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Malaria control in Tanzania: Current status and future prospects

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Abstract
In 2017, Tanzania was among the seven countries accounted for fifty three percent of all global malaria deaths by five percent. In other words, vector control and antimalarial drugs have insufficiently controlled malaria morbidity and mortality. Hence, there is a need of adding other interventions such as malaria vaccine. Despite that, there is no available perfect effective malaria vaccine to date but promising malaria vaccines candidates are still entering the clinical trials. RTS, S is the first licensed malaria vaccine and currently administered in children up to two years in Malawi, Ghana and Kenya. The vaccine is imperfect with almost forty percent effectiveness but will at least lower malaria incidences and health-associated problems in children when compared to the standard care.

Keywords: Malaria vaccine; RTS, S; Tanzania

Introduction
The estimated 20 million cases reduction in 2017 than in 2010 describe insignificant progress made when the time frame of 2015- 2017 is considered [1]. In some countries there has been an increase in malaria incidence [2] and even within countries there can be regional variations in trends i.e. Tanzania malaria indicator survey of 2017 among children between 6-59 months [3] reported variations in prevalence (0.0 to 24.0%) between the regions.
On the other hand, the development of affordable, safe and effective malaria vaccine to form part of malaria control and elimination program is a priority of researchers and many countries, especially where malaria continues to cause health problems [4]. More importantly, malaria vaccine will supplement the existing malaria control tools such as vector control and antimalarial drugs, which have insufficiently controlled malaria morbidity and mortality [1].
Therefore, this article attempts to summarize the epidemiology of malaria and discusses malaria vaccine prospects in Tanzania.

Malaria situation in Tanzania
Tanzania, which comprises of Tanzania Mainland and Zanzibar has eight geographical zones for Tanzania mainland; Lake, Western, Northern, Eastern, Central, Southern, Southern Highlands and Southern West Highlands zone plus Zanzibar (Figure 1a).
Tanzania Malaria Operational Plan of 2018 [5] highlighted that 93% of the population on the Mainland and the entire population of Zanzibar lives in areas where malaria is transmitted. Seasonal variation in malaria transmission was unstable in approximately 20% of the country, while stable malaria with seasonal variation occurs in another 20%. The remaining part of the country (60%) is characterized as malaria endemic areas with stable perennial transmission. Regarding the distribution of Plasmodium species, *Plasmodium falciparum* accounts for 96% of malaria infection in Tanzania, with the remaining 4% due to *P. malariae* and *P. ovale* [5].
On the other hand, Malaria Control Program Strategic Plan for 2015-2020 [5] set the following goals i) to reduce malaria morbidity and mortality levels by 80% by 2020, ii) to reduce malaria prevalence from 10% in 2012 to 5% in 2016 and to 1% in 2020 and iii) to increase the proportion of women receiving two or more doses of sulfonamide-pyrimethamine (SP) during their pregnancy from 32% in 2012 to 80% by 2016 [5].
However, the National Malaria Indicator Survey of 2017 found an overall malaria prevalence of about 7% using rapid diagnostic test (RDT) in children with age between six months and below five years [6]. This was a decrease of almost half when compared to that of 2015-2016 [7]. Prevalence varied by region from <1% in the highlands of Arusha to as high as 24% in Kigoma region (Figure 1b). The same survey showed malaria prevalence of less than 1% by RDT (TMIS, 2017) in Zanzibar. In addition to that, the survey found 56% of pregnant women received at least 2 doses of SP and only 26% received at least 3 doses [6] which is lower than the set goal of 80% by 2016 [5].
Moreover, both Mainland and Zanzibar malaria strategic plans advocate universal coverage of the population with an insecticides treated bed nets (ITNs) through routine distribution and mass campaigns in order to reduce the burden of malaria [5]. About 63% of people have access to ITNs [6] where majority (62%) of ITNs owned by households were obtained from mass distribution campaigns, 15% from Shehia coupons, 10% from a shop/market, 4% from the School Net Program, 4% from antenatal care visits, and 1% from routine immunization visits [6].

