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ABSUMSAJ

*Research Article*

# African Perspective of Medication Safety in the Management of Covid-19: A Narrative Review

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## Abstract

### Background

This study highlights the current medication of use for COVID-19 treatment and management in the health care system and the available drugs of use were evaluated for safety profiles. The findings highlight the need for medications such as Remdesivir, Ibuprofen, non-steroidal drugs, and corticosteroids to be extensively studied in the proper management of COVID-19 while reducing its potential side effects. The study also emphasized the need for strong scientific evidence to support the usage of these drugs among those infected with COVID-19. Remdesivir was reported to have no adverse effects related to its usage. In combination with Ritonavir, Lopinavir has shown more promise in managing SARS-CoV and MERS-CoV. There is no available data yet on the use of Ibuprofen, while Umifenovir and Oseltamivir have no scientific basis for an effective fight against the COVID-19 virus. Methylprednisolone and steroids are not recommended for COVID-19 treatment, excluding those affected with Acute Respiratory Distress Syndrome (ARDS), while Tocilizumab was only suggested as a possible COVID-19 medication. These findings have contributed to revealing the kind of COVID-19 medications that are safe for use, a possible suggestion of use, and not recommended. It has abreast us with all the approved medications employed in the care of COVID-19, as it is vital for therapeutic success.

### Methods

This study reviewed the safety profiles of various medications that have been used to treat COVID-19. A literature search was conducted using the PubMed/MEDLINE and Google Scholar search engines. Articles published in English without a date restriction were reviewed.

### Results

The results of the study showed that there is limited evidence to support the use of some medications for the treatment of COVID-19. For example, there is no evidence that ibuprofen is effective against the virus. Other medications, such as remdesivir and corticosteroids, have shown some promise in clinical trials, but more research is needed to confirm their safety and efficacy.

**Conclusion**

The study concluded that there is a need for more research to determine the safety and efficacy of medications for the treatment of COVID-19. In the meantime, healthcare professionals should carefully consider the risks and benefits of using any medication for this purpose.

**Keywords:** COVID-19, drug safety, Remdesivir, corticosteroids, Africa, SARS-CoV, pandemic, healthcare

## Introduction

The COVID-19 disease enormously impacted healthcare services worldwide, these impacts vary in different countries with a high impact in developing countries. Developed countries such as the United States have implemented measures such as employing excess health professionals and providing health care resources such as ventilators for hospitals to help combat the pandemic.[1] The system of healthcare in low- and middle-income countries where the health system is weak has already been severely affected by the pandemic. [2] Vaccinations are one of the most important, influential, and preventive measures in medicine, and significant medical success can be achieved through vaccinations.[3] Numerous vaccines have been subjected to review and clinical trials due to these challenges in addressing the COVID-19 pandemic. The U.S. Food and Drug Administration (FDA) issued Pfizer-BioNTech, Moderna, and Janssen vaccines. However, on 13 April 2021, the FDA and the Centers for Disease Control and Prevention (CDC) withheld Janssen due to cases of blood clotting and cerebral venous sinus thrombosis.[4] Given the pandemic, various countries have implemented countermeasures to help with COVID-19 cases, such as lockdowns and restrictions on the movement of people. Several health workers have been dispatched during this lockdown to treat hospitalized patients. Meanwhile, the fear of getting infected has prevented many patients from accessing good health facilities and consultations. Also, many self-medication cases have recently been discovered, as infected people resorted to getting non-prescribed drugs from outlets claiming to cure COVID-19.[2]In terms of this, several unconfirmed drugs have been manufactured and promoted in societies and social networks, making patients trivialize the consultation of health professionals in fear of contracting the virus and introducing unconfirmed drugs to them. [2]

Furthermore, people's perceptions and attitudes toward drugs and vaccine acceptance have fluctuated with the flow of information on various social networks and the severity of clinical cases.[5] Therefore, managing several COVID-19 medications has become important in the healthcare system. The constant evaluation of various drug safety profiles on a large scale is a greater priority. Therefore, this study aimed to review various available medications used for COVID-19 treatment and management and evaluate their safety profiles.

