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Life Expectancy and SARS-CoV-2 Genomic Variations Plays Key Role in COVID-19 Transmission and Low Fatality Rate in Africa

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Abstract

The novel coronavirus disease (COVID-19) has claimed lots of lives, posing a dire threat to public health and the global economy. The present study determined the severe acute respiratory syndrome-2 (SARS-CoV-2) genomic variability and the contributory factors to the observed low fatality rate in Africa. To assess the SARS-CoV-2 mutational landscape, 924 viral sequences from the Africa region with their sociobiological characteristics mined from the GISAID database were analyzed. The age of infected patients, the number of tests done, confirmed cases, recovery, fatality, and countries' age distribution were obtained to determine the age distribution, testing, recovery, and fatality rate. Mutational analysis of the SARS-CoV-2 sequences revealed highly recurrent mutations in the Spike glycoprotein D614G (97.2%), concurrent R203K, and G204R (65.2% respectively) in the N protein region, and P4715L (97.2%) in the RNA dependent RNA polymerase region. COVID-19 is more severe in older people (> 65 years), Africa has a low percentage of people within this age group (4.36%). The average age of the 924 infected patients in this study is 46 years with only 47 infected patients (5.1%) above 65 years in comparison to 13.12% in countries in other continents with the highest prevalence of COVID-19. Africa's young generation, the late incidence of the disease, and adherence to public health guidelines are important indicators that may have contributed to the observed low COVID-19 deaths in Africa. However, sufficient data is still unavailable due to low testing rate to ascertain the epidemiology, transmission, genomic variation, and the true impact of the pandemic in Africa

Keywords: Coronavirus, mutations, low fatality, SARS-CoV-2, pandemic, Africa.

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative pathogen of the novel coronavirus disease 2019 (COVID-19) was first reported in December 2019 in Wuhan, China [1,2]. The highly infectious SARS-CoV-2 has spread globally within 3-months of its first outbreak and has posed dire stress on public health and global economy [1,3]. Globally, as of September 13, 2020, there have been 29,474,968 confirmed cases and 933,423 reported deaths due to COVID-19 [4]. It was predicted that the coronavirus outbreak in the African population would be very lethal and result to economic devastation owing to the prevalence of immune-compromised population (due to HIV/AIDS, tuberculosis, hepatitis virus, malaria etc.), poverty, low lifespan, fragile health care systems, poor economic decisions, and lifestyle factors [3,5]. Africa was the last continent to be hit, and surprisingly boast of about 80 % recovery rate as at this stage of the pandemic [6]. Africa accounts for 3.5 % of the fatality rate recorded globally with the highest death toll reported in Americas (55.1 %) and Europe (25.7 %) which are developed regions with high standard of living and healthcare structure [6,7]. In line with public health and World Health Organization guidelines, African governments and policy-makers were quick to institute policies (restrictions such as partial/full-scale lockdowns, physical distancing, accelerated contact tracing, self-isolation and quarantine) and adopt public health measures in light of the index case in the continent [7–9]. Africa's index case of COVID-19 was on 14th of February, 2020 in Egypt [10], North Africa, and on 27th of February, Nigeria, sub-Saharan Africa reported its index case from an European traveller [11]. As of September 13, 2020 there have been 1,359,569 confirmed cases and 32,678 deaths in Africa, out of which South Africa has the highest toll with 649,793 confirmed cases and 15,447 deaths [4].

Coronaviruses are single-positive-stranded RNA viruses with the largest genome (ranging from 26 to 32 kb) among all RNA viruses consisting of ORF1ab polyprotein (7096 amino

acids), ORF3a (276 aa), ORF6a (62 aa), ORF7a (122 aa), ORF7b (44 aa), ORF8 (64 aa), ORF10 (39 aa) and four structural proteins; nucleocapsid phosphoprotein (N), membrane protein (M), envelope protein (E), and the spike glycoprotein (S) [1,12–14]. Accumulation of mutation is central to viral evolution, transmission and virulence. This gives virus selective advantage for host invasion and adaptation, higher transmissibility of more virulent strains and drug resistance [9,14,15]. Identifying the mutational pattern of coronaviruses and monitoring their spread can be important in guiding drug/vaccine development, and in making decisions to curtail the transmission [16]. The present study aims to gain insight into the mutational landscape of the SARS-CoV-2 genome in African population which may serve as eventual targets for drug design and/or vaccine development. This study also assesses the contributory factors to the low fatality rate due to COVID-19 in the African continent.

