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# Predictors of Mortality in COVID-19 Patients -A One-year Institution ObservationalRetrospective Case-Control Study

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Running title: Predictors of Mortality in COVID-19 Patients

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#### ABSTRACT

**Introduction:** To identify risk factors of mortality based on symptoms, comorbidities, vital signs, and laboratory examinations, we retrospectively assessed predictors of mortality in COVID-19 patients and analyzed data from a recognized COVID-19 tertiary care center, in South India.

**Patients and Methods:** A total of 176 patients with COVID-19 who died in hospital served ascases and a total of 680 COVID-19 patients who were discharged during the same period served as control. Data on clinical manifestations, comorbidities, vital signs, lab investigations, HR- CT, and treatment details were collected in this single-centered, retrospective, observational study who were hospitalized in tertiary care center in South India. Univariate and multivariate logistic regression was performed to investigate the relationship between each variable and therisk of death of COVID-19 patients.

**Results:** Among 856 COVID-19 patients hospitalized [680"survivors" and 176 "non- survivors" (deaths)], there was a male predilection [77%, 524/746)] among survivors and 90% (159/176) among non-survivors. The mean age was 62 years among cases and 50 years among the control group. Comorbid conditions hypertension 83/176(47%) and Type 2 diabetes mellitus 98/176(55.7%) having a significant impact on mortality. Significant other variables predicting mortality were: symptomology, type of steroid used, and inflammatory markers.

**Conclusion:** Hypertension, cardiovascular disease, and diabetes were the most common comorbidity in patient's death due to COVID-19. Inflammatory markers have a prognostic significance with higher levels being associated with worse outcomes. The clinician can better manage and treat patients by identifying those who are at risk of death with the aid of COVID-19 mortality predictors.

Keywords: COVID-19, Inflammatory markers, Mortality predictors.

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#### **INTRODUCTION**

In December 2019, SARS CoV-2, a novel coronavirus based infectious illness first surfaced in Wuhan City, China, which became a pandemic soon, taking many lives creating havoc in all aspects and shattered the life whole mankind.<sup>1</sup> The COVID-19 pandemic's first case was identified in the India in Karnataka on March 8, 2020. As of October 25, 2022, there were 40,097 fatalities and 40,01,655 confirmed cases in Karnataka with 9,135 current cases and 39,52,381 recoveries.<sup>2</sup> On March 11, 2020, the World Health Organization declared the disease brought on by the novel severe respiratory syndrome coronavirus 2 to be a Pandemic.<sup>3</sup> Advanced age, male gender, and comorbidities such as diabetes mellitus, systemic hypertension, renal disease, and coronary artery disease were all reported as risk factors for mortality in COVID-19 patients.<sup>4</sup>

A higher plasma level of biomarkers like D-dimer, C-Reactive Protein (CRP), serum ferritin, Interleukin-6 (IL-6), and procalcitonin (PCT) provided early clues to the severity of disease.<sup>5</sup> In addition, symptoms such as fever, cough, dyspnea, weakness might give early indications of the severity of the illness.<sup>6</sup> Studies that have already been published include limitations in their design, such as single-center data analysis and relatively small sample numbers.<sup>7</sup> To identify the risk factors of mortality based on vital signs, symptoms, comorbidities, and laboratory examinations, we assess the predictors of mortality in COVID-19 patients and analyze the data retrospectively from a recognized COVID-19 tertiary care center in South India.

#### **Patient and Methods**

**Source of Data**: The data was collected retrospectively from patients diagnosed with COVID-19 pneumonia admitted at a tertiary care center in Belagavi, South India. A one-year institution-Observational retrospective case-control study. During the period from January 2021 to December 2021. A total of 856 diagnosed cases of COVID-19 pneumonia were analyzed in the study.

#### **Inclusion criteria:**

1. Patients diagnosed with SARS-CoV2 through RT PCR positive or Rapid antigen test positive or CBNAAT positive with the age group of more than 18 years will be included in the study.

