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Research Article

Profile and Outcome of Hospitalized Patients with Severe COVID-19 in a Tertiary Hospital in Southern Nigeria

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Abstract

Background: The reporting of profile and outcomes of patients with severe COVID-19 provides an opportunity to evaluate treatment protocols, understand epidemiologic peculiarities and provides opportunities to improve care.

Objective of the Study: The objective of this study is to describe the demographic, clinical profile and disease outcome in patients hospitalized with severe COVID-19 disease in a tertiary hospital, Nigeria.

Methods: This was an observational retrospective study of patients admitted for care with COVID-19 in the University of Port Harcourt Teaching Hospital, Port Harcourt, Nigeria, from the 1st of May to 31st September 2020.

Results: A total of 90 hospitalised patients, comprising of 62 (68.9%) males with a median age of 44 years were recruited. A comorbid disease condition was present in 46 (51.1%), with hypertension in 35 (38.9%) and diabetes 17 (18.9%) as the leading comorbidities. Fever 56 (62.2%), dyspnoea 46 (51.1%) and dry Cough 31 (34.4%) were the leading symptoms. Thirty-seven (41.1%) patients had a severe disease while 7 patients died. Predictors of severity were male gender (O.R = 3.44, CI = 1.226 - 9.64, p = 0.02), presence of a comorbidity, (OR = 3.12, CI = 1.98 - 4.86, p = < 0.001), hypertension (OR = 2.88, CI = 1.65 - 5.01, p = < 0.001) and heart disease (LR = 7.61, CI = 0.79 - 0.99, p = 0.02). The predictors of mortality were hypertension and presence of comorbidity with, (p = < 0.001, O.R = 3.18 and CI = 3.587 - 7.814) and (p = < 0.001, O.R = 1.176 and CI = 2.389 - 5.786), respectively. Case fatality in all patients and patients with severe disease was 7.8% and 18.9% respectively.

Conclusion: The demographic profile, risks for severe disease and predictors of outcome and fatality rate is similar to existing trends. Risk communication on the factors predictive of severity and mortality such as hypertension and the presence of comorbidity is recommended. A significant proportion of patients in this cohort had severe disease requiring respiratory support with mortality rates below globally observed rates for COVID-19 patients in ICU.

Keywords: *COVID-19; SARS-CoV-2; Disease Profile; Outcomes; Nigeria*

Abbreviations

"AWaRe": Access, Watch, Reserve; (Adj O.R): Adjusted Odds Ratio; COVID-19: Coronavirus Disease 2019; HDU: High Dependency Unit; HCQ/CQ: Hydroxychloroquine/Chloroquine; ICU Settings: Intensive Care Unit; LPV/r: Lopinavir/Ritonavir; MEWS: Modified Early Warning System Score; NCDC: Nigeria Centre for Disease Control; OR: Odds Ratio; RT-PCR: Reverse-Transcriptase-Polymerase-Chain-Reaction; SARI: Severe Acute Respiratory Infection; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus-2; SoC: Standard of Care; UK: United Kingdom; WHO: World Health Organisation

Introduction

The spectrum of Coronavirus disease 2019 (COVID-19) associated with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection ranges from asymptomatic and mild, to moderate and severe to critical disease [1,2]. The majority (80% - 81%) of pa-

tients diagnosed with COVID-19 usually have asymptomatic to mild disease, with an associated low risk of morbidity and death in contrast to the (19 - 20%) of patients with the severe and critical disease [1,3,4].

Studies on COVID-19 disease outcome in various populations' show that patients with severe to critical COVID-19 disease are at risk of severe morbidity and death even with care in the best intensive care unit (ICU) settings [5-7].

Reports from the International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC) COVID-19 database for May and June 2020, respectively reveal mortality of 1567 (32.97%) out of 4752 and 2441 (33.1%) out of 7374, among hospitalised patients who were admitted at some point of their illness into an intensive care unit (ICU) or high dependency unit (HDU) [8, 9]. The outcome data of a prospective observational cohort study from the United Kingdom (UK) [10], involving 20133 hospitalised people using the ISARIC World Health Organisation (WHO) clinical characterisation protocol reported death in 5165 (26%) of hospitalised patients. A meta-analysis [11] of prospective cohort studies on outcomes from ICUs for patients with COVID 19 focusing on death in ICU consisting of 10150 patients from centres across Asia, Europe and North America, reported a range of 0 to 84.6%, in ICU mortality for all studies and combined ICU mortality of 41.6%, in patients with completed ICU admissions. It was noted that ICU mortality from COVID-19 is higher than that seen in ICU admissions from other viral pneumonia's [11].

