



Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2): What Can Africa Learn from Ongoing Research in Epidemiology, Clinical Manifestations, Chemotherapy and Prevention?

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

The world is experiencing an outbreak due to the new and mysterious SARS-CoV-2. Information regarding its source and transmission dynamics in different environments as well as medications for its prevention and cure is weak. This review seeks to document on the epidemiology, clinical signs, control, prevention, and present some perspectives for SARS-CoV-2 research in Africa. There are geographical differences in morbidity and mortality rates of this disease all over the world. The scientific community strongly reject claims regarding the fact that the virus has been genetically manipulated, but supports the theory that it has a natural origin from animal host as any other emerging viral disease. Although animals are thought to be the original source of global spill over, person-to-person transmission is well comprehended. Transmission could be enhanced by symptomatic and asymptomatic individuals with high contaminations reported in dense urban environments. Scientific evidences from the Center for Disease Control (CDC) and other publications reported that contaminated surfaces and air could possibly be the underlying mechanism through which SARS-CoV-2 spreads. Cohort studies reveal that children as well as adults could be vulnerable to the disease, but others attribute it to health care workers, some risky habits (drinking and smoking) and comorbid individuals due to their immune suppressed status. There is no drug of choice for SARS-CoV-2, but clinical studies including several antiviral drugs are underway. Similarly, vaccine studies and clinical trial studies are ongoing. Because there is no medication, preventive measures such as Personal Protective Equipments (PPEs), ventilators, sanitation, social distancing, and quarantine are the gears globally used to curb the spread of this virus. The African continent does not have high morbidity and mortality compared to other continents that are highly affected. The following lessons could be learned by Africans from ongoing research: that the SARS-CoV-2 originated from an animal host, individuals could be infected irrespective of their age, sex, race, and origin, there is a broad spectrum of clinical signs and confirmatory diagnosis is required, there is no approved drug of choice, vaccine trials are ongoing and community-based prevention is required, the recommendations put in place by the Government and the WHO to curb the spread of this virus should be strictly followed. From the above lessons, a research project to study the ecological epidemiology of SARS-CoV-2 in tropical African settings by including the following aspects: socio-cultural, economic, and political characteristics as well as the evaluation of measures taken by the different countries to combat the disease is required.

Keywords: SARS-CoV-2; epidemiology; clinical signs; chemotherapy; prevention; Africa.

1. INTRODUCTION

The first case of an unknown pneumonia was reported in Wuhan, Hubei Province in China in December 2019. The Scientists at the Chinese Centers for Disease Control reported that this mysterious pneumonia was caused by the 2019 novel coronavirus [1]. The WHO named the disease 'COVID-19'. The International Committee on the taxonomy of Viruses named the virus 'Severe Acute Respiratory Syndrome Coronavirus 2' (SARS-CoV-2). The disease has spread to more than 200 countries outside China. There is no published data about the COVID-19 pandemic in Africa that recorded its first confirmed cases between February and March 2019. Till 9 am of 22/05/2020, 100069 cases have been confirmed and 3102 deaths recorded in Africa (<http://covid-19-africa.sen.ovh/>). Despite the global struggle to curb the spread of COVID-19, a lot is still

unknown about its source and its transmission dynamics in different environments. Efficacious and safe medications for its prevention and cure are not available yet. To support urgent research to combat the ongoing coronavirus disease pandemic, the present review seeks to provide updated scientific information on the epidemiological, clinical, prevention, and therapeutic aspects of this disease as well as to provide some perspectives for research in Africa based on ongoing research in other continents.

1.1 Data Collection

Information from 60 articles published in peer-reviewed journals was extracted based on the objective of the articles. For this reason, only articles that reported on the epidemiology, clinical signs, prevention and control measures were retained (Fig. 1).

