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Attitudinal, regional and sex related vulnerabilities to COVID-19: Considerations for early flattening of curve in Nigeria

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Abstract

Background: In Nigeria, the policies and interventions due to the COVID-19 pandemic are majorly directed at businesses and relief. There are no clear plans to identify individuals with comorbidities associated with high morbidity and fatality rates. This paper identifies comorbidities associated with high morbidity and fatalities of COVID-19 across countries and vulnerable groups in Nigeria.

Methods: Peer-reviewed articles published between 2010 and 2020 retrieved from Google scholar, African Journal Online, EMBASE, Scopus, and MEDLINE/PubMed (central) were systematically reviewed.

Results: The pooled prevalence of hypertension is the lowest in North Central Nigeria (22.0%) and the highest in South-Eastern Nigeria (33.6%) while the pooled prevalence of diabetes mellitus (DM) is lowest in North-Western Nigeria (3.0%) and highest in South-Southern Nigeria (9.8%). Significant differences in the frequency of comorbidities (hypertension, DM, cardiovascular disease, cancer, and chronic kidney disease; CKD) and complications (cardiac injury and acute respiratory disease syndrome; ARDS) were observed between fatal and non-fatal cases of COVID-19 ($p<0.0001$). There were significant correlations between hypertension and ARDS ($p=0.002$), DM and ARDS ($p=0.010$), hypertension and ($p<0.0001$), DM and CKD ($p=0.033$), and hypertension and DM ($p=0.001$).

Conclusion: High prevalence of comorbidity may be predictive of high COVID-19 morbidity and mortality. Thus, to flatten the curve early intervention funds should be appropriately allocated based on the prevalence of comorbidities in the geopolitical zones. Such high-risk groups should be identified, stratified and actively monitored during treatment to prevent the development or progression of complications such as cardiac injury and ARDS.

Keywords: COVID-19, Comorbidities, Fatality, Cardiac injury, Cancer

Conflicts of Interest: *None declared*
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↑What is "already known" in this topic:
Global reports from affected countries revealed that high morbidity rate is associated with high prevalence of comorbidities. Current intervention funds for COVID-19 are being allocated based on previous budget formula and the number of confirmed cases of COVID-19 in different Nigerian States. No consideration is presently been given to regional difference in the prevalence of some comorbidities to the disease and prior utilization of preventive healthcare services.

→What this article adds:
In this study, a higher prevalence of comorbidities was observed in Southern Nigeria than in Northern Nigeria. The study suggests that the level of awareness and utilization of preventive healthcare services, and the treatment and control of comorbidities prior to the pandemic may accounts for sex and regional differences of confirmed cases of COVID-19 infection. It also suggests that the higher morbidity and fatality observed in Southern Nigeria compared to Northern Nigeria could be associated with the high prevalence of comorbidities in the region.

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Introduction

In late 2019, a certain type of progressive pneumonia caused by a novel coronavirus, COVID-19, was reported in Wuhan, China. Earlier reports suggested an animal-to-human transmission but recent findings show human-to-human transmission. As of 15 April 2020, over 1.9 million cases have been confirmed and over 120,000 deaths have been documented (1). In Nigeria, Africa's most populous country, the first case of COVID-19 was reported on 27 February 2020. So far, efforts to prevent the spread of the disease by the National Emergency Operations Centre (NEOC) in collaboration with the Nigeria Centre for Disease Control (NCDC) have been less effective. As of 17 April 2020, the NCDC stated that with over 6,649 samples tested, Nigeria now has a total number of 493 confirmed cases and 17 deaths (2). Although the number of confirmed cases in Nigeria appears to be fluctuating, the number of COVID-19 cases and deaths could increase in the next few weeks since over 4000 persons who came in contact with confirmed cases are yet to be traced (Figs. 1 and 2). The expected increase is largely due to partial compliance to isolation and social distancing regulations, and lack of protective equipment and late closure of international airports and land borders in the country. Case fatality rate (CFR) is higher in Italy (7.2%) than in China

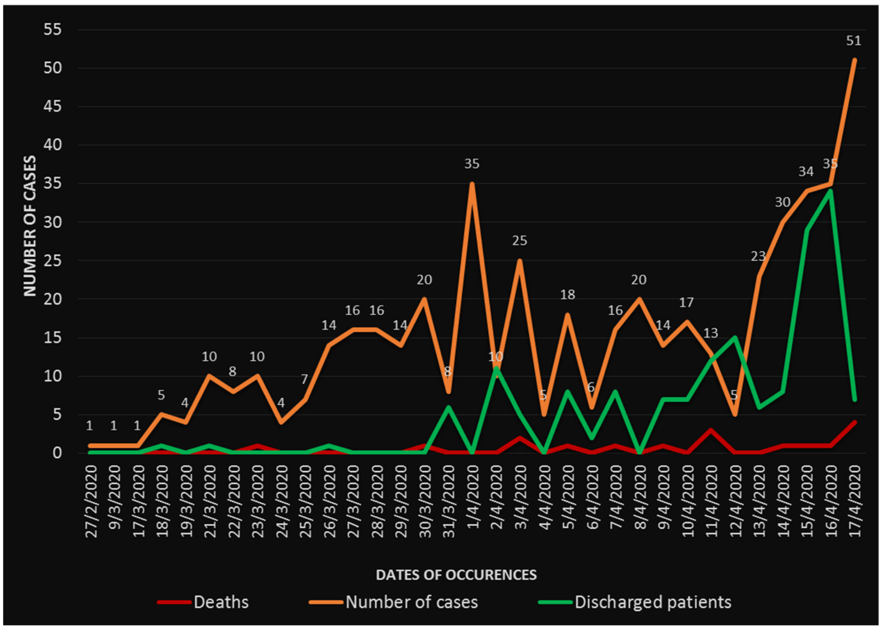

Fig. 1. Number of confirmed COVID-19 cases per day in Nigeria, 17 April 2020, NCDC (2)

