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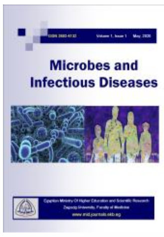

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Review article

Malaria endemicity in sub-Saharan Africa: Past and present issues in public health

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ABSTRACT

The World Health Organization (WHO) reported an estimated 241 million malaria cases with nearly half of the world's population at risk in 2020. Since time immemorial, malaria has been one of the most endemic parasitic diseases, which has caused a great menace to public health. This infectious disease has spread worldwide, with a cumulative mortality rate. Despite the significant developments in the healthcare sector, parasitic infectious diseases still exist, causing life-threatening diseases and leading to high mortality and morbidity rates worldwide. This review article discussed malaria as a public health endemic infection in general while exposing the associated past and present issues. This is done using articles published in peer-reviewed journals.

The endemic nature of malaria was investigated through the past and present issues in its prevalence, multiple causative agents and epidemiological survey. Its morbidity and mortality rate, especially in Africa, where poverty and many other favorable conditions have proven it life-threatening and a serious public health concern. Investigation on the report of various drug resistance to malaria treatment, wide association with other infectious diseases which could aggravate malaria pathogenicity and pose a threat on diagnosis; culminate into a more threat. However, the investigation into various management, prevention and control practices in many African countries has given a glimpse of hope in mitigating endemic malaria.

Background

The World Health Organization (WHO) reported an estimated 241 million malaria cases with nearly half of the world's population at risk in 2020 [1]. Malaria, a mosquito-borne infectious disease, is caused by the protozoan parasite *Plasmodium*. Malaria is typically transmitted through the bite of an infected female Anopheles mosquito, although infections can also arise by introducing contaminated blood products (transfusion malaria) and inborn transmission. Generally, clinical signs and symptoms appear after 7–10 days of the initial mosquito bite. The infection has varying degrees of

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severity depending on the species and host variables, such as the level of host immunity, which is connected to the intensity of parasite exposure in the past [2].

Malaria is commonly divided into asymptomatic, uncomplicated, and severe (complicated). Low-grade fever, shaking chills, muscle aches, and, in youngsters, stomach issues are common first symptoms. These symptoms may appear quickly (paroxysms), followed by drenching sweats, a high fever, and tiredness. Severe malaria is generally fatal, and it causes severe anemia and a variety of multi-organ damage symptoms, including brain malaria [2]. This review article discusses malaria as a public health endemic infection in general while exposing the associated past and present issues.

Main text

Method

A literature search was performed by using the keywords “sub-Saharan Africa” and “malaria”. Thirty-four (34) studies from sixteen (16) countries in sub-Saharan Africa published between 1881 and 2022 were included in the review. The studies included were those that discussed the malaria discovery, etiology, epidemiology, surveillance, treatment, prevention and management in sub-Saharan Africa.

Epidemiology

According to **Snow et al.** [3], the epidemiology of malaria varies across geographical locations, depending on the local malaria transmission intensity or the class of endemicity. Malaria infection has been transmitted in 108 countries among approximately 3 billion people. In 2020, there were an estimated 241 million new cases of malaria infection and 627,000 malaria-related deaths in 85 countries, an increase of 69000 over the previous year. More than two-thirds of malaria-related deaths were among children under 5 years of age living in the WHO African Region [4]. While disturbances caused nearly two-thirds of these deaths (47000) during the COVID-19 pandemic, the remaining one-third (22,000) was caused by a recent adjustment in WHO’s malaria mortality methodology, irrespective of COVID-19 disruptions [4].

The new cause-of-death methodology was tested in 32 countries in sub-Saharan Africa, which account for nearly 93% of all malaria deaths worldwide. With the aid of the methodology, it was discovered that malaria had killed far more African children yearly since 2000 than it was previously. The worldwide malaria burden continues to fall disproportionately on the WHO African Region. In 2020, the Region accounted for 95% of all malaria cases and 96% of deaths [4].

Nigeria (31.9%), the Democratic Republic of the Congo (13.2%), the United Republic of Tanzania (4.1%), and Mozambique (4.1%) accounted for just over half of all malaria deaths globally. Over half of the world's population is at risk for malaria, with prevalence in sub-Saharan Africa being the highest globally. Currently, 43 countries in sub-Saharan Africa are endemic to malaria. Due to the unexpected cost burden of treatment, control, and prevention, the high malaria incidence and prevalence rate have resulted in a rising poverty rate. Furthermore, time wasted due to illness negatively influences the economy and productivity [5].

