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Article

Investigating the Factors Affecting SARS-COV-2 Transmission and Mortality Rate in Sub-Saharan Africa

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Abstract: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), also known globally as COVID-19, originated in December 2019 in Wuhan, Hubei province in China and has rapidly spread across the globe ever since. The first recorded case in sub-Saharan Africa was in Nigeria, on the 25th February, 2020. The virus continues to spread, and new variants of the disease have emerged, the number of deaths and new infections in the countries of sub-Saharan Africa has been relatively low compared to predictive models. This could be due to several factors, such as slower transmission dynamics of the virus, a lower-case fatality rate, or a lack of testing or reliable data. Whilst this may also, in part, be due to the robustness of the nations' public health responses, there is scarce reporting on the specifics of this. However, emerging research has demonstrated that various environmental factors could influence virus transmission. The study adopted collected meteorological data that was critically analysed and discussed. The impact of three factors in the context of sub-Saharan African nations: temperature, ultraviolet (UV) exposure and pre-existing infection with Plasmodium (malaria) were discussed. These factors were discussed critically in light of the reduced rates of transmission and mortality observed.

Keywords: COVID-19; coronavirus; transmission; meteorological impact

1. Introduction

Following the emergence of SARS-CoV-2 in Wuhan, China, in December 2019, it was declared as a Public Health Emergency of International Concern by the World Health Organisation (WHO) in January 2020, and a pandemic on 11th March 2020. This prompted many governments to impose public health interventions to reduce transmission of the virus, including national lockdowns and social distancing measures. Such measures were also implemented in the nations of sub-Saharan Africa, such as closing borders and limiting travel to returning residents and essential workers (Muzvidziwa, Muza, 2020). Contact tracing and testing and admission of those who tested positive to designated isolation areas with medical assistance (Umviligihozo et al, 2020), among other measures.

Despite implementing the aforementioned measures, it was expected that countries in sub-Saharan Africa would be markedly affected in terms of mortality, given the fragile infrastructure of healthcare systems in these nations and limited global knowledge surrounding the novel Coronavirus. However, these nations have had lower case and mortality statistics relative to predictive models. As of 27th February 2022, there have been 5, 965, 639 deaths and 435, 234, 549 confirmed cases of COVID-19 (WHO Coronavirus Dashboard, 2021), with the USA, Brazil and India being the worst hit, with 972, 930; 648, 989 and 513, 756 fatalities respectively. On the other hand, the nations of sub-Saharan Africa have totalled 164, 251 fatalities, accounting for 2.75% of total global fatalities.

There are several potential reasons why outcomes in these nations have been better than predicted, including the strength of nations' public health responses or lacking accuracy in data collection. However, with the emergence of SARS-CoV-2, more recent research has been conducted into the impact of various environmental factors on its transmission. With the rapid spread of the virus, much attention has been paid to the rate of an epidemic, transition ways, prevention methods and remaining time of the virus in the environment – hence the consideration of virus behaviour in response to environmental factors is vital (Pirouz et al, 2020). There are a substantial number of environmental factors, in this research, we have focussed on three main areas, both as they are factors affecting and relevant to the sub-Saharan Africa region. They are areas of research that are still very much developing.

Regarding temperature, there has been significant debate as to its effect on transmission is. Initially, most studies about the topic suggested an inverse relationship between temperature and SARS-CoV-2 transmission; a number of studies have denied or underestimated the effect on the transmission of the virus. It has also been proposed that temperature only affects the transmission of the virus in its early stages and that once transmission reaches a critical mass following a successive exponential increase, temperature no longer has a significant effect on transmission (Kassem et al, 2020). Few studies have also attempted to suggest a quantitative representation of temperature's effect and identify the threshold. Xie and Zhu (2020) proposed a 4.861% increase in the daily number of confirmed COVID-19 cases per 1^{o}c increase in temperature, up to a threshold of 3^{o}c.

Furthermore, recent research published in the British Journal of Dermatology found that COVID-19 transmission is sensitive to Ultraviolet-A (UVA) exposure. Individuals living in areas with the highest level of exposure to UVA rays tended to have a lower risk of dying from COVID-19 than those with lower levels (Cherrie et al, 2021). Further research has suggested that Ultraviolet B (UVB) radiation also impacts the transmission of the virus. While potential biological mechanisms have been hypothesised, it is believed that each type of UV radiation pertains to its biological pathway, which will be explored further by this study. Suppose there is proven to be a link between UV exposure and COVID-19 transmission and mortality. In that case, it could lead to interventions that could be tested as potential treatments – current studies have called for further research to establish if it causes a reduction in mortality rates. Globally, regarding COVID-19 transmission, observed is a tropism as we move towards the poles of the Earth (Bezabih et al, 2020). The decrease in incidence with decreasing latitude could be associated with higher climates and UV exposure, and thus it is relevant to consider in the context of sub-Saharan Africa.