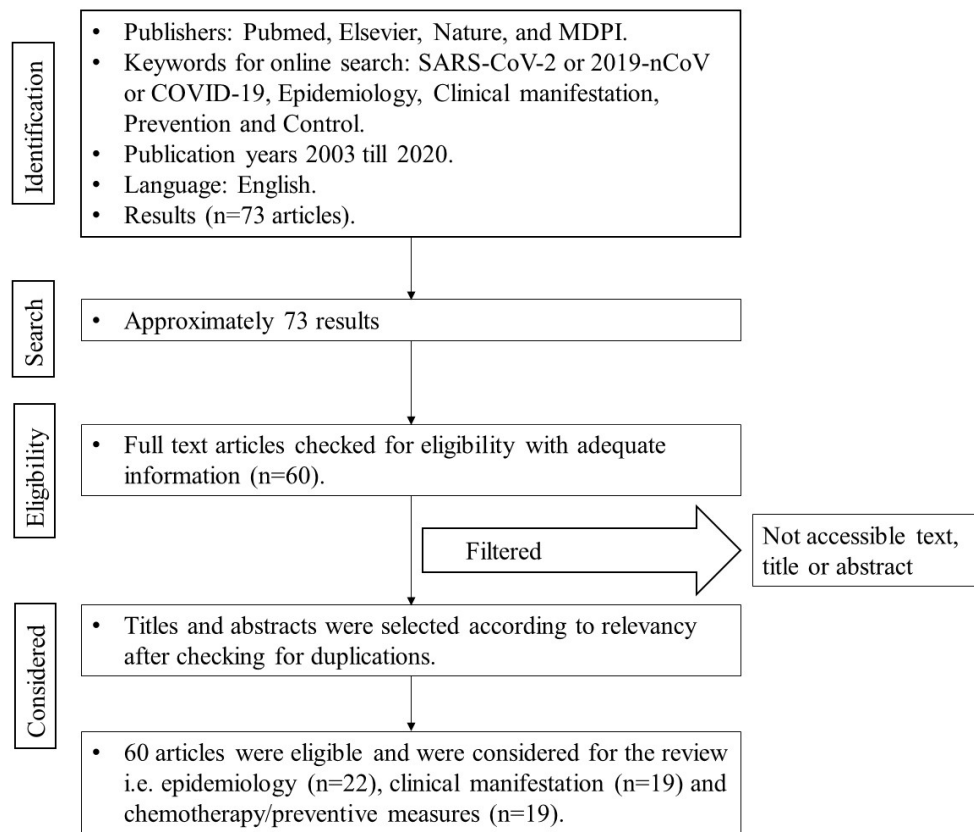


Fig. 1. Study article selection and characteristics

2. EPIDEMIOLOGY

The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2, SARS2, 2019-nCoV or COVID-19 virus), is a newly emerging zoonotic agent that appeared in December 2019 at a sea food wholesale wet market (Huanan market) in Wuhan Hubei China [1]. This region of China represents the hotspot of this mysterious disease that has spilled over the globe with more than 200 countries currently affected. The updated statistics on confirmed new COVID-19 cases, confirmed deaths, and confirmed recovered individuals in the various affected countries can be accessed via this link: <https://gisanddata.maps.arcgis.com/apps/opsdashboard/index.html>.

The morbidity rate of the 2019-nCoV is different in African countries with Egypt, South Africa, Morocco and Algeria leading the statistics on confirmed cases of COVID-19 (<http://covid-19-africa.sen.ovh/>). The geographical differences in the morbidity and mortality have been reported in the USA [2] and these variations could be

attributed to the differences in cultural practices, demographics, climate, political, mitigation approaches, and health infrastructure [3].

The coronaviruses (CoVs) family is a class of enveloped, positive-sense single-stranded RNA viruses having an extensive range of natural roots [4,5]. The CoVs are genotypically and serologically divided into four subfamilies: α , β , γ , and δ -CoVs. Human CoV infections are caused by α - and β -CoVs [6,7]. SARS coronavirus (SARS-CoV) and MERS coronavirus (MERS-CoV) are members of β -CoVs [6]. These are enveloped positive-strand RNA viruses isolated from bats (*Rhinolophus affinis*) that share sequence similarity (>90%) at the whole genome level with isolates from humans, suggesting them as natural hosts and reservoirs [8-10]. The other vertebrate hosts that are suspected to have been contaminated apart from the natural bat host include pangolins (*Manis javanica*) [11,12], civets, camels, monkeys, horses, mice, dogs, pigs, cats, goats, snakes, fishes, tigers etc. [13]. According to Kristian et al. [14] and Xu et al. [15], this animal virus might have jumped host species

boundaries to infect humans. A study conducted in North East of Gabon by Maganga et al. [16], suggested that cave-dwelling bats harbored potentially zoonotic CoVs with probable seasonal variation of infection in them.

