Research Output Journal of Biological and Applied Science 5(3):73-86, 2025

ROJBAS Publications ONLINE ISSN: 1115-9200

https://rojournals.org/roj-biological-and-applied-science/ PRINT ISSN: 1115-6120

https://doi.org/10.59298/ROJBAS/2025/537386

Pregnancy-Associated Malaria: Evidence and Interventions

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ABSTRACT

Pregnancy-associated malaria (PAM) is a critical public health concern in endemic regions, particularly sub-Saharan Africa, where it significantly contributes to maternal and neonatal morbidity and mortality. Immunological and hormonal changes during pregnancy heighten women's susceptibility, especially among primigravidae and those with HIV co-infection. PAM is primarily caused by Plasmodium falciparum, which sequesters in the placenta, impairing nutrient and oxygen transfer and leading to adverse outcomes such as maternal anaemia, miscarriage, stillbirth, preterm delivery, and low birth weight. Globally, more than 125 million pregnancies annually are at risk, with prevalence influenced by geographic distribution, socioeconomic conditions, and immunological factors. Diagnosis remains challenging due to placental sequestration and low peripheral parasitemia, with microscopy and rapid diagnostic tests often missing infections. Molecular techniques and placental histology improve detection but are not widely accessible. Preventive measures recommended by the World Health Organization include insecticide-treated nets (ITNs), indoor residual spraying (IRS), and intermittent preventive treatment in pregnancy (IPTp) with sulfadoxine-pyrimethamine. These interventions have proven effective in reducing parasite prevalence, maternal anaemia, and adverse birth outcomes, but challenges persist with drug resistance, limited coverage, and sociocultural barriers. Effective management of PAM requires integrated strategies that combine improved diagnostics, equitable access to preventive interventions, and strengthened antenatal care. Addressing PAM holistically is essential to safeguard maternal and child health and accelerate global malaria elimination efforts.

Keywords: Pregnancy-associated malaria, Placental sequestration, Maternal and neonatal outcomes, intermittent preventive treatment (IPTp), and Malaria elimination.

INTRODUCTION

Malaria constitutes a persistent public health challenge in tropical and subtropical regions, afflicting more than 400 million individuals and engendering nearly a million fatalities annually, predominantly among children under the age of five [1]. The disease is instigated by a eukaryotic parasite of the genus Plasmodium, transmitted through the bite of Anopheles mosquitoes. The infection cycle commences when sporozoites enter the human bloodstream, subsequently migrating to hepatocytes for replication, followed by erythrocytic invasion where symptomatic manifestations arise. Pregnancy-associated malaria (PAM) denotes the Plasmodium infection occurring during gestation [2]. This condition engenders heightened vulnerability in expecting women due to immunological and hormonal alterations [3]. The pathogenesis of PAM culminates in diverse deleterious effects on both maternal and fetal health, including but not limited to anaemia, fetal growth restriction, premature delivery, stillbirth, miscarriage, and low birth weight, which collectively exacerbate maternal and infant mortality rates. Certain high-risk groups, such as primigravida women and those with human immunodeficiency virus (HIV) co-infection, demonstrate an increased susceptibility to adverse outcomes [1, 3].

Overview of Malaria

Malaria is a complex infectious disease transmitted by the bite of infected female Anopheles mosquitoes and caused by protozoan parasites of the genus Plasmodium [1, 4]. Plasmodium parasites possess a complex life cycle, which in humans involves two stages: a sexual phase in the mosquito vector and an asexual phase in the vertebrate host. Plasmodium parasites undergo a pre-erythrocytic (liver) stage during which sporozoites mature to yield tens of thousands of exoerythrocytic merozoites; these enter erythrocytes, producing a widespread erythrocytic infection

responsible for the clinical symptoms of the disease [1], which include fever, chills, and headache, anemia, and splenomegaly [4].

Impact of Malaria on Pregnancy

Pregnancy-associated malaria (PAM) entails the sequestration of Plasmodium falciparum parasites in the placenta, leading to adverse outcomes for both the mother and fetus[4]. These include maternal anaemia, miscarriage, prematurity, intrauterine growth retardation, low birth weight, stillbirth, neonatal mortality, and developmental deficits in childhood [4]. Understanding the effects of malaria during pregnancy is vital due to the associated health risks. The Plasmodium parasite lifecycle initiates when an infected Anopheles mosquito injects sporozoites into the human bloodstream during a blood meal. Fed sporozoites enter hepatocytes and mature into schizonts, which subsequently burst, releasing merozoites into the bloodstream. Merozoites infect erythrocytes and transform into ring-stage trophozoites, which develop into schizonts. Each schizont produces new merozoites that infect additional red blood cells [1, 5]. Some trophozoites differentiate into sexual forms known as male and female gametocytes, which are ingested by another anopheline mosquito during feeding, completing the cycle. The asexual replication process spans 36 to 48 hours, contingent upon the specific Plasmodium species involved [4]. Malaria transmission via the bite of an infected female Anopheles mosquito introduces Plasmodium sporozoites into the bloodstream [1, 4]. The parasites traverse the circulatory system and invade liver cells. In the hepatic phase, sporozoites develop into thousands of merozoites, which reenter the peripheral circulation to infect red blood cells. In erythrocytes, merozoites undergo asexual replication, culminating in the formation of additional merozoites that perpetuate the infectious cycle. Some parasites differentiate into gametocytes, the sexual forms responsible for transmission back to the mosquito vector. The generalized Plasmodium lifecycle is emphasized in the context of host-vector-host interactions [1].

Maternal Health Outcomes

Malaria infection during pregnancy can adversely affect maternal health and fetal development [5]. Pregnant women living in malaria-endemic areas are more susceptible to the disease than their nonpregnant counterparts. Malaria in pregnancy may lead to maternal anaemia, increased risk of miscarriage and stillbirth, premature delivery and low-birth-weight babies [6]. Indeed, reports of adverse birth outcomes associated with Plasmodium falciparum malaria in pregnancy were first published nearly 100 years ago, with reduced birth weight and anaemia most frequently documented in relation to infection[5, 6].

Fetal Development and Outcomes

Malaria exerts detrimental effects on pregnancy and fetal development, particularly in Plasmodium falciparum endemic regions [5]. Malaria infection during pregnancy damages the placenta, disrupting nutrient transfer and fetal growth, thereby causing stillbirth, prematurity, low birth weight (LBW), and increased neonatal mortality [7]. Excessive placental deposits of malarial pigment further harm foetal development. Malaria in pregnancy affects more than 25 million women annually in endemic areas, mainly in Sub-Saharan Africa. Non-immune pregnant women are more exposed to high-density parasite infection and severe clinical manifestations. Predominantly attributable to Plasmodium falciparum, the condition is associated with maternal anemia, stillbirth, preterm birth, and LBW[2, 7]. Maternal anemia and LBW constitute the most common severe consequences. Malaria infection is implicated in up to 14% of LBW infants worldwide and 11% of LBW-associated infant mortality in Sub-Saharan Africa, representing the foremost cause of adverse newborn outcomes. Malaria exposure in utero modulates fetal immune cell development with potential long-term health effects. While a malaria-specific antibody response is evident in children born to infected mothers, placental malaria does not generally induce an acute fetal humoral immune response [5]. The timing of parasite exposure profoundly influences fetal immune profiles at birth, impacting childhood susceptibility to the parasite [2, 5].

