

Research



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Risk factors associated with COVID-19 morbidity and mortality at a national tertiary referral treatment centre in Ghana: a retrospective analysis

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Abstract

Introduction: *there is a substantial variation in COVID-19 case fatality rates across different locations, which may be due to differences in population age structure, patient factors, or health system factors. The study evaluated the clinical features and risk of COVID-19 morbidity and mortality among confirmed cases at COVID-19 referral treatment centre. **Methods:** the study was a retrospective analysis of routine data of cases admitted and treated between March 2020 to March 2021 at Greater Accra Regional Hospital (Ridge Hospital). The data were analysed using descriptive statistics, simple and multiple logistic regression. **Results:** the overall mortality rate among this cohort of patients was 34.4%. Compared to survivors, non-survivors were older patients, non-insured, had a higher frequency of hypertension, diabetes, heart disease, and were more prone to suffer from a severe form of COVID-19 infection. Compared to survivors, non-survivors showed elevated levels of white blood cell count, platelets, higher heartbeat per minute and lower levels of haemoglobin, creatinine, and oxygen saturation. The independent risk factors for COVID-*

*19 mortality in the national treatment centre were shorter stay of hospitalizations, having a heart disease, difficulty in breathing, increased in concentration of platelets, and creatinine. A 1% increase in oxygen saturation decreased a patient's likelihood of dying from COVID-19 by 29.0%. **Conclusion:** this study showed COVID-19 mortality was associated with a shorter stay in hospital, having heart disease, dyspnoea, elevated levels of platelets and creatinine, and decreased oxygen saturation. There is a need for awareness creation about these risk factors to clinicians and public health officials.*

Introduction

The clinical features of Coronavirus disease 2019 (COVID-19) range from asymptomatic to severe pneumonia and death [1-4] with an average incubation period of 5-6 days [1]. Common clinical symptoms of COVID-19 are fever, dry cough and shortness of breath [4,5]. In the Ghanaian context, fever, cough, difficulty in breathing, headache and sore throat are clinical characteristics among COVID-19 patients [4,6-8]. COVID-19 is more severe in old age patients, males and in people with comorbidities such as hypertension, diabetes and obesity [9,10]. Evidence suggests that sepsis, acute respiratory distress syndrome, and heart failure are COVID-19 complications requiring admission to the Intensive Care Unit (ICU) [5]. Evidence from 61 studies shows that the overall case fatality rates of COVID-19 range from 0.00% to 1.63% [11]. This indicates a substantial case fatality rate variation across different locations, which may be due to differences in population age structure, patient characteristics, viral characteristics and health systems factors [11]. Therefore, identifying the risk factors responsible for COVID-19 mortalities in the Ghanaian context is urgently required. This is crucial for policymakers and healthcare workers for effective surveillance, case management, risk communication, laboratory response and infection prevention and control. Preliminary studies indicate that old age, male, low hemoglobin, high lactate dehydrogenase

(LDH), hypertension, cardiovascular diseases, diabetes and a wide range of sociodemographic factors are associated with COVID-19 mortality [12-15]. Most of these studies were designed and conducted in developed countries with limited evidence about risk factors for COVID-19 mortality in the Ghanaian context [16]. Furthermore, several COVID-19 studies conducted in Ghana have largely focused on the clinical characteristics, treatment and duration of hospitalization of COVID-19 patients [4,7,8,16]. Therefore, this study aims to identify the risk factors for COVID-19 morbidity and mortality among a cohort of patients admitted at Greater Accra Regional Hospital of Ghana.

Methods

Study design and settings: the study was a retrospective review of records of confirmed COVID-19 patients admitted and treated at Greater Accra Regional Hospital. The Greater Accra Regional Hospital is a 420-bed capacity referral hospital and additionally serves as a national COVID-19 treatment and referral center for Ghana's COVID response. The record review included confirmed COVID-19 patients who were either discharged alive or dead. A confirmed case of COVID-19 had a patient with laboratory confirmation of SARS-COV-2 as was detected in respiratory specimens by a polymerase chain reaction assay. In all, medical records of 244 cases of COVID-19 admitted at the ridge hospital between March 2020 to March 2021 were reviewed in the study including Ghana's first two confirmed cases of COVID-19.