2. HR-CT/CT -COVID-19 suspect individuals were also included in the study. A chest CT scan can be classified according to the likelihood that a patient has verified COVID-19 with lung involvement using the COVID-19 Reporting and Data System (CO-RADS) assessment method. If one or more of the clearly described signs, such as ground-glass opacities in a typical

peripheral subpleural distribution, subpleural/interlobular interstitial thickening, the atoll sign, halo, and reverse halo signs, were present, HR-CT was considered "positive" for the diagnosis of COVID-19 pneumonia.

#### **Exclusion criteria:**

- 1. Patients in the age group less than 18 years of age were excluded
- 2. Pregnant and lactating women

#### Methodology

The study was approved by the Institutional Ethical and Research Committee and requested for waiver of consent which was accepted. The study was a retrospective observational casecontrol study. A questionnaire concerning: age, sex, oxygen saturation at the time of presentation, date of symptom onset to hospital, laboratory biomarkers (Hscrp, D-dimer, Procalcitonin test, IL6, ferritin) comorbidities (Hypertension, Type 2 diabetes mellitus, Ischemic Heart diseases, Chronic Kidney disease, Chronic liver disease, cerebral vascular accident), any past pulmonary disease (as defined by chronic obstructive pulmonary disease, asthma, tuberculosis, bronchiectasis etc), mode of respiratory support (IMV, noninvasive mechanical ventilation [NIV], oxygen mask) at the time of admission, medications were recorded. All patients with a diagnosis of COVID-19 pneumonia as per inclusion criteria were included in the study. For the 856 individuals with confirmed COVID-19, this retrospective observational study will look at clinical traits and potential risk factors for mortality. The purpose of this study was to look into any clinical traits and laboratory measurements that might be indicators of mortality among COVID-19 patients who were admitted.

#### Statistical analysis

Categorical variables are expressed as number of patients and percentage of patients and compared across the groups using Pearson's chi-square test for independence of attributes /Fishers' exact test as appropriate. Continuous variables are expressed as mean and standard deviation and compared across the groups using independent sample t-test/Mann-Whitney U-test as appropriate. For graphical representation of data pie diagrams and bar diagrams are used. The statistical software SPSS version 25 has been used for the analysis. An alpha level of 5% has been taken. i.e; if p-value is less than 0.05 it has been considered as significant. The relationship between clinical traits and laboratory values and the likelihood of death was examined using univariate and multivariate logistic regression. Stepwise selection was used to

select the multivariate logistic model. This approach uses a combination of forward and backward selection methods. We began by using the forward selection method, which gradually incorporated important predictors from the univariate logistic model into the model. Each time we added a predictor, we examined the model's existing predictors. Any that weren't statistically significant (p-value >0.05) were removed from the model. Only predictors with a statistically significant (p-value of <0.05) were included in the final multivariate model. The stepwise selection method's benefit is that it enables the use of different models for testing

#### Results

The research comprised a total of 856 COVID-19 patients with a mean age being 52.816 years. Around 683 patients (79.7 %) were male. 176 patients out of the 856 died who were included in the case group (non-survival group). 680 patients out of the 856 patients who survived were included in the control group. The age group of the patients in the case and control group are displayed in Table 1 The area under this ROC curve of the test variable: age is 0.706 which shows how accurately a logistic regression model distinguishes positive and negative outcomes at all potential cutoffs. Age shows higher sensitivity and specificity in predicting the mortality of COVID-19 patients (Figure 1a). The mean age of the patients in the mortality group was  $62.1\pm13.2$ years and in the control group, it was  $50.3\pm16.7$  years (p < 0.001). There were 159 males (90%) in the case group and 17 females (9.7 %) in the case group whereas in the survival group, there were 524 males (77%) and 156 female patients (23%).

It was found that the mean admission respiratory rate in the case group ( $29.8\pm8.9$  cycles/min) was higher than the control group ( $20.9\pm4.2$  cycles/min) thereby showing its statistical significance (p<0.001). Among the case group, 176 died in the hospital. Initial oxygen saturation ( $85.2\pm13.9\%$ ) was associated with a risk for mortality which showed its statistical significance (p<0.001) compared with the control group ( $95.4\pm39.3\%$ ). The mean duration of the time to hospital from symptom onset was higher in the case group ( $4.9\pm3.5$  days), although it was not statistically significant (p<0.215). The area under this ROC curve of the test variable: Respiratory rate is 0.840 which shows the significance of our logistic regression model. Respiratory rate at the time of admission shows higher sensitivity and specificity in predicting the mortality of COVID-19 patients (Figure 1b). The area under this ROC curve of the test variable: Nariable: Admission SpO<sub>2</sub> is 0.246. Admission SpO<sub>2</sub> shows low sensitivity and higher specificity in predicting the mortality of COVID-19 patients (Figure 2a).

