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RESEARCH ARTICLE

Predictors of mortality among inpatients in COVID-19 treatment centers in the city of Butembo, North Kivu, Democratic Republic of Congo

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Abstract

Determining the risk factors for severe disease and death among hospitalized Covid-19 patients is critical to optimize health outcomes and health services efficiency, especially in resource-constrained and humanitarian settings. This study aimed to identify the predictors of mortality of Covid-19 patients in North Kivu province in the Democratic Republic of Congo.A retrospective cohort study was conducted in 6 Covid-19 treatment centers in the city of Butembo from 1 January to 31 December 2021. The time to event (death), the outcome variable, was visualized by Kaplan-Meier curves and the log-rank test was used to confirm differences in trends. Cox regression was used for all the predictors in the bivariate analysis and multivariate analysis was done using predictors found statistically significant in the bivariate analysis. The following variables were considered for inclusion to the Cox regression model: Age, Sex, Disease length, Treatment site, History of at least one co-morbidity, Body mass index, Stage according to SpO2 and the NEWS-modified score.Among the 303 participants (mean age of 53 years), the fatality rate was 33.8 deaths per 1000 patient-days. Four predictors were independently associated with inpatient death: age category (≥ 60 years) (adjusted HR: 9.90; 95% CI: 2.68–36.27), presence of at least one comorbidity (adjusted HR: 11.39; 95% CI: 3.19–40.71); duration of illness of > 5 days before hospitalization (adjusted HR:1.70, 95% CI: 1.04–2.79) and peripheral capillary oxygen saturation (SpO2) < 90% (adjusted HR = 14.02, 95% CI: 2.23–88.32). In addition to advanced age, comorbidity, and length of disease before hospitalization, ambient air SpO2 measured by healthcare providers using low-tech, affordable and relatively accessible pulse oximetry could inform the care pathways of Covid-19 inpatients in resource-challenged health systems in humanitarian settings.

in the City of Butembo, North Kivu, Democratic Republic of Congo. Retrieved from osf.io/qevm4.

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I. Introduction

Corona Virus Disease 2019 (COVID-19) is an infectious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Since the discovery of the first group of cases in Wuhan City, Hubei Province, in China on December 31st, 2019, the initial COVID-19 outbreak has become one of the most significant global health threats.

It was declared a public health emergency of international concern on January 30th, 2020, by the World Health Organization (WHO) and a pandemic on March 11th, 2020 [1, 2]. By 2021, COVID-19 had affected almost all countries around the world.

According to the WHO situation reports, as of October 4th, 2022, the number of confirmed COVID-19 cases reached more than 615,777,700 cases and 6,527,192 deaths (1.06% case- fatality rate) [3]. In the African region, the first case of COVID-19 was reported on February 14th, 2020, in Egypt and on February 17th, 2020 in sub-Saharan Africa (Nigeria). Since then, all 54 African states have been affected. As of September 21st, 2021, the WHO African Region has recorded 8,166,634 cases and 206,740 deaths (2.53% case-facility rate) [4–7]. The Democratic Republic of Congo (DRC) recorded its first case on March 10th, 2020. Since then, the cumulative number of cases up to September 3rd, 2022 was 92,942 cases, of which 92,940 were confirmed, with 1,357 deaths, representing a case-fatality rate of 1.5% [8]. According to the epidemiological report in North Kivu, as of may 22nd, 2022, the province recorded 10,049 cases, of which 9,144 recovered (91.0%) and about 600 died (5.9%). These figures place the province in second place after the provincial city of Kinshasa in terms of disease burden [9]. On the same date, the report indicates that the city of Butembo, with its two health zones, had 1280 cases, of which 1157 (90.4%) recovered and 116 (9.1%) died. These two health zones concentrated 20% of the province's mortality [9].

The signs and symptoms of COVID-19 vary considerably, with clinical features ranging from asymptomatic presentation to fatal respiratory distress and multiorgan failure [10, 11]. COVID-19 does not exert an equal impact on the different affected regions in the world, with a wide variation in the reported proportion of patients with severe disease and death [12, 13]. Morbidity accounts for 6% of cases in the Eastern Mediterranean region, 30% in Europe, 39% in the American region, 19% in South Asia, 3% in the Pacific and 4% in Africa [4, 14]. The consequences are palpable worldwide at all levels with significant economic, social, health and financial costs [15].

Strategies to prevent COVID-19 transmission have included border closures, the creation of quarantine centers, self-isolation, enforcement of containment measures, surveillance, routine screening, and, recently, vaccination, with the first vaccine deliveries to Africa in March 2021 [15].

Studies were done worldwide to determine COVID-19 risk factors and patient characteristics and recently the impact of vaccination on hospitalization [1, 2, 6, 15]. Overall, risk factors for severe disease and death included advanced age, male sex, history of comorbidity, poor nutritional status, a severe form of the disease on admission, vaccination status, delay in admission to intensive care, etc. To our knowledge, by the time we conducted our research in 2021, such a study had not yet taken place in the region. Therefore, our study proposed to identify the predictors of mortality of COVID-19 patients who were hospitalized in the city of Butembo from January 1st to 31 December 31st, 2021.

II. Methods

This study was conducted in six COVID-19 treatment centers (CTC) in the Katwa and Butembo health zones of the city of Butembo, North Kivu province, Democratic Republic of Congo. The CTCs were located at the Hospital of Women Committed to the Promotion of

Integral Health, the Kitatumba Referral General Hospital, the Graben University Clinics, the Katwa Referral General Hospital, the Matanda Hospital and the Ngote Hospital.

A retrospective cohort study was conducted from 1 January to 31 December 2021.The study population included all patients hospitalized in one of the CTCs in the city of Butembo in 2021 with a positive reverse transcriptase-polymerase chain reaction result (RT-PCR +). The statistical units were the COVID-19 patients registered in each health center. We excluded patients without investigation forms or whose clinical records could not be found. In total, 303 Covid-19 patient records were found. Delay between symptom onset and hospital admission was the exposure variable. Patients were divided into two groups: 188 patients hospitalized for $\leq$ 5 days (Short delay) and 115 patients hospitalized for$>$ 5 days (long delay). Data was extracted by the authors who are all medical doctors.