Epidemiology of Pregnancy-Associated Malaria

Malaria parasites expose over 125 million pregnant women annually throughout malaria-endemic regions and pose an increased risk of maternal and fetal mortality and morbidity [2, 8]. Understanding the epidemiology of pregnancy-associated malaria is essential to guide treatment and prevention [2]. Malaria transmission is highly heterogeneous; the estimated number of pregnant women at risk in different intensity areas varies considerably and geographical hotspots exist [8].

Prevalence Rates

Pregnancy-associated malaria (PAM), resulting predominantly from Plasmodium falciparum infection, is a major cause of morbidity and mortality in pregnant women and their fetuses in malaria-endemic areas [8]. In sub-Saharan Africa, more than 30 million women become pregnant annually, with nearly 60% residing in malaria transmission areas. Globally, an estimated 125 million pregnancies occur each year in regions with stable malaria transmission [2]. The prevalence of Plasmodium falciparum in pregnant women varies geographically: 50% in West and Central Africa, 35% in East and Southern Africa, 15% in low-transmission parts of Asia, and approximately 5% in Latin America[8]. Data from 2005 indicate that an estimated 24 million annual pregnancies

in sub-Saharan Africa were exposed to malaria infection. Despite this widespread exposure, only a fraction of affected women access effective preventive and curative services [21, 28].

Geographic Distribution

Malaria has been a major global health challenge, especially for low- and middle-income countries (LMICs). Among parasitic diseases, it is the second most deadly after schistosomiasis[9, 17]. Estimates indicate that approximately 50% of the global population remains at risk of contracting malaria. The disease is caused by parasitic protozoans known as Plasmodium, with P. falciparum being the most common parasite. Primarily transmitted through mosquito bites during blood-feeding, malaria parasites multiply first in the liver and subsequently in the red blood cells of humans [1, 3, 7]. This multiplication can lead to death due to brain and kidney damage, as well as profound anemia. Malaria imposes a high burden on fetal development. In 2007, around 54.7 million pregnancies occurred in areas with stable P. falciparum malaria, and 70.5 million took place in regions with low malaria transmission or exclusively P. vivax infections [9]. The aforementioned prevalence rate is elevated by socioeconomic factors, environmental conditions, and the immunological status of patients[1, 2, 25].

Risk Factors for Infection

Immunological and hormonal changes in pregnancy increase susceptibility to malaria [1]. The combination of endemicity, exposure, and immunity determines the epidemiology and clinical presentation of pregnancy-associated malaria[1]. In high-transmission areas pregnant women have some level of immunity; they can control but not clear infections, resulting in common asymptomatic infections but only rare clinical malaria. Age is an important confounder of the effect of pregnancy on susceptibility to infection and disease [8]. Pregnant women who develop clinical disease tend to be young and primigravid. In areas of low, entirely unstable transmission they have little or no pre-existing immunity and a significantly increased risk of developing clinical disease; they may also have more infections with Plasmodium vivax. Outside pregnancy, in high-transmission settings the risk of infection is generally assumed to increase towards the end of the rainy season[8, 9]. The overwhelming majority of infections detected in pregnant women are attributable to the six months preceding the first antenatal visit. Alcohol use, marital status, distance to the nearest health centre and use of insecticide-treated bed nets are also important. Age, parity and gestational age also influence the risk of P. falciparum infection during pregnancy; younger, primigravidae in middle-to-late pregnancy are most at risk. There is limited data on the burden of malaria in the first trimester, and uncertainty about the point during pregnancy when the risk of malaria begins to increase[8, 9, 19].

Socioeconomic Factors

Malaria during pregnancy remains a significant source of morbidity and mortality worldwide, with the majority of cases concentrated in the World Health Organization's African Regions [10]. Among the numerous factors affecting the prevalence of pregnancy-associated malaria (PAM), socioeconomic status is of particular importance [11]. Socioeconomic status encompasses both economic position and social class; the latter can be defined as a group of people within a society distinguished by prevailing social standards, occupation, and income. These factors influence malaria risks through variations in living standards, economic resources, housing quality, and the capacity to prevent or seek treatment for the disease[10]. Malaria in pregnancy has long-standing social implications firmly linked to poverty, as malaria is more common among socially and economically disadvantaged populations. Existing evidence correlates the distribution of malaria infection with income and education indicators of socioeconomic position even in endemic populations [11]. For example, in The Gambia, higher malaria prevalence in poorer villages is attributed to socioeconomic disparities, and in Tanzania, infection and disease are linked with poverty and social position. An important route by which socioeconomic status influences infection and clinical episodes involves the differential coverage of efficient preventive measures such as insecticide-treated mosquito nets. Ownership and use of such nets during pregnancy also varies with socioeconomic status and further explains differences in malaria frequency among pregnant women [9, 10, 11]. The prevalence of PAM differs considerably across socio-political regions and is affected by various risk factors, including cultural, economic, occupational, and social influences. Malaria continues to be a leading preventable cause of adverse birth outcomes and maternal mortality in Africa, yet the underlying social causes of malaria remain poorly understood. Both poor housing and low incomes can increase vulnerability to malaria, but it is not clear which of these is the fundamental social cause [9, 12, 15]. To effectively combat one of the most socio-economically determined diseases known, a strategic public health approach must address its fundamental social causes.

Environmental Factors

Environmental determinants at the household level such as quality of housing construction, indoor residual spraying, and use of insecticide-treated nets have the potential to influence the risk of malaria in pregnant women [11]. There is growing awareness that such factors may modify infection rates, although few studies have addressed this association specifically amongst pregnant women [8]. In Uganda, for example, younger and less

educated women face higher risks of malaria during gestation, yet interventions including intermittent preventive treatment and indoor residual spraying confer measurable protection [8]. Temporality also emerges as an important consideration: in areas where transmission varies seasonally, a substantial proportion of infections detectable at first antenatal visit were likely acquired prior to conception and persist through early pregnancy [8, 11].

