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Malaria Epidemiology: Specific Vulnerable Group in the Population

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ABSTRACT

Malaria is a potentially fatal vector borne disease caused by the blood protozoan, *Plasmodium* spp. The number of species of *Plasmodium* spp continues to grow; even nowadays there is zoonosis based species that infect human. Morbidity and mortality still difficult to control, with sub Sahara Africa and south East Asia still the epicentrum of persistent transmission. Human behavior is one of the predisposing factors and actually there is a specific vulnerable group in the Population. It consists of pregnant women, children (especially under five years old) and travellers. They are at risk and very vulnerable with separated specific reason. There is no single action can be successfully applicable for them, because preventive approach must be conducted based on each group specific characteristics. In order to prevent the spread of transmission, active surveillance is one of the tools used. Preventive action conducted tailor made based on each specific group with adjustment when applicable in different region. Lesson learned from the effort to tackle malaria so far and to try to adjust it into specific vulnerable population and future direction being made in order to eliminate malaria and to create world free malaria.

Keywords: Blood protozoa; children; pregnant women; travellers; active surveillance; vector.

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1. INTRODUCTION

Malaria is still a big challenge and a global health problem. Malaria known with their complex spectrum disease pathologies caused by formerly known five distinct species Plasmodium (Plasmodium vivax, P. falciparum, P. ovale, P. malaria, and P. knowlesi) [1,2]. Restricted to some region of the world, there are also known zoonosis based malaria named, P. knowlesi. as viable targets for eradication; because the latter two will always connected to certain animal as their primary definitive host [1]. Considering their global epidemiology, with high number and persistent morbidity and mortality, the two major causative agent of malaria, P. falciparum and P. vivax supposed to be the focus of global malaria eradication efforts [3]. Annually, the number of malaria cases globally remains constant and worrying in some region of the Some population groups are considerably higher risk of infecting malaria, and developing severe form of the disease, than others. These include pregnant women, infants with children under 5 years of age and nonimmune travellers, labourer and migrants. These group remain specific vulnerable group and the aim of this review article is to discuss about factors related to or influencing their vulnerability to malaria [4].

2. GLOBAL EPIDEMIOLOGICAL DATA: WHO IS AT RISK?

It is still very challenging to try to count the exact number related the burden of malaria in limited area, e.g. sub-Saharan Africa and even if effort being made to measure other country in the world. Measurement effort always counting on epidemiological data based modeling to analyses local parameters and providing an in-depth evaluation regarding progress and trends in malaria response, locally and even in greater scale, globally [5].

In some African malaria-endemic countries, there is increasing use of routine surveillance data to define their own dynamic estimation and prediction of malaria case, national strategic targets and achievement, and to measure control progress to identify priorities scale to be conducted based on time limit [6]. Existing research targets strongly on the capabilities of these availability and trustworthy data; with less emphasis on possible existing challenges and opportunities that might be presented [7].

In the year of 2018, it is estimated that malaria reaching almost 228 million cases, globally. It has reduced from 251 million of cases in 2010 and 231 million in 2017. Majority of malaria incidence in the year of 2018 were happened in the African continent (epidemiologically estimated it reached 213 million or 93% of all cases of malaria worldwide), and then in the 2nd place is the South-East Asia Region (3.4% of all global cases) and the last region, the Eastern Mediterranean Region in 3rd place (2.1%) of all global cases. The global incidence rate of malaria declined between the year 2010 and 2018, from previously 0.071 and then declined to 0.057 population at risk (per 1,000 people). But instead all success that before mentioned, the rate of change slowed dramatically, and not changes since 2014 and remain the same until 2018 (stagnant) [4].

Global mortality due to malaria is also the cause of concern to all stakeholders, in Fig. 1 there is a 3 year global morbidity number caused by malaria. Among the three group of vulnerable to malaria, children (mostly < 5 years) are the most prone to be infected by malaria. Just in the year 2018, 67% of cases of all malaria related morbidity, globally, are happened in children. The global health organization (WHO) African Region even estimated further as much as 94% of all malaria deaths happened in Africa just in the year 2018.

With so much recent information on the epidemiology of malaria, this mini review aim to dig further on the epidemiology and its related factor related to the three most vulnerable group in the population (1) Pregnant women, (2) children (especially under 5) and (3) travellers (tourists, laborer, refugee) which all at risk and very prone to get infected with malaria in an endemic region where transmission occurred in constant rate due to the availability of the vector, the mosquito *Anopheles* spp [7]. Without proper intervention, these three group remain prone to infection. Sociopolitically, these group might not able to access proper health care when they need it.

2.1 Pregnant Women

Just in the year 2018, global health organization accounted about as much as 11 million pregnancies took place in endemic region [4]. These women unfortunately living in location of with moderate and high-rate of malaria transmission, most of them located in the region

of sub-Saharan African countries [8]. It means that these poor pregnant women would have been exposed to malaria parasite in a greater amount compared to other pregnant women who live in non-endemic area. This facilitates by the existence and bite of Anopheles spp mosquito which transmit the disease [7]. Perhaps poverty and lack of education become the basis for poor personal hygiene and bad environmental sanitation [9]. Geographically, West African sub region and Central Africa (35% each) bear the brunt of the burden of exposure to malaria related pregnancy, the 2^{nd} place is the East and Southern Africa. Nigeria and the Democratic Republic of the Congo bear as much as 39% of all malaria related pregnancy in Africa continent [4].

