39.4 (68.4)	87.5 (89.4)	< 0.001
O2 Saturation (%)	94.9 (4.2)	79.6 (12.4)	< 0.001	96.4 (1.7)	84.7 (9.8)	< 0.001
Duration of hospital stay	13.5 (5.8)	6.8 (5.4)	< 0.001	13.6 (5.6)	10.7 (7.2)	< 0.01

AST: aspartate aminotransferase; ALT: alanine aminotransferase; CRP: C-reactive protein; NR: international normalized ratio; LDH: lactate dehydrogenase; NLR: neutrophils-lymphocytes ratio; PNR: platelets neutrophils ratio; WBCs: while blood cell count.

Table 4. Scores assigned to each predictor of COVID-19 severity (COVEG score).

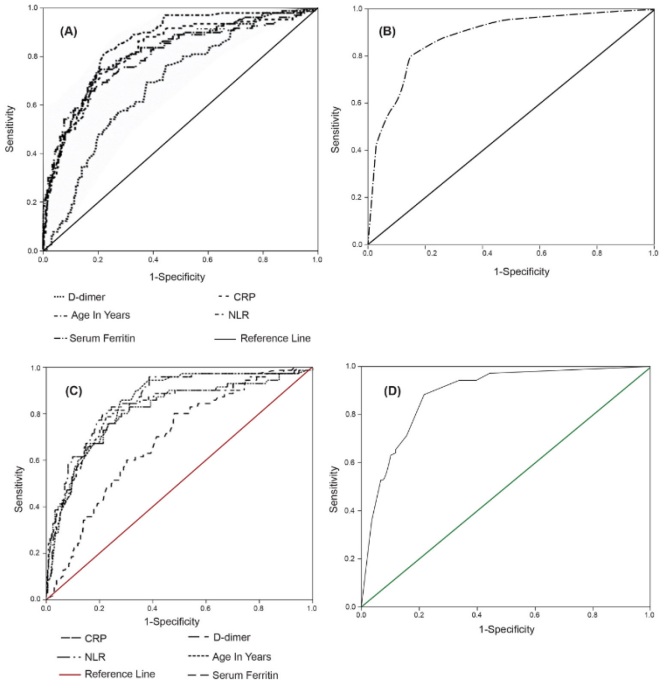
Variables	Point
D-dimer (mg/L)	
≥ 0.795	2
< 0.795	0
Age (years):	
≥ 54	3.5
< 54	0
Ferritin (ng/mL)	
≥ 406	3.5
< 406	0
CRP (mg/L)	
≥ 30.1	2
< 30.1	0
NLR	
≥ 2.88	3
< 2.88	0
Total score	
Moderate disease	< 14
Severe disease	≥ 14

CRP: C-reactive protein; NLR: neutrophils-lymphocytes ratio.

develop the severity score (Figure 1A), with an AUC of the COVEG severity score of 0.882, [Severity Score = D-dimer × 2 (if ≥ 0.795) + Age × 3.5 (If age ≥ 54) + Ferritin × 3.5 (If ≥ 406) + CRP × 2.0 (If ≥ 30.1) + NLR x 3.0 (If 2.88), Cut-off point for severity score = 8.00 Carrying a sensitivity of .723 and a specificity of 0.862. Fatality Score = Severity Score × 1.5 (If ≥ 8.0) + Cardiac Diseases × 1.3 (If Present), Cut-off point for fatality score = 8.75 carrying a sensitivity of 0.714 and a specificity of 0.842] (Figure 1B).

For COVID-19 mortality prediction, a severity score and relevant comorbidities were introduced for binary logistic regression analysis. The final model included the disease severity score and cardiac diseases as predictors of COVID-19 mortality. The Hosmer–Lemeshow test determined the model's fitness to the data (internal validity) (Table 5). The model reveals an overall classification prediction of 86.8 with the Hosmer–Lemeshow test ($p > 0.05$). A score had been assigned to each severity score and cardiac disease as comorbidity, using the odds ratio generated from the regression model. The odds ratio of the two included variables was used to develop the score, being 1.5 for the severity score and three for cardiac diseases, summing up to a maximum score of 21 (Table 6).