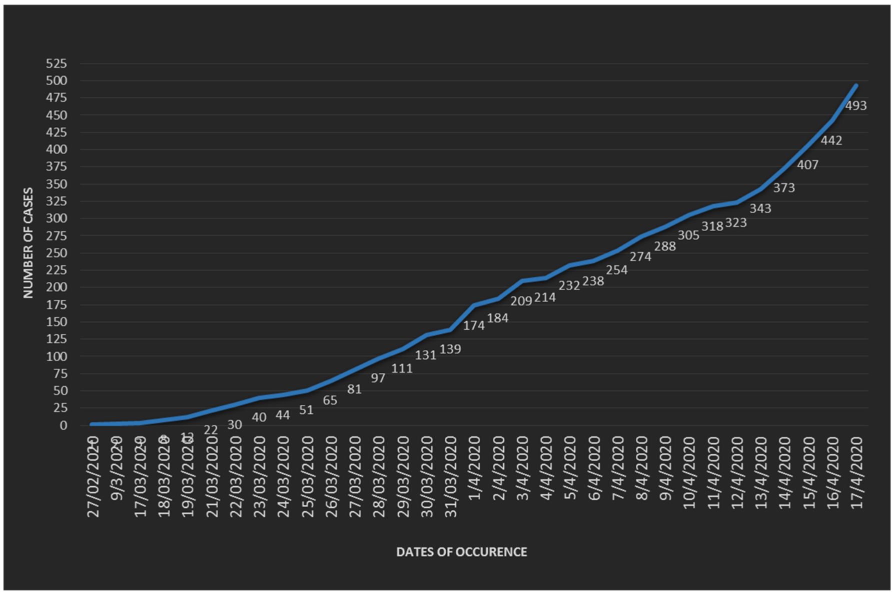

Fig. 2. Cumulative frequency of confirmed COVID-19 cases in Nigeria, 17 April 2020, NCDC (2)

(2.3%) (3). Although the CFR values at the initial phases of an epidemic are not totally dependable due to day-to-day fluctuations, however it is important to indicate the initial values in Nigeria which is currently estimated at 3.4% (2). Presently, a higher prevalence of confirmed cases of COVID-19 and fatality rate is seen in Southern Nigeria (73.9% and 4.1%) than in Northern Nigeria (26.1% and 2.3%, respectively) (2). The reason for the high difference is yet to be elucidated. There are few isolation centers in Nigeria. Thus, with increasing hospitalization of infected persons, the rate of mortality could rise among already hospitalized COVID-19 uninfected patients due to nosocomial spread. Already, Wang et al. stated that 12.3% of infected persons are hospitalized patients (4). The fatality rate may depend on the progress phase of the epidemic at a given calendar time in a country, the prevalent comorbidity in infected population and the country's preparedness for the pandemic. To reduce the impact of the disease, it is only logical that healthcare resources be directed at vulnerable groups. Thus, identifying comorbidities associated with COVID-19 fatality will assist healthcare workers, especially those with inadequate healthcare facilities, to stratify individual patients, guide high-risk groups, predict and control the rate of disease progression. Interestingly, studies have compared severe cases with non-severe cases of infection so as to identify comorbidities associated with COVID-19 fatality (4, 5). The word 'severe', a primary composite end point, connotes admission to an intensive care unit (ICU) or death. Mounting evidence suggests that the prevalence of COVID-19 and its associated fatality vary across regions (6). The regional variation may depend on the prevailing comorbidity in the region. In Seattle, a greater percentage of COVID-19 patients had diabetes mellitus (58%) and 21% had chronic kidney disease (7) while hypertension appears to be the prevalent comorbidity in COVID-19 patients in China. Thus, to reduce the impact of COVID-19, healthcare workers and the government must consider the peculiarities of their region or county either by considering self-reported medical history or by conducting simultaneous testing for comorbidities and COVID-19. This review paper highlighted current policies and interventions on COVID-19 pandemic and their limitations. It identified comorbidities that are associated with high morbidity and mortality in the six geopolitical zones of Nigeria; North Central Nigeria (NCN), North Eastern Nigeria (NEN), North Western Nigeria (NWN), South Eastern Nigeria (SEN), South Western Nigeria (SWN) and South Southern Nigeria (SSN). It also elucidates the relationship between COVID-19 and comorbidities such as diabetes mellitus (DM), hypertension, and cancer.