The final factor considered is if previous infection with Plasmodium, universally known as malaria, may have a protective effect in the context of SARS-CoV-2 infection. Annually, there are estimated to be 230 million malaria cases in sub-Saharan Africa (Dyer, 2020). So if a link is demonstrated, it could explain the marked difference in COVID-19 incidence and mortality in North America, Western Europe, and South Asia compared to malaria-endemic nations of sub-Saharan Africa (Hussein et al, 2020). Several biological mechanisms have been proposed, including both a potential genetic basis and modifications to the immune system. Initially, there was much speculation as to whether chloroquine and hydroxychloroquine (anti-malarial medication) could be used as prophylaxis or treatment for COVID-19. However, a recent Cochrane review (Singh et al, 2021) stated that the drugs most likely do not reduce mortality. Despite this, pre-existing infection with malaria still may be closely linked with COVID-19 susceptibility and mortality.

Table 1 presents some existing literature with different findings on the impact of environmental factors on Covid 19 transmission and mortality rate. These studies observe a significant effect of temperature

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Table 1. Studies on the relationship between Covid 19 infection and environmental factors.

Authors	Title
(Kassem, 2020)	Does Temperature Affect COVID-19 Transmission?
(Tan et al., 2005)	An initial investigation of the association between the SARS outbreak and weather: With the view of the environmental temperature and its variation
(Ma et al., 2020)	Effects of temperature variation and humidity on the death of COVID-19 in Wuhan, China
(Smit et al., 2020)	Winter is coming: A southern hemisphere perspective of the environmental drivers of sars-cov-2 and the potential seasonality of covid-19
(Morris et al., 2020)	Mechanistic theory predicts the effects of temperature and humidity on inactivation of SARS-CoV-2 and other enveloped viruses
(Chan et al., 2011)	The effects of temperature and relative humidity on the viability of the SARS coronavirus
(Ozyigit, 2020)	Understanding Covid-19 transmission: The effect of temperature and health behavior on transmission rates
(Sharma et al., 2020)	Structural stability of SARS-CoV-2 degrades with temperature.
(Biryukov et al., 2020)	Increasing Temperature and Relative Humidity Accelerates Inactivation of SARS-CoV-2 on Surfaces
(Ali & Islam, 2020)	The Effects of Air Pollution on COVID-19 Infection and Mortality—A Review on Recent Evidence
(Riddell et al., 2020)	The effect of temperature on persistence of SARS-CoV-2 on common surfaces

Given this background and the positions of several studies on demography, weather changes have a significant impact on covid 19 spread. It is observed that with higher temperature and UV light , the covid 19 spread rate is decreased. Studies like (Merow & Urban, 2020) supports this notion stating that UV light is associated with reduced disease growth. This is supported by (Chen et al., 2021). Based on this background and the widely held notion, countries like Nigeria experienced a lesser impact of the Coronavirus. This study collected weather data on humidity and temperature to understand the reason behind the low figures.

2. Method

The methodological framework for the study is represented graphically in Figure 1. The study conducted an extensive literature review to understand the impact of climatic variables on the spread and survival of the Coronavirus. In the second stage, the study collected weather data.

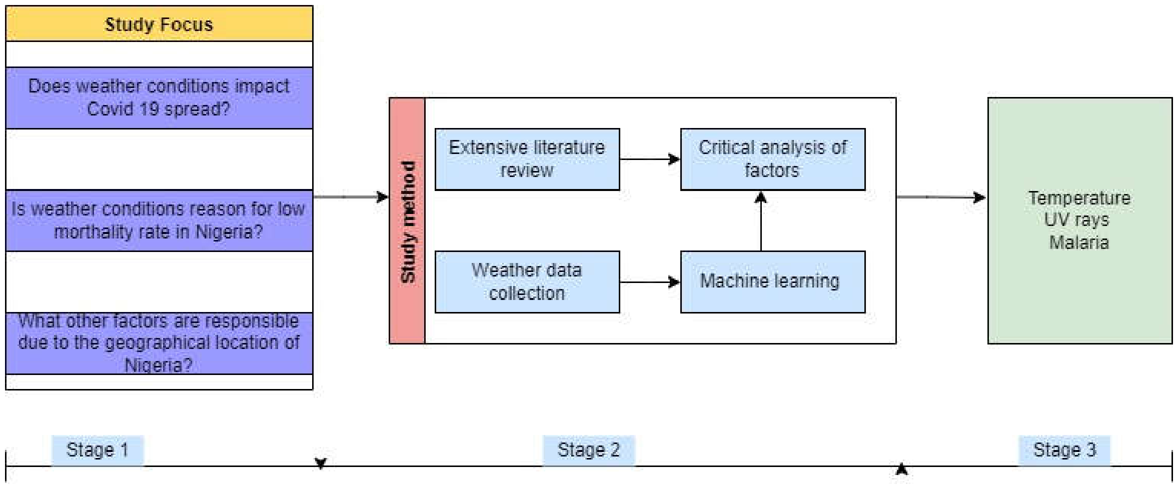

Figure 1. Methodological flowchart for the study.