Immunological Factors

Pregnant women constitute a risk group with a higher susceptibility to Plasmodium falciparum infections [12], which has a tendency to decrease as successive pregnancies occur, suggesting that protective immunity is acquired [13]. In women with pregnancy-associated malaria (PAM), P. falciparum parasitemia develops almost exclusively with parasites expressing the VAR2CSA adhesion phenotype. These parasitized red blood cells sequester selectively in the placenta, accumulating on the syncytiotrophoblast cell layer[13]. Women experiencing a first pregnancy therefore lack protective immunity to the VAR2CSA-type infected erythrocytes, making PAM particularly common among primigravidae. As the lack of protective immunity is thought to be parity dependent, the prevalence and incidence of PAM are greatest in women who are pregnant for the first or second time. Multiple birth pregnancies and the postpartum period are times when pregnant women are more vulnerable to malaria [13, 24]. Several mechanisms are likely to be involved in the increased susceptibility to infection and the clinical severity of plasmodial infections during pregnancy. Pregnancy temporarily depresses cell-mediated immunity in most women, causing a reduction in resistance to infectious agents that are normally controlled by lymphocyte activation. Pregnant women therefore experience a general immunosuppression and higher susceptibility to infections, like malaria. In areas of stable malaria transmission, a cellular immune response to P. falciparum 'parasite recall' antigens is suppressed during pregnancy and may take several months to recover after women have delivered[13, 15].

Clinical Manifestations

Pregnancy-associated malaria (PAM) is a life-threatening condition, particularly during the first pregnancy[1]. The disease dramatically alters the anatomy and physiology of the placental wall, threatening the lives of both mother and fetus[13, 23]. In areas with high malaria transmission, infected women are often asymptomatic, resulting in the presence of parasites in the placenta. The general physiological adaptations that take place during pregnancy increase susceptibility to malaria infection. When clinical symptoms are present, they are often non-specific and lack the paroxysmal cycles of fever seen in non-pregnant individuals [20, 25]. It is hypothesized that the observed decrease in febrile response to parasitemia during pregnancy results from pregnancy-induced modulation of the cytokine immune response. Despite the recognized importance of PAM, there is a relative scarcity of data describing its clinical features. Clinical manifestations vary according to the level of immunity and malaria transmission; infected women in stable transmission areas (e.g., sub-Saharan Africa) seldom seek treatment because they are frequently pyrogenic and asymptomatic [1, 32]. The most severe clinical manifestation during pregnancy is severe malarial anemia, which is a complex event that may result from low levels of parasitemia combined with high rates of red blood cell destruction, dyserythropoiesis, and iron deficiency. Severe anemia during pregnancy is associated with fetal loss, prematurity, and low birthweight (LBW)[1].

Symptoms in Pregnant Women

The fever, chills, and headaches of uncomplicated malaria are often less prevalent in pregnancy due to the majority of parasites being sequestered in the placenta, rather than circulating in the peripheral blood [14]. Moreover, Plasmodium falciparum parasites bound in the placenta cause very few surface-agglutinating antibodies, which means that the infection usually progresses without obvious symptoms. Most diagnoses thus occur only when there is already high parasitemia and moderate anemia [11]. The severity of illness depends on three factors: the immune status of the mother, the endemicity of the parasite, and the time in pregnancy at which the infection occurs. Pregnant women experiencing their initial infection (or reinfection) within an endemic area tend to develop more serious illnesses because of an altered immune response or higher parasitemia[13]. In areas where malaria is not endemic, such as parts of Europe and the Americas, the disease also tends to be more serious because the mother has not developed any immunological memory against the parasite, rendering her more susceptible to infection. The illness is most severe during the first and second trimesters, but severe cases can still occur up to delivery[12].

Complications Associated with Malaria

Complications associated with malaria can vary greatly, depending on the infecting species, the age of the patient, immunity, and several other factors [14, 18]. Severe malaria occurs mostly in young children and in individuals who have either not developed protective immunity or have lost it, such as pregnant women and travelers from nonendemic to endemic areas [22, 28]. Death in uncomplicated malaria may occur as a result of acute anemia or damage to vital organs. Falciparum infection can cause complications affecting almost all organ systems. The most striking differences between complicated malaria in adults and children are a higher incidence of renal failure in

the former and coma in the latter. Changes in the brain of the children are associated with seizures and increased intracranial pressure. Severe malaria and death are uncommon in indigenous adults but may be common among tourists and immigrants who have lost their immunity [24, 25]. During and following a bout of malaria, existing chronic conditions such as cardiac, renal, or pulmonary disease may be aggravated. Infection with Plasmodium falciparum during pregnancy has been shown to be associated with low birth weight, premature labour, and increased neonatal and infant mortality [17, 29]. These can be attributed to placental infection, maternal anemia, secondary bacterial infection, poor nutritional status of the mother, and congenital malaria. Damage to the kidney, hepatitis, and pulmonary edema have also been occasionally documented in women suffering from malaria during pregnancy[17, 19].

Diagnosis of Malaria in Pregnancy

Malaria illness in the general population is diagnosed by microscopy and/or rapid diagnostic tests (RDT). Malaria in pregnancy is characterized by high parasite sequestration in the placenta and low peripheral parasitemia[2, 26]. High placental sequestration of infected erythrocytes with relatively low peripheral parasitemia in pregnancy can result in peripheral blood microscopy, RDT, and PCR showing negative for parasitemia while placental histology is positive[7, 18].

Diagnostic Methods

Malaria diagnosis relies on rapid diagnostic tests (RDTs), microscopy, and PCR. RDTs have become widely used for quick detection in resource-limited settings, but their performance varies, especially during pregnancy. In Tanzania, RDTs were compared to placental histology, microscopy, and PCR, with evaluations of associated adverse pregnancy outcomes [14, 15]. Analysis of RDT performance necessitates consideration of different reference standards [15]. PAM diagnosis is often challenging because parasitized erythrocytes sequestrate in the placenta, reducing peripheral blood parasitemia to below detection thresholds of routine diagnostics. Submicroscopic infections associate with maternal anemia, pre-term delivery, and low birth weight [15, 16]. Accurate and prompt PAM diagnosis prevents poor outcomes and reduces parasite reservoirs. Conventional clinical diagnosis is unreliable in endemic areas because malaria symptoms overlap with other infections; presumptive treatment leads to over-diagnosis and inappropriate use of drugs. Rational anti-malarial prescription decreases costs and the risk of parasite resistance development and selection [11, 15]. Likewise, detection of submicroscopic infections during pregnancy is crucial, since untreated cases link to low birth weight and maternal anemia[2, 19]. In sub-Saharan Africa, PAM by Plasmodium falciparum is characterized by sequestration of infected erythrocytes in the placenta, limiting oxygen and nutrient transport to the fetus and causing adverse outcomes such as intra-uterine growth retardation [17, 25]. Infected erythrocytes in peripheral blood are therefore difficult to detect, and infections frequently remain asymptomatic in endemic regions. Although microscopic examination of blood smears has been the gold standard method for malaria diagnosis, deployment in rural areas is hindered by lack of infrastructure and trained personnel, and by sensitivity and time consumption limitations [23, 30].