Methods

Data search and analysis

Peer-reviewed articles published between 2010 and 2020 which retrieved from Google scholar, African Journal Online, EMBASE, Scopus, and MEDLINE/PubMed (central) were systematically reviewed. Search phrases included, Nigerian policies and interventions on COVID-19 pandemic, uptake of Medical check-up, utilization/awareness of preventive healthcare services, prevalence/occurrence of fatal/severe (the occurrence of death or admission to the intensive care unit) cases of COVID-19 disease in China/US/Italy/UK, cardiac injury and COVID-19, Prevalence of diabetes mellitus (DM; fasting plasma glucose ≥ 7.0 mmol/L, random plasma glucose ≥

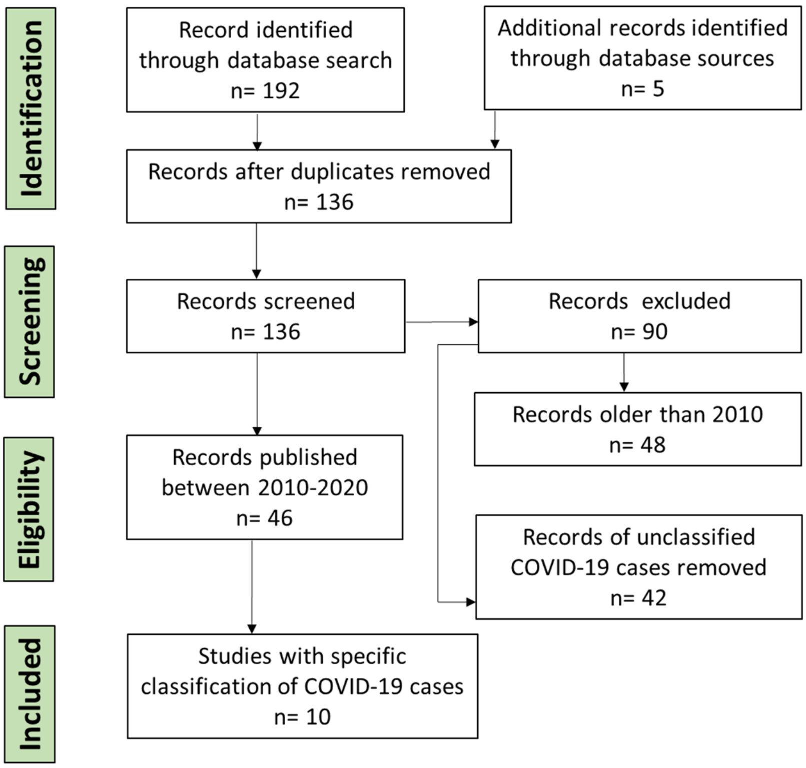

Fig. 3. PRISMA Flow Diagram on COVID-19 and comorbidities related literature search

11.1 mmol/L, 2 hour post-prandial plasma glucose ≥ 11.1 mmol/L) and hypertension (blood pressure ≥ 140/90 mmHg) in COVID-19 patients, and systematic reviews and meta-analysis on prevalence of DM/hypertension/cancer in Nigeria/Africa. The pooled prevalence of DM and hypertension were extracted from the systematic reviews and meta-analyses as well as the upper and lower frequency limits of DM and hypertension in each geopolitical zone. Studies were selected based on relevance (Fig. 3). Chi-square analysis was carried out to determine the association of some comorbidities to fatal cases of COVID-19. Pearson's correlation was carried out to determine the relationship comorbidities.

Results

Significant differences in the frequency of comorbidities (Hypertension, DM, cardiovascular disease, cancer and chronic kidney disease; CKD) and complications (cardiac injury and ARDS) was observed between fatal and non-fatal cases of COVID-19 ($p< 0.0001$). There were significant correlations between hypertension and acute respiratory disease syndrome (ARDS; $p= 0.002$), DM and ARDS ($p= 0.010$), hypertension and CKD ($p< 0.0001$), DM and CKD ($p= 0.033$), hypertension and DM ($p= 0.001$), CKD and ARD ($p< 0.0001$), hypertension and cardiac injury ($p= 0.055$), DM and cardiac injury ($p= 0.078$), and CKD and cardiac injury ($p= 0.142$).

Discussion

Policies and interventions following COVID-19 pandemic

Following COVID-19 pandemic, most of the policies announced in Nigeria were designed to protect small and medium enterprises. The federal government through the Central Bank of Nigeria (CBN) slashed the interest rates of intervention programmes from 9 to 5% per annum. The bank also extended the loan repayment of affected beneficiaries by one year. A reduction of petrol pump price from 145 to 125 naira was also made. However, only a few healthcare related policies and interventions were also made. One of which is the 100 billion naira healthcare loan to pharmaceutical companies and healthcare facilities for capacity building. No fund was injected into the health sector to allow for simultaneous testing for and treatment of comorbidities associated with high COVID-19 morbidity and mortality. To reduce the fatality rate individuals with family history of cancer and cardiovascular diseases should be properly investigated whether they are positive or negative for the virus. Another 1 trillion naira loan was introduced to boost production across critical sectors of the economy, especially agriculture (8). In another wave of response, the Nigerian House of Representatives (HORs) passed a Bill which seeks to forestall job loss due to COVID-19 by granting 50% income tax rebate to Nigerian companies who retain all their employees. Although the HORs suspended all import duties on medical equipment, medicines and personal protective equipment required for COVID-19 control for a period of three months effective from the 1 of March, borders and international airports remain closed. This appears to have a cancelling impact on the desired effect of the Bill. Interestingly, these interventions were only possible following a proposed budget cut on education and health by the Nigerian government. The initial budget covered the cost of health awareness and the treatment of cancer, vaginal fistulae and other debilitating diseases. Thus, these interventions may ameliorate the short term effects of the pandemic, but the long term impact may reverberate for another century. More importantly, there is no explicit formula or criteria for disbursement of loan or intervention fund among the Nigeria States. Current disbursements are made based on States with the highest number of COVID-19 cases. This plan may be catastrophic since other States with low funds may not be able to adequately prepare for their individual peak incidence.

