ORIGINAL ARTICLE

# Factors Contributing to COVID-19 Mortality In-hospital and after Discharge: Results of an Ambivalent Cohort Study from a Tribal District of Kerala, India

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## Abstract

**Introduction:** The morbidity and mortality burden of the COVID-19 pandemic was high in socioeconomically deprived areas. Identifying the factors associated with in-hospital mortality in such settings will help physicians prioritize the scarce resources for the more needy individuals.

**Objective:** To study the demographic, clinical, and biochemical factors associated with in-hospital mortality in COVID-19 patients in Wayanad, Kerala, India. We also report the incidence of post-COVID symptoms and the mortality rate in the survivors of COVID-19 pneumonia.

**Materials and methods:** The study design was a record-based retrospective cohort, and the study participants were 402 patients admitted with moderate to severe COVID-19 at the secondary care hospital of Wayanad, Kerala, India, during late 2020 and early 2021. In-hospital mortality was the major outcome variable, and we expressed the mortality risk in terms of relative risks (RRs). Factors associated with the same were assessed using Chi-square, Fisher's exact tests, and *t*-tests depending upon the type of exposure variable. Dose-response relationships were assessed using Chi-square for trend. A subgroup of consented survivors ($n = 156$) was followed to study the post-COVID symptoms and mortality rate outside the hospital. We constructed binary logistic models to find out the independent predictors of mortality.

**Results:** The patient group ($n = 402$) was composed of individuals aged 18–95 years, and two-thirds ($n = 258$) were men. The in-hospital mortality rate was 17.7%. The risk of mortality increased with age, multimorbidity, and extent of hypoxia, peripheral oxygen saturation/fraction of inspired oxygen [$SpO_2/FiO_2$ (SF)] ratio, D-dimer, serum glutamic-oxaloacetic transaminase (SGOT), serum glutamic-pyruvic transaminase (SGPT), serum creatinine, and blood urea. The case fatality rate (CFR) had a dose-response relationship with the number of comorbidities. Out of the individual comorbidities analyzed, systemic arterial hypertension [RR = 1.5 (1.16–1.83)], cancer [RR = 4.7 (1.38–15.6)], and neurological disorders [RR = 5.8 (1.6–21.16)] were significantly associated with mortality in the hospital. According to the binary logistic regression analysis, age, hypoxia at the time of admission, intensive care unit (ICU) admission, serum creatinine, and SF ratio were the significant predictors of mortality. Most of the patients (73%) complained of some symptoms during follow-up. Easy fatigability and tiredness were the most common post-COVID symptoms, followed by exertional breathlessness, myalgia, decreased sleep, weight loss, and cough.

**Conclusion:** The physician should prioritize patients with multimorbidity and markers of organ involvement to save lives in resource-poor settings during pandemics and large infectious disease outbreaks affecting the community. The early diagnosis and management of comorbidities should be included in pandemic or outbreak preparedness to reduce morbidity and mortality.

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## Introduction

The global impact of COVID-19 has been profound, with significant loss of life and considerable social and economic upheaval. The impact of the pandemic was not equal for every health system. Limited infrastructure and human resources posed significant obstacles to the health systems of the global south.[1,2] Mitigation strategies of the pandemic were multifaceted. Public health activities, including vaccinations, reduced the death toll of the surging infection. Saving the lives of patients admitted with COVID-19 pneumonia is the last opportunity on the ladder of the preventive and therapeutic activity spectrum. Large numbers of ill patients will come to hospitals at the time of any pandemic, and the lessons learned at hospitals while treating those patients are an important learning to build resilience against impending outbreaks of infectious diseases and future pandemics. There is significant overlap among factors contributing to mortality and clinical features of near-miss deaths among most infectious diseases, as many of the infections act through common immunological cascades, including cytokine storm and organ involvement.[3]

The physicians working in the setting where the present study was conducted faced significant challenges in managing their patients in terms of infrastructure, diagnostics, and therapeutics. The government of Kerala brought the treatment of COVID-19 under universal health coverage, which reduced the out-of-pocket expenditure significantly.[4] The government published updated evidence-based treatment guidelines and ensured the supply of essential diagnostic mechanisms and therapeutic agents.[5] Strong public health measures prevented the COVID-19 caseload from overwhelming the capacities of the state throughout the pandemic.[6] However, Wayanad is one of the most backward districts of the state; it is deprived socially as well as in terms of health system amenities. It is the only district in Kerala categorized as an "aspirational district," and a significant proportion of the population is tribal.[7] The mountainous terrain and remote areas make accessing healthcare facilities difficult in the Wayanad district. It is important to

