

Predictors of Mortality in Hospitalized Patients with COVID-19 Infection. A Single Center Follow Up Study

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ABSTRACT

Background: Coronavirus disease 2019 (COVID-19) is a condition brought on by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It is a significant global cause of illness and mortality. Finding modifiable risk variables might help lower COVID-19 infection-related mortality. **Objective:** The aim of the current study to identify the factors associated with mortality in patients admitted with COVID-19 in our Minia University Cardiothoracic Hospital. **Patients and methods:** A total of 329 real-time polymerase chain reaction (PCR) confirmed COVID-19 infected patients were subjected to complete history taking, general and local chest examination, and some laboratory investigations (Total leucocytic count "TLC", lymphocyte count, serum ferritin, D dimer, C-reactive protein "CRP" and Lactic Dehydrogenase "LDH"). Patients were followed up from admission to discharge. They were assessed regarding need for non-invasive (NIV) or invasive mechanical ventilation (IMV) and duration spent on them if present and also regarding length of hospital stay and mortality.

Results: The study showed that non-survivors had significantly higher age than survivors (*P-value 0.0001*). Hypertension was more prevalent in non-survivor group (72.1%) than survivors (47.3%) (*P-value 0.0001*). Also, Diabetes Mellitus was significantly found to be more in non-survivors (65.4%) than in survivors (41.8%) (*P-value 0.0001*). Moreover, comorbid cardiac disease was presented more in non-survivors (15.4%) than survivors (8.00%) (*P-value 0.036*). Regarding laboratory parameters, significantly higher TLC, serum ferritin, D dimer, CRP and LDH and lower lymphocytic count were observed in the non-survivor group (*P-value 0.0001 for all*). Regarding mechanical ventilation use, more non-survivor patients required NIV and IMV with more days spent on them (*P-value 0.0001 for all*). **Conclusions:** Older age, hypertension, DM, cardiac disease, higher TLC, serum ferritin, D dimer, CRP, LDH and lower lymphocytic count are associated with higher mortality in COVID-19 infected patients. Also, need for mechanical ventilation whether invasive or non-invasive is associated with higher mortality.

Keywords: COVID-19, Survivors, Non-survivor, Follow up study, Minia University.

INTRODUCTION

Since its initial appearance in Wuhan, China in December 2019, the coronavirus disease 2019 (COVID-19) has spread quickly around the world ⁽¹⁾. The severity of the outbreak and the extraordinary rates of transmission led to the World Health Organization classifying it as a pandemic ⁽²⁾.

A large portion of the information describing the traits and risk factors of patients for fatal illness and severe sickness comes from Chinese case series with unadjusted analysis. It is unclear whether such results can be applied to other populations. Through multivariable analysis of 171 patients in Wuhan, older age and D-dimer levels more than 1 g/ml were found to be independent predictors of hospital mortality ⁽³⁾. Heart disease, hypertension, chronic lung disease, chronic renal disease, and other conditions have also been linked to severe illness or mortality in China ^(4, 5). In addition to other chronic illnesses, in a study of 20133 hospitalized UK patients, **Docherty et al.** also discovered these characteristics as separate risk factors for mortality ⁽⁶⁾.

Black and Asian ethnic groups are more likely in the UK to test positive and require hospitalization, raising concerns about the danger of mortality from Covid-19 in these communities ⁽⁷⁾. For effective patient treatment, it's crucial to be aware of the risk factors for COVID-19-related hospital mortality, including as clinical and collaborative decision-making, prompt

escalation of care for respiratory support, and targeted use of possible antiviral or immunomodulatory drugs. Identification of modifiable risk factors allows alleviation of risk prior to infection.

The aim of the current study to identify the factors associated with mortality in patients admitted with COVID-19 in our Minia University Cardiothoracic Hospital.

PATIENTS AND METHODS

The current follow-up study was conducted in Minia Cardiothoracic University Hospital, during the period from January to August 2021.