Epithelial cells in the respiratory and gastrointestinal tract of host are the primary target cells for the replication of the SARS-CoV-2. Therefore, viral shedding occurs through these systems and transmission can occur via different routes: fomites, airborne, and fecal-oral. Two phenomena best explains such risks: 1) the original clustering of patients at the Wuhan China hospital with respiratory distress (December 2019) and approximately 10 days later, the same hospital facility reported patients outside this cohort as positive. It was presumed that the new cases in this hospital could be linked to the contamination that occurred in its premises [17]; 2) approximately 700 of the 3,711 passengers on board the princess diamond (approximately 19%) contracted the COVID-19 during their 14 days quarantine in the ship [18,19]. The above scenarios indicate the high contagious nature of the novel coronavirus disease as estimates of its reproductive ratio (R_0) (the number of secondary infections caused by an infectious individual introduced in a susceptible population) ranged from 1.5 to 3 and could increase (between 5 and 15) in confined environments [5]. Considering the scenarios of the golden diamond ship and the Wuhan hospital, the increasing COVID-19 cases could be linked to the proximity of infected passengers/patients, and the general layout of such structures [18]. The mechanisms through which this transmission could occur in the environment happens when individuals get in direct and indirect contact with surfaces around them. Viral particles can be directly deposited and resuspended due to natural air flow patterns, mechanical air flow patterns, or other sources of turbulence in the indoor or outdoor environment such as foot fall, walking, and thermal plumes from warm natural host/human bodies. These resuspended viral particles can then contaminate fomites that can indirectly infect susceptible individuals. The major source of the viral particle into the environment occur through some actions of infected individuals like coughing, sneezing, talking, and vomiting [20,21]. The duration of persistence of COVID-19 differs with the type of environmental matrix as follows: 3 hrs for aerosols, 72 hrs for plastics, 48 hrs for stainless steel, 4hrs for copper, and 24 hrs for cardboard [22,23].

The above stated epidemiological discoveries on COVID-19 are based on Western data but no such data exists for African settings with different environmental, socio-cultural, and political policies.

3. CLINICAL MANIFESTATIONS

The symptoms of COVID-19 infection appear after an incubation period of approximately 2-14 days [5,24,25]. This disease has a relatively low mortality rate and can be highly deadly and lethal especially in high risk patients. The period from the onset of COVID-19 symptoms to death range from 6 to 41 days with a median of 14 days [1]. The associated risk factors include individuals with age ≥ 50 years [15], males, smokers as well as comorbid individuals [26] with Chronic Kidney Diseases (CKDs) [27], CerebroVascular Diseases (CVDs), tumors, diabetes, hypertension etc. [28,29]. A cohort study revealed that the extent to which SARS-CoV-2 infections may be asymptomatic, or present as subclinical and with non-specific symptoms is still unclear [30]. In addition, children like adults are vulnerable to COVID-19 [30,31]. According to Huang et al. [1], there are similarities in the symptoms of COVID-19 and those of other betacoronavirus such as fever, dry cough, dyspnea, and bilateral ground-glass opacities on chest CT scans. However, COVID-19 shows some unique clinical features that include the targeting of the lower airway as evident by upper respiratory tract symptoms like rhinorrhoea, sneezing, and sore throat [32]. The common clinical signs identified in COVID-19 patients are presented in Table 1.