The mortality associated with severe cases of COVID-19 stated above exemplifies how the ongoing pandemic of COVID-19 is severely challenging healthcare systems all around the world. These challenges include the unprecedented requirements for HDU/ICU care for a previously inconceivable number of patients even in settings with low HDU/ICU availability like Nigeria.

The assessment and reporting of the outcomes in patients with severe COVID-19 disease in Nigeria are required as it will provide the opportunity for the evaluation of treatment protocols, sharing of local experience and provide learning opportunities to improve care and outcomes.

The assessment will also contribute evidence to assess the impact of demographic factors such as race and ethnicity on COVID-19 outcomes as studies in certain countries suggest worse outcomes in patients of Black Asian and Minority Ethnicity (BAME) [12].

Objective of the Study

The objective of the report is to describe the demographic and clinical profile and disease outcome with emphasis on severe disease among patients hospitalized with COVID-19 disease in a tertiary hospital, Nigeria.

Materials and Methods

Study design and setting: This was an observational retrospective study of patients admitted for care with COVID-19 in the University of Port Harcourt Teaching Hospital, Port Harcourt, Nigeria.

Study population: The records of all consenting patients who were hospitalized for COVID-19 at the University of Port Harcourt Teaching Hospital, COVID-19 treatment centre from 1st May 2020 to 31st September 2020 were analysed. The patients were symptomatic and diagnosed with laboratory-confirmed COVID-19 infection defined by a positive result on a reverse-transcriptase-polymerase-chain-reaction (RT-PCR) assay for SARS-CoV-2, using nasopharyngeal and oropharyngeal swab specimens. Patients were categorized into severe and non-severe disease based on criteria in the interim national guidelines for case management of COVID-19 in Nigeria, by the Nigeria Centre for Disease Control (NCDC) [13], as outlined below. Adolescents or adult: with fever > 38°C or suspected respiratory infection, plus one of: respiratory rate > 30 breaths/min; severe respiratory distress; SpO_2 ≤ 93% on room air and presence of co-morbid conditions such as diabetes, asthma, hypertension. Children: with cough or difficulty in breathing and at least one of the following central cyanosis or SpO_2 < 92%; severe respiratory distress e.g. grunting and very severe chest in-drawing and signs of pneumonia with a general danger sign.

Sample size: This was determined by the number of all consenting patients who were hospitalized with COVID-19 from 1st May to 31st September 2020.

Treatment: All patients were managed following the facility-based treatment protocol for COVID-19 in line with the NCDC [13], and WHO Clinical management of COVID-19 interim guidance May 2020 [14] and the WHO Clinical care for severe acute respiratory infection (SARI): toolkit: COVID-19 adaptation [15]. The facility treatment protocol and standard of care comprised of supportive care with maintenance of fluid balance with isotonic crystalloids in line with fluid management guidelines [16], and oral rehydration using oral rehydration salt solutions and zinc in patients with diarrhoea. Antipyretics were given if temperature ≥38°C specifically paracetamol 2 tablets 2 times a day ≤ 3 days (with no NSAIDs use policy). Prophylactic anticoagulation with enoxaparin and therapeutic anticoagulation for the patient's already on anticoagulation and with thromboembolic risk was administered during hospitalisation and for at least 10 days after discharge. Intravenous Hydrocortisone at a dose of 160 mg per day in two divided doses not exceeding 7 days was administered preceding the preliminary release of the RECOVERY trial outcome in July 2020. Dexamethasone at a dose of 6mg daily for ≤ 10 days was commended after the RECOVERY trial preliminary report in July 2020. Treatment of superimposed bacterial infection was based on community-acquired pneumonia protocols and WHO Access, Watch, Reserve ("AWaRe") antibiotic use protocol [17]. Respiratory support and oxygen therapy was administered for patients with hypoxemia and respiratory failure in line with WHO SARI care toolkit guidance [15] escalating from nasal prongs, face mask, non-rebreather mask with reservoir bag and Continuous positive airway pressure (CPAP) therapy. Antiviral therapies were administered under compassionate use and trial conditions in an open-label randomised trial approach with Ethical clearance approval in line with the NCDC guidelines [13] and the WHO Initial Solidarity trial options [1,18]. Therapeutic options were Lopinavir/Ritonavir (LPV/r) at a dose of 400/100 mg tablets orally twice a day for 14 days (use paediatric formulation for children); or Hydroxychloroquine/Chloroquine (HCQ/CQ) tablets at a dose of 400mg twelve hourly on day 1 and 200 mg twelve for 4 days, with a Paediatric dosing of 6.5 mg/kg/per dose twelve hourly for day 1, then 3.25 mg/kg/per dose twelve hourly for 4 days (up to adult maximum dose) plus Azithromycin 500 mg daily for 5 days and Standard of Care (SoC). Trial and compassionate use was discontinued following the interim release of WHO Solidarity trial data. Patients also received oral zinc at 50 mg daily and vitamin C at 500 mg daily. Exiting comorbidities such as hyperglycaemia, hypertension and other conditions were treated as appropriate. The Modified early warning system score (MEWS) and charts were used to monitor patients with the aim of early identification of deterioration, triaging and escalation of care. Patients were discharged per the NCDC guidelines [13], with a first follow up visit at one week post-discharge.

