

# Predictors of Mortality among COVID-19 Patients - A Case Control Study at Tertiary Care Center, Nanded (Maharashtra)

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## Abstract

**Background:** The novel Coronavirus is belonging to the family of SARS & MERS-CoV, the impact of the earlier is more dreadful as demonstrated by the steady increase in morbid cases. The average incubation period of COVID-19 is 1–14 days with a mean of 6 days. **Aim -** To evaluate predictors of mortality among COVID-19 patients. **Objectives –** 1. To assess risk predictors associated with mortality among COVID-19 patients 2. To suggest prediction model for preventing mortality in future outbreaks. **Materials and Methods:** Study design – A case-control study. Study place -Tertiary care center, Nanded, Maharashtra. The present study included 400 cases that died off due to Covid-19 and 400 controls survived COVID-19 disease in a 1:1 proportion. **Results:** On admission, a significant difference was observed among cases and controls with reference to the percentage of SpO<sub>2</sub> ( $p < 0.05$ ). The proportion of associated co-morbidities among cases was very high i.e., 75.75% as compared to controls with a proportion of 29.25% co-morbidities. The median days of hospital stay were significantly lower in cases compared to controls (3 days vs 12 days,  $P < 0.001$ ). **Conclusion:** Length of hospital stay (in days) was showing a significant difference among cases and control (3 days Vs 12 days); hospital stay was less (median 3 days) for cases, as they reported late and thus died earlier; hence concluded that early hospital admission will decrease chances of death due to COVID-19.

**Keywords:** Co-morbidities, COVID-19, hospital stay, neutrophil-lymphocyte ratio, ROC, SpO<sub>2</sub>

## INTRODUCTION

The novel Coronavirus is belonging to the family of SARS and MERS-CoV, and the impact of the earlier is more dreadful as demonstrated by the steady increase in morbid cases.<sup>[1]</sup> The average incubation period of COVID-19 is 1–14 days with a mean of 6 days,<sup>[2]</sup> during this period asymptomatic patient carries a virus that can transmit the disease to healthy people, as proved by the evidence of person-to-person transmission via tiny droplets or close contacts.<sup>[3]</sup> According to the standards of International Health Regulations (2005) declared by the World Health Organization (WHO), COVID-19 has been a Public Health Emergency of national and international concern at the end of January- 2020.<sup>[4]</sup>

All age groups are susceptible to COVID-19 (SARS-CoV-2). Infection is transmitted through coughing and sneezing from symptomatic patients but it can also be transmitted from the asymptomatic person before the symptoms appear.<sup>[5]</sup> The small droplets can spread up to 1–2 meters and get deposited on surface/inanimate objects. The virus can remain viable

on surfaces for days together in a favorable atmosphere and is destroyed within a minute by disinfectants viz. sodium hypochlorite, hydrogen peroxide, etc.<sup>[6]</sup> Clinical features include from the asymptomatic stage to fever, running nose, cough, sore throat, headache, malaise, loss of appetite, and difficulty in breathing in some patients, at the end of the first week, the disease can progress to pneumonia, respiratory failure, and even death also.<sup>[7]</sup>

The first case of COVID-19 has been reported in Kerala, India on 30<sup>th</sup> January 2020. This notified case was a student who came from Wuhan city of China and this case had been

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isolated in a hospital.<sup>[8]</sup> As per the MOHFW, Govt. of India, COVID-19 transmission is mainly concerned with travel in and out, local contacts of imported cases, and overall community transmission, which was initially reported on 30<sup>th</sup> March 2020.<sup>[9]</sup> Contrary to that, Klein *et al.*<sup>[10]</sup> assumed that in India, community transmission most likely started at the beginning of March 2020.

On March 14<sup>th</sup>, 2020 Govt. of India reported two COVID-19 deaths. These two cases had ages >65 years and associated co-morbidities were noted. Throughout the first week after the COVID-19 onset, India's case-fatality ratio remained at the rate of 3.2%. As of 9<sup>th</sup> June, the case-fatality ratio dropped to 2.8%. Overall, India's CFR resembled the average CFR from South East Asia.<sup>[11]</sup>

