Presenting Symptoms and Predictors of Poor Outcomes Among 2,184 Patients with COVID-19 in Lagos State, Nigeria

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A R T I C L E   I N F O

A B S T R A C T

Introduction: Lagos state remains the epicentre of COVID-19 in Nigeria. We describe the symptoms and signs of the first 2,184 PCR-confirmed COVID-19 patients admitted at COVID-19 treatment centers in Lagos State. We also assessed the relationship between patients' presenting symptoms, sociodemographic and clinical characteristics and COVID-19 deaths.
Methods: Medical records of PCR-confirmed COVID-19 patients were extracted and analyzed for their symptoms, symptom severity, presence of comorbidities and outcome.
Results: The ages of the patients ranged from 4 days to 98 years with a mean of 43.0 (16.0) years. Of the patients who presented with symptoms, cough (19.3%) was the most common presenting symptom. This was followed by fever (13.7%) and difficulty in breathing, (10.9%). The most significant clinical predictor of death was the severity of symptoms and signs at presentation. Difficulty in breathing was the most significant symptom predictor of COVID-19 death (OR:19.26 95% CI 10.95-33.88). The case fatality rate was 4.3%.
Conclusion: Primary care physicians and COVID-19 frontline workers should maintain a high index of suspicion and prioritize the care of patients presenting with these symptoms. Community members should be educated on such predictors and ensure that patients with these symptoms seek care early to reduce the risk of deaths associated with COVID-19.

1. Introduction

Since the discovery of the index case of COVID-19 in Nigeria in February 2020,(*NCDC Coronavirus COVID-19 Microsite*, 2020) the spread of the virus has increased exponentially due to community-based human-to-human transmission.(Odukoya et al., 2020) Lagos state was the first state to record and manage that case and has remained the epicentre of the pandemic, accounting for 36% of the cases and 22% of deaths as at July 26, 2020. (NCDC 2020, Odukoya et al., 2020)

COVID-19 is a novel disease with seemingly variable clinical presentation and progression. In several parts of the world, commonly reported symptoms include fever, dry cough, fatigue,

myalgia, headache, sore throat, abdominal pain and diarrhea. (Kim et al., 2020; Koh et al., 2020; Lapostolle et al., 2020; Lechien et al., 2020) There is limited research on the symptom profile of COVID-19 patients in Nigeria.

The first and only study in Nigeria that reported the symptomatology of COVID-19 in Lagos State found that admitted early cases of COVID-19 had an average age of 38.1 years, were mostly male and had moderately severe symptoms (66%), while only 16% were asymptomatic.[7] The validity of the findings of this study is limited by its small sample size (only 32 patients) and the fact that the data was obtained from a single isolation centre in Lagos state. (Bowale et al., 2020)

COVID-19 is a new and rapidly evolving disease. Understanding the symptoms profile of the infection is important in formulating a practicable approach to rapidly identify cases and assess the course of infection. This will improve treatment outcomes and reduce disease transmission and death rates. Assessing the relationship between symptom severity and COVID-19 outcomes may provide some insights into the understanding of the disease and its risk or protective factors. The objective of this study is to use data from a large cohort of the first 2184 patients with PCR confirmed COVID-19 admitted in nine isolation and treatment centres in Lagos State, to describe the pattern of symptoms and predictors of mortality from COVID-19. It is hoped that these findings will fill some critical gaps in research on COVID-19 in Nigeria and provide locally relevant evidence on COVID-19 among Nigerians. The findings will also inform state and national policy and decision-making to improve health outcomes for the rapidly rising number of COVID-19 patients in Nigeria.

2. METHODS

Study sites: The cases reported in this study were patients admitted at all of the nine treatment centres in Lagos state, Southwest Nigeria, though their places of residence were diverse in the Lagos Metropolis. Treatment centers refer to a place that provides in-patient hospital care specifically for COVID-19 cases.

