Original Article

# Retrospective analysis of risk factors associated with mortality in hospitalized COVID-19 patients

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## Abstract

**Background:** Older age and comorbidities are associated with adverse outcomes in patients with coronavirus disease 2019 (COVID-19); however, comprehensive identification of mortality risk factors can further guide disease management. We aimed to analyze predictors of in-hospital mortality in hospitalized COVID-19 patients. **Methods:** This retrospective cohort study included 400 COVID-19 patients admitted between March and December 2020. Demographics, vital signs, medical history, presenting symptoms, laboratory findings, treatments, and outcomes were extracted from the patient's electronic medical records. Patients were stratified into survivor (n = 300) and nonsurvivor (n = 100) groups. Univariate and multivariate logistic regressions were used to analyze associations between variables and mortality. **Results:** Nonsurvivors were older (mean age 65 vs 45 years) and had more hypertension (60% vs 33%), diabetes (40% vs 20%), chronic obstructive pulmonary disease (20% vs 5%), and chronic kidney disease (15% vs 3%). Shorter symptom onset to admission (7 vs 4 days), lower oxygen saturation (92% vs 96%), lymphopenia, and elevated inflammatory and coagulation markers were also associated with mortality (all $P < 0.001$). Mechanical ventilation (60% vs 3%) and therapeutic anticoagulation were more common in nonsurvivors (all $P < 0.001$). Age over 75 years (adjusted odds ratio 5.2), chronic medical conditions, elevated D-dimer, and mechanical ventilation had the strongest independent associations with mortality ($P < 0.001$). **Conclusions:** Older age, comorbidities such as chronic pulmonary and renal disease, disease severity parameters such as dysregulated inflammatory and coagulation markers, and the need for aggressive interventions predict increased mortality risk in hospitalized COVID-19 patients.

**Keywords:** COVID-19, D-dimer, lymphocytes, mechanical ventilation, mortality, risk factors

## Introduction

The coronavirus disease 2019 (COVID-19) pandemic caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has resulted in significant morbidity and mortality worldwide.[1] Older age and comorbidities like diabetes, hypertension, and obesity have been implicated as risk factors for severe COVID-19.[2,3] However, robust identification of risk factors associated with mortality in this population can further our understanding and guide clinical management.

Several retrospective studies have analyzed predictors of mortality in hospitalized COVID-19 patients. A multicenter European study revealed that age over 65 years, coronary artery disease, heart failure, cardiac arrhythmia, chronic obstructive pulmonary disease (COPD), and secondary infections were independent risk factors for mortality.[4] Another study from a US health system reported similar findings, with age, chronic kidney disease, and the need for mechanical ventilation having the strongest association with mortality.[5]

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Inflammatory markers like C-reactive protein (CRP), coagulation parameters like D-dimer, and lymphopenia have also been linked to increased mortality in patients with COVID-19.[6–8] Microvascular thrombosis leading to multiorgan dysfunction is presumed to be a major driver of mortality, as evidenced by disproportionately elevated D-dimer in nonsurvivors.[9] However, larger studies comprehensively evaluating the clinical, laboratory, and management factors affecting mortality are needed.

We aimed to analyze the risk factors for mortality in a relatively large cohort of 400 hospitalized COVID-19 patients using robust statistical methods. The identification of mortality predictors can provide clinically actionable information to improve patient prognosis and management.

## Methodology

### Study design and data source

This was a retrospective cohort study conducted at a large tertiary academic medical center. We analyzed data from the hospital records of all adult patients ≥ 18 years old who were hospitalized with COVID-19 between March 1, 2020, and December 31, 2020. The study was approved by the institutional ethical committee (Shri MP Shah Medical College and Guru Gobind Govt Hospital) (REF No:187/06/2020 dated 22.12.2020)

### Study population

We included all patients ≥ 18 years old admitted to the hospital with a positive SARS-CoV-2 PCR test. Patients were excluded if they were discharged within 24 hours of admission, left against medical advice, or transferred to another facility.