Ethics: Ethical approval was obtained from the Health Research and Ethics Committee (HREC) of the University of Port Harcourt Teaching Hospital, Port Harcourt. Consent was obtained from all patients enrolled in the study. Confidentiality was maintained by the removal of patient identifiers from the dataset.

Data analysis: Demographic and clinical data were analysed using the statistical package software for windows (SPSS) version 23. Continuous and categorical variables were presented as percentages with median, mean ± standard deviation and confidence intervals as appropriate. Comparisons of means were done using the independent t-test while proportions were compared using the mantel haenszel corrected chi-square test with odds ratios (O.R), likelihood ratio and fishers exact test of significance. Spearman and Pearson correlations and logistic regression analysis were done to evaluate the associations of independent variables as predictors of dependent variables such as disease severity and outcome, with adjusted odds ratio (Adj O.R). A p-value ≤ of 0.05 was considered significant.

Results

Demographics of the study population

A total of 90 hospitalised patients were recruited over the period. The age distribution and comparisons of age in different groups of patients are displayed in table 1.

The mean age of all patients was 44.69 ± 14.55 years, with a median of 44 years and a range of 12 to 77 years. The majority of patients were in the 41 - 50 year (27.8%), 31 - 40 year (22.2%), 51 - 60 year (15.6%) and 18 - 30 year (15.6%) age groups, as shown in table 1.

The mean age of Males was 47.48 ± 13.84 vs. 38.50 ± 14.41 in females, (p = .0006) (Table 1), while the mean age of patients with severe vs. non-severe disease was 53.06 ± 14.898 vs. 39.11 ± 11.395, (p = 0.000 < 0.001), (Table 1).

The mean age of dead vs. discharged patients was 52.59 ± 14.174 vs. 44.05 ± 14.485, (p = 0.151), (Table 1).

Age descriptive and age group distribution				
Age Group	**N**	**Mean ± SD**	**Median**	**% of Total N**
< 18	1	12.00	12.00	1.1%
18 - 30	14	24.93 ± 4.19	26.00	15.6%
31 - 40	20	34.20 ± 2.82	33.50	22.2%
41 - 50	25	45.76 ± 2.82	45.00	27.8%
51 - 60	14	54.93 ± 2.10	54.00	15.6%
61 - 70	12	64.08 ± 2.64	63.50	13.3%
> 70	4	73.75 ± 2.75	73.50	4.4%
Total	90	44.69 ± 14.55	44.00	100.0%
Comparison of mean age by demographic and clinical outcome variable				
Variable	**Category (N)**	**Mean ± SD**	**CI**	**p-value**
Gender	Male (62)	47.48 ± 13.84	2.64-15.33	0.006
	Female (28)	38.50 ± 14.41		
Disease severity	Severe disease (37)	53.06 ± 14.89	8.43-19.46	
	Non-Severe Disease (53)	39.11 ± 11.39		< 0.001
Disease outcome	Discharge (83)	52.59 ± 14.17	-19.71-2.99	
	Death (7)	43.93 ± 14.53		0.147

Table 1: *Age description, distribution and comparisons by demographic and outcome variables.*

The patient population included 62 (68.9%) males and 28 (31.1%) females (See table 2).

The pattern of clinical characteristics and outcomes

Patients with the non-severe disease were 53 (58.9%) compared to 37 (41.1%) with severe disease (See table 2). A comorbid disease condition was present in 46 (51.1%) patients while 44 (48.9%) had no comorbidity (See table 2).

The distribution of comorbid disease conditions in the patients is presented in table 2. The leading comorbid disease conditions were Hypertension in 35 (38.9%), Diabetes 17 (18.9%) and Heart Disease in 4 (4.4%).

One of the patients with severe disease was a 12 years old female diagnosed with the multi- inflammatory syndrome in children (MIS-C).

Eighty-three (92.2%) of the patients were discharged and 7 (7.8%) died giving a case fatality rate of 7.8% (See table 2).

The 7 deaths occurred in the 37 patients with severe disease resulting in a mortality rate of (18.9%) in patients with severe disease (See table 2).