Study design and population: This was a retrospective study using medical records of 2184 PCR confirmed COVID-19 patients. Laboratory confirmation of COVID-19 was done with naso-oropharyngeal and sputum specimens that tested positive for the SARS-CoV-2 virus using real-time reverse transcription-polymerase-chain-reaction (RT-PCR) assay for SARS-CoV-2 in accordance with the protocol established by the World Health Organisation.(WHO, 2020) Patients were considered negative and discharged after a negative PCR-based SARS-CoV-2 virus test. All patients were treated with Lopinavir-Ritonavir, Vitamin C, Vitamin D and Zinc.

Data extraction and analysis: Data were extracted from electronic medical records of the 2,184 patients as maintained by the case management teams at the hospital or isolation centres. We obtained data on patients age, gender, admitting facility, presenting symptoms, severity of initial presenting symptoms, the presence of co-morbidities and patient's final outcome (i.e. Dead or Discharged).

Patient's severity at presentation was based on clinical parameters and the need for oxygen and assisted ventilation. Mild patients are those who were asymptomatic at presentation; Moderate, if patient presented with fever, cough, respiratory rate <30breaths per minutes and peripheral capillary oxygen saturation (spO2) >90% for adults and >92% for children. A patient with grunting respiration, respiratory rate >30 breaths per minute, spO2 <90% for adults and <92% for children requiring oxygenation was classified as severe while a patient with respiratory failure requiring mechanical ventilation was classified as critical. Our case definition was adapted from a handbook on clinical experience in

China (Yu, 2020) STATA version 16 (StataCorp, USA) was used to conduct the data analysis.

Normally distributed continuous variables were presented as means (SD) while categorical variables were presented in tables as frequencies and percentages. To determine the variables associated with COVID-19 deaths, we first of all conducted a bivariate analysis using the student's T test and the Pearson's chi square tests for continuous or categorical variables respectively. Thereafter, we conducted two multivariable logistic regression models using variables that were significant at p < 0.2. (Hosmer et al., 2013, Lee, 2014)The first model was designed to determine the socio-demographic and clinical predictors of COVID19 death, while the second model was designed to identify the presenting symptoms most predictive of COVID-19 death among our COVID-19 patients. Variables that were collinear were dropped from the analysis. Results were presented in adjusted odds ratios and 95% confidence intervals. p values of <0.05 were considered statistically significant.

Ethics: Ethical approval was obtained from the Health Research and Ethics Committee of the Lagos State University Teaching Hospital. All patient data was anonymized and handled only by authorized personnel in order to ensure confidentiality.

3. Results

3.1. Patients socio-demographic and clinical presentation

Data from two thousand one hundred and eighty-four (2,184) laboratory confirmed COVID-19 patients presenting in nine treatment facilities in Lagos state. The ages of the patients ranged from 4 days to 98 years with a mean of 43.0(SD16.0) years. More than half (53.2%) were aged between 30 and 50 years. Only 2.9% were children i.e. less than 18 years of age) while 3.8% were aged 70 years and older. The patients were mostly male (65.8%) and seen in in government owned COVID-19 treatment facilities (97%). More than half (57.5%) were tested within a hospital setting while 42.4% were tested at designated ambulatory centreand thereafter referred to the isolaton and treatment centres.

At presentation, majority were considered to have mild disease, while 6.8% of them were either in severe or critical condition at presentation. Less than a quarter (22.5%) presented with at least one other comorbidity. Of these, 25.4% presented with more than one comorbidity. The cases fatality rate was 4.3% (Tables 1 and 2).

Table 1
Patients age, gender and admitting facility of the COVID-19 patients.

Variable	Frequency	%
Age in years (N = 2,175)		
<10	52	2.4
10-19	69	3.2
20-29	365	16.8
30-39	631	29.0
40-49	526	24.2
50-59	321	14.8
60-69	128	5.9
70-79	55	2.5
80 and older	28	1.3
Mean age (SD)	43.0(16.0)	43.3-44.7*
Gender (N = 2182)		
Female	746	34.2
Male	1436	65.8
Admitting facility (N = 2,184)		
Government-owned	2118	97.0
Privately run	66	3.0

95% Confidence interval

Table 2
Patients' clinical presentation and outcomes of the COVID-19 patients.

