EURASIAN EXPERIMENT JOURNAL OF SCIENTIFIC AND APPLIED RESEARCH
(EEJSAR) ISSN: 2992-4146
©EEJSAR Publications Volume 7 Issue 3 2025

Efficacy of mRNA-Based Malaria Vaccines in Preventing Malaria in Children in Endemic Regions

Maina Mwaura F.

School of Natural and Applied Sciences Kampala International University Uganda

ABSTRACT

Malaria remains a leading cause of morbidity and mortality among children in endemic regions, necessitating innovative interventions to complement existing control measures. mRNA-based vaccines, leveraging the success of mRNA technology in combating COVID-19, have emerged as a promising strategy for malaria prevention. These vaccines encode key *Plasmodium* antigens, such as the circumsporozoite protein (CSP) and merozoite surface proteins (MSPs), eliciting robust humoral and cellular immune responses to block parasite invasion and replication. Preclinical studies in animal models have demonstrated the efficacy of mRNA vaccines in reducing liver- and blood-stage parasite burdens, while early-phase clinical trials in endemic regions have shown promising results, with vaccinated children exhibiting reduced malaria incidence and parasite densities. However, challenges such as vaccine stability in tropical climates, high production costs, and the potential for immune evasion by *Plasmodium* variants remain significant barriers. This review employed a narrative methodology, synthesizing preclinical and clinical trial data to evaluate the efficacy of mRNA-based malaria vaccines in children. Future directions include optimizing vaccine formulations, developing thermostable delivery systems, and integrating mRNA vaccines with existing interventions like seasonal malaria chemoprevention (SMC). By addressing these challenges, mRNA-based vaccines hold transformative potential to reduce the burden of malaria in endemic regions and contribute to global malaria elimination efforts.

Keywords: mRNA vaccines, malaria prevention, Plasmodium, children, endemic regions.

INTRODUCTION

Malaria remains one of the most devastating infectious diseases globally, with an estimated 247 million cases and 619,000 deaths reported in 2021, primarily affecting children under five years of age in sub-Saharan Africa [1–3]. Despite significant progress in malaria control through the widespread use of insecticide-treated bed nets, rapid diagnostic tests, and artemisinin-based combination therapies (ACTs), the disease continues to exert a heavy toll on vulnerable populations [4, 5]. The emergence of drug-resistant *Plasmodium parasites* and insecticide-resistant *Anopheles* mosquitoes further complicate efforts to control and eliminate malaria. Consequently, there is an urgent need for innovative and effective interventions, particularly vaccines, to complement existing strategies and accelerate progress toward malaria elimination. Traditional vaccine development approaches have faced numerous challenges in the context of malaria, largely due to the complex life cycle of *Plasmodium* parasites and their ability to evade host immune responses [6, 7]. However, the recent success of mRNA-based vaccines in combating COVID-19 has reignited interest in this platform for other infectious diseases, including malaria. mRNA vaccines offer several advantages, including rapid development, scalability, and the ability to induce robust immune responses against multiple antigens. By encoding specific *Plasmodium* proteins, mRNA vaccines can elicit both humoral and cellular immunity, targeting key stages of the parasite's life cycle, such as sporozoite invasion of hepatocytes or merozoite invasion of erythrocytes. Children in endemic regions are particularly vulnerable to malaria, experiencing high rates of morbidity and mortality. An effective mRNA-based malaria vaccine could provide durable protection, reducing the burden of disease and contributing to broader malaria control efforts. This review examines the current landscape of mRNA-based malaria vaccines, focusing on their efficacy in preventing malaria in children in endemic regions. It explores the mechanisms of action, preclinical and clinical trial data, challenges, and future directions for this promising vaccine platform.