Malaria infected pregnant women are at risk delivered neonates with low birth weight, and in case of Africa continent. West Africa suffer the most because they have the highest number of small birth weight neonates as the consequences of malaria that happen during the times of pregnancy [10,11]. Malaria in pregnant women also made them suffered from anemia in various stage, from mild to severe, as the direct consequences of malaria, and this aggravate their condition while struggling maintain their baby during pregnancy [8,11]. Severe malaria pregnant women have deleterious effect, both to the mother and their babies [4].

2.2 Children

Children are prone to all kind of infection, including malaria. Malaria in children bring several complication, one of the commonest is anemia. Within four years, between 2015-2018, countries with status of exactly 21 transmission moderate to high malaria burden in Africa, the prevalence of anemia in children under 5 years thru a positive rapid diagnostic test (RDT) was double in number compared to that of children with a negative RDT. In the children who were positive for malaria, 9% among them had severe anemia and those who had moderate anemia 54% had: in contrast, in the children without malaria, the prevalence of anemia is truly lower. Overall in just the year of 2018, unfortunately, it is estimated about 24 million children, just in sub Saharan African, having malaria falciparum and 1.8 million among them accounted to suffer from severe anaemia [4].

2.3 Travellers

The increase in trips to endemic areas in recent decades means that imported malaria cases are becoming more common [12]. Malaria is endemic throughout the tropics and sub-tropics, regions by an estimated 25-30 international travellers annually, resulting in an estimated 30,000 travel-related malaria infections [13]. Imported malaria may occur more often along certain travel routes in these areas, and may result in secondary transmission if the infection is brought back to a non-endemic country [14]. Most of the reported 17,471 imported malaria infections among US travellers from 2004 to 2014 were acquired while travelling in Africa; P. falciparum or P. vivax comprised the majority of infections. Most P. falciparum exposures cluster in mostly the region of Africa and also the Caribbean (Hispaniola) and P. vivax exposures occur most frequently in the area of South East Asia, Central-South America, and Oceania [13]. Furthermore, some restricted inland areas in Indonesia having all 4 kind of malaria agent (Plasmodium vivax, P. falciparum, P. ovale, P. malaria). travellers are prone to get infected to any of these 4 species if they failed to implement safety standards. [2] all of the before mentioned area were the place for most visited famous vocational destination for tourists. Other groups in which Plasmodium infection should be considered carefully in health care include asymptomatic immigrants (refugees, international adoptees, and others) from endemic areas [15].

3. WHY PREGNANT WOMEN VULNERABLE?

Malaria that took place during pregnancy affected the mother's and her baby's health; and it put them (both) at higher potency of complication, even causing death [8,10] for the fetus, untreated malaria directly causing prematurity and low birth weight, both are major causative predisposition to mortality among neonates and baby [10,11] in other word, what happened to the mother will affect their baby directly. Unicef data told us, in daily basis, every two minutes, a child (age under 5) passed away due to malaria. In the year of 2018, there were 228 million malaria cases that led to 405,000 deaths. Of these 67 percent (272,000) were children under 5 years of age. This translates into a daily toll of nearly 750 children under age

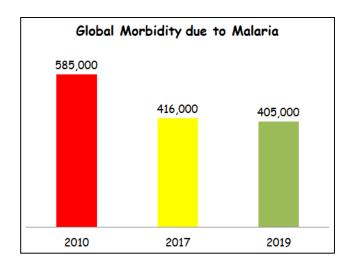


Fig. 1. Global mortality due to Malaria in the year 2010, 2017 and 2019, with modification

The chronic and relapsing nature of *P. vivax* results in repeated episodes of hemolysis and dys-erythropoeisis due to erythrocyte sequestration, especially took place inside microvasculature of tissue and important organ, e.g. Brain, kidney, muscle. [16] when parasite recurrence occurs prior to hematological recovery, there is a cumulative risk of severe anemia which, when accompanied with other comorbid, *e.g.* Hiv, malnutrition and sepsis, can result in a catastrophic outcome [17].

In analysis on population based study conducted by Patriani et al. [18] with subject were southern papuan children aged younger than 5 years that presenting with malaria, they found out that severe anemia (hb < 5 g/dl) was associated with a 2-fold increased risk of delayed mortality and malnutrition with a 3-fold increased risk [18]. Recurrent episodes of malaria may have contributed both directly and indirectly to this malaria vivax high mortality rate in children, especially under five and also for pregnant women.

In the context of travellers, the increasing accessibility of international air travel and changing preferences for travel destinations due to very aggressive advertising or testimony from people that already visited the location. This means that more people visit regions that actually not yet malaria-free, and they do so increasingly in number [19] a detailed itinerary is necessary to assess risk, and also the local status of transmission (low, moderate or high) so that these potential tourists can be well educated on the risk of malaria [20] at least there are 3 factors contributes for potency of risk: (1)

geographic and chronology: variation of area that influence the degree of, even within the same country, and probably also at different times of the year, e.g. Visitor came during the months of the dry or rainy season (2) personal: an individual's risk depends on the activities related geographic undertaken and how long is the time spent in the endemic area, (3) vector: the existence of potential mosquito, *Anopheles* spp, their abundance and vectorial capacity in the environment [21].