Variable	Frequency	%
Initial presentation (N = 2170)		
Mild	1251	57.7
Moderate	770	35.5
Severe	107	4.9
Critical	42	1.9
The presence of symptoms at presentation (N = 2170)		
Symptomatic	906	41.7
Asymptomatic	1264	58.3
Co-morbidity (N = 2184)		
Yes	492	22.5
No	1692	77.5
Number of co-morbidities (n = 492)		
1	367	74.6
2	114	23.2
3 or more	11	2.2
Type of co-morbidities		
Hypertension	365	16.7
Diabetes	149	6.8
Asthma	50	2.3
Cancer	9	0.4
Kidney disease	14	0.6
Sickle cell disease	7	0.3
HIV	7	0.3
Length of hospital stay (days)		
Less than 5	229	12.3
6-10	475	25.4
11-15	912	48.8
16-20	165	8.83
>20	88	4.71
Outcome (n = 1798)		
Discharged	1725	95.9
Died	73	4.1

3.2. Pattern of presenting symptoms among COVID-19 laboratory confirmed cases

Of the patients who presented with symptoms, cough (19.3%) was the most common presenting symptom. This was followed by fever (13.7%), difficulty in breathing, (10.9%) headaches (7.3%), weakness (6.3%), loss of sense of smell and taste (4.9%), throat irritation (4.9%), chest pain (3.8%), body pains (3.2%), nasal congestion (2.4%) and diarrhea (2.4%). All other symptoms were experienced by less than 1% of the patients.

Figure 1 displays symptoms profile of patients. We report all symptoms that were presented by at least 2 patients. All other symptoms were presented by only one patient and include: hoarse voice, tooth pain, easy satiety, dry mouth, dark urine, frequent urination, stained mucus, body rash, bleeding, hemiparesis, increased thirst, hiccups, hearing impairment, metallic taste, swollen feet, leg shaking, tingling sensations, anorexia, osteoarthritis, vaginal discharge, weight loss, anxiety, convulsion, ear heaviness, excessive sweating, constipation and body itching (Fig. 2).

3.3. Socio-demographic and clinical factors associated with COVID-19 deaths

The bivariate analysis showed that more deaths occurred among older patients, males and patients admitted in non-government treatment facilities (p < 0.05). Also, more deaths occurred in patients who were considered as being severe or critical at presentation also had more deaths. More deaths also occurred in persons with existing co-morbidities and this increased with increasing number of co-morbidities. The most significant predictor of death was the severity of initial presentation. Patients presenting in a severe/critical state were 153 times more likely to have died (95%CI:30.74-766.35) while those presenting in a moderate state were 6.33 times (95%CI: 1.13-35.20) more likely to have died, compared to those presenting in as mild cases.

Patients with at least one co-existing morbidity were 2.45 more likely to have died, (95%CI: 1.26-4.76) compared to those without comorbidities. Males were 2.21 times (95%CI: 1.06-4.58) more likely to have died. For every additional year of life, the likelihood of death increased by 1.04 times (95%CI: 1.02-1.06) (Tables 3 and 5)

3.4. Presenting symptoms as predictors of COVID-19 deaths

A bivariate analysis showed that deaths occurred more in patients who presented with difficulty in breathing, weakness, loss of appetite, fever, cough, weakness, and hemoptysis. Of the symptoms, difficulty in breathing was the most significant predictor of COVID-19 death (OR:19.26 95% CI 10.95-33.88). Patients who presented with body weakness were 3.04 times more likely to have died, while those presenting with cough were 1.87 times more likely to have died (Tables 4 and 6).