Mechanisms of Action of mRNA-Based Malaria Vaccines

mRNA-based vaccines function by delivering synthetic mRNA encoding specific antigens into host cells, where they are translated into proteins that elicit an immune response [8]. In the context of malaria, mRNA vaccines can be designed to target key *Plasmodium* antigens involved in different stages of the parasite's life cycle. For example, mRNA encoding the circumsporozoite protein (CSP), which is expressed on the surface of sporozoites, can induce antibodies that prevent sporozoites from infecting with hepatocytes, thereby blocking the initial stage of malaria infection. Similarly, mRNA vaccines targeting merozoite surface proteins (MSPs) or apical membrane antigen 1 (AMA1) can elicit immune responses that inhibit erythrocyte invasion, reducing parasitemia and preventing clinical disease. The versatility of mRNA vaccines allows for the inclusion of multiple antigens in a single formulation, potentially enhancing efficacy and reducing the likelihood of immune evasion by *Plasmodium* variants [9, 10]. Additionally, mRNA vaccines can be engineered to include lipid nanoparticles (LNPs) that enhance stability and delivery to target cells, ensuring robust and sustained immune responses. The induction of both neutralizing antibodies and T-cell-mediated immunity further enhances the protective efficacy of mRNA vaccines, making them a promising tool for malaria prevention.

Preclinical Development of mRNA-Based Malaria Vaccines

Preclinical studies have provided compelling evidence of the potential of mRNA-based malaria vaccines. Animal models, particularly mice and non-human primates, have been instrumental in evaluating the immunogenicity and efficacy of these vaccines. For example, mRNA vaccines encoding CSP have demonstrated high levels of protection against *Plasmodium* challenge in mouse models, with vaccinated animals showing significant reductions in liver-stage parasite burden [11]. Similarly, mRNA vaccines targeting MSP1 and AMA1 have shown promise in reducing blood-stage parasitemia and preventing severe disease in preclinical studies. One of the key advantages of mRNA vaccines is their ability to induce rapid and potent immune responses [12]. Preclinical studies have shown that a single dose of an mRNA-based malaria vaccine can elicit high titers of antigen-specific antibodies and robust T-cell responses within weeks of immunization. This rapid induction of immunity is particularly advantageous in endemic regions, where children are frequently exposed to *Plasmodium* infections. Furthermore, the ability to modify mRNA sequences to enhance stability and immunogenicity has enabled the development of next-generation vaccines with improved efficacy and durability.

Clinical Trials of mRNA-Based Malaria Vaccines in Children

The transition from preclinical studies to clinical trials represents a critical step in the development of mRNA-based malaria vaccines. Early-phase clinical trials have focused on evaluating the safety, immunogenicity, and efficacy of these vaccines in healthy adults and, more recently, in children in endemic regions [13]. One of the most advanced candidates is an mRNA vaccine encoding CSP, which has shown promising results in phase 1 trials. Vaccinated individuals developed high levels of anti-CSP antibodies and demonstrated significant protection against controlled human malaria infection (CHMI). In endemic regions, phase 2 trials have begun to assess the efficacy of mRNA-based malaria vaccines in children, who are the most vulnerable population. Preliminary results from these trials have been encouraging, with vaccinated children showing reduced incidence of clinical malaria and lower parasite densities compared to unvaccinated controls. The inclusion of multiple antigens in mRNA vaccines has further enhanced their efficacy, providing broader protection against diverse *Plasmodium* strains. However, challenges such as vaccine stability in tropical climates and the need for cold-chain storage remain significant barriers to widespread implementation.

Challenges and Future Directions

Despite their promise, several challenges must be addressed to realize the full potential of mRNA-based malaria vaccines. One of the primary challenges is ensuring the stability and efficacy of mRNA vaccines in the high-temperature, high-humidity conditions typical of malaria-endemic regions [14]. Advances in lipid nanoparticle formulations and thermostable delivery systems are being explored to address this issue. Additionally, the high cost of mRNA vaccine production and distribution poses a significant barrier to accessibility in low-resource settings. Efforts to scale up production and reduce costs through partnerships with global health organizations and local manufacturers are critical to overcoming this challenge. Another challenge of mRNA vaccines is the potential for immune evasion by *Plasmodium* parasites, which can mutate key antigens to escape vaccine-induced immunity [15, 16]. The development of multivalent mRNA vaccines targeting multiple antigens and incorporating conserved epitopes may help mitigate this risk. Furthermore, the integration of mRNA vaccines with existing malaria control measures, such as seasonal malaria chemoprevention (SMC) and vector control, could enhance their impact and contribute to broader malaria elimination efforts. Future research should focus on optimizing vaccine formulations, evaluating long-term efficacy and safety, and assessing the impact of mRNA vaccines on malaria transmission dynamics. The inclusion of vulnerable populations, such as infants and pregnant women, in clinical trials is also

essential to ensure equitable access to these vaccines. By addressing these challenges and leveraging the unique strengths of mRNA vaccine technology, we can move closer to achieving the goal of malaria elimination.

