

Coronavirus Pandemic

COVID-19 imported cases and severity: expected information from genomic characterization of SARS-CoV-2 strains in Mozambique

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Abstract

Introduction: The novel coronavirus, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), etiological agent of coronavirus disease 2019 (COVID-19) was first reported in China in December 2019 and spread worldwide. As of March 6th, 2021, there have been 116,670,105 million confirmed cases globally including 2,592,085 deaths. COVID-19 cases have been reported in 219 countries and territories, creating global panic. Mozambique has witnessed the evolution of COVID-19 epidemic associated with the weakness of health system, mostly in terms of laboratory diagnosis capacity, concerns on compliance to effective public health measures including physical distancing, use of masks in crowded indoor areas, hand hygiene, isolation and quarantine of people.

Methodology: The data included in this study were collected from published articles regarding COVID-19 imported cases and severity in Africa, especially in Mozambique. Additionally, official documents of COVID-19 epidemiology from Minister of Health and National Institute of Health of Mozambique from 22nd of March 2020 to 1st of August 2020 were included.

Results: The SARS-CoV-2 strains imported mainly from South Africa and European countries might have been playing an important role on COVID-19 epidemic evolution in Mozambique.

Conclusions: These circulating strains in the country, might be similar enough to the strains found in other countries, yet the genomic characterization is needed particularly during the phase of borders reopening through understanding the source of infections and guiding the implementation of containment and mitigation measures in the country.

Key words: COVID-19 imported cases; severity; genomic characterization; SARS-CoV-2; Mozambique.

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Introduction

The novel coronavirus, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), emerged in Wuhan, Hubei Province (China) in December 2019 and in less than three months spread throughout the globe causing a highly contagious disease called coronavirus disease 2019 (COVID-19) [1-3].

The World Health Organization (WHO) officially declared the outbreak a pandemic on March 11st, 2020 [4]. To date (March 6th, 2021), COVID-19 has spread to 219 countries and territories, including 57 African countries. According to Worldometer, 03:32 GMT (a reference website that provides real-time worldwide statistics), 3,975,048 COVID-19 cases have been reported in Africa as the last continent to be hit by the pandemic with 105,405 deaths, mostly in South Africa, Egypt, Morocco, Tunisia, Algeria, Ethiopia and Libya [5].

The first COVID-19 cases have been travel-related (imported cases) in several countries. The first SARS-

CoV-2 case in Africa was reported on February 14th, 2020 in Egypt, which was from a contact of a person with a history of travel to China. In the sub-Saharan region, the first COVID-19 case was reported in Nigeria on February 27th, 2020 from an Italian citizen who worked in Nigeria [6], and the first case in Southern Africa was reported on March 5th, 2020, in South Africa from a citizen returning from Italy [7]; whilst in Mozambique the first COVID-19 case, was reported on March 22nd, 2020 from a 75-year-old Mozambican man, who returned from United Kingdom [8].

The tracking and analyses of demographic, clinical patient as well as genomic information have been accomplished worldwide to understand the transmissibility and COVID-19 severity. The COVID-19 severity has been associated with several factors including people with underlying comorbidities, such as chronic lung disease, serious heart conditions, high blood pressure, obesity and diabetes and age, where individuals older ≥ 65 years are at higher risk [9-11].

For instance, fatality case of 1.38 % was reported from China, with substantially higher ratios in older age groups; 0.32 % in those aged < 60 years vs. 6.4 % in those aged ≥ 60 years, up to 13.4 % in those aged 80 years or older [12]. In addition to this, genomic variation of virus has medical and biological impacts on the prevention, diagnosis, and therapy of the diseases [13].

The current emergence of newer SARS-CoV-2 variants in many countries underlines the significance of enhancing efforts to sequence the genome of the virus from across the globe including Mozambique [14]. In the present study the COVID-19 imported cases and severity were analyzed to understand the epidemiology of the disease and to highlight the future information that might be obtained through genomic characterization of SARS-CoV-2 strains in Mozambique.