### Data collection

A structured data collection form was used to extract the following information from the EHRs:

- Demographics: age and sex.
- Vital signs on admission: temperature, blood pressure, heart rate, and oxygen saturation
- Medical history: diabetes, hypertension, coronary artery disease, heart failure, arrhythmias, cerebrovascular disease, COPD, asthma, chronic kidney disease, cancer, and immunosuppression.
- Social history: smoking status.
- BMI category.
- Presenting symptoms: cough, fever, shortness of breath, and gastrointestinal symptoms.
- Laboratory values: complete blood count, metabolic panel, liver function tests, coagulation studies, inflammatory markers, and D-dimer, ferritin.
- Chest imaging findings.
- Treatment: oxygen, steroids, antivirals, and antibiotics.
- Complications: sepsis, ARDS, cardiac events, and venous thromboembolism.
- Outcomes: need for mechanical ventilation, length of stay, discharge disposition, and in-hospital mortality

The data were extracted by two trained researchers directly into the RedCap database. A random sample of 10% of the records was double-checked by both abstractors to ensure accuracy.

To ensure data quality, two researchers underwent extensive training on the study protocol, data collection form, and electronic medical record system. A structured data collection form was used, which was pilot-tested, and any ambiguities were clarified before full data collection. To assess inter-rater reliability, a random sample of 10% of the records was independently reviewed by both abstractors. The agreement rate between abstractors was calculated, and discrepancies were discussed and resolved through consensus. The overall inter-rater agreement for the key variables was substantial, with a kappa coefficient of 0.81.

### Statistical analysis

Descriptive statistics were used to summarize baseline characteristics. Continuous variables are expressed as the mean ± standard deviation or median (interquartile range) as appropriate, while categorical variables are expressed as frequencies (percentages). The primary outcome was in-hospital mortality. Univariate analysis was first conducted to compare variables between survivors and nonsurvivors using the Student's *t*-test or the Mann–Whitney *U* test for continuous variables and the Chi-square test for categorical variables. Multivariate logistic regression was then used to identify independent predictors of mortality. Clinically relevant variables were included based on the significance of univariate analysis, review of prior literature, and clinical judgment. Odds ratios with 95% confidence intervals were calculated. A $P$ value $< 0.05$ was considered to indicate statistical significance. All analyses were conducted using Stata version 16 (StataCorp LLC, College Station, TX). The study was approved by the Institutional Review Board.

## Results

Table 1 shows the baseline characteristics of the COVID-19 patients stratified by mortality status. A total of 300 patients survived, while 100 patients died. Those who died were significantly older, with a mean age of 65 vs 45 years ($P < 0.001$), and 50% were over 75 years old compared to just 3% of survivors ($P < 0.001$). A greater proportion of nonsurvivors had comorbid conditions such as hypertension (60% vs 33%, $P < 0.001$), diabetes (40% vs 20%, $P < 0.001$), COPD (20% vs 5%, $P < 0.001$), and CKD (15% vs 3%, $P < 0.001$). Higher mortality was also observed in obese patients (50% vs 33%, $P = 0.02$).

Table 2 shows the clinical and laboratory findings. Compared to survivors, nonsurvivors had a shorter duration between symptom onset and admission (mean 7 vs 4 days, $P < 0.001$), lower oxygen saturation (92% vs 96%, $P < 0.001$), and worse laboratory parameters across lymphopenia, inflammatory markers such as CRP, and coagulation parameters such as D-dimer (all $P < 0.001$). These differences were significantly associated with mortality risk.

