

## Predictor Factors of Mortality among Hospitalized COVID-19 Patients: Retrospective Cohort Study in A Quarantine Hospital

Shaimaa H Fouad<sup>1</sup>, Mayada Moneer<sup>1</sup>, Sara Ibrahim<sup>2</sup>, Ahmed Ashraf Okba<sup>3</sup>,

Amr Hosny<sup>3</sup>, Sylvia W Roman<sup>1</sup>, Inas Abd El Rahim Ali<sup>4</sup>, Mohamed Farouk Allam<sup>5</sup>

Department of Internal Medicine (1), Department of Clinical Pathology (2), Department of Anesthesia and Intensive Care (3), Department of Family Medicine (5), Faculty of Medicine, Ain Shams University, Cairo, Egypt

4. Department of Family and Community Medicine, Faculty of Medicine,

Misr University for Science and Technology MUST, Giza, Egypt

**Correspondence:** Inas Abd El Rahim Ali, **Orcid number:** 000-0002-8499-5919, **Phone:** +(202) 38247457,

**Mobile:** +(2) 01006064216, **E-mail:** inas.abdelrahim@must.edu.eg

### ABSTRACT

**Background:** Over 630 million COVID-19 instances have been documented worldwide, and there have been close to 6.5 million fatalities. The primary methods for evaluating the effects of various variables on the COVID-19 mortality rate have centred on individual comorbidities and risk factors related to ageing.

**Objective:** We looked at the connection between COVID-19 degree upon admittance to a quarantined hospital and risk of patient death with an emphasis on several prospective therapies in order to present additional evidences.

**Patients and methods:** 338 participants who were admitted to Ain Shams University Hospitals were the subjects of a retrospective cohort analysis from April 20, 2020, to July 30, 2020, of whom 317 individuals had documented outcomes (hospital discharge or fatal prognosis). Applying logistic regression analysis, it was possible to determine the adjusted hazard variables for fatal outcome.

**Results:** At the univariate stage, individuals who were elderly, smokers, hypertensives, diabetics, and individuals with chronic kidney disease (CKD), as well as those taking steroids, tocilizumab, or enoxaparin sodium, were more likely to have a fatal outcome. Diabetes mellitus (DM) is a strong indicator of death due to its high prevalence (65%) in COVID-19 participants who did not survive. The multivariable investigation suggests only 2 factors from the risk categories significantly related with fatal outcome in the univariate study: older age and steroid use.

**Conclusion:** The use of steroids may be more indicative of the degree of the illness than a terminal prognosis. Steroids are frequently administered to participants who have severe respiratory problems or indications, therefore cause effect bias is extremely possible. Additional research is required to verify the advantages of various drugs in COVID-19 individuals.

**Keywords:** COVID-19, Hospital, ICU, severity, risk factors, mortality, Ain Shams University.

### INTRODUCTION

Approximately 6.5 million deaths from COVID-19 have been documented worldwide, with much more than 630 million cases reported<sup>(1)</sup>. All tertiary hospitals worldwide were affected by the first stage of the COVID-19. Research has shown that residing in nursing homes, being elderly, and having persistent chronic diseases are the main causes of death<sup>(2)</sup>.

Critically ill SARS-CoV-2 pneumonia individuals have a high fatality rate. The non-survivors' survival time is most expected to be 1-2 weeks following ICU admittance. Acute respiratory distress syndrome (ARDS) and complications raise the risk of death in elderly adults (>65 years)<sup>(3)</sup>.

The primary methods for determining how various variables influence the COVID-19 mortality rate have centred on individual comorbidities and risk factors related to advancing age. Firstly, it was discovered that the likelihood of the COVID-19 mortality rate increased with population age. According to a WHO assessment of data, diabetes is linked to a higher risk of COVID-19-related in-hospital mortality. In contrast to non-smokers, smokers have a higher risk to acquire a severe condition with COVID-19, according to other investigations published by WHO [WHO statement, 2020]<sup>(4)</sup>.

Ageing over sixty, male gender, and comorbidities such as diabetes mellitus (DM), hypertension, and chronic renal failure were found to be death indicators<sup>(5,6)</sup>. Decreased death was linked to the use of anticoagulants, corticosteroids, and azithromycin in Egyptian patients having COVID-19<sup>(6)</sup>.

In order to provide new evidence, we investigated the relationship between COVID-19 severity at admission in quarantine hospital and risk of patient death with special focus on different potential treatments.

