



Commentary

Prospects of malaria vaccination in Nigeria: Anticipated challenges and lessons from previous vaccination campaigns

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ABSTRACT

Malaria is a severe public health issue in Nigeria, with higher morbidity and mortality rates than any other country. An estimated 100 million malaria cases and over 300,000 deaths are recorded yearly in Nigeria. Vaccination is an effective strategy in combating and eliminating infectious diseases such as malaria, thus, the deployment of a prospective malaria vaccine in Nigeria offers hope to the country's health sector. However, vaccination programmes face challenges, particularly in communities that are difficult to reach geographically or culturally, and these obstacles can only be overcome through continued international, national, and individual commitment. There is a need for expanded and continuous public health information, education, and communication particularly on contemporary health issues such as malaria and vaccination hesitancy. This will enable easier implementation and compliance to strategies for the sustainable control and eventual elimination of malaria. This article highlights some of the lessons learned from previous vaccination programs in Nigeria and how the insight gotten can be pivotal in ensuring the success of a prospective malaria vaccination programme in Nigeria.

1. Introduction

The prospect of a world free of malaria has fueled significant development, and the remarkable drop in malaria mortality between 2000 and 2015 can be described as a victory of modern public health, as the global number of malaria cases has fallen by 22% and malaria-related deaths have decreased by 50% (Shretta et al., 2018) [1]. However, malaria still causes over one million deaths each year, largely in Africa, with more than 250,000 children dying yearly from the disease in Sub-Saharan Africa (Adepoju, 2019) [2]. Despite the use of drugs, insecticide-treated nets, and other interventions to reduce the impact of the disease, malaria remains a formidable foe (Otarigho, 2012) [3]. The distribution of an effective and affordable malaria vaccine would help curb the adverse health and socioeconomic effects of the disease.

1.1. Burden and endemicity of malaria in Nigeria

Nigeria has the highest malaria burden worldwide, with an estimated 100 million cases every year and over 300,000 deaths, and together with the Republic of Congo, accounts for 36% of all worldwide malaria cases (Thornton, 2020) [4]. Nigeria recorded the largest number of malaria cases (25% of global malaria cases) and the highest number of deaths (24% of global malaria deaths) in 2018, according to the 2019 World Malaria Report (Thornton, 2020) [4]. Malaria is endemic in Nigeria due to the climatic and environmental conditions that favour mosquito breeding, such as stagnant water bodies, land pollution, and poor sewage disposal. This leaves most Nigerians vulnerable to malaria, as a large proportion of the population live in rural areas. The most vulnerable groups are children, pregnant women and non-immune individuals, as malaria is responsible for 11% and 30% of maternal and infant mortality, respectively (Thornton, 2020) [4]. Malaria is also a leading

cause of miscarriage, low birth weight, maternal anemia, and maternal death (Kidanto et al., 2009) [5]. Besides the morbidity and mortality [26, 27], the high costs of malaria treatment and eradication activities have created a major economic burden for the Nigerian health sector. The availability of a cost-effective and accessible malaria vaccine in Nigeria will strengthen malaria eradication efforts and public health quality.

1.2. Status of *P. falciparum* malaria vaccine candidates

The development of a malaria vaccine is an active area in vaccine research and development but is accompanied by challenges associated with the complex life cycle, morphological changes, and varying antigenic sites of the malaria parasite *Plasmodium falciparum* (Arama & Troye-Blomberg, 2014) [6]. The malaria vaccine candidates target specific stages of the parasite's life cycle, and mainly include the transmission-blocking vaccines (TBVs), the pre-erythrocytic vaccines (PEVs), and the blood-stage vaccines (BSVs). Details of the various malaria vaccine candidates and their clinical trial status are outlined in Table 1.

1.3. Progress of malaria vaccination trials in African countries

Data from malaria vaccine trials so far show good levels of efficacy in immunogenicity and protection of the trial subjects, mostly children with severe malaria or high vulnerability to the disease. Malaria vaccine trials have been successfully implemented in 7 African countries, including Kenya, Burkina Faso, Malawi, Ghana and Mali, amongst others. The earlier approved RTS,S malaria vaccine has undergone completion of phase III clinical trials, with recorded efficacies of 55% within 12 months and a cumulative 39% over a period of four years (Nakkazi, 2021) [8]. Also, phase III clinical trials have commenced for

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Table 1

P. falciparum malaria vaccine candidates undergoing clinical trials in African subpopulations (National Library of Medicine, n.d.) [7].

Vaccine candidate	Vaccine category	Immunogen type	Current status
RTS,S	PEV	Subunit	Phase 4
R21	PEV	Subunit	Phase 1/2
Full-length CSP	PEV	Subunit	Phase 1
PfSPZ Vaccine	PEV, WSV	Whole sporozoite (radiation attenuation)	Phase 2
Chemoprophylaxis vaccination (CVac)	PEV, WSV	Whole sporozoite (chemical attenuation)	Phase 2
Genetically attenuated parasite (GAP) vaccines	PEV, WSV	Whole sporozoite (genetic attenuation)	Phase 1
PfRH5	BSV	Subunit	Phase 1
AMA1-RON2	BSV	Subunit	Preclinical
PfSEA-1	BSV	Subunit	Preclinical
PfGARP	BSV	Subunit	Preclinical
Chemically attenuated parasite (CAP) vaccines	BSV	Whole blood-stage parasite	Phase 1
VAR2CSA (Placental malaria)	BSV, PMV	Subunit	Phase 1
Pfs25	TBV	Subunit	Phase 1
Pfs230	TBV	Subunit	Phase 2
Pfs48/45	TBV	Subunit	Preclinical

