



OPINION

Prior Use of Chloroquine May Partially Explain the Low Number of Cases of COVID-19 in Sub-Saharan Africa

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INTRODUCTION

As of November 3, 2021, over 248, 000,000 confirmed cases of COVID-19 were reported worldwide, with about 5, 024, 200 deaths (2.0%) and 224, 686, 130 recoveries¹. Presently, the United States (US), India, Brazil, and the United Kingdom (UK) are the top four countries with the highest reported cases of the COVID-19¹. All African countries have officially reported at least one positive case of the virus, with over 8, 500, 000 confirmed cases (3.4% of reported worldwide cases)². In brief, the number of reported cases of COVID-19 is lower in African countries compared to other continents.

Although vaccines are now available for the COVID-19 infection, the cure for the virus is still under investigation. Recently, two experimental antiviral drugs discovered by US companies (Merck and Pfizer) have been shown to reduce hospitalizations and death from the COVID-19 virus³. Merck's antiviral agent has been approved in the UK and might soon be authorized in the US. Fortunately, a recent report has shown that the widely used drug "Hydroxychloroquine" has a promising effect against the COVID-19 virus, mainly, among the population infected with the disease in the US and Europe⁴. Hydroxychloroquine is a chloroquine derivative that has been used widely in the

treatment of Malaria in Africa since 1940. Thus, the decades use of this drug by most people in the continent could be one of the reasons for the low cases of COVID-19 virus infection in the African countries.

Chloroquine is an antimalarial drug of the chemical group 4-aminoquinolines. It is used to prevent or treat malaria caused by mosquito bites. It is active against the erythrocytic forms of sensitive strains of all species of malaria, and it is also gametocidal against *P. vivax*, *P. malariae*, and *P. ovale*. First introduced in the 1940s, chloroquine for many decades served as a cheap and reliable drug for the treatment of malaria caused by *Plasmodium falciparum* in most tropical countries⁵. Over the years, *P. falciparum* developed resistance to chloroquine. Its derivative, hydroxychloroquine, is used as an anti-inflammatory drug for systemic lupus erythematosus and rheumatoid arthritis (RA)⁶.

The characteristics of COVID-19 as a protein enveloped by fatty substances has been identified earlier. The reported successes in treating or preventing COVID-19 with chloroquine in combination with azithromycin, zinc Sulphate gives hope that contracting the disease should not be seen as a kind of 'death sentence'. The dominant product is obviously chloroquine and although the prescription is not an authoritative first line treatment regimen, it

nevertheless has been reported to be beneficial for some individuals in the US. The former US President, Donald Trump encouraged the use of chloroquine for patients receiving treatment for the disease.

It is based on above premises that this paper attempts to draw an analogy between the reported efficacy of chloroquine in the treatment and prevention of COVID-19 infection in the USA and other European countries, and the low cases of the disease in Sub-Saharan African countries. For decades, Sub-Saharan African countries have had a long history of successful experiences in using chloroquine and its derivatives as first line drugs of choice in the treatment of malaria. This included the widespread use of bark and leaves of *Cinchona* that is very rich in quinine, and later, chloroquine, hydroxychloroquine, and other synthetic derivatives of quinine in the treatment of malarial parasite for over 70 years. The use of these compounds was recently abandoned for other alternative products due to resistance⁵. In contrast, malaria parasites cannot survive in regions with temperatures below 20°C. Thus, malaria transmission does not occur in temperate regions such as USA and most of Europe. Therefore, people in the USA and Europe have not been using or are not exposed to chloroquine and its derivatives.

The hypothesis is to establish a relationship whether malaria parasite in Sub-Saharan African countries, have retained some residual amount of the chloroquine substances within their mutated genetic norm after 'surviving' doses of chloroquine within their host⁵. The parasite is known to remain dormant in the human liver for several months and up to four years following infection. It is this likelihood of carrying traces of chloroquine within the genetic makeup of the parasite while in the liver in its dormant form could have provided some residual amount of chloroquine drug within the blood stream of people in sub-Saharan African countries. It could be hypothesized that this residual chloroquine could act as some kind of 'prophylactic' against the COVID-19 virus,

which has now been reported to be effective against the infection.

In addition to the above explanation, other factors responsible for the low COVID-19 cases in Sub-Saharan African countries may include the following: a higher proportion of young population in Sub-Saharan Africa compared to Europe and USA, unfavorable weather (> 20 °C temp) in most of the Sub-Saharan region which may limit the survival of the coronavirus; mitigation measures introduced in Africa largely learnt from previous epidemics such as Ebola virus; and pre-existing immunity which may be due to cross-reacting coronaviruses.

CONCLUSION

Given the trend of low level of COVID-19 infections within the population of Sub-Saharan African countries with a long history of chloroquine exposure, when juxtaposed with the recorded high numbers of those inflicted with the virus in the US and UK, which can be said to have never used chloroquine to cure malaria due to the absence of the disease in these countries, it is safe to conclude or hypothesize as follows:

- (a) That chloroquine has great potentials for the treatment of COVID-19.
- (b) The exposure to chloroquine may be one of the possible explanations for the low number of COVID-19 cases in Sub-Saharan countries compared with the US, and other countries (without history of chloroquine use).
- (c) That most people in the Sub-Saharan Africa countries have malaria parasites obviously in different mutant forms in their system which can cause malaria in the host when immunity is compromised.
- (d) That the genetic makeup of the malaria parasites within people of Sub-Saharan Africa is such that it has developed resistance to chloroquine and that in its present genetic genome, has some characteristics of the chloroquine molecule achieved through several generations of mutation that can still 'behave' as a weakened or diluted form of

chloroquine drug and being present in millions within the liver, will assist the body's defence to comprehensively fight off the coronavirus.

- (e) That while other factors such as inadequate healthcare systems, limited or lack of equipment for screening for COVID-19, and low level of health literacy could be responsible for the low cases in the region, this paper has generated a hypothesis that can be tested in high quality randomized controlled clinical trials to provide more empirical evidence.

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