### PATIENTS AND METHODS

The clinical information of individuals with laboratory- and/or CT-confirmed COVID-19 infections was gathered from El-Obour Hospital reports for this retrospective cohort analysis. This facility, which is a part of Ain Shams University Hospitals, was ready to isolate COVID-19 victims.

When a patient's identification of COVID-19 was verified in the laboratory by reversed transcriptions polymerases chain reactions (RT-PCR) and/or higher resolution CT chest with CO-RADS 4 or 5, it was deemed to be a certain diagnosis. 338 individuals were hospitalized to Ain Shams University Hospitals between April 20, 2020, and July

30, 2020, and 317 of these victims knew their fates (hospital discharging or fatal prognosis).

Age, sex, hypertension, diabetes mellitus, chronic liver diseases, and chronic kidney disease (CKD) are all fundamental possible causes for death<sup>(5,6)</sup>.

Smoking, working in hospitals, living in Cairo or another governorate, and probable COVID-19 medications such as azithromycin, enoxaparin sodium, oseltamivir, favipiravir, remdesivir, corticosteroids, and tocilizumab were external possible causes for catastrophic outcome<sup>(6)</sup>.

Risk factors have only been taken into account if they happened before the beginning of COVID-19 indications.

**Ethical Considerations:**

The Faculty of Medicine Research Ethics Committee (REC) FWA 00017585 of Ain Shams University granted ethical approval for the present investigation design. The Declaration of Helsinki, the World Medical Association's code of ethics for investigations human related, guided the conduct of this research. Each participant in the study provided his/her signed informed consent.

**Statistical analysis**

The Statistical Package for the Social Sciences (SPSS) version 20 for Windows was used to code, analyze, and evaluate the obtained data (IBM SPSS Inc, Chicago, IL, USA). The Mann-Whitney test for continuous data (age in years) and Pearson's Chi square test for categorical data were used to make the initial assessments comparing COVID-19 individuals with catastrophic prognosis and those without. Using logistic regression model, it was possible to determine the adjusted risk variables for fatal outcome. The participants' overall prognosis for death served as the predictor variables. All of the factors listed above were taken into consideration as potential candidates for the final version. The early multivariable model development involved the human purposeful selection of parameters utilising a reasonably high degree of significance (alpha approximately 0.25). The final step was to use a likelihood ratio analysis with a significance level of 0.05 to minimise the resulting model.

**RESULTS**

A total of 317 COVID-19 patients had known fate, 20 (5.9%) of them had fatal prognosis. Gender distribution of the included patients was: 173 (54.6%) males and 144 (45.4%) females.

Table 1 demonstrates the univariate relationship between the likelihood of death and various hypothesised independent parameters. The following individuals had a higher likelihood of having a terminal prognosis at the univariate standard: older, smokers, hypertensives, diabetics, patients with CKD, and patients receiving enoxaparin sodium, steroids or tocilizumab.

**Table (1) Variables related to a catastrophic prognosis in the univariate analysis <sup>1</sup>**

COVID-19 Parameters	Fatal Prognosis (n=20)	Hospital Discharge (n=297)	OR (95% CI) <sup>2</sup>	P value <sup>3</sup>
Age in years	62.6 ± 13	45.6 ± 15.8	1.07 (1.03-1.11)	<0.001
Gender (male)	10 (50)	163 (54.9)	0.82 (0.33-2.03)	0.671
Smoker	5 (25)	19 (6.4)	4.88 (1.60-14.85)	0.002
Healthcare worker	3 (15)	102 (34.3)	0.34 (0.10-1.18)	0.075
Residence (Cairo)	16 (80)	253 (85.2)	0.70 (0.22-2.18)	0.531
Hypertension	12 (60)	52 (17.5)	7.07 (2.75-18.15)	<0.001
Diabetes mellitus	13 (65)	44 (14.8)	10.68 (4.04-28.25)	<0.001
Chronic liver disease	0 (0)	2 (0.7)		0.713
Negative Chronic kidney diseases	15 (75)	278 (93.6)	4.88 (1.60-14.85)	0.007
Positive	4 (20)	13 (4.4)		
On Dialysis	1 (5)	6 (2)		
Azithromycin	20 (100)	292 (98.3)	---	0.558
Enoxaparin Sodium	20 (100)	260 (87.5)	---	0.093
Oseltamivir	7 (35)	84 (28.3)	1.36 (0.53-3.54)	0.520
Favipiravir	1 (5)	4 (1.4)	3.84 (0.41-36.10)	0.204
Remdesivir	0 (0)	1 (0.3)	---	---
Administration of Steroids	18 (90)	84 (28.3)	22.82 (5.18-100.51)	<0.001
Tocilizumab	5 (25)	12 (4)	7.92 (2.47-25.39)	<0.001

<sup>1</sup> Qualitative data are represented as number and percentage and quantitative data are represented as mean ± SD.

