EXPLOITABLE OPTIONS FOR CURBING THE DANGER OF SARS-COV-2 IN AFRICA

[1]Yusuf L., [2]Bala J. A., [2]Aliyu I. A., [1]Kabir, I. M.,[3]Haruna. M. W.
[1]Department of medical laboratory science, Kebbi State College of Health Science and Technology Jega, Nigeria, P.M.B 9003.
[2]Department of medical laboratory science faculty of allied health science, Bayero University Kano, Nigeria, P.M.B 3011, Kano, Nigeria,
[3]Department of Anatomy, Bayero University Kano, Nigeria, P.M.B 3011, Kano, Nigeria,
[4]Department of medical laboratory science, Microbiology unit, Aminu Kano Teaching Hospital, Kano, Nigeria
Corresponding author email: Iaaliyu.mls@buk.edu.ng: +2348065882020

ABSTRACT

Background: It is understood that coronavirus is highly mutated, in December, 2019 a new strain of coronavirus emerged which originated in Wuhan, from seafood. The pathogen was named novel coronavirus, while the disease it causes is known as Covid-19, the 2019 coronavirus disease. Bat is the major reservoir host of the virus. By putting bats in touch with other mammals will promote viral spillovers, which is a dominant condition for SARS-CoV-2, while also the effect of climate anomalies on food scarcity, behavioral flexibility, and bat immune modulation is likely to increase the risk of disease emergence. Over 34 million Covid-19 cases were registered between 31st of December 2019 and October 1st 2020 with Africa reporting about 1.4 million cases in this period.

Aim: This review was design to highlight possible options that can be exploited in curbing the Covid-19 menace in Africa.

Method: We reviewed articles from online databases for relevant documents written in English language. These includes NCBI, PubMed and Google scholar. We included both original and review papers that provided information on current SARS-CoV-2 trends and meta-analysis in Africa and globally.

Results: Of the 15 articles selected from the 128 available citations, approximately 40 million people worldwide have been diagnosed with SARS-CoV-2, while only 1.4 million people in Africa have been confirmed to be positive for the virus as of October 1, 2020, although the prevalence in Africa is low in relative to other continents. However, most African nations do not have the economy to buy the vaccines that are accessible. The availability of phytoterapeutic agents, on the other hand, would provide a cost-effective way to tackle the Covid-19 threat in Africa.

Conclusion: Cell lines adaptation in vaccine production, proteomic analysis of the viral-host interactomes, treatment approaches using natural occurring compounds, which will provide cost effective options to low-income countries can be adopted to curb the menace of Covid-19 in Africa.

INTRODUCTION

Coronavirus belong to the order *Nidovirales*, family *Coronaviridae*, subfamily *Coronavirinae*, and genus *Betacorona virus* (Siddiqe and Ghosh, 2021), is an enveloped non-segmented, single stranded, positive-sense RNA virus. Coronavirus got its name from it crown-like surface projections (Li *et al*., 2020). The 2019 coronavirus disease (COVID-19), now a global pandemic is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It started as pneumonia from unknown cause that occurred in Wuhan, Hubei province, China in December 2019 (Li *et al*., 2020), although was later identified as SARS-CoV-2 in a patient's throat swab sample on 7 January 2020.

World Health Organization announced the disease caused by SARS-CoV-2 as coronavirus 2019 (COVID-19), which has since affected over 70 countries globally making it a pandemic (Lai *et al*., 2020). The virus can be transmitted mainly through droplets though was later reported to be airborne, and is generally susceptible to crowding. Covid-19 thrive better in immunosuppressed individuals, as increased mortality rate been reported in patients with compromised immune system. Patients with HIV, tumor, diabetics, asthma, and high blood pressure are at high risk for this pathogen because of impaired immune function and organ (Lai *et al*., 2020). Symptoms include dry cough, fever, and sore throat, loss smelling sensation, dyspnea, fatigue, body ache and pain. Early detection of patients with this underlying illnesses infected with the novel coronavirus disease Covid-19 and also understanding its dissemination characteristics will help increase patient cure rates and better control of the SARS-Cov-2 epidemic and growth (Bloukh *et al*., 2020).