Materials and methods

Data acquisition

A total of 924 available SARS-CoV-2 genomic sequences in Global Initiative on Sharing All Influenza Data (GISAID) database as of September 2, 2020 filtered as "high coverage only, *Homo sapiens*, complete, all clades and low coverage excl", with patient's status, Africa were mined from the GISAID web interface (https://www.epicov.org/epi3/frontend) and analyzed. Patient's age of all the sequences were also obtained to determine the age distribution of the infected patients. The accession numbers and laboratories in Africa that sequenced and deposited complete SARS-CoV-2 genomes on the GISAID database used in this study are provided as Supplementary file S1.

Country data of number of confirmed cases, recoveries, reported deaths due to COVID-19 were obtained from Worldometer and WHO database [4,7]. The number of tests done per country and each nation's population was obtained from worldometer database [4]. The age distribution of countries with highest prevalence of COVID-19 cases were obtained from the World Fact book [17].

Sequence and mutational analysis

In this study, the mined 924 SARS-CoV-2 viral sequences were used to analyze the genomic variability since the index case of COVID-19 pandemic in Africa in February 2020 to identify the frequency and spread of mutations in the African population. The evolution of COVID-19 outbreak with respect to the transmission in the mutational hotspots was assessed and evaluated on the GISAID web interface (https://www.epicov.org/epi3/frontend). Recurrent mutations observed were focused on as they are likely to confer viral-host structure-function relationship promoting higher transmission rate.

Determination of Testing, Fatality and Recovery Rate

The testing rate was determined for each African country as percentage of total test done from the country's population. The fatality rate was determined as percentage of total reported deaths due to COVID-19 from each country's number of confirmed cases. The recovery rate was determined as percentage of number of infectious patients who recovered from all reported confirmed cases in each country.

Results

Genomic variabilities dispersed at various sites in the SARS-CoV-2 sequence were observed, few mutations occurred more frequently (represented as Table 1). Mutational analysis of the 924 SARS-CoV-2 sequences revealed highly recurrent mutations in D614G (898 viral sequences) which falls in the S glycoprotein region, and was observed concurrently with P4715L variant (898 viral sequences) in the ORF1ab polyprotein region. More so, R203K and G204R mutations (602 viral sequences respectively) in the nucleocapsid phosphoprotein region, Q57H (60 viral sequences) in the ORF3a region, L84S (16 viral sequences) in the ORF8 region and L3606F (45 viral sequences), G3278S (73 viral sequences), T265I (26 viral sequences) in ORF1ab polyprotein region were observed. It is worthy of note, 97.3% of viral sequences with the nsp5 G3278S mutation were from South Africa. The distribution of the mutations flags the Spike S1 domain (D614G), N protein R203K and G204R and nsp12 P4715L as SARS-CoV-2 mutational hotspots in the African population. According to mutational pattern, the viral sequences were characterized into the GISAID six (6) clades; GR (598), G (240), GH (57), S (16), O (7), V (4) and L (2).