4. CHEMOTHERAPY

To date, there is no validated curative and preventive medication for COVID-19. The main approaches are community health care, such as keeping vital signs, maintaining oxygen saturation and blood pressure, and treating complications, such as secondary infections or organs failure. Because of the potential mortality of COVID-19, several therapeutic trials are underway and include interferons nebulization and various antivirals such as Nafamostat, Nnitazoxanide, Ribavirin, Penciclovir, Ffavipiravine, Rritonavir, Baricitinib, Lopinavir, Oseltamir and Arbidol [39]. The mechanism of action of some potential drugs currently investigated for their efficacy and safety against COVID-19 are as follows:

Table 1. Clinical signs common in COVID-19 patients

Clinical signs	References
Fever	[17,25,32-35].
Cough	[17,25,26,32-35].
Fatigue	[17,25,33].
Diarrhoea	[10,17,25,33].
Chronic Kidney disease	[10,27].
Dysnoea	[25,32,35].
Myalgias	[35].
Sore throat	[17,34].
Headache	[17,25,34,35].
Sputum production	[1,17,25,36-38].
Haemoptysis	[1,17,25,36-38].
Lymphopenia	[1,17,25,36-38].
CT-Scan showing pneumonia	[1,17,25,36-38].
RNAemia	[1,17,36-38,37,38].
Acute respiratory syndrome	[1,17,36,37,38].
Cardiac injury	[1,10,17,25,36-38].
Ground-glass opacities	[1,17,25,26].

4.1 Remdesivir

It is an experimental drug and a novel nucleotide analogue prodrug in development by Gilead Sciences, Inc. It is also an unapproved antiviral drug being developed for Ebola and SARS. In April 2020, Remdesivir was approved by the FDA as emergency drug for critically ill COVID-19 patients in the USA. The anti-infective mechanism of action of Remdesivir is that it interferes with virus cell entry [34,40-42].

4.2 Ribavirin

It is an approved drug with synthetic guanosine nucleoside mode of action. Its anti-infective mechanism of action is that it interferes with the synthesis of viral mRNA (a broad-spectrum activity against several RNA and DNA viruses). This drug target diseases like SARS, MERS, and HCV [43,44].

4.3 Lopinavir/Ritonavir

This drug has been tried to treat SARS disease with apparent favorable clinical response. *In vitro* antiviral activity against SARS-associated coronavirus at 48 hours for Lopinavir and Ribavirin was demonstrated at concentrations of 4 and 50 µg/mL respectively. The anti-infective mechanism of this drug is that it inhibit HIV-1 protease for protein cleavage, resulting in non-infectious viral particles. However, randomized controlled trials are needed to determine the safety and efficacy of these candidate drugs for

treatment of patients with the 2019-nCoV infection [29,45-49].

4.4 Chloroquine

It is a repurposed drug with great potential to treat COVID-19. Chloroquine has been used to treat malaria for many years [50], with a mechanism that is not well understood against some viral infections. However, recent publications [38,51,52] attempt to describe the antiviral effects of chloroquine against coronavirus. The possible anti-infective mechanisms already reported include:

- Chloroquine can inhibit pH-dependent steps of the replication of several viruses [51].
- Chloroquine has immunomodulatory effects, suppressing the production/release of TNF-α and IL-6, and
- Chlorine works as a novel class of autophagy inhibitor [53], which may interfere with viral infection and replication. Several studies have found out that chloroquine interfered with the glycosylation of cellular receptors of SARS-CoV-2 [54] and functioned at both entry and at post-entry stages of the COVID-19 infection in Vero E6 cells [38].

A combination of remdesivir and chloroquine as well as Hydroxychloroquine and Azithromycin [55,56] were proven to effectively inhibit the recently emerged SARS-CoV-2 *in vitro*, but clinical trials to test for the efficacy and safety of these formulations are underway.

4.5 Epoxomicin, Bortezomib and Carfilzomib

These drugs act as ubiquitin–proteasome system (UPS) inhibitors, which were proven to be powerful tools in reducing the cytokine storm and in inhibiting virus replication for other coronaviruses [39]. Also, they have the potential to affect both viral replication as well as pneumonia and acute respiratory distress syndrome. Further studies are now needed in order to establish their clinical efficacy and safety for COVID-19 patients.

4.6 Ivermectin

It is an FDA approved drug that acts as inhibitor of the causative virus (SARS-CoV-2) *in vitro* in vero cells (Australian isolates) [57].