Challenges in Diagnosis

A variety of diagnostic approaches are available, although diagnosis of PAM remains challenging [1]. Microscopic examination of blood smears is widely used but requires skilled personnel [6]. Rapid diagnostic tests (RDTs) offer quick results but face logistic and interpretive difficulties. Identification of histopathological changes in placental tissue provides insight, yet placental biopsies are feasible mainly at delivery[6, 10]. More recently, molecular diagnostic methods targeting histidine-rich protein 2 are able to detect placental infection during the antenatal period[11, 32].

Interventions for Prevention

Prevention of pregnancy-associated malaria is crucial and relies heavily on vector control measures [1]. The World Health Organization strongly recommends the use of insecticide-treated nets (ITNs) for pregnant women and others at risk [3, 9]. Properly worn, these nets provide a physical and insecticidal barrier against mosquito bites. Evidence from Cochrane meta-analyses demonstrates that both ITNs and indoor residual spraying (IRS) significantly reduce infections in pregnant women and the associated risk of low birth weight in their newborns. Proactive community-level vector control strategies such as larviciding and source reduction can also decrease malaria burden [3, 27]. For instance, the Metropolitan Manila Development Authority in the Philippines conducts regular larviciding operations targeting mosquito breeding sites. However, cultural perspectives can impede the widespread adoption of environmental management [27, 30]. As Gilbert and colleagues illustrate in the Solomon Islands, although community members recognize the benefits of environmental management for malaria reduction and are willing to participate, misconceptions about its purpose sometimes hinder participation [5, 18].

Insecticide-Treated Nets

It is well established that using insecticide-treated mosquito nets reduces malaria cases and related deaths. Nevertheless, operational challenges remain in expanding net coverage within vulnerable populations in many malaria-endemic countries [1, 21]. Where appropriate, other measures to avoid contact between mosquitoes and pregnant women can reduce the risk of PAM and its consequences for example, by ensuring that windows and doors have screens or closure at night, staying in the centre of houses, and avoiding exposing arms and legs to mosquito bites during the hours of maximum mosquito activity; these measures are often culturally expected and used naturally [13, 26].

Indoor Residual Spraying

Indoor residual spraying (IRS) involves applying a broad-spectrum insecticide to interior walls and ceilings of dwellings, effectively targeting vectors resting indoors [17]. When sprayed surfaces remain undisturbed, they retain insecticidal properties that help prevent malaria transmission for several months.

Environmental Management

Environmental management encompasses the control of all vector breeding sites and the improvement of house design [18]. These measures were deployed in Colombia during the 1940s and 1950s but were later discontinued.

Treatment Options

The treatment of malaria during pregnancy remains a critical component of overall disease management [12, 15]. Pregnant women with malaria should be treated only after parasitological confirmation to ensure safety and avoid unnecessary exposure to antimalarial drugs. During the first trimester, which is a period of heightened vulnerability, the use of chloroquine, quinine, clindamycin, and proguanil can be considered safe. For uncomplicated malaria, a regimen combining quinine and clindamycin administered over seven days is recommended [6,17, 27]. In situations where treatment cannot be delayed and parasitological confirmation is unavailable, parenteral artesunate and quinine may be considered despite ongoing uncertainties surrounding the safety of artemisinins in early pregnancy [1]. Prevention strategies centered on the use of insecticide-treated bed nets (ITNs) have been shown to significantly reduce the incidence of malaria. Intermittent preventive treatment during pregnancy (IPTp) with sulfadoxine-pyrimethamine (SP) constitutes another cornerstone of prophylactic intervention, although the efficacy of this approach continues to be undermined due to growing resistance; mefloquine has emerged as a potential alternative with prevention efficacy comparable to that of SP. In geographic regions characterized by low transmission, systematic screening of all pregnant women and subsequent treatment of those testing positive may represent a viable prophylactic method[23, 24].

Antimalarial Medications

Malaria infection during pregnancy is a major preventable cause of maternal and infant mortality in malaria-endemic areas [1]. Current WHO guidelines recommend treatment only after parasitological confirmation to reduce exposure to potentially harmful antimalarials. Artemisinin-based combinations, chloroquine, quinine, clindamycin, and proguanil are preferably used [1, 26]. Only quinine combined with clindamycin is considered safe during the first trimester. Frequently available antimalarials include amodiaquine, chloroquine, sulphadoxine–pyrimethamine (SP), mefloquine, quinine, and artemisinin derivatives. Several safety-related concerns limit the use of amodiaquine, SP, and mefloquine during pregnancy [27]. From the second trimester onwards, addition of an artemisinin derivative to long half-life antimalarials constitutes the most effective treatment option. Challenges remain concerning the treatment of asymptomatic infection and intermittent preventive treatment in areas of declining transmission, and prophylactic interventions to prevent re-infection [30, 32].

Guidelines for Treatment in Pregnancy

The choice of antimalarial drugs for treating infected pregnant women is limited due to potential risks of abortion or fetal harm; the selection depends on gestational age and malaria species [16, 230]. In the first trimester, quinine is recommended for any Plasmodium species, in combination with clindamycin when possible. In the second and third trimesters, artemisinin-based combination therapies (ACT) are preferred for treating Plasmodium falciparum malaria. For Plasmodium vivax infection in the second and third trimesters, chloroquine is the drug of choice, and primaquine remains contraindicated during pregnancy[24, 29].

Public Health Strategies

Public health approaches must focus on reducing malaria in pregnancy (MIP) to lower the risks of low birthweight, severe anaemia, stillbirth and premature birth[1, 25]. Interventions that have proved promotional value in the control of MIP include the widespread use of effective case management and insecticide treated nets, as well as the introduction of intermittent preventive treatment [11, 15]. The links between PAM prevalence and some of the risk factors identified, coupled with the substantial impact on maternal health and foetal development, as well as the already proven efficacy of existing intermittent preventive treatments, provide additional emphasis on the wider significance of PAM for community health and the need to further extend their implementation and availability [18]. There is a need for public health campaigns to increase awareness and confidence in the

effectiveness of anti-malaria treatment in pregnancy, leading to improved treatment, quicker recovery and reduced impact for both mother and foetus[5, 9, 20]. Detection methods are equally important and there is a need for accurate, affordable field detection kits that can be deployed widely and in quantity [2, 29]. In addition to raising awareness of the risks present, once the dangers of PAM are better mediated through prevention and treatment, PAM should cease to be a major problem. Community education about preventive measures and timely treatment should be the clear focus of all public health efforts to reduce the burden of PAM and bring about positive change. Population-wide improvements in housing and sanitation are also likely to lower overall burden [13, 23].