As per the press release by the Ministry of Health and Family Welfare, GOI, on 6<sup>th</sup> April 2020, 76% of diagnosed cases were male. The age distribution of the cases was reported as given - 47% of cases were of <40 years of age, 34% of cases were between the age group of 40 to 60 years, and 19% were >60 years and above. Further, mortality data were presented as genderwise 73% of COVID-19 deaths were male and 27% of death cases happened in female; only 19% of death cases were among the elderly, and 63% of notified deaths contributed among the age group >60 years. 30% of deaths were between the age group of 40 to 60 years, and 7% of patients were of the age group <40 years. Importantly, a total of 86 percent of the morbid patients have suffered from co-morbidities.<sup>[12]</sup>

Globally, there have been 271,963,258 confirmed COVID-19 cases including 5,331,019 deaths worldwide by 17<sup>th</sup> December 2021. Meanwhile in India, from 3<sup>rd</sup> January 2020 to 17<sup>th</sup> December 2021; there have been 3,47,33,194 confirmed COVID-19 cases with 4,77,158 deaths reported to World Health Organization. Just prior to submission, Maharashtra counted 66, 47, 840 positive cases on 17<sup>th</sup> December 2021, with the total number of patients deceased being 1, 41, 329 with a case fatality rate of 2.12%.<sup>[13-15]</sup>

On this background, a case-control study was carried out to find out the risk predictors associated with mortality among COVID-19 patients. The aim of our study is to evaluate predictors of mortality among COVID-19 patients and the objectives were, to assess risk predictors associated with mortality among COVID-19 patients and to suggest a prediction model for preventing mortality in future outbreaks.

## METHODOLOGY

**Study design:** A case-control study.

**Study place:** Tertiary care center, Nanded, Maharashtra.

**Study period:** April 2020 to December 2020.

**Sampling and sample size:** By using the complete enumeration method, all deaths due to COVID-19 during the study period from April 2020 to December 2020 were reported

and included in the study; thus 1:1 proportion of cases and control were taken as depicted in the table.

**Inclusion criteria:** All Real-Time Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) or Rapid Antigen Test (RAT) positive COVID-19 diagnosed patients admitted to tertiary care center; having the status of discharged or COVID-19 death as an outcome.

**Exclusion criteria:** All Covid suspected patients were found Covid negative on RT-PCR or RAT test. Patients Discharged Against Medical Advice (DAMA) from the hospital were excluded from the study.

## Definitions

**Case:** Study participants done with RT-PCR or Rapid Antigen Test, found COVID-19 positive, and admitted to a tertiary care center with definite COVID-19 death as an outcome.

**Control:** Participants with RT-PCR test or Rapid Antigen Test, seen positive for COVID-19, admitted to the tertiary care center, and got survived or discharged as an outcome during the same period.

**Study plan:** A case-control study was conducted among COVID-19 died and recovered patients fulfilling the inclusion criteria. A well-structured questionnaire consisting of demographic characteristics, personal habits, co-morbidities, and clinical and hematological parameters was used as a data collection tool. Interviews of the recovered patients and relatives of cases who died were taken. Institutional Ethical Committee (No. 147/2020 dated 03/06/2020) approval was sought at the start of the study.

The consecutive admission records of the patient were reviewed and information about the patient was taken for the period from April 2020 to December 2020. Cases and controls were gender-matched and selected with a 1:1 proportion. Two Groups were divided based on their outcome; death event (cases) and recovered or discharged (controls). Clinical details including initial symptoms, SpO<sub>2</sub> on admission, Pulse rate, Respiratory rate, Past medical history, Co-morbidities, ICU admission details, Hospital stay and Hematological findings were obtained through a structured questionnaire.

**Statistical analysis:** Statistical analysis was performed using statistical software such as IBM SPSS Statistics Software (version 21), Epi-info, and MedCalc. Quantitative data were presented as mean or median and also as the frequency and percentages of the total. The associations and comparisons of data were initially assessed by using the bivariate analysis viz. Odds ratio, Confidence interval, Chi-square test with *P* value, and latter Binary Logistic Regression (BLR) model applied for finding out the independent association of risk predictors with the outcome. The area under Receiver Operating Characteristic Curve (ROC) has been plotted for SpO<sub>2</sub>, Neutrophil Lymphocyte ratio, and Hemoglobin levels.

## RESULTS

All the risk factors affecting the outcome of COVID-19-infected patients were analyzed by using Bivariate and Binary Logistic Regression (BLR) analysis. The Receiver Operating Characteristic Curve (ROC) of SpO<sub>2</sub>, Neutrophil Lymphocyte ratio, and Hemoglobin as diagnostic tests of significance for predicting prognosis and the future outcome was also analyzed.

