

# MALARIA PREVENTION IN PREGNANCY: EFFECTIVENESS AND FUTURE STRATEGIES

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## Abstract

*Malaria remains a significant global health challenge, particularly for pregnant women in malaria-endemic regions. Malaria in pregnancy poses substantial risks to both the mother and the developing fetus, leading to adverse maternal and neonatal outcomes. Despite considerable progress in prevention and control efforts, there is a need for innovative and sustainable strategies to further reduce the burden of malaria in pregnancy. This review explores future preventive strategies for addressing this issue, focusing on advances in malaria prevention, antimalarial drugs, vaccines, vector control, and health system strengthening. By examining recent research and ongoing initiatives, on malaria prevention in pregnancy, we provide key findings on the effectiveness of the current interventions and challenges and provide insights into promising interventions that can be integrated into comprehensive malaria control programs to safeguard the health of pregnant women and their unborn children.*

**Keywords:** *Malaria Prevention, Pregnancy, Effectiveness, Future Strategies*

## Introduction

Malaria is a life-threatening human disease caused by *Plasmodium* parasites transmitted through a bite of infected female Anopheles mosquitoes (WHO 2014). Malaria burden disproportionately occurs among pregnant women alongside less than five-year-olds. Currently, malaria in pregnancy (MiP) is still of great public health concern, especially in areas where the disease is endemic (Uneke 2008). The burden of MiP is particularly significant in sub-Saharan Africa, where the majority of global malaria cases occur, and where the disease is a leading cause of maternal and infant mortality (Desai et al 2007).

The immune system undergoes changes during pregnancy that dampen immune responses so as to accommodate the developing foetus. These changes increase susceptibility of pregnant women to infections, including malaria. MiP poses risks to both the mother and the developing baby. One of the main complications of MiP is maternal anaemia which can lead to severe weakness, fatigue, and even death. Malaria may also lead to poor pregnancy outcomes that manifest as low birth weight and preterm delivery; a leading cause of infant mortality especially in sub-Saharan Africa (Desai et al. 2018). The presence of malaria parasites in the placenta can impair the exchange of nutrients and oxygen between the mother and the foetus, further compromising the health of the pregnant women and the foetus (Wu et al, 2012). Thus, babies born to mothers with malaria are at higher risk of long-term developmental challenges such as cognitive impairments (Fried et al. 2017). This may also increase risk of preterm birth or even stillbirth (Desai et al, 2018).

Owing to the apparent impact malaria exerts on pregnant women, the unborn child and less than five-year olds, multifaceted strategies are currently being implemented to prevent infection as well as avert and/or reduce mortality and morbidity. These interventions include the use of insecticide-treated bed nets, intermittent preventive treatment during pregnancy, and prompt diagnosis and treatment of malaria infections (Desai et al 2018 and Rogerson 2017). These interventions are further reinforced by conducting early malaria diagnosis and educating pregnant women on malaria preventive measures during antenatal care.