## Methodology

A literature review was conducted to determine the types and extent of drug safety in treating COVID-19 in African countries. This article summarizes the safety of medication in the management of COVID-19. PubMed/MEDLINE and Google Scholar search engines were searched with the terms 'Medication', 'COVID-19', 'Management' and "Africa," and articles published in English without a date restriction placed on the search were reviewed. The results are discussed in detail under various sub-headings below.

## Results

Standard medication safety aims to ensure that healthcare professionals prescribe, dispense, administer drugs, and monitor the use of drugs safely. It is expedient for healthcare professionals to improve medication safety by ensuring that patients are taking the correct medications at the right doses, monitoring the patients for any side effects as well as educating them about their medications. Quality medical care is the heartbeat of an effective and robust response to an outbreak. Prevention strategies play an important role in reducing the relentless spread of the unexpected virus, as well as in community containment and successful disease isolation.[6] According to the World Health Organization (WHO),[7] more than 600 million COVID-19 cases have been reportedly confirmed, together with more than 6 million deaths reported since the emergence of COVID-19.

COVID-19 has quickly become a global pandemic that has caused numerous deaths and catastrophic economic consequences worldwide. It has been reported as a global public health problem in 2020.[4,6] COVID-19 is said to be caused by the SARS-CoV-2 virus and is spread through various transmission

routes, including direct contact, droplet, and aerosol.[8,9] However, airborne spread through aerosol formation is suspected to be the primary route of transmission.[8,10] Clinical characteristics are reported to occur most frequently between days 4 and 5 after exposure. However, several research studies have revealed that incubation can often last up to 14 days.[11] A wide range of symptoms of COVID-19 is reported to be cough, fever, fatigue, loss of smell or taste, and shortness of breath.[7] During the season of the covid-19 pandemic emergency, several countries have had to make serious decisions to protect their citizens. Therefore, Clinical researchers are testing various treatments such as immunotherapy, cell therapy, and Chinese herbal medicine. [12] However, the WHO suggests that the only way to reduce and curb transmission of all forms is to be informed of the virus and transmission routes and stay at least 1 meter away from the public and in closed spaces. The CDC recommends at least 1.8 meters, including putting on a well-fitting facemask, washing hands regularly, or applying an alcohol-based hand sanitizer to prevent infection, vaccinations at the appropriate time, and following all local instructions.[7]

Many people can get the coronavirus without showing symptoms. In only mild cases, this could lead to the unintentional spread of the virus if public health measures are not practiced, such as using a face mask and washing hands frequently, and physical distancing. More health seminars and outreach education exercises are needed to curb and control the widespread prevalence of COVID-19. The WHO, recognizing the fragility of many health systems and services worldwide considering the havoc posed by this pandemic on health systems globally, has proposed guidelines to maintain significant health reinforcement and services throughout the globe during the pandemic for all countries which includes strengthening the surveillance system to COVID-19, increasing testing capacity and provision of financial support to healthcare workers.[7] These steps include activating restrictions and restrictions on the movement of people and mobilizing health workers on the front lines of COVID-19 transmission. This can be a huge problem for chronically ill patients due to return visits, follow-up visits, tests, and prescription refills, as access to healthcare facilities to receive treatment could be deprived. Furthermore, the increased likelihood of contracting the disease in and around hospitals has convinced almost all patients to reject medical facilities for consultation by the doctor. [13]

Again, to fulfil their duty of maintaining necessary services regularly, pharmacists in the community must involve individual clients in transparent communication regularly, especially those with serious conditions, to determine their medication needs and provide the appropriate support. High community involvement will ensure confidence in the community health system because it will ensure the

continuity of health services to meet their essential needs at the grassroots community level. It is also necessary to ensure that clients always seek appropriate care when necessary. [2]

Ensuring patient isolation is essential to prevent the spread to other innocent patients, members of the family, and caregivers. Quarantine measures should be implemented to isolate symptomatic and asymptomatic infected people who might be in close contact with an infected person in some way. Individuals should minimize using time outside and all forms of social contact. Self-isolation at home is the most preferred option for mild cases while staying well hydrated and nourished, treating any symptoms that arise, such as sore throat, fever, and cough**.** [14] The safety of medications such as Remdesivir, Ibuprofen, non-steroidal drugs, and corticosteroids during the COVID-19 pandemic has received little attention in the literature. The use of these medications in the general population, who may have COVID-19, or in people severely infected with the virus is currently not supported by scientific evidence. However, in the narrative review, only a few results of the impact of these highlighted drugs on the treatment of COVID-19 were addressed.