According to **Diuk-Waser et al.** [6], malaria is one of the most common vector-borne infectious diseases affecting human populations. In 2000, **Hays et al.** reported that malaria has the highest toll in most sub-Saharan African countries, where about 70% of the populace resides in areas infested with potential malaria vectors [7]. Malaria was once a threat to over 80% of the population of Africa and Asia and a considerable proportion of Americans and Europeans, while Australia was generally free of the disease [8].

Discovery of malaria

Malaria comes from the Italian words mal' and aria, which means spoilt air, and malaria fever has been thought to be caused by miasmas rising from swamps. The discovery of malaria did not just surface but followed a sequential pattern. Bacteria and microorganisms were first discovered by Antoni Van Leuwenhoek in 1676 also, scientific study of the parasite that causes malaria became possible after it was elucidated by Alphonse Laveran in 1880 [9]. In 1879, the miasma theory that malaria is caused by spoilt air faded away when the two questions, if microorganisms responsible for malaria either come through inhalation or by water and ingestion, could not be answered [9].

Theodor Albrecht Edwin klebs and Corrado Tommasi-crudeli, who were the two scientists first to see the bacteria responsible for typhoid and diphtheria, claimed that they isolated bacterium from the water of pontine marshes where malaria was prevalent, and they called the name

Bacillus malariae which caused enlarged spleen following the miasma's theory [10].

Laveran, a French scientist in Algeria, detected a pigment first in leucocytes and erythrocytes in malaria patients by examining two hundred patient blood samples, out of which 148 patients' erythrocytes showed pigment in all cases of malaria and none in those without malaria. He also noted that quinine removed this pigment from the blood; this discovery made him name the parasite inside the erythrocytes (parasitic protozoa) *Oscillaria malariae* [11]. Vassily Danilewsky discovered many parasites, including trypanosomiasis and others he named pseudo-vacuoles, by examining the blood of reptiles and birds [9]. In 1885, Danilewsky recognized three genera of intra-erythrocytes blood parasites of birds: *Plasmodium, Haemoproteus* and *Leucocytozoon* [9]. In 1890 it was established that a protozoan parasite caused malaria and that there were three species *Haemamoeba vivax, Laverania malariae* and *Haemamoeba malariae* which is presently referred to as *Plasmodium vivax, P. falciparum* and *P. Malariae* respectively [9].

Causative organisms, prevention and management of malaria

Plasmodium spp. is a single-celled eukaryotic organism belonging to the phylum Apicomplexa, named after the apical complex used for host cell invasion by the organism. Five species of the genus *Plasmodium* are primarily involved in human infection. These include *Plasmodium falciparum, Plasmodium vivax, Plasmodium malariae, Plasmodium knowlesi*, and *Plasmodium ovale* [12], with *Plasmodium ovale* recently recognized as two sub-species called *Plasmodium ovale curtisi* (classic type) and *Plasmodium ovale wallikeri*.

Malaria transmission can be prevented in numerous ways, including being aware of the risk of malaria, using insect repellant called permethrin, and covering the arms and legs. However, the distribution of insecticidal-treated Nets (ITNs) by governments or by some Non-governmental Organizations (NGOs) should be encouraged [13]. Using antimalarial tablets when traveling to an area where malaria occurs can also prevent malaria. They get prompt diagnosis and treatment if someone thinks they may have the disease. Vaccine administration is also important in endemic areas [13]. Routinely unblocking of stagnant water channels in the environment and kerosene can be poured on the eggs mosquitoes lay in the stagnant water. Also, regularly cutting down grasses can serve as a reservoir for mosquitoes [13].

It is very important to start treating malaria as soon as possible. Medical practitioners can prescribe medications to kill the malaria parasite. However, some parasites are resistant to malaria drugs. Some drugs are prescribed in combination with other drugs [14]. The nature of the malaria parasite will determine the type of medication to prescribe and how long it will take to use the drugs [15]. The following are examples of antimalarial drugs which are effective in treating malaria.

- Artemisinin drugs (combination of artemether and artesunate). The best treatment for *Plasmodium falciparum* malaria is artemisinin combination therapy.
- Atovaquone (Mepron®).
- Chloroquine. Some parasites are resistant to this medication.
- Doxycycline (Doxy-100®, Monodox®, Oracea®).
- Mefloquine.
- Quinine.
- Primaquine.

Prevalence of malaria in Nigeria

Studies from various part of Nigeria shows an overview of malaria prevalence. The determinant factors of malaria prevalence in Nigeria were stated by **Bassey and Izah** [16], which showed that malaria prevalence depends on certain factors, which include medical condition, environment/season and human status viz: pregnancy, blood group, Rhesus factor, age, gender and educational status.