2.1. Study area

The study area adopted by the study is Lagos state in Nigeria. Lagos is the commercial nerve centre and former administrative capital of Nigeria. The state has a high population influx and is one of the most populated cities in the country. It is, therefore, a place that could have experienced similar covid 19 figures like other highly populated cities globally.

The study installed the EarthSense Zephyr air quality sensor to collect data on the meteorological variables. With the equipment, data was collected for temperature and humidity, among other variables. Data was collected from July 2020 to March 2022. This period consists of the covid 19 pandemic high points. The data was collected at 15minutes intervals during the period. This is similar to the data collection adopted by (Ejohwomu et al., 2022).

According to the body overseeing the coronavirus management in Nigerian, the Nigerian centre for disease control (NCDC), Lagos state, since the outbreak of the disease, has recorded a total of 99322 cases, out of which 491 are on admission, 98, 062 discharged and 769 deaths (NCDC, 2022) as at 27 April 2022. The records (Figure 2) from the same source show an undulating record and periodic surge in recorded cases. Overall, it can be deduced that the documented cases in Lagos state are not profoundly affected compared with the death and recovery records from other parts of the globe, according to the WHO (NCDC, 2022).

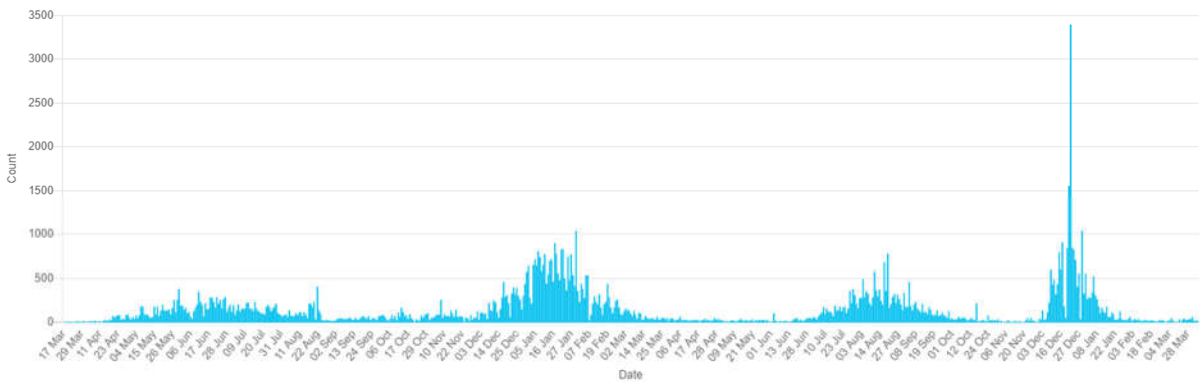

Figure 2. Coronavirus records in Lagos state(NCDC, April 2022).

2.2. Data Analysis

The collected data was analysed to understand the temperature trend over the period.

3. Results and Discussion

The study discussed the findings under the headings below:

3.1. Temperature

It is understood that climate change and variability have significantly impacted human health. Climate affects the intensity of vector(tick, rodent), food and water-borne diseases and the prevalence of diseases associated with air pollutants and aeroallergens (Amuakwa-Mensah, Marbuah, Mubanga, 2017). In fact, Zivin and Neidell (2013) modelled an individual's health production as a function of four variables: climate variability, given its impact on illness incidence, cost of medical care, and all other consumption goods. Climate change could also alter or disrupt natural systems, making it possible for disease to proliferate and emerge in areas where they had not existed or was scarce.