Utilization of preventive healthcare services and impact of comorbidities

During any pandemic, stratifying high-risk groups remains a key aspect to reducing fatality rate. In countries with developing economies, chronic diseases are associated with a high mortality rate due to low utilization of preventive healthcare services (PHSs). The PHSs allows for early identification of symptomless diseases. Interestingly, the awareness of PHSs could be high in some regions but the uptake is uniformly low across Nigerian States. Since many individuals cannot be risk-stratified due to their unawareness of any undiagnosed comorbidities, a high rate of COVID-19 infection and fatality is expected in Nigeria. For example, in NWN, the awareness of PHSs is approximately 93% and 89% among public and private sector workers but only 44% and 42% of such workers utilize the services, respectively. The awareness is lower in males (39%) than in females (61%) (9). In NCN, the awareness of PHSs is very low (13%). The awareness and the utilization are lower among men (39% and 37%) than among women (61% and 63%) while the uptake is also lower among persons 44 years and younger than those who are 44 years and older (10). Furthermore, the uptake of PHSs is lower in SSN (33%) than in NWN and NCN (43-48%) (9-11). The location of residents may also determine access rate to healthcare facilities. Hence, the high rate of HPHs utilization in urban areas (40%) than in rural areas (22%). A recent study show that about 56% and 66% of people living in SSN have never checked their blood pressure and blood glucose level, respectively (11). This suggested that there could be a high incidence and fatality rate in SSN due to undiagnosed hypertension, diabetes mellitus and cardiovascular diseases. Studies have shown that the barriers to optimum utilization of PHSs include lack of health insurance, cost, low income, proximity of healthcare facility, lack of education, fear of positive result, cultural and religious believes (9, 10). In the US, 85.7% of critically ill patients (with COVID-19) who are transferred to the intensive care unit (ICU) have one or two comorbidities while 50-52.4% of these patients die in ICU and only 9.5-17% are discharged from the ICU (8, 12). In Italy, 68% of patients admitted into the ICU have one or two comorbidities but only 26% of such patients die in the ICU while 16% of the patients are discharged

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(13). Although sample size influences study finding, the reason for the difference in mortality rate between the US and Italy may depend on patient's age and types of comorbidities present. This is buttressed by the fact that the prevalence of DM in severe cases of COVID-19 is higher in the United States (33.3-58.3%) than in China (14.3-31.5%) and Italy (17.0%). The prevalence of CKD in severe cases of COVID-19 is also higher in the US (20.8-57.1%) than in China (1.7-6.7%) and Italy (3.5%). However, higher prevalence of hypertension is reported in China and Italy than in the United States (Tables 1-3). Thus, identifying individuals with comorbidities and evaluating accrued to the individual comorbidities are essential parts of any plan directed at reducing the impact of COVID-19.

Diabetes mellitus and zonal vulnerabilities to COVID-19

COVID-19 has been reported across all ages, but reports have shown that older age to a large extent determines the severity of the disease. According to the reports of Chen et al. in China, 83.2% of COVID-19 associated deaths occur among those who are above the age of 60 years while the remaining deaths occur among those within the age range of 40 to 60 years (14). Similar findings were observed by Onder et al. in Italy. There, 96.4% of the patients are 60 years and above, 3.3% of the patient are within the age group of 40 to 59 years while the remaining patients are within the age group of 30 to 39 years. The susceptibility of older patients could be linked to immunologic aging or dysfunction and a higher prevalence of comorbidities, especially DM and hypertension (13). Diabetes mellitus has been found to increase the vulnerability of individuals to COVID-19 infection. The prevalence of DM is higher in patients with severe COVID-19 disease than in patients with mild symptoms (Tables 1 and 2). A systematic review carried out in 2016 on DM related studies reveal a pooled prevalence of 2.2% while another study in 2018 reveal a pooled prevalence of 5.8% (15, 16). This also suggests that the prevalence of DM increased in Nigeria by 2.6% in a space of 2 years. Evidently, the prevalence of undiagnosed DM ranges from 27 – 41% across Nigerian States, and 7 to 67% of these individuals develop complications. About 34% of the complications are cardiac autonomic neuropathy (17). The high prevalence of undiagnosed DM has been linked to lack of effective screening practices due to partial adherence to screening guidelines. In a country where there is a high prevalence of undiagnosed DM, the fatality due to COVID-19 infection is expected to be high. In Korea, about 18% of hospitalized patients had one or two comorbidities and DM is the most common (7.1%). This is contrary to the reports coming from China where hypertension is the most common comorbidity (Tables 1 and 2). This suggests that geographical location may determine the fatality rate of the disease. Furthermore, the prevalence of DM is higher in urban communities (0.8-7.9%) than in rural communities (0.8-4.4%) of Nigeria (15-17). Just like in urban and rural communities, differences have also been observed be-

Table 1. Comparison of comorbidities of COVID-19 in severe and non-severe cases in China