Salwa et al. [17] in 2016 assessing the prevalence of Malaria among the Hausa community in Kano state, recorded that malaria prevalence is 60.6 % out of 334 sample size, and 15 Rapid Diagnostic Test (RDT) positive cases gave negative results with microscopy while five of them were confirmed positive by Polymerase chain reaction (PCR). It was noted that all infection was of *Plasmodium falciparum*, and 70.1% constituted < 1000 parasite /µL of blood. It was further observed that male prevalence is like that of females (61.2 vs. 59.7%) and that prevalence differs among age groups. The age group 12-17 years has the highest prevalence (66.7%), and < 12 years has a prevalence of 42.9%, while children below 5 years have the lowest prevalence of about 37.5%.

Recent studies by **Awosolu et al.** [18] showed a cross-section of malaria transmission prevalence in Ibadan. The study indicated that malaria infection was observed to be caused by *P. falciparum* and out of 300 selected individuals observed, 56.4% of malaria infection was categorized as low (< 1000 parasite/µL of blood), and 43.6% were classified as moderate with a range of 1000≤9999 parasite /µL of blood. He noted that the male gender has a higher prevalence of 60.2% compared to 50.9% in females. Education has also been noted as a factor. Prevalence in patients with no formal education is higher than in those with formal education ($p< 0.05$). Traveling to villages highly contributed to the higher malaria prevalence (74.4%) in patients without formal education.

In Ogun state, **Olasehinde et al.** [19] determined malaria prevalence among infants and children. 215(80.4 %) of the 267 children investigated were infected with malaria, and under 5 years age group showed the highest frequency rate of 84.7 %. It was also observed that the prevalence rate of malaria was significantly low (47.9%) among children who used insecticide-treated bed nets and 55.2% among those who used antimalaria drugs as prophylaxis compared with patients who did not use any (92.5 %).

Assessment of malaria prevalence by **Benjamin et al.** [20] in Kaduna state showed that from 300 samples screened, the prevalence of malaria based on the age group of participants in selected hospital is highest at age group ≤ 10 years (33.3%), followed by the age group 31 -40 (31.3%), 11- 20 (17.21%). The age group ≥ 41 years has the lowest prevalence (9.1%) at $p≤0.029$. According to educational status, the highest prevalence of 30.6 % was found among patients with no education, followed by a prevalence of 28.6% among those who only passed through adult literacy, primary school education (27.0%), secondary school education (26.6%) and tertiary education (17.2%). Occupational status was also assessed, Civil servants had the least prevalence of 17.1%, and the highest prevalence was shown in other forms of occupation apart from farmer, unemployed and artisan. Prevalence according to blood group also shows the highest in those with genotype AA. (73%), followed by those with hemoglobin genotype AS (23%), AC has a 3 %, and SS has a 1% prevalence rate. .

Management of malaria in different parts of sub-Sahara Africa

Malaria infection is endemic to people living in the tropics and subtropics [19]. The highest effect and burden of malaria was seen in Africa in the year 2017, where there were 92% of the estimated cases of malaria and malaria-associated deaths. Some African countries with a high rate of malaria are seen in **table (1)** below.

Table 1. Table showing management of malaria in different parts of Africa.

Country	Malaria index	Predisposing Factors	Mode of treatment	Synthetic drug	References
Congo	The Republic of Congo (RoC) is one of the 54 countries where malaria transmission is still high, and the disease accounts for 12 % of the causes of death. It is estimated that 30-47 % of hospitalizations are malaria-related.	Age, HIV infection status, education and wealth index	Local and Synthetic	Artesunate, amodiaquine (ASAQ) or Artemether, lumefantrine (AL).	[21-24]

Nigeria	Fifty-one million cases and 207,000 deaths were reported annually, approximately 30 % of the total malaria burden in Africa), while 97% of the total population (approximately 173 million) is at risk of infection.	Lack of education and the non-usage of insecticide-treated nets were the major factors associated with an increased risk of malaria infection.	Local and Synthetic	Artesunate, artemether, quinine and quinidine.	[25-28]
Tanzania	About 14–18 million new malaria cases are reported in Tanzania, resulting in 120,000 deaths. Of these deaths, 70,000 are in children less than five years of age, and the annual incidence rate is 400–500/1,000 people and this number doubles for children less than five years of age.	Crowding, household insecticide-treated nets ownership, age, gender.	Local and Synthetic	Artemisinin combination therapy (ACT)	[29-31]

Drug resistance

The progressive resistance of antimalarial drugs is one of the main oppositions to managing and eradicating malaria in Africa. Misuse or exclusive drug use can stimulate the selection of resistant strains [32].

