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Original article

Mortality-related risk factors in critically ill COVID-19 in a developing country: An observational study

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ABSTRACT

Background: Mortality rates of coronavirus disease-2019 (COVID-19) were too high across the globe. The impact of several risk factors on coronavirus mortality has been previously reported in several studies with different results. In this study, we aimed to investigate the relation between the patients' comorbidities and risk of mortality from critically ill COVID-19 disease. **Methods** This is a prospective observational cohort study. Seventy-two patients with critically ill COVID-19 were included. All patients were adult and diagnosed after SARS-CoV-2 PCR. All patients were admitted to isolation ICUs in Critical Care Department, Cairo University Hospitals. **Results** Old age (> 70 years-old) , DKA on presentation, receiving corticosteroids prior to presentation, thrombotic events (STEMI, N-STEMI, DVT) and tachypnea on admission were all risk factors for mortality with *p*-values 0.033, 0.031, 0.046, 0.013 and <0.001 respectively. Whereas, pre-existing pulmonary diseases did not have statistically significant relationship with mortality. **Conclusion** Chronic comorbidities, complications, and demographic variables including old age, DKA, receiving corticosteroids prior to admission, thrombotic events and tachypnea are clinical risk factors for a fatal outcome associated with critically ill COVID-19 disease.

Introduction

Coronarvirus disease 2019 (COVID-19) has been a health disaster resulting in a global pandemic declared in 2020. This pandemic has caused huge loss of lives as well as socio-economic losses [1].

COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which is a Betacoronavirus family member. However, SARS-CoV-2 is characterized by having greater rate of spread [1].

Hence, several researchers have been studying risk factors affecting COVID-19 severity and mortality [2,3]. This study aims at enhancing our knowledge and understanding about the disease mortality risk factors among critically ill patients in developing countries.

Methods

This is a prospective observational cohort study involving patients diagnosed with critically ill COVID-19 disease. All were admitted to COVID-19 isolation ICUs in critical care department- Cairo university hospitals. Consent was obtained from all patients or their next of kin.

All patients were 18 years old or older and diagnosed after obtaining positive SARS-CoV-2

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PCR via nasal swabs. Exclusion criteria were mild and moderate disease.

After approval of research ethics committee (MD-284-2021) – Faculty of Medicine – Cairo University and fulfilling inclusion criteria, recruited patients' data were collected but not their names. Age, Gender & Co-morbidities as well as history of prior corticosteroid or immunosuppressant therapy. Bleeding, thrombotic events as well as secondary infection were all recorded. Mortality was recorded.

Statistical analysis

Statistical analysis was done using IBM SPSS® Statistics version 26 (IBM® Corp., Armonk, NY, USA). Numerical data was expressed as mean and standard deviation or median and range as appropriate. Qualitative data was expressed as frequency and percentage. Pearson's Chi-square test or Fisher's exact test was used to examine the relation between qualitative variables.

Results

This prospective observational study included seventy-two patients diagnosed with critically ill COVID-19 disease.

Old age, DKA on ICU admission, receiving corticosteroids at home and occurrence of thrombotic events *(STEMI, N-STEMI & DVT)* before presenting to hospital, all were associated with mortality (*p*-values 0.033, 0.031, 0.046 & 0.013 respectively) as shown in **table (1)**. Respiratory rate on admission was higher in the mortality group (*p*-value <0.001) as shown in **table (2)**. Mechanical ventilation was associated with high mortality (*p*-value < 0.001) as shown in **table (3)**.

Table 1. Relation of various comorbidities & risk factors with mortality.

		Group		Total	***p*-value**
		Survival	Mortality		
Age ≥ 70 years	Count	8	25	33	**0.033**
	% within Group	24.2%	75.8%	100.0%	
Male	Count	19	27	46	0.375
	% within Group	41.3%	58.7%	100.0%	
Smokers	Count	2	2	4	0.375
	% within Group	50.0%	50.0%	100.0%	
Pre-existing pulmonary disease	Count	2	4	6	1.000
	% within Group	33.3%	66.7%	100.0%	
Hypertension	Count	15	29	44	0.454
	% within Group	34.1%	65.9%	100.0%	
Diabetes Mellitus	Count	8	23	31	0.454
	% within Group	25.8%	74.2%	100.0%	
Diabetic Ketoacidosis (DKA)	Count	0	7	7	**0.031**
	% within Group	0.0%	100.0%	100.0%	
Chronic coronary artery disease	Count	9	15	24	1.000
	% within Group	37.5%	62.5%	100.0%	
Malignancies	Count	5	6	11	0.554
	% within Group	45.5%	54.5%	100.0%	
Immunosuppressive therapy	Count	1	6	7	0.244
	% within Group	14.3%	85.7%	100%	
Home steroids	Count	2	12	14	**0.046**
	% within Group	14.3%	85.7%	100.0%	
Upper GI bleeding	Count	1	7	8	0.121
	% within Group	12.5%	87.5%	100.0%	
Thrombotic events	Count	0	9	9	**0.013**
	% within Group	0.0%	100.0%	100.0%	
Secondary infection	Count	4	10	14	0.442
	% within Group	28.6%	71.4%	100.0%	

Table 2. Relation of respiratory rate on admission with mortality.

			Mean	SD	Median	Minimum	Maximum	*p*-value
RR on admission	Group	Survival	27.3	5.1	**26**	**22**	**40**	**<0.001**
		Mortality	32.4	6.1	**33**	**22**	**46**	

Table 3. Relation of mechanical ventilation (MV) with mortality.