4. DISCUSSION

This is the firststudy that reports the pattern of presenting symptoms and predictors of death among a large cohort of PCR confirmed COVID-19 patients in Nigeria, and one of the first in sub Saharan Africa. COVID-19 patients with dyspnea may have a higher risk of severe and critical disease outcomes. In our study, difficulty in breathing was the most significant predictive symptom of COVID-19 death. Fu et al. observed that there was no statistically significant association between shortness of breath and COVID-19 severity [2] however a systematic review and meta-analysis of risk factors for critical and morbid cases of COVID-19 indicated that shortness of breath/dyspnea was positively associated with the severe illness and death but with a lower odds than ours (OR = 4.16, 95% CI [3.13−5.53][1] Fever on the other hand as reported by Zheng et al was negatively associated with severe illness and death (OR = 0.56, 95% CI [0.38−0.82], P = 0.003) though Fu et al and a systematic review by Shi et al reported no associations similar to our findings. Both systematic reviews however were predominated by studies in China with only one study from the UK and none from Africa.

More than half (58.3%) of patients in our study were asymptomatic and often reluctant to be admitted into isolation units. These patients though asymptomatic, can transmit the virus to others and as a result serve as an important source of hospital and community-based transmission. Two separate reviews of asymptomatic SARS-CoV-2 infections report slightly lower figures, ranging from 1.6% to 51.8% in the first review and 40%- 45% of asymptomatic cases in the second review. None of these reviews had patient representation from sub Saharan Africa. (Gao et al., 2020; Oran & Topol, 2020). Another systematic review and meta-analysis of asymptomatic COVID-19 patients showed that up to 40% of patients present with abnormal computed tomography (CT) findings. (Kronbichler et al., 2020) Public health messages tend to focus on symptoms as an indicator of COVID-19 disease. Our findings suggest that the focus of public health preventive measures should not be only placed on symptomatic persons, as the majority of COVID-19 cases may be asymptomatic. In addition, public health infection prevention guidelines for both the symptomatic of asymptomatic must be provided to the general public. Asymptomatic COVID-19 infection may be associated with sub-clinical CT lung abnormalities; however, CTs were not conducted for the asymptomatic cases in our study. National guidelines for the management COVID-19 cases should include
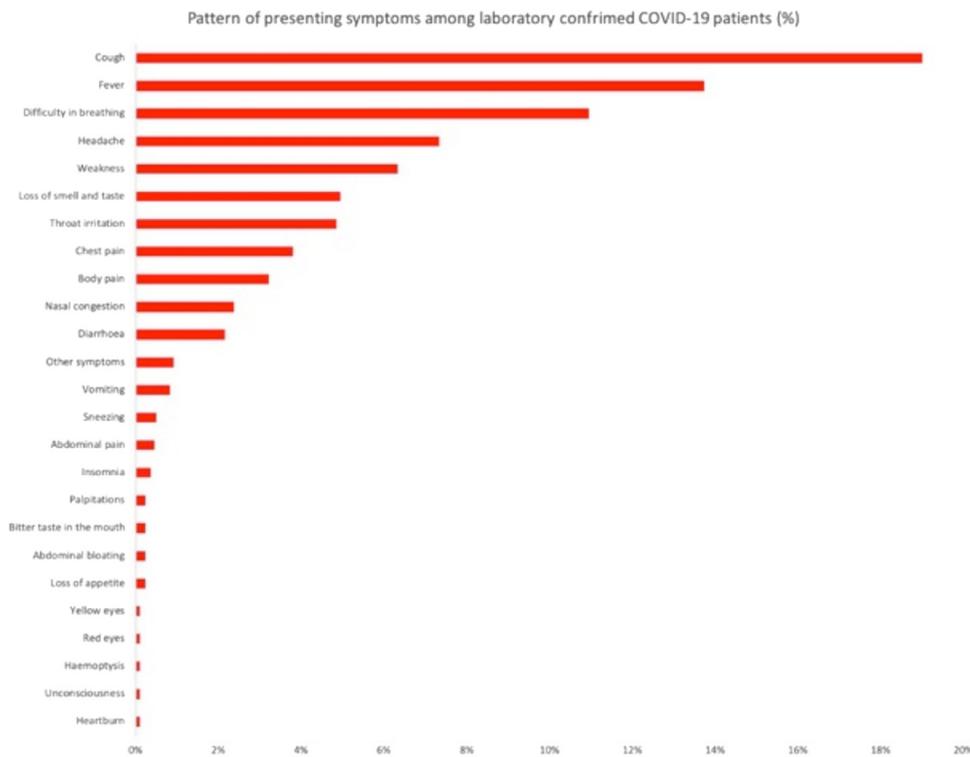
Fig. 1. Pattern of presenting symptoms among laboratory confirmed COVID-19 patients.
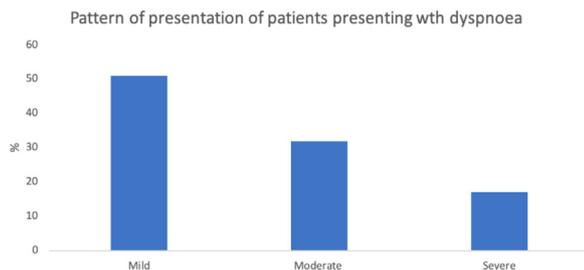
Fig. 2. Pattern of presentation of patients presenting wth dyspnoea.