Out of 176 COVID-19-positive patients who died, it was found that the majority of the patients were on rebreathing masks (48.86%) at the time of admission, followed by patients maintaining a room comprising up to 22.15%. The mode of ventilation on admission is shown in Table 2. 14.2 % of the study group required invasive/non-invasive mechanical ventilation at the time of admission. It was also found that only 4.5% of the study group was on oxygen mask and 2.2% on High-flow nasal cannula (HFNC). Out of 680 COVID-19-positive patients who survived, it was found that the majority of the patients were maintaining room air comprising up to 429 individuals (63.08%) at the time of admission. 11.4 % (78 patients)of the control group required a rebreathing mask. It was also found that only 0.5% (4 patients) of the control group required mechanical ventilation and 0.2% (2 patients) on HFNC. In both the group, we had missing data on the mode of ventilation at the time of admission comprising up to 14 (7.9%)and 143 (21.02%) in the study and control group. The comparison of symptoms and clinical is findings between groups shown in Table 3. Dyspnoea, fever, and cough were the most frequently reported symptoms upon admission; dy spnoea was considerably more common in patients who died, whereas fever, cough, and wea kness were more frequent in those who survived. The association of comorbidities is represented in Table 4. Hypertension, diabetes mellitus, and IHD were the most common comorbid conditions present in the patients with COVID-19 pneumonia thereby showing its statistical significance in leading to mortality. It was found that the CT severity score had a prognostic significance with higher levels being associated with worse outcomes. The mean CT severity score in non survival group (14.8±6.1) was higher compared to the survival group  $(12.4\pm5.4)$  thereby showing its statistical significance (p < 0.025) (Figure 2b). The area under this ROC curve of the test variable: CT severity score is 0.633. CT severity score shows higher sensitivity and specificity in predicting the mortality of COVID-19 patients.

The majority of patients had baseline measurements that were consistent with an acute inflammatory response, such as high levels of procalcitonin, CRP, and ferritin; these measurements were all noticeably altered in patients who died. Urea, creatinine, and LDH serum concentrations were all considerably greater in the mortality group than in the survivor group (Table 5). Additionally, D dimer, S. ferritin, and IL-6 levels were higher in non-survivors. Figure 3 shows the ROC for both groups' outcomes of hospitalization for inflammatory biomarkers, which in turn shows its sensitivity and specificity in predicting mortality in COVID-19 patients.

Remdesivir injection was relatively safe, and in both the groups no major adverse events were reported. When intravenous methylprednisolone was given to hospitalized COVID-19 pneumonia patients instead of dexamethasone, it resulted in shorter hospital stays, better clinical outcomes, and higher survival rates (Table 6). Finally, admission respiratory rate, spo2, older age, higher inflammatory markers at admission, and elevated inflammatory markers were found to be independent predictors of mortality in the multivariate Cox proportional hazard model. The other significant indicators of greater mortality in these patients were blood urea, creatinine, and CT severity (Table 7).

#### Discussion

The primary goal of this observational retrospective study was to evaluate and characterize the key clinical predictors and risk factors for mortality in COVID-19 participants. A total of 856 COVID-19 patients were enrolled in this observational retrospective case control study.176 patients who died were included in the case group (non-survival group). 676 patients who survived were included in the control group. Demographic data, oxygen saturation at the time of presentation, day of onset of symptoms to hospital, laboratory biomarkers (Hscrp, D-dimer, S. PCT, IL-6, S.ferritin) comorbidities (HTN/T2DM/ IHD/CKD/CLD/ CVA), mode of respiratory support (IMV, noninvasive mechanical ventilation [NIV], oxygen mask) at the time of admission, medications were recorded.