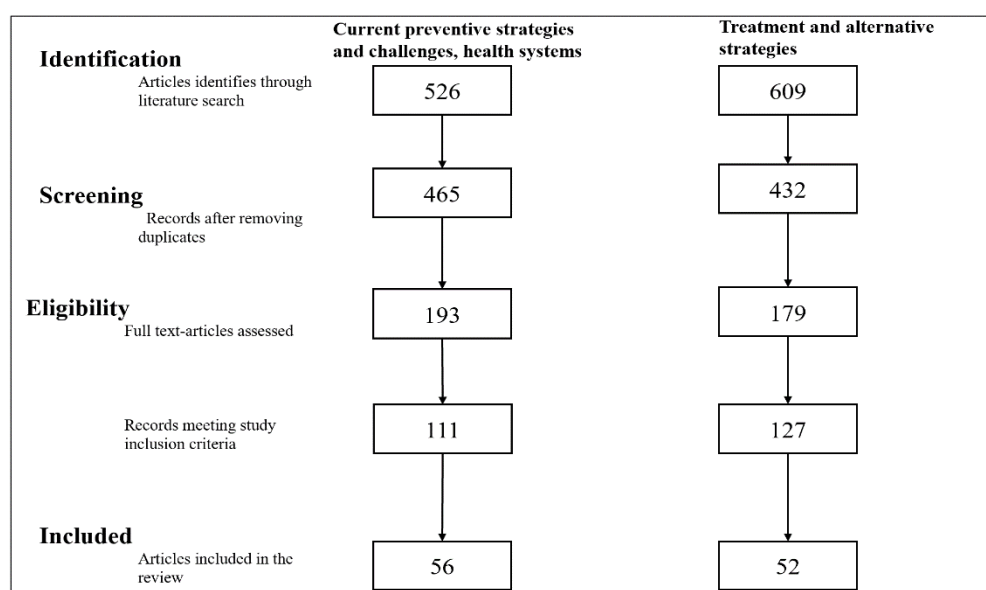
Efforts to combat MiP are made through national and international initiatives, such as the national malaria control programs, Roll Back Malaria Partnership and the World Health Organization's Global Malaria Program (Fried et al.2017). These initiatives aim to increase access to malaria preventive measures and effective treatment, as well as to improve overall quality of antenatal care. While tremendous progress has been made in reducing the burden of MiP over the years, there is still much work to be done to safeguard the well-being of pregnant women and their babies. Continued research, funding, and implementation of effective strategies are essential for the fight against MiP and safeguard good pregnancy outcomes for affected populations. This review aims to provide an update on the effective treatment and preventive strategies for MiP.

## Methods

A systematic literature search was conducted to identify relevant studies on MiP treatment and preventive strategies. The search included electronic databases and academic journals, focusing on studies published between January 1, 2013 and January 1, 2023 in sub-Saharan Africa. Key terms used to retrieve published articles included "malaria", "malaria AND pregnancy", "malaria AND MiP prevention", "malaria AND MiP prevention" and "MiP AND treatment." Studies were included if they assessed the impact of at least one MiP preventive or treatment strategy such as intermittent preventive treatment (IPT), insecticide-treated bed nets (ITNs), and vector control strategies. The review excluded all studies that did not involve MiP.

## Results

A total of 1,135 articles published between 2013 and 2023 were identified. Of these, 526 and 609 were publications on MiP preventive and treatment strategies, respectively (Figure 1). Fifty-six (56) studies on MiP prevention and 52 studies on MiP treatment were reviewed after removal of duplicated articles and after removal of articles that failed to meet the inclusion criteria.



**Fig 2: Selection Chart**

## Discussion

Over the past ten years, significant progress has been made towards bridging prevailing research gaps in MiP prevention and management. This study seeks to review MiP prevention and management strategies for a ten-year period based on studies published between 2013 and 2023.

Intermittent Preventive Treatment in Pregnancy (IPTp) is a key strategy recommended by the World Health Organization (WHO) for the prevention of MiP among pregnant women living in areas in moderate to high malaria transmission. IPTp involves administration of an antimalarial drug during pregnancy, typically sulfadoxine-pyrimethamine (SP) at specified intervals (Shulman et al, 2003). This approach helps to

prevent malaria infection during pregnancy, reduce maternal anaemia, and improve pregnancy outcomes. Current WHO guidelines recommend that at least three IPTp doses should be administered from the second trimester of pregnancy with a minimum of one month between doses (Al Khaja et al 2021).

IPTp is mostly administered during routine antenatal care visits (Shulman 2003). Its popularity has grown over the years because it is cost-effective and substantially reduces the risk of malaria-related complications. These benefits are best realized where malaria parasites are sensitive to SP. However, when SP resistant malaria is prevalent, alternative antimalarial drugs may be used (Rogerson 2017) and (WHO 2004). Since IPTp is a valuable tool for MiP control, emergence of resistance to antimalarial drugs for IPTp would reverse gains attained so far (WHO 2014). This implies therefore that antimalarial drugs for IPTp ought to be used with caution to avert an increase and spread of antimalarial drug resistance. One strategy to delay increase of SP resistance is active surveillance of antimalarial drug resistance patterns and adopting IPTp accordingly. To date, efficacy of alternative antimalarial drug combinations of IPTp have been assessed. The efficacy of an IPTp comprising amodiaquine and SP was shown not to be superior to SP-based IPTp (Mlugu et al 2021). Nevertheless, mefloquine has been reported to be a promising alternative for SP IPTp because it has long elimination half-life that provides an extended period of post-treatment prophylaxis and prevents low birthweight (LBW) (D'Alessandro, 2007). In addition, mefloquine prevents placental malaria, clinical malaria, and maternal anaemia at delivery. Poor mefloquine tolerability, however, poses a major challenge for widespread use in IPTp (Figueroa-Romero et al 2022).