Variable	Grouping	Frequency (N)	Percentage (%)
Gender	Male	62	68.9
	Female	28	31.1
Comorbidity	Present	46	51.1
	None	44	48.9
Disease Severity	Non-Severe	53	58.9
	Severe	37	41.1
Disease Outcome	Discharged	83	92.2
	Died	7	7.8
Disease Outcome in patients with severe disease (N = 37)	Discharged	30	81.1
	Died	7	18.9
Distribution of Comorbidity	**Categories**	**Frequency (N)**	**Percentage (%)**
	Hypertension	35	38.9
	Diabetes	17	18.9
	Asthma	2	2.2
	Heart Disease	4	4.4
	Kidney Disease	2	2.2
	HIV/AIDS	1	1.1
	COPD	1	1.1

Table 2: *Frequency distribution of demographic and clinical variables.*

The pattern of comorbidities and symptoms of the disease

The spectrum of symptoms and comparison of symptoms by disease severity is displayed in table 3.

The leading symptoms at presentation were Fever 56 (62.2%), Dyspnoea 46 (51.1%), Dry Cough 31 (34.4%) and Productive Cough 21 (23.3%), Fatigue 18 (20.0%), Anosmia 16 (17.8%) and Aguesia 13 (14.4%).

Fever, dyspnoea, and fatigue were significantly more predominant in patients with severe disease with the following odds ratio (OR) and p values respectively (OR = 4.14, P = 0.003, OR = 20.15, P = < 0.001, OR = 4.17, p = < 0.001), as shown in table 3.

Symptom	Overall Frequency (N = 90)	Overall Percentage (%)	(%) Frequency in severe disease (N = 37)	(%) Percentage Frequency in non-severe (N = 53)	Odds Ratio	X^2	P value
Fever	56	62.2	80.6	50.0	4.14	8.58	0.003
Dyspnoea	46	51.1	88.6	27.8	20.15	31.43	<0.001
Dry Cough	31	34.4	44.4	27.8	2.64	2.66	0.081
Productive Cough	21	23.3	34.4	16.7	2.61	3.66	0.501
Fatigue	18	20.0	34.4	11.1	4.17	7.07	0.009
Anosmia	16	17.8	8.6	24.1	0.296	3.46	0.054
Aguesia	13	14.4	5.7	31.2	0.39	1.29	0.223
Diarrhoea	11	12.2	20.0	7.8	3.06	2.98	0.820
Sore Throat	10	11.1	11.4	11.1	1.03	0.00	0.609
Myalgia	9	10.0	8.6	11.1	0.75	0.15	0.479
Vomiting	7	7.78	5.7	9.4	0.58	0.39	0.420
Headache	5	5.6	5.7	5.6	1.01	0.00	0.665
Rhinorrhoea	3	3.33	2.9	3.8	0.75	0.05	0.653

Table 3: *Frequency of symptoms and association of symptoms with disease severity.*

Comparison of baseline clinical parameters by disease severity and outcome

The comparison of baseline clinical parameters in patients with severe and non-severe disease and discharged and dead patients are shown in table 4. Age (Years) (53.06 ± 14.89 vs. 39.11 ± 11.395, p = < 0.001), Respiratory Rate (/minute) (34.47 ± 7.512 vs.23.14 ± 4.567, p = < 0.001), Temp (°C) (37.10 ± 1.004 vs. 36.57 ± 0.53, p = 0.003), Pulse rate (Beats/Minute) (106.86 ± 15.871 vs. 88.70 ± 13.048, p = < 0.001) and MEWS Score (6.36 ± 2.206 vs. 1.81 ± 1.415, p = < 0.001) respectively were significantly higher in patients with severe disease; while SPO_2 (%) (77.72 ± 19.27 vs. 96.94 ± 2.612, p = < 0.001), was significantly lower in patients with severe disease (Table 4).

Patients who died when compared to those discharged, had higher respiratory rate per minute (39.14 ± 18.55 vs. 26.89 ± 7.41, p = < 0.001), pulse rate per minute (116.14 ± 7.105 vs. 94.33 ± 16.243, p = 0.001), diastolic blood pressure (mmHg) (96.00 ± 21.457 vs. 79.71 ± 10.954, p = 0.002) and MEWS Score (6.86 ± 2.193 vs. 3.36 ± 2.793, p = 0.001), respectively. The SPO_2 (%) was lower in patients who died (61.29 ± 22.889 vs. 91.55 ± 12.285, p = < 0.001) (Table 4).