In this case-control study, older people, the male sex, and people with pre-existing diabetes and/or hypertension predominated and showed a positive correlation for the probability of dying from COVID-19. There were 159 males (90%) and females (10%) in the mortality group with the mean age of the patients being  $62.1\pm13.2$  years. Whereas in the control/survivor group, there were 524 males(77%) and 156 females patients(23%) with the mean age being  $50.3\pm16.7$  years(p<0.001). A study by Nguyen et al revealed that men have a higher respiratory rate, mechanical ventilation, a longer length of hospital stay, and a higher death rate even when compared across age groups, race/ethnicity, and comorbidity.<sup>[13]</sup> According to a study by Bart G. Pijls et al, individuals over the age of 70 and men have a higher risk of COVID-19 infection, severe illness, ICU hospitalization, and mortality. This risk is based on meta-analyses of 59 studies that included 36,470 people.<sup>[14]</sup>

In this study, all patient's oxygen saturation levels at the time of admission were noted. When compared to the survival group, which had a mean spo2 of 95.439.3, it was found that the non-survival group's was 85.213.9, demonstrating its statistical significance. (p<0.001). According to a study by Fernando Mejia et al, oxygen saturation below 90% at entry is a significant

predictor of in-hospital mortality in patients with COVID-19.<sup>[61]</sup> Another study by Praveen V. et al it was found that SPO2 < 90% at admission is a reliable indicator of mortality in COVID-19 patients.<sup>[15]</sup>

Before being admitted to our hospital, the average symptom duration was  $4.6\pm3.2$  days. However it was found that there was no statically significance in between the two groups in presenting to the hospital since the symptom onset (p< 0.215). One can speculate that some of the patients in the case or control group experienced hypoxemia sooner before being admitted because the median time for symptom onset was similar for both groups. This suggests that we require a more effective, quicker method of identifying hypoxemia in the community.

According to our study, the respiratory rate upon admission was likewise related to a relative risk for mortality. It was found that mean respiratory rate in non survival group was  $29.8\pm8.9$  cpm compared to survival group being  $20.9\pm4.2$  cpm thereby showing its statistically significance. (*p*< 0.001). In accordance with a study conducted by Yuriy Pya et al<sup>[16]</sup>. It was discovered that CRP and respiratory rate were separate predictors of mortality.

Respiratory rate being one of the components of systems like CURB65 score (Confusion, Urea, Respiratory Rate, Blood Pressure, Age > 65 years) and APACHE "(Acute Physiology and Chronic Health Evaluation-II)" score shows its importance.[17] The majority of patients in the control group, which included 429 patients (63%) maintained at room air compared to the 39 patients (22.15%) in the non-survival group.Additionally, it was discovered that the majority of patients on NIV/IMV at the time of admission had a greater death rate, demonstrating the importance of this finding in predicting the mortality of covid patients.

Nearly 50% of patients in the non-survival group were using non-rebreathing masks at the time of admission, compared to only 11% in the control group. IMV was required more frequently and for a shorter period of time in the patients who died, indicating a more serious respiratory injury. The early symptoms that people with COVID-19 have experienced symptoms can be moderate or severe tiredness, dyspnea, and fever The minor symptoms include cough, anorexia, and sore throat.<sup>[18,19]</sup>

In our study, we observed that dyspnea (87%) was much more common in patients who died, but fever(61%), loss of taste, and cough were more common in patients who lived. These symptoms were most frequently reported upon admission. It was also found out that major symptom common present in these two groups was cough which was upto 60% in the both groups. Fever, dry cough, exhaustion, productive cough, and shortness of breath were the most prevalent symptoms in a research by Liang W et al. <sup>[20]</sup>

Similarly a study done by Lan Yang et al showed that fatigue, expectoration, hemoptysis, dyspnea, and chest tightness were the independent predictors of death in COVID. In our study we found that both groups had high rates of comorbid conditions such hypertension, diabetes mellitus with HTN alone contributing upto fifty percentage of the patients in the mortality group. It was also noticed that diabetes were present in 32 % of patients in mortality group and 26 % in survival group. However, in our investigation, having two or more comorbidities was linked to mortality.