For the age distribution, the average age of the infected patients is 46 years with only 47 infected patients (5.1%) above 65 years. According to demographic data from world fact book, the percentage of population of Africans ≥ 65 years is 4.36% in comparison to 13.12% in countries in other continents with highest prevalence of COVID-19 (as shown in Figure 1). As at this stage of the pandemic, Africa still face the challenge of low testing as none of the African countries meet up with the 15% testing rate standard, as South Africa has the highest testing rate (6.59%) in Africa. Nevertheless, there is a high recovery rate and low fatality rate observed across the Africa continent. The trend and distribution of confirmed cases, discharged cases, fatality and recovery rate are as shown in Table 2

Table 1. Recurrent mutations observed in the viral samples (N = 924 viral sequences)

S/N	SARS-CoV-2 region	Mutation observed	Occurrence
1	Spike protein; S1 domain	L18F	2
2		A222V	4
3		D614G	898
4	Spike protein; S2 domain	E780Q	2
5	Nucleocapsid phosphoprotein	P13L	2
6		R203K	602
7		G204R	602
8	ORF3	Q57H	60
9		G251V	4
10	ORF8	L84S	16
11	ORF1ab; nsp2	T265I	26
12		D448del*	6
13		I739V	3
14		P765S	3
15	ORF1ab; nsp5	G3278S	73
16	ORF1ab; nsp6	L3606F	45
17	ORF1ab; RdRp	A4489V	3
18		P4715L	898

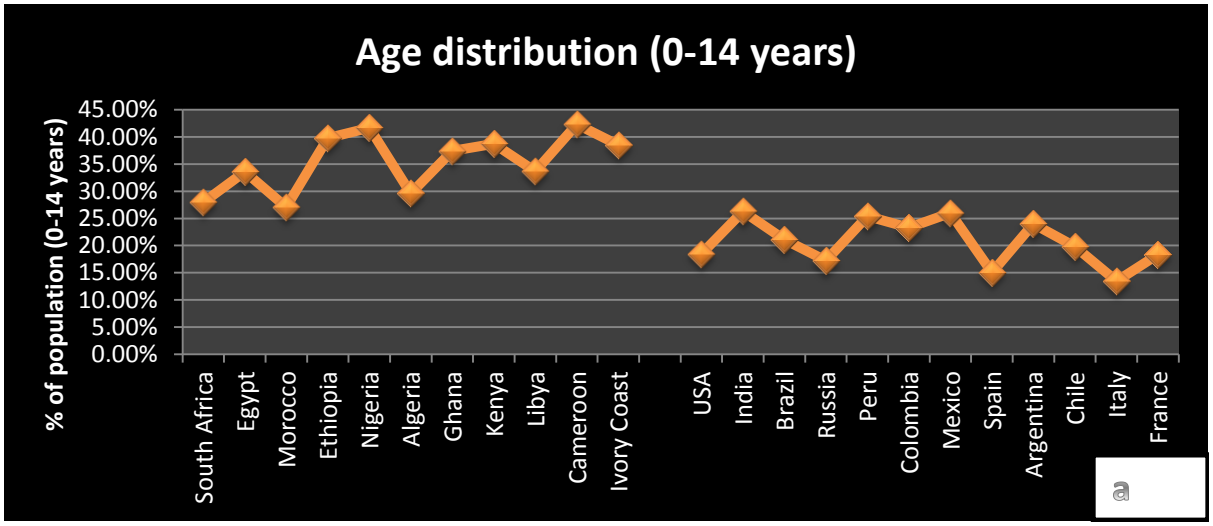
Highly recurrent mutations were observed in the spike protein, nucleocapsid phosphoprotein and ORF1ab, flagging these regions as SARS-CoV-2 mutational hotspots.