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understand the challenges and the resilience the system faced, specifically in the Wayanad district, and this learning will help in preparing for future pandemics and will be useful for places with similar struggles. It is always a priority to document the pandemic impact in terms of morbidity and mortality in such deprived settings and to identify the priority patients in the clinical setting.

The current study evaluates the demographic, clinical, and biochemical factors contributing to in-hospital COVID-19 mortality of patients admitted at a COVID hospital in Wayanad, Kerala, India. We also report the features of long COVID syndrome and the 1-year mortality rate in survivors of COVID-19 pneumonia in a subgroup of patients.

## Materials and Methods

This study was conducted in two phases. The first phase was the analysis of a record-based retrospective cohort of COVID-19 patients who were admitted to the secondary care hospital (Government District Hospital), Mananthavady, Wayanad, Kerala, India. Patients with RT-PCR/TrueNAAT/CBNAAT-confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and features of COVID pneumonia aged 18 years or more were included. The patients were admitted between July 1, 2020, and February 28, 2021. The second phase was a follow-up study on discharged patients during March to April 2022.

Data collection from hospital records was done using a validated structured questionnaire. For the first part of the study, which was record-based, data were collected from 402 COVID-19-confirmed patients who were admitted to the hospital during the study period. According to Kerala State's COVID treatment protocol, asymptomatic and mildly symptomatic patients were managed at their homes or COVID first-line treatment centers in the community. As our cohort of patients was enrolled from a COVID hospital, they were suffering from moderate to severe symptoms of COVID pneumonia or had some vulnerabilities for complications as assessed by the treating physician. Data regarding the sociodemographic characteristics, comorbidities, clinical profile, including the need for oxygen support, intensive care unit (ICU) admission, vitals, laboratory investigations at the time of admission, treatment given, and the outcome in terms of hospitalization and in-hospital mortality were recorded for most of the patients. A team of clinicians, epidemiologists, and biostatisticians compiled and reviewed the data.

For the follow-up, a telephonic interview was conducted using a pretested semi-structured questionnaire to gather information from willing participants who could be reached through the information they provided in the hospital record at the time of admission. From 38% of patients from the initial cohort (156/402) who consented to telephonic interviews and were followed up after discharge, information regarding demography, symptoms, comorbidities after discharge, reinfection, vaccination, addictions, and mortality after discharge was documented. The calls were connected to the subjects hospitalized earlier or to a close relative who answered the call.

A COVID-19 death was defined as per the World Health Organization (WHO) as the major outcome variable, which is death resulting from a clinically compatible illness in a probable or confirmed COVID-19 case, unless there is a clear alternative cause of death that cannot be related to COVID-19 disease without a period of complete recovery between illness and death.

The data were entered in Microsoft Excel and analyzed using the Statistical Package for Social Science (SPSS version 27). Continuous variables such as age, temperature, blood pressure, oxygen saturation level, lab indices, and duration of ICU admission were expressed as mean (SD) or median (IQR), and frequency and percentage for categorical variables like gender, socioeconomic status, occupation, addictive habits, comorbidity status, symptomatology, treatment, and presence of coinfection. We used the Chi-square or Fisher's exact test to evaluate the univariable analysis. Chi-square for trend was used to compare differences in mortality in different groups, and the Mann–Whitney *U* test was used to compare the difference in scores. Imputation was done using the expectation maximization (EM) method for quantitative variables whose data were incomplete, and those with <10% of missing data were included in the analysis. The relevant variables, along with the ones that showed a significant association, were included for binary logistic regression.

The Institutional Ethics Committee (IEC) approved the study (GMCKKD/RP 2024/IEC/37) dated February 16, 2024.