Similarly in a study done by Je-Wook Chae et al research, patients with diabetes who also had end-organ damage (51.1%), congestive heart failure (9.9%), coronary artery disease (8.1%), and stroke (6.8%) were more likely to die than those without these conditions. [21] The risk of death from COVID- 19 is dramatically increased by comorbidities.Patients with COPD and CKD had a greater risk of dying. [22]

A meta-analysis of 1389 COVID-19 patients, 19.7% of whom had severe disease, revealed a strong correlation between CKD and severe COVID-19.[22] In one of the study from South Korea, which found that patients with diabetes had a much higher mortality rate than those without it (20.0% vs. 4.8%). Analysis of a study by Mammen JJ et al revealed that the presence of diabetes was not significantly different between survivors and non-survivors (42.5% vs. 49.2%, p=0.310). <sup>[23]</sup>

In this study it was demonstrated that, compared to survivors at admission, non-survivors with confirmed COVID-19 had greater levels of inflammatory markers (such as ferritin, CRP, IL-6, procalcitonin, and d-dimer) thereby showing its significance in predicting the mortality in covid patients (p<0.001). According to a retrospective study by Aditi Parimoo et al higher levels of inflammatory markers were linked to a worse outcome of 142 patients admitted with COVID 19. [24]

Similarly in a study done by Rahman T et al, Age, Lymphocyte count, D-dimer, CRP and serum creatinine acquired upon hospital admission were revealed as the primary predictors of hospital death.

Patients who did not survive showed multi organ involvement, like acute renal failure, an increase in a number of cardiac involvement and procoagulant activity indicators. The majority of patients who experienced acute renal failure received conservative treatment. [25] Numerous studies have been carried out to determine the correlation between these markers and patients

with COVID19 overall prognosis. A severe illness course has been independently related with high blood ferritin concentrations at the time of admission. One of the main causes of death in patients with severe COVID-19 disease has been related to the cytokine storm brought on by the release of proinflammatory factors, which is similar to that observed in other diseases.[26] In this study, the median IL-6 level was 341.6+860.7pg/ml in non-survivors against 84.7+299.3 pg/ml in survivors. Higher IL-6 levels were related to more COVID deaths (p = 0.006).

In the absence of a specific treatment for the illness, early detection of key laboratory markers such as C-reactive protein (CRP), urea, creatinine, interleukin-6 (IL-6), D-dimer, ferritin, and CT-severity score for disease severity may help in monitoring and preventing disease development towards a severe form. The prognosis and course of the illness are shown to be related to these lab indicators.

In one of the study done by Chaochao Tan et al ,it showed Greater CT severity scores and significant lung involvement were linked to higher CRP levels in the early stages of the disease [27].

Our findings demonstrated that patients with greater CT-Severity score had significantly higher mortality rates. Mean CT severity score in non survival group( $14.8\pm6.1$ ) was higher compared to survival group ( $12.4\pm5.4$ ) thereby showing its statistically significance .

Similar findings were reported by Abbasi et al after study being done on 262 patients, discovered that COVID-19 patients with elevated CT-SS had considerably higher death rates. [28]

In another study done by Yilmaz et al on 130 covid patients, serum ferritin and D-dimer levels were found to be elevated and to have a moderately correlation with CT severity.[29]

Similarly a recent study by Akdur G. et al on 655 patients

revealed that patients with a higher CT severity score

had a significant mortality risk and needed an extended stay in the intensive care unit (ICU) of more than five days thereby correlating with the data of our study showing its significance in predicting the mortality in covid patients. [30]

Temporal variations in chest CT severity scores and characteristics may be useful for detecting severe cases early and ultimately lowering the COVID-19 death rate.[31]

When intravenous methylprednisolone was given to hospitalised COVID-19 pneumonia patients instead of dexamethasone, it resulted in shorter hospital stays, better clinical outcomes, and higher survival rates.

Based on "the theory that methylprednisolone has stronger lung penetration, it can operate as a better immunosuppressive agent in the treatment of COVID-19 and in improving respiratory problems."

Our data demonstrated that methylprednisolone had a substantial positive impact on the patient's treatment process resulting in decreased requirement for mechanical ventilation thereby reducing duration of hospital stay. [32, 33]

The Randomised Evaluation of COVID-19 Therapy (RECOVERY Trial) is a clinical trial with a sizable enrollment that examines potential therapies for patients in the United Kingdom who have been admitted to the hospital with severe COVID-19 infection.