Community Education and Awareness

Achieving a long-term reduction in the malaria burden will require a comprehensive approach that not only targets the vector and the parasite but also establishes effective educational programs, promotes preventive measures, detects carriers, implements timely treatment, and ensures the surveillance of drug resistance [19]. Malaria during pregnancy is a serious threat to health and survival, yet it receives relatively little attention in awareness campaigns, potentially leaving pregnant women vulnerable to infection [19, 20]. Therefore, community education and awareness should be considered integral components of strategies to control and reduce the malaria burden in endemic settings [12, 15]. Community discussions represent a straightforward and promising strategy for improving access to appropriate prevention and treatment services, understudied as part of efforts to scale up the use of effective prevention measures for malaria during pregnancy [10, 21]. Lack of information and widespread misunderstandings about the possible consequences of malaria during pregnancy, as well as uncertainty about the safety and effectiveness of preventive measures, constitute important barriers to access and use, and these barriers can only be addressed through appropriate communication, education, and information campaigns at different levels and through different channels [20].

Monitoring and Surveillance Programs

Monitoring and evaluation of malaria control in pregnancy are essential for assessing the efficacy and effectiveness of health interventions aimed at reducing disease burden among women in endemic areas [1]. Current recommendations call for intermittent preventive treatment during pregnancy with sulphadoxine-pyrimethamine in higher transmission areas, combined with insecticide-treated bed nets and case management [1, 20]. In lower transmission settings, emphasis is primarily on case management [1]. Monitoring approaches include assessments of drug efficacy, reductions in parasite prevalence, seasonal effects, rapid assessment methodologies, birthweight and anaemia measures, case-coverage methods, maternal mortality indices, operational indicators, and safety surveillance of antimalarials [18]. These measures should be incorporated into national programmes to improve surveillance and identify high-risk groups. Data systems require strengthening, with increased focus on safety and pharmacovigilance, especially in the context of new therapies and the risk of early pregnancy exposure to artemisinins[1, 2, 14]. Integrating monitoring activities within malaria control and reproductive health services is critical for effective implementation [2, 9].

Global and Regional Initiatives

The World Health Organization (WHO) developed evidence-based guidelines to support implementation of effective interventions for malaria in pregnancy: vector-control methods such as insecticide-treated nets (ITNs) and indoor residual spraying (IRS), intermittent preventive treatment during pregnancy (IPTp), and effective case management of malarial illness [18]. Vector-control strategies aim to reduce contact between host and vector, which in turn reduces transmission of infection, and currently serve as the most effective method for protecting pregnant women from malaria. Countries belonging to the Roll Back Malaria Partnership and other global initiatives have made significant progress in disseminating ITNs to target populations [21]. Collaborative efforts between the countries most affected by malaria in pregnancy and organizations such as the Global Fund to Fight AIDS, Tuberculosis, and Malaria, as well as Jhpiego.org and the Centers for Disease Control and Prevention (CDC), are aimed at addressing the burden of malaria on maternal health [24, 25]. These collaborative efforts reflect a renewed focus on malaria in pregnancy and are based on frameworks such as the Roll Back Malaria Partnership Global Malaria Action Plan (2008–2015), the 2017 World Malaria Report, and updated WHO policy on IPTp[20, 21, 23].

WHO Guidelines

WHO encourages the integration of widespread parasite screening at each scheduled antenatal care visit in areas with moderate and high malaria transmission [9, 10]. The objective of this screening is to facilitate prompt treatment to prevent anemia and adverse birth outcomes. Intermittent preventive treatment in pregnancy (IPTp) with sulfadoxine–pyrimethamine (SP) is recommended in moderate or high transmission areas of sub-Saharan Africa; the medication should be administered starting from the second trimester, with successive doses spaced at least four weeks apart, up until delivery, provided that doses are given at least one month apart. Pregnant women are also advised to use long-lasting insecticidal nets (LLINs), and management of fever during pregnancy should

consider malaria as a potential cause [1, 12]. WHO advises that, wherever possible, malaria prevention and treatment services should be delivered as an integral component of antenatal care programmes[16, 17]. The continued spread of resistance to SP in Africa threatens the effectiveness of IPTp, underscoring the need for the development of alternative drugs. Maternal vaccination constitutes another potential approach to tackle pregnancy-associated malaria; however, further research is required to accurately assess the implications of placental malaria during the earliest trimester of pregnancy [16].

Partnerships and Collaborations

In addition to the joint work already underway within the World Health Organization (WHO), addressed in the preceding sections, a number of partnerships are further supporting the response to pregnancy-associated malaria[17, 18]. The Global Fund, Jhpiego, the Centers for Disease Control and Prevention, WHO and the United States Agency for International Development are working together to improve access to intermittent preventive treatment (IPTp) with sulfadoxine/pyrimethamine in sub-Saharan Africa, at the national and local levels, by: better defining and quantifying the risk of malaria in pregnancy, particularly in urban areas; identifying the factors that influence the delivery and uptake of IPTp and long-lasting insecticidal nets (LLINs); and accelerating implementation, scale-up and coverage of IPTp and LLINs [21, 23]. Several other reports, policies and scientific papers also endorse and encourage rolling out effective interventions for preventing malaria in pregnancy in countries where malaria is endemic, including the Malaria Policy Advisory Committee's recommendations and the Global Malaria Action Plan[20, 21].

Research Gaps and Future Directions

Pregnancy-associated malaria (PAM) remains a critical public health concern, yet persistent gaps hinder optimal management. Rigorous longitudinal studies are warranted to quantify the relative contributions of pregnancy-specific and general risk factors to infection and morbidity over time [4]. Furthermore, the development of new tools to prevent infection and morbidity during pregnancy remains an important priority. Certain populations, such as HIV-infected pregnant women, continue to face disproportionately high risk, calling for targeted solutions. Enhanced research into the safety of medications during pregnancy is needed, particularly for new antimalarials that may serve as alternatives to sulfadoxine-pyrimethamine (SP)[5]. In response, a WHO expert committee has embarked on developing guidelines to improve safety data collection and pharmacovigilance throughout pregnancy, encompassing early-stage development and post-marketing activities. Ethical considerations remain indispensable; the advancement of clinical research on pregnancy-associated malaria hinges on ethical standards that protect vulnerable populations and prioritize informed consent. Addressing these research gaps and upholding ethical imperatives are prerequisites to refining PAM control strategies[10].