Among sociodemographic factors studied, Age, Family type, Occupation, Residence, Diet type, Previous BCG vaccination status, Tobacco chewing, Smoking, and Alcoholism were

found to have significant differences among cases and controls [Table 1]. As participants were gender-matched; the mean age of cases was 59.66 years, out of which the proportion of males was 70.75% and that of females was 29.25%; while the mean age of controls was 49.30 years, of which male proportion was 283 (70.75%) and that of female was 117 (29.25%).

It was very obvious that 51% of cases required ICU for admission compared to 4.25% of controls required ICU. Of the total cases in ICU, 59% of cases were put on ventilators and NIV. Saturation of peripheral Oxygen (SpO<sub>2</sub>), and the respiratory rate has shown significant differences among

**Table 1: Sociodemographic factors affecting Mortality among patients**

| Parameter              | Cases (n=400) | Controls (n=400) | Odds Ratio | 95% CI       | P        |
|------------------------|---------------|------------------|------------|--------------|----------|
| Age (in years)         |               |                  |            |              |          |
| Mean (SD)              | 59.66 (14.05) | 49.30 (11.25)    |            |              |          |
| 0-9                    | 1             | 2                | 0.25       | 0.18 to 0.34 | P< 0.001 |
| 10-19                  | 2             | 7                |            |              |          |
| 20-29                  | 14            | 48               |            |              |          |
| 30-39                  | 18            | 65               |            |              |          |
| 40-49                  | 46            | 79               |            |              |          |
| 50-59                  | 79            | 83               |            |              |          |
| 60-69                  | 135           | 70               |            |              |          |
| 70-79                  | 80            | 38               |            |              |          |
| > 80                   | 25            | 8                |            |              |          |
| Family type            |               |                  |            |              |          |
| Nuclear                | 88            | 233              | 4.94       | 3.63 to 6.73 | P< 0.001 |
| Joint                  | 312           | 167              |            |              |          |
| Occupation             |               |                  |            |              |          |
| Housewife              | 87            | 136              | 1.85       | 1.35 to 2.53 | P< 0.001 |
| Farmer                 | 123           | 93               |            |              |          |
| Service                | 50            | 47               |            |              |          |
| Laborer                | 36            | 30               |            |              |          |
| Self employed          | 67            | 41               |            |              |          |
| Unemployed/ Students   | 37            | 24               |            |              |          |
| Doctor                 | 00            | 29               |            |              |          |
| Residence              |               |                  |            |              |          |
| Rural                  | 230           | 138              | 2.56       | 1.92 to 3.41 | P< 0.001 |
| Urban                  | 170           | 262              |            |              |          |
| Diet                   |               |                  |            |              |          |
| Mixed                  | 324           | 284              | 1.74       | 1.25 to 2.42 | P< 0.001 |
| Veg.                   | 76            | 116              |            |              |          |
| BCG vaccination status |               |                  |            |              |          |
| BCG                    | 226           | 268              | 1.57       | 1.17 to 2.11 | P0.007   |
| BCG and MMR            | 15            | 14               |            |              |          |
| No                     | 159           | 118              |            |              |          |
| Tobacco chewing        |               |                  |            |              |          |
| Yes                    | 71            | 34               | 2.32       | 1.50 to 3.58 | P0.001   |
| No                     | 329           | 366              |            |              |          |
| Smoking                |               |                  |            |              |          |
| Yes                    | 42            | 25               | 1.75       | 1.05 to 2.94 | P0.031   |
| No                     | 358           | 375              |            |              |          |
| Alcoholism             |               |                  |            |              |          |
| Yes                    | 43            | 11               | 4.25       | 2.16 to 8.38 | P< 0.001 |
| No                     | 357           | 389              |            |              |          |
| Total                  | 400           | 800              |            |              |          |

study participants ( $p < 0.05$ ). Pulse rate was found to have insignificant differences among cases and controls ( $p > 0.05$ ). Cases were having a higher proportion of co-morbidities i.e., 75.75% compared to controls with a proportion of 29.25% co-morbidities [Table 2]. Laboratory parameters viz. Hemoglobin, White Blood Cells count, Neutrophil count, Lymphocyte count, Neutrophil Lymphocyte ratio, and Platelet

count were showing significant differences among study subjects ( $p < 0.05$ ) [Table 3].