Besides mefloquine, other antimalarial drugs have been explored for IPTp or intermittent screening and treatment (IST). This includes co-trimoxazole and antimalarial drug artemisinin-based combination therapy. IPTp with a combination of co-trimoxazole and mefloquine in IPTp has been shown to be more efficacious than co-trimoxazole among HIV-positive women, than IPTp treatment with co-trimoxazole alone (Green et al 2016). However, use of this IPTp combination is limited by mefloquine's poor tolerability and propensity to increase maternal HIV viral load as well as mother-to-child HIV transmission (Suthar et al, 2015). Other studies have shown co-trimoxazole and SP efficacy to prevent LBW among HIV-positives is similar (Rogerson 2017 and Saito et al 2020). A three-day regimen of artemisinin-based combination therapy is currently being considered as alternative drugs to replace the single-dose regimen for SP-based IPTp or SP-based IST (Figueroa-Romero et al. 2022).

A clinical trial assessing acceptability of IPTp and IST treatment with dihydroartemisinin-piperaquine in Kenya highlighted concerns among pregnant women and health care providers on treatment compliance in field settings despite being acceptable in a clinical trial setting. Adherence to multi day regimens was perceived to be more common in the case of ISTp, as women could see positive results from the blood tests. Pregnant women generally found ISTp acceptable despite the discomfort of finger pricks. Conversely, health providers in Kenya, Ghana, and Malawi have been reported to favor IPTp over IST whereas some participants prefer hybrid strategy of IPTp and ISTp (Rogerson 2017). IST is amenable to field settings especially is the availability of cost effective and easy to use

diagnostic methods. Thus, even though rapid diagnostics tests are suitable for low malaria transmission settings, more sensitive diagnostics are necessary in moderate to high malaria transmission settings due to high risk of reinfection.

Case management and treatment of MiP are crucial to ensure well-being of both the pregnant woman and the developing foetus. Equally prompt and effective management of malaria cases in pregnant women can reduce complications and improve pregnancy outcomes (Green et al, 2016). Diagnosis of malaria in pregnancy follows similar principles as that of the general population which rely on detection of malaria parasites using microscopy or rapid diagnostic tests (RDTs). It is important to note that pregnant women may have lower parasite densities, thus limiting detection of malaria parasites (Suthar 2015, Hill 2016). It is therefore recommended that healthcare providers should test for malaria, especially when mild malaria symptoms are observed and prompt malaria treatment should be given to malaria positive cases because of the likelihood of significant risks to both the mother and the foetus (Fried et al 2012). The choice of antimalarial treatment for MiP depends on several factors, namely severity of the infection, local drug resistance patterns, and safety profile of the drug in pregnancy (Saito et al, 2020). Artemisinin-based combination therapies (ACTs) are currently recommended as the first-line treatment for uncomplicated malaria in pregnant women (Briggs et al, 2019).

In severe malaria cases, hospitalization and parenteral therapy with intravenous artesunate are usually required. Supportive care should be provided to manage symptoms and complications in addition to antimalarial treatment. This may include interventions to address anaemia, such as iron supplementation or blood transfusions when necessary (D'Alessandro et al, 2018). Regular follow-up visits are essential to monitor treatment response, detect potential complications, and provide additional care as needed. This reinforces the importance of integrating malaria case management into antenatal care services. Healthcare providers involved in case management of MiP should thus, be trained regularly especially when treatment guidelines and protocols specific to pregnant women have been amended. Additionally, efforts to enhance availability and accessibility of quality-assured antimalarial drugs and diagnostic tools are essential to ensure effective case management (D'Alessandro et al. 2018).