## Results

The patient group ($n$ = 402) consisted of 258 (64.2%) men. The mean (SD) age of the patients was 62.1 (14.7), ranging from 18 to 95 years. The major symptoms at the time of admission included breathlessness 78.8% ($n$ = 317), fever 50.2% ($n$ = 202), and cough 45% ($n$ = 181). Most patients [77.1% (310/402)] had at least one known comorbidity. The most frequent comorbidities were diabetes mellitus [$n$ = 192 (47.8%)], systemic arterial hypertension [$n$ = 180 (44.7%)], and coronary artery disease (CAD) [$n$ = 73 (18.1%)]. Most patients [316 (78.6%)] required ICU admission. The duration of ICU stay was between 1 day and 38 days, with a median (IQR) of 7 (4.5–11) days. The most common reasons for ICU admission were desaturation and hypoxia, breathlessness, prolonged cough, and uncontrolled fever. The number of patients who needed ventilator support was 45 (11.1%), among them 40 patients (88.8%) received noninvasive ventilation. Most of the patients [353 (87.8%)] required HFNC/$O_2$ support.

The in-hospital mortality rate experienced by the cohort is 17.7% ($n$ = 71). The case fatality rate (CFR) among men was 17.4% (45/258), while among women it was 18.1% (26/144). Among ICU-admitted patients, the CFR was 22.1% (70/316). The risk of mortality increased with age, multimorbidity, and the extent of hypoxia on admission and among ICU-admitted patients. The $SpO_2/FiO_2$ (SF) ratio, D-dimer, serum glutamic-oxaloacetic transaminase (SGOT), serum glutamic-pyruvic transaminase (SGPT), serum creatinine, and blood urea exhibited a dose-response gradient with the mortality risk (Table 1). The mortality risk was higher in those with elevated serum ferritin levels, although the relationship was not statistically significant.

The CFR has a dose-response relationship with the number of comorbidities. Odds ratios showed an increasing trend, with seven times the odds of mortality in multimorbidity with two existing diseases compared to people without any reported comorbidities (Chi-square for linear trend $p$-value <0.001). Of the individual comorbidities analyzed, only systemic arterial hypertension [relative risk (RR) = 1.5 (1.16–1.83)], cancer [RR = 2.97 (1.54–5.73)], and neurological disorders [RR = 3.31 (1.77–6.18)] were significantly associated with mortality in the hospital (Table 2).

We didn't observe a significantly different symptomatology in the expired group compared to the survivors at the time of presentation (Table 3). The major symptoms at the time of admission were breathlessness (85.7 vs 89.8%), fever (57.1 vs 56.7%), and cough (49.2 vs 51.4%) in both groups. Chest skiagrams of all the patients showed evidence of pleural effusion, alveolar opacities, and ground-glass appearance. The median (IQR) radiographic assessment of lung edema (RALE) score of the 197 patients was 16 (9–24), which was higher in patients who expired [25 (20–34)] compared to the survivors [14 (8–21)], $p < 0.0001$. Regarding medications, steroids