Data collection and sources: the data were collected using a data extraction tool designed by the research team and used to extract data physically from the medical records to obtain sociodemographic information, the severity of COVID-19 infection, length of stay, clinical characteristics, comorbidities (diabetes, heart disease, hypertension, asthma), smoking, alcohol, treatment received, vital signs and laboratory

investigations. The data was then reviewed for completeness, accuracy, and quality. Medical records with incomplete data (11) were excluded from the study.

Study variables: the explanatory variables for the study include sociodemographic characteristics (age, gender, occupation, marital status and National Health Insurance status), length of hospital stay, comorbidities (diabetes mellitus, heart disease, hypertension and asthma), clinical characteristics (fever, diarrhea, dry cough, vomiting, breathlessness, loss of smell, loss of taste, headache, chest pain and sore throat), treatment received (Hydroxychloroquine, Chloroquine phosphate, Azithromycin, Doxycycline, Methylprednisolone, Vitamin C, Zinc), vital signs (temperature, heart rate, oxygen saturation, systolic blood pressure, diastolic blood pressure), laboratory investigations [white blood cell (WBC), lymphocytes, neutrophils, platelets, haemoglobin, Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), Albumin, Globulin, Blood urea nitrogen (BUN) and creatinine] and severity of COVID-19 infection (mild, moderate, severe and critical). A mild COVID-19 infection refers to asymptomatic or symptomatic patients with uncomplicated upper respiratory tract viral infection, and non-specific symptoms such as fever, cough, sore throat, diarrhoea, etc. Moderate COVID-19 infection refers to adult patients with pneumonia but not in respiratory distress and with oxygen saturation on admission (SpO_2) $>93\%$ on room air. Severe COVID-19 infection relates to patients with fever or suspected respiratory infection, plus either respiratory rate >30 breaths/min or severe respiratory distress, or $SpO_2 \leq 93\%$ on room air. Critical illness refers to life-threatening organ dysfunction caused by a dysregulated host response to suspected or proven infection. They may have acute respiratory distress syndrome, sepsis, septic shock that may represent virus-induced distributive shock, cardiac dysfunction, an exaggerated inflammatory response, and others. The outcome variable for

the study was the patient's discharge status (survival and non-survival).

Statistical analysis: data were analysed using STATA 16.0. The data were summarized using mean/standard deviation or median (Interquartile range, IQR) for continuous variables and number (percentage) for continuous variables. We explored risk factors for COVID-19 mortality using simple and multiple logistic regression. Variables that showed significant differences after the univariate analysis were qualified for multivariate analysis. Results was considered significant at a p-value less than 0.05. To determine the factors associated with death from COVID-19 among patients, a univariate logistic regression model was fitted to select significant variables into a final multivariate logistic regression model.

Ethical clearance: ethical clearance was sought from the Ghana Health Service Ethics Review Committee (GHS-ERC: 013/10/21). The authors also sought permission from the management of Ridge Hospital and records department to retrieve records.

Results

Comparison of sociodemographic characteristics, clinical symptoms and treatment regimen of survivors and non-survivors: a total of 244 patients treated for COVID-19 in the Greater Accra Regional Hospital (Ridge Hospital) in Ghana were included in the final analysis. The overall mortality rate among this cohort of patients was 34.4%, while the survival rate was 65.6%. We found that the mortality rate was significantly higher among patients aged 60 years and above ($p=0.007$). Male patients form the majority (57.0%) in this cohort of COVID-19 patients, and mortality was common among males (62%) compared to females (38%). The mean age (SD) of the patients was 55.98 ± 8 (17.5), and non-survivors were significantly older than survivors (62.1 ± 16.2 vs 52.8 ± 17.4 years; $P < 0.001$) (Table 1). The majority (76.2%) of non-survivors reported a severe form of the COVID-19 infection compared to survivors (18.8%). Non-