Variables	Guan et al. 2020 Mainland (5)		Shi et al. 2020 Wuhan (30)		Chen et al., 2020 Wuhan (14)		Zhou et al., 2020 Wuhan (33)	
	Severe n= 173	Mild n= 923	Severe n= 49	Mild n= 438	Death n= 113	Survivor n= 161	Death n= 54	Survivor n= 137
Median age (years)	52	45	56	45	68	51	69	52
Female	73 (42.2)	386(41.8	13 (26.5)	215 (49.1)	30 (26.5)	73 (45.3)	16 (29.6)	56 (40.9)
Male	100 (57.8)	537(58.2)	36 (73.5)	223 (50.9)	83 (73.5)	88 (54.7)	38 (70.4)	81 (59.1)
Hypertension	41 (23.7)	124(13.4)	26 (53.1)	73 (16.7)	54 (47.8)	39 (24.2)	26 (48.1)	32 (23.4)
Diabetes	8 (22.2)	53 (5.7)	7 (14.3)	22 (5.0)	24 (21.2)	23 (14.3)	17 (31.5)	19 (13.9)
Cardiovascular disease	--	--	4 (8.2)	7 (1.6)	16 (14.2)	7 (4.3)	--	--
Cancer	3 (1.7)	7 (0.8)	2 (4.1)	3 (0.7)	5 (4.4)	6 (3.7)	--	2 (1.5)
Chronic kidney disease	3 (1.7)	5 (0.5)	2 (4.1)	5 (1.1)	4 (3.5)	1 (0.6)	2 (3.7)	0 (0.0)
Compt.; Cardiac injury	--	--	--	--	72 (68.1)	18 (11.2)	32 (59.3)	1 (0.7)
ARDS	27 (15.6)	10 (1.1)	--	--	113 (100)	83 (51.6)	50 (92.6)	9 (6.6)

	Wang et al., 2020 Wuhan (4)		Shi et al., 2020 Wuhan (27)		Lei et al., 2020 Wuhan (28)		
	ICU n= 34	NICU n= 102	SCWCI n= 82	SCWTCI n= 334	Death n= 7/15	ICU n= 15	NICU n= 19
Median Age (years)	66	51	74	60	55	55	47
Female	14 (38.9)	49 (48.0)	38 (46.3)	173 (51.8)	4 (57.1)	10 (66.7)	10 (52·6)
Male	22 (61.1)	53 (52.0)	48 (53.7)	161 (48.2)	3 (42.9)	5 (33.3)	9 (47.4)
Hypertension	21 (58.3)	22 (21.6)	49 (59.8)	78 (23.4)	3 (42.9)	9 (60.0)	4 (21.1)
Diabetes	8 (22.2)	6 (5.9)	20 (24.4)	40 (12.0)	1 (14.3)	6 (40.0)	2 (10.5)
Cardiovascular disease	9 (25.0)	11 (10.8)	13 (15.9)	9 (2.7)	4 (57.1)	6 (40.0)	1 (5.3)
Cancer	4 (11.1)	6 (5.9)	7 (8.5)	2 (0.6)	4 (57.1)	5 (33.3)	4 (21.1)
Chronic kidney disease	2 (5.6)	2 (2.0)	5 (6.1)	9 (2.7)	--	1 (6.7)	0 (0.0)
Compt.; Cardiac injury	8 (22.2)	2 (2.0)	--	--	4 (57.1)	5 (33.3)	0 (0.0)
ARDS	22 (61.1)	5 (4.9)	48 (58.5)	49 (14.7)	7 (100)	9 (60.0)	2 (10.5)

Keys: Compt.= Complication, ARDS= acute respiratory distress syndrome, COPD= Chronic obstructive pulmonary disease, ICU= Intensive Care Unit, NICU= Non-intensive care unit, WCI= Severe cases with cardiac injury, WTCI= Without cardiac injury, WBC= White cell count

Table 1 shows that the fatality cases are higher in males than in females. It also shows that the three most prevalent comorbidities in severe COVID-19 disease when compared with non-severe cases in China were hypertension, diabetes and cardiovascular diseases in decreasing order and frequency of occurrence. Hypertension is the most prevalence comorbidity in China. In China, the difference in the prevalence of hypertension and diabetes between severe and non-severe cases ranges from 13.4 to 60.0% and 5.0 to 40%, respectively. The prevalence of cardiac injury and ARDS are higher in death outcome (59.0-68.1% and 92.6-100) than in those who received (60-61.1% and 22.2-33.3%) and did not receive intensive care (0.0-2.0% and 4.9-10.5%, respectively).

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Table 2. Comparison of comorbidities of COVID-19 in severe and non-severe cases outside China

Variable	Bhatraju et al., 2020 US (7)	Arentz et al., 2020, US (12)	Grasselli et al. 2020, Italy (13)	Total cases		Chi-square
	ICU N= 24	ICU N= 21	ICU N= 1591	Fatal N= 2490	Non-fatal N= 1780	p-value
Median age (years)	64	70	63	63.4	48.5	< 0.0001
Female	9 (37.5)	10 (47.6)	287 (18.0)	673 (27.0)	789 (44.3)	< 0.0001
Male	15 (62.5)	11 (52.4)	1304 (82.0)	1823 (73.0)	991 (55.7)	< 0.0001
Hypertension	--	--	509/1043 (48.8)	813 (41.9)	294 (16.5)	< 0.0001
Diabetes mellitus	14 (58.3)	7 (33.3)	180/1043 (17.3)	331 (17.0)	125 (7.0)	< 0.0001
Cardiovascular disease	--	--	223/1043 (21.4)	280 (14.4)	26 (14.6)	< 0.0001
Cancer	0 (0.0)	--	81/1043 (7.8)	109 (5.6)	28 (1.6)	< 0.0001
Chronic kidney disease	5 (20.8)	10 (57.1)	36/1043 (3.5)	79 (40.7)	13 (0.7)	< 0.0001
Compt.; Cardiac injury	--	--	--	199 (8.0)	21 (1.2)	< 0.0001
ARDS	--	--	--	318 (12.8)	109 (6.1)	< 0.0001