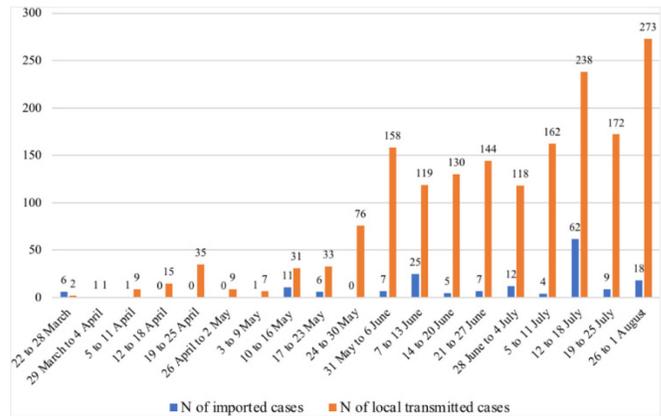
COVID-19 epidemic in Mozambique, from March 22nd to August 1st, 2020

COVID-19 imported cases

COVID-19 epidemic was firstly related to imported cases like in other countries, where the first case was reported on March 22nd 2020, from a 75-year-old Mozambican man, who returned from United Kingdom [8].

Within the analyzed 19 epidemic weeks the COVID-19 cases raised steadily in the country. On August 1st, 2020, 1,907 cases were reported, of which,

Figure 1. Local and imported in Mozambique, from 22nd of March 2020 to 1st of August 2020.



175 (9 %) imported and 1,732 (91 %) locally transmitted (Figure 1 and Table 1). In the first epidemic week (March 22nd to March 28th, 2020), the COVID-19 disease was dominated by imported cases (in total 6), from the UK, South Africa, Portugal and France. From April 5th to April 11st, 2020 the imported cases started to decrease, where from April 12nd to May 2nd no imported cases were reported, whilst the local transmitted cases increased.

Notably, in five epidemic weeks, May 10th to May 16th; June 7th to June 13th; June 28th to July 4th; July 12nd to July 18th; and July 26th to August 1st, 2020; 11, 25, 12, 62 and 18 COVID-19 imported cases, respectively, were reported.

Table 1. Evolution of COVID-19 epidemic and imported in Mozambique.

Epidemic week	N of tested cases	N of reported cases	N of imported cases	N of local transmitted cases	Countries
22 to 28 March	174	8	6	2	United Kingdom, South Africa, Portugal, France and England
29 March to 4 April	136	2	1	1	Portugal
5 to 11 April	210	10	1	9	Portugal
12 to 18 April	299	15	0	15	-
19 to 25 April	619	35	0	35	-
26 April to 2 May	751	9	0	9	-
3 to 9 May	1,402	8	1	7	Portugal
10 to 16 May	1,964	42	11	31	South Africa*
17 to 23 May	2,203	39	6	33	South Africa*
24 to 30 May	2,312	76	0	76	-
31 May to 6 June	3,133	165	7	158	South Africa*
7 to 13 June	4,647	144	25	119	South Africa*
14 to 20 June	5,043	135	5	130	South Africa*
21 to 27 June	4,852	151	7	144	Malawi*
28 June to 4 July	4,543	130	12	118	South Africa*
5 to 11 July	6,593	166	4	162	South Africa*
12 to 18 July	6,098	300	62	238	Eswatini and South Africa*
19 to 25 July	6,255	181	9	172	South Africa and Malawi*
26 to 1 August	7,547	291	18	273	Zimbabwe and South Africa*
Total	58,871	1,907	175 (9 %)	1,732 (91 %)	-

* Other countries might be involved.

From May 10th to August 1st, 2020, COVID-19 imported cases were mainly from African countries including South Africa, Malawi, Eswatini and Zimbabwe. These countries share borders with Mozambique.