Variables

The time to event (death) was the outcome variable. Predictor variables were age, sex, occupation, clinical stage of disease based on signs and symptoms, ambient air oxygen saturation (SpO2), respiratory rate, NEWS-modified score (National Early Warning Score), history of comorbidities, number of comorbidities, types of comorbidities, body mass index (BMI), duration of disease before hospitalization, date of discharge or last news about the patient. NEWS comprises seven parameters: respiration rate, SpO2, any supplemental oxygen, temperature, systolic pressure, heart rate, level of consciousness (Table 1). It allows the classification of COVID-19 patients into three severity categories: low (aggregate 1–4), medium (aggregate 5–6), and high (aggregate 7 or more). Because some parameters (blood pressure, supplemental oxygen) in the patient's records were missing, we modified the scoring of some parameters to obtain the NEWS-modified score with five parameters. The time variable was calculated from the date of enrolment (admission at the hospital) to the end point (death, discharge or end of the study).

Data collection

An Excel database was used to collect data from the patient records, registers and CTC databases. After verification and validation, it was imported into SPSS (Statistical Package for the Social Sciences) version 26 and Stata 17 (StataCorp, College Station, TX) for analysis. Before the actual analysis, we transformed the variables of age, BMI, respiratory rate, ambient air oxygen saturation, number of comorbidities, and Hb level into categorical variables.

Statistical analysis

Descriptive statistics were used to describe the basic characteristics of the study data. For continuous variables, means and standard deviation (SD) were calculated for normally distributed

Table 1. Score NEWS–adapted from the NEWS2 scoring matrix.

Vital signs	3	2	1	0	1	2	3
Temperature	Hypothermia		Fever	No fever			
Heart rate				Normal			Abnormal
Respiratory rate	$\leq$ 8		9–11	12–20		21–24	$\geq$ 25
Ambient air SpO2	$\leq$ 91	92–93	94–95	$\geq$ 96			
Consciousness level				Lucid/alert			Confused

Classification: mild or moderate (NEWS score $<$ 5); severe (NEWS score $\geq$ 5) [16]

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continuous variables and median with interquartile range (IQR) for non-normally distributed continuous variables; for categorical data, proportions and their respective 95% confidence intervals were calculated. We used the chi-square test and Fisher´s exact test when appropriate.

We calculated proportions, where the main outcome variable was death. We determined the incidence rate of recorded death events per 1000 patient-day (p-d) from the date of enrollment. The survival probabilities of participants according to the predictor variables were visualized by Kaplan-Meier curves and the log-rank test was used to confirm differences in trends. Cox regression was used for all the predictors in the bivariate analysis and multivariable analysis was done using predictors found statistically significant in the bivariate analysis. The following variables were considered for inclusion to the Cox regression model: Age, Sex, Disease length, Treatment site, History of at least one co-morbidity, Body mass index, Stage according to SpO2 and the NEWS-modified score. The interaction age and SpO2 was not significant and was not included in the model. The interaction between the comorbidity and «the delay between symptom onset and hospital admission» was not significant and was not included in the model. The interaction between age and «the delay between symptom onset and hospital admission» was not significant and was not included in the model. The interaction age and comorbidity was significant and was included in the model. We then compared the model with the interaction to the model without the interaction using the lrtest command. The significant lrtest indicated that we reject the null hypothesis that the two models fit the data equally well and concluded that the bigger model with the interaction fits the data better than the smaller model which did not include the interaction.

The proportionality test based on Schoenfeld residuals verified compliance with the assumption of the proportionality of risks (refer to S1 Table). The Test of proportional hazards shown that the assumption was not violated as presented in S1 Fig. Regarding the goodness of fit of the final model, we have seen that the hazard function follows the 45-degree line very closely except for very large values of time. Overall, we would conclude that the final model fits the data very well (refer S2 Fig). We assessed multicollinearity using variance inflation factors (VIFs) greater than 2.1. The proportionality test based on Schoenfeld residuals verified compliance with the assumption of the proportionality of risks. All tests were two-tailed with 95% confidence intervals and considered statistically significant when p-value < 0.05. Dataset can be found in osf:

https://osf.io/qevm4/?view_only=9da898c21cb94c0385e3c0d5342b283d

Ethical considerations

Prior authorizations were obtained from the health authorities in North Kivu province (Head of the Health Division, Coordinator of the DPS/Butembo branch, the Head of Katwa and Butembo Health Zone and the Directors of the selected hospitals). To ensure confidentiality, we deidentified the variables in the database. With regard to informed consent, we did not have any contact with the patients, so no biological procedures were used in the collection or processing of the data. The use of the results of this study will be limited to the strict exploitation related to its objectives and the authors have reported no conflict of interest. The protocol for this study had received ethical approval from the School of Health Ethics Committee (reference number: ESP/CE/138/2021).

All the study sites have had a blanket data policy informing their patients of the following: "For all rare and emerging diseases for which science still needs further data, hospitalized patients have accepted that their data be used for research in order to improve treatment." The Kinshasa School of Public Health Ethics Committee approved the study.

III. Results

There were 303 participants who had a mean age of 53 ± 22 years. Those who consulted within 5 days of symptom onset were younger than those who consulted ≥ 5 days (51 vs. 57 years; p = 0.014). Overall, 43% were at least 60 years old, 46% were male, and 6.4% were healthcare professionals. The distribution of patients in the population from which the two groups were drawn was identical according to sociodemographic characteristics, except for age and site (Matanda and Katwa particularly) (Table 2).

Of 303 patients included, 45.9% had at least one comorbidity of whom 25.2% had at least two comorbidities. The most frequent comorbidities were hypertension 18.8% (57/303) and diabetes 17.8% (54/303). The distribution of patients in the ≤ 5 days (short) and > 5 days (long) hospitalization groups was similar in terms of comorbidities (Table 2).