All patients (total 329 patients) who were hospitalized with COVID-19 infection during the study period were included in the analysis. Our cohort included any patient above the age of 18 years old who were admitted to our hospital and had a nasopharyngeal swab tested positive for SARS-CoV-2 before to or during their stay.

Patients were subjected to complete history taking, a thorough general and local chest examination, and a few laboratory tests (total leucocytic count, lymphocyte count, serum ferritin, D dimer, C-reactive protein, and lactate dehydrogenase). From admission through release, patients were monitored.

Patients were followed up from admission to discharge. They were assessed regarding need for non-invasive (NIV) or invasive mechanical ventilation

(IMV) and duration spent on them if present and also regarding length of hospital stay and mortality.

Ethical approval:

This study was ethically approved by the Institutional Review Board of the Faculty of Medicine, Minia University. Written informed consent was obtained from all participants. This study was executed according to the code of ethics of the World Medical Association (Declaration of Helsinki) for studies on humans.

Statistical analysis

The collected data were introduced and statistically analyzed by utilizing the Statistical Package for Social Sciences (SPSS) version 20 for windows. Qualitative data were defined as numbers and percentages. Chi-Square test and Fisher’s exact test were used for comparison between categorical variables as appropriate. Quantitative data were tested for normality by Kolmogorov-Smirnov test. Normal distribution of variables was described as means and SD, and independent sample t-test was used for comparison

between groups. P value ≤0.05 was considered to be statistically significant.

RESULTS

A total of 329 patients were included in the study; 209 males and 120 females. Only 104 patients died during their course of treatment and follow up, while 225 patients survived.

Comparison was made between survivors and non-survivors regarding age, gender, body mass index “BMI” and comorbidities. **Table 1** revealed that non-survivors had significantly higher age than survivors. Gender and BMI were insignificantly different between both groups. More non survivors (50%) had smoking history than survivors (38.7%). Hypertension was more presented in non-survivor group (72.1%) than survivors (47.3%) with statistically significant difference. Also, diabetes mellitus was significantly found to be more in non-survivors (65.4%) than in survivors (41.8%). Moreover, both groups were statistically different regarding presence of comorbid cardiac disease which was presented in 15.4% of non-survivors and in only 8% of survivors.

Table (1): Comparison between both groups regarding; age, gender, BMI, smoking history and comorbidities.

Variable		COVID-19 patients		P-value
		Survivor N= 225	Non survivor N= 104	
Age	Mean ± SD	56.1 ± 12.7	66.3 ± 11.5	0.0001*
Gender:	N %			
Male		138 (61.3%)	72 (69.3%)	0.163
Female		87 (38.7%)	32 (30.7%)	
Smoking	N %	87 (38.7%)	52 (50.00%)	0.04*
BMI	Mean ± SD	26.1 ± 3	26.3 ± 4	0.533
Hypertension	N %	106 (47.3%)	75 (72.1%)	0.0001*
DM	N %	94 (41.8%)	68 (65.4%)	0.0001*
Chronic chest diseases	N %	43 (19.1%)	15 (14.4%)	0.374
Cardiac diseases	N %	18 (8.00%)	16 (15.4%)	0.036*
CKD	N %	4 (1.8%)	6 (5.8%)	0.14

COVID-19: Coronavirus disease 2019. N: number. SD: Standard Deviation. BMI: Body Mass Index. DM: Diabetes Mellitus. CKD: Chronic Kidney Disease. *: Significant level at P value <0.05.

Table 2 revealed that fever, loss of taste or appetite and abdominal pain were significantly more presented in survivors than in non- survivors.

Table (2): Clinical parameters among survivors and non survivors.

