



Looking Beyond the Malaria Vaccine Approval to Acceptance and Adoption in Sub-Saharan Africa

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INTRODUCTION

Growing up in the Malaria-endemic region of sub-Saharan Africa, one becomes inescapably aware of the devastating effect of malaria. From the common experiences of pyrexia, hospital admissions, and daily intramuscular injections to the early childhood trauma of learning that a classmate will not be returning to school because they did not recover from a severe bout the illness, to the sudden, painful loss of loved ones. In many instances of illness, there is an emergency demand for blood transfusion due to severe anemia secondary to malarial infection. Malaria remains a public health threat to sub-Saharan regions of Africa, with enormous health and economic implications, hence the global attention.

MALARIA

Malaria is a vector-borne infectious disease that is caused by Plasmodium species (1). Five species of Plasmodium can infect and be spread by humans - *P. falciparum*, *P. vivax*, *P. ovale*, *P. malariae*, and *P. knowlesi* (1). Of the five species, *P. falciparum* is the protozoan parasite associated with severe disease and accounts for most malaria deaths. Malaria spreads to humans through the bites of infected hosts, the female Anopheles mosquitoes. The sporozoites, which are a motile infective form, are transmitted into the host human. The sporozoites spread through the bloodstream into the liver, where the sporozoites mature into schizonts. The schizonts form in the liver, rupture, and release merozoites into the bloodstream, infecting new red blood cells (blood stage). The parasite in the red blood cells matures into schizonts, which rupture and release merozoites. The erythrocyte/blood stage of the parasites is responsible for the symptoms in individuals infected with malaria. Of note,

Abbreviations: P, Plasmodium; ARDS, acute respiratory distress syndrome; IUGR, Intrauterine growth restriction; LBW, Low birth weight; RDT, Rapid diagnostic tests; ACTs, Artemisinin-based combination therapies; WHO, World Health Organization.

plasmodium *ovale* and plasmodium *vivax* can remain dormant in the liver as hypnozoites which can persist and cause relapses if left untreated.

The transmission/distribution of malaria is mainly dependent on climatic factors, especially in the warmer regions of the tropics (2, 3). Lesser malaria transmission has been established in some tropical and subtropical areas of Africa, including the deserts (except the oases), due to the prevalence of colder seasons, very high altitudes, and successful control/elimination of malaria (3).

Presentations and Implications

Malarial infection can present as asymptomatic or symptomatic, with low to high-grade intermittent fever, headache, chills, and fatigue. Severe cases can result in renal failure, pulmonary edema, acute respiratory distress syndrome (ARDS), jaundice, seizures, coma, or death (4). Children and the elderly are more prone to the complications of malarial infection. Pregnant mothers with malaria can have complications including premature delivery (before 37 weeks of gestation), miscarriages, intrauterine growth restriction (IUGR) of the baby, and low birth weight (LBW) (4).

Sub-Saharan Africa accounts for more than 90% of the world's deaths due to malaria (5). According to the latest World malaria report, in 2019, there were 229 million malaria cases globally that led to 409,000 deaths (6). Of these deaths, 67 percent (274,000) were children under five years of age, which translates into a daily toll of nearly 750 children under age 5 (6). The under-five mortality rate is devastating. Every two minutes, a child under five dies of malaria. Many of these deaths are preventable. The cost associated with the treatment of malaria and lost labor, in sub-Saharan Africa, is estimated at 12 billion USD every year (7).

Diagnosis and Treatment

The diagnosis of malaria can be made through several means, including clinical diagnosis using symptoms, microscopic examinations in the medical laboratory, and antigen-based rapid diagnostic tests (RDTs) (8). Over the decades, several measures have been implemented for malaria prevention, including vector control with insecticide-treated nets and indoor residual spraying and seasonal malaria prophylactics. Pharmacotherapy, such as the Artemisinin-based combination therapies (ACTs), has been the mainstay for treating uncomplicated and severe *P. falciparum* malaria, including the symptomatic management of malaria complications. Pharmacotherapy mainly targets the blood stage of the life cycle (9). Despite these management strategies, resistance to the available anti-malaria medications has continued to grow, resulting in more deaths (10).