Cough and asthenia were present in more than 80% of cases, anorexia, headache and dyspnea in 50–79% of cases, and fever, digestive, and taste disorders and other signs in less than 50% of cases. The distribution of patients between the short and long-hospitalization groups differed in terms of symptoms, except for cough, headache, loss of taste, and digestive and cardiac disorders (Table 2).

The mean oxygen saturation on admission was 85.60% ± 12.72% (81.91 ± 14.29 in the exposed (> 5 days (long) hospitalization group) and 87.85 ± 11.11 in the unexposed (in the ≤ 5 days (short) hospitalization group)). Patients admitted early had higher oxygen saturation than those who visited late. Patients with a severe form accounted for 61% of all participants based on the m-NEWS score, 49% based on their SpO2 level and 55% based on symptoms at admission. Regardless of the classification used, the distribution of patients between the short and long-hospitalization groups differed according to disease severity upon admission (Table 3).

The fatality rate was 33.8 deaths per 1000 patient-days. The rate was 46 deaths per 1000 patient-days in the exposed group (> 5 days (long) hospitalization group) versus 25.6 deaths per 1000 patient days in the unexposed group (in the ≤ 5 days (short) hospitalization group) (Table 4).

After adjustment, four predictors were independently associated with inpatient death: older patients (≥ 60 years) had a higher risk of death than the reference group(<40 years) (adjusted HR: 9.90; 95% CI: 2.68–36.27) (see Fig 1 and Table 4), having at least one comorbidity had a higher risk of death than patients without comorbidity (aHR: 11.39; 95% CI: 3.19–40.71) (see Fig 2 and Table 4); patient admitted after "long delay" between symptom onset and hospital admission duration of illness of > 5 days before hospitalization had a higher risk of death than patients admitted after "short delay" (aHR:1.70, 95% CI: 1.04–2.79) and Patients with SpO2 < 90% had a higher risk of death than patients with SpO2 ≥ 95% (HRa = 14.02, 95% CI: 2.23–88.32) (Table 4). The interaction age and comorbidity was significant and was included in the model.

IV. Discussion

This study focused on the predictors of survival of Covid-19 patients hospitalized from 1 January to 31 December 2021 in the city of Butembo. Advanced age above 60 years, low free air SpO2 on admission, history of comorbidity and late admission (> 5 days after symptom onset) were predictors of mortality. Overall, these predictors have been previously reported in studies conducted in China, Europe, the USA and other African countries [2, 4, 10, 17–27]. Another new predictor introduced in the present study was the duration of illness > 5 days before hospitalization. Knowledge of these factors is an important advocacy tool for covid-19 patients in humanitarian and resource-limited settings. The use of NEWS-modified or original NEWS score, the measurement of oxygen saturation and search for co-morbidities must be

Table 2. Socio-demographic characteristics and clinical signs of Covid-19 patients on admission to the Covid-19 treatment centers in the city of Butembo from January 1st, to December 31st, 2021.

Characteristics on admission	All cases		Delay between symptom onset and hospital admission				
			> 5 days		≤ 5 days		p
	n = 303	%	n = 115	%	n = 188	%	
Age (median, IQR)	55.0(40–71)		53.0 (39–68)		60.5 (40–75)		**0.032***
Age(range)							0.139
< 40 years	83	27.4	27	23.5	56	29.8	
40–59 years	89	29.4	30	26.1	59	31.4	
≥ 60 years	131	43.2	58	50.4	73	38.8	
Gender							0.313
Male	139	45.9	57	49.6	82	43.6	
Female	164	54.1	58	50.4	106	56.4	
Profession*	n = 234		n = 90		n = 144		0.601
Cultivator	72	30.8	32	35.6	40	27.8	
Housekeeper	50	21.4	19	21.1	31	21.5	
Shopkeeper	30	12.8	10	11.1	20	13.9	
Health care professional	15	6.4	7	7.8	8	5.6	
None and other professions	67	28.6	22	24.4	45	31.3	
Signs and symptoms							
Fever on admission	140	46.2	38	33.0	102	54.3	**<0.001**
Dry or wet cough	286	94.4	109	94.8	177	94.1	0.816
Dyspnea	164	54.1	78	67.8	86	45.7	**<0.001**
Shortness of breath	247	81.5	107	93.0	140	74.5	**<0.001**
Asthenia	180	59.4	63	54.8	117	62.2	0.2
Headache	163	53.8	80	69.6	83	44.1	**<0.001**
Anorexia	23	7.6	8	7.0	15	8.0	0.744
Loss of taste	41	13.5	18	15.7	23	12.2	0.399
Digestive disorders	11	3.6	5	4.3	6	3.2	0.605
Heart rhythm disorders	17	5.6	11	9.6	6	3.2	0.019
Altered consciousness	4	1.3	2	1.7	2	1.1	0.979
HIV positive	57	18.8	23	20	34	18.1	0.679
Hypertension	54	17.8	23	20	31	16.5	0.438
Diabetes	6	2	4	3.5	2	1.1	0.299
Obstructive lung disease	6	2	3	2.6	3	1.6	0.825
Obesity	139	45.9	58	50.4	81	43.1	0.213
Sites							**<0.001**
Pepsi	19	6.3	7	6.1	12	6.4	
Kitatumba	42	13.9	15	13.0	27	14.4	
CUG	52	17.2	33	28.7	19	10.1	
Katwa	75	24.8	17	14.8	58	30.9	
Matanda	60	19.8	28	24.3	32	17.0	
Ngote	55	18.2	15	13.0	40	21.3	

CUG: Cliniques Universitaires du Graben (Graben University Clinics); *Median test

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systematic. These parameters may help to select the most at-risk patients with a poor prognosis and to intensify surveillance. In almost all hospitals in Africa in general, and in the DRC in particular, the measurement of oxygen saturation was not systematically used of times due to the absence of an oximeter.

Table 3. Clinical stage of inpatients on admission to Covid-19 treatment centers in the city of Butembo from January 1 to December 31, 2021.

