EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 5
Issue: 2
979-987
Year: 2018

THE SUCCESSES AND FAILURES OF MALARIA CHEMOPROPHYLAXIS IN PREGNANCY: A NARATIVE REVIEW

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Article Received on 21/12/2017 **Article Revised on 10/01/2018** **Article Accepted on 31/01/2018**

ABSTRACT
Malaria is an age-long parasitic disease which is preventable and treatable, but has defied all eradication efforts so far in developing countries. Though it is still endemic in some ecological zones of the world, it has drastically declined globally over the years and eliminated within the borders of United States of America and other countries. This decline is owing to the sustained global efforts at its prevention and control. Most prevention and control efforts are centered on pregnant women and children being the most susceptible population to malaria infection and clinical disease. The integrated application of insecticide treated nets (ITNs), indoor residual sprays (IRS), intermittent preventive treatment (IPT) and prompt case detection and management of clinical cases in the last two decades have gone a long way in helping communities cope with disease. Efforts at improving the performance of current prevention and control measures as well as new trends and innovations in malaria control paint a picture of a brighter future in the fight against the disease. What is needed is a sustained political will at funding current interventions, training of personnel and a robust research into new technologies in malaria prevention and treatment and malaria disease will be a thing of the past. This paper reviews and showcases the trends in malaria prevention and control in pregnancy.

KEYWORDS: Challenges, Malaria prevention, pregnancy, review.

I INTRODUCTION
Since its discovery, malaria remains an important cause of illness and death in children and adults in countries in which it is endemic. Pregnant women and children below 5 years old are the most vulnerable to the adverse consequences of malaria infection. Malaria infection during pregnancy poses substantial risk to the mother, her fetus and the neonate. First and second pregnancies have greater risk of malaria infection than subsequent pregnancies. Parasitaemia in pregnancy is greatest in the second trimesters when immunity is much reduced with gestational age which may span through to the early post-partum stage. Malaria endemicity leads pregnant women to acquire some level of immunity to it but is susceptible to sub-clinical infection which may lead to adverse effects to both mother and child. Pregnancy quadruples a woman's risk to malaria and other infections and doubles her risk of death.

The discovery of the role of mosquitoes in the transmission of malaria provided malariologists with a new strategy to combat this ancient disease thus the possibility of controlling the disease by reducing contact with infected mosquitoes had become evident. This was followed later, exploring methods to prevent mosquito bites by avoidance, screening and mosquito proofing dwellings and anti-mosquito measures such as by the use of oils and larvivorous fish and draining mosquito habitats had become common place.[1]

II THE ADVENT OF MALARIA PREVENTION AND CONTROL
Modern day malaria control efforts started during the United State occupation of Cuba and the construction of the Panama Canal at the turn of the 20th century when the United States Public Health Service (USPHS) established the malaria control activities around military bases in the malarious regions of the Southern United States to allow soldiers to train all year round.

This effort received a great boost when in 1933 the U.S. President Franklin D. Roosevelt signed a bill that created the Tennessee Valley Authority[2] which provided agricultural and industrial development of the valley and later integrated Malaria Control with Economic Development. The law gave the federal government a centralized body to control the Tennessee River's potential for hydroelectric power and improve the land and waterways for development of the region.[3] An organized and effective malaria control program

stemmed from this new authority in the Tennessee River valley.

In the early 1950s, Pyrimethamine (Daraprim®) was discovered as a useful agent for malaria chemoprophylaxis. Administered in a dose of 25mg weekly was highly effective preventing and affording complete protection against an overt malaria attack in subjects exposed to repeated infection with Plasmodium falciparum.[4] It was reported to affect both the asexual erythrocytic and the pre-erythrocytic forms of the parasite and thus, a true causal prophylactic of falciparum malaria. Further studies observed that 25mg Daraprim weekly demonstrated effective suppressive action against malaria.[5] Afterwards, Daraprim (nick-named Sunday-to-Sunday medicine for pregnant women) became a licensed, effective and economical agent for the chemoprophylaxis of malaria especially for pregnant women and children.