asymptomatic cases, as they may have undetected sub-clinical abnormalities. (Kronbichler et al., 2020; Singhal, 2020) To reduce the risk of nosocomial transmission, health care workers need to maintain a very high index of suspicion when treating their patients, as the majority may be asymptomatic. The role of asymptomatic carriers in community-based transmission is also important and public health messages designed to emphasize this should be prioritized.

Majority of the symptomatic cases in our study had mild symptoms. This is consistent with findings observed in other places like Beijing, (Tian et al., 2020) Hubei province of China (Novel, 2020) and South Korea. (Kim et al., 2020) Cough, fever and difficulty in breathing were the most common symptoms observed in the patients in this study. Similar findings were observed in France where cough and fever were reported in more than 90% of cases (Lapostolle et al., 2020). Body pains, headaches, shortness of breath, ear-nose-throat symptoms and chest pain were also common symptoms a the French aamong patients in France (Lapostolle et al., 2020). Similarly, only 3% of patients presented with haemoptysis in the French study, comparable to our study findings. Consistent with the literature, COVID-19 symptoms among the patients in our study are primarily respiratory, ear-

nose and throat, gastrointestinal and generalised symptoms. (Lapostolle et al., 2020; Lechein et al., 2020; Koh et al., 2020)

Loss of smell and taste was the most peculiar symptom observed among the COVID-19 patients. However, this occurred in less than 5% of our of the patients in our study. Studies in other parts of the world suggest that such peculiar symptoms may serve as an important clue for the diagnosis of the infection. (Lee et al., 2020; Jan et al., 2020) In Korea and the United States, up to 15.3% of patients presented with acute loss of smell and taste, (Lee et al., 2020; Moein et al., 2020) and this was more common in females and young individuals at the early stages of the infection. (Lee et al., 2020) Further research is needed to determine whether loss of taste and smell may also serve as important early signs of COVID-19 among patients in sub Saharan African settings.

Of the symptoms, difficulty in breathing was the most significant predictor of COVID-19 deaths. This is consistent with studies in Wuhan, Guangzhou and Italy (Wang et al., 2020; Liang et al., 2020; De Vito et al., 2020) Also consistent with the literature, increasing age, male gender, and the presence of co-existing morbidities are strong predictors of COVID 19 deaths in Nigeria. (Figliozzi et al., 2020; Galloway et al., 2020; Imam et al., 2020; Du et al., 2020)

Late presentation appears to be the most significant predictor of poor outcomes e as patients presenting in severe or critical states were more likely to have died compared to those presenting in mild clinical states. Effective home management of COVID-19 may therefore play a critical role in reducing late presentations and deaths as suggested by McCullough et al. Targeted and consistent public sensitization on effects of late presentation should be considered in social mobilisation and communication drive to achieve the needed behavioural change in a pandemic as this. Majority of testing in this study was in treatment centers, and not done earlier. This is congruent with the early American experience that a majority of patients waited until becoming very ill to have testing done at the hospital. (McCullough et al., 2020)

Table 3
Patients age, gender, admitting facility and clinical presentation by final outcome N = 1802