3.1 What Makes Them Prone?

Underlying condition that made pregnant women at risk of infection can be caused by physiological changes, both happened in her hormone levels and also in immune system. Physiologically, pregnancy shifted homeostatic of a woman, e.g. Hemodilution, additional body weight [22]. First-time mothers are especially prone to malarial infection compared to multiparous women [23]. Malaria infected pregnant women might suffer from anemia miscarriage with and short interpregnancy interval, and when their having their babies, it has the potency of stillbirth, prematurity, intrauterine growth retardation (IUGR), and low birth weight (LBW). [24,25] compared to other group in the community. These pregnant women are more prone to suffer from the complications of malaria, once they get infected [26]. Complications may include hemolysis, multi-organ failure, rhabdomyolisis and cerebral malaria [2,27]. This increased risk proceed even into the early postpartum period [28].

Pregnant women that already having HIV infection are at even facing bigger risk of to have placental malaria (this a very serious condition because rapid replication of malarial parasites that took place in the placenta; this condition surely blocks oxygen and nutrient exchange between the mothers with their fetus). An already HIV infected pregnant women when they also infected with malaria usually will have more fatal and severe malarial infections, and they unable to promote the same manner of anti-malarial resistance as happened in women without HIV [29.30]. HIV infection impairs the ability of the host's antimalarial immunity, especially responses to placental type variant surface antigen (vsa). The impairment is greatest in the most immunosuppressed women and could explain the increased susceptibility to malaria seen in pregnant women with HIV infection [31].

In general, immunity against malaria parasite, when it is developed successfully, characterized by an age-related lowering of the parasite count, clinical appearance, and the potency and number of severe malaria cases among individuals living in endemic areas [32]. The fact that clinical condition due to malaria is often less clear in older adults than in children because of they already develop enough immunity capable to minimize malaria parasite attack, a condition which develop along with increasing age [33]. Any children, when infected with malaria, are thus at very prone to suffer from severe malaria, since probably they have not yet adequate acquired natural immunity. Pregnant women, particularly in the primi-gravid women/having their baby for the first time, sometimes or transiently, lose some of their acquired immunity too, and this is due to their pregnancy [34].

Recent data showed us, when malaria and HIV infection happened in the same time, and their interaction caused dysregulation to the host's immune system and its armamentarium [35]. HIV and malaria, each will interact with their host's immune system to make complex pronounced activation of the host's immune cells. This causes dysregulated cytokine function and also the production of adequate antibody [30] in addition, the host's CD4+ T cells, that supposed to play an important role in the development and maintenance of anti-malaria properties, then being disrupted by HIV, the mechanism of which includes (1) systemic lymphoid cell rupture alongside the organ of lymph nodes, spleen, and gut mucosae, (2) hyperactivation of CD4+ and CD8+ effector cells to produce cytokines that in the end might cause cytokine storm, (3) direct hiv-induced down regulation of CD4+ T cells, (4) lowering the CD8+ T-cell counts, and (5) promotes and up regulated parasitemia due to the condition predisposed by no 1 until 4; and altogether these caused to the increased risk of fatal malaria together with a rapid worsening to AIDS [35].

In children, vulnerability related to their naïve immunity [36]. The well-known function of naturally acquired immunity is to establish the host's antibody responses especially against infection or corpus alienum. This protective role of antibodies also developed in fighting malaria infection, and at the beginning, it was first formed by passively transfer antibodies (Immunoglobulin G /lgG) from already developed clinically immune adults into their babies [37]. This in fact, has been supported by the result of the study on immuno-epidemiological basis of malaria, where the properties of antibodies against parasite antigens actually have been discovered; it give specific and sufficient protection from the potency of repetitive clinical episodes that might develop in endemic areas. These kind of antibodies have the ability to prevent or limit the development of any type of blood-stage malaria parasites, and also with their ability to induce and develop typical clinical symptoms of malaria by several already notable mechanisms, and these incorporated as follows: (1) erythrocyte invasion by this obligate intracellular organism, (2) opsonizing infected red blood cell (IRBC's) so that it is ready for phagocytic elimination, (3) making ready the monocytemediated antibody-dependent cellular killing of parasite, and (4) complement-mediated lysis of the IRBC's, and in addition (5) interfere in the adherence of IRBC's to vascular endothelium, these steps prevent the very early stage of erythrocyte sequestration.[37]

If the patient unable to inadequately produced sufficient level of antibodies against *Plasmodium* antigens (due to several condition, *e.g.* Malnutrition, HIV) and their subsequent loss in the case of persistent exposure to infection has been indicated to directly affect the progress of B-cell immunological memory advancement, which is very important for the host's future defense against malaria [38]. In case of malaria, just as other type of infection, memory B-cells play a critical role in enduring host's resistance to any different pathogens by way of boosting the host's immune response if the secondary exposure happened [39].

Multiple (and possibly recent) episodes of malaria are associated with the modification of the immune system in children [36]. Individuals who have experienced repeated episodes demonstrate enhanced activation of neutrophils, B cells and CD8+ T cells; up regulation of interferon-inducible genes; and a clear increase in circulating levels of the immunoregulatory cytokine IL-10. Such elevated IL-10 levels suggest a degree of immune modulation that may be important for avoiding immunopathology but could interfere with parasite clearance [36,39,40]. This condition may also affect the induction of protective immune responses by vaccines and hence have significant implications for the efficacy of such vaccines in endemic populations [37-40].