Malaria vaccine studies
SPf66 malaria vaccine in Tanzania
After the Global Malaria Eradication program in the late

1950s went unsuccessful, research scientists thought of malaria vaccine as the promising tool that may supplement the existing fights for malaria eradication [8]. Since that time different malaria candidate vaccines were studied [9], most of them failed at the earlier stage of development [4].

The discovery of a synthetic peptide polymer (SPf66) by a Columbian pathologist, Manuel Elkin Patarroyo [10] attracted more attention and enabled the development of the first vaccine candidate in 1987 where Tanzania became one of the countries where the SPf66 trial was conducted [11–15]. The SPf66 initial trial was promising but clinical trials conducted in Tanzania, Gambia and Thailand indicated lack of efficacy [10].

RTS, S malaria vaccine in Tanzania

RTS,S is the first approved malaria vaccine where Malawi had started giving this vaccine to children below two years of age (16). This candidate was designed by research scientists at the Walter Reed Army Institute of Research (WRAIR) in the 1980s and has since been developed by the pharmaceutical company Glaxo Smith Klein (GSK) with financial support from the Bill the Melinda Gates Foundation (BMGF) [4].

RTS,S is made to target the sporozoites stage, however the candidate faced some challenges due to having limited immunogenicity that prompted the design of adjuvants AS01 [17, 18] and AS02 [19, 20]. Therefore, there are on-going studies to further address its limited efficacy, recently, a matched case-control study nested within the multicentre African RTS,S/AS01E phase 3 trial was conducted in children and infant with clinical malaria and found that Interleukin (IL) 2 and IL-5 ratios were associated with RTS,S/AS01E vaccination (adjusted P ≤. 01) [21].

Previously the world has witnessed different contributions toward RTS, S vaccine development from Tanzania as discussed below. The study by Abdulla *et al*., 2008 [19], was conducted with the aim of assessing the feasibility of integrating RTS,S/AS02D into a standard Expanded Program on Immunization (EPI) schedule in infants. One month after vaccination, the study found that 98.6% of infants receiving the RTS, S/AS02D vaccine had seropositive titers for anti-circumsporozoite antibodies on enzyme-linked immunosorbent assay (ELISA). During the 6-month period after the third dose of vaccine, the efficacy of RTS, S/AS02D vaccine against the first infection with *P. falciparum* malaria was 65.2% (95% CI, 20.7 to 84.7; P = 0.01). On the other hand, the use of RTS, S/AS02D vaccine in infants had a promising safety profile and did not interfere with the immunologic responses to co-administered EPI antigens, and reduced the incidence of malaria infection.

Other studies by Lusingu *et al*., 2010 [17] and Selidji *et al*., 2010 [18] on infants reported that the candidate vaccine RTS,S/AS01$_E$ demonstrated an acceptable safety profile in infants living in a malaria-endemic area in East Africa with a favourably safety and immunogenicity when integrated with EPI. The findings on safety profile were similar from the studies conducted on young children [22]. However there has always been the challenge regarding the age and efficacy i.e. the candidate malaria vaccine RTS,S/AS01 reduced episodes of both clinical and severe malaria in children 5 to 17 months of age by approximately 50% [23] but when infants 6 to 12 weeks of age recruited for the same trial were studied the efficacy was reduced to 30% [24]. To summarize, RTS, S is an imperfect vaccine but may help to reduce the current malaria incidences and its associated health consequences in children.

Future malaria control prospects in Tanzania

The World especially sub-Saharan countries have demonstrated limitations on the current available malaria control tools such as use of ITNs and antimalarial in the eradication of malaria[1]. Almost eighty percent of global malaria deaths in 2017 were concentrated in seventeen WHO African Region and India; seven of these countries accounted for 53% of all global malaria deaths: Nigeria (19%), Democratic Republic of the Congo (11%), Burkina Faso (6%), United Republic of Tanzania (5%), Sierra Leone (4%), Niger (4%) and India (4%) (25). Unfortunately none of these countries were reported to form part of the on-going and the coming RTS,S immunization program, at present the first malaria proven vaccine (RTS,S) with 40% efficacy is administered to Malawian children with age below 2 years with expectations of Ghana and Kenya to join in, as part of a large-scale pilot program backed by WHO [16].