survivors had a shorter duration of hospitalization, median (IQR) of 3 (2-6) days compared to survivors 9 (5-16) days. Spending lesser days in hospital was associated with death from COVID-19 infection ($p < 0.001$) (Table 1). Comorbidities were common among non-survivors. For instance, hypertension (35.7%), diabetes (53.6%), and heart disease (39.3%) were significantly higher in non-survivors compared to survivors, hypertension (8.8%), diabetes (26.3%) and heart disease (11.3%). These commodities (hypertension, heart disease and diabetes) significantly predicted higher COVID-19 mortality. Higher rates of fever (52.4%) and difficulty in breathing (47.6%) were observed among non-survivors compared to survivors. On the contrary, survivors experienced high rates of diarrhea (5%), dry cough (23.8%), loss of taste (8.8%) and headache (13.8). COVID-19 mortality was significantly higher among patients with fever ($P < 0.001$) and difficulty in breathing ($P < 0.001$) (Table 1). The median (IQR) temperature recorded among all patients was 37.0 (36.0 -37.0) degrees celsius, heart rate 96 (80-112) beats per minute, Oxygen saturation 92% (85- 97), systolic blood pressure 133 (116 - 155) mmHg and diastolic blood pressure 81 (70- 92) mmHg. There were significant differences in heart rate among non-survivors and survivors (103 vs 91; $P=0.001$). Lower oxygen saturation was observed among non-survivors compared to survivors (84 vs 94; $P < 0.001$). They were no significant differences in temperature, systolic and diastolic blood pressure among survivors and non-survivors. Increased heart rate beats per minute and lower oxygen saturation were significantly associated with death from COVID-19 among patients (Table 1). Commonly prescribed medications were azithromycin 144 (46.7%), doxycycline 70 (28.7%), vitamin C 161 (66.0%) and zinc tablet 163 (66.8%). Patients who survived received a higher amount of hydroxychloroquine (7.5%), chlorine phosphate (7.5%), azithromycin (45.6%) and doxycycline (31.9%) with no significant differences compared to the non-survivors. Similarly, survivors significantly received more of vitamin C compared

to non-survivors ($P=0.003$). This is also the same for Zinc tablets ($P=0.021$) (Table 1).

Comparison of laboratory findings among survivors and non-survivors: we observed significantly elevated levels of white blood cell amount in non-survivors compared to survivors ($P=0.001$). Platelets levels were markedly higher among non-survivors compared to survivors ($P < 0.001$). On the contrary, we found significantly higher levels of hemoglobin and creatinine among survivors than non-survivors ($P=0.020$; $P < 0.001$, respectively (Table 2). Higher WBC count, platelets, creatinine, and lower hemoglobin levels were significantly associated with COVID-19 mortality (Table 2).

Factors associated with the risk of COVID-19 mortality among COVID-19 patients at Greater Accra Hospital: in the univariate analysis, we found a significant association between age, insurance status, days of hospitalization, diabetes, hypertension, heart disease, fever, difficulty in breathing, heart rate, oxygen saturation, vitamin C, Zinc tablet, WBC count, hemoglobin, platelets, creatinine and risk of dying from COVID-19 infection (Table 1, Table 2). Therefore, we modelled the probability of patients dying from COVID-19 infection and adjusted for the above-stated variables in Table 1, Table 2. The multivariate logistic regression analysis revealed, an additional day of hospitalization decreases the odds of death from COVID-19 by 13% [OR = 0.87 (95% CI: 0.78 – 0.97), $p=0.012$]. COVID-19. The risk of death was 1.3 times likely among patients with heart disease compared to those without heart disease (OR= 1.31 (95% CI: 1.10 - 2.01) (Table 3). Patients with symptoms of difficulty in breathing were 2.3 times likely to die from COVID-19 compared to those who did not experience difficulty in breathing (OR = 2.32 (95% CI: 1.04 - 4.30)). A 1% increase in oxygen saturation decreases a patient's likelihood of dying from COVID-19 by 29.0% (OR = 0.71 (95% CI: 0.62-0.81). A unit increase in platelets and creatinine increases a patient's odds of dying from COVID-19 by 1.02 (OR = 1.02 (95% CI: 1.01-1.03) and 1.07

(OR = 1.07 (95% CI: 1.03-1.12) times, respectively (Table 3).