	Mean ± SD		P-value	Mean ± SD		P-value
Baseline variables	Severe (N = 37)	Non-Severe (N = 53)		Dead (N = 7)	Discharged (N = 30)	
Age (Years)	53.06 ± 14.89	39.11 ± 11.39	<0.001	52.29 ± 14.17	44.05 ± 14.49	0.151
SPO_2 (%)	77.72 ± 19.27	96.94 ± 2.61	<0.001	61.29 ± 22.89	91.55 ± 12.29	<0.001
Respiratory Rate (/minute)	34.47 ± 7.51	23.14 ± 4.57	<0.001	39.14 ± 18.55	26.89 ± 7.41	<0.001
Temperature (°C)	37.10 ± 1.00	36.57 ± 0.53	0.003	36.88 ± 0.45	36.78 ± 0.82	0.798
Pulse (Beats/ Minute)	106.86 ± 15.87	88.70 ± 13.05	<0.001	116.14 ± 7.11	94.33 ± 16.24	0.001
Systolic Blood Pressure (mmHg)	130.11 ± 20.74	124.29 ± 12.81	0.112	140.50 ± 13.55	132.14 ± 18.92	0.053
Diastolic Blood Pressure (mmHg)	80.15 ± 15.94	81.33 ± 9.74	0.671	96.00 ± 21.46	79.71 ± 10.95	0.002
MEWS Score	6.36 ± 2.21	1.81 ± 1.42	<0.001	6.86 ± 2.19	3.36 ± 2.79	0.001

Table 4: *Comparison of baseline age and clinical parameters by disease severity and outcomes.*

Impact of demographic and comorbid factors on disease severity and outcome

The effect of demographic and comorbid factors on disease severity and outcome is shown in table 5.

Males had a higher frequency of severe disease (48.4%) compared to women (21.4%), p = 0.02, χ^2 = 5.84, O.R = 3.44, CI = 1.226 - 9.64 (Table 5).

There was a significant correlation between severe disease and gender with the Spearman correlation coefficient (R = -0.255, p = 0.015) (Table 5).

Patients with Hypertension had a higher frequency of severe disease (63.9%) compared to (36.1%) patients without hypertension, p = < 0.001, χ^2 = 15.78, OR = 2.88, CI = 1.65 - 5.01 (Table 5).

There was a significant correlation between severe disease and hypertension with the Spearman correlation coefficient (R = 0.42, p = < 0.001) (Table 5).

Patients with heart disease also had higher frequency of severe disease (100%) vs compared to patients without heart disease (37.2%), p = 0.02, χ^2 = 6.28, LR = 7.61, CI = 0.79 - 0.99 (Table 5).

There was a significant correlation between severe disease and heart disease spearman correlation coefficient (R = 0.25, p = 0.01) (Table 5).

Patients with a comorbid disease had a higher frequency of severe disease (67.4%) compared to (2.3%), patients without comorbidities, p = < 0.001), χ^2 = 29.42, OR = 3.12, CI = 1.98 - 4.86 (Table 5).

There was a significant correlation between severe disease and the presence of a comorbid disease condition with the Spearman correlation coefficient (R = 0.572, p = < 0.001) (Table 5).

	Outcome variable	**Disease Severity**					
Variable	**Variable category**	**Frequency of severe disease (%)**	**Chi-square (X^2)**	**Odds Ratio**	**(95% C.I)**	**P-value**	**Spearman's R (p-value)**
Gender	Male	48.4	5.841	3.44	1.23-9.63	0.020	-.0.255 (0.015)
	Female	21.4					
Comorbidity	Comorbidity Present	67.4	29.415	3.12	1.99-4.86	<0.001	0.572 (<0.001)
	No comorbidity	11.4					
Hypertension	Hypertensive	63.9	15.779	2.86	1.65-5.01	<0.001	0.419 (<0.001)
	Non-Hypertensive	36.1					
Heart disease	Heart disease Present	100	6.279	*7.61	0.79-0.99	0.023	0.246 (0.012)
	No heart disease	37.2					
	Outcome Variable	Disease Outcome (Death)					
Presence of comorbidity	Comorbidity present	100	8.399	*11.49	NA+	0.015	NA
	Comorbidity none	0					
NA: Not applicable because O.R was not computed for variables with values of 0 in any cell							
*Reflects likelihood ratios where O.R is not computed							

Table 5: *Association between demographic, comorbidity variables and disease severity and outcome.*

All the 7 (100.0%) patients who died had a comorbidity, p = 0.015), χ^2 = 8.40, Likelihood ratio = 11.49.

Predictors of disease outcomes

With multinomial logistic regression analysis hypertension and presence of comorbidity were the significant predictors of death with, (χ^2 = 93.32, p = <0.001, Adj O.R = 3.18 and CI = 3.59 - 7.81) and (χ^2 = 4488.96, p = < 0.001, Adj O.R = 1.18 and CI = 2.39 - 5.79), respectively (Table 6).

Variable	Chi square	Sig.	Adj O.R	CI
Age	41.76	0.838		
Gender	5.19	0.07		
Hypertension	93.32	< 0.001	3.18	3.587-7.814
Heart disease	2.08	0.354		
Comorbidity present	4486.96	< 0.001	1.18	2.389-5.786
Drug Arm	0.17	0.679		

Table 6: *Regression table for predictors of death among patients with severe disease.*

Use of repurposed trial antiviral drugs

The distribution of therapeutics with repurposed drugs for patients with severe disease is displayed in table 7.