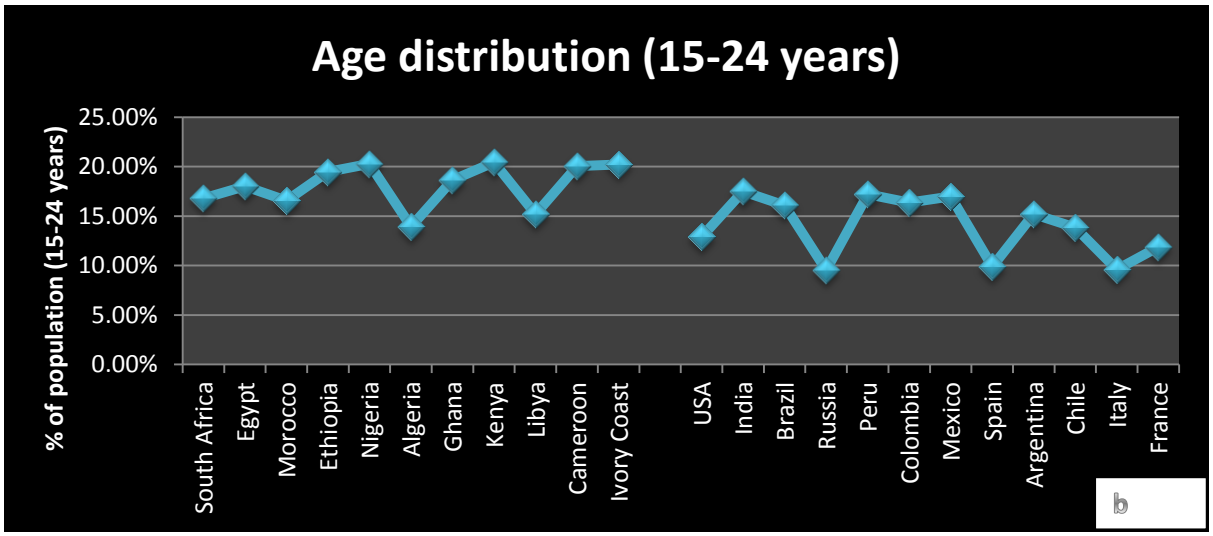
*Key: RdRp – RNA dependent RNA polymerase. One letter code for corresponding amino acid: A – alanine, D – aspartic acid, G – glycine, E – Glutamate, R – arginine, K – lysine, Q – glutamine, H – histidine, V – valine, L – leucine, S – serine, T – threonine, I – isoleucine, P – proline, and F – phenylalanine.

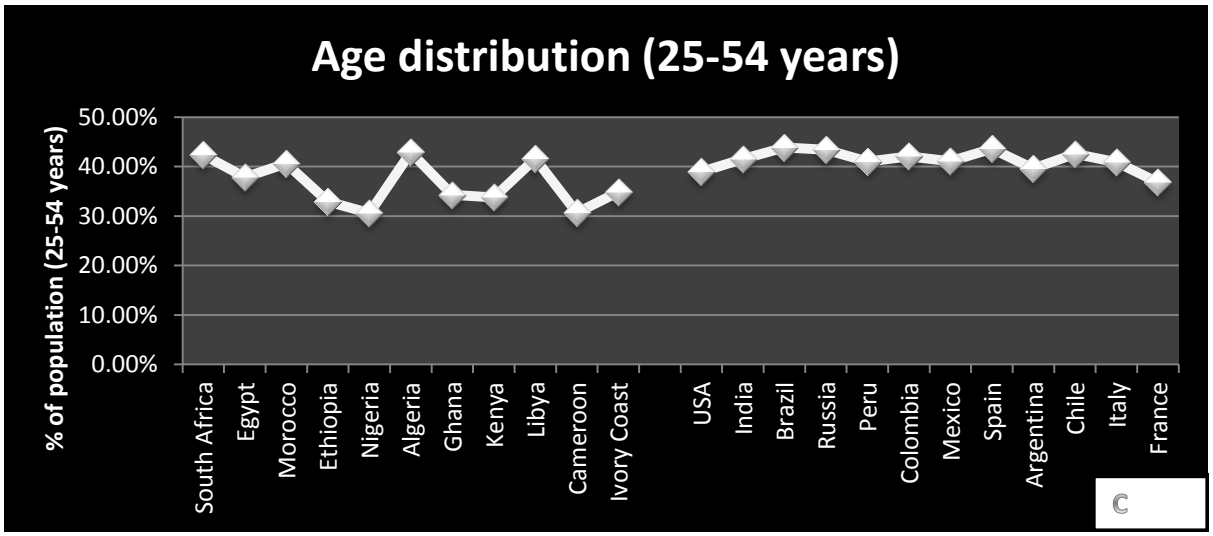
Table 2. Trend and distribution of confirmed cases, discharged cases and fatality rate across Africa