In this trial consisting of 2104 patients it was found that dexamethasone treatment reduced mortality in patients hospitalised with Covid-19 who were getting invasive mechanical ventilation or oxygen supplementation but not in those individuals maintaining at room air.[34]

If taken at the right moment during the course of the disease, glucocorticoid medications are known to be effective in calming the inflammatory storm by inhibiting the expression of pro-inflammatory genes and lowering cytokine levels. [35]

A study by Wang et al. found that patients who had taken 1-2 mg/kg/day of methylprednisolone for 5-7 days had shorter hospital stays and need of lesser incidence of mechanical ventilation. [36]

In this study also, those who took methylprednisolone had lower fatality rates than those who received dexamethasone in our study. (p < 0.001)

The Cox regression model was then used to assess each variable that had a significant p-value in the univariate analysis.

Inflammatory indicators, age, respiratory rate, admission spo2, symptoms, comorbidities, and CT severity all underwent multivariate logistic regression analysis. Age, sex, RR, admission spo2, CT severity score, and inflammatory biomarkers are factors that were statistically significantly linked to a higher risk of mortality in COVID-19 disease.

In a meta-analysis done by Mehraeen E et al , age, hypertension, and diabetes mellitus were found to significantly increase the risk of mortality among COVID-19 patients that included 114 studies and 310,494 patients from throughout the world. Only diabetes mellitus showed an independent connection with higher mortality in the multivariate analysis.[37]

In another meta analysis study done by Shi C et al they found 36 observational studies out of which 27 were used . The following significant risk factors were found to be associated with mortality : old age, male sex, preexisting comorbidities (especially chronic kidney, respiratory, and cardio-cerebrovascular diseases), dyspnea symptoms, complications during hospitalisation, corticosteroid therapy, and a severe condition. Furthermore, a number of aberrant laboratory indicators related to renal parameters, inflammation, coagulation were linked to poor outcomes.[38]

There were 7106 COVID19 patients in total that were found through a meta-analysis study done by Zakariaee et al. The findings of this study suggest a link between CT-SS and COVID-19 patient death.[39]

Our study revealed a number of important variables like age, RR, spo2 at the time of admission, comorbidities, investigation which included CT scan and the Covid inflammatory marker, and finally steroid treatment linked to elevated mortality risk which was consistent with all these studies. These variables can be used as a useful predictor marker to identify high-risk COVID19 patients at an early stage for early disease management.

Lastly, regarding the impact of vaccination in reducing the mortality of covid patients, it was found that COVID19 vaccine has significantly changed the pandemic's trajectory and saved tens of millions of lives worldwide. [40]

The effect of vaccination couldn't be determined because the Covid vaccinations hadn't yet been released, and our study was conducted in the group that was affected by the first wave of Covid in 2020. In the existence of vaccinations, the Case fatality rate depends not only on how well they work to prevent mortality but also on how well they work to identify emerging illnesses.[41] In order to provide early preventative measures for a better outcome, it is crucial to understand sickness severity and outcome predictors.

The risk of death linked with COVID-19 may be greatly decreased by implementing proper protection and interventions for COVID-19 patients in general and in particular male patients with age 50 years who have comorbidities.[42]

#### Conclusion

Hypertension, cardiovascular disease, and diabetes were the most common comorbidity in patients death due to COVID-19. Inflammatory markers have a prognostic significance with higher levels being associated with worst outcomes. The clinician can manage and treat patients

by identifying those who are at risk of death with the aid of COVID19 mortality predictors in

a better way.

## **Conflict of Interest: None**

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|             | Total No (%)      | Non-survival group No (%) | Survival Group<br>No (%) | p-value |  |  |
|-------------|-------------------|---------------------------|--------------------------|---------|--|--|
| Patients    | 856               | 176                       | 680                      |         |  |  |
|             | Mean age in years |                           |                          |         |  |  |
| Age in year | 52.8±16.7 years   | 62.1±13.2 years           | 50.3±16.7 years          | < 0.001 |  |  |
| Sex         |                   |                           |                          |         |  |  |
| Male        | 683(79.7%)        | 159(90.3%)                | 524(77.1%)               | <0.001  |  |  |
| Female      | 173(20.3%)        | 17(9.7%)                  | 156(22.9%)               | <0.001  |  |  |

 Tables

 Table 1. Age group of the patients in the case and control group.