**Clinical Case Management/ Review of Covid-19 Drugs**

**Remdesivir**

Gao et al. (2020) study on the antiviral drug Remdesivir revealed that the drug has in vitro action against the COVID-19 virus, while Ebola studies had validated its safety. [15] Wang et al. (2020) showed that chloroquine, a former malaria drug with evident efficacy and safety against COVID-19-caused pneumonia, was suggested as another drug remedy.[16]Holshue et al. (2020) documented the first case in the United States, which served as a proof point for using remdesivir to treat COVID-19. On the seventh day of the patient's hospital stay, the antiviral was administered for compassionate use because the patient's clinical state had worsened with only supportive treatment. The next day, the patient allegedly showed improvement in oxygen saturation, clinical findings, and symptoms. The viral loads of the oropharyngeal swabs gradually decreased and became negative. Holshue et al. (2020) have stated that there were no adverse effects related to its use.[16] **Table 1** summarizes the COVID-19 drugs and their side effects.

**Lopinavir-ritonavir**

Combining Lopinavir with Ritonavir increases Lopinavir's bioavailability by inhibiting cytochrome P450 3A4, the lopinavir enzyme, and lopinavir, which inhibits viral 3-chymotrypsin-like protease. [17]

Yao et al. (2020) stated in their study that this combination of lopinavir with ritonavir has also shown promise in the treatment of SARS-CoV together with MERS-CoV.[17]

**Ibuprofen**

According to Quaglietta et al. (2021), ibuprofen has been associated with severe necrotizing soft tissue infections (NSTI) during chickenpox. Using ibuprofen before going to a hospital makes kids more likely to have severe pneumonia. Quaglietta et al. (2021) stated in their review that ibuprofen is safe and effective when used in exacerbations of cystic fibrosis (CF), despite conflicting results for septic youth. However, data on the course of ibuprofen use during COVID-19 are not yet available.[18]

**Umifenovir and Oseltamivir**

Although intriguing, no scientific basis exists to determine whether anti-influenza drugs such as oseltamivir and Umifenovir effectively combat the COVID-19 virus. However, its effectiveness in treating other viral respiratory infections, such as influenza, has not yet been shown.[19,20]

**Methylprednisolone**

According to Kolifarhood et al. (2020), methylprednisolone and steroids seem to be employed in the present COVID-19 cases. However, the WHO-2020 report revealed that methylprednisolone and steroids are not recommended for administration as a drug for COVID-19, except for those with an acute form of respiratory distress syndrome (ARDS), since it has been shown to extend the availability of the virus in the case of MERS.[21]

**Tocilizumab**

Patients with severe macrophage activation syndrome due to COVID-19 infection often develop acute respiratory distress syndrome. Interleukin 6 (IL-6) levels that are high due to persistent infections are associated with the intensity of COVID-19 and the death rate in ARDS.[22,23] An anti-IL-6 monoclonal antibody called Tocilizumab is used to treat rheumatoid arthritis and has been suggested as a possible COVID-19 drug in this situation.[24,25]

**Vitamin D**

The most recent findings revealed a positive effect of vitamin D on COVID-19. Vitamin D was reported to reduce the risk of respiratory infections. This was reinforced by Grant et al., who have suggested that vitamin D supplementation may reduce the risk of contracting COVID-19.[31]

**Zinc**

Zinc has been reported to have antiviral effects against viruses such as Covid-19 and the influenza virus due to its potency in increasing immune system function and inhibiting COVID-19 replication by preventing RNA synthesis [32,33]. Zinc ensures natural tissue barriers, such as the respiratory

epithelium, inhibits pathogen invasion**,** and is necessary to maintain functional immune and redox systems.[34]

**Hydroxychloroquine and chloroquine**

These two antimalarial drugs are immunomodulatory and commonly used to treat systemic lupus erythematosus and rheumatoid arthritis. These two drugs have been reported in the treatment of COVID-19,which are currently being studied as the mechanism of action is not well understood.[35]