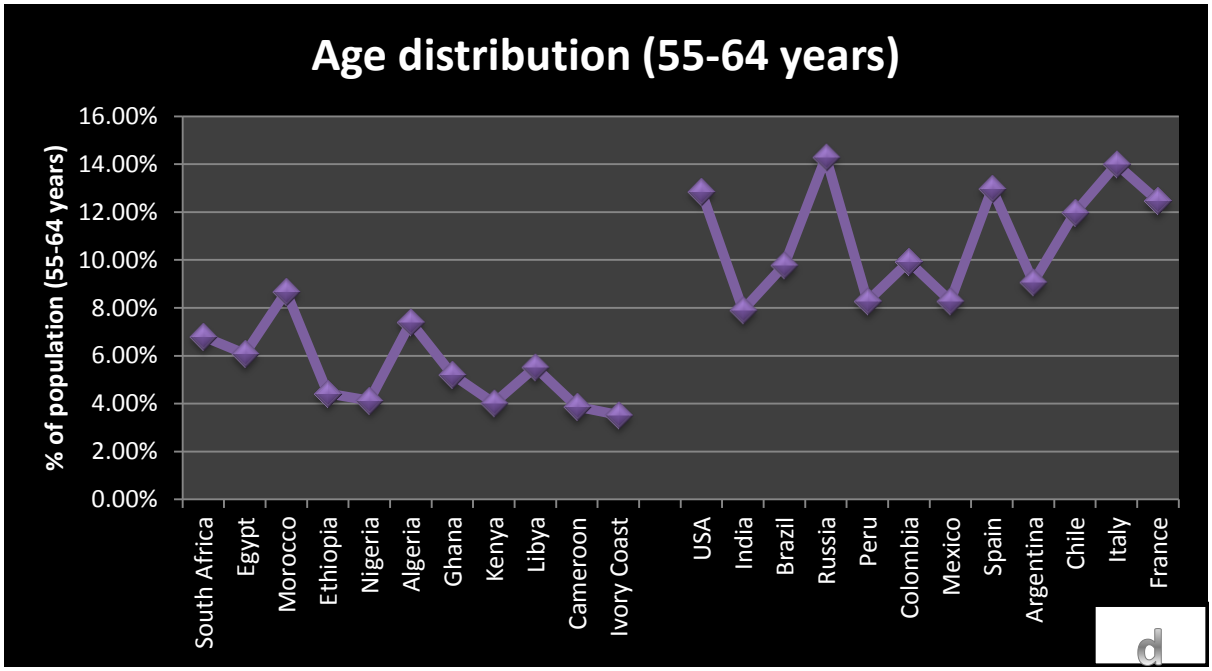
S/No	Country	Confirmed cases	Total deaths	Recovered cases	Total test done	Population	Testing rate	Fatality rate	Recovery rate
	Africa	1,359,569	32,678	1,104,047				2.40%	81.21%
1	South Africa	649,793	15,447	577,906	3,918,478	59,461,240	6.59%	2.38%	88.94%
2	Egypt	101,009	5,648	84,161	135,000	102,722,504	0.13%	5.59%	83.32%
3	Morocco	86,686	1,578	67,528	2,230,069	36,999,965	6.03%	1.82%	77.90%
4	Ethiopia	64,301	1,013	24,983	1,138,012	115,528,092	0.99%	1.58%	38.85%
5	Nigeria	56,256	1,082	44,152	440,248	207,152,368	0.21%	1.92%	78.48%
6	Algeria	48,254	1,612	34,037		44,010,565		3.34%	70.54%
7	Ghana	45,434	286	44,342	450,872	31,202,737	1.44%	0.63%	97.60%
8	Kenya	36,157	622	23,067	481,982	54,007,662	0.89%	1.72%	63.80%
9	Libya	22,781	362	12,183	157,481	6,890,311	2.29%	1.59%	53.48%
10	Cameroon	20,167	415	18,837	149,000	26,676,814	0.56%	2.06%	93.41%
11	Ivory Coast	19,013	120	18,112	142,248	26,507,763	0.54%	0.63%	95.26%
12	Madagascar	15,757	211	14,368	64,174	27,831,811	0.23%	1.34%	91.18%
13	Senegal	14,280	297	10,520	158,751	16,831,055	0.94%	2.08%	73.67%
14	Zambia	13,539	312	12,260	131,034	18,485,203	0.71%	2.30%	90.55%
15	Sudan	13,516	835	6,757		44,052,920		6.18%	49.99%
16	DRC	10,390	264	9,756		90,093,630		2.54%	93.90%
17	Guinea	10,045	63	9,292	28,140	13,203,001	0.21%	0.63%	92.50%
18	Namibia	9,719	101	6,543	80,352	2,550,174	3.15%	1.04%	67.32%
19	Gabon	8,643	53	7,706	135,615	2,236,175	6.06%	0.61%	89.16%
20	Zimbabwe	7,526	224	5,678	154,733	14,906,868	1.04%	2.98%	75.45%