**Table 1:** Patient characteristics at the time of admission and their association with in-hospital mortality

| *Variable* | *Categories* | *Total n = 402* | *Dead (CFR) n = 71* | *OR* | *Chi-square for linear trend p-value* |
|---|---|---|---|---|---|
| Age (in years) | <40 | 29 (7.2%) | 1 (3.4%) | Ref = 1 | <0.001 |
| | 40–49 | 46 (11.4%) | 1 (2.2%) | 0.62 | |
| | 50–59 | 85 (21.1%) | 8 (9.4%) | 2.91 | |
| | 60–69 | 107 (26.6%) | 18 (16.8%) | 5.66 | |
| | 70 and above | 135 (33.6%) | 43 (31.9%) | 13.09 | |
| Comorbidity | No comorbidity | 92 (22.9%) | 4 (4.3%) | Ref = 1 | <0.001 |
| | Single comorbidity | 100 (24.9%) | 13 (13%) | 3.28 | |
| | Multimorbidity—two | 95 (23.6%) | 23 (24.2%) | 7.02 | |
| | Multimorbidity—three | 69 (17.2%) | 14 (20.3%) | 5.6 | |
| | Multimorbidity—four and more | 46 (11.4) | 17 (36.9%) | 12.9 | |
| Hypoxia at admission | No hypoxia (>94) | 151 (37.6%) | 14 (19.7%) | Ref = 1 | <0.001 |
| | Mild (93–94) | 79 (19.7%) | 11 (15.5%) | 1.27 | |
| | Moderate (90–92) | 77 (19.2%) | 8 (11.3%) | 0.91 | |
| | Severe (<90) | 95 (23.6%) | 38 (53.5%) | 5.24 | |
| Oxygen support while in hospital | No | 47 (11.7%) | 5 (7%) | Ref = 1 | 0.179 |
| | Yes | 355 (88.3%) | 66 (93%) | 1.92 | |
| ICU admission | Yes | 316 (78.6%) | 70 (98.6%) | Ref = 1 | <0.001 |
| | No | 86 (21.3%) | 1 (1.4%) | 24.18 (3.30–176) | |
| SF ratio *n* = 350 | >315 | 118 (29.4%) | 2 (2.8%) | Ref = 1 | <0.001 |
| | ≤315 | 232 (57.7%) | 61 (85.9%) | 20.69 | |
| D-dimer *n* = 402 | <5 | 383 (95.3%) | 62 (16.2%) | Ref = 1 | 0.002* |
| | ≥5 | 19 (4.7%) | 9 (47.3%) | 0.21 (0.08–0.55) | |
| SGOT *n* = 402 | <40 | 344 (85.6%) | 61 (85.9%) | Ref = 1 | 0.023* |
| | 40–120 | 51 (12.7%) | 6 (11.8%) | 0.62 | |
| | >120 | 7 (1.7%) | 4 (57.1%) | 6.19 | |
| SGPT *n* = 402 | <40 | 211 (52.5%) | 36 (17.1%) | Ref = 1 | 0.011* |
| | 40–120 | 174 (43.3%) | 27 (15.5%) | 0.89 | |
| | >120 | 17 (4.2%) | 8 (47.1%) | 4.32 | |
| Serum creatinine *n* = 402 | <2 | 343 (85.3%) | 46 (13.4%) | Ref = 1 | <0.001* |
| | ≥2 | 59 (14.6%) | 25 (42.3) | 0.211 (0.11–0.38) | |
| Blood urea *n* = 402 | <40 | 241 (60%) | 21 (29.6%) | Ref = 1 | <0.001* |
| | ≥40 | 161 (40.0%) | 50 (31.0%) | 0.21 (0.12–0.37) | |
| Serum ferritin *n* = 358 | ≥1000 | 56 (15.6%) | 15 (26.8%) | Ref = 1 | 0.058 |
| | <1000 | 302 (84.4%) | 49 (16.2%) | 0.52 (0.27–1.03) | |

* Corresponds to *p*-value of fisher's exact test

were administered to 333 (82.8%) patients, anticoagulants to 314 (78.1%), remdesivir to 93 (23.1%), other antivirals to 215 (53.4%), hydroxychloroquine (HCQ) to 125 (31.1%), and azithromycin to 233 (58%) patients. We didn't compare the mortality rates between people who received medication because such medications were given to patients with severe disease and the groups were not comparable.

Binary logistic regression was done to find out the determinants of mortality for COVID-19 patients admitted to the hospital. Factors that were significant at a 5% level were included in the model. The dependent variables were age, presence of comorbidity, hypoxia, SF ratio, ICU admission, D-dimer, serum creatinine, blood urea, hypertension, heart condition, neurological disorder, and cancer, and nonsignificant variables like SGPT and SGOT. The model was found to be significant at *p*-value <0.001, and the Hosmer and Lemeshow Chi-square goodness-of-fit test illustrates *p*-value >0.05 (0.781), indicating