Genomic structure of SARS-CoV-2

Coronavirus is an enveloped virus with a positive sense single stranded RNA and has a crown-like spike on its outer surface (Cui *et al*., 2019), they have the largest genome of all RNA viruses, with an average genome size of 32 kilobase pairs and a diameter of around 125 nm (Cui *et al*., 2019). The viral G-C content is about 43%. The viral genome is packed inside a helical capsid formed by the nucleo-capsid protein (N), which is further encircled by envelope (Su *et al.*, 2016). The viral envelope is linked to at least 3 structural proteins, for the viral assembly, the envelope protein (E) and the membrane protein (M) are responsible, while the spike protein (S) mediates the entry of the virus into the host cells. SARS-CoV-2 binds through its spike to ACE2 (angiotensin-converting enzyme 2) and enables Covid-19 to enter the host cells. A hemagglutinin-esterase (HE) protein is also contain in certain coronaviruses (Su *et al.*, 2016).

The Covid-19 menace

The patient characteristics of covid-19 show many sign of disease vulnerability and severity. Both symptomatic and asymptomatic person in the same vicinity of positive case may get infected. This can occur through respiratory tract droplets transporting the virus or contact with infected surfaces and then using that contaminated hand to touch the mouth, nose and eyes (Bloukh *et al.*, 2020). The virus is transmitted to everyone in close contact with the infected carrier without restrictions. Coronavirus pneumonia development is directly linked with old age, history of smoking, metabolic disorder, and cardiovascular diseases. The global Covid-19 outbreak triggered fear, vulnerability and depression due to its rapid rate of infection, people showing no symptoms with high transmission potential, unspecific symptoms and control mechanisms imposed on the public (Bloukh *et al.*, 2020). Despites this, there is no specific antiviral therapy for Covid-19 until now, and the available vaccine are limited, at this point any effective therapeutic agent will do, despite the fact there is a need for reliable, and cost effective drugs as an appropriate response to the outbreak.

Prevalence of Covid-19, as of October 1st 2020

Over 34 million Covid-19 cases were registered between 31st of December 2019 and October 1st 2020, specifically 34 029 923 cases (Who, 2020). The continent with the highest reported cases is America as shown in Table 1, with almost half the global reported cases, registering approximately 16.7 million cases. Oceania reported the least cases, as depicted in figure 1.0, while Asia registered higher number of cases they have reported better number of cases to death ratio. Europe has recorded a large number of deaths to cases ratio.

Table 1: Prevalence of Covid-19, as of October 1st 2020

Continent	Number of cases reported	Number of deaths reported
Africa	1 482 752	35 861
Asia	10 580 764	193 485
America	16 794 190	560 388
Europe	5 138 206	224 330
Oceania	33 315	972