The Binary Logistic Regression model revealed that, of the total factors added in the model, Age ( $> 50$  yrs), co-morbidities viz. Hypertension, CKD, COPD, CVD, No previous BCG vaccination, SpO<sub>2</sub> on admission ( $< 89\%$ ), Hemoglobin ( $< 10$  gm/dl), WBC count ( $> 11000$  cells/cm) emerged as risk

**Table 2: Clinical parameters of study participants**

| Parameters  | Cases ( $n=400$ ) | Controls ( $n=400$ ) | Odds Ratio | 95% CI           | P           |
|---|-------------------|----------------------|------------|------------------|-------------|
| Required ICU on admission   |                   |                      |            |                  |             |
| Yes   | 204               | 17                   | 23.44      | 13.88 to 39.59   | $P < 0.001$ |
| No  | 196               | 383                  |            |                  |             |
| Saturation of peripheral O <sub>2</sub> on admission (SpO <sub>2</sub> %) |                   |                      |            |                  |             |
| $\geq 94$   | 91                | 270                  | 7.05       | 5.15 to 9.65     | $P < 0.001$ |
| 89-93   | 75                | 77                   |            |                  |             |
| 84-88   | 53                | 25                   |            |                  |             |
| 79-83   | 36                | 11                   |            |                  |             |
| $\leq 78$   | 145               | 17                   |            |                  |             |
| Mode of O <sub>2</sub> supply during hospital stay                        |                   |                      |            |                  |             |
| On Ventilator   | 147               | 01                   | 231.83     | 32.23 to 1667.29 | $P < 0.001$ |
| NIV   | 89                | 3                    |            |                  |             |
| HFO <sub>2</sub>  | 76                | 17                   |            |                  |             |
| Nasal canula  | 88                | 69                   |            |                  |             |
| No  | 00                | 310                  |            |                  |             |
| Pulse rate  |                   |                      |            |                  |             |
| $\leq 60$   | 2                 | 3                    | 1.08       | 0.78 to 1.49     | $P 0.852$   |
| 61-80   | 95                | 101                  |            |                  |             |
| 81-100  | 277               | 274                  |            |                  |             |
| $\geq 100$  | 26                | 22                   |            |                  |             |
| Respiratory rate  |                   |                      |            |                  |             |
| $\leq 24$   | 340               | 372                  | 2.34       | 1.46 to 3.75     | $P < 0.001$ |
| 25 to 30  | 49                | 24                   |            |                  |             |
| $\geq 30$   | 11                | 4                    |            |                  |             |
| Hospital stay (in days)   |                   |                      |            |                  |             |
| Median  | 3                 | 12                   | 16.55      | 11.61 to 23.60   | $P < 0.001$ |
| $\leq 7$  | 298               | 60                   |            |                  |             |
| $> 7$   | 102               | 340                  |            |                  |             |
| Co-morbidity  |                   |                      |            |                  |             |
| Cardiovascular  |                   |                      |            |                  | $P < 0.001$ |
| Hypertension  | 101               | 37                   |            |                  |             |
| HTN and DM  | 76                | 32                   |            |                  |             |
| CVD   | 21                | 7                    |            |                  |             |
| CVA   | 6                 | 1                    |            |                  |             |
| Metabolic   |                   |                      |            |                  |             |
| Diabetes  | 32                | 24                   |            |                  |             |
| CKD with HTN  | 26                | 3                    |            |                  |             |
| Hypothyroidism  | 5                 | 3                    |            |                  |             |
| Lung disease  |                   |                      |            |                  |             |
| Asthma  | 15                | 4                    |            |                  |             |
| COPD  | 8                 | 2                    |            |                  |             |
| PTB   | 7                 | 2                    |            |                  |             |
| HIV   | 6                 | 2                    |            |                  |             |
| No  | 97                | 283                  |            |                  |             |
| Proportion of Co-morbidities  | 303/400 (75.75%)  | 117/400 (29.25%)     | 7.55       | 5.51 to 10.34    | $P < 0.001$ |

[Note- NIV- Non-invasive ventilator, HFO<sub>2</sub> - High flow oxygen, HTN- Hypertension, DM- Diabetes Mellitus, CVD- Cardiovascular disease, CVA- Cerebrovascular accidents, CKD- Chronic Kidney Disease, COPD- Chronic Obstructive Pulmonary Disease, PTB- Pulmonary Tuberculosis.]