Discussion

This retrospective data analysis provides insight into the risk factors for COVID-19 mortality at a national treatment center in Ghana. This study revealed mortality rate in this treatment center was higher than reported by previous studies in Ghana [8], China [15] and Kuwait [5]. The discrepancies may be explained by the fact that our study site serves as a referral center for severe and critical cases across the country. Late referral of cases may thus also be contributing to these discrepancies. Compared to survivors, non-survivors were older, had a higher frequency of hypertension, diabetes and were more prone to suffer from a severe form of the COVID-19 infection. These findings are similar to other published studies across the globe [13,15,17,18]. In line with studies in Ghana [4,6,8] and elsewhere [5,9,10], the top clinical symptoms were fever, dry cough, difficulty in breathing and headache. Fever and dyspnoea were higher among non-survivors. In China, fever was higher among survivors, while dyspnoea was higher among non-survivors [15]. Perhaps, dyspnoea may indicate the severe form of COVID-19, which could predict mortality in COVID-19 patients. We observed elevated levels of white blood cell count and platelets among non-survivors in this cohort of patients. Higher levels of WBC have implications on COVID-19 mortality. For instance, a recent study in Wuhan province showed that the elevated levels of WBC is significantly correlated with COVID-19 mortality [19]. Hence, in managing COVID-19 cases, clinicians should pay more attention to COVID-19 patients with elevated levels of WBC count. In variance with our findings, a study in Iran found lower levels of platelets among non-survivors [20].

Some scholars suggest that platelets activation is a potential contributory factor for worsening the conditions of critically ill patients [21] and that it

could be responsible for the long-term mortality of critically ill patients [22]. We found significantly lower levels of hemoglobin among non-survivors. This is in accordance with a previous study where lower Hb concentration predicted mortality among COVID-19 patients [20]. In accordance with similar studies [23,24], a higher rate of heart beats per minute and lower oxygen saturation was found among non-survivors. Oxygen saturation is a predictor of COVID-19 mortality [23-25]. We found that non-survivors died within 3 days of admission to the treatment center. The reason for this finding is unclear, but it may be because the treatment centre is a referral centre for severe and critically ill patients. However, several factors come into play in the duration of hospitalizations [26]. The risk of dying was more likely among COVID-19 patients with heart disease. This agrees with similar studies that found heart conditions as independent risk factors for COVID-19 mortality [27-29]. This indicates that people with underlying diseases such as heart disease should be more concerned about adherence to COVID-19 protocols and that clinicians should aggressively manage COVID-19 patients with heart disease. We found that having difficulty in breathing increased the likelihood of mortality among the COVID-19 patients. Previously published studies confirmed our findings that difficulty in breathing elevates the risk of mortality in COVID-19 patients [30,31]. Our results showed an increase in oxygen saturation decreases the likelihood of mortality in COVID-19 patients in the treatment centre. This has also been described by previously published studies where lower oxygen saturation was a risk factor for COVID-19 mortality [23,32]. Elevated levels of platelets and creatinine were associated with the risk of mortality in this group of COVID-19 patients. Findings from published studies showed an increase in platelets activity is associated with poor prognosis [21,22]. Elevated creatinine levels in COVID-19 patients may be a marker of impaired kidney function. Kidney disease has been figured in increasing COVID-19 mortality [33,34]. COVID-19 patients with elevated levels of creatinine

should be closely monitored during the management of COVID-19.

Limitations of the study: the study is not without limitations. The study did not independently collect the data used in the analysis but relied on routine hospital data. We could not obtain full records of the patient's laboratory markers, which may have impacted our findings. Also, several sociodemographics were missing in the hospital data. This is a single-center study; hence readers should cautiously interpret our findings in relations to other studies and other treatment centers in Ghana. Notwithstanding these limitations, the study provides an insight into risk factors responsible for COVID-19 mortality in Ghana.