# Table 2. Mode of ventilation on admission.

|   | Gro                         | Total                   |               |
|---|-----------------------------|-------------------------|---------------|
|   | Non-survival cases<br>n (%) | Survived cases<br>n (%) |               |
| Missing Data                                    | 14 (7.90%)                  | 143 (21.02%)            | 157 (18.30%)  |
| High Flow Nasal cannula                         | 4(2.27%)                    | 2(0.20%)                | 6 (0.70%)     |
| Non-Invasive/Invasive<br>mechanical ventilation | 25(14.20%)                  | 4 (0.50%)               | 29 (3.30%)    |
| Non-rebreathing mask                            | 86 (48.86%)                 | 78 (11.47%)             | 164 (19.15%)  |
| Oxygen Mask                                     | 8 (4.5%)                    | 24 (3.52%)              | 32 (3.70%)    |
| Room air  | 39 (22.15%)                 | 429 (63.08%)            | 468 (54.67%)  |
| Total   | 176 (20.60%)                | 680 (79.40%)            | 856 (100.00%) |

# Table 3. Symptoms in the case and control groups.

| Symptoms         | Total no (%) | Mortality cases<br>no (%) | Survived cases<br>no (%) | P value |
|------------------|--------------|---------------------------|--------------------------|---------|
| Dyspnea          | 512(59.8)    | 154(87.5)                 | 358(52.6)                | 0.002   |
| Cough            | 493(57.6)    | 104(59.1)                 | 389(57.2)                | 0.673   |
| Chest pain       | 29(3.4)      | 6(3.4)                    | 23(3.4)                  | 0.712   |
| Fever            | 517(60.4)    | 101(57.4)                 | 416(61.2)                | 0.325   |
| Weakness         | 80(9.3)      | 11(6.3)                   | 69(10.1)                 | 0.014   |
| Mylagia          | 49(5.7)      | 35(19.9)                  | 14(2.1)                  | 0.007   |
| Loss of smell    | 21(2.5)      | 6(3.4)                    | 15(2.2)                  | 0.822   |
| Loss of taste    | 40(4.7)      | 4(2.2)                    | 36(5.3)                  | 0.042   |
| Loose stools     | 37(4.3)      | 1(0.6)                    | 36(5.3)                  | 0.003   |
| Vomiting         | 7(0.8)       | 5(2.8)                    | 2(0.3)                   | 0.001   |
| Sore throat      | 25(2.9)      | 4(2.2)                    | 21(3.1)                  | 0.562   |
| Loss of appetite | 10(1.2)      | 9(5.1)                    | 1(0.1)                   | 0.001   |

| Comorbidities            | Total no (%) | Non-survival cases<br>no (%) | Survival case<br>no (%) | P value |
|--------------------------|--------------|------------------------------|-------------------------|---------|
| Hypertension             | 238(27.8)    | 83(47.2)                     | 155(22.8)               | 0.041   |
| Diabetes mellitus        | 277(32.4)    | 98(55.7)                     | 179(26.3)               | 0.047   |
| Chronic kidney disease   | 17(2.0)      | 8(4.5)                       | 9(1.3)                  | 0.012   |
| Chronic liver disease    | 5(0.6)       | 1(0.6)                       | 4(0.6)                  | 0.899   |
| Thyroid disorder         | 11(1.3)      | 4(2.3)                       | 7(1.1)                  | 0.031   |
| Bronchial asthma         | 13(1.5)      | 5(2.8)                       | 8(1.2)                  | 0.019   |
| Ischemic Heart disease   | 65(7.6)      | 26(14.8)                     | 39(5.7)                 | 0.022   |
| Cerebrovascular accident | 4(0.5)       | 1(0.6)                       | 3(0.4)                  | 0.231   |
| Psychiatric disorder     | 4(0.5)       | 1(0.6)                       | 3(0.4)                  | 0.231   |

Table4. Association of comorbidities in the case and control group.