With the discovery of chloroquine and its subsequent adoption, chemoprophylaxis of malaria in pregnancy with chloroquine then took the center stage. Administered in a dose of 300mg per week in pregnancy was very safe and effective in preventing malaria in pregnancy. During this period, Several trials of chloroquine chemoprophylaxis (with or without the addition of proguanil) demonstrated protective effects against the adverse consequences of malaria during pregnancy.[6-9]

Since then, chloroquine (CQ) has been the only drug recommended by the National Malaria Control Programme of many countries in line with the World Health Organization (WHO) recommendations for use in chemoprophylaxis against malaria in pregnant women. However, the increasing resistance of P. falciparum to chloroquine coupled with poor compliance of pregnant women to observe the weekly regimen reduced the efficacy of CQ to protect against malaria.[10,11] With the evidence of the efficacy of IPT in pregnant women using sulphadoxine-pyrimethamine (SP), new guidelines were issued in February 2005 for a policy change regarding the chemoprophylaxis of malaria during pregnancy.

III ADVANCES IN THE PREVENTION AND CONTROL OF MALARIA IN PREGNANCY

Despite the toll that malaria exacts on pregnant women and their babies, yet for various reasons malaria control during pregnancy has not received broad programme support in the past. First, the fact that malaria infection in women is largely asymptomatic in areas of greatest burden mandates a preventive approach, which has usually been given low priority. Second, the lack of effective linkages between malaria control and antenatal care programmes has also limited the success of efforts to control malaria during pregnancy. The promising news is that during the past decade more effective control approaches have been identified to address these limitations.

Among these approaches is ensuring effective case management of malaria illness though not without challenges because (1) malaria infection in pregnancy is often asymptomatic, (2) peripheral parasitaemia may be absent even when the placenta is heavily parasitized, (3) implementing diagnosis and treatment of malaria within a routine antenatal service may be difficult and (4) antimalarial treatment options available to pregnant women are limited due to resistance to Chloroquine (CQ) and Sulfadoxine-Pyrimethamine(SP) and paucity of safety and efficacy data on other antimalarial drugs in pregnancy, particularly artemisinin-based combination treatments (ACTs). The most viable option is therefore to prevent vector contact and chemoprophylaxis such as using ITN and intermittent preventive therapy (IPT) respectively.

There is a wide range of malaria control interventions in pregnancy whose efficacy and effectiveness have been reportedly demonstrated over many years. These include insecticide treated nets[12], indoor residual spray[13], IPTp[14] and interventions that have recently received increasing attention such as improved diagnosis using rapid diagnostic tests (RDTs)[15] and treating infected cases with ACTs as first line therapy.[16]

Use of insecticide-treated nets (ITNs): Sleeping under an ITN is probably the most effective method for preventing mosquito bites because mosquitoes bite most often at night when the pregnant woman is asleep. ITNs prevent mosquito bites by repelling them or killing them if they land on the net. A controlled trial in Gambia has demonstrated that provision and use of ITNs to multi-gravids may provide adequate protection against malaria in pregnancy without the need for IPT.[17]

Indoor residual spray (IRS): This involves spraying the walls of living rooms with insecticides that kill or repel the mosquitoes and keep them away from contact with man and thereby prevent malaria. Indoor residual spraying (IRS) is effective in areas where the predominant mosquito species bite and rest indoors. This is in the majority of Africa and a number of other areas in Asia, although in areas of Asia and Latin America most transmission is outdoors.

Case management of malaria illness: Prompt and effective treatment of clinical cases of malaria in pregnancy is an essential component of malaria control because **d**espite preventive measures, some pregnant women will still become infected with malaria. These women should adequately be treated to prevent complications as well as prevent transmission to others.

Use of Intermittent Preventive Treatment (IPT): Intermittent preventive treatment of malaria during pregnancy (IPTp) is based on the assumption that every pregnant woman living in areas of high malaria transmission has malaria parasites in her blood or placenta, whether or not she has symptoms of malaria.

Therefore every pregnant woman needs a prophylactic dose of an antimalarial during her period of pregnancy to prevent or treat asymptomatic malaria. Intermittent Preventive Therapy (IPT) with Sulphadoxine-Pyrimethamine has been used for several years in parts of Africa, and has shown to be effective. This is an evidence-based approach and is recommended for all pregnant women in malaria endemic regions.

Presently, Sulfadoxine-Pyrimethamine (SP) is the only antimalarial medicine for which data on efficacy and safety for IPT is available from controlled clinical trials, and WHO recommends that at least 2 doses of SP are given after quickening during the second and third trimesters, at least one month apart. The IPT policy has been studied extensively and reviewed to improve delivery and efficacy.