Need for Longitudinal Studies

Most data on malaria in pregnancy (MiP) derive from cross-sectional studies of delivery cohorts [6]. Such designs, combined with the heterogeneity of malaria infection and the imbalance in the timing of diagnosis, are major limitations for understanding how malaria adversely affects reproduction throughout pregnancy. Two large prospective studies of MiP in Benin and Uganda involved enrolment before 24 weeks of gestation and followed longitudinally during pregnancy[7, 8]. Early or recurrent malaria infections with high parasite densities increased the risks of low birthweight and preterm birth in Benin, but placentas were not collected for histological analysis. Symptomatic malaria diagnosed by microscopy was common, estimated to cause one in five and one in seven stillbirths in Benin and Uganda, respectively, but no assessment of placental malaria was described[7, 8, 14]. The level of parasitaemia was often very low and infections were particularly difficult to detect by microscopy, which is a major limitation for assessing the burden of malaria during pregnancy and ultimately hampered attempts to distinguish maternal malaria from placental malaria[3]. A much larger study conducted in Malawi used a combination of qPCR and histology to explore the relationship between submicroscopic infection, placental malaria and birth outcomes. Severe anaemia phenotypes (haemoglobin <75 g/l) were preferably used rather than all adverse outcomes combined. A statistically significant association was found between submicroscopic malaria and histology-confirmed placental malaria, but no association was observed between submicroscopic malaria and birth outcomes[12, 25, 28]. More frequent sampling to ascertain the timing of infection and additional investigations are required to accurately describe the effects of parasitaemia on placental malaria and foetal growth restriction. Taken together, current evidence emphasises the need for longitudinal studies to investigate the burden of malaria during pregnancy, its relationship with placental malaria and the association with adverse birth outcomes [1, 25, 30].

Innovative Intervention Strategies

Conventional vector control methods, such as the use of insecticide-treated nets (ITN), intermittent preventive treatment with sulfadoxine–pyrimethamine (IPTp-SP) and indoor residual spraying (IRS) are effective strategies recommended by the World Health Organization (WHO) [22]. Although these interventions have contributed to decreasing maternal mortality and stillbirths associated with pregnancy-associated malaria (PAM), the prevalence

of infections during pregnancy persists, especially in rural communities with limited access to prevention and care services [23]. Intermittent screening and treatment in pregnancy (ISTp), which involves screening for asymptomatic malaria during antenatal care visits and treating only infected women with an artemisinin-based combination therapy (ACT), could be a promising alternative for the prevention of PAM[23, 27, 29]. The approach was designed to reduce the unnecessary drug exposure associated with IPTp and could therefore avoid the selection of parasites resistant to sulfadoxine–pyrimethamine and prevent potential adverse drug effects[1]. However, a robust debate prevails about the safety of ACT among pregnant women. Since pregnant women are not included in most clinical control studies, there is an important lack of data necessary to guide policy development[21, 24, 29]. Additional evidence is needed to establish whether the approach can provide a better individual protection than the current strategy. In addition, the effectiveness of ISTp has not been thoroughly addressed with epidemiological and qualitative data of acceptability at community level [12, 22, 27]. Although a randomized controlled trial suggested that ISTp-AL was not inferior to IPTp-SP in an area of high SP resistance in West Africa, further investigations are required to provide detailed evidence on the impact of screening during pregnancy on prematurity and low birth weight at a larger scale and in areas where SP is still effective. Efforts towards developing more effective approaches for the prevention of malaria during pregnancy could play an important role in reducing the mortality in sub-Saharan Africa where the burden of PAM is the heaviest [25, 30].

Ethical Considerations

Ethical considerations are paramount in the management of pregnancy-associated malaria (PAM) due to the potential risks to both the mother and fetus during study participation [16]. Sustainable interventions must be implemented and evaluated within ethical frameworks that encompass equity, respect for persons, beneficence, and non-maleficence [15, 16]. Informed consent stands as a foundational principle; pregnant women must receive complete information prior to participation in research or other interventions involving malaria screening, treatment, or prevention [21, 25, 26]. The concept of respect for persons extends beyond information disclosure to ensure individuals are treated with dignity and privacy throughout program delivery.The principle of justice demands that the benefits of effective malaria control interventions are equitably shared, both within and between populations [11, 13, 19]. Pregnant women require preferential access to efficacious preventive and therapeutic measures because they face higher morbidity and mortality risks than other groups[13, 23, 27]. Collaboration among malaria control programs and related sectors is necessary to facilitate access and resolve competing priorities that may hinder appropriate service delivery. Adherence to these ethical principles underpins public health efforts aimed at reducing the PAM burden [15, 28, 31].

Informed Consent in Research

Pregnant women are considered a vulnerable population in biomedical research, as pregnancy raises distinctive safety concerns for the developing fetus, as well as for the woman [2, 29]. Ethical guidelines emphasize that when research involves pregnant women, the purpose of the research should be to better understand the woman's condition to benefit both her and the fetus; cannot offer greater than minimal risk to the fetus; be conducted with participants or their legal representatives providing informed consent; and, in the absence of direct benefits for the woman, only proceed if risks to the fetus are no greater than minimal [2, 19]. Nevertheless, formal regulations governing provision of informed consent during pregnancy are generally inadequate, as specific guidance is typically scattered throughout distinct documents and inadequate for addressing the structural and practical complexities of conducting research involving pregnant women [4].

Equity in Access to Treatment

Malaria during pregnancy, also called pregnancy-associated malaria (PAM), contributes to increased risks for low birth weight, spontaneous abortion, stillbirth, premature delivery, as well as maternal anaemia and maternal death [23, 27]. Nearly 125 million pregnancies occur annually in areas with Plasmodium falciparum and Plasmodium vivax transmission, and large numbers of women also reside in dengue-endemic countries [24, 26]. An estimated 25 million pregnancies occur each year in areas of stable P. falciparum transmission across Africa. Malaria is transmitted from infected humans to uninfected humans by female Anopheles mosquitoes [12, 26, 30]. The parasite life cycle includes sexual development within female Anopheles mosquitoes, of the genus Anopheles, and asexual multiplication in vertebrates. Malaria infection in pregnancy is probably more common than recognised in many countries in malaria-endemic parts of Africa [13, 15, 17]. The clinical manifestations of malaria during pregnancy are diverse: an increased risk of miscarriage, stillbirth, prematurity, low birth weight and neonatal death, maternal anaemia, and even maternal death [1, 3]. Reduced miscarriages and increased birth weights may have contributed to the decline in all-cause mortality among children under 5 years of age that has been observed in some sites in Africa[5, 6]. Prevention of malaria in pregnancy with effective drugs and vector control will decrease the morbidity and mortality for mothers and their unborn children [4, 20, 25]. Public-health information, education campaigns and education through the mass media are essential to provide pregnant women and mothers with information about dengue, appropriate protective measures, and early diagnosis and treatment of suspected

disease. Epidemiological studies on the dengue burden in pregnancy and effects on both the mother and the foetus should be undertaken with appropriate approvals and informed consent [2, 5, 7].