Moreover, WHO has declared only 38 malaria-free countries after the recent add of two countries, Argentina and Algeria [26]. Factors such as false negative diagnosis due to histidine rich protein 2 (HRP-2) deletion [27–29], insecticides and antimalarial resistance are among the challenges indicated to affect the archiving of malaria free world [30]. In Tanzania, artemether-lumefantrine (AL) and dihydroartemisinin-piperaquine (DP) are the first-line for uncomplicated malaria treatment [31]. Currently, molecular marker, in vitro test or blood dosage levels could not confirm lumefantrine resistance nor artemisinin resistance in Africa [30] but other parts of the world have reported resistance to artemisinin combination therapy [32]. Therefore other approaches such as vaccines should supplement existing malaria control and elimination tools.

Conclusion

Tanzania was among the first countries outside Columbia where SPf66 clinical trials were conducted. Such a notable history indicates the epidemiological advantage the country, Tanzania hold. This is also an important history for researchers to consider Tanzania when designing malaria vaccines trials because series of trials and huge investments are needed before coming up with an effective malaria vaccine and should include a range of epidemiological evaluations, covering different intensities of transmission and allowing the antigenic variability of the parasite.

Moreover, the current malaria epidemiology and National Malaria Control Program Strategic Plan for 2015-2020, indicates children with age below five years and pregnancy women as the mostly affected group but unlike pregnant women who are given SP as an intermittent preventive therapy (IPTp-SP), at present no intervention is given to Tanzanian children to prevent them from the disease (malaria) burden.

Therefore, this article recommends to the responsible authorities to plan to include Tanzania in the current RTS, S malaria vaccine pilot program. RTS, S vaccine is imperfect with almost forty percent effectiveness but will at least lower malaria incidences and their associated health consequences in children. Furthermore, zonal and regional differences in malaria transmission intensities i.e. less than 1% malaria prevalence in highland regions to 24% in

Kigoma region highlights the need for the country to employ regional or zonal approaches for fight against malaria. Zero malaria in Tanzania is possible.

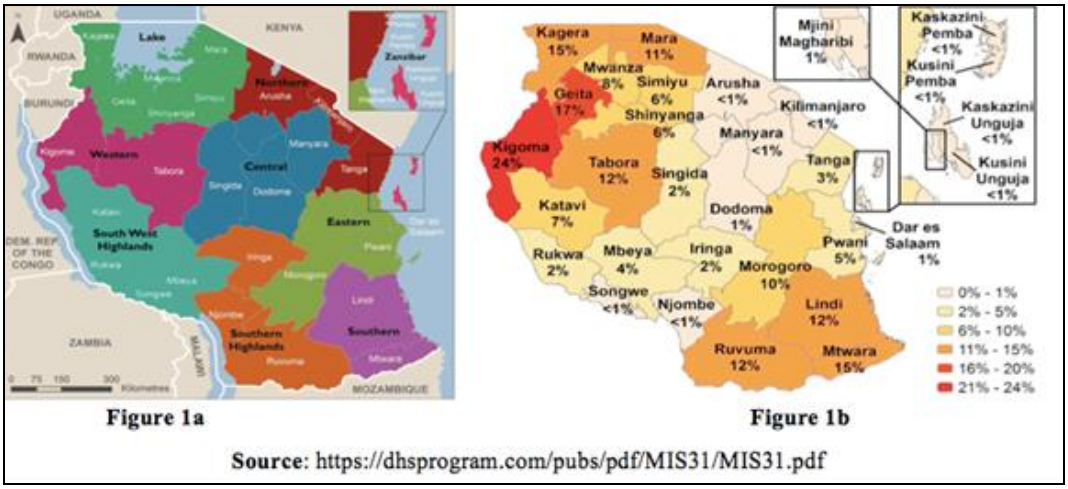

Fig 1: Tanzania map. The map indicating different eight zones from Tanzania mainland with their respective regions plus Zanzibar (Figure 1a). Tanzania map indicating prevalence of malaria by region using rapid diagnostic test in children with age between 6 months and below 5 years (Figure 1b)