Reports of the efficacy and or superiority of the dosing schedule of SP-IPT has been conflicting. Some studies report superiority of more than 2 doses over the 2-dose schedule while others do not. As a result, some malaria endemic countries in Sub-Saharan Africa such as Nigeria, Ghana and Zambia now use 3 doses while Malawi and Kenya have revised their strategies from 2-dose regimen to recommending SP at each monthly ANC visit beginning from 16weeks gestation.[18] Data from meta-analysis showed that adding a 3rd and 4th doses improves birth weight in human-immunodeficiency virus (HIV)-negative women.[19] Similarly, a recent study in Mali comparing the efficacy and safety of a 3-dose verse a 2-dose SP-IPT regimen has demonstrated the superiority of the 3-dose regimen in reducing the incidence of placental parasitaemia, low birth weight or pre-termed birth, showing that the 2-dose regimen may not have been the optimal dose.[20]

Another study has demonstrated the need for review of the 2-dose SP in a study that found as high as 41% of the pregnant women who took the 2-dose SP had malaria parasitaemia with 53.4% of the parasitamic women found to be late in the third trimester from 31 weeks.[21] This finding is supported by the finding of Maiga[20] in Kenya that the 2-dose regimen may not have been the optimal dose for SP-IPTp. However, the use of SP-IPT by the pregnant women was reported to partly account for the low prevalence of anaemia and hospitalization for clinical malaria during pregnancy and the overall outcome can be considered a reflection of the quality of care of IPT in the facility.

A postulated disadvantage of the 2-dose regimen is that women get their second SP dose early, leaving them unprotected for about 6 – 8 weeks in the later part of their pregnancy with risk of malaria infection at an important period for fetal growth.

Parasitologic Assessment of 2-dose SP-IPTand monthly SP-IPT for prevention of malaria in pregnancy (MiP) has shown that none of the women developed clinical malaria during the period of follow-up and none tested positive for *P.falciparum* on assessment of placental parasitaemia, suggesting that the monthly dosing was not significantly superior to the 2-dose regimen.[22]

The major constraints to implementation of the SP-IPT strategy have been reported to hover around access barrier and perception and practice of malaria prophylaxis in pregnancy among health workers.

A study reported that access barrier still exist to higher degrees for those in the rural areas despite a decade of implementation of the policy and that overall low coverage occurred despite high antenatal clinic (ANC) attendance implying that high ANC attendance does not guarantee high IPT coverage.[23]

The implementation of SP-IPT is generally weak in the African sub-region. A questionnaire based survey has assessed the views of healthcare providers with respect to malaria prophylaxis in pregnancy and found providers to have good knowledge of all the WHO strategies for malaria prevention in pregnancy including SP-IPT[24] but the absence of clean water and cups in some health facilities limits the ability of health workers to ensure compliance with the Directly Observed Treatment (DOT) strategy. Lack of knowledge of or poor observance of the DOT strategy in the administration of SP-IPTp by caregivers at the ANCs reduces the effectiveness of the programme.[23]

The MPAC meeting of 16-18th September 2015[25], reviewed the existing SP-IPTp policy and the ongoing search for alternative options put forward by researchers stated that there is currently no evidence of a threshold level of malaria transmission below which SP-IPTp is no longer cost-effective to be discontinued and so recommended the continued use of SP-IPTp. However, the SP-IPTp policy was reviewed to be administered monthly from quickening till delivery.

IV SEARCH FOR ALTERNATIVE TO SULPHADOXINE/PYRIMETHAMINE FOR INTERMITTENT PREVENTIVE TREATMENT

The following efforts have been made in search for effective replacement for SP for IPTp with little success because none has actually overcome the strengths inherent in SP. Some of these attempts include:

- **Mefloquine (MQ) monotherapy**: When used for IPT, Mefloquine may have more side effects than SP. The tolerability of MQ for IPTp in HIV negative pregnant women has been reported to be poorer than SP[26] (Raquel *et al*., 2014a). This finding is in agreement with an IPT trial in which MQ presented poorer tolerability than SP with higher frequencies of adverse events.[27]
  The information to date regarding MQ for IPT is limited to 2 trials carried out in Benin which provided encouraging results[27,28]

Mefloquine has been reported to increase viral load of HIV positive pregnant women at delivery and increase frequencies of mother-to-child transmission of HIV which further raises concern about the use of MQ in this context[29]

The use of MQ to prevent malaria in pregnancy should therefore be based on risk-benefit analyses that balances the likelihood of adverse effects against the risk of acquiring the infection.