Malaria Vaccine

Due to the unrelenting morbidity and mortality from malaria infections, researchers have sought for more robust preventative measures. Years of clinical trials have led up to the World Health Organization's (WHO) recent approval of the groundbreaking four-dose malaria vaccine, RTS, S/AS01 (Mosquirix), on October 6, 2021, designed to target the sporozoite (pre-blood) stage of *P. falciparum* before they infect liver cells (10–12). Preceding this approval, a phase 3 efficacy study in 7 sub-Saharan African countries revealed that the 4-dose schedule vaccine efficacy was 25.9% (95% CI, 19.9 to

31.5) among a population of 6537 children between the ages of 6-12 weeks and 36.3% (95% CI, 31.8 to 40.5) among a population of 8922 children between the ages of 5-17 months with clinical malaria. The vaccine efficacy against severe malaria was 17.3% (95% CI, -9.4 to 37.5) among a population of 6537 children between age of 6 to 12 weeks and 32.2% (95% CI, 13.7 to 46.9) among a population of 8922 children 5 to 17 months of age (8). The newly approved malaria vaccine will be administered intramuscularly. The first three doses have some flexibility in administration, starting at five months and must be completed at nine months, while the fourth dose is expected to be administered at 15-18 months of age.

DISCUSSION

As a sequel to the varied degree of malaria endemicity and the differing needs, we may expect differing implications of the malaria vaccine across the sub-Saharan Africa regions. Considering the vaccine's efficacy was tested in seven sub-Saharan African countries (Burkina Faso, Gabon, Ghana, Kenya, Malawi, Mozambique, and the United Republic of Tanzania) while excluding other endemic regions poses some limitations (13). Nigeria, which contributes to about 31.9% of the global malaria deaths, being the highest malaria disease burden, was excluded from the vaccine efficacy testing (14). This narrative, therefore, limits the generalizability of the malaria vaccine efficacy.

The malaria vaccine is undoubtedly a giant innovation with a promising outlook. However, we know that history is replete with examples of novel vaccines met with vaccine hesitancy due to low confidence in the safety and efficacy of the vaccines (15). In the wake of the recent approval, public awareness and perception about the malaria vaccine are scant. For example, the online search for the keyword "Malaria vaccine," as expressed on google trends, has remained scanty in the last 12 months, with pockets of search in only 8 of the 36 states in Nigeria (**Figure 1**).

Considering the knowledge gaps, we recommend initiating studies that assess public awareness and explore perceptions of the malaria vaccine especially around its acceptability. This will inform public health and policy measures targeted at maximizing the health benefit of the malaria vaccine, including health education and promotion. We also recommend that studies be initiated to assess the safety and efficacy of the malaria vaccine in other vulnerable populations like the elderly, pregnant mothers, persons living with sickle cell disease, and immunocompromised individuals. While there are studies that have assessed the prevalence of malaria and challenges with the acceptance of the malaria vaccine before its approval, no study has examined these variables after the vaccine's approval, further necessitating the need to initiate awareness and acceptability studies.

To address the scourging effect of malaria, we hope that every willing resident of malaria-endemic regions (not only in the tropical areas of Africa but also in other endemic parts of the world), will eventually have the option of being a recipient of the malaria vaccine. Structured public health education and massive campaigns, in collaboration with stakeholders, including community and faith-based leaders, may be resourceful in achieving this feat. The potential to reduce and possibly eliminate the burden of malaria

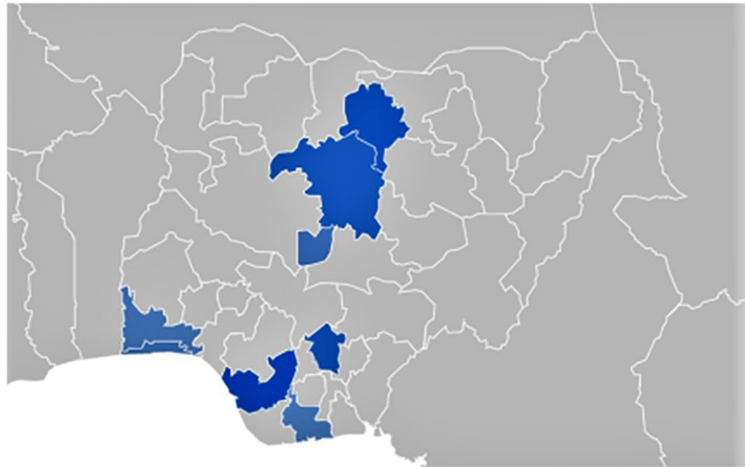


FIGURE 1 | Google trend showed that the keyword “malaria vaccine” was searched online in 8 of 36 states in Nigeria (November 14, 2020 – November 14, 2021).

in endemic regions will translate to significant economic gains. Considering that malaria-endemic areas are mainly developing countries, the malaria vaccine, if proven to have sustained efficacy across the life span, will free up resources that can be channeled towards addressing other challenges. The malaria vaccine is a welcome development and efforts must be sustained to ensure that its approval culminates in actual adoption and administration.

AUTHORS CONTRIBUTIONS

Conceptualization, TA, OA, and OEO. Methodology, TA, OA, OEO, and ONO. Writing—original draft preparation, TA and OA. Writing—review and editing, TA, OA, OEO, KA, SD, and ONO. All authors contributed to the article and approved the submitted version.

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