**Table 2:** Known comorbidities and risk of mortality

| *Comorbidity* *n = 402* | *Expired* *n = 71* | *Survived* *n = 331* | *RR (95% CI)* | *p-value* |
|---|---|---|---|---|
| Diabetes mellitus, *n* = 192 (47.8) | 38 (53.5%) | 154 (46.5%) | 1.1 (0.8–1.4) | 0.26 |
| Hypertension, *n* = 180 (44.7) | 43 (60.6%) | 137 (41.4%) | 1.5 (1.16–1.83) | 0.001 |
| CAD, *n* = 73 (18.1) | 15 (21.1%) | 58 (17.5%) | 1.2 (0.72–2.00) | 0.46 |
| COPD, *n* = 67 (16.6) | 14 (19.7%) | 53 (16%) | 1.23 (0.72–2.09) | 0.44 |
| CKD, *n* = 31 (7.7) | 9 (12.7%) | 22 (6.6%) | 1.74 (0.96–3.15) | 0.084 |
| DLP, *n* = 14 (3.4) | 1 (1.4%) | 13 (3.9%) | 0.36 (0.04–2.69) | 0.48* |
| Cancer, *n* = 10 (2.4) | 5 (7%) | 5 (1.5%) | 2.97 (1.54–5.73) | 0.018* |
| Neurological diseases, *n* = 9 (2.2) | 5 (7%) | 4 (1.2%) | 3.31 (1.77–6.18) | 0.011* |
| CLD, *n* = 6 (1.4) | 3 (0.9%) | 3 (0.9%) | 2.91 (1.27–6.67) | 0.071* |
| Other lung condition, *n* = 3 (0.7) | 2 (2.8%) | 1 (0.3%) | 3.86 (1.68–8.83) | 0.082* |
| Musculoskeletal disorders, *n* = 4 (0.9) | 2 (2.8%) | 2 (0.6%) | 2.88 (1.06–7.86) | 0.145* |

* Corresponds to *p*-value of fisher's exact test

**Table 3:** Symptoms at the time of admission and risk of mortality

| *Symptoms* *n = 356* | *Expired* *n = 63* | *Survived* *n = 293* | *RR (95% CI)* | *p-value* |
|---|---|---|---|---|
| Breathlessness | 54 (85.7%) | 263 (89.8%) | 0.95 (0.85–1.06) | 0.402 |
| Cough | 31 (49.2%) | 150 (51.4%) | 0.96 (0.73–1.26) | 0.777 |
| Fever | 36 (57.1%) | 166 (56.7%) | 1 (0.79–1.27) | 0.94 |
| Diarrhea | 3 (4.8%) | 20 (6.8%) | 0.69 (0.21–2.27) | 0.55 |
| Tiredness | 29 (46%) | 101 (34.5%) | 1.3 (0.97–1.82) | 0.067 |
| Body ache | 9 (14.3%) | 52 (17.7%) | 0.80 (0.41–1.54) | 0.51 |
| Sore throat | 4 (6.3%) | 31 (10.6%) | 0.60 (0.21–1.63) | 0.31 |

**Table 4:** Post-COVID symptoms at the time of follow-up

| *Reported post-COVID symptom* | *Total* *n = 156* | *Reported post-COVID symptom* | *Total* *n = 156* |
|---|---|---|---|
| Easy fatigability and tiredness | 49 (31.4) | Wheezing | 7 (4.5) |
| Exertional breathlessness | 41 (26.2) | Palpitation | 6 (3.8) |
| Myalgia | 25 (16) | Chest pain | 5 (3.2) |
| Decreased sleep | 22 (14.1) | Stroke | 4 (2.6) |
| Weight loss | 19 (12.2) | DVT | 4 (2.6) |
| Cough | 18 (11.5) | MI | 4 (2.6) |
| Hair loss | 11 (7.1) | Constipation | 3 (1.9) |
| Lack of concentration | 11 (7.1) | Nightmare | 3 (1.9) |
| Deficit of memory | 11 (7.1) | Rash | 4 (2.6) |
| Headache | 10 (6.4) | Loss of bladder control | 3 (1.9) |
| Anxiety | 7 (4.5) | Pedal edema | 2 (1.3) |
| Depressed mood | 7 (4.5) | | |

a good fit for the model. The model could explain 51.2% of the determinants of mortality (Nagelkerke's $R^2$ = 0.512). The significant predictors of in-hospital mortality were age ($p < 0.001$), hypoxia at the time of admission ($p < 0.001$), ICU admission ($p = 0.015$), serum creatinine ($p = 0.028$), and SF ratio ($p = 0.026$).