Variable	Recovered n = 1725 Freq.(%)	Died n = 73 Freq.(%)	Total N = 1798 Freq.(%)	Chi-square	P-value
Age (in years)					
<10	48(100)	0 (0.0)	48(100.0)	173.14	0.000
10-19	55(98.2)	1 (1.8)	56(100.0)		
20-29	294(98.7)	4 (1.3)	298(100.0)		
30-39	529(99.1)	5 (0.9)	534(100.0)		
40-49	444(98.0)	9(2.0)	453(100.0)		
50-59	234(92.5)	19(7.5)	253(100.0)		
60-69	83(81.4)	19(18.6)	102(100.0)		
70-79	23(69.7)	10(30.3)	33(100.0)		
80 and older	15(71.4)	6(28.6)	21(100.0)		
Mean (SD)	41.7(15.0)	61.2(17.1)	42.5(15.6)	−10.8	0.000
Gender					
Female	611(97.3)	17 (2.7)	628(100.0)	4.54	0.033
Male	1114(95.2)	56 (4.8)	1,170(100.0)		
Admitting facility (n = 1802)					
Government-owned	1689(96.2)	66 (3.8)	1,755(100.0)	16.9	0.00
Privately run	36(83.7)	7 (16.3)	43(100.0)		
The presence of symptoms at presentation					
Symptomatic	1092(99.1)	10(0.9)	1102(100.0)	72.64	0.000
Asymptomatic	633(91.0)	63(9.0)	696(100.0)		
Initial presentation					
Mild	1,089(99.6)	4 (0.4)	1,093(100.0)	981.177	0.000
Moderate	584(97.3)	16 (2.7)	600(100.0)		
Severe	52(76.5)	16(23.5)	68(100.0)		
Critical	0(0.0)	37(100.0)	37(100.0)		0.000
Prescence of co-morbidity					
Yes	336(86.8)	51(13.2)	387(100.0)	105.26	0.000
No	1389(98.4)	22(1.6)	1411(100.0)		
Number of co-morbidities (n = 387)					
1	270(91.2)	26(8.8)	296(100.0)		
2	61(72.6)	23(27.4)	84(100.0)		
3 or more	5(71.4)	2(28.6)	7(100.0)	21.26	0.000

Table 4
Pattern of presenting symptoms by patient's outcome.

Symptoms profile	Recovered n = 1725 Freq.(%)	Died n = 77 Freq.(%)	Total N = 1802 Freq.(%)	Chi-square	p-value
Fever	**198(89.6)**	**23(10.4)**	**221(100.0)**	**26.06**	**0.000**
Cough	**281(90.3)**	**31(9.7)**	**311(100.0)**	**30.13**	**0.000**
Vomiting	14(93.3)	1(6.7)	15(100.0)	0.26	0.607
Abdominal pain	8(100.0)	0(0.0)	8(100.0)	0.34	0.560
Loss of appetite	**23(85.2)**	**4(14.8)**	**27(100.0)**	**8.13**	**0.004**
Weakness	**81(83.5)**	**16(16.5)**	**97(100.0)**	**40.70**	**0.000**
Headache	**114(98.3)**	**2(1.7)**	**116(100.0)**	**1.73**	**0.188**
Difficulty in breathing	**126(71.6)**	**50(28.4)**	**176(100.0)**	**296.95**	**0.000**
Diarrhoea	**35(89.7)**	**4(10.3)**	**39(100.0)**	**3.92**	**0.047**
Chest pain	68(95.7)	3(4.2)	71(100.0)	0.00	0.943
Body pain	**55(100)**	**0(0)**	**55(100.0)**	**2.40**	**0.121**
Throat irritation	**82(98.8)**	**1(1.2)**	**83(100.0)**	**1.82**	**0.177**
Insomnia	6(100)	0(0)	6(100.0)	0.25	0.614
Sneezing	11(100)	0(0)	11(100.0)	0.47	0.494
Loss of smell and taste	**77(98.7)**	**1(1.3)**	**78(100.0)**	**1.62**	**0.204**
Abdominal bloating	4(100)	0(0.0)	4(100.0)	0.17	0.680
Nasal congestion	39(100.0)	0(0.0)	39(100.0)	1.69	0.194
Bitter taste in the mouth	3(100.0)	0(0.0)	3(100.0)	0.13	0.721
Palpitations	2(100.0)	0(0.0)	2(100.0)	0.08	0.771
Heartburn	2(100.0)	0(0.0)	2(100.0)	0.08	0.771
Haemoptysis	**0(0.0)**	**2(100.0)**	**2(100.0)**	**47.31**	**0.000**
Red eyes	2(100.0)	0(0.0)	2(100.0)	0.08	0.771
Other symptoms	**13(86.7)**	**2(13.3)**	**15(100.0)**	**3.34**	**0.068**