Conclusion

Evidence from this study showed that risk factors for COVID-19 deaths include presence of heart disease, dyspnoea, decreased oxygen saturation on admission, and elevated levels of platelets and creatinine. Our analysis also showed non-survivors were older patients, non-insured, had a higher frequency of comorbidities, and were more prone to suffer from a severe form of the COVID-19 infection. Laboratory analysis revealed detection of elevated levels of white blood cell count, platelets, and lower levels of hemoglobin, creatinine, and oxygen saturation in non-survivors. There is a need for awareness creation about these risk factors to all concerned stakeholders. This is particularly important in assisting clinicians and public health officials in identifying COVID-19 patients with poor prognoses for prioritization.

What is known about this topic

- *There is a substantial variation in COVID-19 case fatality rates across different locations, which may be due to differences in population age structure, patient factors, characteristics of the virus or health system factors;*

- *There is limited evidence about COVID-19 morbidity and mortality risk factors in Ghana.*

What this study adds

- *This study showed COVID-19 mortality was associated with a shorter stay in hospital, having heart disease, dyspnoea, elevated levels of platelets and creatinine, and decreased oxygen saturation;*
- *There is a need for awareness creation about these risk factors to all concerned stakeholders;*
- *This is particularly important in assisting clinicians and public health officials in identifying COVID-19 patients with poor prognoses for prioritisation.*

Competing interests

Authors declare they have no competing interests.

Authors' contributions

All authors contributed equally to this research. All the authors have read and agreed to the final manuscript.

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Tables

Table 1: univariate logistic regression analysis of clinical characteristics and determinants of mortality among COVID-19 patients

Table 2: univariate logistic regression analysis of laboratory findings and determinants of mortality among COVID-19 patients

Table 3: multivariate logistic Regression analysis of determinants of mortality among COVID-19 patients

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Table 1: univariate logistic regression analysis of clinical characteristics and determinants of mortality among COVID-19 patients

Variables	Total (n=244)	Non-survivors (n=84)	Survivors (n = 160)	OR	95% CI	p-value
Age, years median (IQR)	59 (42-68)	65 (55 – 72)	57 (36 – 66)	1.03	1.03 – 1.05	< 0.001
Gender, n (%)						
Male	139 (57.0)	52 (61.9)	87 (54.4)	Reference		
Female	105 (43.0)	32 (38.1)	73 (45.6)	0.73	0.43 – 1.26	0.260
NHIS status, n (%)						
Non- insured	166 (68.0)	65 (77.4)	101 (63.1)	Reference		
Insured	78 (32.0)	19 (22.6)	59 (36.9)	0.50	0.27 – 0.92	0.025
Severity of illness, n (%)						
Mild	150 (61.5)	20 (23.8)	130 (81.3)	Reference		
Severe	94 (38.5)	64 (76.2)	30 (18.8)	13.87	7.31 – 26.30	< 0.001
Days of hospitalization, median (IQR)	6 (3 – 13)	3 (2 – 6)	9 (5 – 16)	0.87	0.82 – 0.91	< 0.001
Comorbidity, n (%)						
Diabetes	44 (18.0)	30 (35.7)	14 (8.8)	5.79	2.86 – 11.75	< 0.001
Hypertension	87 (35.7)	45 (53.6)	42 (26.3)	3.24	1.86 – 5.65	< 0.001
Heart Disease	51 (20.9)	33 (39.3)	18 (11.3)	5.10	2.65 – 9.85	< 0.001
Symptoms, n (%)						
Fever	76 (31.2)	44 (52.4)	32 (20.0)	4.40	2.47 – 7.84	< 0.001
Diarrhoea	10 (4.1)	2 (2.4)	8 (5.0)	0.46	0.10 -2.23	0.338
Dry cough	57 (23.4)	19 (22.6)	38 (23.8)	0.94	0.50 – 1.76	0.843
Difficulty in breathing	69 (28.3)	40 (47.6)	29 (18.1)	4.12	2.28 – 7.39	< 0.001
Loss of smell	6 (2.5)	0 (0.0)	6 (3.8)	-	-	-
Vital Signs, median (IQR)						
Temperature, ° C	37.0 (36.0-37.0)	37.0 (36.0-37.0)	37.0 (36.0-37.0)	0.80	0.59 – 1.09	0.162
Heart rate (bpm)	96 (80 – 112)	103 (83 – 121)	91 (75 – 106)	1.02	1.01 – 1.03	0.001
Oxygen saturation (%)	92 (85 – 97)	84 (62 – 90)	95 (87 – 98)	0.76	0.71 – 0.82	< 0.001
Treatment received, n(%)						
Methylprednisolone	4 (1.6)	0 (0.0)	4 (2.5)	-	-	-
Vitamin C	161 (66.0)	45 (53.6)	116 (72.5)	0.44	0.25 – 0.76	0.003
Zinc tablet	163 (66.8)	48 (57.1)	115 (71.9)	0.52	0.30 – 0.91	0.021