Most infections occur in travellers resident of an European country, rather than in visitors to that country. They got the infection while travelling to an endemic area, e.g. Country in Africa or South East Asia which already known with malaria endemicity [12-14,20,21]. Malaria is a major risk for travellers if they do not take chemoprophylaxis or if they take incorrect prophylaxis [41]. Less than half of travellers who acquire malaria actually have taken advice before travelling [21].

Analysis of imported malaria indicates that certain groups among these travellers are at particular risk with a typical characteristics, including such as those (1) picking last minute holidays (not well planned) and those (2) visiting friends and relatives abroad [42]. Travellers visiting friends and relatives abroad (also known as VFR travellers) account for 70% of all of the malaria imported into the United Kingdom; limited evidence suggests that these travellers do not think of malaria as a serious or potentially fatal disease, and they are also less likely to consult practitioners or travel general medicine specialists pre-departurely, and often travel to areas of high risk such as West Africa [21,42].

Using intervention strategies for travellers visiting friends and relatives, pre-departure action should always be encourage for them—such as steps as follows: stay alert, increasing awareness in the community, dispelling myths about immunity or subsidizing antimalarial—could considerably reduce imported malaria [12-14,20,21,42].

3.2 Surveillance as Important Tools

Improved surveillance for malaria cases and deaths helps authorities to determine which

areas and/or population groups are most affected and enables countries to monitor changing [1-3]. Strong patterns surveillance systems also help countries design effective health interventions and evaluate the impact of their malaria control programmes [4,7]. Malaria surveillance is currently weakest in countries with the highest malaria burden, rendering it difficult to accurately assess disease trends and plan interventions. In countries that account for 85% of the global malaria burden, trends are based on empirical models and not conducted as a routine surveillance. With improved diagnostic and reporting systems, surveillance systems are, however, gradually improving in these countries, but more effort is necessary to ensure quality data across all sectors of the health system 43-45].

Intervention without previous active surveillance is like to enter the rain without an umbrella. Surveillance should precede any intervention in order to successfully obtain elimination. The global health organization had declared success story of several countries that already able to eliminated malaria. Actually in the beginning, those countries have built and established basic fundamental electronic information systems and somehow using this advancement to maintain the national programme and also helped them to prevent the re-establishment of the disease [6,43]. Previous assessments conducted by several researchers has identified the potency of gaps in that advance system using it; especially those area which is (1) faraway and remote (geographical restriction), (2) high-risk areas (moderate to high transmission), (3) reporting conducted from private providers (potency of conflict of interest), (4) integration of various data elements, (5) user-friendly visualization of system information (easy to read and interpret), and (6) the routine use of available data to make programmatic decisions [44].

Coordination and cooperation what is really needed from all stake holders. While the holding of a very perfect technology/systems are not really required in case of elimination, these gaps, as long as it exists, it will make it more difficult to distribute all resources to all stakeholder in ways that, making elimination aspirations more difficult to achieve [45].

In response to the result and recommendation of these assessments, several countries actually managed to have made their own vital adjustments that leads to improvements in area

considered as priority in the context of upgrading their surveillance systems. They even able to include and extend the system to reach more issues in the society, e.g. additional important points of care, shifting from classic aggregate to modern case-based reporting, and pushing beyond the limit on the usage of 'the just daily routine use' of surveillance data [4]. Means that, successful country to eliminate malaria uses all of their resources and put them together as their strength to fight and eliminate malaria.

Beyond the future, this geographical based approach can lead to the effort of developing a more standardized toolkit that can be used for malaria surveillance assessments in any region of the world [46]. Countries managed to improve their system of malaria surveillance and resulted in the declines of the prevalence/incidence, but the performance and sustainability of these systems will need to be re-evaluated continuously due to the dynamics of hostmalaria-environment relationship. Other aspect of this approach is also linking and integrating this system to a more broader public health surveillance systems; the system which is open and continuously updated. [6] in short term, spending resources on high priority gaps to increase the quality of information and its routine use by programs might be expensive and difficult, but for long term, this approach may enable countries to be more effective and efficient, e.g. They can provide targeted programs with better tools to achieve and maintain malaria elimination [4,5].

3.3 Preventive Action

In general, preserving all member of the populations at risk of get infected with malaria actually is the main target of a global effort to "roll back malaria" (this become the tagline of global venture to fight malaria) [47]. The availability of anti-malaria medicine, includina supporting treatment for complication and the campaign for using protective bed nets are actually two important approach in reducing the prevalence of malaria in several African countries. The first is to handle the sick ones and the latter prevent people to become sick. Pregnant women, children especially under five years old and travellers continues to become specific vulnerable group that need to be watch over and protected [15,18,48].

Who keep recommending the use of insecticidetreated mosquito nets (ITNs) and preventive antimalarial medicines made available in the primary health care in order to protect and save pregnant women from malaria, in Africa [49,50]. Both shows progress, in a positive manner. Even though there were still found pregnant woman that did not use ITNs in their bed and in case of preventive anti-malaria therapy also found pregnant women that did not receive it properly.

But in case of children, efforts to expand access to preventive antimalarial medicines are seems to be promising because in some Africa's subregion, the global health organization pushed the local authority to provide seasonal malaria chemoprevention and made them available in the primary health care center, especially when the time of peak transmission occured [51]. Almost all of children living in areas eligible for this preventive therapy already received it [4].