Stade de la maladie à l'admission			Delay between symptom onset and hospital admission				p-value
	Number of cases		> 5 days		≤ 5 days		
	(n)	%	(n)	%	(n)	%	
SpO2 (mean, SD)	**85.60 ± 12.7**		**81.91 ± 14.3**		**87.85 ± 11.1**		**<0.001**
Stage according to SpO2							**0.001**
Mild	61	20.1	12	10.4	49	26.1	
Moderate	94	31.1	34	29.6	60	31.9	
Severe	148	48.8	69	60.0	79	42.0	
Modified national early warning score							**<0.001**
< 5	119	39.3	29	25.2	90	47.9	
≥ 5	184	60.7	86	74.8	98	52.1	
Disease severity on admission							**0.001**
Mild	23	7.6	5	4.3	18	9.6	
Moderate	114	37.6	31	27.0	83	44.1	
Severe	166	54.8	79	68.7	87	46.3	
Total	**303**	**100**	**115**	**100**	**188**	**100**	

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Our study found that the risk of death increases with age. Compared to patients under 40 years of age, the risk of death is four times higher in patients > 60 years. It is well established that older age groups are more likely to have comorbidities and are more susceptible to acquire SARS-CoV-2, severe forms of the disease, and higher mortality risk than younger patients [28]. The difference between the age groups lies in the ability to fight the infection [29]. Several studies have proposed multiple pathogenic mechanisms for severe disease in the elderly population, including low levels of angiotensin-converting enzyme 2 (ACE2) in the elderly [30], age-related difficulty in clearing particulate matter from small airways [31], excessive release of inflammatory mediators in the elderly ("inflammaging") [32]. This finding is similar to recent retrospective studies from Egypt [33], Iran [27] and Pakistan [34] and Kinshasa [35–38]. This is also consistent with other reports from outside the Eurogio Meuse-Rhine (EMR) countries [39, 40].

Our study also revealed that the risk of death for patients with a history of at least one comorbidity (the most common being hypertension and diabetes) is more than double. Indeed, the high expression of ACE2 receptors in highly differentiated airway epithelial cells underlies susceptibility to SARS-CoV-2. When hypertensive patients are infected with the SARS-CoV2, blood pressure regulation becomes more complicated and difficult to control, and the cardiovascular risk is amplified [27, 41]. Diabetic patients are more likely to have severe Covid-19 complications because their high blood glucose levels promote viral growth and impair their immune function and ability to resist infection, setting the stage for secondary bacterial and viral co-infections. In addition, if diabetes complications occur, the risk of multiorgan failure and death is significantly increased. One study reported that mortality and multiorgan injury were significantly higher in Covid-19 patients with type-2 diabetes than in patients without diabetes (HR, 1.5). Such an association has been demonstrated by numerous studies worldwide, reminding us of the need to control chronic non-communicable diseases and pay special attention to people with comorbidities during epidemics [23, 26, 27, 41–50].

Regarding SpO2 at admission, our study demonstrated the risk of death for patients admitted with SpO2 < 90%, which is more than 13 times compared to patients with normal saturation (≥95%). Low ambient air SpO2 is strongly associated with poor outcomes on admission to the hospital and, therefore, is part of the classification of disease severity [47, 51]. Indeed,

Table 4. Predictors of mortality of Covid-19 inpatients in the city of Butembo from January 1 to December 31, 2021.

Variables	(n)	Death	patient-day	Death incidence /1000 patient-day	aHR	95% CI	p-value
Delay between symptom onset and hospital admission							
≤ 5 days	188	37	1507	24,6	1		
> 5 days	115	45	1001	45,0	1.70	1.04–2.79	0.035
Age (years)							
< 60	172	26	1465	17,7	1		
≥ 60	131	56	1042	53,7	9.9	2.68–36.27	0.001
Gender							
Female	164	41	1320	31,1	1		
Male	139	41	1188	34,5	1.39	0.86–2.24	0.182
Treatment site							
FEPSI	19	3	212	14,2	1		
KITATUMBA	42	12	326	36,8	1.62	0.34–5.04	0.400
CUG	52	13	648	20,1	0.27	0.05–0.79	0.022
KATWA	75	18	574	31,4	0.69	0.16–2.15	0.425
MATANDA	60	29	422	68,7	1.31	0.30–3.64	0.950
NGOTE	55	7	326	21,5	0.61	0.12–2.18	0.367
History of at least one co-morbidity							
No	164	20	1361	14,7	1		
Yes	139	62	1147	54,1	11.39	3.19–40.71	< 0.001
Stage according to SpO2							
Mild	61	2	487	4,1	1		
Moderate	94	10	738	13,6	3.56	0.71–17.82	0.122
Severe	148	70	1283	54,6	14.02	2.23–88.32	0.005
m-NEWS							
< 5	119	9	1088	8,3	1		
≥ 5	184	73	1420	51,4	0.72	0.22–2.27	0.571
Age(≥ 60)#History of at least one co-morbidity					0,15	0.04–0.61	0.008
Total	303	82	2508	32,7			

CUG: Cliniques Universitaires du Graben (Graben University Clinics)