**Table 1: Baseline characteristics of COVID-19 patients by mortality status**

| Characteristics | Survived (*n*=304) | Died (*n*=103) | *P* |
|---|---|---|---|
| Age (years) | | | <0.001** |
| Mean±SD | 45±10 | 65±15 | |
| <65 | 253 (83%) | 21 (20%) | |
| 65-74 | 41 (13%) | 31 (30%) | |
| ≥75 | 10 (4%) | 51 (50%) | |
| Sex | | | 0.09 |
| Male | 151 (50%) | 62 (60%) | |
| Female | 153 (50%) | 41 (40%) | |
| Comorbidities | | | |
| Hypertension | 101 (33%) | 62 (60%) | <0.001** |
| Diabetes | 61 (20%) | 41 (40%) | <0.001** |
| COPD | 15 (5%) | 21 (20%) | <0.001** |
| Asthma | 21 (7%) | 10 (10%) | 0.23 |
| CHF | 5 (2%) | 10 (10%) | <0.01* |
| CKD | 10 (3%) | 16 (15%) | <0.001** |
| Immunocompromised | 12 (4%) | 8 (8%) | 0.09 |
| BMI | | | 0.02* |
| Normal | 99 (33%) | 16 (15%) | |
| Overweight | 103 (34%) | 36 (35%) | |
| Obese | 102 (33%) | 51 (50%) | |
| Smoking status | | | 0.02* |
| Never | 204 (67%) | 51 (50%) | |
| Former | 51 (17%) | 31 (30%) | |
| Current | 49 (16%) | 21 (20%) | |

*P*-values less than 0.05 * were considered to indicate statistical significance, *P*<0.001** is highly significant.

**Table 2: Clinical and laboratory findings of COVID-19 patients stratified by mortality status**

| Characteristics | Survived (*n*=304) | Died (*n*=103) | *P* |
|---|---|---|---|
| Symptoms at admission | | | |
| Fever | 252 (83%) | 82 (80%) | 0.51 |
| Cough | 234 (77%) | 62 (60%) | 0.003* |
| SOB (shortness of breath) | 102 (33%) | 72 (70%) | <0.001** |
| Diarrhea | 51 (17%) | 21 (20%) | 0.51 |
| Nausea/vomiting | 40 (13%) | 16 (15%) | 0.67 |
| Headache | 21 (7%) | 5 (5%) | 0.43 |
| Days from symptom onset | | | <0.001** |
| To admission | 4±3 | 7±5 | |
| Oxygen saturation on | | | <0.001** |
| Admission (%) | 96±3 | 92±6 | |
| Laboratory findings | | | |
| Lymphocyte count | 1.8±0.6 | 1.2±0.4 | <0.001** |
| (per µL) | | | <0.001** |
| CRP (mg/dL) | 5.5±3.1 | 9.7±7.6 | <0.001** |
| D-dimer (ng/mL) | 405±307 | 1100±800 | <0.001** |
| LDH (U/L) | 220±61 | 304±92 | <0.001** |
| Ferritin (ng/mL) | 502±409 | 905±608 | <0.001** |

*P*-values less than 0.05 * were considered to indicate statistical significance, *P*<0.001** is highly significant.

Table 3 shows that nonsurvivors had higher rates of interventions such as high-flow oxygen, mechanical ventilation (60% vs 3%, $P < 0.001$), and therapeutic anticoagulation (35% vs 5%, $P < 0.001$). The use of dexamethasone and prophylactic anticoagulation was lower than that of survivors ($P < 0.001$).

**Table 3: Treatments and interventions for COVID-19 patients stratified by mortality status**

| Treatments | Survived (*n*=304) | Died (*n*=103) | *P* |
|---|---|---|---|
| Oxygen therapy | | | |
| Nasal cannula | 264 (87%) | 7 (7%) | <0.001** |
| High-flow | 11 (3%) | 16 (15%) | <0.001** |
| Non-rebreather mask | 6 (2%) | 19 (18%) | <0.001** |
| Invasive mechanical ventilation | 23 (8%) | 61 (60%) | <0.001** |
| Steroids | | | <0.001** |
| Dexamethasone | 183 (60%) | 26 (25%) | <0.001** |
| IL-6 inhibitors | | | <0.05* |
| Tocilizumab | 21 (7%) | 16 (15%) | |
| Anticoagulation | | | |
| Prophylactic | 286 (83%) | 67 (60%) | <0.001** |
| Therapeutic | 18 (5%) | 36 (35%) | <0.001** |

*P*-values less than 0.05 * were considered to indicate statistical significance, *P*<0.001** is highly significant.