An extensive review study analyzing previous studies of antimalarial interventions in pregnant women actually found that by providing effective drugs during pregnancy locally and made them easy to access and available in the primary health care, then it will minimize sign and symptom of illness and reduce complaint from the mother side; and in the end it is prove to be able to prevent the occurrence of low birth weight infants and anemia, especially if this treatment started to be given in multi-parity pregnant women, as early as possible [34].

Intermittent presumptive malaria treatment (IPT) for pregnant women is an approach for susceptible women. It is already proven efficient and cost-effective to improve maternal and child health, especially for nully-parity women that unfortunate enough living in endemic areas in African region [52]. IPT when combined with the classic anti-malarial drug sulfadoxinepyrimethamine (SP, also known as Fansidar) when given during pregnancy can minimize the possibility of severe anemia in pregnant women. and by doing that to the mother, it is also minimize the incidence of low birth weight infants in region where resistance to chloroquine were found [53]. By giving pregnant women two or more doses of SP helped to reduce the prevalence of low birth weight infants by more than one-half [54].

It was measured in african endemic region, that with only US\$12 (at a cost of for two doses of SP given to pregnant women in areas with no SP resistance) healthy year of life can be gained [55]. The WHO now recommends that women in areas where moderate to high transmission malaria is widespread receive IPT with an

effective, preferably one-dose, antimalarial drug as part of routine antenatal care during their first and second pregnancies [56]. While the availability of SP that made it mostly become the drug of choice for the technique of intermittent treatment in chloroquine resistant areas, it is less effective in women who have HIV, and in those who do not return for their second dose [57]. SP resistance has been seen in some areas of Eastern Africa, so the need for new, effective drugs continues [58]. The search and the development of potential substance that work as better antimalarial drug is a must, compared to the already exist anti-malaria drugs.

Preventing malaria among children living in endemic areas also conducted by the use of the the use of insecticide-treated mosquito nets (ITNs) and preventive antimalarial medicines [49,50]. Management of acute malaria in children must include both acute treatment of peripheral parasitaemia, malnutrition management and reversing the condition of severe anemia, as well as interventions to prevent subsequent malaria recurrence. It need such community medicine approach, e.g. Insecticide treated bed nets, prophylaxis or even radical curative treatment [19]. It will be very interesting to study the impact of this approach on this specific vulnerable group, directly for their health and also indirectly for other aspect of their life.

Travellers to endemic areas can reduce their risk of malaria substantially by adopting preventive measures: avoiding mosquito bites and using appropriate chemoprophylaxis. Effective uptake of such measures is, however, largely dependent on the traveller's recognition and understanding of the risk. This in turn depends on an accurate risk assessment by healthcare workers who advise them; these risks change over time with shifts in the global epidemiology of malaria, changes in travel habits and patterns of migration (visits to friends and relatives are a common reason for travel), and changes in patterns of drug resistance [7,12,13].

3.4 Lesson Learned and the Future of Malaria Eradication by Approaching Specific Vulnerable Group in the Population

Malaria eradication is defined as the permanent reduction to zero of the worldwide incidence of malaria infection caused by all species of human malaria parasites. Once eradication has been achieved, intervention measures are no longer needed. Lessons learned from the history of global malaria eradication effort so far highlighted the fact that not even a single strategy can be successfully applicable everywhere; means that it is always need adjustment based on local characteristics. Continous epidemiological and clinical study combined with a long-term commitment from the higher authority with a dynamic and ready to adjust strategy that always includes community participation and this must involve the integration with ready to support national health systems, and the development of active and trustworthy surveillance systems is needed.

Many experts discussions re-affirmed that eradication will result in millions of lives saved and a return on investment of billions of dollars. Lesson learned from some countries that is successfully eradicated malaria recently. Actually, no biological or environmental barriers identified to malaria eradication. In addition, by measuring a variety of global trends in the human and biophysical environment over the next decades suggests that the world of the future will have much less malaria to contend with.

Strengthening this specific vulnerable group in the population conducted by educating them and expecting their cooperation by the change of attitude and practice on malaria prevention, so this disease can be controlled and eliminated with hard work and big efforts from every global and local stake holder. When these critical foundations are laid, the author believes that the world will be in a much stronger position to make the final and credible push for eradication.

4. CONCLUSION

Pregnant women, children (especially under five years old) and travellers are specific vulnerable people in the context of malaria; and among them children are the most brittle. Their vulnerability to this parasite is case specific and actually can be prevented. Prevention also a case specific, and intervention must be adjusted according type of the group and the form of intervention must be adapted carefully and cannot be mix and match. Success story of malaria elimination in some countries in Africa using the advancement of IT and support from the authority and all stake holders with their focus on this vulnerable group exist in the population.

COMPETING INTERESTS

Author has declared that no competing interests exist.