## Result of Follow-up Data (*n* = 156)

Out of the participants who were followed up, the majority were males, 109 (69.8%). The mean age was 59.4 ± 14.1 years, ranging from 18–87 years. Most of the patients [73% (114/156)] complained of some symptoms at the time of follow-up (Table 4), and 23 (14.7%) reported hospitalization after discharge. Easy fatigability and tiredness were the most common symptoms, followed by exertional breathlessness, myalgia, decreased sleep, weight loss, and cough. About 53 (34%) patients suffered from some symptoms, dominated by easy fatigability, tiredness, exertional dyspnea, and cough, even after 1 year of follow-up. A significant association was found between gender and post-COVID symptoms (RR = 0.59 (0.37–0.94), *p*-value = 0.029). Females were at lower risk of having post-COVID symptoms (Table 5).

A number of 13 patients had a history of reinfection after discharge, and the median duration of reinfection was 12 months after the previous infection. Only three (1.9%) were immunized against COVID at the time of initial hospitalization, but most of them, 143 (91.6%), got vaccinated after the event. At the time of follow-up, the majority of them received two doses [79.4% (124/143)], 9.6% (15/143) received three doses, and 2.5% (4/143) received one dose of vaccination. Most of them were immunized with Covishield (adenovirus vector vaccine), 121 (84.6%); Covaxin (whole-virion inactivated vaccine), 20 (14%); one person with

**Table 5:** Factors associated with the reporting of post-COVID symptoms

| *Variables* | *Categories* | *Post-COVID symptoms n = 156* | | *Total* | *RR (95% CI)* | *p-value* |
|---|---|---|---|---|---|---|
| | | *Yes n = 114* | *No n = 42* | | | |
| Gender | Female | 29 (61.7) | 18 (38.3) | 47 | 0.59 (0.37–0.94) | 0.029 |
| | Male | 85 (78) | 24 (22) | 109 | | |
| Hospitalization after discharge | Yes | 22 (95.7) | 1 (4.3) | 23 | 8.1 (1.1–58.2) | 0.037 |
| | No | 92 (69.2) | 41 (30.8) | 133 | | |
| Reinfection with COVID | Yes | 10 (76.9) | 3 (23.1) | 13 | 1.23 (0.35–4.24) | 0.74 |
| | No | 104 (72.7) | 39 (27.3) | 143 | | |
| Vaccination at the time of follow-up | Yes | 104 (74.2) | 39 (27.8) | 143 | 0.98 (0.88–1.08) | 0.73 |
| | No | 10 (62.5) | 3 (18.7) | 13 | | |
| Smoking *n* = 133 | Yes | 6 (75) | 2 (25) | 8 | 1.33 (0.28–6.34) | 0.71 |
| | No | 86 (68.8) | 39 (31.2) | 125 | | |
| Alcohol consumption *n* = 148 | Yes | 7 (70) | 3 (30) | 10 | 0.92 (0.25–3.40) | 0.906 |
| | No | 99 (71.7) | 39 (28.3) | 138 | | |
| Vaccinated at the time of hospitalization *n* = 144 | Yes | 3 (100) | 0 | 3 | Not calculated because of empty cell in the table | |
| | No | 100 (70.9) | 41 (29.1) | 141 | | |

**Table 6:** Factors associated to mortality at the time of follow-up

| *Variables* | *Categories* | *Expired n = 15* | *Alive n = 141* | *Total n = 156* | *RR (95% CI)* | *p-value* |
|---|---|---|---|---|---|---|
| Sex | Female | 2 (4.3) | 45 (95.7) | 47 | 0.41 (0.11–1.55) | 0.192 |
| | Male | 13 (11.9) | 96 (88.1) | 96 | | |
| Post-COVID symptoms | Yes | 13 (11.4) | 101 (88.6) | 114 | 1.2 (0.96–1.51) | 0.09 |
| | No | 2 (4.8) | 40 (95.2) | 42 | | |
| Hospitalization after discharge | Yes | 11 (47.8) | 12 (52.2) | 25 | 8.61 (4.62–16.03) | 1.08 |
| | No | 4 (3) | 129 (52.2) | 133 | | |
| Reinfection | Yes | 0 (0) | 13 (100) | 13 | Not calculated because of empty cell in the table | |
| | No | 15 (10.5) | 128 (89.5) | 143 | | |
| Vaccination | Yes | 5 (3.5) | 138 (96.5) | 143 | 0.34 (0.16–0.69) | 0.003 |
| | No | 10 (62.5) | 3 (18.5) | 16 | | |
| Smoking | Yes | 3 (37.5) | 5 (62.5) | 8 | 6.05 (1.64–22.25) | 0.006 |
| | No | 9 (7.2) | 116 (92.8) | 125 | | |
| Alcohol consumption | Yes | 1 (10) | 9 (90) | 10 | 1.15 (0.15–8.40) | 0.887 |
| | No | 12 (8.7) | 126 (91.3) | 138 | | |
| Vaccinated at the time of hospitalization *n* = 144 | Yes | 1 (33.3) | 2 (66.7) | 3 | 4.3 (0.41–44.64) | 0.221 |
| | No | 14 (9.9) | 1 27 (90.1) | 141 | | |

