INTRODUCTION

Beginning in December 2019 a novel corona virus spread from Wuhan, China to the whole World and being accepted as a pandemic by WHO since March 11, 2020. The first case diagnosed in our country was 11th March 2020. Since then there are numerous cases infected by COVID-19 and hospitalised because of disease severity. Urging early identification for severe cases is needed because thousands of people died from COVID-19 pandemic.

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Abstract

Objective: The aim of this study is to find out the potential risk factors including charlson comorbidity index (CCI) score associated with death in COVID-19 patients hospitalised because of pneumonia and try to find a novel COVID-19 mortality score for daily use.

Methods: All patients diagnosed as confirmed or probable COVID-19 pneumonia whom hospitalised in our Chest Diseases Education and Research Hospital between March 11, 2020 and May 15, 2020 were enrolled. The optimal cut-off values, sensitivity and specificity values and odds ratios to be used in mortality prediction of the novel scoring system created from these parameters were calculated by ROC analysis according to the area under the curve and Youden index.

Results: Over 383 patients (n: 33 deceased, n: 350 survivors) univariate and multivariate regression analysis showed that CCI and lymphocyte ratio were prognostic factors for COVID-19-related mortality. Using this analysis, a novel scoring model CoLACD (CoVID-19 Lymphocyte ratio, Age, CCI score, Dyspnoea) was established. The cut-off value of this scoring system, which determines the mortality risk in patients, was 2.5 points with 82% sensitivity and 73% specificity (AUC = 0.802, 95% CI 0.777-0.886, P < .001). The risk of mortality was 11.8 times higher in patients with a CoLACD mortality score higher than 2.5 points than patients with a score lower than 2.5 (OR = 11.8 95% CI 4.7-29.3 P < .001).

Conclusion: This study showed that by using the CoLACD mortality score, clinicians may achieve a prediction of mortality in COVID-19 patients hospitalised for pneumonia.
cardiovascular and cerebrovascular disease, lactate dehydrogenase and d dimer levels, level of CD3+CD8+ T-cells are studied for predictors of mortality, however, there is still a need for a simple scoring system for predicting mortality and determining severe disease for early intervention. Also, as this breakout now accepted as a pandemic not all hospitals have the capacity or the availability to have sophisticated laboratory equipment.

Charlson comorbidity index (CCI) score is developed in 1987 and since then used for the impact of comorbidities on mortality prediction is several studies. Since COVID-19 pneumonia severity is affected by age and comorbidity, we believe that this simple index, symptoms and basic laboratory findings may be used in order to predict mortality in COVID-19 infected hospitalised patients. Therefore, the aim of this study is to find out the potential risk factors including CCI score associated with death in COVID-19 patients hospitalised because of pneumonia and try to find a novel COVID-19 mortality score for daily use.

2 | METHODS

2.1 | Study population

This study was approved by both the Scientific Committee of our hospital and Ministry of Health COVID-19 Scientific Research Evaluation Committee date/number 21.05.2020/4329. For this retrospective, non-interventional, a single-centre case cohort study, we enrolled all patients diagnosed as confirmed or probable COVID-19 pneumonia whom hospitalised in our Chest Diseases Education and Research Hospital between March 11, 2020 and May 15, 2020. The probable and definite diagnosis of COVID-19 pneumonia and all treatment strategies were based on the Guidelines by the Scientific Committee of Ministry of Health (8). All patients hospitalised for COVID-19 pneumonia underwent nasopharyngeal swab test for SARS-CoV-2 virus using real-time reverse-transcriptase-polymerase-chain-reaction (RT-PCR). Positive result on RT-PCR assay of nasal and pharyngeal swab specimens were accepted as laboratory-confirmed patient. Severity of the disease is based on the Guidelines by the Scientific Committee of Ministry of Health.8

2.2 | Data collection

The information for all participants including demographic data, co-morbidities, clinical characteristics, laboratory parameters and outcomes, were collected prospectively. Charlson comorbidity score is calculated from the collected data and information needed is gained from hospitals e-database settings. Mortality data are obtained from hospitals e-information and operating system. Two researchers reviewed and double checked the e-data collection forms. Missing data are mentioned by numbers in the tables.

What's known?

- There are few scoring systems for predicting mortality in COVID-19 infected patients which were clinically impractical.

What's new?