REFERENCES

- Molyneux D. Malaria eradication. The Lancet, 2020;395:10233, e71.
 DOI: https://doi.org/10.1016/S0140-6736(20)30240-3
- Siagian F, Ronny, Sirra A, Susiantoro U, Siregar M. Malaria related myalgiaarthralgia: an imported case report treated with antimalarial drug. Int J Basic Clin Pharmacol. 2020;9(10):1603-6 DOI: 10.18203/2319-2003.iibcp20203964
- Garrido-Cardenas JA, Cebrián-Carmona J, González-Cerón L, Manzano-Agugliaro F, Mesa-Valle C. Analysis of Global Research on Malaria and Plasmodium vivax. Int J Environ Res Public Health. 2019;16(11):1928. DOI: 10.3390/ijerph16111928. PMID: 31159165; PMCID: PMC6603864.
- 4. World Health Organization; 2019.World .2019malaria report Available:h/iris/int.who.apps//:httpsandle/1 0665/330011. License: CC BY-NC-SA 3.0 IGO. 185 p. ISBN. 9789241565721.
- Alegana VA, Okiro EA, Snow RW. Routine data for malaria morbidity estimation in Africa: challenges and prospects. BMC Med. 2020;18:121.
 Available:https://doi.org/10.1186/s12916-020-01593-y
- Lourenço C, Tatem AJ, Atkinson PM, Cohen JM, Pindolia D, Bhavnani D, et al. Strengthening surveillance systems for malaria elimination: a global landscaping of system performance, 2015-2017. Malar J. 2019;18(1):315. DOI: 10.1186/s12936-019-2960-2. PMID: 31533740; PMCID: PMC6751607.
- Ryan SJ, Lippi CA, Zermoglio F. Shifting transmission risk for malaria in Africa with climate change: a framework for planning and intervention. Malar J. 2019;19:170. Available: https://doi.org/10.1186/s12936-020-03224-6
- 8. Takem EN, D'Alessandro U. Malaria in Pregnancy. Mediterranean Journal of Hematology and Infectious Diseases. 2013;5(1):e2013010.

 DOI: 10.4084/MJHID.2013.010
- 9. Degarege A, Fennie K, Degarege D, Chennupati S, Madhivanan P. Improving

- socioeconomic status may reduce the burden of malaria in sub Saharan Africa: A systematic review and meta-analysis. PLOS ONE. 2019;14(1):e0211205. Available:https://doi.org/10.1371/journal.po ne.0211205
- Menendez C, Ordi J, Ismail MR, Ventura PJ, Aponte JJ, Kahigwa E, et al. The Impact of Placental Malaria on Gestational Age and Birth Weight, The Journal of Infectious Diseases. 2000;181(5):1740–5. Available:https://doi.org/10.1086/315449
- Steketee RW. Weighing in on malariaattributable low birthweight in Africa. The Lancet Global Health. 2014;2(8):e434e435
- García MD, Solana CF, Ugarriza AV, Moreno CB, Palazón EM, Botaya RM. Imported malaria cases: the connection with the European ex-colonies. Malar J. 2019;18:397 Available:https://doi.org/10.1186/s12936-019-3042-1
- Angelo, K.M., Libman, M., Caumes, E. Malaria after international travel: a GeoSentinel analysis, 2003–2016. Malar J. 2017;16:293.
 Available:https://doi.org/10.1186/s12936-017-1936-3
- Tatem AJ, Jia P, Ordanovich D, Falkner M, Huang Z, Howes R, Hay SI, Gething PW, Smith DL. The geography of imported malaria to non-endemic countries: A meta-analysis of nationally reported statistics. Lancet Infect Dis. 2017;17(1):98-107.
 - DOI: 10.1016/S1473-3099(16)30326-7. Epub 2016 Oct 21. PMID: 27777030; PMCID: PMC5392593.
- Cohee LM, Laufer MK. Malaria in Children. Pediatr Clin North Am. 2017;64(4):851-866.
 - DOI: 10.1016/j.pcl.2017.03.004. PMID: 28734514; PMCID: PMC5733786.
- Franke-Fayard B, Fonager J, Braks A, Khan SM, Janse CJ. Sequestration and Tissue Accumulation of Human Malaria Parasites: Can We Learn Anything from Rodent Models of Malaria?. PLOS Pathogens. 2010;6(9):e1001032. Available:https://doi.org/10.1371/journal.pp at.1001032
- Ssentongo P, Ba DM, Ssentongo AE, Ericson JE, Wang M, Liao D, Chinchilli VM. Associations of malaria, HIV, and coinfection, with anemia in pregnancy in sub-Saharan Africa: a population-based