**Table 3: Laboratory parameters of the study subjects**

| Laboratory parameters    | Cases (n=400) | Controls (n=400) | Odds Ratio | 95% CI       | P        |
|--------------------------|---------------|------------------|------------|--------------|----------|
| Hemoglobin (gram/dl)     |               |                  |            |              |          |
| < 7                      | 37            | 9                | 1.66       | 1.24 to 2.24 | P< 0.001 |
| 7-7.9                    | 34            | 26               |            |              |          |
| 8-8.9                    | 48            | 25               |            |              |          |
| 9-9.9                    | 45            | 55               |            |              |          |
| 10-10.9                  | 52            | 63               |            |              |          |
| 11-11.9                  | 77            | 71               |            |              |          |
| 12-12.9                  | 52            | 75               |            |              |          |
| >13                      | 55            | 76               |            |              |          |
| WBC Count (per cmm)      |               |                  |            |              |          |
| < 4000                   | 23            | 21               | 3.04       | 2.18 to 4.24 | P< 0.001 |
| > 11000                  | 154           | 70               |            |              |          |
| 4001-11000               | 223           | 309              |            |              |          |
| Neutrophils              |               |                  |            |              |          |
| < 50                     | 11            | 10               | 2.95       | 2.14 to 4.06 | P< 0.001 |
| > 70                     | 311           | 224              |            |              |          |
| 51-70                    | 78            | 166              |            |              |          |
| Lymphocytes              |               |                  |            |              |          |
| < 20                     | 218           | 137              | 2.20       | 1.64 to 2.95 | P< 0.001 |
| > 40                     | 18            | 36               |            |              |          |
| 21-40                    | 164           | 227              |            |              |          |
| NLR                      |               |                  |            |              |          |
| ≥3.50                    | 227           | 141              | 2.41       | 1.81 to 3.20 | P< 0.001 |
| < 3.50                   | 173           | 259              |            |              |          |
| Platelet count (per cmm) |               |                  |            |              |          |
| < 150 000                | 212           | 130              | 2.36       | 1.77 to 3.15 | P< 0.001 |
| > 400 000                | 8             | 9                |            |              |          |
| 150 001-400 000          | 180           | 261              |            |              |          |
| Total                    | 400           | 400              |            |              |          |

[Note- gm/dl- gram per deciliter, cmm- cubic millimeter]

predictors showing independent association with mortality of COVID-19 patients [Table 4].

SpO<sub>2</sub> had an area under the Receiver Operating Characteristic (ROC) curve of 0.772. The AUC of NLR was 0.779, indicating a high diagnostic value in predicting disease severity. While Area under ROC for Hb is quite low i.e., 0.618. [Table 5].

**Validation tests for Binary Logistic Regression (BLR):** Nagelkerke R Square value 0.744 (74.4%) shows that 74.4% variation in the outcome variable (Dependent variable) is explained by this model. R square is also known as the coefficient of determination which measures the strength of this model. Hosmer and Lemeshow Test p value is 0.901; it shows that the model is a good fit for data for prediction purposes.

## DISCUSSION

The present study depicted the relationship between gender-matched cases and controls with reference to sociodemographic factors, previous vaccination status, and personal habits viz. tobacco chewing, smoking, and alcoholism. Thus, joint family type, occupation particularly

farmers, rural residence, mixed diet, no BCG vaccination, tobacco chewing, smoking, and alcoholism were found to have significant differences among participants ( $P < 0.05$ ).

Saturation of peripheral Oxygen (SpO<sub>2</sub>) at the time of admission was significantly lower (<89%) and thus showed significant association ( $P < 0.001$ ) and it came out to be a decisive factor for the disease prognosis of patients. On comparing co-morbidity, we found significant differences with regard to HTN, DM, CVD, CKD, and COPD ( $P < 0.001$ ). Also, a significant difference was observed in the duration of hospital stay, as cases with a median of 3 days (3 days Vs 12 days,  $P < 0.001$ ) of hospital stay were showing a higher proportion of deaths that happened within the first week of admission as compared to controls.