Twenty six patients (15 on LPV/r and 11 on HCQ/CQ) received repurposed trial drugs compared to 11 on standard of care (SoC) alone (Table 7).

The proportion of patients receiving repurposed drug who died was (3.8%) compared to (54.5%) on standard of care with fishers exact p value = 0.003, with (O.R = 3, 25, p = 0.007) (Table 7).

		Outcome variable					
Variable: Drug Treatment		Discharged	Death	Fishers Exact	X^2	O.R (p value)	C.I
Yes	LPV/r	15	0				
	HCQ	10	1	0.003	8.131	3.25 (0.007)	0.91-5.61
None	SoC	5	6				
Total		30	7				

Table 7*: Pattern of repurposed drug use and association with disease outcomes among patients with severe disease.*

There was no significant difference on the use of either HCQ/CQ or LPV/r on disease outcome (death).

There was no significant effect of drug arm in predicting disease outcome (death) (See table 6).

Discussion

The analysis of the demographic, clinical profile and outcomes of hospitalised COVID-19 patients provides information on the epidemiologic trends, predictors of disease patterns and outcomes distinctive to the population. The study of clinical outcomes also indirectly assesses the standard of care, provides data for comparisons with the global outcome and provides opportunities for quality improvement.

In this study of hospitalised patients in a tertiary hospital in South-South Nigeria, the demographic pattern concerning age and gender distribution of patients is similar to existing trends within Nigeria [19-21], other countries in Africa [22,23], and globally [3,24].

The mean and median age of 44.69 ± 14.55 years and 44 years respectively observed in this study is comparable to 43 years reported by Osigbogun., *et al*. [19] in Lagos, Nigeria. Otounye., *et al*. [21] in Lagos, Nigeria also reported a mean age of 46 years, while Zamparini., *et al*. [22] in South Africa and Nachega., *et al*. [23] in the Democratic Republic of the Congo (DR Congo) reported median age of 42 and 46 years respectively.

Other studies have however reported higher median and mean ages in their cohort of hospitalised patients. These include a median of 53.75 ± 16.58 years in Iran by Shahriarirad., *et al*. [24], 54 years by Matangilia., *et al*. [25] in Kinshasha, DR Congo, 59 years documented by De Souza., *et al*. [26] in Brazil and 52.9 years in a Bulgarian cohort [27].

The age trends and pattern seen in this study reflects patterns in Nigeria and other countries. Observed variations may be explained by the higher proportion of elderly citizens in those patient populations.

The majority (68.9%) of the patient population in this study were males. This finding is consistent with other reports and the pattern across the globe which report more males than females though with varied proportions [7]. Three reports from Nigeria [19-21] also reported more male prevalence with rates of 65.8%, 66.7% and 74.7% respectively. The observations from other countries are similar, with Nachega., *et al*. [23] in DR Congo reporting that (65.3%) patients were male. Studies from Iran [24], Bulgaria [27], China [3], Brazil [26] and Spain [28] also reported higher male proportions of 63%, 62%, 62.8%, 57.5% and 52.5% respectively.

Though few studies reported almost approximate proportions of males compared to females with rates of 51%, [25] and 52.6% [29]. There is a consistency in the trend of more males with COVID-19 with a higher predisposition to more severe disease compared to women. The higher risk of men for SARS-CoV-2 infection and severe COVID-19 is thought to be due to biopsychosocial factors related to genetic-based immune responses which confer more protection on women, the expression of the angiotensin converting enzyme (ACE) receptor genes and social attitude of men which confers more risk for COVID-19 transmission [30].

The presence of comorbidities has been associated with the risk of severe disease and adverse outcomes in patients with COVID-19. In this study, 51.1% of the patients had at least one comorbidity with Hypertension (38.9%), Diabetes (18.9%) and Heart Disease (4.4%) as the leading comorbidities. These findings are comparable with that of other studies reporting a frequency of comorbidities in the hospitalised populations of 34.6% in DR Congo [23]; 46% in Kinshasha, DR Congo [25]; 49.4% in Nigeria [20]; 56.8% in Brazil [29] and 50% in Bulgaria [27].

The finding of hypertension and diabetes and cardiovascular risk conditions such as heart disease as leading comorbid diseases is also similar to the findings in various populations though with varying frequencies and ranking. Other studies in Nigeria [19,20] correspondingly reported hypertension and diabetes as the leading comorbidities with frequencies of (74.2%) and (33.8%) for hypertension and (30.3%) and (15.6%), for diabetes, respectively. Studies [22,23,25,27,29,31] outside Nigeria have likewise documented hypertension and diabetes as the leading comorbidities with a range of (25.4% - 52.9%) for hypertension and (14% - 29.6%) for diabetes. The comorbidity pattern in this study is consistent with the global pattern and reflects the increasing burden of hypertension and diabetes as leading non-communicable diseases which contribute to global morbidity and mortality.