The analyzed period shows that from March 22nd to May 9th, 2020, the imported cases were originated from European countries and from May 10th to August 1st are tracked to African countries. However, there is a paucity of published data related to the profile of COVID-19 imported cases, so there might have been involvement of other countries [8].

The number of COVID-19 positive tests were considerably higher from May to August 1st, 2020 following the increased testing capacity. In total 58,871 COVID-19 tests were done during the analyzed period as an essential step in fighting COVID-19 (Table 1).

By July 26th, 2020, 51.7 per 1 million of habitants were positive against the 11.3 registered on June 5th that might be related to increased testing capacity in Mozambique [8].

COVID-19 severity

Individuals of all ages are at risk for infection and severe COVID-19 disease, but it has been noticed that serious COVID-19 disease is higher in people aged \geq 60 years, and in those with chronic medical conditions. On August 1st, 2020, 1907 confirmed COVID-19 cases were reported in Mozambique, with 645 patient (34 %) recovered and 12 (0,6 %) died. Death rate was 0.4 % per 1 million of habitants by July 26th, 2020 [8].

Most of recovered patients were observed in the last two analyzed epidemic weeks, July 19th to July 25th and July 26th to August 1st, with 135 and 102 cases, respectively (Table 2). In addition, 49 patients were hospitalized and only 10 (20 %) remained in hospital by August 1st, 2020.

The COVID-19 fatalities included children (4) and adults (8), the majority were male and occurred in Nampula followed by Maputo city provinces (both provinces having community transmission) and were associated mainly with comorbidities including hypertension, pulmonary and cardiac diseases (Table 3).

Expected information and role of genomic characterization

Strains imported from Europe and African countries might have been playing important role in the evolution of COVID-19 in the country. It is expected that these strains of SARS-CoV-2 from these countries are evolving in Mozambican population and a typical profile could emerge. The rapid spread of SARS-CoV-2 associated with non-compliance of COVID-19 measures, and also regional or international travels that contribute to the importation of SARS-CoV-2 might be important factors in the emergence of a newer strains in Mozambique. Several efforts with the aim to slow down the transmission of COVID-19 have been implemented in the country including the improvement of laboratory diagnosis capacity and monitoring the compliance to preventive measures.

Table 2. COVID-19 severity in Mozambique.

Epidemic week	N of reported cases	N of recovered patients*	N of deaths**
22 to 28 March	8	0	0
29 March to 4 April	2	1	0
5 to 11 April	10	1	0
12 to 18 April	15	2	0
19 to 25 April	35	5	0
26 April to 2 May	9	10	0
3 to 9 May	8	16	0
10 to 16 May	42	9	0
17 to 23 May	39	8	0
24 to 30 May	76	39	2
31 May to 6 June	165	36	0
7 to 13 June	144	25	0
14 to 20 June	135	25	2
21 to 27 June	151	48	1
27 June to 4 July	130	31	2
5 to 11 July	166	93	2
12 to 18 July	300	59	1
19 to 25 July	181	135	1
26 to 1 August	291	102	1
Total	1,907	645	12

Limited information is available regarding the SARS-CoV-2 strains characterized by Whole Genome Sequencing (WGS) in Mozambique according to our knowledge. Thus after borders reopening and allowing the international travel, the genomic characterization of SARS-CoV-2 strains could be very important tool to better understand and to monitor the COVID-19 epidemiology in the country. This is a very important tool to monitor the emergence of new pathogenic strains including SARS-CoV-2 strains [14,15].

Genome tools such as WGS provide highest resolution information about an organism with accurate identification of virulence factors, path of disease transmission within a population and provide information on the probable source thereby facilitating infectious disease management [15,16].

SARS-CoV-2 has been spreading worldwide, allowing the emergence of distinct lineages of viruses circulating in different regions. The rapid genomic surveillance by WGS is helpful in comparing sequences in order to quickly rule out possible lines of transmission of SARS-CoV-2 infections. This powerful tool is also useful in monitoring the spread and identifying the source of some cases, where contact tracing fails and when international travel resumes [15,17].