Figure 1. D-dimer, age, ferritin, C-reactive protein (CRP), and neutrophils-lymphocytes ratio are COVID-19 severity and mortality predictors. ROC curve displaying the discriminating ability of different severity predictors (**A**) and AUC of the COVEG severity score (**B**). ROC curve displaying the discriminating ability of different mortality predictors (**C**) and AUC of the COVEG mortality score (**D**).



The ROC curve of different mortality predictors (Figure 1C) displays D-dimer with the least AUC compared with the other variables included (age, CRP, ferritin, and NLR). Figure 1D displays the performance of the developed COVEG mortality score in predicting death in patients with COVID-19. AUC for the COVEG mortality score was 0.883, with a cut-off point of 8.00 showing higher sensitivity than specificity and 9.25 showing higher specificity than sensitivity.

Table 6. Score assigned to mortality predictors generated from logistic regression (COVEG mortality score).

Variables	Odds ratio	Score
Severity score	1.412	× 1.5
Coronary diseases	2.951	× 3
Total score	1.5 × 14	21

Table 5. Binary logistic regression for identification of independent COVID-19 mortality predictors.

Variables	B	S.E.	Wald	*p* value	OR	95% CI	
						Lower	Upper
Severity score	0.345	0.041	71.770	0.000	1.412	1.304	1.530
Presence of coronary diseases	1.082	0.492	4.844	0.028	2.951	1.126	7.736
Constant	− 4.190	0.399	110.283	0.000	0.015		
Hosmer and Lemeshow test		4.195	*p* value	0.522			
Classification table overall percentage		86.8					

Discussion

By the end of January 2021, Egypt had more than 161,000 confirmed cases and more than 8,000 deaths due to COVID-19 [1]. The possible causes of these relatively lower infection rates than in other countries could be related to high temperature, humidity, early Bacillus Calmette–Guérin (BCG) vaccination, or a different viral subtype [16].

We believe that this is the most comprehensive study of COVID-19 infection in Egypt, which included 1,308 hospitalized patients with SARS-CoV-2. This is also the first Egyptian study to develop a novel score for predicting in-hospital severity and mortality. The recorded data of these patients aided in the development of COVEG severity and mortality scores with a high predictive value. The values of serum ferritin, CRP, D-dimer, NLR, and age are independent factors for predicting case severity in patients with COVID-19. We developed and validated this easy-to-use five-variable score that allows for accurate stratification of COVID-19 patients admitted to hospitals based on their mortality risk at the time of admission. This method may help clinicians make decisions like care escalation. One of the main goals of risk stratification is to help clinicians make better decisions.

Aged patients with COVID-19 had higher mortality rates. In general, age > 60 years is a cut-off value for higher mortality in several studies [9,17-20]. In our study, age > 54 years is associated with severe outcomes. This difference can be attributed to the age distribution in Egypt. Individuals aged > 55 years represent only 10.5% of the Egyptian population [21]. Similarly, in a single-center Egyptian study, Ramadan *et al.* reported that age > 53 years was a significant predictor of severe COVID-19 [22].

In SARS-CoV-2 infection, the severity of the disease and the fatal outcome are linked to the cytokine-storm syndrome [23]. The infection stimulates the iron release into the reticuloendothelial system, reduces ferritin storage in the liver and spleen, and increases ferritin intracellularly [24,25]. Elevated serum ferritin levels are a poor prognostic indicator for influenza-infected hospitalized patients. [26]. Several studies report that serum ferritin is increased markedly in severe COVID-19 cases compared with mild and moderate cases [22,27-29]. Reports of raised ferritin are also linked to increased mortality in COVID-19 patients [30-34]. In this study, ferritin values of > 406 ng/ml are associated with a 3.6-fold increased risk of a severe disease course.

CRP is a liver-produced acute-phase reactant that rises in inflammatory conditions [35-37]. CRP is usually elevated modestly with viral infection compared with bacterial infection [38,39]. Higher levels in the patients included in this study were tied to increased severity and mortality, reported in several studies [40-44]. D-dimer is another factor related to poor outcomes in patients with COVID-19. D-dimer is a degradation protein resulting from fibrinolysis of a blood clot, which helps diagnose thrombosis [45,46]. Elevated D-dimer levels are a predictive factor for death and a severe outcome [47,48], which is also documented in our cohort.