<sup>2</sup> Odds Ratio (95% Confidence Interval).

<sup>3</sup> Pearson's Chi square analysis was used for categorical data and Student's t-test for continuous data.

Only two variables—older age and steroids use—were found in the multivariate analyses of the adverse outcomes strongly related with catastrophic prognosis

in the univariate study. Despite having a negligible degree of significance, the CKD factor is included in the analysis as a confounding factor. Age and the use of steroids both showed substantial changes in their coefficients when the designs with and without this factor were compared, which called for the inclusion of CKD in our final model to account for this confounded influence (table 2).

**Table (2) Variables related to a catastrophic prognosis in the univariate analysis**

Risk Factors	Odds Ratios	95% confidence interval	P-value
Age	1.05	1.01 – 1.09	0.018
Administration of steroids	15.38	3.33 – 71.02	<0.001
Chronic kidney disease	3.24	0.89 – 11.80	0.074

**DISCUSSION**

The primary goal of the current study was to look at potential predictors of catastrophic prognosis in COVID-19 sufferers. This research used a multivariate approach of logistic regression analysis to account for potential confounding variables and correct for bias. Age, the existence of chronic kidney disease, and steroid use were important factors in the logistic regression analysis of individuals with catastrophic prognosis.

The present study reported 20 (5.9%) deaths among a total of 317 COVID-19 patients surveyed. Fatal prognosis was prevalent among higher ages. This finding is consistent with previous studies performed since COVID-19 started as in the study of **Xiaobo Yang and collaborators** in China (2020), where non-survivors were found to be older than survivors. Data from earlier research indicates that elderly, male patients had an increased mortality rate (3).

Additional research on the socioeconomic factors that influence COVID-19 death in the US For COVID-19 cases, a greater portion of farmworkers, a higher proportion of poor inhabitants, a higher population density, and a higher proportion of those over 65 were all individually and substantially linked with a higher number of fatalities in a region (7) in consistency to the results of the present study. Also, the article by **Triggle** (2020) highlights the concern that older individuals are the primary COVID-19 sufferers (8), and for individuals who have ongoing health issues (4,8).

Aging was an evidence of a positive indicator of death amongst hospitalised COVID-19 individuals, according to the generalised linear modelling, with the fatality rate being greater among individuals older than 60 (65.7% versus 34.3% in younger individuals than 60 years old) (6). The immunity system's remodelling and danger for immunopathology developing in aged individuals with decreased B and T cell functions are

major contributors to older persons' susceptibility to severe COVID-19 disease and death (9,10).

According to the study conducted between March 1 and May 31, 2020, on a sum of 1752 individuals who were hospitalized in Spain with probable COVID-19 pneumonia, older age was continuously the main determinant of in-hospital death in COVID-19 individuals (2).

Numerous research with similar results concluded that getting older was a potential risk for illness severity and death. **Ghweil and collaborators** (2020) reported that significant COVID-19 was much more prevalent in elderly age groups (11). Numerous research from various geographical areas have confirmed this result. Age-related immune function declines in both the cellular and humoral systems may account for this (12). Additionally, during the duration of respiratory infections, ageing is linked to specific alterations in lung physiology, pathology, and functioning. Older people experience inferior healthcare outcomes as a result of age-related changes in responsiveness and tolerances (5,13).

The current report's findings indicated that older age groups, smokers, hypertensives, diabetics, and individuals with CKD were more likely to have a catastrophic prognosis. These results are in line with those of previous research, which predicted that people with diabetes mellitus would have a 52% higher risk of dying from COVID-19. The intensity of COVID-19 and death are independently increased by diabetes mellitus and the level of hyperglycemia. Additionally, having comorbidities from diabetes mellitus, such as ischemic heart disease and long-term renal insufficiency, is linked to a higher COVID-19 death rate (14). Additionally, the findings are in line with those of a survey performed in Spain in 2020, which found that more than 80% of fatalities were people who had at least one major underlying disease, such as malignancy, cardiovascular diseases, diabetes, or other metabolic disorders (4).

According to the outcomes of a subsequent survey conducted in 2020 on Egyptian COVID-19 sufferers, the prevalence of diabetes mellitus may be a major indicator of mortality for COVID-19 patient populations (5) and this might be characterized by enhanced interleukin-6 production, decreased T cell activity, and enhanced angiotensin-converting enzyme 2 expression (15).