https://doi.org/10.1371/journal.pgph.0002020.t004

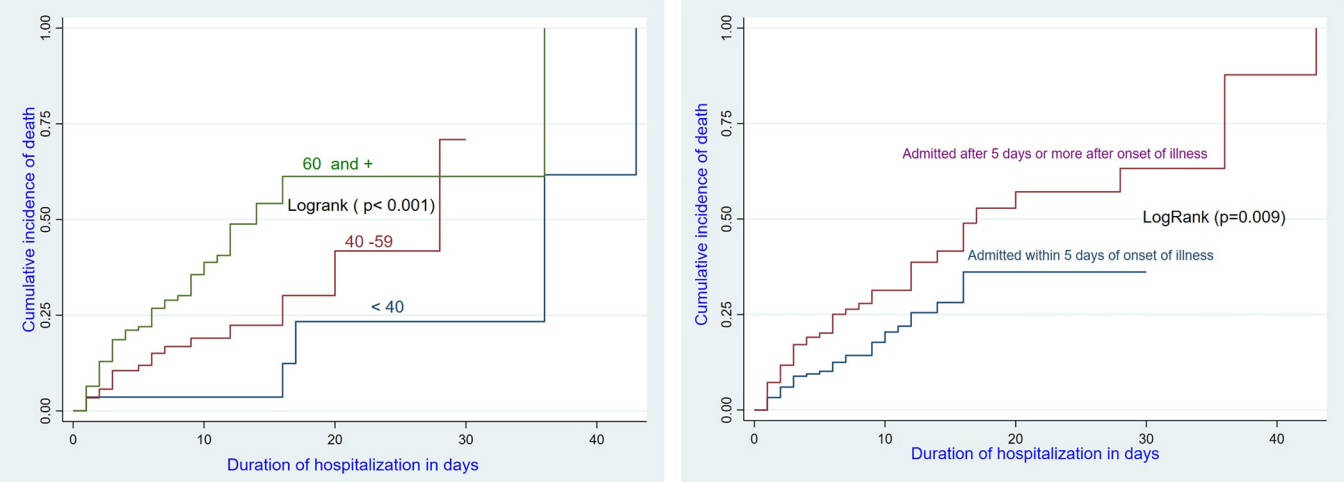

Fig 1. Survival of hospitalized COVID-19 patients by age and time from disease onset to admission.

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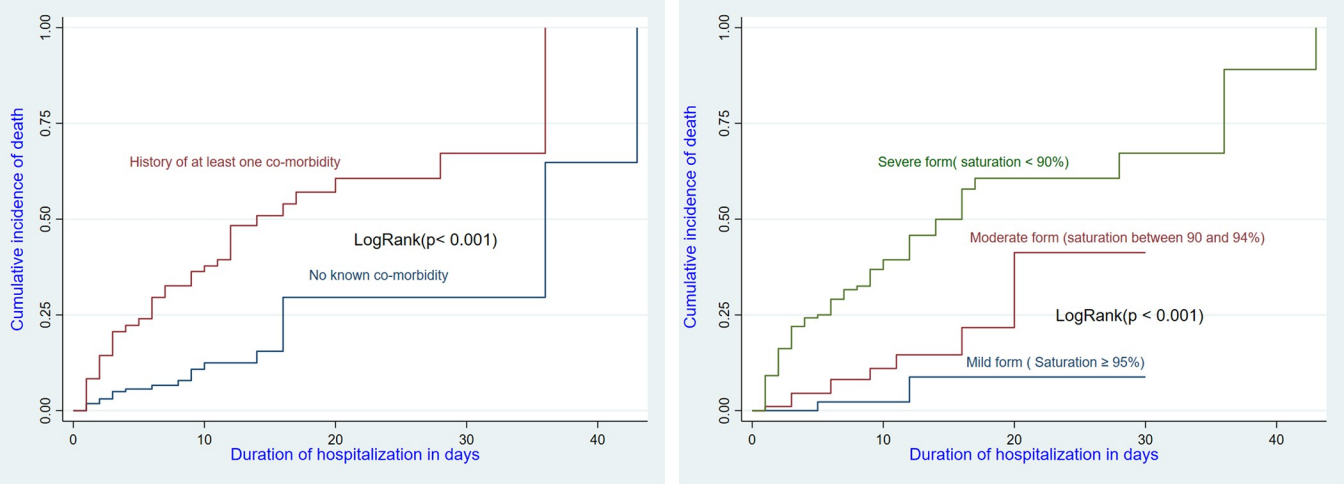

Fig 2. Survival of hospitalized COVID-19 patients by presence of comorbidity and disease stage (based on saturation) at admission.

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the degree of ambient air O2 saturation reflects the level of the respiratory system function [38]. Such observation has been made by other authors and reiterates the need to take into account SpO2 levels in the prioritization of patients for admission to intensive care units [35, 38, 39, 44]. The wide confidence interval for SpO2 is due to the small number of events in the reference group, we have only 2 cases of death in mild severe patients.

In our study, delay in consulting was significantly and independently associated with mortality, with a risk of more than doubling. Indeed, in all infectious diseases, the duration of symptoms before hospitalization has an impact on the outcome. In fact, delayed onset of supportive care affects clinical outcomes by enabling immuno-inflammatory and thrombotic responses [44]. This result mirrors the findings of other studies, such as that of Wen-Hua Liang et al. in China [52].

On the other hand, our study did not establish a significant association between gender and death as in the study of Cummings MJ et al. [44]. Similarly, Nasiri et al. showed that there was no significant difference between men and women in terms of admissions to intensive care units [53]. Another Egyptian study of 260 patients with COVID-19 showed no significant association between male gender and risk of severe disease [54]. In Italy, Ciceri et al. reported no significant association between the female gender and the risk of severe disease [55]. Other reports from the Eurogio Meuse-Rhine countries demonstrated similar findings [27, 33, 37]. Although recent surveillance has shown that male patients were more likely to acquire severe infection and die with COVID-19 [56], This sex-specific difference was observed in previous SARS outbreaks [57].

The interpretation of the results of the present study should consider some of its limitations. First, although we tried to be as complete as possible, the retrospective nature of this study limited the availability of data due to issues of archiving records, quality of the data found in the patient records, and possible errors in assessing patient parameters at admission. Second, record incompleteness, and the limited capacity in diagnosing other comorbidities could have biased the outcome as we could not input more predictors that could have explained mortality. The fact that we did not have the opportunity to analyze the impact of COVID vaccination in our study is another limitation. Regarding COVID-19 vaccines, the roll-out started on April 19th, 2021. However, the uptake was slow initially, by the time of data collection, only about 7% of the target population (entire population >18) had received at least one dose in the entire

country. This low coverage may affect case fatality. This may have also substantial impact on study results as not all cases may have ended up to the hospital thereby creating reporting bias of the outcome.

Finally, because the date of symptom onset is based on self-report, a bias related to the patient's recollection may have misclassified patients at admission. However, to reduce the risk of error, we linked the different sources of data (patient and investigation forms, registers, and databases). We ensured the streamlining of clinical assessment and equipment used to collect patient parameters upon admission in each CTC.