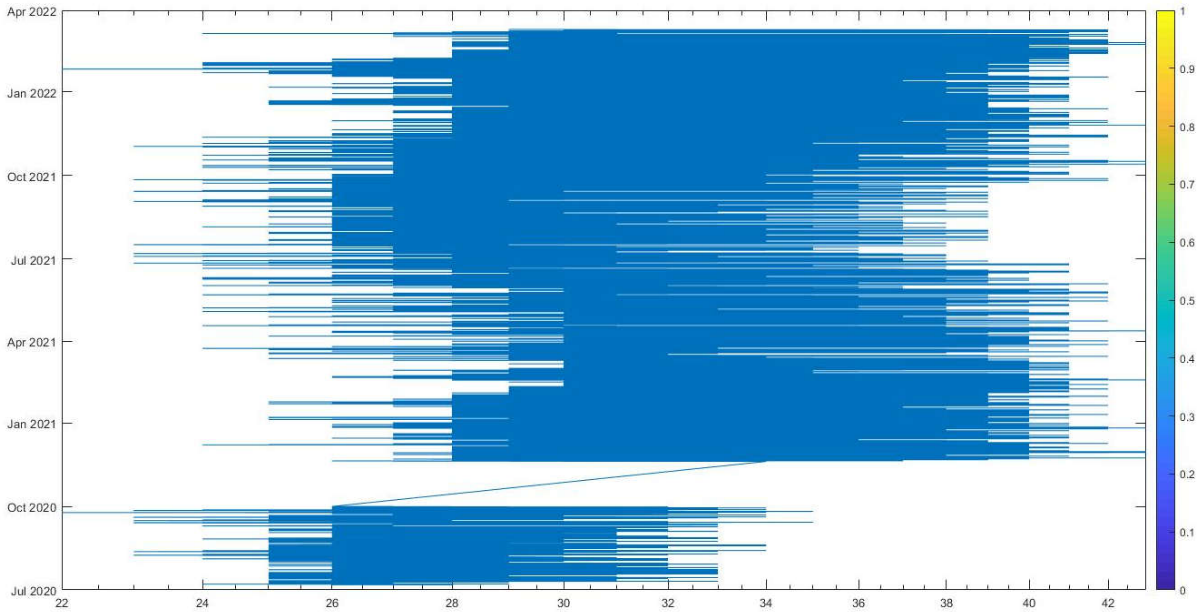

Figure 3. Time series analysis of temperature.

However, what is less well understood is the impact of climate variability on airborne disease, even less so, a more recently emerging disease as COVID-19. Among all other environmental factors, there is the possibility that temperature could be a distinct factor, vital in controlling public health responses with regard to epidemic growth and control (Das et al, 2020). As a respiratory pathogen, the virus has been able to reach every corner of the globe, however, there have been variations in transmissibility in different countries, particularly striking is that of those in sub-Saharan Africa (as referenced in 'Introduction'). Variation between nations has been thought to be related to climatic variability, particularly as the structure of the virus in not stable and is sensitive to temperature external to the host (Bezabih et al, 2020).

In considering the impact of temperature on COVID-19, it is vital to consider the changes occurring on a molecular level. The SARS-CoV-2 molecule contains an outermost Spike protein, which interacts with the Angiotensin Converting Enzyme 2 (ACE2) and gains access to the respiratory system. Kassem et al (2020) found that the Spike protein showed active and inactive states at different temperatures. Rath and Kumar (2020) investigated this further by performing an all-atom molecular dynamics simulation involving 200ns of stimulation at different temperatures and obtaining a root mean square deviation (RMSD) of the trajectory to investigate the effect of temperature on the Spike protein - they established several interesting phenomena.

The virus consists of 4 major structural proteins: the Spike glycoprotein (as aforementioned), the Envelope protein, the Membrane protein and the Nucleocapsid. These structural proteins are vital for virus transmissibility and enabling the virus to exert its effects. Following the molecular dynamics simulation, the RMSD showed that the spike protein was most stable at temperatures of 10°c and 50°c. Structural studies suggested the presence of several charged residues on the surface of the N-terminal domain of S1, and that they are optimally oriented at temperatures between 10°c and 30°c, which could have implications for binding to ACE2, as well as other receptors in the body. Furthermore, they found that the receptor binding motif (RBM), present on the receptor binding domain (RBD) of S1, begins to close at around 40°c, with its three chains coming very close together to seal the visibility of the trimeric pore. At temperatures above 50°, it attains a completely closed conformation – this closed conformation inhibits binding to ACE2, due to closure of receptor binding residues, and thus prevents entry to the respiratory system. Bezabih et al (2020) further supported that infectivity loss at higher temperatures are associated with Spike glycoprotein processing defects.

Despite the study, Rath and Kumar still stated that understanding molecular-level changes in the virus in different temperature environments is still fairly limited. For example, Rhinoviruses are unable to replicate at 37°c, whereas 33-35°c is ideal for their survival in the nasal cavity, whilst SARS can persist at temperatures between 22-25°c for five days. Still, viability is lost when the temperature is raised to 38°c (Edwards et al, 2020). In terms of virus viability on surfaces, Chin et al (2010) found that virus droplets survived at 4°c but quickly deactivated at temperatures higher than 50°c. Data collected by the study (Figure 3) shows the minimum temperature to be 22°C. A critical look at the temperature trend and the covid 19 records in Lagos state, it is safe to say temperature affected transmission. Also, temperature higher than 20°C inhibits the impact of coronavirus transmission.

Studies of previous epidemics have supported studies on the behaviour of SARS-CoV-2 at different temperature environments. Viruses of similar homology have shown inverse transmission relationship with temperature, for example, studies of SARS during the 2003 epidemic showed that the risk of daily incidence was 18.18 fold higher on days with lower air temperatures in Hong Kong and other regions (Chan et al, 2020). As warm weather increased, a gradual decrease was seen in the 2003 outbreak in Guangdong, with a complete resolve at the end of July 2003, during the summer (Thangariyal et al, 2020). Furthermore, Influenza and Middle East Respiratory Syndrome (MERS) also show greater persistence on surfaces at lower temperatures (Wang et al, 2020). Based on studies conducted on SARS and the Influenza virus, some reasons have been proposed why the virus remains viable at lower temperatures but is thought to be degraded at higher temperatures. Lower temperatures are thought to demote host immunity, thus increasing susceptibility. This may be due to cold air causing vasoconstriction of the respiratory tract, weakening the immune system. The virus is more stable in cold temperatures and can reproduce more rapidly, and respiratory droplets, which contain viral particles, remain in suspension for longer (Mecenas et al, 2020).