5. PREVENTION

In May 2020, vaccine centers in the USA, UK, China, etc. are in the race for a vaccine candidate against COVID-19. Based on the long period taken to develop previous vaccines, there is no evidence of having a vaccine for COVID-19 before the end of 2020. Therefore, it is important to devise other strategies to stop its propagation. For general population, travel to epidemic area of COVID-19 and contact with infected people as well as animals is not recommended [58]. The following preventive measures could be adopted:

- Individuals who have come in contact with infected counterparts or travelled from the epidemic region in the recent two weeks, 14 days quarantine is recommended to monitor for compatible symptoms of COVID-19 as well as conduct laboratory confirmatory tests. If such individuals are tested positive, they should be treated in isolation centers.
- For front line health workers, personal protective equipments (PPEs) should be put on when receiving and working with confirmed patients.
- In public places, the wearing of face masks and shields is compulsory where physical distancing (keeping a distance of at least 1 m from each other) is not respected.
- As most countries in the world are gradually reopening, the regular disinfection of public spaces, regular washing of hands, and respecting the CDC guidelines for reopening is important. Users of household disinfectants and hand sanitizers should respect manufacturer

instructions because they could be toxic to users and the environment (WHO communication of May, 2020). Because the virus is sensitive to some chemicals, the following could be used for disinfection: sodium hypochlorite (0.1%–0.5%), 70% ethyl alcohol, povidone-iodine (1% iodine), chloroxylonol (0.24%), 50% isopropanol, 0.05% benzalkonium chloride, 1% cresol soap, or hydrogen peroxide (0.5%–7.0%).

- For health facilities in affected countries, increasing bed capacity to isolate COVID-19 cases is important as this helped to contain the widespread of the disease in Wuhan in China [12].
- Data driven models indicates that the lock down policy successfully helped to curb the spread of COVID-19 in China, Italy, and Spain [12,59,60]. Based on the consequences of lockdown in Africa such as economic hardship, most countries have not been able to include this approach in their list of measures to stamp out the disease from the continent. However, other mitigation and suppression measures such as case-based isolation, shielding of vulnerable groups, school closures, and restricting public events have been adopted in most African countries to minimize person-to-person transmissions of SARS-CoV-2 through social distancing.
- While the world is focusing on the prevention of SARS-CoV-2, the control and treatment of other dangerous diseases should not be neglected [61,62,63,64].
- The investigation of Miller et al. [3] on Bacillus Calmette-Guérin (BCG) childhood vaccination revealed that the national policy for BCG vaccination by some nations has reduced the number of reported COVID-19 cases in those countries.
- Convalescent therapies (plasma from recovered COVID-19 patients) is a strategy that has been used to support passive immunization, but trials on it to boost the immune system of COVID-19 patients is underway.

6. PERSPECTIVES FOR RESEARCH STUDIES IN AFRICA

The research perspectives for Africa will include:

- To conduct an ecological epidemiological study to understand the drivers of COVID-19 in the African settings.

- To study the survival and contamination sources of the COVID-19 in tropical African settings.
- To evaluate the Knowledge Attitudes and Practices in different African countries towards COVID-19.

7. CONCLUSION

The SARS-CoV-2 is a zoonotic disease with low to moderate mortality rate. Eco-epidemiological data on the disease is weak and lacking for Africa. The lessons Africans could learn are that:

- The virus might have originated from an animal species such as bats and pangolins.
- The virus could infect any individual irrespective of age, sex, race, and geographical origin.
- There is no treatment for the disease and prevention is the only strategy.
- The SARS-CoV-2 clinical signs frequently encountered in publications include cardiac injury, RNAemia, cough, sputum, haemoptysis, lymphopenia, CT scan showing pneumonia, acute respiratory syndrome, fever, diarrhoea, headache, and ground-glass opacities.
- Although many experimental trials are underway to put in place an efficient and safe vaccine and drug against SARS-CoV-2, stringent local infection control operation is required.
- Health infrastructures with many beds to isolate and take care of COVID-19 patients should be put in place.
- Front line healthcare providers should be highly aware of appropriate infection prevention measures for suspected patients.
- Nation-based strategies together with the recommendations of the WHO should be considered in the fight against this disease.

Finally, research projects to gain new insights on the eco-epidemiology of this disease in Africa should be supported.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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