PEV – Pre-erythrocytic vaccine; WSV – Whole sporozoite vaccine; BSV – Blood stage vaccine; PMV – Placental malaria vaccine; TBV – Transmission-blocking vaccine

the R21 malaria vaccine after previous trial studies in Burkina Faso showed an efficacy of 77%, surpassing the World Health Organization (WHO) benchmark of 75% efficacy for malaria vaccines (Hill, 2021) [9]. Overall, the RTS,S vaccine has successfully reduced malaria susceptibility and rendered immunological protection to over one million children in Africa (WHO, 2022) [10]. Funding for the wide distribution of the malaria vaccines have kicked in as Gavi, the Vaccine Alliance, has invested over US\$150 million in the procurement and delivery of the malaria vaccine to several countries in Sub-Saharan Africa (Kuehn, 2022) [11]. The reality of access to malaria vaccines has given a new ray of hope to malaria control efforts, with the WHO 2030 target of a 90% reduction in malaria mortality looking much more feasible (Patouillard et al., 2017) [12].

1.4. Anticipatory challenges of a malaria vaccine and lessons from previous vaccination campaigns in Nigeria

1.4.1. The need to address misinformation and vaccine hesitancy

In African countries like Nigeria, vaccination has always been impeded by vaccine hesitancy due to the fear of adverse vaccine effects (Adebisi et al., 2021) [13]. For example, during the onset of the COVID-19 vaccination programme in Nigeria, certain negative propagandas surfaced, such as the belief that the vaccines were administered with an ulterior motive to render males sterile, implant tracking microchips, or even cause death in vaccine recipients in Africa (Asishana, 2021; Schönbauer, 2022) [14,15]. Similar vaccine misconceptions occurred in the past during the introduction of the polio vaccination programme in Northern Nigeria (Renne, 2014) [16], and could likely emerge during a prospective malaria vaccination campaign. These challenges were resolved through collaborations between the vaccination staff and rural community leaders, including traditional and religious authorities (Effiong et al., 2021; Elebesunu & Ubani, 2021) [17, 18]. Thus, a successful malaria vaccination programme in Nigeria requires sufficient involvement of community stakeholders to enhance vaccine acceptance among the community indigenes. Also, a comprehensive information surveillance program should be implemented at all levels of the Nigerian government to identify and correct any misinformation concerning the prospective malaria vaccine.

1.4.2. Lesson 2: The need to address vaccine storage and transportation challenges

For the storage and distribution of the RTS,S malaria vaccine to take place, an effective cold chain system at defined temperatures is necessary (Asante et al., 2016) [19]. Currently, the malaria vaccine is stored at 2–8 °C, while other malaria vaccine candidates in development are stored and transported at even lower temperatures [19]. Insufficient cold chain infrastructure, coupled with power supply interruptions, are probable challenges to vaccine storage and distribution in Nigeria, as poor storage may compromise the quality of the vaccine. For instance, during the polio vaccination campaigns, poor storage and transportation systems led to the expiration of some of the polio vaccines, and according to reports, those who received such vaccines remained susceptible to the virus (Arita & Nakane, 2008) [20]. In this regard, it is important for the Nigerian government and health policy makers to channel resources into the establishment of quality cold chain equipment for the storage and transportation of vaccines.

1.4.3. Lesson 3: The need to include larger population subgroups in clinical trials

Vaccine efficacy and safety are often measured through randomized clinical trials (RCTs), which have a limitation of never being conducted in all the subpopulations where the vaccine will eventually be administered (Poland et al., 2009) [21]. This may not reflect a complete real-world scenario, as it is possible that vital subpopulations might be overlooked. Most clinical trials for the RTS,S malaria vaccine are targeted at infants and young children (RTS, 2014) [22], and as a result, there is a dearth of information on the efficacy and safety of these vaccines among older populations. Understandably, the younger population is at higher risk of mortality from malaria, but a malaria-endemic country like Nigeria would not be favoured if the efficacy of these vaccines is not tested in older subpopulations. Also, most final stage clinical trials (phase III) only assess the efficacy and safety of vaccines in a well-defined population, limiting the participants to a narrow age range. For instance, pregnant women, infants, and young adolescents were not included in various clinical trials for the COVID-19 vaccines (Principi & Esposito, 2021) [23]. The results generated from such trials might not be completely suitable for generalizing the data to a larger population, and for special cases. Also, the geriatric population has often been excluded from most clinical trials, and as a result, reports have shown lower responsiveness of elderly individuals to vaccines such as the Hepatitis B vaccine, Herpes Zoster vaccine, Influenza vaccine, and even the COVID-19 vaccine (Cherubini et al., 2010; Veronese et al., 2021) [24,25, 28]. This paucity of data among certain demographic populations may limit vaccine coverage and possibly encourage vaccine hesitancy. There is a need for the malaria vaccine clinical trials to extend to other subpopulations for equal demographic representation and improved chances of herd immunity.

2. Conclusion

The deployment of the malaria vaccine offers great promise, as seen in the African countries fielding the clinical trials, however, certain hurdles must be overcome to ensure the reality of an effective vaccination programme in Nigeria. Synergised efforts at the national and subnational levels are necessary to address these challenges, with a view to enabling easier implementation of a malaria vaccination programme in Nigeria. This will ensure significant progress towards the successful control and elimination of malaria in Nigeria, and in Africa as a whole.

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Consent

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Data availability statement

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No conflicts of interest declared.

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Abbreviations

- PEV – Pre-erythrocytic vaccine
- WSV – Whole sporozoite vaccine
- BSV – Blood stage vaccine
- PMV – Placental malaria vaccine
- TBV – Transmission-blocking vaccine
- WHO – World Health Organization
- COVID-19 – Coronavirus Disease - 2019
- RCTs – Randomized Clinical Trials

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