- **Chloroquine-Azithromycin (AZ-CQ)**: A fixed-dose combination of AZ-CQ is currently under investigation as potential replacement for SP for IPTp.[30] The combination has demonstrated additive to synergistic activity against Plasmodium falciparum in vitro.[31,32] However, there are concerns that the use of AZ-CQ in IPT could encourage the emergence and spread of resistance to a variety of organism.[33] Acceptance and adherence to a 3-day regimen of AZ-CQ could be another barrier to its use for IPT.
- **Pyronaridine**: Pyronaridine represents an ideal candidate for combination therapy with artemisinin derivatives such as Artesunate. This is because of its high efficacy against Chloroquine and Amodiaquine resistant strains of malaria and the reassurance of many years of successful use in China as monotherapy without the development of widespread resistance. It is being investigated as a fixed-dose combination in a 3:1 ratio.[34] The drawback of its use for IPT is the fact that treatment requires a 3-day course not ideal for IPT which requires DOT administration to guarantee adherence and compliance.
- **Dihydroartemisinin/Piperaquine (DHA/PPQ)**: In a study that compared dihydroartemisinin/piperaquine-intermittent screening and treatment (IST) [DHA/PPQ-IST] with SP-IPT and DHA/PPQ- IPT, the result showed that malaria infection during pregnancy was higher in the IST-DHA/PPQ than SP-IPT and DHA/PPQ-IPT but DHA//PPQ-IPT was significantly associated with lower incidences of malaria during pregnancy than SP-IPT.[35] DHA/PPQ is therefore a promising alternative to SP for IPTp. However, further studies on the efficacy, safety, operational feasibility and cost-effectiveness analysis are needed to support this claim.

V SEARCH FOR ALTERNATIVE TO INTERMITTENT PREVENTIVE TREATMENT FOR PREVENTION AND CONTROL OF MALARIA IN PREGNANCY

Several alternative strategies to contend malaria in pregnancy have been explored. One of such is intermittent screening and treatment (IST) of malaria in pregnancy. This has been compared with IPT in a randomized controlled non-inferiority trial.[36] This study compared the pregnancy outcomes of IST and IPT using SP-IST, and artesunate/amodiaquine (AsAq)-IST compared with SP-IPT. The result showed that baseline anaemia was associated with asymptomatic malaria by microscopy and no difference between the prevalence of peripheral blood parasitaemia between the treatment groups at weeks 36 – 40 or at six weeks post-partum. Authors concluded that though SP-IST or AsAq-IST is not as effective as SP-IPT in preventing infection of the placenta, IST is a potentially promising strategy for the control of MiP especially in areas with decreasing or seasonal malaria incidence.

More so, it is estimated that African population increased by 43% between 2000-2013 while malaria infection declined by 26% and malaria mortality declined by 54% during the same period.[37] This is achieved through advocacy, prompt case detection and management and scale-up use of LLIN along with emerging interventions in vulnerable populations such as pregnant women and children. The effectiveness of IPTp is greatly reduced in countries or regions or communities where malaria has been reduced to low and unstable transmission. It will therefore become more cost effective to screen pregnant women and to treat only those who are positive for malaria in addition to encouraging the use of ITNs.

The humanistic outcome of the IST intervention has been reported to be indeed a promising alternative to the IPT intervention.[38,39] The first reported humanistic study was conducted in Ghana to assess the acceptability of SP-IPT compared with IST of MiP among users. Data were collected through a series of FGDs and the result showed that even though the tests associated with the IST procedures were painful, the women said they were prepared to accept them for the sake of their health. Authors concluded that overall, both IST and IPT seem to be equally acceptable to pregnant women as strategies for control of MiP in this setting.[38] Furthermore, structured interviews conducted with 134 health workers spread across 67 ANCs to assess their knowledge and opinions on IPT and IST. The knowledge of the national policy for IPTp was very high among the respondents and many midwives expressed support for RDTs and thus ISTp as this reduce the reliance on microscopy which can only be performed by trained personnel and with the supply of electricity though more respondents tended to favor SP-IPTp over ISTp stating the old adage that prevention is better than cure'. This study concluded that if ISTp was considered by policy makers to be a viable alternative to SP-IPTp for implementation as part of routine ANC activities, considerable attention would need to be paid to improving the knowledge and practice of ANC staff in relation to appropriate treatment of confirmed MiP.[39]