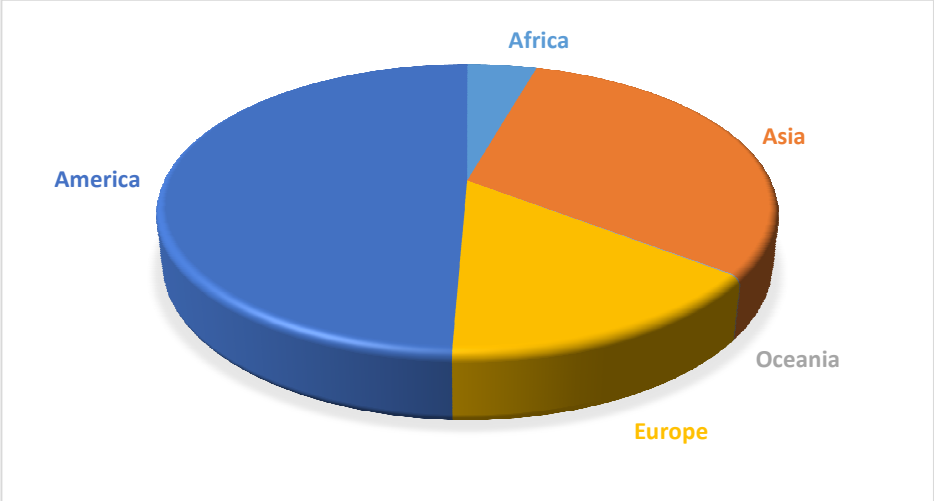

Figure 1.0: Prevalence of Covid-19, as of October 1st 2020(WHO, 2020)

Early treatment options used in management of Covid-19

Antiviral treatment

Some of the antiviral used includes: Oseltamivir, ganiciclovir, arbidol and ritonavir (Liu *et al.*, 2020).Antiviral agents were given to more than 85% of patients, including oseltamivir (75 mg orally every 12 hours), ganciclovir (0.25 g intravenously every 12 hours), and lopinavir/ritonavir tablets (400/100 mg twice daily). Remdesivir, which has been shown to prevent MERS-CoV, is currently being studied at more than ten medical institutions in Wuhan(Cunningham *et al.*, 2020).None of these antiviral agents, however, has been effective in treating Covid-19

Antibiotic therapy

The most employed antibiotics used in Covid-19 management is Azithromycin which was at a time combined with the antimalarial hydroxychloroquine, while other antibiotics used were Vancomycin, Moxifloxacin, Meropenem, Cefaclor, Cefepime, and Tazobactam(Barlow *et al.*, 2020). Existing antimalarial medication known aschloroquine phosphate that's known to exhibit antiviral and anti-inflammatory properties has been found to be effective in preventing pneumonia exacerbation(Cunningham *et al.*, 2020). This medication was explored during the early stage of Covid-19 pandemic, despite its documented antiviral activity, no scientific evidence that it does have an Anti-Covid effect. Inspite that most of these drugs failed to undergo a clinical trial before being used, though this may be because desperate times call for desperate measures, it is however necessary to provide evidence based treatment options. Hence, the need for proper research on therapeutic agents against SARS-CoV-2 especially the exploration of plant extract of African origin.

SARS-CoV-2 Vaccines

To prevent and mitigate the morbidity and mortality caused by SARS-CoV-2 infection, SARS-CoV-2 vaccines that elicit protective immune response are crucial.

The knowledge available suggests that for the defense from Covid-19 and the prevention of vaccine-enhanced disease, a balanced humoral and Th-1 directed cellular immune response may be essential (Graham, 2020). Different candidate vaccines are being manufactured and evaluated, these includes vaccines for the viral nucleic acids, live attenuated vaccines, vaccines for protein or peptides subunits, vaccines for the viral vectors (Poland *et al*., 2020). It is not worth discounting the function of mucosal immunity, and several formulations of intranasal vaccines are being investigated (Hassan *et al*., 2020; Poland *et al*., 2020a). Several phase 3 clinical vaccine trials of tens of thousands of participants were being initiated, as at August 2020 and preliminary results were made available as at December 2020(He *et al*., 2021). In the USA, guidance has been provided by the Food and Drug Administration (FDA), stated that to be deemed successful, a Covid-19 vaccine will have to protect at least 50 percent of vaccinated individuals(Leiker and Wise, 2020). All studies done excluded pregnant women, a lot of SARS-CoV-2 mutation were recognized (Long *et al.*, 2020). Therefore, if the virus subsequently evades immunity to the spike glycoprotein used to create the vaccine, vaccine production could be obstructed (Lin *et al.*, 2020).Vaccines were made available for use in early 2021, having met both FDA and WHO requirements.Here are a handful of the vaccines that are currently available:

AstraZeneca

A chimpanzee adenovirus-vectored investigational vaccine (ChAdOx1/AZD1222) has been developed by AstraZeneca and Oxford University, the vaccine encodes the SARS-CoV-2 glycoprotein spike(Maciorowski *et al*., 2020). In non-human primates, the vaccine has shown to be highly immunogenic. Study showed that this vaccine elucidate humoral immune response in human. When a vaccine user developed symptoms associated with transverse myelitis, the phase 3 trial was halted and continued on October 5th 2020, this vaccine needs cold chain system, which may be difficult for low-income countries to use (Maciorowski *et al.*, 2020).