Of the important notified laboratory parameters studied, Hemoglobin <10.00 gm/dl, WBC >11000, Neutrophil count >70, Lymphocyte count <20, Neutrophil Lymphocyte ratio (NLR) with cut off >3.5, and platelet count <150 000 were found to have a significant association as a risk factor with death outcome ( $p < 0.05$ ). On admission, SpO<sub>2</sub> ≤89%, increased Neutrophil %, decreased lymphocytes %, and increased NL ratio played decisive role in the deadly process of COVID-19



**Table 4: Binary Logistic Regression (BLR) model to identify independent risk factors associated with COVID-19 outcome**

| Risk Factors                 | B      | Sig. or P          | Exp (B)/ Odds Ratio | 95% C.I. for Exp (B) or Odds Ratio |         |
|------------------------------|--------|--------------------|---------------------|------------------------------------|---------|
|                              |        |                    |                     | Lower                              | Upper   |
| Age (> 50 years)             | 4.898  | 0.000**            | 134.082             | 36.468                             | 492.984 |
| Tobacco Chewing (Yes)        | -0.138 | 0.759 <sup>#</sup> | 0.871               | 0.361                              | 2.103   |
| Smoking (Yes)                | 0.577  | 0.323 <sup>#</sup> | 1.780               | 0.567                              | 5.588   |
| Alcoholism (Yes)             | -0.155 | 0.798 <sup>#</sup> | 0.857               | 0.261                              | 2.808   |
| Hypertension (Yes)           | 1.689  | 0.000**            | 5.414               | 2.296                              | 12.765  |
| Diabetes Mellitus (Yes)      | 0.520  | 0.247 <sup>#</sup> | 1.683               | 0.698                              | 4.056   |
| CKD (Yes)                    | 2.302  | 0.005*             | 9.993               | 1.995                              | 50.040  |
| COPD (Yes)                   | 1.853  | 0.014*             | 6.381               | 1.447                              | 28.134  |
| CVD (Yes)                    | 1.202  | 0.043*             | 3.326               | 1.036                              | 10.671  |
| BCG vaccination (No)         | 0.744  | 0.016*             | 2.105               | 1.151                              | 3.848   |
| SpO <sub>2</sub> (< 89%)     | 2.435  | 0.000**            | 11.416              | 6.291                              | 20.715  |
| Respiratory rate (> 24)      | 0.719  | 0.095 <sup>#</sup> | 2.053               | 0.881                              | 4.780   |
| Hemoglobin (< 10 gm/dl)      | 4.647  | 0.000**            | 104.316             | 31.351                             | 347.099 |
| WBC count (>11000/cmm)       | -0.814 | 0.029*             | 0.443               | 0.213                              | 0.920   |
| Platelet count (<150000/cmm) | 0.077  | 0.798 <sup>#</sup> | 1.080               | 0.598                              | 1.951   |
| NLR (≥ 3.5)                  | 0.061  | 0.851 <sup>#</sup> | 1.063               | 0.561                              | 2.015   |
| Hospital stay (≤7 days)      | 0.243  | 0.693 <sup>#</sup> | 1.275               | 0.382                              | 4.253   |
| Constant                     | -6.622 | 0.000              | 0.001               |                                    |         |

\* Statistically Significant ( $P < 0.05$ ) \*\* Statistically Highly Significant ( $P < 0.001$ ) <sup>#</sup>Statistically Non-Significant ( $P > 0.05$ ) [Note- CKD- Chronic Kidney Disease, COPD- Chronic Obstructive Pulmonary Disease, CVD- Cardiovascular disease. NLR- Neutrophil Lymphocyte Ratio]

**Table 5: Area under the curve (AUC) of SpO<sub>2</sub>, NLR, Hemoglobin**

| Test Variable    | Area  | Std. Error | P Value  | Z statistic | Sensitivity | Specificity | Yoden index (YI) | 95% Confidence Interval |             |
|------------------|-------|------------|----------|-------------|-------------|-------------|------------------|-------------------------|-------------|
|                  |       |            |          |             |             |             |                  | Lower Bound             | Upper Bound |
| SpO <sub>2</sub> | 0.772 | 0.0177     | < 0.0001 | 15.370      | 60.42       | 82.27       | 0.4269           | 0.741                   | 0.802       |
| NLR              | 0.779 | 0.0214     | < 0.0001 | 13.059      | 60.76       | 100.00      | 0.6076           | 0.742                   | 0.813       |
| Hemoglobin       | 0.618 | 0.0244     | < 0.0001 | 4.831       | 38.19       | 97.57       | 0.3576           | 0.577                   | 0.658       |