- We created a novel mortality model called CoLACD with four prognostic parameters only; CoVID-19 lymphocyte ratio, age, charlson comorbidity index score, dyspnoea.
- This study showed that by using the CoLACD mortality score, clinicians may achieve a prediction of mortality in COVID-19 patients hospitalised for pneumonia.

2.3 | Statistical analysis

Analyses were performed with SPSS software v 25.5 (IBM, NY, USA). To determine whether continuous data are normally distributed, Shapiro-Wilk and Kolmogorov-Smirnov normality tests were used. Mann-Whitney U-test was used to compare parameters that were not normally distributed and $\chi^2$ and Fisher’s exact test were used for comparison of categorical data. Results were given as median (min-max), number and percentage (%). $P$ value <.05 was considered statistically significant. The predictive values of the parameters for mortality were calculated with univariate and multivariate logistic regression analyses. The optimal cut-off values, sensitivity and specificity values and odds ratios to be used in mortality prediction of the scoring system created from these parameters were calculated by ROC analysis according to the area under the curve and Youden index. The results were presented with 95% confidence intervals.

3 | RESULTS

3.1 | Clinical data

Between March 11, 2020 and May 15, 2020 there were 485 patients admitted to our Chest Diseases Education and Training Hospital in Izmir with a confirmed or suspected diagnosis of COVID-19 infection. After excluding outpatient patients and absence of pneumonia there remained 383 patients whom hospitalised for COVID-19 pneumonia in a between March 11, 2020 and May 15, 2020 (Figure 1). There was a male predominance in the cohort (57.2%). The median hospitalisation time was 6 (1-34) days in the cohort. Demographic data of the whole cohort, the characteristics of the deceased and survivors are showed in Table 1. The median CCI score was 1 (0-11) in the cohort, the median score of the deceased groups was significantly higher compared with survivors [5 (0-11) to 1 (0-10)], ($P < .001$) (Table 1). If we look at the distribution of the age groups between deceased and survivors, there were older patients...
in the deceased group (P = .05). When we compared the 16 different symptoms on admission, only dyspnoea was significantly different between two groups (P < .001) (Table 1). Of the three physical examination findings on admission none of them were different between groups (Table 1).

4 | Laboratory findings

54.5% of the patients were RT-PCR confirmed COVID-19 pneumonia, being PCR confirmed was not different between the deceased and the survivor groups (Table 2). Number of leucocytes, number of lymphocytes and lymphocytes % were statistically significantly different between groups (Table 2). Other laboratory findings which are different between groups are mentioned in Table 2. Of the whole cohort 68.9% of the patients had an abnormal finding on their Chest X-Ray, however, 95.6% had a High-Resolution Computerised Tomography (HRCT) finding.

5 | Predictors of mortality

When the predictive power of risk factors determined for mortality was evaluated with univariate analysis, it was found that patients with dyspnoea had a 7.3 times higher mortality risk (OR = 7.3 95% CI 3.1-17.3). Likewise, mortality risk of patients over 65 years of age was higher than other age groups (Table 3). The cut-off value of lymphocyte%, which determines the mortality risk, was 17.65% with 88% sensitivity and 63% specificity (AUC = 0.802, 95% CI 0.726-0.878, P < .001), while the cut-off value of the CCI score for mortality was determined as 2.5 with 78% sensitivity and 74% specificity (AUC = 0.853, 95% CI 0.787-0.920, P < .001). Patients with lymphocyte% value below 17.65 had a 9.7 times higher mortality risk compared with patients with lymphocyte% above this percentage (OR = 9.7; 95%CI 3.7-25.8; P < .001). And the mortality risk of patients with a CCI score above 2.5 was 10.7 times higher than those with a CCI score of less than this value (OR = 10.7; 95%CI 4.5-25.6; P < .001) (Table 3).

6 | A novel scoring model

To create a simple score and facilitate clinical use, a novel scoring model was established CoLACD (COVID-19 Lymphocyte ratio, Age, CCI score, Dyspnoea) mortality score which scores from 0 to 5 points (Table 4). The cut-off value of this scoring system, which determines the mortality risk in patients, was 2.5 points with 82% sensitivity and 73% specificity (AUC = 0.802, 95% CI 0.777-0.886, P < .001) (Figure 2). The risk of mortality was 11.8 times higher in patients with a CoLACD mortality score higher than 2.5 points than patients with a score lower than 2.5 (OR = 11.8; 95% CI 4.7-29.3; P < .001).