Case Studies

Malaria and pregnancy remain an important public health challenge in most tropical regions [1, 4]. Pregnant women are at higher risk of infection and disease, with adverse consequences that affect both mother and foetus[1]. In areas of high transmission, such as in most of sub-Saharan Africa, pregnant women have a higher parasite density and more severe maternal anaemia than their non-pregnant counterparts [7]. Between 2007 and 2016, Mali piloted community case management of malaria that included seasonal malaria chemoprevention and annual screening and treatment for malaria in pregnancy [5, 8]. The country witnessed major public health achievements, including a 75%, 54%, and 55% decline in all-cause mortality in children under 5 years of age, in the general population, and children under 10 years of age, respectively. These case studies of successful and failed community-based malaria control programmes illustrate that concerted efforts from multiple stakeholders during both implementation and scale-up phases are critical to minimise the burden of malaria. Resources do not necessarily guarantee success and, conversely, limited resources do not automatically result in failure. Ensuring implementation fidelity pays dividends and can constitute the single most important ingredient for an effective and sustainable community-based malaria control programme[13, 23]. Equipping healthcare providers with appropriate in-service training on malaria management in pregnancy remains a key element towards more effective control in high transmission settings [11, 13]. It enables a broader range of providers to diagnose and treat uncomplicated malaria, thus allowing for effective management of cases in the community amongst hard-to-reach populations [30, 31]. At the same time, integrating community-based programmes into a stronger and adaptable health system and securing long-term community acceptance for these programmes is necessary to fully realize their potential at scale [2, 16]. The challenge is formidable and multifaceted: financial commitments along the entire continuum of malaria control and elimination; strengthening the public health infrastructure to allow a more efficient use of scarce resources; and reliable forecasting and procurement systems to ensure uninterrupted supply of drugs, commodities, and essential medical equipment. A malaria-free generation remains a distant goal in most endemic areas and malaria in pregnancy remains a major public health concern in most tropical regions [1, 17, 19, 29]. The combined effectiveness of LLINs, IPTp, and effective case management in all WHO African Region countries that have adopted the Roll Back Malaria Partnership strategies adopted in 2005 must therefore be urgently confirmed[8, 9]. Filling this gap will provide a foundation on which operational research questions and impact evaluation can be based, thereby providing national governments, multilateral and bilateral agencies, and public health policy makers with concrete evidence on where and how to invest limited financial resources[27]. Regardless of the progress achieved so far and the large availability of tools, there is an urgent need to explore the development and incorporation of new ones, such as vaccines against placental-binding parasites, particularly in highly endemic areas that lag behind[5, 24].

Successful Interventions

The three principal preventive interventions for pregnancy-associated malaria (PAM) are long-lasting insecticidal nets (LLINs), intermittent preventive treatment during pregnancy (IPTp), and effective case management [1, 23, 24]. LLINs have substantially reduced malaria morbidity and mortality; during pregnancy, they decrease maternal parasitaemia, maternal anemia, and the incidence of low birth weight [2, 14, 31]. IPTp, currently recommended in certain regions, involves administration of sulfadoxine-pyrimethamine (SP) at least twice after quickening, generally once in the second and once in the third trimester [2, 7]. Intervals between doses of at least one month are preferable. WHO advocates for continued use of SP-IPTp in settings where HIV prevalence is less than 10% and antifolate resistance has not reached high levels; otherwise, alternative regimens or strategies for effective prevention are necessary [24, 31]. WHO guidelines endorse LLINs combined with IPTp to reduce the adverse consequences of PAM on placental health and perinatal development. Where ongoing transmission and infection risk persist, large-scale, high-coverage distribution of LLINs should continue and be routinely provided through antenatal clinics. Concurrently, treatment of symptomatic infection during pregnancy calls for the widespread provision of diagnostics and effective case-management services. In regions where IPTp is inapplicable due to low transmission or widespread SP resistance, promotion of consistent LLIN use alongside prompt diagnosis and treatment addresses the risk of PAM and its consequences [1, 29, 32].

Lessons Learned from Failures

In Africa, up to 200,000 infants may die annually as a consequence of their mother's infection with Plasmodium falciparum during pregnancy [3, 7]. Prevention and treatment strategies implemented according to the World Health Organization (WHO)-recommended framework address the central pathologies of pregnancy-associated malaria (PAM)-related adverse birth outcomes, which, in turn, inform operational research aimed at designing sustainable programmes and shaping future policy[1, 6]. PAM is a major public health problem in Africa, where an estimated 25 million pregnancies occur each year during malaria transmission seasons [4, 9]. Up to 50% of

these pregnancies can be complicated by malaria infection in regions of stable endemicity. Plasmodium falciparum infections are more frequent and last longer, and are associated with higher parasite density, in primigravidae and secundigravidae 7. Maternal illness and anaemia disproportionately affect this group. Lack of acquired immunity to PAM can also render multigravidae at risk [8, 11]. Failures to prevent and control this infection during pregnancy can be related to parasite-, patient, and programme-associated factors. Most evaluations focus on the individual level, such as socio-demographic determinants of refusal, incorrect use, or non-compliance. From a programme perspective, failure to prevent infection can result from the inappropriate service delivery of an otherwise effective regimen [2, 5, 9].

Role of Healthcare Providers

Ensuring the availability and quality of the malaria-control arsenal is a major challenge. For optimal effectiveness at the outset, health workers must be trained adequately; cost must be contained; and individualized care and follow-up must be assured to name but a few imperative conditions that apply equally well to prevention and treatment[16. 20]. Yet, all too often, insufficient attention has been accorded to how appropriate services can be built and sustained. Recognizing that well-structured health systems constitute a critical foundation, the necessity of a strong and well-supported health infrastructure comes to the fore. It is an indispensable part of the solution, even if not always the sole remaining gap. Healthcare workers at all levels must be equipped with the knowledge and resources necessary to provide guidance to pregnant women, both during routine contacts and when the opportunity arises [10, 17]. The performance of front-line providers exerts a direct influence on the effectiveness of prevention and treatment interventions [11, 13]. Several studies have highlighted poor quality of service provision across both public and private sectors, underscoring an urgent need to identify and implement quality-improvement interventions targeting both users and providers [16]. Addressing these circumstances warrants multifaceted strategies, including intensified training programmes, mHealth initiatives, team-based quality-improvement approaches, and supportive supervision [10, 12]. Interventions should be tailored separately for health facilities and drug outlets, reflecting the distinct qualifications of their providers and the corresponding health-seeking behaviours of patients [25]. Enhancing practice within the informal sector is especially important, given that this segment constitutes a substantial part of treatment provision and experiences minimal regulatory oversight. Implementation and evaluation of such strategies will be key to reducing the morbidity and mortality attributed to PAM, particularly in sub-Saharan Africa[25, 27].