This shows the countries with highest prevalence of COVID-19 in Africa, the data for all African countries is available as Suppl. file S2. The fatality due to COVID-19 in Africa is 2.4% with 81.21% recovery rate. South Africa has the highest COVID-19 testing rate (6.59%) in Africa.


Age distribution (0-14 years)
% of population (0-14 years)
45.00%
40.00%
35.00%
30.00%
25.00%
20.00%
15.00%
10.00%
5.00%
0.00%
South Africa
Egypt
Morocco
Ethiopia
Nigeria
Algeria
Ghana
Kenya
Libya
Cameroon
Ivory Coast
USA
India
Brazil
Russia
Peru
Colombia
Mexico
Spain
Argentina
Chile
Italy
France
a


Age distribution (15-24 years)
% of population (15-24 years)
25.00%
20.00%
15.00%
10.00%
5.00%
0.00%
South Africa
Egypt
Morocco
Ethiopia
Nigeria
Algeria
Ghana
Kenya
Libya
Cameroon
Ivory Coast
USA
India
Brazil
Russia
Peru
Colombia
Mexico
Spain
Argentina
Chile
Italy
France
b


Age distribution (25-54 years)
% of population (25-54 years)
50.00%
40.00%
30.00%
20.00%
10.00%
0.00%
South Africa
Egypt
Morocco
Ethiopia
Nigeria
Algeria
Ghana
Kenya
Libya
Cameroon
Ivory Coast
USA
India
Brazil
Russia
Peru
Colombia
Mexico
Spain
Argentina
Chile
Italy
France
c