			Mortality		Total	*p*-value
			Survival	Mortality		
MV	No	Count	20	3	23	
		% within Mortality	74.1%	6.7%	31.9%	**<0.001**
	Yes	Count	7	42	49	
		% within Mortality	25.9%	93.3%	68.1%	
Total		Count	27	45	72	
		% within Mortality	100.0%	100.0%	100.0%	

Discussion

COVID-19 disease has been a serious nightmare for the past few years. Several efforts have been made to control disease spread, alleviate disease severity, deal with complications and even prevention of infection and reinfection. [1] However, lack of prognostication of disease severity and mortality did lead to improper use of certain medications such as immunomodulatory drugs or futile management thus multiple studies were published aiming to identify risk factors for disease mortality. [4, 5] Our study aims to identify risk factors of disease mortality in critically ill patients.

In our data, patients of $\geq$ 70 years of age did show statistically significant relation with mortality (p=0.033). This was echoed by **Du et al.** in a prospective study including 179 patients with COVID-19 pneumonia, they concluded that age $\geq$ 65 years was associated with high mortality (p<0.001) [6]. Where **Auld et al.** in another multicenter observational cohort study including 217 critically ill COVID-19 patients concluded that age $\geq$ 75 years was associated with mortality (p=0.004) [7].

In the same context, **Lu et al.** in a systemic review with meta-analysis confirmed advanced age has been associated with high mortality in COVID-19 patients [3]. **Figliozzi et al.** in another systematic review confirmed the same finding [8].

Similarly, **Zimmerman et al.** in their retrospective cohort study including 304 mechanically ventilated COVID-19 patients observed that patients over 71 years old had greater risk of mortality compared to patients ages 61-70 [9].

According to our study, there was no statistically significant relation between gender and mortality. In agreement with this finding, **Codesido et al.** in a retrospective multicentric study including 1246 patients concluded that gender did not have statistically significant relationship with mortality [10]. On the contrary, **Kharroubi et al.** in a retrospective study including 62310 patients concluded that males had higher mortality. However, they stated that the male group had more comorbidities, which were associated with mortality [11].

Our data concluded that smoking and pre-existing pulmonary diseases were not associated with mortality. This was confirmed by **Figliozzi et al.** in their huge meta-analysis where they concluded that smoking was associated with disease severity but not mortality [8]. On the contrary, **Li et al.** in a meta-analysis using PubMed, Embase, and Cochrane Library databases concluded that smokers & COPD patients had more severe disease and higher mortality [12].

Our data suggests that hypertension, diabetes mellitus, chronic coronary artery disease, malignancies and chronic immunosuppressive therapy were not associated with mortality. But **Du et al.** in their prospective cohort study including 179 consecutive patients concluded that hypertension and cardiovascular or cerebrovascular diseases were associated with mortality but not diabetes, chronic digestive disorders, tuberculosis, chronic hepatic or renal insufficiency, peripheral vascular disease or malignancy [6]. However, A huge study done by **Sharma et al.** that studied more than twenty systemic reviews/meta-analyses/meta-regression concluded that hypertension, diabetes, any heart

condition and chronic obstructive pulmonary disease (COPD) were associated with adverse disease outcome. And pre-existing comorbidities were associated with less survival, but not a particular comorbidity [13].

Among our patients, diabetic ketoacidosis (DKA) on admission was associated with mortality (p=0.031). In agreement with our finding, a study including 2366 patients from an electronic medical record done by **Stevens et al.** concluded that the combination of DKA & COVID-19 infection was associated with high mortality [14]. As well as, a systemic review/meta-analysis of studies involving 639 DKA patients with confirmed SARS-CoV-2 performed by **Alhumaid et al.** concluded that DKA in COVID-19 patients was associated with mortality ($\geq$ 25%) [15].

According to our study, initial tachypnea (on admission) was associated with high mortality (p<0.001). In agreement with our study**, Chatterjee et al.** in a study including 1095 patients concluded that indices of respiratory compromise at initial presentation that are readily measurable at home—oxygen saturation <92% or a respiratory rate >22 breaths per minute—were each associated with elevated mortality in hospitalized COVID-19 patients. Hypoxemic patients had a mortality risk 1.8 to 4.0 times greater, depending on the patient's blood oxygen levels. Similarly, compared to patients admitted with normal respiratory rates, those with tachypnea had a mortality risk 1.9 to 3.2 times greater [16].

In our study, patients who were mechanically ventilated recorded highly statistically significant relationship with mortality (93%) (p-value < 0.001). In an explanation to this finding, mostly both mechanical ventilation and mortality were sequelae for the disease severity, in other words, mortality is a consequence for severe disease not mechanical ventilation. i.e. association not causation.

This was confirmed in other works, **Nishikimi et al.** conducted a multicenter retrospective cohort study including 1966 mechanically ventilated patients recorded mortality above 60% [17]. The results of our study did not agree with the multicenter observational cohort study including 217 critically ill COVID-19 patients done by **Auld et al.** as it recorded 29.7% mortality for patients receiving mechanical ventilation [7]. **Roedl et al.** in a multicenter observational study of 223 critically ill patients with COVID-19 among 15 hospitals found the mortality was 44% among patients requiring mechanical ventilation [18]. **Zimmerman et al.** in a retrospective cohort study including 304 mechanically ventilated COVID-19 patients found the mortality rate was 53.3% with no mortality difference regarding race [9].

However, the pandemic resolved. Current data could help with future sporadic cases or similar clinical situations as emergence of a new strain, or a new member of the same family. Identifying risk factors for mortality is of major importance as many of them is preventable, modifiable or treatable.

Conclusion

Our data concluded that several demographic data and comorbidities were associated with mortality in critically ill COVID-19 disease such as old age, DKA, receiving corticosteroids prior to presentation and tachypnea on admission.

Disclosure of potential conflicts of interest

No conflict of interest

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