Despite the fact that WGS could provide plenty of data on SARS-CoV-2 infections, it is more important to include the antigenic sequencing approach, since in some cases the virus escapes due to the viral load in the earlier period of the disease or during recovery stage [18].

The antigenic sequencing can help to perform antigen tests to detect the viral presence in symptomatic or asymptomatic individuals. Immunoassays mostly through antigen tests can be used as a complementary method of genomic surveillance due to its advantages that include simplicity of utilisation, lower costs and rapidity of the result which allow an increased volume

of testing and faster isolation of people who test positive. The isolation of positive cases plays important role in breaking chains of transmission.

In summary, data on genetic features of the virus could save lives by forming strategies for public health and clinical care, as well as helping the design of therapies and vaccines to combat the virus. In addition, this tool can enhance surveillance of the virus and provide better understanding of transmission patterns. Next-generation sequencing has been considered an important role to tackle COVID-19.

Discussion

The findings from this study are congruent with current analyses considering that in Africa most of the first COVID-19 cases were imported from Europe rather than from China where the virus emerged [19,20] (Table 4). It is, however, believed that under-reporting is widespread in several African countries due to the less developed healthcare systems associated with lower capacity of COVID-19 testing [21].

In 2020, nine African countries such as Algeria, Cameroon, Egypt, Morocco, Nigeria, Senegal, South Africa, Togo and Tunisia reported over 40 cases showing the spreading of the disease by the end of the first week of March and most index cases originated in Europe [21].

European countries played an important role for early spread of the pandemic on the African continent since Europe was the epicenter by March 13rd, 2020 [22].

The African continent has been preparing to deal with imported cases of COVID-19, led by the Africa CDC, Nigerian CDC, African Union, PANDORA-ID-NET and other research and capacity development and training consortia [21]. For instance, the early implementation of measures to tackle COVID-19, such as travel bans to most affected Asian and European countries and mandatory quarantine periods for most

Table 3. COVID-19 Fatalities in Mozambique.

	Date	Age	Sex	City	Region	Comorbidities
1	25 May	13	unknown	Nampula	Nothern	+
2	28 May	45	F	Pemba	Nothern	+
3	15 June	84	M	Nampula	Nothern	+
4	16 June	6	M	Nampula	Nothern	?
5	18 June	38	M	Maputo	Central	+
6	26 June	37	M	Nampula	Nothern	+
7	2 June	58	M	Tete	Central	+
8	4 July	17 days	F	Maputo	Southern	+
9	9 June	54	M	Quelimane	Central	?
10	18 July	54	M	Xai-Xai	Southern	+
11	20 July	26	F	Tete	Central	?
12	1 August	12	M	Maputo	Southern	+

travelers [23] played an important role in decreasing the imported and locally transmitted cases as well as the fatalities in Mozambique.

Currently, most of COVID-19 imported cases are from other African countries that share borders with Mozambique. This situation might be influenced by repatriation of Mozambican citizens and clandestine entry and trade market with neighboring African countries. For instance, 589 Mozambican citizens were repatriated from South Africa on May 11st, 2020, during the second period of the state emergency [24].

The early limitation of travel through the state emergency declared on March 30th, 2020, (that was implemented from April 1st to April 30th, 2020 and extended to May 30th, 2020), contributed to decrease the number of imported COVID-19 cases in some weeks during the analyzed period, such as: April 12nd to April 18th, April 19th to April 25th, April 26th to May 2nd, May 3rd to May 9th, April 19th to April 25th, and April 26th to May 2nd (Table 1), showing the role of this measure in tackling COVID-19. The issuance of entry visas to Mozambique were suspended during the state emergency period and the control of land, sea and air borders were strengthened by Mozambican authorities.