# Table 5. Association of Inflammatory markers among the control and case group.

| Variable                      | Total no (%)     | Non-survival<br>Cases no (%) | Survival cases<br>no (%) | P value |  |  |  |
|-------------------------------|------------------|------------------------------|--------------------------|---------|--|--|--|
| Remdesvir (No of doses)       | 5±3              | 5±3.1                        | 5±2.3                    | 0.911   |  |  |  |
| Tocilizumab (No.<br>of Doses) | 2±1              | 2±1.3                        | 2±1.3                    | 0.894   |  |  |  |
| Type of Steroid used          |                  |                              |                          |         |  |  |  |
| Methylprednisolone            | 576              | 142 (24.6 %)                 | 434 (75.3 %)             | <0.001  |  |  |  |
| Dexamethasone                 | Dexamethasone 98 |                              | 89 (90.8 %)              | <0.001  |  |  |  |

# Table 6. Multivariate logistic regression analysis

| Variable                    | Total no (%) | Non survival<br>cases<br>no (%) | Survived<br>cases<br>no (%) | P value |
|-----------------------------|--------------|---------------------------------|-----------------------------|---------|
| <b>Ferritin</b> 569.6±854.5 |              | 1015.3±97.05                    | 448.2±778.1                 | 0.001   |
| LDH                         | 420.6±282.5  | 678.2±419.1                     | 357.9±191.7                 | 0.001   |
| hsCRP                       | 110.9±224.8  | 195.9±165.5                     | 76.7±236.6                  | 0.001   |
| IL-6                        | 13.6.1±478.9 | 341.6±860.7                     | 84.7±299.3                  | 0.006   |
| d-Dimer                     | 942.2±3473.7 | 1370.6±1569.3                   | 837.6±3790.4                | 0.025   |
| <b>Urea</b> 44.5±39.8       |              | 74.9±57.7                       | 35.4±26.7                   | < 0.001 |
| Creatinine                  | 3.9±45.5     | 1.9±2.1                         | 4.6±52.0                    | 0.558   |

| Variable                | р      | C E   | <b>1</b> | OD     | 95% CI for OR |        |
|-------------------------|--------|-------|----------|--------|---------------|--------|
| variable                | В      | 5.E.  | p-value  | UK     | Lower         | Upper  |
| Age                     | -0.066 | 0.02  | 0.001    | 0.936  | 0.9           | 0.973  |
| Sex                     | 1.614  | 0.868 | 0.063    | 5.021  | 0.916         | 27.524 |
| Admission RR            | -0.217 | 0.05  | 0.001    | 0.805  | 0.73          | 0.887  |
| Admission spo2          | 0.058  | 0.034 | 0.085    | 1.06   | 0.992         | 1.133  |
| CT severity score (/25) | -0.08  | 0.043 | 0.061    | 0.923  | 0.849         | 1.004  |
| Ferritin                | -0.001 | 0     | 0.014    | 0.999  | 0.998         | 1      |
| LDH                     | -0.007 | 0.002 | 0.001    | 0.993  | 0.99          | 0.997  |
| hsCRP                   | -0.009 | 0.003 | 0.005    | 0.991  | 0.985         | 0.997  |
| IL-6                    | 0      | 0     | 0.87     | 1      | 0.999         | 1.001  |
| d-Dimer                 | 0      | 0     | 0.651    | 1      | 1             | 1      |
| Urea                    | -0.044 | 0.007 | 0.001    | 0.957  | 0.945         | 0.97   |
| Creatinine              | 0.253  | 0.148 | 0.088    | 1.287  | 0.963         | 1.722  |
| Constant                | 2.925  | 0.307 | 0.001    | 18.628 |               |        |

 Table 7. Cox proportional hazard model.

# **Figure Legends**

# Figure 1. RoC curve of age and respiratory rate.



1a. ROC curves with Age



1b. ROC curves with Respiratory Rate



# Figure 2. RoC curve of specificity and sensitivity.

Figure 3. RoC curve for Inflammatory parameters.



ROC curves with significant inflammatory parameters