- cross-sectional study. BMC Pregnancy Childbirth. 2020;20(1):379. DOI: 10.1186/s12884-020-03064-x. PMID: 32600355; PMCID: PMC7324981.
- Patriani, D., Arguni, E., Kenangalem, E. Early and late mortality after malaria in young children in Papua, Indonesia. BMC Infect Dis. 2019;19:922.
 Available:https://doi.org/10.1186/s12879-019-4497-y
- Behrens R, Carroll B, Hellgren U, Visser L, Siikamäki H, Vestergaard L, et al. The incidence of malaria in travellers to South-East Asia: Is local malaria transmission a useful risk indicator?. Malaria journal. 2010;9:266. DOI: 10.1186/1475-2875-9-266
- 20. Franco-Paredes C, Santos-Preciado JI. Problem pathogens: prevention of malaria in travellara Lancot Infrat Dia 2006: 6:
- in travellers. Lancet Infect Dis 2006; 6: 139–49
- Lalloo DG, Hill DR. Preventing malaria in travellers. BMJ. 2008 Jun 14;336(7657):1362-6. doi: 10.1136/bmj.a153. PMID: 18556317; PMCID: PMC2427103.
- Soma-Pillay P, Nelson-Piercy C, Tolppanen H, Mebazaa A. Physiological changes in pregnancy. Cardiovasc J Afr. 2016 Mar-Apr;27(2):89-94. doi: 10.5830/CVJA-2016-021. PMID: 27213856; PMCID: PMC4928162.
- 23. Accrombessi M, Fievet N, Yovo E, Cottrell G, Agbota G, Massougbodji A, et al. Prevalence and Associated Risk Factors of Malaria in the First Trimester of Pregnancy: A Preconceptional Cohort Study in Benin, The Journal of Infectious Diseases, 2018; 217(8):1309–17, https://doi.org/10.1093/infdis/jiy009
- 24. Adam I, Ismail MH, Nasr AM, Prins MH, Smits LJM. Low birth weight, preterm birth and short interpregnancy interval in Sudan, The Journal of Maternal-Fetal & Neonatal Medicine, 2009;22(11):1068-71. DOI: 10.3109/14767050903009222
- Dhiman S, Yadav K, Goswami D, Das N, Baruah I, Singh L. Epidemiology and Risk Analysis of Malaria among Pregnant Women. Iran J Public Health. 2012;41(1):1-8. Epub 2012 Jan 31. PMID: 23113116; PMCID: PMC3481657.
- 26. Osaro E, Abdullahi A, Tosan E, Charles AT. Risk factors associated with malaria infection among pregnant women of African Descent in Specialist Hospital

- Sokoto, Nigeria. Obstet Gynecol Int J. 2019;10(4):274–80. DOI: 10.15406/ogij.2019.10.00454
- Piñeros JG, Tobon-Castaño A, Alvarez G, Portilla C, Blair S. Maternal clinical findings in malaria in pregnancy in a region of northwestern Colombia. Am J Trop Med Hyg. 2013;89(3):520-6.
 DOI: 10.4269/ajtmh.12-0205. Epub 2013 Jul 29. PMID: 23897991; PMCID: PMC3771293.
- Saba N, Sultana A, Mahsud I. Outcome and complications of malaria in pregnancy. Gomal Journal of Medical Sciences, 2008;6(2):98-101
- 29. Briand V, Badaut C, Cot M. Placental malaria, maternal HIV infection and infant morbidity. Annals of Tropical Paediatrics International Child Health, 2009;29(2):71-83.

 DOI: 10.1179/146532809X440699
- 30. McLean AR, Ataide R, Simpson JA, Beeson JG, Fowkes FJ. Malaria and immunity during pregnancy and postpartum: a tale of two species. Parasitology. 2015;142(8):999-1015. DOI: 10.1017/S0031182015000074
- Mount AM, Mwapasa V, Elliott SR, et al. Impairment of humoral immunity to Plasmodium falciparum malaria in pregnancy by HIV infection. Lancet (London, England). 2004;363(9424):1860-1867. DOI: 10.1016/s0140-6736(04)16354-x.
- 32. Rochford, R, Kazura, J. Introduction: Immunity to malaria. Immunol Rev. 2020;293:5–7.
- Available:https://doi.org/10.1111/imr.12831 33. Doolan DL, Dobaño C, Baird JK. Acquired immunity to malaria. Clin Microbiol Rev. 2009;22(1):13-36, Table of Contents. DOI: 10.1128/CMR.00025-08. PMID: 19136431; PMCID: PMC2620631.
- 34. Rogerson SJ, Mwapasa V, Meshnick SR. Malaria in Pregnancy: Linking Immunity and Pathogenesis to Prevention. In: Breman JG, Alilio MS, White NJ, editors. Defining and Defeating the Intolerable Burden of Malaria III: Progress and Perspectives: Supplement of American Journal of Tropical Medicine and Hygiene. Northbrook (IL): American Society of Tropical Medicine and Hygiene; 2007;77(6).
 - Available:https://www.ncbi.nlm.nih.gov/books/NBK1710/

- 35. Kwenti TE. Malaria and HIV coinfection in sub-Saharan Africa: prevalence, impact, and treatment strategies. Res Rep Trop Med. 2018;9:123-136.
 Available:
 - https://doi.org/10.2147/RRTM.S154501
- Bediako Y, Adams R, Reid AJ. Repeated clinical malaria episodes are associated with modification of the immune system in children. BMC Med, 2019;17:60.
 Available: https://doi.org/10.1186/s12916-019-1292-y
- Lugaajju, A, Reddy, SB, Wahlgren M. Development of Plasmodium falciparum specific naïve, atypical, memory and plasma B cells during infancy and in adults in an endemic area. Malar J. 2017;16:37. Available:https://doi.org/10.1186/s12936-017-1697-z
- Anna-Karin PE, Carole H. Remembrance of Things Past: Long-Term B Cell Memory After Infection and Vaccination. Frontiers in Immunology, 2019;10:1787.
 DOI:10.3389/fimmu.2019.01787
- Ly A, Hansen DS. Development of B Cell Memory in Malaria. Front Immunol. 2019;10:559.
 DOI: 10.3389/fimmu.2019.00559. PMID: 31001244: PMCID: PMC6454213.
- 40. Bucşan AN, Williamson KC. Setting the stage: The initial immune response to blood-stage parasites. Virulence. 2020;11(1):88-103. DOI:10.1080/21505594.2019.1708053
- 41. Schlagenhauf P, Petersen E. Malaria chemoprophylaxis: strategies for risk groups. Clin Microbiol Rev. 2008;21(3):466-72.