Keys: US= United States, Compt.= Complication, ARDS= acute respiratory distress syndrome, COPD= Chronic obstructive pulmonary disease, ICU= Intensive Care Unit, NICU= Non-intensive care unit, WCI= Severe cases with cardiac injury, WTCI= Without cardiac injury, WBC= White cell count. Chi-square analysis

Table 2 shows significant differences in the frequency of comorbidities (Hypertension, DM, cardiovascular disease, cancer and chronic kidney disease) and complications (cardiac injury and ARDS) between fatal and non-fatal cases of COVID-19 (p< 0.0001). A high frequency of DM and chronic kidney disease were found in severe cases in US, though fewer samples were included.

Table 3. Comparison of in systematic studies on frequency of cancer, diabetes and hypertension between geopolitical zones

Variables	Cancer		Diabetes mellitus		Hypertension		
	Morounke et al. 2017 (39) ASR		Dahiru et al., 2016 (15)	Uloko et al., 2018 (16)	Ogah et al., 2012 (43)	Adeloye et al., 2014 (21)	Akinlua et al., 2015 (23)
	Males	Females					
North West	40.5-40.8	59.2-59.5	0.8-6.0	0.8-10.0	24.8-25.7	24.8	3.8-30.2
North East	39.1-45.6	54.4-60.9	2.6	7.0	27.8-40.0	25.2	15.2
North Central	32.4-55.1	44.9-67.6	1.5-2.9	4.0-8.3	27.1	21-27.1	10.1-19.3
South West	25.1- 44.7	55.3-74.9	0.8-11.0	4.4- 7.0	10.1-34.8	9.3-52	0.1-47.2
South East	40.0-42.3	57.7-60.0	3.6-6.7	3.0-10.0	25.1-46.4	31.8-46.4	5.4-46.4
South South	37.9-47.0	53.0-62.1	6.8-10.5	5.0-23.1	13.3-43.0	15-47	2.1-47.0
Males	25.1-55.1	--	0.5-11.6	--	7.9-50.2	10.4-52	6.2-48.9
Females	--	53.0-74.9	0.3-11.2	--	3.5-68.8	7.1-49.3	10.0-47.3
Children	--	--	--	--	--	--	0.1-17.5
Adult	--	--	--	--	--	--	2.1-47.2
Urban	--	--	--	--	13.5-46	9.3-50.5	9.5-51.6
Rural	--	--	--	--	8.1-42	20.2-46.4	4.8-43

Key: NA= Not available, ASR= Age Standardize Incidence Rate

Table 3 shows a higher prevalence of diabetes mellitus and hypertension in Southern Nigeria and males than in Northern Nigeria and females. It also shows higher frequency of hypertension in urban areas and adults than in rural areas and children (≤18 years). The prevalence of cancer is higher in females than in males.

tween geopolitical zones of Nigeria. The pool prevalence of DM in NWN, NCN, SEN, SWN, NEN and SSN is 3.0%, 3.8%, 4.6%, 5.5%, 5.9%, and 9.8%, respectively in increasing order of preponderance (16). The difference should be considered when allocating healthcare resources so as to reduce the fatality of COVID-19 disease in the zones. Mounting evidence show that the prevalence of DM is higher in men than in women (Table 3). This could be related to lower utilization of PHSs among men than women (10). Apart from acute respiratory distress syndrome (ARDS), an adverse clinical outcome found in patients with COVID-19, hypertension have also been linked to DM. The prevalence of co-existing ARDS and DM is 22%, and 8.2% of these patients experience fatal disease (18).

Hypertension, sex and zonal susceptibilities to COVID-19

Following standardization by age and sex, Sub-Sahara Africa, Nigeria inclusive, has the highest proportion of individuals with hypertension (24.9%) when compared with the rest of the world (9.6% in East Asia to 21.0% in Europe). It also have the highest proportion of individuals with uncontrolled blood pressure in those on treatment than the rest of the world (51.0% vs 31.9-48.7%) (19).

Considering the impact of hypertension on COVID-19 progression (Tables 1 and 3), the high prevalence may be predictive of high fatality rate in the region. The prevalence of hypertension, diagnosed as increase blood pressure ≥140/90 mmHg, among individuals with mild and fatal/severe COVID-19 disease is approximately 13-24% and 24-60%, respectively (Tables 1 and 2). In Italy, 65.6% of patients with COVID-19 have one or two comorbidities. Among patients with hypertension, 63% and 40% die in and are discharged from the ICU, respectively (13). Since hypertension increases the fatality rate of the disease, identifying individuals with hypertension is an important step for early flattening of curve in Nigeria. As of 2010 in Sub-Sahara Africa, the prevalence of hypertension was estimated at 74.7 million. It is projected that the number of affected individuals will increase to 110.7 million by the year 2020 (20). Similarly in Nigeria, a total of 20.8 million people who have attained the age of 20 years was estimated to have hypertension in 2012 while 25.4 million people are expected to have hypertension in 2020 (21). This suggests that higher COVID-19 infection rate and fatality may be observed in Nigeria than is currently being predicted. Although the prevalence of hypertension varies from 18 to 54.2% across Nigeria States, the pooled prevalence in men, women, urban and rural communities is 29.5%, 25.0%, 30.6% and 26.4%, respectively (21, 22). The difference between urban and rural communities may be diet related while the difference between men and women may be PHSs related. More so, the pooled prevalence of hypertension in NCN, NWN, NEN, SWN, SSN and SEN is 22.0%, 22.4%, 24.8%, 25.6%, 27.9% and 33.6%, respectively in increasing order of preponderance (20, 21, 23). The high prevalence of hypertension may be due low awareness of hypertension. In Nigeria, the treatment and control among individuals diagnosed with DM ranges from 5 to 77% and 3 to 29%, respectively. Interestingly, higher awareness and treatment are seen in Nigerian males (40% and 24%) than their female counterparts (25% and 17.5%, respectively) however lower control is achieved in men (5%) than in females (18%) (20, 22). Taken together, this suggests that the infection rate of COVID-19 could be 2 times higher in men than in women (20). Again, the prevalence of hypertension is higher in individuals without any formal education (48.5%) than those with any form of formal education (27-33.4%) (24). Education increases the chances of awareness and the likelihood of utilizing PHSs. Thus, individuals without any form of education may have undiagnosed DM and increased chance of COVID-19 infection.