When the predictive power of risk factors included in the CoLACD scoring system for mortality risk was evaluated by multivariate logistic regression analysis, CCI score and Lymphocyte% value was found to be important risk factors for mortality. (OR = 1.5; 95% CI 1.2-1.8; P < .001 and OR = 0.9; 95% CI 0.8-1.0; P = .002, respectively) (Table 5).

7 | DISCUSSION

During the COVID-19 pandemic, with using a simple scoring system during the first admission, for the prediction of patients who will have a severe course, can be life-saving. Therefore, with this study a novel scoring model CoLACD, is developed for prediction of mortality at admission. This study showed that the risk of mortality was 11.8 times higher in patients with a CoLACD mortality score higher than 2.5 points than patients with a score lower than 2.5 points.

In several studies it has been shown that comorbidities play an important role in COVID-19 infected patients. Charlson comorbidity index which is a component of our novel score is valid and a reliable tool for predicting mortality. However, its impact on COVID pneumonia is not studied properly. With this study, we showed that having a high comorbidity score increases the like hood of mortality 10.7 times. A cut off value of 2.5 (which means >3 points) is an independent risk factor for mortality prediction. Our second component age is the basic factor of severity, which has become a consensus in the recent publications in COVID-19 and also in severe acute respiratory syndrome (SARS) infection.
of the first studies determining the characteristics of COVID-19 infection Guan et al showed that Lymphopenia was observed in 82.1% of patients. In several studies it has been found that the lymphocyte percentage descend with the disease, which indicates the direct result of viral infection. And last component of this novel scoring model is the absence of a respiratory symptom dyspnoea; in a meta-analysis by Hu et al showed that the incidence of dyspnoea was 21.4% (95CI 15.3%-27.5%) in COVID-19 infected patients. In a review by Pesola et al investigating 10 studies, suggested that dyspnoea was an independent predictor of mortality with point estimates by odds ratio, rate ratio or hazard ratios ranging from 1.3 to 2.9-fold greater than baseline. Therefore, a symptom predictor of mortality can be used a component of a mortality scoring system.

### TABLE 1 Comparison of demographic and clinical findings of COVID-19 patients who died and survived

| Demographic and clinical data | Total n = 383 | Deceased n = 33 | Survivors n = 350 | P value |
|-------------------------------|--------------|-----------------|-------------------|---------|
| **Age groups n (%)**          |              |                 |                   |         |
| 15-49 y                       | 171 (44.6%)  | 6 (18.2%)       | 165 (47.1%)       | 0.005   |
| 50-64 y                       | 129 (33.7%)  | 15 (45.5%)      | 114 (32.6%)       |         |
| ≥65 y                         | 83 (21.7%)   | 12 (36.4%)      | 71 (20.3%)        |         |
| **Gender n (%)**              |              |                 |                   |         |
| Male                          | 219 (57.2%)  | 24 (72.7%)      | 195 (55.7%)       | 0.059   |
| Female                        | 164 (42.8%)  | 9 (27.3%)       | 155 (44.3%)       |         |
| **Charlson comorbidity index score median (min-max)** | 1 (0.0-11.0) | 5.0 (0.0-11.0) | 1.00 (0.0-10.0) | <0.001 |
| **Smoking history**           |              |                 |                   |         |
| Non-smoker                    | 171 (58.0%)  | 7 (29.2%)       | 164 (60.5%)       | <0.001  |
| Ex-smoker                     | 73 (24.7%)   | 15 (62.5%)      | 58 (21.4%)        |         |
| Active-smoker                 | 51 (13.3%)   | 2 (8.3%)        | 49 (18.1%)        |         |
| **Symptoms on admission**     |              |                 |                   |         |
| Fever                         | 145 (37.9%)  | 9 (27.3%)       | 136 (38.9%)       | 0.190   |
| Conjunctival concession n (%) | 1 (0.3%)     | 0 (0.0%)        | 1 (0.3%)          | 1.000   |
| Nasal concession n (%)        | 9 (2.3%)     | 0 (0.0%)        | 9 (2.6%)          | 0.617   |
| Headache n (%)                | 31 (8.1%)    | 2 (6.9%)        | 29 (9.2%)         | 0.759   |
| Cough n (%)                   | 242 (63.2%)  | 19 (57.6%)      | 223 (63.7%)       | 0.485   |
| Sore throat n (%)             | 72 (18.6%)   | 2 (6.1%)        | 70 (20.0%)        | 0.050   |
| Fatigue n (%)                 | 141 (36.8%)  | 12 (36.4%)      | 129 (36.9%)       | 0.955   |
| Sputum n (%)                  | 41 (10.7%)   | 7 (21.2%)       | 34 (9.7%)         | 0.069   |
| Haemoptysis v                 | 4 (1.0%)     | 1 (3.0%)        | 3 (0.9%)          | 0.304   |
| Dyspnoea n (%)                | 144 (37.6%)  | 26 (78.8%)      | 118 (33.7%)       | <0.001  |
| Nausea and vomiting n (%)     | 31 (8.1%)    | 5 (15.2%)       | 26 (7.4%)         | 0.169   |
| Diarrhoea n (%)               | 28 (7.3%)    | 1 (3.0%)        | 27 (7.7%)         | 0.493   |
| Myalgia n (%)                 | 77 (20.1%)   | 4 (12.1%)       | 73 (20.9%)        | 0.231   |
| Chills n (%)                  | 27 (7.0%)    | 1 (3.0%)        | 26 (7.4%)         | 0.494   |
| Anosmia n (%)                 | 13 (3.4%)    | 0 (0.0%)        | 13 (3.7%)         | 0.396   |
| Anorexia n (%)                | 50 (13.1%)   | 6 (18.2%)       | 44 (12.6%)        | 0.360   |
| **Physical examination findings** |              |                 |                   |         |
| Redness in the throat n (%)   | 21 (6.3%)    | 0 (0.0%)        | 21 (6.8%)         | 0.239   |
| Swelling of the tonsils n (%) | 3 (0.9%)     | 0 (0.0%)        | 3 (1.0%)          | 1.000   |
| Enlarged lymph node n (%)     | 2 (0.5%)     | 1 (3.7%)        | 1 (0.3%)          | 0.155   |