The first-line therapy introduced for treating malaria infection *Plasmodium falciparum* in the mid-1940s was Chloroquine (CQ), which became widely used by the 1950s [32]. The acceptance of chloroquine results from its cost-effectiveness, low toxicity, relative ease to manufacture, and chemical stability, making it easy to store and transport under extreme climatic conditions. By 1977 there came the emergence of chloroquine-resistant *Plasmodium falciparum* (CRPF), with the entire establishment in Sub-Saharan Africa and the whole continent by 1989 [33]. On 06 October 2021, WHO recommends using RTS, S/AS01 (Mosquirix) among children in Sub-Saharan Africa and other regions of moderately to high *P. falciparum* malaria transmission [34]. However, the malaria vaccine efficacy cannot be generalized, thus undisputable colossal transformation [34].

Surveillance of malaria intervention programs in Nigeria

Malaria control is historically the oldest control program in Nigeria, having existed since 1948. It has undergone several transitions from the

National Malaria Service to the National Malaria Control Programme in 1986 to the National Malaria Elimination Programme in 2013 as a reflection of the country's desire for a malaria-free nation [35].

The National Malaria Strategic Plans (NMSP) have, over the years, served as the blueprint of malaria control and elimination objectives and targets. Four NMSPs have been in use, with the latest being the NMSP 2014-2020. This latest NMSP aims to reduce the malaria burden to pre-elimination levels and bring malaria-related mortality to zero' through activities under seven strategic objectives [35].

The malaria elimination strategy faces challenges due to the operational deficiencies, resistant strains and poor health system management across various malaria-endemic countries, resulting in inadequate monitoring and surveillance of the reported cases. The current global IT-based Malaria Information System (MIS) could not provide quick and timely enough information about malaria cases, which delays the infection transmission and management of severe malaria cases [35].

The NMSP 2014-2020 listed five key intervention areas for malaria prevention activities. These include universal access to Long-Lasting Insecticide-treated Nets (LLINs), Indoor Residual Spraying (IRS), Larval Source Management (LSM), and provision of Intermittent Preventive Treatment of Malaria in pregnancy (IPTp) to all pregnant women attending antenatal clinics in targeted districts, vector sentinel surveillance and resistance monitoring and quality assurance of commodities [35]. Insecticide-treated nets (ITNs) remain one of the most effective means of mitigating malaria morbidity and mortality. From 2000 to 2015, national malaria control programs have distributed over one billion ITNs. There have not been significant improvements in the use of ITNs in Nigeria. It is severally reported that millions of ITNs have been distributed annually since the Abuja summit. Only 17% of Nigerians owned at least one net (but not necessarily an insecticide-treated one) in 2008, compared with 12% in 2003 [35].

However, In sub-Saharan Africa, the number of people sleeping under an ITN has increased substantially from 5% in 2005 to 53% in 2015 [35]. However, much work remains to attain the goal of universal coverage. As the scale of ITN distribution increases, so does the need for effective methods to identify, prevent and mitigate fraud and ensure that the ITNs reach beneficiaries in need.

Nigeria has specific malaria control goals. The major impediment to achieving them has always been frail or insubstantial action-oriented exertions. The Abuja target (to halve the burden of malaria by 2010) has not been realized. Although funding for malaria control increased from $17 million (US) in 2005 to $80 million in 2008 [36], the amount is unlikely to be sufficient to reach national targets for prevention and cure [36].

Malaria in the face of COVID-19 outbreak (infectious disease co-infection)

Malaria is endemic in sub-Sahara Africa due to its burden and mortality and its occurrence and association with other infectious diseases like the Covid-19 virus. Coronavirus infection 2019 (COVID-19), caused by SARS-COV-2, took emergence from Wuhan, China, in December 2019, with pandemic proportions affecting more than 8 million cases worldwide and total death exceeding 400,000 [37]. It negatively influences the management of epidemic vector-borne and infectious diseases due to increasing workload, understaffing in intensive care units and lack of resources, particularly in many African countries handling simultaneously malaria endemic [38]. Although malaria is caused by protozoan disease and has different routes of infection from Covid-19, there have been reports of interactions between the two in the same host [39]. Some COVID-19 issues have similarities with malaria infection or may impact malaria morbidity and mortality due to disruption in the milieu, including clinical presentation, the control measures, transmission, treatment and stigma [39]. In clinical presentations, the similarities of symptoms between COVID-19 and malaria include fever, chills, headache, sweats, vomiting, and body throbs [38].