Training and Capacity Building

Malaria eradication remains a priority for the World Health Organization (WHO) and national malaria control programmes (NMCPs). Strengthening the capacity of key personnel is fundamental to sustaining programmes and making malaria eradication feasible in the effort to achieve a malaria-free world [19, 27]. One crucial skill among programme officers is monitoring and evaluation (M&E), which helps to identify strengths and weaknesses and correct underperforming or inefficient activities [20, 23, 26]. From 2010 to 2014, regional in-person workshops on malaria M&E for Anglophone and Francophone African countries were organized in collaboration with partners from Ghana and Burkina Faso. Additionally, complementary open-source online courses in English were made available. From 2010 to 2014, these 5-day training workshops strengthened the capacity of 181 M&E personnel from 28 malaria-endemic countries in Africa and the Asia-Pacific region. Participants mainly represented NMCPs, the ministries of health, partner institutions, non-governmental organizations (NGOs) and international development agencies [28]. In 2015, a post-workshop assessment was conducted to evaluate the effects of this regional capacity-building strategy and to address remaining gaps. Results showed that key M&E knowledge and competencies acquired during the workshops were retained and extensively used in participants' work[12, 28]. There is a need, however, for a new module on malaria surveillance systems adapted to the epidemiological context of countries transitioning towards pre-elimination [25]. These findings will inform the development and restructuring of future workshops as well as the conduct of country-specific capacity needs assessments. Antimalarial drug resistance and the changing malaria landscape with increasing numbers of countries intensifying their malaria-control programmes will require innovative M&E strategies such as a stronger focus on surveillance and responsive information systems [24].

Integration of Services

Intermittent preventive treatment during pregnancy (IPTp) with sulfadoxine–pyrimethamine (SP) is delivered through antenatal clinics to mitigate adverse pregnancy-associated malaria (PAM) outcomes [16, 27]. Healthcare providers' knowledge and motivation, supervision, supply logistics, and the broader health system context remain influential determinants of IPTp coverage and effectiveness. Research assessing pregnant women's preferences for IPTp delivery highlights a demand for integrated services; the logistics and trust engendered by such combined provision could boost intervention uptake and coverage [25, 27]. A national assessment in Mali reinforced the logic of service integration as the foundation for scaling the WHO strategy targeting PAM control 28. Recent

scale-up in the integration of preventive, promotive, and curative reproductive health services similarly stresses the role of healthcare providers, indicating that full implementation of the WHO policy depends critically on their training, coverage, and engagement [16, 27].

Cultural Perspectives

Cultural beliefs and practices constitute important constructs that can help to explain the local perceptions of symptoms, treatment options and barriers to the uptake of interventions against malaria in pregnancy [1, 29]. These may, in turn, inform the design of culturally sensitive service-delivery approaches, which are more likely to be effective, efficient and accessible when incorporated within antenatal care services [2, 29]. Health-care professionals and stakeholders who are involved in migratory-work programmes need to take these cultural and social barriers into account when promoting the uptake of effective interventions, especially in the case of displaced persons who are less likely to have been sensitized during previous health promotion programmes. Within this context, there is an urgent need to adapt the delivery of services to improve quality, uptake and adherence to evidence-based interventions to prevent the negative effects of malaria in pregnancy [3, 29].

Beliefs and Practices Related to Malaria

Malaria is among the most important parasitic diseases affecting maternal and infant health in developing countries [30]. During pregnancy, malaria is associated with an increased risk of maternal mortality, stillbirth, spontaneous abortion and low birth-weight [28]. The impact of pregnancy-associated malaria is particularly high in sub-Saharan Africa, providing one of the strongest arguments for malaria control in Africa to focus on pregnant women [30]. Health care providers need to understand beliefs and practices surrounding pregnancy in order to identify potentially harmful attitudes and behaviour. In this context, qualitative research is important to explore local beliefs and customs, social and cultural factors and the limited perception of the susceptibility of pregnant women to malaria [4] Management of symptoms, perceived danger and acceptable treatment options are conditioned by cultural concerns; awareness of these elements will help the design of better health education materials and the dissemination of interventions aimed at the reduction of pregnancy-related malaria risks, thereby allowing health workers to implement appropriate strategies to reduce maternal and perinatal mortality and morbidity in these settings[7,30].

Addressing Cultural Barriers

In sub-Saharan Africa, cultural barriers have long limited the effectiveness of malaria interventions during pregnancy [19]. The World Health Organization (WHO) recommends a package of interventions to reduce malaria in pregnancy and its associated morbidity and mortality: insecticide-treated nets, intermittent preventive treatment (IPT), and effective case management [30]. However, the effectiveness of each intervention depends on the attitudes and behaviours of the pregnant women who are intended to benefit. Social and cultural factors also influence compliance with intervention policy and the use of services for preventive treatment, case management of malaria and pregnancy, and the use of ITNs. Cultural barriers affect women's access to services and their ability to prevent and treat malaria both before and during pregnancy [32]. Furthermore, the influence of these cultural barriers differs between community settings and varies according to each individual intervention. One key factor influencing uptake of interventions is women's use of antenatal care (ANC) [29]. Qualitative research to explore cultural factors influencing malaria in pregnancy interventions has provided valuable insight to the conceptual framework of cultural constraints to healthcare access and effective health-seeking behaviour [29]. This evidence has also led to the development of pilot interventions to help remove these cultural barriers to uptake [31]. An improved understanding of the wider social and cultural environment is therefore fundamental to the successful prevention, control, and treatment of malaria in pregnancy and to the effective implementation and delivery of intervention programmes and policies [32].

CONCLUSION

Pregnancy-associated malaria remains a leading cause of preventable maternal and neonatal morbidity and mortality in malaria-endemic regions. The unique pathophysiology of placental sequestration underpins its devastating consequences, including maternal anaemia, miscarriage, stillbirth, and low birth weight. Despite progress with ITNs, IRS, and IPTp, significant challenges persist, particularly in the areas of diagnosis, drug resistance, socioeconomic inequities, and cultural acceptance of interventions. Addressing PAM effectively requires a comprehensive and context-sensitive approach that integrates sensitive diagnostic tools, accessible preventive and curative measures, robust antenatal health services, and sustained community engagement. Strengthening health systems, advancing research, and prioritizing maternal health in malaria control programs are essential to reduce the burden of PAM. Ultimately, tackling this hidden but deadly form of malaria will be pivotal in improving maternal and child survival and achieving global malaria elimination goals.

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CITE AS: Kibibi Muthoni L. (2025). Pregnancy-Associated Malaria: Evidence and Interventions. Research Output Journal of Biological and Applied Science 5(3):73-86.
https://doi.org/10.59298/ROJBAS/2025/537386