Sinopharm

Sinopharmdeveloped 2 inactivated whole-viruses (Xia *et al.*, 2020) and there researchers announced at the end of August 2020 that they had already started delivering the vaccine to health care workers and groups at elevated risk of infection. While the Beijing Institute of Biological Products produced the second vaccine candidate being evaluated by Sinopharm. In the UAE, a phase 3 trial took place and emergency use of the vaccine was granted by the UAE to health care personnel. Hundreds of thousands of individuals were reportedly given these experimental vaccines by Sinopharm under emergency use condition approved by the government of China(Poland *et al*., 2020a).

Gamaleya

The findings of two phase 1/2 clinical trials of a Covid-19 vaccine which consists of recombinant adenovirus vector serotype 26 (rAd5) and recombinant adenovirus vector serotype 5 (rAD5) wasreleased by the Gamaleya National Research Centre for Epidemiology and Microbiology (Logunov *et al.*, 2020).

Johnson and Johnson

A randomized, placebo-controlled, double-blind, phase 3 trial was conducted by the Janssen Pharmaceutical Companies of Johnson & Johnson of their Ad26.COV2.S which is a replication-defective vaccine that expresses glycoprotein spike full-length (Poland *et al*., 2020b). It was reported that with this vaccine, a single immunization in rhesus aged 6 to 12 years, induces strong neutralizing antibody responses and provides defense against SARS-CoV-2 challenges (Vashishtha & Kumar, 2020). It was reported that clinical trials of the vaccine showed that a single dose of the vaccine had an efficacy rate of about 72%(Poland *et al*., 2020b).

Pfizer and Biotech

Pfizer and Biotech developed a Covid-19 vaccines based on mRNA.They reported BNT162b1, an mRNA vaccine formulated with lipid nanoparticle, nucleoside-modified, induced RBD-binding IgG and neutralizing antibodies, with mainly mild side effects (Mulligan *et al.*, 2020). Individuals vaccinated with BNT162b2 had higher CD4+ and CD8+ T-cell responses to spike glycoprotein and RBD than the participants with BNT162b1 (Mulligan *et al.*, 2020). The candidate chosen for evaluation in phase 3 trials was BNT162b2, although it requires storage at -80^0C, a fact that is posing logistical issues.

Moderna

An mRNA-based vaccine (mRNA-12733) has been jointly developed by Moderna and National Institutes of Health. Comprising of sequence optimized mRNA encoding the lipid nanoparticles encapsulated spike protein (Corbett *et al.*, 2020). In non-human primates, the vaccine has shown to be highly immunogenic. This vaccine caused both spiked glycoprotein binding and virus-neutralizing antibody responses in recipients in a phase 1 dose-escalating study (Jackson *et al.*, 2020). The humoral responses were identical to those found by patients recovering from Covid-19 in convalescent plasma. Cellular responses, primarily biased towards CD4+ Th1 cells, were also produced by the vaccine recipients (Jackson *et al.*, 2020). For vaccine deployment, one potential problem is storage requirement of -20^0C temperature is needed.

Casino Biologics

On 25th of June 2020, prior to the initiation of phase 3 trials, Casino Biologics and Institute of Biology at the Academy of Military Medical Sciences announced the approval of their adenovirus serotype 5 vector vaccine which is a recombinant adenovirus serotype 5 vectored Covid-19 vaccine, engineered to express the Wuhan-Hu-1 virus strain of SARS-CoV-2 full length spike glycoprotein (Zhu *et al.*, 2020).