Furthermore, in Lagos, where this study was conducted, poor hospital seeking practices and late presentation occur commonly (Roberts et al., 2015; Awofeso et al., 2018; Anorlu et al., 2004; Ugochukwu et al., 2019). Strong public health advisories encouraging people to seek care early. and guidelines for the effective home management of COVID-19 should be instituted to prevent COVID-19 deaths.

5. Study strengths and limitations

To our knowledge, this is the first study in Nigeria and one of the first in sub Saharan Africa to explore the symptomatology and predictors of mortality using data from a large cohort of COVID 19 patients in several treatment facilities. It however has some important limitations and the findings should be interpreted with

Table 5
Socio-demographic and clinical predictors of COVID-19 outcome (Death) among COVID-19 patients

Variables	Adjusted OR	95% CI	p value
Age in years	**1.04**	**1.02-1.06**	**0.000**
Male gender	**2.21**	**1.06-4.58**	**0.034**
Is asymptomatic at presentation	1.16	0.31-4.37	0.831
Has at least one co -morbidity	**2.45**	**1.26-4.76**	**0.008**
Being admitted in a government own facility	1.99	0.66- 6.16	0.222
Severity of presenting symptoms			
Mild	Ref		
Moderate	6.33	1.13-35.20	0.035
Severe/Critical	**153.47**	**30.74-766.35**	**0.000**

Table 6
Symptoms as a predictor of COVID-19 death controlling for age, gender, co morbidity and admitting facility.

Variables	Adjusted OR	95% CI	p value
Fever	1.58	0.82-3.07	0.172
Cough	**1.87**	**1.04-3.37**	**0.038**
Weakness	**3.04**	**1.44-6.42**	**0.003**
Loss of Appetite	1.87	0.44-7.91	0.397
Headache	0.48	0.10-2.32	0.367
Difficulty in breathing	**19.26**	**10.95-33.88**	**0.000**
Diarrhoea	1.12	0.31-4.02	0.861
Throat irritation	0.15	0.02-1.29	0.084
Loss of taste/smell	0.36	0.04-3.09	0.321
Other symptoms	1.85	0.18-19.40	0.609

some caution. First, data on symptoms was obtained by self-report and may be subject to recall or reporting bias. Secondly, inferences on causality cannot be made due to the cross-sectional nature of data extraction. Thirdly, this represents finding from the early stages of a dynamic and rapidly changing pandemic and the evidence provided may change over time or as more data becomes available. Nevertheless, this study provides valuable evidence on the symptom profile and predictors of mortality for COVID-19 at a time where evidence from African countries is sparse.

6. Conclusion

Respiratory symptoms i.e. cough and difficulty in breathing, as well as fever are the most common presenting symptoms for the COVID-19 patients in our study. Difficulty in breathing is the most important symptom predictive of COVID-19 death. Body weakness and cough are also predictive symptoms of poor outcomes. Severe symptoms at presentation, which may be brought about by late presentation, is the most significant predictor of death. Males, patients with co-existing morbidities and increasing age have poorer COVID-19 outcomes. Primary care physicians and COVID-19 frontline workers should maintain a high index of suspicion and prioritize the care of patients presenting with these symptoms. Emphasis should be placed on older males with co- morbid conditions. Community members should ensure that patients with these symptoms seek care early to reduce the risk of deaths associated with COVID-19.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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