The World Health Organization (WHO) recommends artemisinin-based combinations (ACTs) as first line treatment of *P. falciparum* in the second and third trimester of pregnancy.[40] Artemether-Lumefantrine is currently the most widely used ACT for acute uncomplicated *P. falciparum* malaria and reported to be

very safe in a study that ompared the safety of artemether/lumefantrine (AL) with SP.[41]

This finding substantiates the safety of AL in particular and artermisinins in general in the later stages of pregnancy in African women in line with previous findings that AL exposure during this period is well tolerated and has no adverse outcomes for the mother or her exposed fetus.[42,43]

A systematic review of the safety and efficacy of AL against uncomplicated *Plasmodium falciparum* malaria during pregnancy[44] revealed that children up to 1 year of life did not show any serious maternal adverse events, adverse birth outcomes or neurological development deficit in the infants.[45]

Several studies have demonstrated the safety of AL in the second and third trimester of pregnancy.[46-50] In all these, no significant adverse events were recorded on pregnancy and fetal outcomes, deliveries and early childhood development and all the pregnant women tolerated the doses of AL.

Authors in this review concluded that the use of AL for the treatment of uncomplicated *P. falciparum* malaria in pregnancy is supported by a large body of evidence and that the available safety data support the use of AL in second and third trimesters. AL may be preferable to quinine in the second and third trimesters as AL efficacy is non-inferior to quinine but AL is associated with fewer adverse events as supported by study findings.[49]

Tagbor et al 2015[51] in their report on a study of AL-ISTp in some West African countries submitted that the level of malaria transmission below which SP is no longer useful is not known, and consequently there is reluctance to stop SP-IPTp in low transmission settings without an alternative. In such situation both within and outside Sub-Saharan Africa, AL-ISTp could be an effective alternative until malaria is no longer a significant threat. AL-IST therefore presents a potential future option for the control of malaria in pregnancy in West Africa if SP resistance continues to increase in this region as seem likely.

However, though highly acceptable among users and providers alike, AL-ISTp is likely to be associated with higher cost. It is hoped that the performance of urine malaria test (UMT) kits for diagnosis of malaria[52] to replace RDT kits will reduce the cost of an IST intervention programme.

The MPAC meeting of 16-18th September 2015[25] reviewed carefully documented safety data on women exposed to only ACTs (AL) compared to those exposed to only quinine in the first trimester of pregnancy showed that ACT exposure was associated with a significantly reduced rate of miscarriage compared to quinine. The committee therefore recommended that if available, AL should be considered as the preferred ACT treatment option in the first trimester. The safety of ACTs in first trimester of pregnancy is supported by a body of evidence.[25]

The ultimate hope at prevention of malaria remains an effective vaccine. An effective vaccine for malaria has been sought for more than three decades, with significant resources devoted to this research. Over that time, substantial progress has been made in understanding the basic biology and immunology of malaria which might underlie an effective malaria vaccine. However, to date only one vaccine has made it through to the late stages of clinical development i.e. the RTS,S/AS01.[53] Newly published results from a phase 3 trial showed promise for the vaccine

The recombinant subunit vaccine consists of the hepatitis B surface antigen linked to epitopes derived from the circumsporozoite surface protein of the *P. falciparum* sporozoite. Targeting the sporozoite phase of the parasite lifecycle is beneficial since it attacks the parasite as it enters the host following the Anopheles bite.[54] In order to eradicate the parasite, the host must mount a robust immune response. In initial studies, the vaccine was shown to stimulate a strong antibody and Th1 cell-mediated response.[55] The difficulty in developing a malaria vaccine in part reflects the complexity of malaria and the immune response to it.

A Systematic Review of studied interventions such as ITNs, IRS, IPTp, vaccines, malaria diagnostics, treatment of uncomplicated malaria, treatment of severe malaria in health centres or hospitals, larviciding, larvivorous fish, malaria early warning systems, environmental management, drug treatment, rapid diagnostics, and combined prevention and treatment programmes, reported study outcomes such as median financial cost per ITN distributed to be $7.03 (range $2.97-$19.20), $3.91 (range $1.11-$12.87) per household for IRS, and $2.06 (range $0.47- $3.36) for IPT in pregnant women. The median financial cost of diagnosing a case of malaria was $4.32 (range $0.34-$9.34). The median financial cost of treating an episode of uncomplicated malaria was $5.84 (range $2.36-$23.65) and the median financial cost of treating an episode of severe malaria was $30.26 (range $15.64-$137.87).[56]

The wide ranges in the estimates of unit costs represent different durations of protection, and are a consequence of the wide variation in the type of costing study reviewed. One of the key drawbacks of costing studies is that they are often not undertaken alongside an evaluation of the clinical and epidemiological effect of the intervention under investigation.