*Bold indicates statistical significant results.*
Factors associated with poor prognosis have been shown in several studies, including age, comorbidities, lymphocytes, laboratory parameters such as serum ferritin, cardiac troponin, lactate dehydrogenase-dimer, IL6, level of CD3⁺CD8⁺ T-cells. But surely a single parameter will not be enough for predicting severe patients. Therefore, there are new scores developed for COVID severity (CALL) and also some well-known scores which were nowadays adapted to COVID-19 (MuLBSTA, qSOFA, CURB-65 and NEWS2).

Ji et al developed a novel scoring model for obtaining the severe COVID-19 patients called CALL score. It was developed for progressive risk estimation using four parameters; comorbidity, age, lymphocyte number and LDH. Using a cut-off value of 6 points, the positive and negative predictive values were 50.7% (38.9%-62.4%) and 98.5% (94.7%-99.8%), respectively, in this model. In the CALL model comorbidity was not specified properly and there was only with/without option, however, in this novel CoLACD model, a verified comorbidity index CCI score is used.

Zang et al developed a scoring model for predicting severity for COVID-19 patients using age, WBC, neutrophil, GFR and myoglobin. This score was not mortality specific but predictor for severity. The scoring system was applied to calculate the predictive value

TABLE 2  Comparison of laboratory and radiological findings of COVID-19 patients who died and survived