Despite these limitations, this study has nevertheless the merit of having shown a new factor in the arsenal of predictors of survival of patients hospitalized for COVID-19 in the city of Butembo from January to December 2021. These results can also be used to prioritize actions according to the characteristics of the population and the triage of patients upon admission to the health facilities in the city of Butembo and in similar resource-limited contexts.

V. Conclusions

Advanced age, history of comorbidity, low level of ambient air SpO2 at admission and long duration of the disease before hospitalization were predictors of survival of patients hospitalized for COVID-19 in Butembo. Therefore, the following actions are recommended: (a) health policymakers and authorities must strengthen barrier measures and make them mandatory to protect the elderly and those with a history of comorbidity; (b) health authorities, along with technical and financial partners, should incentivize symptomatic patients to seek care at dedicated health structures as early as possible; and (c) health care providers should measure ambient air SpO2 as part of criteria for admission to intensive care units.

Supporting information

S1 Table. Test of proportional hazards assumption.
(DOCX)

S1 Fig. Test of proportional hazards assumption by predictor.
(ZIP)

S2 Fig. Goodness of fit of the final model.
(TIF)

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References

1. World Health Organization (2020) Rolling Updates on Coronavirus Disease (COVID-19). http://www.who.int/emergencies/diseases/novel-coronavirus-2019/events-as-they-happen (accessed on 28/09/2021).
2. Mahalmani VM, Mahendru D, Semwal A, Kaur S, Kaur H, Sarma P, et al. COVID-19 pandemic: A review based on current evidence. Indian J Pharmacol. 2020 Mar-Apr; 52(2):117–129. doi: doi: 10.4103/ijp.IJP_310_20. Epub 2020 Jun 3. PMID: 32565599; PMCID: PMC7282680.
3. WHO. Tableau de bord de l'OMS sur le coronavirus, www.who.int. (accessed on 28/09/2021)
4. Directives de l'OMS pour la surveillance du COVID-19 et définition des cas: https://www.who.int/publications/i/item/who-2019-nCoV-surveillanceguidance-2020.7 (accessed on 20/10/2021)
5. Africa CDC_COVID-19: « Bulletin d'information n° 88: sur la pandémie de la maladie à Coronavirus (Covid-19) » sur CACM, 21 septembre 2021 (consulté le 24 septembre 2021), p.1
6. OMS, Bulletin hebdomadaire sur les épidémies et autres urgences 2020 disponible sur https://apps.who.int/iris/bitstream/handle/10665/331892/OEW17-20226042020.pdf /
7. Ihekweazu C., Agogo E. Africa's response to COVID-19. BMC Med 18, 151 (2020). https://doi.org/10.1186/s12916-020-01622-w PMID: 32438912
8. RDC CMR COVID-19, SECRETARIAT TECHNIQUE: Covid-19/ Bulletin n°636 dimanche, le 19 Décembre 2021: Situation épidémologique Covid-19.
9. RDC-Ministère de la santé. Situation épidémiologique du Nord-Kivu au 29/09/2021. Rapport épidemiologique
10. CDC. Symptoms of Coronavirus. https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html (consulted January 15, 2022)
11. Hui DS I Azhar E, Madani TA, Ntoumi F, Kock R, Dar O, et al. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health—The latest 2019 novel coronavirus outbreak in Wuhan, China. Int J Infect Dis. 2020 Feb; 91:264–266. https://doi.org/10.1016/j.ijid.2020.01.009 PMID: 31953166
12. CDC Africa. Impact en Afrique de la pandémie de Covid-19, https://africacdc.org/consulted 07/09/2021
13. European Centre for Disease Prevention and Control. Situation update worldwide, as of 6 March 2020 08:00. 2020.
14. Yang J, Zheng Y, Gou X, Pu K, Chen Z, Guo Q, et al. Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis. Int J Infect Dis. 2020 May; 94:91–95. https://doi.org/10.1016/j.ijid.2020.03.017 PMID: 32173574
15. RDC-Ministère de la santé. Impacts sanitaires et socioéconomiques de la covid– 19 en rdc. Analyse prospective et orientation de la riposte multisectorielle, Kinshasa, Mai 2020.
16. Cr P, Vanidassane I, Pownraj D, Kandasamy R, Basheer A. National Early Warning Score 2 (NEWS2) to predict poor outcome in hospitalised COVID-19 patients in India. PLoS One. 2021 Dec 15; 16(12): e0261376. https://doi.org/10.1371/journal.pone.0261376 PMID: 34910789
17. Jaspard M, Saliou Sow M, Juchet S, Dienderé E, Serra B, Kojan R, et coll. Présentation clinique, survie et facteurs associés à la mortalité: une étude prospective dans trois centres COVID-19 en Afrique de l'Ouest. Infect Dis Now. 2021 Aug; 51(5): S59. French.
18. Gottlieb M, Sansom S, Frankenberger C, Ward E, Hota B. Clinical Course and Factors Associated with Hospitalization and Critical Illness Among COVID-19 Patients in Chicago, Illinois. Acad Emerg Med. 2020 Oct; 27(10):963–973. https://doi.org/10.1111/acem.14104 PMID: 32762106
19. Ho FK, Petermann-Rocha F, Gray SR, Jani BD, Katikireddi SV, Niedzwiedz CL, et al. Is older age associated with COVID-19 mortality in the absence of other risk factors? General population cohort study of

470,034 participants. PLoS One. 2020 Nov 5; 15(11): e0241824. https://doi.org/10.1371/journal.pone.0241824 PMID: 33152008

20. Ioannou GN, Locke E, Green P, Berry K, O'Hare AM, Shah JA, et al. Risk Factors for Hospitalization, Mechanical Ventilation, or Death Among 10 131 US Veterans With SARS-CoV-2 Infection. JAMA Netw Open. 2020 Sep 1; 3(9):e2022310.