[Note- SpO<sub>2</sub> – Saturation of peripheral oxygen, NLR- Neutrophil Lymphocyte Ratio.]

disease progression to death. Male subjects were in a higher proportion of the risk of death, which is in agreement with a retrospective study report in a cohort of 44,672 patients, where male subjects >60 years of age having co-morbidities had noticed increased death risk, which was showing similarity with our study, as our study observed that more than 50% male patients having age over 60 years with various co-morbidities succumbed to COVID-19.<sup>[16]</sup>

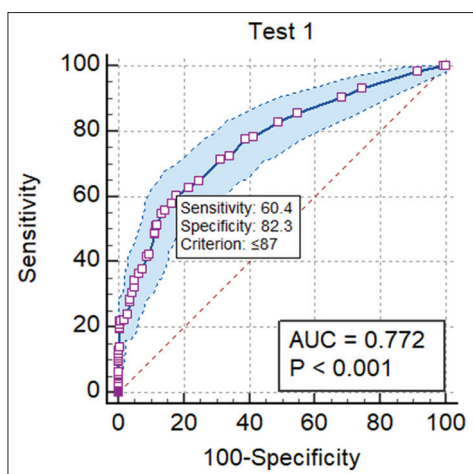
In Correspondence to previous study reports, older patients with a median age of 68 yrs (IQR 61-75 yrs) presenting with morbid conditions like Hypertension and CVD were at more risk of developing severe COVID-19, which is quite in conformity with our findings of old age cases with a mean age of 59.66 (SD-14.05) presenting with morbidities Viz. Hypertension, Diabetes, and chronic airway diseases were likely to succumb to COVID-19 as compared to controls with a mean age of 49.30 (SD-11.25).<sup>[17]</sup>

The prevalence of Hypertension and Hypertension with CKD was significantly higher (25.25% Vs 9.25%) and (6.5% Vs 0.75%) respectively in died compared to recovered patients found in our study, which was in conformity with the findings

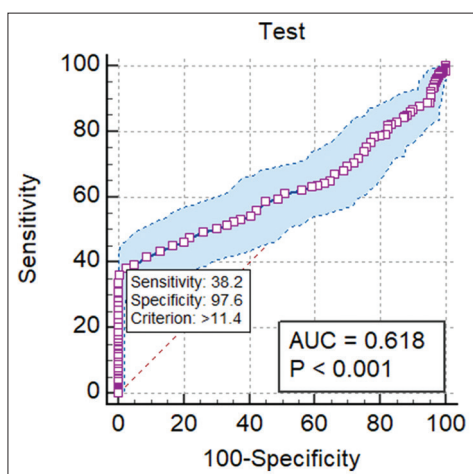
noted by Cheng *et al*, he observed that there was a statistically significant association between kidney disease and increased risk of hospital deaths in their study on 701 patients of COVID-19.<sup>[18]</sup>

The Neutrophil Lymphocyte Ration (>3.5) calculated at the time of admission was significantly related to the outcome of COVID-19-infected patients. Although attention should be given to early diagnosis and treatment; as in the control group, the mean duration of hospital stay was 12 days (from symptom onset to admission) compared to 3 days of stay observed in cases, before leading to severe progression of the disease which was very similar to the study done by Pan F *et al*.<sup>[19]</sup>

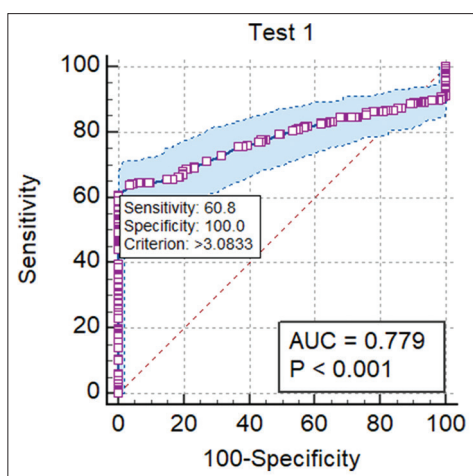
With relative importance, Hemoglobin (gm/dl), WBC count, Neutrophil percentage, Lymphocyte percentage, Platelet count, and advanced age are the most critical parameters of prediction for in-hospital mortality due to COVID-19. Among the significant factors of mortality reported in the present study, three are in a similarity to the findings of Kun Wang study's viz. neutrophilia, lymphopenia, and advanced age. Our study also confirmed that, in addition to NLR, neutrophilia was significantly higher in cases (50.75%) compared to