Pathophysiology of DM and hypertension, and treatment related fatality

The high prevalence of hypertension, especially in blacks, has been attributed to mutation in some genes including T594M and R563Q, and polymorphism in G-protein receptor kinase-4 and Cytochrome P450, subfamily IIIA, polypeptide 5 (CYP3A5) (20). This may not be unconnected to the high mortality rate in blacks due to cardiovascular disease when compared with in whites (65 vs 55.8 per 10,000 person-year) (25). Treatment for comorbidities such as diabetes and hypertension using angiotensin II type-I receptor blockers (ARBs) and ACE inhibitors or thiazolidinedione and ibuprofen for hypertension result in elevated levels of angiotensin-converting enzyme 2 (ACE2). Current hypotheses suggest that such treatment induced elevated levels of ACE2 which facilitates the entry of the virus. To mitigate the effects of elevated ACE2 in such patients, antihypertensive calcium channel blockers has been suggested as an alternative treatment option (26). On the other hand, a higher prevalence of cardiac injury, described as significant elevated cardiac troponins, has been reported in older patients than younger patients (27). An infection with the virus may trigger the progression of cardiac injury to death. Thus, the development of cardiac injury pre- or during treatment may account for the difference in mortality rate across affected countries, especially Italy, Spain and Germany (28). Apart from age, sex has also been shown to impact on disease prevalence and severity. A recent report from Seattle (United States) shows that COVID-19 disease is preponderant in males (63%) than in females (38%) (7). Grasselli et al. also reported higher prevalence in males (82%) than in females (18%) (13). The difference could be attributed to the variation of cardiac injury between the two sexes due to levels of ACE2. This is because estrogen in females upregulates the levels and activity of ACE2, a cardiovascular protective agent, thereby reducing the risk of cardiac injury in females (29). This might explain why Shi et al. observed higher prevalence of cardiac injury in males than in females (27) and also accounts for the higher number of severe cases of COVID-19 disease in males (73.5%) than in females (26.5%) (30). Based on multivariate Cox regression analysis carried out by Shi et al. cardiac injury is independently associated with severe COVID-19 disease ($p< 0.001$) (27); it shortens the duration of symptoms onset in affected persons and increases mortality rate (5, 27). Evidence shows that there are higher presentations of comorbidities such as cardiovascular disease, chronic heart failure, cancer, and 4.1:1 in patients with cardiac injury than those without the injury, with ratios of 5.8:1, 9.7:1, 9:1, and 4.1:1, respectively (27). Intriguingly, about 22 to 33% of patients with COVID-19 develop acute cardiac injury while in ICU (Tables 1 and 2). COVID-19 associated cardiac injury arises from fulminant myocarditis following increased circulation of pro-inflammatory cytokines and aggressive inflammatory reaction (31). It can also occurs due to impaired myocardial oxygen demand and supply event following hypoxia and acute respiratory disease syndrome (ARDS) (32). Cardiac injury accounts for over 50-68% in-hospital deaths (14, 27, 28, 33). Since 57-68% of COVID-19 associated deaths are linked to ARDS, it could be suggested that ARDS plays a critical role in the development of cardiac injury; higher prevalence of ARDS predicts higher prevalence of cardiac injury and eventual mortality (Tables 1 and 2). Thus, it is imperative to forestall or monitor the development of ARDS and cardiac injury in hospitalized COVID-19 positive patients in other to reduce mortalities. Fortunately, studies have shown that high levels of hypersensitive cardiac troponin I (>15.6 pg/ml/> 0.009 µg/La) and creatinine kinase–myocardial band (> 1.3 ng/mL) are indicative of poor prognosis among COVID-19 patients with cardiac injury (14, 27).