Many studies have supported the hypothesis that COVID-19 transmission is reduced by higher temperatures, and so regions with lower temperatures are more prone to infection. Underpinning this hypothesis is the fact that COVID-19 cases increased towards the Earth's poles with increasing latitude – additionally, virus peaks occur during the winter, a period with lower-than-average temperatures, taking the form of local epidemics that last a few weeks or months (Kassem et al, 2020). Mecenas et al (2020) found that the Coronavirus is able to retain its infectivity for up to two weeks in a low temperature and low humidity environment, which could be thought to facilitate the virus transmission in a communities located in subtropical climates.

Additionally, a study by Bezabih et al (2020) analysed 748, 555 confirmed COVID-19 cases worldwide, and concluded that the total number of patients with the virus decreased with increasing atmospheric air temperature and decreased with increasing latitude. Their study observed the correlation between increasing latitude and confirmed COVID-

19 cases. There is a presumed decrease in air temperature and UV exposure with increased latitude. They concluded that increasing latitude was associated with a significant increase in COVID-19 cases. For example, an increase in latitude from 25°, South Africa, to 50°, United Kingdom (countries with similar COVID-19 testing strategies) corresponded to a 16-fold-increase in the number of detected cases (from 2 to 32 per 100,000 population). Most studies concur that the relationship between COVID-19 transmission and air temperature has opposite directions, despite the level of significance varying. The variation observed in statistical significance may be due to differences in selection criteria of countries but does not affect the direction of the relationship.

In a letter to Nature, Rice et al (2020) remarked on the variation in SARS-CoV-2 outbreaks across sub-Saharan Africa. At the time of completion in December 2020, all sub-Saharan African countries, with the exception of South Africa and Ethiopia, reported fewer than 100,000 total cases and fewer than 1800 deaths – considerably lower than those observed in Asia, Europe and the Americas. Whilst there may exist a number of potential reasons for this, a core reason identified in the letter was warmer environments in these countries. It is imperative for us to consider temperature and its role on transmission in these countries, as temperature has thought to affect transmission and could play a significant role in recovery rates, deaths, and critical cases around the globe (Das et al, 2020).

3.2. Ultraviolet exposure

The impact of ultraviolet (UV) exposure has not been as widely researched as that of temperature, it is an area of significant potential with regard to COVID-19 transmission. Decreasing latitude has been associated with decreasing COVID-19 incidence and, as aforementioned, increasing air temperature; however, there is also associated higher levels of UV radiation from the sun (Bezabih et al, 2020).

Whilst research on the area is developing, the majority of studies to date support the hypothesis that a greater degree of UV exposure decreases transmission and mortality rates from COVID-19. As discussed in 'Temperature', with decreasing latitude, there is a decrease in transmission rate, but equally increased levels of sunlight exposure towards the equator – it can be said that the two variables go hand-in-hand. For example, a meta-regression study of Japanese prefectural data showed a significant negative trend for mean air temperature (coefficient = -0.314) and mean daily maximum UV index (coefficient = -0.852) (as well as sea level air pressure) – the study concluded that the variables collectively could be negatively associated with COVID-19 prevalence (Takagi et al, 2020).

Carleton et al (2020) combined a spatially resolved dataset of confirmed COVID-19 cases, involving 3235 regions across 173 countries. Using a statistical method to quantify the causal effect of environmental parameters in observational data, they found that UV exposure shows a significant inverse correlation with daily COVID-19 growth rates. With one SD increase in UV exposure lowering the growth rate of cases by 1 percentage point over the following 2.5 weeks. The peak effect of UV exposure occurs between 9-11 days which corresponds with the timescale of incubation, testing and reporting.

Deep ultraviolet (UVC) has been shown to inactivate coronaviruses on surfaces, and whilst germicidal UVC rarely reaches the Earth's surface, solar radiation has been reported to inactivate bacteria and viruses alike (Aboubakr et al, 2020). One prominent, recent study that has identified UVA exposure as an area of interest in COVID-19 research is that by Cherrie et al (2021), published in the British Journal of Dermatology. Their study focused predominantly on UVA exposure in the USA, with replication studies in Italy and England. A ZINB regression model was used, with inclusion of random effect, and the results showed that study subjects living in areas with the highest level of exposure to UVA rays, which constitutes 95% of the sun's UV rays, had a lower rate of disease-related mortality. UVA has also previously been shown to be effective against coronaviruses – UVA, along with light-activated DNA and RNA cross-linking agent amotosalen, was shown to effectively inactivate MERS-CoV particles (Hindawi et al, 2018).