Data to analyze COVID-19 severity still lacks in Mozambique. However, the emerging data suggests that subjects with comorbidities are at higher risk, that is consistent with previous studies. Higher rates of comorbidity conditions (*e.g.*, cardiac disease, diabetes, hypertension, obesity, pulmonary, chronic lymphocytic leukemia disease) and more advanced age (≥ 65 years), increase the risk for symptom manifestations and COVID-19 severity [25,26] and this has been observed also in Mozambique; although, the fact that most of fatalities in adults ranged from 26 to 58 years of age highlights the major role of comorbidities.

Additionally, most of the patient remained asymptomatic (58%) or experienced few and mild symptoms (34%) [8], that is of particular concern based on an increasing number of studies describing that asymptomatic individuals can transmit SARS-CoV-2 [27-29], even though the mechanism remains unknown. However, this type of transmission may be contributing to a substantial amount of community transmission. Maputo city, Nampula and Pemba reported this type of COVID-19 transmission [8,30]. Therefore, physical distancing, face coverings and frequent handwashing are still effective preventive measures in reducing SARS-CoV-2 infections.

Table 4. Origin of the first COVID-19 cases (imported cases) in some African countries.

African country	Country of importation**	Continent	Confirmation date
Algeria	Italy	Europe	25 February
Angola*	Portugal	Europe	21 March
Botswana*	United Kingdom and Thailand	Europe/Asia	30 March
Cameroon	France	Europe	6 March
Comoros*	France	Europe	30 April
Djibouti	Spain	Europe	18 March
Eswatini*	United States	America	14 March
Ivory Coast	Italy	Europe	11 March
Gabon	France	Europe	12 March
Kenya	United States or other	America	12 March
Lesotho*	Saudi Arabia	Asia	13 May
Malawi*	India	Asia	2 April
Madagascar*	France	Europe	20 March
Mali	France	Europe	25 March
Mauritius*	United Kingdom and other	Europe	19 March
Moroco	Italy	Europe	2 March
Mozambique*	United Kingdom	Europe	22 March
Namibia*	Spain	Europe	14 March
Nigeria	Italy	Europe	27 February
Republic of the Congo*	France	Europe	14 March
Sierra Leone	France	Europe	31 March
Senegal	France	Europe	2 March
Seychelles*	Italy	Europe	14 March
South Africa*	Italy	Europe	5 March
Tunisia	Italy	Europe	2 March
United republic of Tanzania*	Belgium	Europe	16 March
Zambia*	Italy	Europe	18 March
Zimbabwe*	Italy	Europe	21 March

*Member state of Southern African Development Community (SADC); **Data was taken from World Organization Health (WHO) Africa (2020). External Situation Report 2 to 7 [50].

COVID-19 fatality rate in Mozambique is 0.4 by one million inhabitants, which is lower than other African countries including Botswana, Tanzania, Angola, Zimbabwe, Namibia, Malawi, Lesotho, Eswatini, Zambia and South Africa. The latter country was the most affected in the Southern African Development Community (SADC) with 137.5 fatalities in each one million of inhabitants [31,32].

Notwithstanding the rapid spread of COVID-19 in developing countries worldwide, many African countries including Mozambique, having a weak health systems and poor testing capacity, have been largely spared by this pandemic disease. The global death toll remains highly concentrated in few high-income, middle income or upper-middle countries [22], such as the United States, Brazil, Russia, Spain, and Kazakhstan, and South Africa on the African continent that has reported 8,366 deaths, although the deaths decreased in the past 7 days [33]. In some European high-income countries hit by COVID-19 pandemic, such as Luxembourg, Spain, Belgium, and San Marino, 110.23, 139.62, 175.59, and 942.90 fatalities per million, respectively were reported [34].