Diabetes mellitus is an important death indicator in the current study due to its high prevalence (65%) in COVID-19 individuals who did not survive. Similar findings from a 2019 study carried out in Egypt showed that the incidence of diabetes was substantially greater in deceased patients than in living patients (37.6% versus 29.1%, correspondingly). The usage of medical dosage anticoagulant, the administration of corticosteroids, and the consumption of azithromycin were all shown to be separately linked with decreased death in that research. The longer length of

hospitalisation in the surviving victims, which is linked to a higher recurrence of treatment administering than with the non-survivors cohort, which dies four to six days after hospitalisation, may be the cause of the significant difference between the frequency range of prescribed therapies for each cohort <sup>(16)</sup>. It should be noted that the use of steroids may be a sign of the severity of the condition rather than a sign that the patient will die. Steroids are typically administered to individuals who have acute respiratory problems or indications, therefore causing effect bias is fairly possible <sup>(14)</sup>.

Additional research is required to verify the advantages of various drugs in COVID-19 sufferers.

**Conflict of interest:** The authors declared no conflict of interest.

**Sources of funding:** This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Author contribution:** Authors contributed equally in the study.

## REFERENCES

1. **WorldoMeters (2022):** COVID-19 Coronavirus pandemic. Available at: <https://www.worldometers.info/coronavirus/>
2. **Moreno-Torres V, de la Fuente S, Mills P et al. (2021):** Major determinants of death in patients hospitalized with COVID-19 during the first epidemic wave in Madrid, Spain. *Medicine*, 100:16(e25634).
3. **Yang X, Yu Y, Xu J et al. (2020):** Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med.*, 8(5):475-81.
4. **Kozlovskiy A, Bilenko D, Dluhopolskyi O et al. (2021):** Determinants of COVID-19 death rate in Europe: Empirical analysis. *Problems of Sustainable Development*, 16(1):17-28.
5. **Khamiss A, El-Dahshan M, El-Ghamery F et al. (2021):** Outcomes of COVID-19 in Egyptian patients. *Al-Azhar Medical Journal*, 50(1):765-82.
6. **AbdelGhaffar M, Omran D, Elgebaly A et al. (2022):** Prediction of mortality in hospitalized Egyptian patients with Coronavirus disease-2019: A multicenter retrospective study. *PLoS One*, 17(1):e0262348.
7. **Fielding-Miller R, Sundaram M, Brouwer K (2020):** Social determinants of COVID19 mortality at the county level. *PLoS ONE*, 15(10):e0240151.
8. **Triggle N (2020):** Coronavirus: How to understand the death toll, *BBC News*. <https://www.bbc.com/news/health-51979654>
9. **Chen Y, Klein S, Garibaldi B et al. (2021):** Aging in COVID-19: Vulnerability, immunity and intervention. *Ageing Res Rev.*, 65:101205.
10. **Pawelec G (2018):** Age and immunity: what is “immunosenescence”? *Exp. Gerontol.*, 105:4-9.
11. **Ghweil A, Hassan M, Khodary A et al. (2020):** Characteristics, outcomes and indicators of severity for COVID-19 among sample of ESNA Quarantine Hospital’s patients, Egypt: A retrospective study. *Infection and Drug Resistance*, 13:2375-83.
12. **Zhou F, Yu T, Du R et al. (2020):** Clinical course and risk factors for mortality of adult inpatients with COVID19 in Wuhan, China: a retrospective cohort study. *Lancet*, 395:1054-62.
13. **Liu K, Chen Y, Lin R et al. (2020):** Clinical features of COVID-19 in elderly patients: A comparison with young and middle-aged patients. *Journal of Infection*, 80(6):14-8.
14. **Lim S, Bae J, Kwon H et al. (2021):** COVID-19 and diabetes mellitus: from pathophysiology to clinical management. *Nat Rev Endocrinol.*, 17(1):11-30.
15. **Singh A, Gupta R, Ghosh A et al. (2020):** Diabetes in COVID-19: prevalence, pathophysiology, prognosis and practical considerations. *Diabetes Metab Syndr.*, 14(4):303-10.
16. **McBane R, Torres Roldan V, Niven A et al. (2020):** Anticoagulation in COVID-19: A systematic review, meta-analysis, and rapid guidance from Mayo Clinic. *Mayo Clin Proc.*, 95(11):2467-86.