Conflict of interest

None to declare

References

1. WHO. World Malaria Report. 2018. ISBN 978 92 4 156469 4. [Internet], 2018. Available from: www.who.int/malaria
2. Okiro EA, Kazembe LN, Kabaria CW, Ligomeka J, Noor AM, Ali D, *et al*. Childhood Malaria Admission Rates to Four Hospitals in Malawi between 2000 and. PLoS One. 2010-2013; 8:4.
3. NBS. Tanzania Malaria Indicator Survey Key indicators 2017. Decis Support Syst [Internet]. 2017; Available from: https://dhsprogram.com/pubs/pdf/PR103/PR103.pdf
4. Von Seidlein L, Bejon P. Malaria vaccines: Past, present and future. Arch Dis Child. 2013; 98(12):981-5.
5. URT. President's Malaria Initiative and Tanzania Malaria Operational Plan. United Republic of Tanzania (URT). 2018.
6. TMIS. Tanzania Malaria Indicator Survey (TMIS) 2017 [Internet]. 2017. Available from: https://dhsprogram.com/pubs/pdf/MIS31/MIS31.pdf
7. NBS. Tanzania dermographic and health survey 2015-2016. National Bureau of Statistics (NBS) [Internet]. 2015. Available from: http://www.tzdpg.or.tz/fileadmin/documents/dpg_internal/dpg_working_groups_clusters/cluster_2/health/Key_Sector_Documents/Monitoring___Evaluation/TDHS_2015-16_final_report.pdf
8. Das P, Horton R. Malaria elimination: Worthy, challenging, and just possible. Lancet. 2010; 376(9752):1515–7.
9. Girard MP, Reed ZH, Friede M, Kieny MP. A review of human vaccine research and development: Malaria. Vaccine. 2007; 25(9):1567-80.
10. Graves PM, Gelband H. Vaccines for preventing malaria (SPf66). Cochrane Database Syst Rev. 2006; 2.
11. Alonso PL, Tanner M, Smith T, Hayes RJ, Armstrong Schellenberg J, Lopez MC, Bastos de Azevedo C. A trial of the synthetic malaria vaccine SPf66 in Tanzania: rationale and design. Vaccine. 1994; 12(2):181-6.
12. Acosta1 CJ, Galindo1 CM, Schellenberg D, Aponte JJ, Kahigwa Urassa E, Armstrong H, Schellenberg JRM. Evaluation of the SPf66 vaccine for malaria control when delivered through the EPI scheme in Tanzania. Trop Med Int Heal. 1999; 4(5):368-76.
13. Schellenberg JA. Humoral immune responses during a malaria vaccine trial in Tanzanian infants. Parasite Immunol. 2000; 22(9):437-43.
14. Danielopol DL, Geiger W, Lderer-farmer MT, Orellana CP, Terrat MN. Cr ; R L. 1985; 367-72.
15. Safety in infants of SPf66, a synthetic malaria vaccine, delivered alongside the EPI. Trop Med Int Heal. 1999; 4(5):377-82.
16. Maxmen A. First proven malaria vaccine rolled out in Africa — but doubts linger. Vol. 569, Nature. 2019, 14–5.
17. Lusingu J, Olotu A, Leach A, Lievens M, Vekemans J, Olivier A, *et al*. Safety of the malaria vaccine candidate, RTS,S/AS01E in 5 to 17 month old Kenyan and Tanzanian children. PLoS One. 2010; 5(11):1-9.
18. Agnandji ST, Asante KP, Lyimo J, Vekemans J, Soulanoudjingar SS, Owusu R, *et al*. Evaluation of the Safety and Immunogenicity of the RTS,S/AS01 E Malaria Candidate Vaccine When Integrated in the Expanded Program of Immunization. J Infect Dis [Internet]. 2010; 202(7):1076–87. Available from: https://academic.oup.com/jid/article-lookup/doi/10.1086/656190
19. Abdulla S, Oberholzer R, Juma O, Kubhoja S, Machera F, Membi C, *et al*. Safety and Immunogenicity of RTS,S/AS02D Malaria Vaccine in Infants. N Engl J Med. 2008; 359(24):2533-44.
20. Abdulla S, Salim N, Machera F, Kamata R, Juma O, Shomari M, *et al*. Randomized, controlled trial of the long term safety, immunogenicity and efficacy of RTS,S/AS02D malaria vaccine in infants living in a malaria-endemic region. Malar J [Internet]. 2013; 12(1):1. Available from: Malaria Journal
21. Moncunill G, Mpina M, Nhabomba AJ, Aguilar R, Ayestaran A, Sanz H, *et al*. Distinct helper t cell type 1