With malaria symptoms 10-15 days after an infective bite, there is an increase in multi-organ failure in adults and respiratory distress not frequent in children with malaria, mimicking what is often recorded and seen in COVID-19 patients [39]. Hence, making the right diagnosis by health practitioners is challenging. The synergistic interactions pose a serious threat and hence require urgent attention from healthcare professionals, policymakers, and the entire populace. As a result, if symptoms are used to classify a case without proper testing, a patient with malaria could be misdiagnosed as COVID-19 and vice versa [39].

Limited data address how co-infection with COVID-19 affects immune response and susceptibility to malaria and vice versa [40]. However, the establishment of Africa Taskforce for Coronavirus Preparedness and Response (AFTCOR) to control COVID-19 arises in Africa shows that such an approach raises concern that is tracing, treatment and control of other diseases, such as malaria, is much harder during crises, especially with the increase in COVID-19 cases in sub-Saharan Africa where more than 80% malaria take place followed by southeast and central as well as South America [40].

The use of hydroxychloroquine and chloroquine, although not in a recommendation for use, was an economic advantage to individuals battling COVID-19 and malaria co-infection as it was the only effective prophylaxis to COVID-19 at the early stage of the outbreak, which was the same time useful in the fight for malaria in a host individual. Despite the fall in the COVID-19 cases recently, with the vaccine developed, control measures and stipulated guidelines are to be adhered to. In controlling the COVID-19 and malaria co-infection, individual and synergistic measures must be strictly followed [1].

Conclusions

The endemic nature of malaria has been investigated through its prevalence, multiple causative agents and epidemiological survey through exploration of past and present literature. Its morbidity and mortality rate, especially in Africa, where poverty and many other favorable conditions have proven it a serious public health concern. Investigation on the report of various drug resistance to malaria treatment, wide association with other infectious diseases which could aggravate malaria pathogenicity and pose a threat on diagnosis; culminate into a more threat dating back. However, various management, prevention and control practices in many African countries have given a glimpse of hope in mitigating the endemic malaria in the present time even though the various interventions and fights have not been able to eradicate it, especially in sub-Sahara Africa completely. From this literature, there is a significant effect of surveillance system launched on malaria eradication but was not brought to full actualization owing to shortage or lack of funds and responsive structure. Hence, there is a need for a sustainable working surveillance program with maximum extension to rural settlements. The use of various curative methods for malaria varies across sub-Saharan African countries, each having a broad spectrum of synthetic drug utilization. This broad drug utilization can lead to adverse drug reactions and resistance and should be mitigated early through a stewardship program. This work also highlights the potential of malaria co-morbidity with other infections. Sometimes, the co-infection can be beneficial, while at other times, harmful. Although there were colossal interactions between malaria and COVID-19, response to the treatment of COVID-19 using anti-malarial drugs was an economic advantage to patients with both infections.

This work embodies knowledge in that it explored, evaluated and bridged the literature gap between past and existing findings on Malaria to reveal the current state of the fight against malaria in sub-Saharan Africa, particularly Nigeria. It will also serve as handy information for government management decisions, policy making, and malaria intervention programs.

List of abbreviations

WHO- World Health Organization
AFTCOR- Africa Taskforce for coronavirus Preparedness and Response
LLITN- long-lasting insecticide-treated net
ITNs- insecticidal treated Nets
NGOs- Non-Governmental Organization
PCR- polymerase chain reactions
RDT- Rapid diagnostic test
IRS- indoor residual spraying
IPTp- Intermittent Preventive Treatment of Malaria in pregnancy
LSM- larval source Management
MIS- Malaria Informative System
CRPF- chloroquine-resistant *Plasmodium falciparum*
NMSP- National Malaria Strategic Plans
ACT- Artemisinin combination therapy
ASAQ- Artesunate, amodiaquine; AL- Artemether, lumefantrine.

Competing interest

The authors have declared that no competing interest exists.

Ethical approval and consent to participate

Not applicable.

Consent for publication

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Authors contribution

EO Conceived the concept, all authors designed the study, while coordination was done by SE Literature search, critical and detailed study, and manuscript drafting was collaboratively done with specificity on contributions to introduction; Discovery of Malaria and Prevalence of Malaria in Nigeria; Causative Organisms, Prevention and Management of Malaria; Malaria management in Sub-Sahara Africa; Drug resistance; surveillance of malaria intervention programs in Nigeria; and Malaria in the face of Covid-19 Outbreak (infectious disease co-infection) by SA, ET, BO, AS, TB, EO and SE respectively. All authors edited, visualized and supervised the study, and read and approved the final manuscript.

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