Numerous studies have centred on the effect of UV exposure to SARS-CoV-2 on surfaces. These studies support the inverse relationship between UV exposure and confirmed COVID-19 cases. One such study conducted by Ratnesar-Shumate et al (2020) used simulated sunlight to observe the effect of its exposure on the virus – the study was among the first to observe the impact of UV exposure on SARS-CoV-2 surfaces. They found that ninety percent of the virus was inactivated every 6.8 minutes in the simulated saliva culture and every 14.3 minutes in a different culture medium. The artificial light source simulated light conditions of a summer solstice at 40°N latitude at sea level on a clear day – based on the results, the authors suggested the use of UV as a disinfectant for SARS-CoV-2 on surfaces. Other studies using simulated sunlight found a similar degenerative effect on SARS-CoV-2 – the virus showed a half-life of less than 6 minutes, and 90% of the virus was inactivate in less than 20 minutes (Schuit et al, 2020).

Some studies have suggested potential confounding by the human behavioural impact of UV exposure. Sunnier days are likely to be better weather, prompting individuals to go outside more. With a greater proportion of the population outside as opposed to an indoor environment, there would be a reduced transmission rate. Nevertheless, in the context of sub-Saharan Africa, where countries have a much lower climatic variability, such behavioural patterns do not tend to occur; thus, this confounding element can be disregarded, and the correlation can be regarded as strong. Whilst the relationship between UV exposure and COVID-19 transmission and mortality is still a developing area of research, there is a great need for studies involving data from the regions of sub-Saharan Africa, given that such confounding is not applicable to these nations, and equally due to the reduced rate of transmission compared to predictive models.

3.3. Malaria

It has been speculated that there is a link between SARS-CoV-2 and malaria. These speculations arose from statistics of confirmed COVID-19 cases in malaria-endemic countries being considerably lower than predictive models (Hussein et al, 2020) – as of August 2020, the number of confirmed COVID-19 cases in Africa accounted for 4.53% of confirmed global cases, despite the population of Africa accounting for 16.72% of the global population at the time (Worldometer, 2021). Several countries within sub-Saharan Africa known to have high rates of malarial transmission also showed significantly low rates of not only infection, but also mortality. For instance, Nigeria, there were 43, 151 confirmed cases and 879 deaths; Uganda, there were 1,154 confirmed cases and 11 deaths, and Mozambique where there were 1864 confirmed cases and 11 deaths. For context, Nigeria, Uganda and Mozambique account for 25%, 5% and 4% of global malaria cases, respectively. The low confirmed cases and even lower mortality statistics have led to the hypothesis that pre-existing infection with malaria may have a protective effect against COVID-19, thus explaining the lowered mortality rates observed.

A number of physiological theories have been suggested to provide basis for the potential protective effect of malaria in COVID-19 infection. The primary hypothesis pertains to the role of the aforementioned ACE2 receptor in both malaria and COVID-19. One of the key roles of ACE2 is the production of vasodilator agents Ang-(1-7) from angiotensin II (ANG II), and conversion of angiotensin I to angiotensin (1-9) (Rice et al, 2004). If the ACE2 receptor was to undergo downregulation, ANGII would accumulate. This is of importance, as ANGII is believed to impair the development of the Plasmodium parasite; it is thought to decrease the build-up of sporozoites, a spore-like stage in the parasitic life cycle, in mosquitoes' salivary glands by directly disturbing the parasite membrane. Hence, it prevents the proliferation of the parasite within the vector, disrupting the process of transmission (Silva et al, 2016). Additionally, a genetic component has been established, linking to the downregulation of the ACE2 receptor. It has been found that when the D allele, on a genetic polymorphism in intron 16 of ACE1 enzyme, is dominant, we observe reduced expression of ACE2 receptor – patients presenting with this genotype presented with milder symptoms of malaria. The presence of a dominant D allele in this polymorphism has been found to be more prevalent in those with African genetic background. With regards to COVID-19, the downregulation of ACE2 that is protective in malaria could potentially prevent the proliferation of the virus within the body, as we established previously that the receptor is the viral site of access to cells.

Furthermore, some studies have indicated that immune mediators produced in infection with malaria, particularly the antibodies produced and the cytokine interferon- γ, could be effective during infection with coronaviruses (King and Lamb, 2015). Regarding antibodies, the IgG antibody produced in malarial infection targets Glycosylphosphatyidylinositol (GPI) molecules, which anchor the Plasmodium parasite. By targeting this anchoring protein, this anti-GPI antibody may neutralise the effects of Plasmodium. Likewise, SARS-CoV-2 demonstrates homology to the Plasmodium parasite in some respects, with the presence of membrane glycoproteins and spike glycoproteins, which also act as anchoring proteins. In turn, IgG could target these proteins, likewise to GPI, and thus work to neutralise the virus or produce milder symptom presentation.