Exploitable options to curb the SARS-CoV-2 menace in Africa

Coronavirus is been known to be highly mutated, is therefore important to study the SARS-CoV-2 novel pathogenic protein this will assist in drug designing and vaccine production, also proteomic analysis of the protein is also paramount in preventing future pandemic. Due to logistical problems, African countries may not be able to afford the available vaccines. Evidently, the distribution pattern of Covid-19 in Africa varies from that in other parts of the world, therefore it is critical to develop an African solution to African problems.Some of the options that can be exploited to curb the menace of Covid-19 in Africa are:

Production of vaccine through culture

Viral isolation could be carried out both on embryonic chicken eggs and on continuous cell cultivation (Bala *et al.*, 2018). These circumstances were also associated with a culture-binding approach to enhanced improved biological products such as insulin remedy for xenotransplantation using the goats' islets (Yusuf *et al.*, 2020). Covid-19 cultivation and isolation can be doneon Air liquıd interface culture, Vero cell line, HEK-293 cells, and Chinese hamster ovary for production vaccine. SARS-CoV-2 can be isolated, clone purified, and elucidated immune reaction can be studied using animal model for vaccine production by employing the available resources in Africa. This approach if successful will also help countries with low incomes reduce the risk of Covid-19 menace in their area, also provides a cost effective and an independent approach to vaccine production in Africa.

Proteomic analysis

The novel upstream SARS-CoV-2 regulator involved in the genesis of the viral pathogenesis must be recognized and be studied thoroughly to avoid future pandemic, it is very important to evaluate the upstream regulator in respect to region.

Intra-viral and virus-host interactomes can be identified following standard method of affinity mass spectrometry (Li *et al*., 2021), Also the deployment of techniques such as a label-free proteomic method using liquid chromatography-tandem mass spectrometry (LC/MS/MS) to analyze the response of SARS-Cov-2 (Davidson *et al.*, 2020)cultivated on Vero cells against African therapeutic agents is a potential area of research to uncover possiblemechanisms for anti-covid effect.

Phytotherapy

In order to explore natural drugs with lesser side effect and cost, a natural compound Purple coneflower, is one among the plant reported to have active components such as chicoric acid, polysaccharides and echinacoside. This plant extract is known to stimulate immune response. The aqueous fractions of the stems, leaves, and flowers of Echinacea purpurea possess potent antiviral activity against HSV1 and HSV2 and hemagglutinin of influenza virus(Yusuf *et al.*, 2020), as coronavirus also possess a similar protein. This activity was attributed to the plant extract components, polysaccharide and cichoric acid. A potent antiviral photosensitiser was seen in the ethyl acetate and ethanol soluble fractions of the plants stem and leaves. Another molecular docking research in which one of the plants components, L-chicoric acid was docked against the protein HIV-1 integrase this is important to understand the host-interactomes responsible for the mortality rate discrepancy recorded in Africa. by, it shows a very good binding modes between the ligand and the viral integrase(Yusuf *et al.*, 2020). This explains its reported potency which is consistent with the experimental data available. Exploring medicinal will give both option of producing an antiviral agent and immune stimulators. This will also serve as a preparedness approach for any possibility of future SARS-CoV-2 mutation (Yusuf *et al.*, 2020). More plant extracts have shown both antiviral properties and ability to confer immunity in human, a good example of such plant is Asparagus africanus which has proven to be important pharmacologically (Kebede *et al*., 2016).

CONCLUSION

Low income countries will find it difficult to meet up with the demand of Covid-19 vaccines currently available, especially in Africa, where, despite discrepancies in the mortality rate compared to other continents, most countries have to borrow money to acquire these vaccines. Adaptation of cell lines in vaccine development, Researches on viral-host interactomes as well as exploitation of medicinal plants of African origin can be used as cost effective solution for infectious agents such as SARS-CoV-2 in Africa.

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