Table2: univariate logistic regression analysis of laboratory findings and determinants of mortality among COVID-19 patients

Variables	Total (n=244)	Died (n=84)	Discharged (n = 160)	OR	95% CI	p-value
White blood cell count x 10 ³ /uL	11.0 (7.9 – 11.7)	11.7 (8.9 – 11.7)	9.7 (7.2 – 11.7)	1.18	1.07 – 1.29	0.001
Neutrophils x 10 ³ /uL	7.1 (5.3 – 8.6)	7.2 (5.4 – 8.6)	7.0 (5.2 – 8.6)	1.01	0.87 – 1.17	0.890
Lymphocytes x 10 ³ /uL	1.7 (1.4 – 2.4)	1.7 (1.4 – 2.4)	1.7 (1.4 – 2.5)	1.05	0.68 – 1.61	0.830
Platelets x 10 ³ /uL	272 (198 – 340)	367 (314 – 400)	232 (179 – 282)	1.02	1.01 – 1.03	< 0.001
Haemoglobin g/dL	11.8 (10.7 – 13.2)	11.2 (9.6 – 12.6)	11.9 (10.8 – 13.8)	0.83	0.71 – 0.97	0.020
Alanine amitransferase, IU/L	31 (21 – 46)	33 (24 – 48)	30 (19 – 44)	1.02	0.98 – 1.05	0.344
Aspartate aminotransferase, IU/L	37 (21 – 46)	39 (20 – 46)	36 (23 – 46)	1.00	0.97 – 1.04	0.780
Albumin, g/L	36 (32 – 39)	36 (32 – 38)	36 (32 – 40)	0.97	0.90 – 1.04	0.342
Globulin, g/l	37 (31 – 40)	35 (27 – 38)	37 (32 – 40)	0.94	0.89 – 1.01	0.072
Creatinine, µmol/L	100 (85 – 124)	124 (110 – 133)	90 (82 – 111)	1.06	1.04 – 1.09	< 0.001

Table 3 : multivariate logistic regression analysis of determinants of mortality among COVID-19 patients

Variables	Odds ratio	95% CI	P-value
Age, years	1.03	0.99 – 1.07	0.171
NHIS status	0.25	0.06 – 1.06	0.060
Days of hospitalization	0.87	0.78 – 0.97	0.012
Diabetes	0.47	0.08 – 2.63	0.387
Hypertension	1.22	0.31 – 4.80	0.776
Heart Disease	1.31	1.10 – 2.01	0.015
Fever	1.03	0.96 – 1.19	0.048
Difficulty in breathing	2.32	1.04 – 4.30	0.002
Heart Rate, cpm	1.02	0.99 – 1.06	0.246
Oxygen saturation	0.71	0.62 – 0.81	< 0.001
Vitamin C tablet	0.07	0.00 – 1.69	0.100
Zinc tablet	2.85	1.14 – 3.97	0.499
White blood cell count x 10 ³ /uL	1.09	0.89 – 1.38	0.442
Platelets x 10 ³ /uL	1.02	1.01 – 1.03	< 0.001
Haemoglobin g/dL	0.82	0.62 – 1.10	0.184
Creatinine, μmol/L	1.07	1.03 – 1.12	0.001