21. Williamson EJ, Walker AJ, Bhaskaran K, Bacon S, Bates C, Morton CE, et al. OpenSAFELY: factors associated with COVID-19 death in 17 million patients. Nature 2020; 584:430–6. http://dx.doi.org/10.1038/s41586-020-2521-4

22. Killerby ME, Link-Gelles R, Haight SC, Schrodt CA, England L, Gomes DJ, et al. Characteristics associated with hospitalization among patients with COVID-19—metropolitan Atlanta, Georgia, march-april 2020. MMWR Morb Mortal Wkly Rep 2020; 69(25):790–4. http://dx.doi.org/10.15585/mmwr.mm6925e1 https://doi.org/10.15585/mmwr.mm6925e1 PMID: 32584797

23. Kim L, Garg S, O'Halloran A, Whitaker M, Pham H, Anderson EJ, et al. Risk factors for intensive care unit admission and in-hospital mortality among hospitalized adults identified through the U.S. coronavirus disease 2019 (COVID-19)-associated hospitalization surveillance network (COVID-NET). Clin Infect Dis 2020: ciaa1012.

24. Ko JY, Danielson ML, Town M, Derado G, Greenlund KJ, Daily Kirley P, et al. Risk factors for COVID-19-associated hospitalization: COVID-19-associated hospitalization surveillance network and behavioral risk factor surveillance system. Clin Infect Dis 2020: ciaa1419.

25. Lassale C, Gaye B, Hamer M, Gale CR, Batty GD. Ethnic disparities in hospitalisation for COVID-19 in England: the role of socioeconomic factors, mental health, and inflammatory and pro-inflammatory factors in a community-based cohort study. Brain Behav Immun 2020; 88:44–9. https://doi.org/10.1016/j.bbi.2020.05.074 PMID: 32497776

26. Hu Xingsheng, Hu Chunhong, Yang Yong, Chen Juan, Zhong Ping, Wen Yajing et al. Clinical characteristics and risk factors for severity of COVID-19 outside Wuhan: a double-center retrospective cohort study of 213 cases in Hunan, China https://doi.org/10.1177/1753466620963035 PMID: 33138694

27. Jalili M, Payandemehr P, Saghaei A, Sari HN, Safikhani H, Kolivand P. Characteristics and Mortality of Hospitalized Patients With COVID-19 in Iran: A National Retrospective Cohort Study. Ann Intern Med. 2020 cited 4 Aug 2020. https://doi.org/10.7326/M20-2911 PMID: 32687717

28. Perrotta F, Corbi G, Mazzeo G, Boccia M, Aronne L, D'Agnano V, et al. COVID-19 and the elderly: insights into pathogenesis and clinical decision-making. Aging Clinical and Experimental Research. Springer; 2020. p. 1.

29. Bi Q, Wu Y, Mei S, Ye C, Zou X, Zhang Z, et al. Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study. Lancet Infect Dis. 2020 Aug; 20(8):911–919. https://doi.org/10.1016/S1473-3099(20)30287-5 PMID: 32353347

30. Alghatrif M, Cingolani O, Lakatta EG. The Dilemma of Coronavirus Disease 2019, Aging, and Cardiovascular Disease: Insights from Cardiovascular Aging Science. JAMA Cardiology. 2020. https://doi.org/10.1001/jamacardio.2020.1329 PMID: 32242886. View Article/PubMed/NCBI/Google Scholar

31. Svartengren M, Falk R, Philipson K. Long-term clearance from small airways decreases with age. Eur Respir J. 2005; 26: 609–615. https://doi.org/10.1183/09031936.05.00002105 PMID: 16204590. View Article/PubMed/NCBI/Google Scholar

32. Aw D, Silva AB, Palmer DB. Immunosenescence: Emerging challenges for an ageing population Immunology. Wiley-Blackwell; 2007. pp. 435–446.

33. Ghweil AA, Hassan MH, Mohamed AK, Mohamed AO, Mohammed HM, Abdelazez AA, et al. Characteristics, Outcomes and Indicators of Severity for COVID-19 Among Sample of ESNA Quarantine Hospital's Patients, Egypt: A Retrospective Study. Infect Drug Resist. 2020;Volume 13: 2375–2383. https://doi.org/10.2147/IDR.S263489 PMID: 32765012

34. Chaudhry A, Ikram A, Baig MA, Salman M, Ghafoor T, Hussain Z, et al. Mortality Analysis of COVID-19 Confirmed cases in Pakistan. MedRxiv. 2020; 2020.06.07. https://doi.org/10.1111/j.1600-0722.2009.00693.x

35. Bepouka BI, Mandina M, Makulo JR, Longokolo M, Odio O, Mayasi N, et al. Predictors of mortality in COVID-19 patients at Kinshasa University Hospital, Democratic Republic of the Congo, from March to June 2020. Pan Afr Med J. 2020 Oct 1; 37:105. https://doi.org/10.11604/pamj.2020.37.105.25279 PMID: 33425138

36. Nachega JB, Ishoso DK, Otokoye JO, Hermans MP, Machekano RN, Sam-Agudu NA, et al. Clinical Characteristics and Outcomes of Patients Hospitalized for COVID-19 in Africa: Early Insights from the Democratic Republic of the Congo. Am J Trop Med Hyg. 2020 Dec; 103(6):2419–2428. https://doi.org/10.4269/ajtmh.20-1240 PMID: 33009770

37. Nlandu Y, Mafuta D, Sakaji J, Brecknell M, Engole Y, Abatha J, et al. Predictors of mortality in COVID-19 patients at Kinshasa Medical Center and a survival analysis: a retrospective cohort study. BMC Infect Dis. 2021 Dec 20; 21(1):1272. https://doi.org/10.1186/s12879-021-06984-x PMID: 34930174

38. Matangila JR, Nyembu RK, Telo GM, Ngoy CD, Sakobo TM, Massolo JM, et al. Clinical characteristics of COVID-19 patients hospitalized at Clinique Ngaliema, a public hospital in Kinshasa, in the Democratic Republic of Congo: A retrospective cohort study. PLoS One. 2020 Dec 18; 15(12):e0244272. https://doi.org/10.1371/journal.pone.0244272 PMID: 33338063

39. Petrilli CM, Jones SA, Yang J, Rajagopalan H, O'Donnell L, Chernyak Y, et al. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: Prospective cohort study. BMJ. 2020;369. https://doi.org/10.1136/bmj.m1966 PMID: 32444366

40. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020; 395: 1054–1062. https://doi.org/10.1016/S0140-6736(20)30566-3 PMID: 32171076.