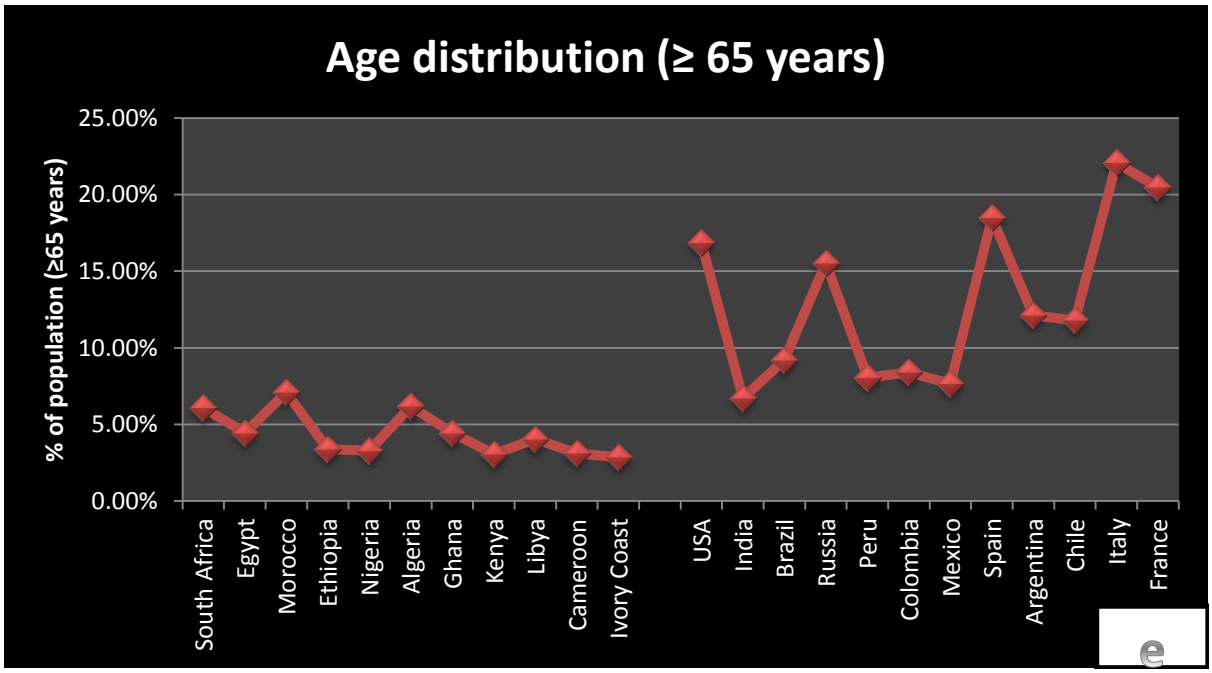


Figure 1a-e. Age distribution of African countries in comparison with nations from other continents with the highest prevalence of COVID-19. This reveals a high prevalence of younger generations in Africa (0-14 years), with equilibrium at age range 15-54 years when compared to older population (≥55 years) in other regions studied with high COVID-19 prevalence.

Discussion

As of September 5, 2020, over 705 million people in the world live in extreme poverty compared to about 651 million people in 2019 [5]. In 2020, 102,125,917 people are reported to be living in extreme poverty from a total population of 205,323,504 people in Nigeria, the most populous African nation compared to 200,369,248 people, among whom 92,441,550 people lived in extreme poverty in 2019 [5]. The COVID-19 has significantly ravaged economies and posed serious threat to public health and social interaction, spreading across the globe within 3 months of its outbreak [3]. It was hypothesized that low- and middle-income countries, especially African nations would be seriously hit by the pandemic due to her vulnerability to infectious diseases and inadequate health structure. Surprisingly, there have been very low mortality rate due to COVID-19 in African nations when compared to developed nations in the Americas and Europe where the pandemic has had its highest toll of infection and fatality [7]. This study assessed the possible factors that could have accounted for the low mortality rate due to COVID-19 in Africa.

The dataset from infected patients helps to understand the COVID-19 infection rate, risks, epidemiology and spread of the disease. The WHO suggested 10 – 30 tests per confirmed case as an indicator of adequate testing [7]. South Africa has the highest test rate of 3,918,478 people in Africa, representing 6.59 % of its 59,461,240 population, which is still a way long off from the adequate testing indicator. Meanwhile, Nigeria has only tested 440,248 people representing 0.21% of its over 207 million population, this trend holds true for many other African countries. Hence, caution should be taken while interpreting these data as the true number of COVID-19 cases in Africa might still remain undetected. However, with the current data available, though with daily increasing incidence, the mortality rate due to COVID-19 in Africa has been minimal. Other factor such as late incidence of the disease [10,18], which gives an advantage for early preparation before the outbreak by enforcing

regulatory guidelines (active surveillance, isolation, quarantine, contact tracing and social distancing among others) in line with World Health Organization guidelines could have played a key role in managing the pandemic in Africa [7,8]. The APM Research laboratory carried out an extensive study in August, 2020 which identified 88.4 deaths per 100,000 Black Americans compared to 54.4 deaths per 100,000 Latino Americans and 36.4 deaths per 100,000 Asian Americans suggesting higher mortality due to COVID-19 in the latter [19]. This raises a concern to understand why Blacks are dying more due to COVID-19 overseas than in Africa.