DOI: 10.1128/CMR.00059-07.

PMID: 18625682; PMCID: PMC2493087.

- Heywood AE, Zwar N. Improving access and provision of pre-travel healthcare for travellers visiting friends and relatives: a review of the evidence, Journal of Travel Medicine, 2018;25(1):tay010.
 Available:https://doi.org/10.1093/jtm/tay01
- World health organization. A framework for malaria elimination. Geneva: World Health Organization; 2017. Licence: CC BY-NC-SA 3.0 IGO.
- 44. **MEASURE** Evaluation. Facilitating Surveillance, Monitoring, and Evaluation in Countries: Malaria-Endemic Α National Malaria Compendium for Programs. Chapel Hill. NC, USA:

- MEASURE Evaluation, University of North Carolina; 2020.
- 45. Wirth DF, Casamitjana N, Tanner M. Global action for training in malaria elimination. Malar J. 2018;17:51. Available:https://doi.org/10.1186/s12936-018-2199-3
- 46. The Global Fund. Strategy Development: Landscape Analysis Malaria. Preliminary version; 2020.
- Shiff C. Integrated approach to malaria control. Clin Microbiol Rev. 2002;15(2):278-93.
 DOI: 10.1128/cmr.15.2.278-293.2002. PMID: 11932233; PMCID: PMC118067.
- Tizifa TA, Kabaghe AN, McCann RS, van den Berg H, Van Vugt M, Phiri KS. Prevention Efforts for Malaria. Curr Trop Med Rep. 2018;5(1):41-50.
 DOI: 10.1007/s40475-018-0133-y. Epub 2018 Feb 8. PMID: 29629252; PMCID: PMC5879044.
- Inungu JN, Ankiba N, Minelli M, Mumford V, Bolekela D, Mukoso B, Onema W, Kouton E, Raji D. Use of Insecticide-Treated Mosquito Net among Pregnant Women and Guardians of Children under Five in the Democratic Republic of the Congo. Malar Res Treat. 2017;2017:5923696.
 DOI: 10.1155/2017/5923696. Epub 2017 Nov 6. PMID: 29234551; PMCID: PMC5694996.
- 50. Boubaker R, Fossati AH, Meige M, Mialet C, Buffat CN, Rochat J, et al. Malaria prevention strategies and recommendations, from chemoprophylaxis to stand-by emergency treatment: a 10-year prospective study in a Swiss Travel Clinic, Journal of Travel Medicine, 2017;24(5):tax043.

Available: https://doi.org/10.1093/jtm/tax043

- 51. Coldiron ME, Von Seidlein L, Grais RF. Seasonal malaria chemoprevention: successes and missed opportunities. Malar J, 2017;16:481.

 Available: https://doi.org/10.1186/s12936-017-2132-1
- 52. Garner P, Gülmezoglu AM. Drugs for preventing malaria in pregnant women. Cochrane Database of Systematic Reviews. 2006;4. Art. No.: CD000169. DOI: 10.1002/14651858.CD000169.pub2.
- 53. Mlugu EM, Minzi O, Asghar M, Färnert A, Kamuhabwa AAR, Aklillu E. Effectiveness of sulfadoxine-pyrimethamine for

- intermittent preventive treatment of malaria and adverse birth outcomes in pregnant women. Pathogens. 2020;9(3):207. DOI: 10.3390/pathogens9030207. PMID: 32168945; PMCID: PMC7157612.
- 54. Anto F, Agongo IH, Asoala V, Awini E, Oduro AR. Intermittent Preventive Malaria in Treatment of Pregnancy: of Assessment the Sulfadoxine-Pyrimethamine Three-Dose Policy on Birth Outcomes in Rural Northern Ghana, Journal of Tropical Medicine; 2019, Article ID 6712685, 10 pages, 2019. Available: https://doi.org/10.1155/2019/6712685
- 55. Hansen KS, Ndyomugyenyi R, Magnussen P, Clarke SE. Cost-effectiveness analysis of three health interventions to prevent malaria in pregnancy in an area of low transmission in Uganda. Int Health. 2012;4(1):38-46.
 - DOI: 10.1016/j.inhe.2011.10.001. PMID: 24030879; PMCID: PMC4197998.
- Peters PJ, Thigpen MC, Parise ME, Newman RD. Safety and toxicity of

- sulfadoxine/pyrimethamine: Implications for malaria prevention in pregnancy using intermittent preventive treatment. Drug Saf. 2007;30(6):481-501.
- DOI: 10.2165/00002018-200730060-00003. PMID: 17536875.
- Shah SN, Smith EE, Obonyo CO, Kain KC, Bloland PB, Slutsker L, et al. HIV Immunosuppression and Antimalarial Efficacy: Sulfadoxine-Pyrimethamine for the Treatment of Uncomplicated Malaria in HIV-Infected Adults in Siaya, Kenya, The Journal of Infectious Diseases, 2006; 194(11):1519–28
- Available: https://doi.org/10.1086/508892
 58. Zhao L, Pi L, Qin Y, Lu Y, Zeng W, Xiang Z, et al. Widespread resistance mutations to sulfadoxine-pyrimethamine in malaria parasites imported to China from Central and Western Africa. International Journal for Parasitology: Drugs and Drug Resistance. 2020;12:1-6.
 - Available:https://doi.org/10.1016/j.ijpddr.20 19.11.002

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