**Graph 1:** Receiver Operating Characteristic Curve (ROC) for Saturation of peripheral oxygen (SpO<sub>2</sub>)



**Graph 2:** Receiver Operating Characteristic Curve (ROC) for Hemoglobin



**Graph 3:** Receiver Operating Characteristic Curve (ROC) for Neutrophil Lymphocyte Ratio (NLR)

controls (36.5%) showing its effect as an early marker of inflammatory processes. In addition to leukocytosis, decreased

Hemoglobin and thrombocytopenia also significantly differed among cases and controls. Increased Neutrophil cell percentage was associated with a higher risk of COVID-19 mortality; our study findings supported the results of 61 patients having 2019-nCoV at Beijing Ditan Hospital, China.<sup>[20]</sup>

The current criteria for classifying mild, moderate, and severe cases are based on Respiratory rate, levels of O<sub>2</sub> saturation, and values of PaO<sub>2</sub>/FiO<sub>2</sub>. These indicators were important lacking specificity for COVID-19. In laboratory examination of patients with mild COVID-19 disease, the absolute value of white blood cells is usually normal or low, and lymphopenia is common.<sup>[21]</sup> However, in the case of severe Covid-19 disease, lymphocytes go on decreasing, while neutrophil count progressively increases. NLR is an important effective marker of the progression and prognosis of COVID-19 easily calculated from routine blood tests. Up till now, four meta-analysis studies have reported that patients with severe COVID-19 disease had a higher Neutrophil Lymphocyte Ratio compared to those having non-severe COVID-19 disease.<sup>[22]</sup>

We analyzed optimal cut-off values of AUC calculated by ROC analysis [Graphs 1, 2 and 3]. Based on clinical and laboratory parameters, we could suggest variables of prognosis for hospital mortality due to COVID-19 viz. AUC for SpO<sub>2</sub> on admission was 0.772 (Sensitivity 60.42 and specificity 82.27), AUC of 0.779 (Sensitivity 60.76 and specificity 100.0) for NLR, and AUC of 0.618 (Sensitivity 38.19 and specificity 97.57) for Hemoglobin.

## CONCLUSIONS

Out of all risk factors studied in Binary Logistic Regression (BLR) model, Age (>50 years), presence of co-morbidities viz. Hypertension, CKD, COPD, CVD, no previous BCG vaccination, SpO<sub>2</sub> on admission (<89%), Hemoglobin (<10 gm/dl), WBC count (>11000 cells/cm) have emerged as risk predictor showing independent association with COVID-19 death outcome.

Level of SpO<sub>2</sub> (< 89%) and laboratory parameters viz. NLR (>3.5), low Hemoglobin levels (<10 gm/dl), and increased WBC count can predict the prognosis of COVID-19 disease when best studied at the time of admission.

Based on Receiver Operating Characteristic Curve (ROC), SpO<sub>2</sub> and NLR area under ROC and their cut-off values can be used as an early signals for COVID-19 severity and mortality. Thus, evaluating SpO<sub>2</sub> and Neutrophil Lymphocyte Ratio will be useful for clinicians to identify severe cases at the earliest, conduction of triage, and initiate COVID-19 case management within time. In addition, Hemoglobin levels can also be used for predicting disease severity, as it came out to be a significant factor in Bivariate and Regression analysis.

Hospital stay was showing a significant difference among cases and controls (3 days vs 12 days); hospital stay was less (median 3 days) for cases, as they reported late and thus died earlier; hence it was concluded that promoting early

hospital admissions will decrease chances of death. Moreover, if the patient survives the first week of admission, chances of survival will increase.

This prediction model consisting of advanced Age, level of O<sub>2</sub> saturation, NLR, Hemoglobin, and associated co-morbidities will be useful in the management of COVID-19 waves; thus can be tried for preventing mortality in future outbreaks of various viruses and pathogens causing emerging and re-emerging diseases, particularly affecting the respiratory and cardiovascular system.

**Limitations:** Not all laboratory tests were done in all patients viz. D-dimer, Lactate dehydrogenase, Interleukin-6, and Serum ferritin; hence their role could not be explained in predicting COVID-19 mortality.

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### Conflicts of interest

There are no conflicts of interest.

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