The symptoms associated with COVID-19 have evolved with documented geographic variations in the pattern and spectrum of symptoms, though there is a consistency in the pattern of leading symptoms globally [31].

The leading symptoms at presentation in this study were fever, dyspnoea, dry cough and productive cough, fatigue, anosmia and aguesia. This pattern was also documented in other studies in Nigeria [20,21,32]. Correspondingly a similar trend of fever, dyspnoea or shortness of breath, dry cough, fatigue, myalgia and headaches as the leading symptoms have also been reported in studies from DR Congo [23,25], South Africa [22], and Brazil [29]. These findings are representative of global trends as shown in a meta-analysis [31] of 13 studies across 8 countries (China, Italy, Australia, Canada, Korea, Taiwan, Singapore, and the USA) which still showed that fever, cough, dyspnoea, sore throat, diarrhoea, nasal congestion, headache, sputum production, fatigue, myalgia remain the leading symptoms, with variations in the pattern of predominance across countries and continents. The symptoms pattern reported in this study is consistent with reports in Nigeria and globally.

The results of this study also show that fever, dry cough, dyspnoea and fatigue were more likely to occur in patients with severe disease. Similar observations were also reported by Matangila., *et al*. [25] and Abayomi., *et al.* [32] with shortness of breath, fever and weakness associated with increased severity and worse outcomes. These symptoms should be taken seriously and patients with these symptoms should be advised to seek care early.

Disease severity patterns in this study showed that 41.1% of patients had severe disease. This pattern of more patients with the non-severe disease is the expected trend for COVID-19 [1,3]. The proportion of patients with severe disease among hospitalised cohorts may be influenced by criteria for hospitalisation and existing referral pathways. In areas where patients are admitted for isolation with mild or moderate disease, the rates of severe disease will be lower compared to facilities where patients are referred on account of severe disease or critical disease requiring HDU/ICU care. The proportion of patients with severe disease in this study parallels observations from other studies of hospitalised patients though with varying percentages of 25%, 31%, 31.2% and 19% reported by Nachega., *et al*. [23], Matangilia., *et al*. [25], Popov., *et al*. [27] and Wu., *et al*. [3], respectively. The knowledge of these figures will help in resurge and contingency planning and resource allocation for patients with COVID-19 especially with relations to bed space, HDU and ICU requirements and therapeutic options.

The overall case-fatality rate among hospitalised patients was 7.8%, however of more interest is the fatality rate of 18.9% among patients with severe to a critical disease requiring HDU/ICU care with respiratory therapy and non-invasive respiratory support.

The fatality rate in patients with severe disease in this study compares to findings from various observational cohort studies across various continents [33-38] with reports of mortality in hospitalised and ICU patients ranging from 11.7% [16] to 67% [13]. These rates usually approximate and exceed 50% among patients in ICU receiving mechanical ventilation [11].

Giesen., *et al*. [28] in Spain reported a lower CFR of 14.7% in a cohort of hospitalised patients while Matangila., *et al*. [25] in DR Congo reported in-hospital mortality of 20% in similarity with this study outcomes. Two other studies by Nachega., *et al*. [23] and Marcolino., *et al*. [29] in DR Congo and Brazil reported an overall in-hospital mortality of 13.2% and 22% respectively. Though the mortality in ICU patients in these two studies were 50% and 47.6% respectively. Analysis of other studies also reports lower, comparative or higher rates of in-hospital mortality. Three observational studies from China by Liu., *et al*. [39], Zhou., *et al*. [36] and Du., *et al*. [37] reported rates (15.3%), (28.27%) and 11.73% while Gracielli., *et al*. [38], in a retrospective case series of 1591 critically ill patients admitted in ICUs in the Lombardy region of Italy from February 20 to March 18, 2020, documented an ICU mortality of 26% [38].

Comparison of the rates in this study with early outcomes reports from the International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC) COVID-19 database show lower rates than the (32.97%) and (33.1%) mortality reported for May and June 2020, respectively among hospitalised patients were admitted at some point of their illness into an intensive care unit (ICU) or high

dependency unit (HDU) [8,9]. The outcome data of a prospective observational cohort study from the UK [10] involving 20 133 hospitalised people using the ISARIC WHO Clinical Characterisation Protocol reported death in 5165 (26%) of hospitalised patients. In a similar pattern a meta-analysis [11] of prospective cohort studies on outcomes from intensive care units for patients with COVID 19 focusing on death in ICU consisting of 10150 patients from centres across Asia, Europe and North America, reported a range of 0 to 84.6%, in ICU mortality for all studies and combined ICU mortality of 41.6%, in patients with completed ICU admissions.