Pfizer (COVID mRNA vaccine); and one person with both Covishield and Covaxin.

On follow-up, 9.6% (15/156) had expired. Out of the 15 patients who had expired, the diagnoses were cancer, CAD, chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), cerebrovascular accident (CVA), heart disease, pneumonia, and post-COVID complications. The median (IQR) duration from discharge to death was 30 (6.5–135) days. A significant association was found between vaccination status (positive) and smoking status (negative) with mortality at the time of follow-up (Table 6).

## Discussion

One out of six patients in our cohort succumbed to death during hospitalization. It is very difficult to compare the mortality rates between different hospital settings. The mortality rate can vary between hospitals based on the clinical severity of patients admitted and the resources available at each hospital to save lives. The general in-hospital mortality rate of COVID-19 in the United States during the initial phase of the pandemic was 11–19%.[8] The hospital where we conducted the analysis was one of the apex hospitals in the backward tribal districts and reports a comparable in-hospital mortality rate. Most of the patients included in our cohort have severe SARS-CoV-2 infections, as indicated by the fact that three-fourths of the cohort needed ICU care. However, our data suggested that most patients received steroids and anticoagulants to support their lives, and antivirals were also tried on compassionate grounds as instructed by the state treatment guideline.[5] Like other settings, in our patients, the risk of death increased with age, comorbidity, and the extent of hypoxia.[9–12]

Comorbidities and multimorbidity as risk factors for death in COVID-19 have been

extensively studied.[10,11,13] In our study, the CFR exhibited a dose-response relationship with the number of comorbidities. In addition to malignancies, systemic hypertension was also associated with an increased likelihood of death. The presence of malignancy is a significant risk factor for mortality due to severe SARS-CoV-2 infection in hospitals.[9] However, the high prevalence of hypertension renders it a factor with a greater population-attributable risk. A meta-analysis involving over 0.5 million individuals from 23 observational studies across five countries revealed that systemic hypertension was the most significant contributor to mortality during the pandemic.[14] The study posits that systemic hypertension indirectly contributed to the elevated rates of COVID-19 mortality among elderly and morbid populations.[14] Lung involvement was evident in the chest X-rays of all patients, with those who expired showing a significantly higher average RALE score compared to the survivor group. The RALE score serves as a reliable predictor of oxygenation and clinical outcomes for patients with acute respiratory distress syndrome (ARDS). A higher RALE score correlated with lower partial pressure of arterial oxygen/fraction of inspired oxygen ($PaO_2/FiO_2$) and poorer survival,[15] a finding consistent for COVID-19-associated lung injury.[16] We identified $SpO_2/FiO_2$ as a risk factor for COVID mortality as reported in other literature.[17] The SF ratio, or $SpO_2/FiO_2$, is a noninvasive surrogate for the $PaO_2/FiO_2$ (P/F) ratio, utilized to assess oxygenation in patients, particularly those with ARDS, and can be helpful in identifying more severe disease and prioritizing transportation and ICU admission in resource-limited settings.