All studies comparing the cost of *P. falciparum* diagnosis by RDT and microscopy found RDTs to be more cost effective. Economics of scale may result in cost-savings

when an intervention is widely implemented and all studies identified, found effective treatment of episodes of uncomplicated or severe malaria with ACT to be highly cost-effective when compared with other antimalarials. This is an added advantage to the IST strategy currently under investigation. A transparent evidence base on the costs and cost-effectiveness of malaria control interventions is therefore important to inform resource allocation by international and domestic financers of health programmes.

VI CHALLENGES OF PREVENTION AND CONTROL OF MALARIA IN PREGNANCY

Drug Faking/counterfeiting: Drug treatment is still recognized as one of the key control strategies to winning the war against the malaria scourge but the high level of counterfeit and fake antimalarials in circulation is a big hindrance to realizing this goal. Fake, counterfeit, adulterated, substandard and unwholesome product by any name or definition is just as inferior in quality and efficacy. This problem is the cause of resistance and suboptimal doses of SP and other antimalarials.

Frequent/prolong stock out of antimalarials: Malaria case management in Africa is weak, suffering from a general absence of diagnostics, a weak supply chain system, and poor delivery of services at the health facility levels. The 2010 MIS revealed that only 3.2% of children under-five with a fever received an Artemisinin-based combination therapy (ACT) the same or next day, slightly higher than 1.1% earlier reported in 2008. The public sector procurement and distribution of essential medicines is extremely fragmented and chaotic leading to stock outs of commodities including the first-line ACT - Artemether-Lumafantrine.

Lack of or poor use of ITNs: Poor implementation of control strategies such as poor distribution and high cost of commercially available ITNs coupled with poor attitude to the use of ITNs by pregnant women remains a great challenge to prevention of MiP. Many households with ITNs do not sleep under it in hot weathers.

Problem of vector control: Vector eradication is also a problem due to the tropical environments where the Anopheles mosquito thrives. Locations like Sub-Saharan Africa are stable zones for transmission due to climate and other less well understood ecological factors that confer a longer lifespan on the mosquito, allowing for increased cycles of reproduction and expansion of both the mosquito and the parasite. In these locations, it is estimated that human exposure may be as high as 1000 mosquito bites per year.[57,58] Further complicating the picture is the limited access to both diagnosis and treatment as a result of cost and civil unrest in some of these locations.[59] Frequent unrest, wars leading to displacements and migrations affect malaria control programmes

Uncertainty of the potential Vaccine in process: The protective efficacy of the vaccine is impressive, but an important question remains to be answered. How long does the protective immunity last? Unlike the smallpox or hepatitis B vaccines which provide natural immunity, it is unclear if long-term immunity can be conferred by RTS,S/AS01 or if repeated boosters are necessary due to waning immunity. Another potential pitfall is the cost. Cost-effectiveness is key, since the highest burden of the infection resides in the poorest nations, with over 90% of worldwide malaria deaths occurring in Africa[40] (WHO 2010).

VII CONCLUSIONS

Great strides have been achieved over the years in curtailing the menace of malaria generally and malaria in pregnancy in particular. It is estimated that malaria infection declined by 26% and its mortality by 54% globally between 2000 and 2013 owing to global efforts at combating the disease but this effort has not reached the elimination or eradication phase. There is a serious threat of resistance to SP (the recommended drug for IPT) and so many pregnancies are still threatened by malaria especially in Sub-Saharan Africa. An effective vector control combined with chemoprophylaxis remains the mainstay of malaria prevention and control in pregnancy.

The outcomes of studies such as using DHA/PPQ for IPT and best still, AL-IST are promising future alternatives strategies for malaria control in pregnancy. Efforts should be stepped up to expand these studies along with concerted efforts to complete the malaria vaccine project to make future elimination and eradication of malaria possible.

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