A highly-contested issue among researchers has been the use of HCQ (hydroxycholorquine) and CQ (chloroquine), a medication that has long been employed to treat malaria. The use of these drugs in treatment against coronaviruses has been studied since the first SARS epidemic (Savarino et al, 2003). HCQ and CQ continue to be used widely in nations of sub-Saharan Africa in the treatment of malaria, despite growing concerns from the WHO surrounding resistance, and the initial hypothesis was that these drugs act as prophylaxis for COVID-19. In-vitro studies demonstrated that CQ could inhibit SARS-CoV-2 replication in both healthy and infected cells (Vincent et al, 2005). One such way HCQ and CQ are thought to have this affect is by preventing binding to ACE2, including altering the affinity of the receptor for the spike protein of the virus (Zhou et al, 2020). After the binding process, the virus uses cell structures known as endosomes to enter the cell, the process requiring a low pH to occur. The accumulation of HCQ and CQ in the endosome subsequently produces a high pH, preventing entry of the virus into the cell (Vincent et al, 2005).

The aforementioned is merely one of a number of hypotheses relating to the role of HCQ and CQ as chemoprophylaxis for COVID-19. Nevertheless, evidence put forward in Cochrane Reviews in 2021 concluded that, following studies on larger cohorts, HCQ was not beneficial for patients of COVID-19 requiring care in hospital. Whilst evidence for its prophylactic effect remains scarce, the study lead hypothesised that the trend would follow suit for prevention. The review included 14 studies, 12 of which were centred on HCQ and CQ use in treating COVID-19, and 2 on the role of HCQ in disease prevention – the study featured 11915 subjects in total. Based on these studies, the authors concluded there was no evidence of a prophylactic effect of these medicines in COVID-19. However, the geographical range covered by the studies may potentially be a confounding factor, the studies included results from Brazil, China, Egypt, Europe, Iran, Taiwan and North America, with only one study adopting a global approach. Thus, there is no study focusing on nations in Africa or sub-Saharan Africa. There is a possibility that the correlation may be otherwise, especially when considering other factors, such as genetic predisposition for reduced expression of ACE2, as well as meteorological factors, such as temperature and UV exposure (Cochrane Reviews, 2021).

4. Limitations

The subject matter of this research paper is an analysis of the influence of various factors, temperature, UV and pre-existing infection with malaria. It is worth mentioning the difficulty in studying these factors in isolation due to their interplay with other elements and the inadvertent effect these external factors will have on the findings.

The lowered infection and mortality rates (relative to predicted models) observed in sub-Saharan Africa generated research interest in the topic. The motivation is fuelled to research the impact of specific factors prevalent in this geographical area. Nevertheless, in doing this, consideration must be given to social, cultural and economic factors that may have contributed to these findings. One such factor is age structure variations and the distribution of older populations. Generally, more developed regions tend to have higher populations of older age due to higher life expectancy than less developed regions. Age is a significant determinant of susceptibility to and outcomes of COVID-19 infections, with older populations faring worse in these respects. In contrast, countries in Africa have been found to have some of the youngest populations, with a median age of < 20 years compared to the median in Europe and Asia of > 38 years. Younger populations are more likely to demonstrate less severe symptoms of COVID-19, and considerably better outcomes with lowered mortality rates – this could be a major factor in the deviation of actual and predicted results (Hussain et al, 2020).

Nevertheless, it could be postulated that despite the younger population, many other factors would likely lead to worse outcomes in these sub-Saharan African countries, ranging from malnutrition, poor working environments, overcrowding in urban settlements, and access to primary care healthcare among other factors. Regarding the review on temperature and UV exposure effects, it is also worth noting that there is a higher median age closer to the Earth's poles, potentially confounding the observed correlation. Nevertheless, this does not align with the finding from numerous studies that increased age is associated only with increased mortality instead of infection rate or susceptibility. Preferential infection of older individuals was not reported, and according to the WHO's 7th daily situational report, the median age of infection was 45 years old (Bezabih et al, 2020) – thus, age can be ruled out as a confounding factor in the context of temperature and UV exposure with decreasing latitude.

In their study, Bezabih et al identified another potential confounding factor associated with decreasing latitude. This is the increased prevalence of policy regarding the Bacillus Calmette-Guérin (BCG) vaccine for tuberculosis at decreasing latitudes. Additionally, they suggested emerging evidence that out-of-date BCG vaccination policies may be associated with decreased infection and mortality rates from COVID-19. Furthermore, the study established increased mortality in countries with a longer duration since mass BCG vaccination policies were introduced. Nonetheless, most countries with BCG vaccination policies are located in the tropics, nearest the equator, where the highest atmospheric temperatures exist, and those countries with outdated BCG policies are located at higher latitudes – thus, the authors anticipate that temperature remains the predominating factor.

Among the studies used in our research, a number pertained to countries beyond the scope of those in sub-Saharan Africa. However, the crude comparison of generally incomparable countries can pose challenges in extrapolating the information, notably as each country differs regarding population density, applied control measures, and the timescales of policy implementation, among other factors. However, in this study, we endeavoured as much as possible to use studies which included countries that had similarities to sub-Saharan Africa in certain regard. For example, closely associated average temperatures. Nonetheless, we believe this challenge highlights the necessity for greater research efforts into the nations of sub-Saharan Africa with regards to SARS-CoV-2, given the remarkable deviation from predictive models.