Lymphopenia in this study was predominant in severe COVID-19 compared with moderate cases. Lymphopenia in COVID-19 is correlated with disease severity and death [34]. In addition, Lympopenia is caused in part by an increase in neutrophil proportions, which might be linked to a cytokine storm triggered by viral infection [49]. The NLR is a readily available indicator of systemic inflammation and has a predictive value in various diseases [50-52]. Several studies have recently shown that NLR can predict COVID-19 disease progression and mortality [53-55]. In a similar Egyptian study, El Kassas *et al.* found that NLR was correlated directly with severe COVID-19 [14]. Liao *et al.* reported that patients with NLR > 9.13 have a 5-fold higher risk of a fatal outcome [55]. Many scoring systems for COVID-19 stated that NLR is a predictor of severity and mortality in infected patients [56-58]. In our study, patients with NLR > 2.88 have an approximate 3-fold risk of developing severe disease, resulting in death.

Our analysis found that the risk of death was significantly higher in patients with diabetes, hypertension, cardiac diseases, and liver or renal diseases. Patients with COVID-19 with other comorbidities share a high risk of a severe disease course and increased fatality [30]. Coronary heart disease is associated with a poor prognosis in influenza and other respiratory viral infections [59-61].

Based on all these different markers of severity and mortality, several scoring systems to predict severity and mortality have been conducted, including different clinical and laboratory parameters. In this study, we developed novel COVEG severity and mortality scores. The COVEG severity score consists of age, D-dimer, ferritin, CRP, and NLR, with a total score of 14. Meanwhile, the novel COVEG mortality score includes the same variables used in the severity score and cardiac diseases, with a total score of 21. Both COVEG severity and mortality scores have high predictive values; AUC is 0.882 and 0.883, respectively. Similar to our COVEG severity score, previous scores are simple and based on

clinical and laboratory data. Dong *et al.* developed a simple severity score system—COVID-19 index and consists of lymphocyte count, D-dimer, and erythrocytic-sedimentation rate [62]. The CALL scoring system proposed by Ji *et al.* includes four parameters; age > 60 years, presence of comorbidity, lymphocyte count, and LDH [63]. The COVID-19-American Association for Clinical Chemistry score is based on comorbidity, albumin, CRP, and age > 60 years [64]. Hui Liu *et al.* also developed a simple score that depends only on age and complete blood count parameters to predict in-hospital mortality for patients with COVID-19 infection [56]. However, some scores consist of 12 parameters, making it challenging to imply in clinical practice [65, 66].

Modified Early Warning Score and Rapid Emergency Medicine Score (REMS) are other mortality scores for critically ill patients. The REMS may provide emergency practitioners with a helpful risk stratification score, particularly for patients over the age of 65 [67]. Similar to our study, Shang *et al.* developed a mortality-scoring system and reported that age > 60 years, coronary heart disease, D-dimer, as well as lymphopenia, and procalcitonin were predictors of in-hospital mortality [49].

Variation in the parameters included in the scoring systems could be attributed to the different sample sizes among the studies, the age distribution and the prevalence of comorbidities in the studied populations, as well as geographical differences in the immune and cytokine responses.

The limitations of this study are that the calculated scores for severity and mortality were created for data collected retrospectively; therefore, some confounders might not have been identified or could have been missed. Finally, a large prospective study requires external validation of COVEG severity and mortality scores.

Conclusions

In this first extended Egyptian study, the COVEG score was developed to predict the severity and mortality of COVID-19 with high accuracy. This provides a guide for clinicians to predict patients who will have progressive disease and will require early ICU admission, thus, providing proper management and reducing mortality.

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Authors' Contributions

The study was designed by MEK, WA, and ME. MAM, HD, EAH, HS, AA, AAA, AFS, EMF, and EM collected study data and oversaw participant visits. KA and HA provided regulatory oversight. ME and MEK provided project management. Data analysis and interpretation were done by MEG and WA. HK, AFS, AA, and MAM wrote the first draft of the article. All authors contributed to the reviewing and editing of the article and approved the final version. Article preparation was done by all study authors and the decision to submit the article for publication was made by all study authors.

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