Cancer related vulnerabilities to COVID-19

Globally, 2.1 million new cases of lung cancer are reported yearly with 18% mortality (34). The cumulative lung cancer risk in Africa (12.8%) is lower than that of the world (18.5%) but the cumulative mortality risk in Africa (9.4%) is high and similar to the pooled prevalence of the world (10.5%) (35). This has to be considered during planning in other to mitigate the effects of COVID-19 in developing countries. The prevalence of cancer is significantly higher in severe/fatal COVID-19 disease than mild cases ($p< 0.0001$; Table 3). Since cancer patients in Africa present at late stage there could be a high number of COVID-19 associated fatalities in African cancer patients than is seen in countries with developed economies. In Nigerian men, the age standardize incidence rate of all aggressive cancer ranges from 58.3 (in the North) to 66.4 per 100,000 (in the South) while that of women ranges from 130.6 (in the South) to 138.6 per 100,000 (in the

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North) (36). This suggests that males in Southern Nigeria have higher frequency of cancer than their Northern counterparts while the reverse is the case for females (Table 3). The frequency of invasive cancer in males ranges from 33.6 to 34% with a mean age of 49.9 to 51.1 years while in females it ranges from 66 to 66.4% with a mean age of 45.4-49.1 years (36). In the US, despite its high screening exercise, about 30% of lung cancer are undiagnosed until its late stages, making lung cancer the most fatal malignancies in the US. Since screening is limited in developing countries the number of undiagnosed cancer could be higher than that of the United States (37). This may influence the fatality rate of COVID-19 disease, especially among those with lung cancer. The frequency of lung cancer, which increased form 2.1% in 2005 to 2.9% in 2009, is higher in men (3.6%) than in women (2.7%) and higher in Southern Nigeria (4.1%) than in Northern Nigeria (2.3%) (38). The difference could be due to tobacco smoking which is higher in men (9.8%) than in women (2.3%) (39). Although the mortality rate among cancer patients decreased from 42% in 2003 to 18% in 2013, the numbers have been seen to fluctuate over the years (40). The level of awareness on lung cancer and its risk factor may have played significant role in the yearly fluctuations in mortality rate in Nigeria. This suggests that the prevalence of COVID-19 could be higher in men than in women, especially those living in Southern Nigeria than in women. This may explain why Lagos State (in South Western Nigeria) has the highest number of COVID-19 morbidity (57.2%) and mortality (3.9%) in Nigeria as of 17 April 2020.

Cancer and angiotensin-converting enzyme 2 and mortality

Apart from age and sex, cancer appears to be another major risk factor for COVID-19 associated death. After the index case, it took about 54 days for Nigeria to record her first COVID-19 related death (23 March 2020). The NCDC stated that the diseased, 67 years old male and a UK returnee, had other comorbidities such as multiple myeloma and diabetes (2). In Wuhan, the prevalence of the virus in cancer patients is 25% with 100% male dominance and 100% fatality (41). Liang et al observed 50% fatality in patients who were both positive for COVID-19 and cancer with 77.7% male predominance (42). This further supports earlier reports which indicate that age, male factor and other underlying diseases such as cancer play critical roles in the severity of the disease. Patients diagnosed with cancer, especially lung cancer, are more susceptible to COVID-19 due to systemic immunosuppression associated with cancer treatment or the cancer cells themselves (42). Liang et al. also observed that cancer patients were older than non-cancer patients (42). The study carried out by Yu et al. shows that the prevalence of COVID-19 is higher in non-squamous cell lung cancer patients who are above the age of 60 years (4.3%) than those below 60 years (1.8%) (41). Since older age has been implicated in COVID-19 susceptibility, the disease could be more fatal in older cancer patients than in young cancer patients, cancer survivors or non-cancer patients. However, there are contrasting reports on the mechanism behind the susceptibility of cancer patients to COVID-19. A study shows that aggressive inflammation and lung injury are linked to cytokine storm which promote the adverse events in COVID-19 disease (43). On the other hand, dysfunctional leukocyte and pro-inflammatory cytokines and decreased maturation of dendritic cells are seen in cancer (44). Studies have shown that the fatality rate is about 2 to 5 times higher in patients with a history of smoking, especially current smokers, than those without any history of smoking (4, 14, 33). Since a majority of cancer patients smoked at one point in their lives, evidence shows that tobacco consumption brokers a truce between the two contrasting pathways of COVID-19 disease and cancer by increasing the level of ACE2 in the body. Evidence suggests that elevated ACE2 increases the risk of mortality in cancer patients. Thus, cancer patients with a history of tobacco consumption require intensive monitoring and less aggressive cancer treatment, decided on a patient-by-patient basis, and psychological counsel during the course of this pandemic.

Prognosticators of COVID-19 disease

According to Zhou et al., older age, elevated d-dimer levels greater than 1 μg/mL, and high Sequential Organ Failure Assessment (SOFA) score in COVID-19 positive patients are early indicators of poor prognosis (33). A recent study shows that a greater number of patients with poor prognosis (35%, 60%, and 82%) have d-dimer, high sensitivity C-reactive protein and lactate dehydrogenase levels of greater than 21 pg/ml, 100 mg/L and 350 U/L, respectively when compared patients with good prognosis (2%, 14%, and 14%, respectively) (14). More so, 39 to 52% of patients with poor prognosis have elevated levels of aspartate aminotransferase greater than >40 U/L (4, 14). Pooled analysis shows that these patients also have significantly lower platelet count (45). These parameters allow for effective monitoring of patients with COVID-19, particularly cancer patients.

Conclusion

To flatten the morbidity and mortality curve of COVID-19 early, the government should appropriately allocate funds to geopolitical zones based on prevalence of comorbidities, especially hypertension and DM. Such high-risk group should be identified, stratified and actively monitored during the course treatment to prevent the development or control the progression of fatal complications such as cardiac injury and ARD. More isolation centres should be built and equipped for the treatment of COVID-19 positive patients away from hospitalized patients. More so, active follow-up and supportive care should be initiated on discharged patients who developed cardiac injury and ARDS during hospitalization to prevent death post-hospitalization.

Conflict of Interests

The authors declare that they have no competing interests.

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