| Laboratory findings | Total n = 383 | Deceased n = 33 | Survivors n = 350 | P value |
|---------------------|--------------|----------------|------------------|--------|
| Leucocyte median (min-max) | 6500 (2600-31 900) | 10 800 (4100-31 900) | 6250 (2600-30 900) | <0.001 |
| Neutrophil median (min-max) | 4400 (400-30 300) | 6900 (2800-28 000) | 4350 (400-30 300) | <0.001 |
| Neutrophil % median (min-max) | 70.0 (26.3-98.1) | 75.8 (26.3-96.2) | 70.0 (34.5-98.1) | <0.001 |
| Lymphocyte median (min-max) | 1200 (100-9600) | 1000 (200-9600) | 1200 (100-5500) | 0.088 |
| Lymphocyte % median (min-max) | 20.1 (1.2-55.8) | 10.7 (1.7-30.5) | 20.6 (1.2-55.8) | <0.001 |
| Monocyte median (min-max) | 500 (0-9000) | 600 (100-8600) | 500 (0-9000) | 0.053 |
| Monocyte % 382 median (min-max) | 7.9 (0.5-24.8) | 6.4 (0.5-16.1) | 8.0 (0.7-24.8) | 0.081 |
| Platelet median (min-max) | 231 000 (45 000-8 40 000) | 300 000 (65 000-6 45 000) | 228 000 (45 000-8 40 000) | 0.007 |
| Neutrophil % median (min-max) | 12.1 (7.8-15.7) | 13.3 (8.0-17.7) | 3.9 (0.1-377.5) | <0.001 |
| CRP 380 median (min-max) | 110 (53-531) | 127 (53-531) | 108 (58-531) | 0.021 |
| BUN 340 median (min-max) | 26.9 (9.2-131.0) | 37.3 (15.5-131.0) | 26.5 (9.2-123.0) | <0.001 |
| Creatinin 382 median (min-max) | 0.8 (0.4-3.2) | 1.0 (0.5-3.0) | 0.8 (0.4-3.2) | 0.093 |
| AST 380 median (min-max) | 20.0 (7.0-134.0) | 29.0 (10.0-132.0) | 20.6 (10.0-134.0) | 0.058 |
| ALT 380 median (min-max) | 21.5 (4.0-255.0) | 22.0 (4.0-78.0) | 21.0 (5.0-255.0) | 0.486 |
| Total protein 246 median (min-max) | 0.38 (0.08-4.73) | 0.38 (0.09-1.17) | 0.37 (0.04-4.73) | 0.857 |
| Total protein 246 median (min-max) | 6.6 (4.3-72.4) | 6.2 (4.2-8.9) | 6.7 (4.5-8.0) | <0.001 |
| Albumin 250 median (min-max) | 4.0 (1.9-5.2) | 3.1 (1.9-3.9) | 4.0 (2.1-5.2) | <0.001 |
| Na 379 median (min-max) | 138 (117-146) | 137 (131-147) | 139 (117-167) | 0.004 |
| K 379 median (min-max) | 4.3 (1.1-6.0) | 4.3 (2.6-5.5) | 4.3 (1.1-6.0) | 0.400 |
| LDH 278 median (min-max) | 217 (97-2246) | 422 (119-2246) | 218 (97-969) | <0.001 |
| Ferritin 261 median (min-max) | 206.7 (8.5-2465.5) | 726.1 (102.0-2465.5) | 190.8 (8.5-1787.2) | <0.001 |
| D-dimer 308 median (min-max) | 670.0 (114-10 000) | 1868.5 (397-10 000) | 662 (114-10 000) | <0.001 |
| Troponin-T 287 median (min-max) | 4.5 (0.0) | 19.4 (0.0-3089.0) | 3.9 (0.0-269.0) | <0.001 |

| Radiological findings | Total n = 383 | Deceased n = 33 | Survivors n = 350 | P value |
|-----------------------|--------------|----------------|------------------|--------|
| Findings on the x-ray n (%) | 264 (68.9%) | 31 (93.9%) | 233 (66.6%) | 0.001 |
| X-ray 264 n (%) | Bilateral | 170 (64.4%) | 20 (64.5%) | 150 (64.4%) | 0.988 |
| Unilateral | 94 (35.6%) | 11 (35.5%) | 83 (35.6%) | 0.720 |
| HRCT findings 367 n (%) | 351 (95.6%) | 31 (96.9%) | 320 (96.9%) | 0.001 |

Note: Abbreviations: ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; BUN, Blood urea nitrogen; CRP, C reactive protein; HRCT, High Resolution Computerised Tomography of the lungs; LDH, lactate dehydrogenase.

*Bold indicates statistical significant results.*
and found that the percentage of ICU admission (20%, 6/30) and ventilation (16.7%, 5/30) in patients with high risk was much higher than those (2%, 1/50; 2%, 1/50) in patients with low risk (P = .009; P = .026).22

Myrstad et al in their study with 66 participants aimed to find the ability of the NEWS2 score and other clinical risk scores at emergency department admission to predict severe disease and in-hospital mortality in COVID-19 patients.23 They found that a NEWS2 score ≥6 at admission predicted severe disease with 80.0% sensitivity and 84.3% specificity (Area Under the Curve (AUC) 0.822, 95% CI 0.690-0.953) and also found that NEWS2 was superior to qSOFA score ≥2 (AUC 0.624, 95% CI 0.446-0.810, P < .05) and other clinical risk scores for this purpose.23

These scores either have multiple parameters or need sophisticated laboratory findings. Some of them need calculation and hard to remember the components of the scores. Therefore, in the current pandemic situation and knowing the importance of early identification of severe patients a simple score may help the clinician. In the first health settings without need of an even pulse oximeter by just asking comorbidities, asking the symptom; dyspnoea, a simple haemogram parameter may be helpful for directing the treatment and determining the course of the disease.