We found that indicators of coagulopathy and organ involvement, such as markers like D-dimer, SGOT, SGPT, serum creatinine, and blood urea, exhibited a dose-response gradient with the risk of mortality. Elevated D-dimer values not only predicted the clinical outcomes of severe COVID-19 infections but also have prognostic significance during the recovery phase of the disease.[18] Liver and kidney involvement were also important predictors of COVID-19 mortality. Both organ injury, as a complication of the clinical severity of SARS-CoV-2 infection, and preexisting chronic diseases contributed to the risk.[19,20] The serological markers of hepatic and renal injury were the most commonly used prognostic factors for recovery from severe infection in hospital settings during the pandemic.[19,20] However, our multiple logistic regression model predicted that the age of the patient, hypoxia at the time of admission, serum creatinine, and ICU admission were the predictors of mortality, accounting for potential confounders. Among these factors, ICU admission serves as a surrogate measure for many clinical and biochemical markers, as the physician bases the decision about ICU admission on clinical judgment and biochemical markers of severity.

We conducted the follow-up study after 1 year of discharge, but we could include only a subgroup of patients in the study. The analysis revealed a 10% additional mortality in the cohort. Still, it is likely to be an underestimation of 1-year mortality outside the hospital because of selection bias, as the relatives of the deceased individuals may be less likely to answer our follow-up calls. However, combining both the data together, at least 25% of patients with severe COVID pneumonia admitted to the COVID hospital might have died either in the hospital or within 1 year of their hospitalization. Only a limited number of studies have analyzed COVID-19 mortality inside and outside of the hospital together. One-year mortality among patients admitted to 60 Spanish ICUs was 14% for noninvasively ventilated patients and 40% for patients who received mechanical ventilation.[21]

One-third of our patients (34%) reported symptoms even after a year following the infection. A systematic review and meta-analysis on the persistence of long COVID after 1 year reported high prevalence rates for persistent symptoms—fatigue/weakness (28%), dyspnea (18%), arthromyalgia (26%), depression (23%), anxiety (22%), memory loss (19%), concentration difficulties (18%), and insomnia (12%).[22] Our patients reported easy fatigability and tiredness as the most common symptoms during the follow-up period, followed by exertional breathlessness, myalgia, decreased sleep, weight loss, and cough. The syndrome complexes are very similar to another study conducted in the southern part of Kerala, India.[23] Easy fatigability is the most commonly reported symptom of long COVID in both severe and nonsevere infections of SARS-CoV-2.[24] Contrary to the reported literature, in our study, men are more prone to the development of post-COVID syndrome.[25]

We noticed that the presence of vaccines was negligible among the patients who were admitted with severe COVID manifestations. Still, almost all of them received the jab after being discharged from the hospital. COVID vaccines taken even after the infection and severe disease manifestation seem to offer significant protection from death. Smoking was found to be a risk factor for mortality among those who survived severe COVID-19 pneumonia. Vaccination against the disease delivers its protection from the progression of the infection to severity and prevention of mortality during the course of the illness.[26] If vaccination was a protective factor, tobacco smoking was a risk for every complication of SARS-CoV-2 infection. Smoking not only reduces lung health, but it is also thought to increase the likelihood of severe infection through extensive expression of angiotensin-converting enzyme 2 (ACE2) receptors in the respiratory passages.[27,28] A major strength of our paper is that we combined the follow-up data with the hospital data for our analysis. There are only a few reports from the deprived districts in India, where the mortality burden of the pandemic may be high because of the scarcity of resources. However, we could only include 39% of the initial cohort in the follow-up part of the study.

## Conclusion

The COVID-19 was the only devastating pandemic that the current clinicians witnessed. It is essential to understand the major challenges the health system faced while navigating these difficulties. In this article, we present how a district with geographical and health-related challenges confronted the COVID-19 pandemic with the facilities available at a secondary care level. What did we physicians learn from this pandemic, and specifically from our study? Multimorbidity and age were two factors that increased mortality and morbidity, including ICU stays. This study also showed that, along with malignancies, systemic hypertension was found to be associated with a higher risk of death in patients with COVID-19 infection. We know there was a complete disruption in treating all other medical conditions during the early part of the pandemic. To prepare for future pandemics, we must focus on managing all multiple long-term conditions, specifically on the management and control of hypertension, as it is often undervalued by those diagnosed, with symptoms typically absent until target organ damage occurs. This study also provided follow-up data of hospitalized patients and emphasized the need for regular follow-up.

## Ethics

Received IEC approval from the Institutional Ethics Committee, Government Medical College, Kozhikode, Ref. no. GMCKKD/RP 2024/IEC/37 dated February 16, 2024.

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