and 2 responses associated with malaria protection and risk in rts,s/as01e vaccinees. Clin Infect Dis. 2017; 65(5):746-55.
22. Vekemans J, Ph D, Mshamu S, Lang T, Ph D, Gould J, *et al*. new england journal, 2010.
23. Agnandji ST, Lell B, Soulanoudjingar SS, *et al*. First Results of Phase 3 Trial of RTS, S/AS01 Malaria Vaccine in. N Engl J Med. 2011; 365(20):2747-57.
24. Agnandji ST, Lell B, Soulanoudjingar SS, *et al*. A Phase 3 Trial of RTS, S/AS01 Malaria Vaccine in African Infants. N Engl J Med. 2012; 367(24):2284-95.
25. WHO. World Malaria Report 2018 [Internet]. 2018. Available from: https://www.who.int/malaria/publications/world-malaria-report-2018/en/
26. Garcia de Jesus EI. Algeria and Argentina declared malaria-free. Nature, 2019.
27. Kozycki CT, Umulisa N, Rulisa S, Mwikarago EI, Musabyimana JP, Habimana JP, *et al*. False-negative malaria rapid diagnostic tests in Rwanda: impact of Plasmodium falciparum isolates lacking hrp2 and declining malaria transmission. Malar J. 2017; 16(1):1-11.
28. Wurtz N, Fall B, Bui K, Pascual A, Fall M, Camara C, *et al*. Pfhrp2 and pfhrp3 polymorphisms in Plasmodium falciparum isolates from Dakar, Senegal: Impact on rapid malaria diagnostic tests. Malar J. 2013; 12(1):1-8.
29. Moges B, Amare B, Belyhun Y, Tekeste Z, Gizachew M, Workineh M, *et al*. Comparison of CareStart HRP2/pLDH COMBO rapid malaria test with light microscopy in north-west Ethiopia. Malar J. 2012; 11:1-6.
30. The WHO. World Malaria Report 2017 [Internet]. World Health Organization. Available from, 2017, 186 p http://apps.who.int/iris/bitstream/handle/10665/259492/9789241565523-eng.pdf;jsessionid=3B05B30235850B2B29A7FFFDD8A874D8?sequence=1
31. United The. of r. the united republic of tanzania standard treatment guidelines and essential medicines list, 2013.
32. Tilley L, Straimer J, Gnädig NF, Ralph SA, Fidock DA. Artemisinin Action and Resistance in Plasmodium falciparum. Trends Parasitol. 2016; 32(9):682-96.
33. WR JVB. Plasmodium falciparum malaria vaccines in development: Expert Review of Vaccines: Vol 7, No 2. Expert Rev Vaccines. 2008; 7(2):223-40.
34. Designing a VAR2CSA-based vaccine to prevent placental malaria. Vaccine [Internet]. 2015; 33(52):7483-8. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L607231992%0Ahttp://dx.doi.org/10.1016/j.vaccine.2015.10.01.