However, this study has some limitations. First of all, this is a single centre study but we have consecutively included all COVID-19 patients hospitalised for COVID-19 pneumonia from the start of the pandemic. Also, the hospital that this study takes place on is the only specific pulmonary diseases education and training hospital in the Aegean region. Because of this study’s retrospective design CoLACD score should be validated prospectively. Also, a single time clinical evaluation at admission may not reflect the course of the disease. And lastly as this study was non-intervention

### TABLE 3

| Univariate analysis of mortality risk factors: dyspnoea, age groups, lymphocyte % and CCI score in patients with COVID-19 |
| OR | 95% CI | P value |
|---|---|---|
| Dyspnoea | | |
| With & without | 7.3 | 3.1-17.3 | <0.001 |
| Age groups | | |
| ≥65 y vs <65 y | 2.3 | 1.1-4.5 | <0.001 |
| ≥65 y vs 50-65 y | 1.3 | 0.6-2.9 | <0.001 |
| ≥50 y vs <50 y | 4.0 | 1.6-9.9 | <0.001 |
| 50-65 y vs <50 y | 3.6 | 1.4-9.6 | <0.001 |
| Lymphocyte % | | |
| <17.6% vs >17.6% | 9.7 | 3.7-25.8 | <0.001 |
| CCI score | | |
| >2.5 vs <2.5 | 10.7 | 4.5-25.6 | <0.001 |

Note: Abbreviation: CCI, Charlson Comorbidity Index score.
*Bold indicates statistical significant results.

### TABLE 4

| The calculation of CoLACD score |
| Points |
|---|---|
| Lymphocytes % | |
| ≥17.6 | 0 |
| <17.6 | 1 |
| Age | |
| <50 | 0 |
| 50-65 | 1 |
| ≥65 | 2 |
| CCI score | |
| ≥3 | 1 |
| <3 | 0 |
| Dyspnoea | |
| With | 1 |
| Without | 0 |

Note: Abbreviation: CCI, Charlson Comorbidity Index score.

### FIGURE 2

ROC curve of CoLACD mortality score.

AUC = 0.831; 95% CI 0.777-0.886; P < .001

### TABLE 5

| Multivariate logistic regression analysis of mortality risk factors for patients with COVID-19 |
| OR | 95% CI | P value |
|---|---|---|
| Age groups | | |
| 50-64 vs <50 y | 1.3 | 0.4-4.4 | 0.652 |
| ≥65 vs <50 y | 0.7 | 0.2-2.7 | 0.634 |
| CCI score | | |
| 1.5 | 1.2-1.8 | <0.001 |
| Dyspnoea | 2.5 | 0.9-6.7 | 0.079 |
| Lymphocytes % | 0.9 | 0.8-1.0 | 0.002 |

Note: Abbreviation: CCI, Charlson Comorbidity Index score.
*Bold indicates statistical significant results.
some laboratory parameters such as LDH, D-Dimer, serum ferritin was absent in some patients. However, all components of CoLACD score were complete in the files and the hospital database system. Therefore, we tried to build a mortality score on basic laboratory parameters which is in routine use in first line health settings.

This study showed that a novel model including four parameters: CCI score, Lymphocyte ratio, age and dyspnoea achieved a prediction of mortality in COVID-19 patients hospitalised for pneumonia. If validated with prospective studies, CoLACD score can be used for effective utilisation of medical resources in the COVID-19 pandemic for decreasing mortality.

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DISCLOSURE

We do not have any financial or non-financial potential conflicts of interest.

AUTHOR CONTRIBUTIONS

Conceptualisation: YV, AKC; Data curation: GP, BK; Formal analysis: BA, CA; Investigation: EB, GB; Methodology: SA, SE; Project administration: EY; Resources: YV, GP; Supervision: AKC, BK; Validation: BA; Writing-original draft: YV, EB; Writing-review and editing: CA, SA, SE.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

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