The present study also looked into the mutational landscape of SARS-CoV-2 genome in Africa. Highly recurrent mutation (D614G) was observed in the S1 domain of S glycoprotein which facilitates viral entry into host by binding to the human angiotensin-converting enzyme2 (ACE2) receptor. The S2 domain of the S glycoprotein which plays a crucial role in viral-host cell membrane fusion was well conserved; this could serve as an important target for antiviral drug design. The T265I mutation that is prevalent in USA which aids SARS-CoV-2 survival in the host cell [20] was only observed in 26 viral sequences, predominantly in Senegal (69.23 %). P4715L mutation hotspot present in the RNA dependent RNA polymerase (RdRp) region was first observed in Italy during the sporadic increase in incidence and fatality of COVID-19 in Europe [15]. This supports the evidence that most Africa's index case originates from European and American travellers [3,18], which could have resulted to the vast distribution of these mutations across the infected patients.

The concurrent R203K and G204R mutation are present in the N phosphoprotein region, which plays an important role in viral interaction with the M protein during virion assemblage [21]. Mutations in the nucleocapsid region alter miRNAs binding, which might contribute to the pathogenesis and progression of infection in the patient [22]. The viral ORF3a and ORF10 proteins can synergistically attack heme on the host's hemoglobin 1-β

chain, thereby disintegrating iron to form porphyrin. This results to reduced hemoglobin carrying oxygen and carbon-dioxide causing extreme poisoning and inflammation of the hepatocytes [23]. Q57H mutation in the ORF3a region was observed to coincide with D614G and P4715L variants. The RdRp P4715L mutation coincides with S protein D614G mutation alongside the concurrent N protein R203K and G204R variants, and in their absence ORF3a Q57H variant. The SARS-CoV-2 membrane, envelope, ORF6, ORF7 and ORF10 proteins were well conserved. These mutational hotspots and conserved domains must be well-considered during drug or vaccine design to avoid vaccine evasion and drug resistance.

Lastly, this study looked at the age distribution of the infected patients as a contributory factor to the low fatality rate. The average life expectancy in Nigeria is 54 years, a reflection of Sub-saharan Africa (61 years) compared to European union (81 years), China (77 years), and USA (79 years) [24]. Earlier report [3] suggests that COVID-19 have high mortality and severity in older people (>65 years) than the younger population, which have high chances of recovery from the infection. From this study, only 5.1 % of the 924 infected Africans whose age are deposited alongside their viral sequences in the GISAID repository are over 65 years. This could have played a major role in the relatively high recovery rate (81.21 %) and low mortality (2.4 %) due to COVID-19 observed in the African population.

Conclusion and perspective

As of now, the highly infectious COVID-19 continues to spread globally, with increasing incidence and mortality. The African continent continues to enjoy the benefit of the swift actions and policies imposed to curtail the pandemic. With the gradual easing of these measures, increasing poverty, poor healthcare structure and a large percentage of immune-compromised population, it is important that the populace adhere to regulatory guidelines. Low life expectancy, low testing rate, late incidence of the disease, adherence to public health

guidelines could be important factors that have contributed to the observed low COVID-19 fatality in Africa. However, sufficient data is still unavailable to ascertain the epidemiology, transmission, genomic variation and the true impact of the pandemic in Africa. Genomic sequences are important in the design and development of antiviral drugs and vaccine. From the over 100,000 complete SARS-CoV-2 sequences available in public repositories, Africa has barely contributed over 2,000 viral sequences (2 %). Collaboration with scientists and research institutes in African nations is highly recommended so as to enhance their delivery capacity.

Conflict of interest

None

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