Malaria transmission prevention and/or control are key pillars of the war on MiP. They complement the contribution of IPTp on MiP prevention as well as safeguard the positive outcome of ISTp and MiP case management. Use of insecticide-treated bed nets (ITNs) provide a physical barrier and prevent mosquitoes from biting during sleep, thereby reducing the risk of malaria transmission akin to ITNs, Vector control, such as indoor residual spraying, helps in reducing contact between pregnant women and malaria infective (Beir JC, 2018) ITNs namely bed nets that have been treated with insecticides are a critical intervention for protecting pregnant women from malaria infections. Pyrethroids are often used to treat bed nets and protect by either repelling and/or killing mosquitoes that come into contact with the nets. Pregnant women are particularly vulnerable to malaria infection because of a dampened immune system. By sleeping under ITNs, pregnant women have reduced exposure to malaria-infected mosquitoes and are at a lower risk of malaria infection.

Previous studies have demonstrated that consistent ITN use during pregnancy can be highly effective in preventing MiP and its potential consequences like maternal anaemia and negative pregnancy outcomes such as low birth weight and neonatal mortality (Mlugu et al, 2021, Figueroa-Romero, 2022). An additional benefit associated with use of ITNs is reduced placental parasitemia in pregnant women (McClure et al 2013). Noteworthy, high coverage and easy access to ITNs in malaria-endemic areas is necessary to effectively protect pregnant women from being infected with malaria parasites. ITNs coverage is currently being boosted by various strategies including the fact that pregnant women receive free INTs under mass INT distribution during campaigns, antenatal care programs, and community-based distribution programs (Bauserman et al, 2019). These efforts are further fortified by incorporating education of pregnant women about the importance of proper and consistent ITN use as well as regular treatment of the nets with effective insecticide.

The aforementioned have been instrumental in achieving key milestones attained so far in the prevention and/or control of MiP. In spite of the progress made over the last decades, studies have revealed that uptake of two doses of IPTp and ITNs among pregnant women in Africa remains unacceptably low (Walker et al 2017, Boene et al 2014). Some of the challenges faced by IPTp distribution programmes include unclear policies and guidance, lack of clarity on timing and regimen of IPTp, lack of data on gestational age, IPTp efficacy and poor knowledge on side effects (Desai et al 2007). These limitations have often led to incorrect administration in the first trimester. Compliance to treatment is uncommon. This is often compounded by frequent lack of IPTp and ITNs owing to heavy dependency of governments in malaria endemic regions on dwindling donor funding of malaria control programmes alongside increasing health care priorities (Desai et al 2018).

### **Outlook of MiP Control**

The outlook for controlling malaria in pregnancy is generally positive, as there have been significant improvements in recent years. However, challenges remain, such as drug resistance and availability of healthcare services in resource-constrained settings. Global and national efforts are essential to sustain and further improve control of malaria in pregnancy.

It's important to note that the specific outlook can vary greatly by region, depending on factors like prevalence of malaria, healthcare infrastructure, and access to resources. The World Health Organization (WHO) and various international organizations continue to work together with the local governments towards reducing the burden of malaria in pregnancy through coordinated efforts and strategies.

### **Conclusion**

Increased funding over the past decade has led to a significant increase in research studies aiming to find new drugs and strategies to replace sulfadoxine-pyrimethamine for IPTp. Valuable insights have been gained, suggesting potential benefits of more sustained protection with monthly regimens starting early in pregnancy. Effectiveness of sulfadoxine-pyrimethamine in improving birth outcomes has remained resilient, even in areas with a high prevalence of quintuple mutations. However,

its effectiveness is compromised in women infected with the sextuple mutant parasite. Among the candidates studied, dihydroartemisinin-piperaquine shows promise as a replacement for IPTp, but further studies are needed to confirm its safety, efficacy, cost-effectiveness, and feasibility in HIV-negative women. Ongoing research is focused on exploring the feasibility and implementation of a 3-day dihydroartemisinin-piperaquine regimen.

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