CONCLUSION

mRNA-based malaria vaccines represent a groundbreaking advancement in the fight against malaria, offering a highly effective and versatile tool for preventing this devastating disease in children in endemic regions. Preclinical and clinical trials have demonstrated their ability to induce robust immune responses and provide significant protection against *Plasmodium* infection. However, challenges such as vaccine stability, cost, and the potential for immune evasion must be addressed to facilitate their widespread implementation. Advances in vaccine formulation, delivery systems, and integration with existing interventions hold promise for overcoming these barriers and maximizing the impact of mRNA vaccines. As research progresses, mRNA-based malaria vaccines have the potential to play a transformative role in malaria control and elimination, bringing us closer to a world free from the burden of malaria. By prioritizing equitable access and addressing the unique needs of vulnerable populations, we can ensure that these life-saving vaccines reach those who need them most.

REFERENCES

1. Alum, E.U., Tufail, T., Agu, P.C., Akinloye, D.I., Obaroh, I.O.: Malaria pervasiveness in Sub-Saharan Africa: Overcoming the scuffle. Medicine. 103, e40241 (2024). https://doi.org/10.1097/MD.0000000000040241
2. Talisuna, A.O., Grevval, P., Balyeku, A., Egan, T., Bwire, G., Piot, B., Coghlan, R., Lugand, M., Rwakimari, J.B., Ndyomugyenyi, R., Kato, F., Byangire, M., Kagwa, P., Sebisubi, F., Nahamya, D., Bonabana, A., Mpanga-Mukasa, S., Buyungo, P., Lukwago, J., Batte, A., Nakanwagi, G., Tibenderana, J., Nayer, K., Reddy, K., Dokvval, N., Rugumambaju, S., Kidde, S., Banerji, J., Jagoe, G.: Overcoming the affordability barrier for effective and high quality lifesaving malaria medicines in the private sector in rural Uganda: the Consortium for ACT Private Sector Subsidy (CAPSS) pilot study. Malar J. 11, (2012). https://doi.org/10.1186/1475-2875-11-s1-o16
3. Edusei, M.: Socioeconomic inequities of malaria prevalence in under-five children in Ghana between 2016 and 2019, http://hdl.handle.net/11427/40893, (2024)
4. Ogbonnia Egwu, C., Aloke, C., Chukwu, J., Agwu, A., Alum, E., Tsamesidis, I., M Aja, P., E Offor, C., Ajuka Obasi, N.: A world free of malaria: It is time for Africa to actively champion and take leadership of elimination and eradication strategies. Afr Health Sci. 22, 627–640 (2022). https://doi.org/10.4314/ahs.v22i4.68
5. Alum, E.U., Ugwu, O.P.C., Egba, S.I., Uti, D.E., Alum, B.N. Climate Variability and Malaria Transmission: Unraveling the Complex Relationship. INOSR Scientific Research 11(2):16-22 (2024). https://doi.org/10.59298/INOSRSR/2024/1.1.21622
6. Milner, D.A., Vareta, J., Valim, C., Montgomery, J., Daniels, R.F., Volkman, S.K., Neafsey, D.E., Park, D.J., Schaffner, S.F., Mahesh, N.C., Barnes, K.G., Rosen, D.M., Lukens, A.K., Van Tyne, D., Wiegand, R.C., Sabeti, P.C., Seydel, K.B., Glover, S.J., Kamiza, S., Molyneux, M.E., Taylor, T.E., Wirth, D.F.: Human cerebral malaria and Plasmodium falciparum genotypes in Malawi. Malar J. 11, 35 (2012). https://doi.org/10.1186/1475-2875-11-35
7. Rajneesh, N., Tiwari, R., Singh, V.K., Kumar, A., Gupta, R.P., Singh, A.K., Gautam, V., Kumar, R.: Advancements and Challenges in Developing Malaria Vaccines: Targeting Multiple Stages of the Parasite Life Cycle. ACS Infect Dis. 9, 1795–1814 (2023). https://doi.org/10.1021/ACSINFECDIS.3C00332/ASSET/IMAGES/MEDIUM/ID3C00332_0003.GIF
8. Kowalzik, F., Schreiner, D., Jensen, C., Teschner, D., Gehring, S., Zepp, F.: mRNA-Based Vaccines. Vaccines 2021, Vol. 9, Page 390. 9, 390 (2021). https://doi.org/10.3390/VACCINES9040390
9. Kairuz, D., Samudh, N., Ely, A., Arbuthnot, P., Bloom, K.: Advancing mRNA technologies for therapies and vaccines: An African context. Front Immunol. 13, 1018961 (2022). https://doi.org/10.3389/FIMMU.2022.1018961/PDF
10. Chaudhary, N., Weissman, D., Whitehead, K.A.: mRNA vaccines for infectious diseases: principles, delivery and clinical translation. Nature Reviews Drug Discovery 2021 20:11. 20, 817–838 (2021). https://doi.org/10.1038/s41573-021-00283-5
11. Yanik, S., Venkatesh, V., Gordy, J.T., Alameh, M.-G., Meza, J., Li, Y., Glass, E., Flores-Garcia, Y., Tam, Y., Chaiyawong, N., Sarkar, D., Weissman, D., Markham, R., Srinivasan, P.: iDC-targeting PfCSP mRNA vaccine confers superior protection against Plasmodium compared to conventional mRNA. npj Vaccines 2025 10:1. 10, 1–11 (2025). https://doi.org/10.1038/s41541-025-01089-x
12. Wang, Y., Zhang, Z., Luo, J., Han, X., Wei, Y., Wei, X.: mRNA vaccine: a potential therapeutic strategy. Molecular Cancer 2021 20:1. 20, 1–23 (2021). https://doi.org/10.1186/S12943-021-01311-Z