Some have hypothesised that the deviation may have stemmed from discrepancy and errors in reporting. For example, one study noted that COVID-19 cases in Portugal that performed 124, 698 tests per million were approximately twice the observed figures. On the other hand, the estimated COVID-19 cases in Togo, which performed 4025 tests per million at best, were 82 times the observed cases (Kassem et al, 2020). This stark figure suggests potential issues with underreporting, but also highlights an overarching issue prevalent in many less developed countries: the provision of testing kits and facilities and accessibility to the general population. Additionally, some studies confirmed that countries lacking proper medical facilities and relatively less hygienic lifestyles were found to register less confirmed COVID-19 cases (Das et al, 2020). Although this would be a significant factor, explanatory of the gap between predicted and confirmed cases. Some studies, including a study in Nature Africa, suggested that even if the potential underreporting of cases, death, and estimates adjusted accordingly, there would likely be significant variation in the results across countries of sub-Saharan Africa, which is noteworthy and researchworthy (Reid, 2021).

Within each nation, transmission and mortality from COVID depends on a substantial number of contextual factors, including, but not limited to, government awareness, social distancing measures, GDP per capita, poverty levels, ethnicity and medical facilities. Whilst there exists variation between the nations of sub-Saharan Africa, there is significant overlap between nations on several of the aforementioned factors, among others, which gives us grounds to study the geographical area as a collective. The studies selected for our research contained some focused on sub-Saharan Africa. Still, sources are based on countries bearing similarities to sub-Saharan Africa in the relevant facet and extrapolated from these areas in developing the hypotheses regarding the perceived effect of these factors in sub-Saharan Africa. Despite this, the use of data from countries with significantly different contextual factors will bear some effect on the validity of our extrapolations. Still, most studies adjusted for external variables or discussed the impact of external variables if an adjustment was not possible, so this could be factored into our decision to use the study as a relevant research source in the context of sub-Saharan Africa.

5. Conclusion

Regarding the effect of temperature, a wealth of research has been emerging, much of it based on the behaviours of other coronaviruses such as SARS and MERS in previous pandemics. Nevertheless, our understanding is limited because there is a wealth of research surrounding bacterial infections, but less so on viral, so the outbreak of COVID-19 stimulated more research interest in the area. Most research sources suggested an inverse relationship between COVID-19 transmission and average temperature. Given that sub-Saharan African nations experience some of the highest atmospheric temperatures, this is a significant factor affecting virus transmission in these nations – some studies exemplified this by demonstrating the relatively lower cases and fatality rates per 1000 population in these nations compared with those at higher latitudes. Based on molecular studies, potential biological mechanisms have been hypothesised, including the closing of receptor-binding motifs and orientation of spike proteins at higher temperatures, thus preventing infiltration of the respiratory tract.

A small number of machine-learning studies have attempted to quantify the effect of a 1^{o}c increase in temperature. While these studies remain limited, those conducted have found a decrease in daily infection rates. Other studies have suggested a potential range of temperatures at which the infectivity of the virus is inhibited or the existence of a critical mass, beyond which temperature no longer affects the spread - research is still required in these areas. It has been postulated that temperature could play a role in recovery rates, deaths and critical cases also – this is a recent conceptualisation, and, whilst bearing significant potential in terms of public health response, requires further research.

From the perspective of pandemic management, government response and policies and access to healthcare facilities differ widely between nations and are imperative factors in predicting transmission and mortality. Furthermore, the relatively lower confirmed cases and deaths observed in sub-Saharan Africa prompted discussion regarding underreporting of cases and issues surrounding testing facilities and the outreach in terms of their distribution. Whilst some study authors have confirmed that even if this is accounted for, results remain significant, it highlights the underlying issue surrounding transparency regarding outcomes in these developing countries since these epidemiological findings guide public health responses.

Temperature and UV exposure have been strongly linked with decreased transmission of COVID-19 with decreasing latitude, thus pertaining to sub-Saharan African nations, and understanding the biological basis to these can guide government policies, as well as indicate when the need for such policies is required, and when there is the capacity for them to be mitigated. Of particular research interest in sub-Saharan Africa is the perceived protective effect of the previous infection with malaria and the genetic factors that may act protectively. Currently, there exists a lack of research pertaining to sub-Saharan Africa. Still, given the remarkable deviation from predictive models, and promising potential of malarial comparison studies, there should be greater focus on these nations and understand how the public health responses may have contributed to the relatively low transmission and mortality. As COVID-19 mutates and its infectious patterns change, it is imperative that we not only identify systemic issues, such as underreporting but equally good governmental responses and promising potential treatments and preventative research areas, as is the case in the nations of sub-Saharan Africa.

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