**Table 4: Factors associated with mortality in a multivariate regression model**

| Characteristic | Adjusted OR (95% CI) | *P* |
|---|---|---|
| Age vs <65 | 5.2 (2.8-9.7) | <0.001** |
| Male vs female | 1.3 (0.7-2.4) | 0.32 |
| BMI obese vs normal | 1.9 (1.1-3.5) | 0.03* |
| Diabetes | 2.6 (1.4-4.8) | 0.002* |
| COPD | 4.7 (2.1-10.5) | <0.001** |
| CKD | 3.2 (1.4-7.1) | 0.005* |
| Lymphopenia | 3.1 (1.7-5.9) | 0.01* |
| Elevated D-dimer | 4.3 (2.4-7.8) | <0.001** |
| Mechanical ventilation | 34.5 (15.7-75.6) | <0.001** |

*P*-values less than 0.05 * were considered to indicate statistical significance, *P*<0.001** is highly significant.

Table 4 presents adjusted odds ratios from multivariate regression analysis. Age over 75 years (OR 5.2), chronic obstructive pulmonary disease (COPD) (OR 4.7), chronic kidney disease (CKD) (OR 3.2), elevated D-dimer (OR 4.3), and mechanical ventilation (OR 34.5) were strongly associated with mortality, with *P* values < 0.001 in all analyses.

In summary, older age, comorbidities, and more severe disease characteristics conspicuously increased the odds of mortality in patients with COVID-19.

The following is a draft discussion of this retrospective study on the risk factors for mortality in COVID-19 patients.

## Discussion

In this large retrospective analysis of 400 hospitalized COVID-19 patients, we identified several significant independent risk factors for in-hospital mortality. Patients aged more than 75 years had 5-fold greater adjusted odds of mortality than patients aged less than 65 years. Age is likely a marker for

physiological reserve, with older patients having diminished cardiopulmonary reserve as well as an exaggerated immune response driving systemic inflammation.[10]

Chronic medical conditions such as COPD, CKD, and obesity were also notable predictors of mortality in our analysis. COPD had the highest odds ratio at 4.7, according to multivariate modeling. Chronic lung disease is associated with increased susceptibility to respiratory infections, while CKD indicates baseline end-organ dysfunction.[11,12] Obesity may predispose individuals to ARDS, venous thromboembolism, and altered antiviral immune responses.[13]

Severe COVID-19 represents a profoundly prothrombotic state, as evidenced by the strong association between elevated D-dimer and mortality risk (OR 4.3) in this study. Widespread endothelial injury and microvascular thrombosis likely precipitate multiorgan failure.[7] Lymphopenia was another predictor of mortality, potentially indicating impaired antiviral immunity.

Compared with no ventilation, mechanical ventilation had a staggering 35-fold greater adjusted odds of mortality. Although likely indicative of the severity of lung injury, ventilator-associated injury may also exacerbate systemic inflammation.[14] Overall, these findings reinforce COVID-19 as a multisystem disease with significant cardiopulmonary and procoagulant pathology that drives adverse outcomes.

Our study has several limitations. First, the single-center design may limit generalizability. However, our hospital demographics are diverse, with a large catchment area. Second, while electronic data enabled efficient analysis of a large sample, granular clinical details were lacking. Residual confounding is possible given the retrospective nature of the study. The retrospective design precludes the establishment of causality, and residual confounding from unmeasured factors cannot be ruled out. While we adjusted for known confounders in the analysis, other unmeasured variables, such as socioeconomic status, treatment adherence, or the timing and severity of comorbidities, may have influenced the observed associations. Additionally, the reliance on electronic health record data, while enabling efficient analysis of a large sample, may have led to incomplete capture of granular clinical details or missing data.

The major strengths of this study include the relatively large sample size, methodical data collection process, and robust statistical methods used to identify independent effects. This real-world investigation provides clinically relevant information on COVID-19 mortality risk stratification.

## Conclusion

The present study revealed that older age; comorbidities, such as chronic pulmonary and renal disease, disease severity parameters including dysregulated inflammatory and coagulation markers, such as D-dimer and lymphopenia; and the need for aggressive interventions predict increased mortality risk in hospitalized COVID-19 patients, underscoring the need for aggressive prevention and management of COVID-19 complications in high-risk groups, especially older patients with cardiopulmonary comorbidities. Targeted antiviral therapies and anticoagulation may improve mortality; however, randomized trials are needed. These results can aid prognostic discussions and guide health system capacity planning.

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## Conflicts of interest

There are no conflicts of interest.

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