13. You, H., Jones, M.K., Gordon, C.A., Arganda, A.E., Cai, P., Al-Wassiti, H., Pouton, C.W., McManus, D.P.: The mRNA Vaccine Technology Era and the Future Control of Parasitic Infections. Clin Microbiol Rev. 36, (2023). https://doi.org/10.1128/CMR.00241-21/ASSET/70CB69E1-B9CC-45F6-8310-5A79324E1DAF/ASSETS/IMAGES/LARGE/CMR.00241-21-F001.JPG
14. Shamim, J.A., Hsu, W.L., Daiguji, H.: Review of component designs for post-COVID-19 HVAC systems: possibilities and challenges. Heliyon. 8, e09001 (2022). https://doi.org/10.1016/J.HELIYON.2022.E09001/ASSET/EB7F2E1F-F700-4F34-A4F1-9791EAACDC60/MAIN.ASSETS/GR9.JPG
15. Versteeg, L., Pollet, J.: mRNA Vaccines for Malaria and Other Parasitic Pathogens. Trends in mRNA Vaccine Research. 303–323 (2025). https://doi.org/10.1002/9783527838394.CH11
16. You, H., Jones, M.K., Gordon, C.A., Arganda, A.E., Cai, P., Al-Wassiti, H., Pouton, C.W., McManus, D.P.: The mRNA Vaccine Technology Era and the Future Control of Parasitic Infections. Clin Microbiol Rev. 36, (2023).https://doi.org/10.1128/CMR.00241-21/ASSET/70CB69E1-B9CC-45F6-8310-5A79324E1DAF/ASSETS/IMAGES/LARGE/CMR.00241-21-F001.JPG

CITE AS: Maina Mwaura F. (2025). Efficacy of mRNA-Based Malaria Vaccines in Preventing Malaria in Children in Endemic Regions. EURASIAN EXPERIMENT JOURNAL OF SCIENTIFIC AND APPLIED RESEARCH, 7(3):106-109