The fatality rates of patients with severe disease seen in this study are comparable to the range reported across the world and generally lower than rates for ICU patients globally, considering that ICU mortality from COVID-19 is higher than that seen in ICU admissions from other viral pneumonia's [11]. The different rates of CFR in the general cohort of hospitalised patients and those with severe disease makes the specific evaluation of outcomes in patients with severe disease important as this provides better insights into the impact of COVID-19 in hospitalised patients in addition to providing a point of reference for the evaluation of the standard of care which may be overlooked if gross case fatality of both severe and non-severe disease is utilised.

The impact and pattern of various demographic and clinical variables on disease severity and hospitalisation outcomes showed that patients with a comorbid disease had a significantly higher frequency of severe disease. Males also had a higher risk of severe disease compared to women. Patients with severe disease were also older than patients with the non-severe disease.

Other observations were the higher risk of severe disease in patients with hypertension and heart disease. The predictors of mortality in this study were the presence of a comorbid condition and hypertension.

The observations on the impact of these demographic and clinical factors as risks and predictors of severe disease and adverse outcomes in patients with COVID-19 have also been documented in other studies.

Hatmi., *et al*. [40] in a systematic review and Huang., *et al*. [41] in a multicentre observational study showed that hypertension and cardiovascular disease were associated with more severe disease and mortality as observed in this study. Mesas., *et al*. [42] also found that age, presence of comorbidity, hypertension and dyspnoea were associated with severity and adverse outcomes in similarity with the findings in this study. The results of other observational studies [19,23,27,29] also document similar patterns with Marcolino., *et al*. [29] and Osigbogun., *et al*. [19] finding hypertension as a predictor of severe disease and death in conformity with the findings of this study. These findings reinforce the observation of hypertension as an independent risk factor for COVID-19 severity and mortality. COVID-19 patients with hypertension should therefore be given additional attention to prevent worsening of their condition [41].

The comparison of baseline demographic and clinical parameter's based on disease severity and outcome showed that patients with severe disease were older than those with the non-severe disease. Also, factors such as higher pulse rate, higher temperature, higher respiratory rates, higher blood pressures, higher MEWS Score and lower SPO_2 were significantly different in patients with severe disease and patients who died. Similar trends of the higher risks of severe disease and worse outcomes associated with increased age increased respiratory rate and lower SPO_2 requiring O_2 supplementation have been reported in previous studies [5,25,29]. These observations show the influences of these baseline parameters in predicting severe disease and adverse outcomes. The baseline vital parameters should be utilised in the early identification of at-risk patients to reduce the requirements for critical care and poor outcomes.

In attempts to find treatment for COVID-19, various drugs have been repurposed and used under trial conditions. In this study, some patients received hydroxychloroquine (HCQ/CQ), while others received Lopinavir/Ritonavir (LPV/r) or routine standard of care (SoC). The frequency of death in patients who received a repurposed trial drug was significantly lower compared to patients with standard of care alone.

The value of this observation is limited by the small patient numbers involved and lack of additional benefit of these drugs in influencing the risk of death in regression models as shown in the preliminary outcomes of the WHO Solidarity trial and other metanalysis [43,44].

Conclusion

The demographic profile of hospitalised patients in this study is similar to existing trends of age and gender patterns of previously reported studies within and outside Nigeria.

The spectrum of symptoms parallels established patterns with fever, dyspnoea and fatigue highly predictive of severe disease. Risk communication of the significance of these symptoms is recommended to promote early presentation in patients with these features.

The observation of hypertension and diabetes as the leading comorbidities, is similar to previous observations, with male gender, presence of comorbidity and hypertension as key predictors of severe disease.

A significant proportion of patients in this cohort had severe disease requiring respiratory support with mortality rates below globally observed rates for COVID-19 patients in ICU. The proportion of patients with severe disease provides useful information for contingency planning and resource allocation for a future surge in COVID-19 cases.

The focus of mortality in the subset of patients with severe disease is important in understanding the impact of COVID-19 in hospitalised cohorts and provides useful information for benchmarking and quality improvement.

The key predictors of death in this study were the presence of comorbidity and hypertension in correspondence with previous observations. Other baseline clinical parameters were also found to be useful predictors of disease severity. The knowledge of these predictive factors identified in this study should be utilised for triaging and risk assessment in the environment.

The repurposed antiviral drugs hydroxychloroquine (HCQ/CQ) and Lopinavir/Ritonavir were not significant variables in predictive models of adverse outcome (death).

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Conflict of Interest

There is no conflict of interest and no financial declaration or funding support for this work.

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