**Amantadine**

This is also an antiviral drug to treat influenza A. It is not yet understood whether this drug is effective in treating COVID-19. However, due to its antiviral characteristics, it was assumed that it would mitigate the symptoms of Covid-19. Amantadine blocks the COVID-19 viral purine channel of COVID-19 and inhibits the release of the viral nucleus into the cell cytoplasm. [36]

**Dexamethasone**

This type of corticosteroid is used mainly to inhibit inflammatory cells and suppress the expression of inflammatory mediators. It is intended for use in the treatment of inflammatory and immune diseases. Recently, this medication has been widely used in the treatment of COVID-19, which was recommended for infected persons in critical condition and in need of oxygen. The National Institute of Health and Care Research (NIHR) in the UK and the National Institutes of Health (NIH) in the US, the Infectious Diseases Society of America (IDSA), the European Medicines Agency (EMA), and the World Health Organization (WHO) also recommend guidelines for severe cases. [37]

**Ivermectin**

Ivermectin is a Food and Drug Administration (FDA) approved antiparasitic drug for treating parasites. The use of Ivermectin for the prevention and treatment of COVID-19 by the public in African Union Member States has been reported. However, a study shows that Ivermectin inhibits SARS-CoV-2 replication. However, due to insufficient data on the drug's efficacy, the FDA has not authorized Ivermectin to treat or prevent COVID-19 infection in humans.[31]

**Paxlovid**

Paxlovid, the newest COVID-19 drug, was authorized by the FDA. This oral medication contains two antiviral drugs: Nirmatrelvir and Ritonavir, packaged together. Paxlovid works by inhibiting the key enzyme that the COVID virus needs to make functional viral particles. Africa Centre for Diseases and

Prevention (CDC) recently signed a memorandum of understanding with Pfizer to access Paxlovid and its distribution throughout African countries.[33,34]

**Table 1: Summary of various drugs used for COVID-19 and their side effects**

| S/N | COVID-19 Drugs | Side Effects | Author(s) |
|---|---|---|---|
| **1.** | Vitamin D | Increases calcium levels in people with sarcoidosis, the growth of tiny collections of inflammatory cells in different body parts that often lead to kidney stones and other problems. The side effects of high doses of vitamin D are more common in women than in men | Nadia et al., 2021 |
| **2.** | Zinc | Headaches, nausea, and vomiting arezinc's most common side effects, usually associated with high doses. | McPherson et al., 2020 |
| **3.** | Hydroxychloroquine and chloroquine | Cardiac, neurological, and psychiatric side effects. Among cardiac-related side effects are disorders such as conduction disorders and cardiomyopathy. Neurological side effects include muscle weakness, diplopia, movement disorders, seizures, myasthenia gravis, and neuropathy. Psychiatric side effects such as insomnia, irritability, psychosis, depression, anxiety, aggression, and confusion | Ferner and Aronson, 2020; Juurlink et al., 2020 |
| **4.** | Remdesivir | The most common adverse events in the Remdesivir studies for COVID-19 included respiratory distress and organ dysfunction, including low albumin, low potassium, low red blood cell count, low platelet count, low blood pressure, and blood pressure clot formation, and yellow skin discoloration are common effects. | Malin et al. 2020 |
| **5.** | Amantadine | The most common side effects of Amantadine are also neurological, such as drowsiness (especially while driving), light-headedness, falls, and dizziness; Cardiovascular, such as orthostatic hypotension, syncope, and peripheral edema; Gastrointestinal, such as dry mouth and constipation; Skin problems; have been reported with Amantadine | Abreu et al., 2020 |

| | | | |
|---|---|---|---|
| **6.** | Dexamethasone | The most common side effects of dexamethasone are also gastritis, vomiting, headache, dizziness, insomnia, restlessness, depression, acne, irregular or absent menstrual periods | Poldermanet al., 2018 |
| **7.** | Ivermectin | Side effects of ivermectin include nausea, vomiting, diarrhoea, decreased consciousness, confusion, hallucinations, central nervous system depression, seizures, coma, and death. | (Caly et al., 2020) and Africa Centre for Diseases and Prevention |
| **8.** | Paxlovid | Paxlovid side effects include diarrhoea, high blood pressure, muscle pain, and taste changes. | (Weng et al., 2020) and (Yale Medicine: Kathy Katella, 2022) |