Variable		COVID-19 patients		P-value
		Survivor N= 225	Non survivor N= 104	
Fever	N %	175 (77.8%)	69 (66.3%)	0.027*
Sore throat	N %	129 (57.3%)	50 (48.08%)	0.14
Cough	N %	141 (62.6%)	64 (61.5%)	0.83
Loss of taste or appetite	N %	23 (10.2%)	1 (0.96%)	0.003*
Diarrhea	N %	34 (15.1%)	16 (15.4%)	0.90
Abdominal pain	N %	80 (35.6%)	23 (22.16%)	0.022*

COVID-19: Coronavirus disease 2019. N: number. *: Significant level at p value <0.05.

Table 3 elucidated that there were statistically significant differences between survivors and non survivors regarding TLC, lymphocytic count, serum ferritin, D dimer, CRP and LDH with significantly higher TLC, serum ferritin, D dimer, CRP and LDH and lower lymphocytic count in non-survivor group.

Table (3): Laboratory investigations differences between survivors and non survivors.

Variable	COVID-19 patients		P-value
	Survivor N= 225	Non survivor N= 104	
	Mean ± SD	Mean ± SD	
TLC	13024.2 ± 342.4	8744.6 ± 274.3	0.0001*
Lymphocytic count	1388.6 ± 338.5	964.9 ± 221.4	0.0001*
Ferritin (ng/mL)	727.9 ± 174.6	1116.5 ± 87.9	0.0001*
D-dimer	1.2 ± 0.2	2.6 ± 0.54	0.0001*
CRP (mg/L)	82.6 ± 17.3	127.1 ± 28.4	0.0001*
LDH (IU/L)	797.2 ± 197.2	1330.2 ± 326.1	0.0001*

COVID-19: Coronavirus disease 2019. N: number. SD: Standard Deviation. TLC: Total Leucocytic Count. CRP: C reactive protein. LDH: Lactic Dehydrogenase. *: Significant level at p value <0.05.

Significant differences were observed between both groups regarding need for NIV or IMV and duration of them and also regarding duration of hospital stay (**Table 4**). More non-survivor patients required NIV and IMV with more days spent on them.

Table (4): Need for Mechanical Ventilation among both groups.

Variable	COVID-19 patients		P-value
	Survivor N= 225	Non survivor N= 104	
	N%	N%	
NIV need	94 (41.8%)	80 (76.9%)	0.0001*
IMV need	4 (1.8%)	73 (70.2%)	0.0001*
Duration of NIV (days)	Mean ± SD	Mean ± SD	0.0001*
	3 ± 5	7 ± 7	
Duration of IMV (days)	0.5 ± 0.3	1.5 ± 1	0.0001*

COVID-19: Coronavirus disease 2019. N: number. SD: Standard Deviation. NIV: Non-invasive Ventilation. IMV: Invasive Mechanical ventilation. *: Significant level at p value <0.05.

DISCUSSION

Growing older was regarded as a significant independent predictor of death in SARS and MERS, and it has also been established that patients with COVID-19 are also connected with mortality ⁽³⁾.

This is confirmed in the current study as it showed that non-survivors are significantly older than survivors (P value 0.0001). This is in agreement with **Zhou et al.** ⁽³⁾ as they found that non survivor group had an older age than survivor group (P value <0.0001).

Li et al. ⁽⁸⁾ found that patients with severe disease are older than those presented with non-severe disease. **Gopalan et al.** ⁽⁹⁾ also reported that age ≥50 years was an independent factor contributing for severity of COVID-19 and that non-survivors were two decades older than survivors. **Alwafi et al.** ⁽¹⁰⁾ documented that age was an important risk factor for mortality in COVID-19.

More non survivors than survivors had smoked in the past (P value 0.04). **Ismail et al.** ⁽¹¹⁾ study backed up the existing research linking smoking to COVID-19 problems and disease progression. In the last MERS-CoV outbreak, investigations conducted in the past revealed that smokers had a higher fatality rate ^(12,13).