Demography (youthful population) and the variant of SARS-CoV-2 strains that circulated in Mozambique by August 1st, 2020, as well as other factors may contribute to the current COVID-19 severity in Mozambique. The number of older adults is lower as people > 60 years of age make up 4.6 % of the population, followed by ages 15-45 years accounting for 38.5%, and ages 0-15 years for 46.7% [35]. Most COVID-19 fatalities (7/12, 58%) affected people \geq 37 years of age [31] thus suggesting that apart from age, other factors including comorbidities may increase the risk of severity. However, it is still insufficient data to understand the severity and proportion of deaths and the dynamics of COVID-19 [34].

Mozambique registered lower infections and deaths by SARS-CoV-2 per 1 million of habitants in the analyzed period when compared to the majority of African countries belonging to the SADC region or member states [8,36]. This situation can be associated with the fact that Mozambique was one of the last countries affected by COVID-19 in the region and related to the type of SARS-CoV-2 strains that circulated.

COVID-19 community transmission could be an important factor in emerging of new virus strains due to the rapid spread of SARS-CoV-2 in the population associated with reduced compliance to COVID-19 preventive measures. Additionally, the delay in patient recovering from COVID-19, which makes

Mozambique as one of African countries with lowest rate [8] might engender novel mutations in the virus [37,38].

Recent studies have shown that a large number of mutations in SARS-CoV-2 may have arisen through intra-host evolution in one or more individuals with prolonged viral replication or infectious over 20 weeks [39,40]. Although this phenomenon of viral evolution has been observed in the context of human immunodeficiency virus (HIV) infection, other mechanisms can be associated with multiple mutations in SARS-CoV-2 or evolution [41-43]. However, further studies are needed for better understanding the mechanisms of emergence of new SARS-CoV-2 strains.

Currently, the circulation of the new South African COVID-19 strain (SARS-CoV-2 lineage 501Y.V2) characterized by eight lineage-defining mutations in the spike protein, including three at important residues in the receptor-binding domain (K417N, E484K and N501Y) [43,44], might play an important role in emerging of new variants in the country.

The SARS-CoV-2 lineage 501Y.V2 and other new variants have shown the trend to replace the wild type in some countries due to its rapid spread and dissemination [45]. The South African lineages have been detected in Botswana, UK, Scotland, France, Sweden, Switzerland, South Korea and Australia [45,46].

The spread of SARS-CoV-2 in Mozambique is of particular concern due to the weakness of the health system, non-compliance of preventive measures and probably due to the circulation of new SARS-CoV-2 strains mainly of the South African lineages 501Y.V2 already confirmed.

Apart from the circulation of South African lineages, other new variants such as clade 20I/501Y.V1, VOC 202012/01 or B.1.1.7 (initially identified in UK) and clade P.1 (initially identified in Brazil) [46-48], might be circulating due to international travel to Mozambique.

Like in other countries, SARS-CoV-2 mutations might arise in Mozambique with effects on human disease prevalence and health outcomes, thus genetic monitoring and biological characterization of new mutations is a high priority in research. Additionally, systematic clinicopathological, genomic and other socio-economic data, together with implementation of preventive measures are important factors to effectively fight against COVID-19.

The new variants are emerging probably due to environmental pressures including vaccine-induced

immunity, antiviral therapies, and public health intervention strategies that could promote virus survival and escape. The selective pressures may drive antigenic variation, promote virus stability and transmissibility, alter virus virulence and pathogenesis of SARS-CoV-2 [49], making WGS including antigenic sequencing very important tools to be used as control and prevention measures.

It is expected that future project for SARS-CoV-2 strains characterization offer insights into the viral dissemination and severity in Mozambique.

Conclusions

The COVID-19 imported cases from European countries might have been playing an important role in Mozambique. Due to the epidemic COVID-19 evolution, the country is currently characterized by an increasing number of confirmed cases, hospitalizations and deaths; genomic surveillance of SARS-CoV-2 including the antigenic sequencing approach might be useful tools in designing new control and prevention measures through understanding the epidemiologic, immunologic, and evolutionary processes in the country and to guide the global pandemic response.

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