## Discussion

The narrative review discusses medication safety in COVID-19 management. Many people with mild symptoms such as sore throat, dry cough, body pain, or low fever visit clinics and health facilities. Patients usually go to the emergency room with symptoms if clinical manifestations worsen after a few days. Research on clinical criteria and biomarkers for prognosis prediction is significant due to the wide range of clinical signs, allowing the differentiation of patients who need additional treatments in the early stages of the disease. Liu et al. (2020) asserted that lopinavir-ritonavir was effective against SARS-CoV-2. One of these reports dealt with 10 patients with COVID-19 cases treated with lopinavir at the Hangzhou Hospital in China. However, the action of the mechanism and the role played by lopinavir in the resuscitation of 7 of the 10 patients was unclear as they received various medicines, such as antibiotics, methylprednisolone, and arbidol hydrochloride granules.[23]

Huang et al. (2020) studied 41 prospectively hospitalized patients from Wuhan, China. This is one of the first studies to explain the importance of methylprednisolone as a component of an overall treatment plan for a subset of patients with COVID-19 with severe community-acquired pneumonia. However, the research did not establish any significant statistical relationship between patients taking or not since it was not intended to examine the effectiveness of corticosteroids in the treatment of COVID-19.[28]Numerous case studies of COVID-19 individuals with particular pre-existing medical illnesses have shown the utility of tocilizumab in those situations. After an initial treatment with lopinavir-ritonavir, Michot et al. (2020) administered two doses of tocilizumab (8 mg/kg dose) each to a metastatic sarcomatoid patient with renal cell. After therapy, the temperature of his body and the

CRP level dropped. On the contrary, his oxygen saturation level increased, and he eventually recovered after experiencing a sudden onset of dyspnea and a decrease in oxygen saturation.[29] Declaring an acceptable short-term with long-term medication safety statistics of all approved medications used in the care of COVID-19 is necessary, as safety will play a significant role in therapeutic success. Safety issues must be viewed in the context of unique disease stages to create an algorithm to decide patient-specific clinical outcomes.

**African Perspective of Covid 19 Medications**

Several medications have been prescribed illegally, which were found to have little or no relation to the pandemic in Africa. [35] For example, the widely accepted use of Ivermectin in South Africa, where there was no evidence that the antiparasitic drug worked against covid 19. Ivermectin is a drug known for treating parasites in animals which was recommended against its use by the U.S FDA, WHO, and South African regulators. Ivermectin usage started in South Africa when the second pandemic wave kicked off at the end of 2020. Importation and usage of Ivermectin in limited circumstances were allowed after the government initially banned it in December 2020. Meanwhile, hydroxy-chloroquine was widely accepted for treatment during the first wave of the pandemic, which was later banned and discredited. However, when cases started reoccurring, indicating the second wave, south Africans turned to the usage of Ivermectin. [35,36,38]

Amid all these hurdles, African populations are still hesitant to get vaccinated. Africans are unsure of the vaccine's efficacy, efficiency, and effects. This has instilled fear in most people in Africa not to embrace it, resulting in criticism of the vaccine. Vaccine uncertainty was reported as the main challenge to vaccine acceptance which is hindering the achievement of herd immunity necessary to protect the marginalized populations in the nation. Most religious and individual groups also made negative claims and discouraged people from accepting the vaccine, as it depicts the end of the universe.[39] For instance, research conducted in sub-Saharan Africa stated that vaccine hesitancy in this region is attributed to the misconstrued information and conspiracy theories widely spread on social media handles about the efficiency of the vaccine.[40]

## Conclusion

The review highlighted that the safety of medications such as Remdesivir, Ibuprofen, non-steroidal drugs, and corticosteroids during the COVID-19 pandemic had received little attention in the literature. The use of these medications in the general population, who may have COVID-19, or in people severely infected with the virus is currently not supported by scientific evidence. Hydroxy-chloroquine

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## Conflict of Interest

The authors declare no conflict of interest

## Authors Contribution

All authors contributed equally to the preparation of this article. We have all read and approved the final draft.

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