Hypertension, cardiac diseases and DM were more prevalent in non-survivor group (P values 0.0001, 0.036 and 0.0001, respectively). **Zhou et al.** ⁽³⁾ also observed that hypertension, coronary heart diseases and DM were more present in non-survivor group (P values 0.0008, <0.0001 and 0.0051, respectively). Similarly, study made by **Li et al.** ⁽⁸⁾ showed that patients presented with severe disease suffered hypertension, coronary heart diseases and DM more than those presented with non-severe disease (P values 0.000, 0.000 and 0.009, respectively).

According to research by **Guo et al.** ⁽¹⁴⁾, patients with underlying cardiovascular illness were more likely to sustain myocardial damage during COVID-19 and are more likely to pass away.

As regards clinical data, fever was shown to be associated with less mortality (P value 0.027). These results are supported by a study performed in Wuhan that showed that fever was associated with lower risk of mortality ⁽¹⁵⁾. Loss of taste or appetite was also linked to lower mortality (P value 0.003). In agreement with these results, **Talavera et al.** ⁽¹⁶⁾ concluded that hospitalized patients with COVID 19 patients who

arrived with anosmia had a reduced death rate and a milder illness.

More survivor patients were presented with abdominal pain than non survivors (P value 0.022). The meta-analysis conducted by **Wang et al.** ⁽¹⁷⁾ revealed that gastrointestinal problems are not related with increased mortality and that the predictive significance of gastrointestinal symptoms in COVID-19 deserves further exploration.

Regarding laboratory parameters, the current study proved that there were significantly higher TLC, serum ferritin, D dimer, CRP and LDH and lower lymphocytic count in non-survivor group (P values 0.0001 for all). **Gopalan et al.** ⁽⁹⁾ found lower lymphocytic percent and absolute lymphocytic count in non-survivor group (P value <0.0001). **Zhou et al.** ⁽³⁾ also reported lower baseline lymphocytic count in the non-survivor group (P value <0.0001). More than 80% of severely sick COVID-19 patients who were examined by **Yang et al.** ⁽¹⁸⁾ had lymphopenia. Due to the targeted invasion by SARS-CoV virus particles that damages and destroys the cytoplasmic components of lymphocytes, lymphopenia is a hallmark characteristic of severely sick individuals with SARS-CoV infection ⁽¹⁹⁾. Lymphocyte apoptosis causes lymphopenia, which is also typical in really sick MERS patients ^(20,21). According to **Zhou et al.** ⁽³⁾ and **Shang et al.** ⁽²²⁾, lymphopenia was linked to greater mortality.

In support to the results of the current study, study of **Zhou et al.** ⁽³⁾ elucidated that leukocytosis, elevated LDH, D dimer and serum ferritin were associated with death. Regarding laboratory parameters, study of **Shang et al.** ⁽²²⁾ also supports the results of the current study as their results showed that elevated D-dimer was connected to COVID-19-associated mortality in severe patients and they found significantly higher CRP levels in the non-survivor group. **Assal et al.** ⁽²³⁾ also found CRP level to be significantly higher in severe COVID-19 than in moderate cases. Study of **Khali et al.** ⁽²⁴⁾ showed that 28-day mortality was independently predicted by higher CRP level.

During hospital stay, more non-survivor patients required NIV and IMV with more days they spent on them. In agreement with these results, According to **Assal et al.** ⁽²³⁾, the use of invasive mechanical ventilation was discovered to be an independent predictor of death. Additionally, **Manal et al.** ⁽²⁵⁾ discovered that a COVID-19 patient's demand for mechanical ventilation is probably related to a greater death rate. According to the current findings, **Wang et al.** ⁽²⁶⁾ discovered that the non-survivor group required greater NIV and IMV (P value <0.001).

CONCLUSION

Among COVID-19 patients, older age, hypertension, DM, cardiac disease, higher TLC, serum ferritin, D dimer, CRP and LDH and lower lymphocytic

count are associated with higher mortality in COVID-19 infected patients. Also, higher NIV or IMV need and longer duration spent on them are associated with higher mortality. On the other hand, fever, loss of taste or smell and abdominal pain were associated with lower mortality.

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