41. Reilev M, Kristensen KB, Pottegård A, Lund LC, Hallas J, Ernst MT, et al. Characteristics and predictors of hospitalization and death in the first 11 122 cases with a positive RT-PCR test for SARS-CoV-2 in Denmark: a nationwide cohort. Int J Epidemiol 2020; 49(5):1468–81.

42. Wang F, Cao J, Yu Y, Ding J, Eshak ES, Liu K, et al. Epidemiological characteristics of patients with severe COVID-19 infection in Wuhan, China: evidence from a retrospective observational study. Int J Epidemiol 2021; 49(6):1940–50. https://doi.org/10.1093/ije/dyaa180 PMID: 33150437

43. Soares RCM, Mattos LR, Raposo LM. Risk Factors for Hospitalization and Mortality due to COVID-19 in Espírito Santo State, Brazil. Am J Trop Med Hyg. 2020 Sep; 103(3):1184–1190.

44. Cummings MJ, Baldwin MR, Abrams D, Jacobson SD, Meyer BJ, Balough EM, et al. Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study. Lancet 2020; 395(10239):1763–70 https://doi.org/10.1016/S0140-6736(20)31189-2 PMID: 32442528

45. McKeigue PM, Weir A, Bishop J, McGurnaghan SJ, Kennedy S, McAllister D, et al. Rapid Epidemiological Analysis of Comorbidities and Treatments as risk factors for COVID-19 in Scotland (REACT-SCOT): a population-based case-control study. PLoS Med 2020; 17(10):e1003374. https://doi.org/10.1371/journal.pmed.1003374 PMID: 33079969

46. Fumagalli C, Rozzini R, Vannini M, Coccia F, Cesaroni G, Mazzeo F, et al. Clinical risk score to predict in-hospital mortality in COVID-19 patients: a retrospective cohort study. BMJ Open 2020; 10(9): e040729. https://doi.org/10.1136/bmjopen-2020-040729 PMID: 32978207

47. Becerra-Muñoz VM, Núñez-Gil IJ, Eid CM, Aguado MG, Romero R, Huang J, et al. Clinical profile and predictors of in-hospital mortality among older patients admitted for COVID-19. Age Ageing 2020: afaa258.

48. Hernández-Galdamez DR, González-Block MÁ, Romo-Dueñas DK, Lima-Morales R, Hernández-Vicente IA, Lumbreras-Guzmán M, et al. Increased risk of hospitalization and death in patients with COVID-19 and pre-existing noncommunicable diseases and modifiable risk factors in Mexico. Arch Med Res 2020; 51(7):683–9.

49. Santos MM, Lucena EE, Lima KC, Brito AA, Bay MB, Bonfada D. Survival and predictors of deaths of patients hospitalized due to COVID-19 from a retrospective and multicenter cohort study in Brazil. Epidemiol Infect 2020; 148: e198.

50. Abdene Weya Kaso Gebi Agero, Hurissa Zewdu, Kaso Taha, Helène Ali Ewune Habtamu Endashaw Hareru, et al. Survival analysis of COVID-19 partients in Ethiopia: A hospital-based study, Mai 2022.

51. Omran D, Al Soda M, Bahbah E, Esmat G, Shousha H, Elgebaly A, et al. Predictors of severity and development of critical illness of Egyptian COVID-19 patients: A multicenter study. PLoS One. 2021 Sep 23; 16(9):e0256203. https://doi.org/10.1371/journal.pone.0256203 PMID: 34555027

52. Liang WH, Guan WJ, Li CC, Li YM, Liang HR, Zhao Y, et al. Clinical characteristics and outcomes of hospitalised patients with COVID-19 treated in Hubei (epicentre) and outside Hubei (non-epicentre): a nationwide analysis of China. Eur Respir J. 2020 Jun 4; 55(6): 2000562. https://doi.org/10.1183/13993003.00562-2020 PMID: 32269086

53. Nasiri MJ, Haddadi S, Tahvildari A, Farsi Y, Arbabi M, Hasanzadeh S, et al. COVID-19 Clinical Characteristics, and Sex-Specific Risk of Mortality: Systematic Review and Meta-Analysis. Frontiers in Medicine. 2020. https://doi.org/10.3389/fmed.2020.00459 PMID: 32793620.

54. Ramadan HK- A, Mahmoud MA, Aburahma MZ, Elkhawaga AA, El-Mokhtar MA, Sayed IM, et al. Predictors of Severity and Co-Infection Resistance Profile in COVID-19 Patients: First Report from Upper Egypt. Infect Drug Resist. 2020; Volume 13: 3409–3422. https://doi.org/10.2147/IDR.S272605 PMID: 33116660

55. Ciceri F, Castagna A, Rovere-Querini P, De Cobelli F, Ruggeri A, Galli L, et al. Early predictors of clinical outcomes of COVID-19 outbreak in Milan, Italy. Clin Immunol. 2020; 217: 108509. https://doi.org/10.1016/j.clim.2020.108509 PMID: 32535188.

56. Aly MH, Rahman SS, Ahmed WA, Alghamedi MH, Al Shehri AA, Alkalkami AM, et al. Indicators of Critical Illness and Predictors of Mortality in COVID-19 Patients. Infect Drug Resist. 2020; Volume 13: 1995–2000. https://doi.org/10.2147/IDR.S261159 PMID: 32617010. View Article, PubMed/NCBI,Google Scholar

57. Karlberg J, Chong DSY, Lai WYY. Do Men Have a Higher Case Fatality Rate of Severe Acute Respiratory Syndrome than Women Do? Am J Epidemiol. 2004; 159: 229–231. https://doi.org/10.1093/aje/kwh056 PMID: 14742282