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Sub-Saharan Africa Pregnant Women: Intermittent Preventive Therapy and Malaria-Related Birth Outcomes

Winniefred Nankya

Department of Clinical Pharmacy Kampala International University Uganda
Email:winniefred.nankya@studwc.kiu.ac.ug

ABSTRACT

Malaria in pregnancy remains a major public health concern in sub-Saharan Africa, where transmission intensity is high and pregnant women are particularly vulnerable to infection. Physiological and immunological changes during pregnancy increase susceptibility to *Plasmodium falciparum*, leading to adverse maternal and fetal outcomes. Intermittent preventive therapy in pregnancy has been adopted as a core strategy to reduce malaria burden and improve birth outcomes. The purpose of this review was to critically examine the biochemical and pathophysiological basis of malaria in pregnancy, assess the effectiveness of intermittent preventive therapy, and evaluate its impact on malaria-related birth outcomes among pregnant women in sub-Saharan Africa. This article was developed through a narrative review of peer-reviewed literature focusing on malaria pathogenesis, pharmacology of preventive therapy, and maternal and neonatal outcomes. Evidence indicated that intermittent preventive therapy significantly reduced placental parasitemia, maternal anemia, low birth weight, and preterm delivery, although effectiveness is influenced by drug resistance, coverage gaps, and health system challenges. Intermittent preventive therapy remained a highly effective intervention for improving pregnancy outcomes in malaria-endemic regions, but sustained optimization of implementation and surveillance is essential to maintain its benefits.

Keywords: Malaria in pregnancy, Intermittent preventive therapy, Sub-Saharan Africa, Birth outcomes, *Plasmodium falciparum*.

INTRODUCTION

Malaria continues to pose a substantial threat to maternal and neonatal health in sub-Saharan Africa, accounting for a significant proportion of preventable morbidity and mortality during pregnancy [1, 2]. Pregnant women represent a uniquely vulnerable population due to immunological modulation, hormonal changes, and the development of the placenta, which creates a niche for *Plasmodium falciparum* sequestration [3, 4]. Malaria infection during pregnancy is associated with adverse outcomes including maternal anemia, placental malaria, low birth weight, preterm delivery, stillbirth, and increased neonatal mortality.

Intermittent preventive therapy in pregnancy was introduced as a public health strategy to reduce the burden of malaria and its consequences among pregnant women in areas of moderate to high transmission [5]. This approach involves the administration of full therapeutic doses of antimalarial drugs at predefined intervals during pregnancy, regardless of infection status. Sulfadoxine-pyrimethamine has been widely used due to its long half-life, safety profile, and ease of administration [6]. Despite its proven effectiveness, challenges such as drug resistance, inconsistent uptake, and health system limitations threaten optimal program performance.

The persistence of malaria-related adverse birth outcomes highlights a critical public health problem, particularly in resource-limited settings where antenatal care access may be suboptimal [7]. Understanding the biochemical mechanisms of malaria pathogenesis, the pharmacological rationale for preventive therapy, and the clinical impact on maternal and fetal outcomes is essential for refining prevention strategies. This review examines the pathophysiology of malaria in pregnancy, the principles and implementation of intermittent preventive therapy, its effects on maternal health and birth outcomes, and the broader public health challenges influencing program success. The purpose of this article is to provide an integrated biochemical, clinical, and public health perspective to inform research, policy development, and improved maternal care practices.

Biochemical and Pathophysiological Basis of Malaria in Pregnancy

Pregnancy induces complex physiological and immunological adaptations that increase susceptibility to malaria infection. A key pathological feature of malaria in pregnancy is placental sequestration of *Plasmodium falciparum-infected* erythrocytes [8]. These parasites express variant surface antigens, particularly VAR2CSA, which bind to chondroitin sulfate A on placental syncytiotrophoblasts. This interaction facilitates parasite accumulation in the placenta, even in women with preexisting immunity to malaria.

Placental malaria triggers a localized inflammatory response characterized by infiltration of monocytes and increased production of proinflammatory cytokines [9]. These biochemical changes impair placental nutrient transport, disrupt oxygen exchange, and compromise fetal growth. Additionally, malaria infection contributes to oxidative stress and altered iron metabolism, exacerbating maternal anemia and reducing oxygen delivery to the fetus.

Primigravidae are particularly vulnerable due to lack of immunity to placental-binding parasite variants, while multigravidae gradually acquire protective antibodies. The biochemical consequences of placental infection provide a mechanistic explanation for adverse birth outcomes and underscore the importance of preventive strategies that reduce parasite exposure throughout pregnancy.

Intermittent Preventive Therapy in Pregnancy: Pharmacological Rationale and Implementation

Intermittent preventive therapy in pregnancy is designed to clear existing parasitemia and prevent new infections during critical stages of fetal development [10]. Sulfadoxine-pyrimethamine, the most commonly used drug for this intervention, acts by inhibiting folate synthesis pathways essential for parasite DNA replication [11, 12]. Its long elimination half-life allows sustained antimalarial activity between doses.

From a pharmacological standpoint, administering therapeutic doses at scheduled antenatal visits ensures adequate drug exposure while minimizing the need for diagnostic testing. The strategy is particularly effective in high transmission settings where asymptomatic infections are common and contribute significantly to placental malaria.

Implementation of intermittent preventive therapy in sub-Saharan Africa is typically integrated into routine antenatal care services. World Health Organization guidelines recommend administration of intermittent preventive therapy beginning in the second trimester, with repeated doses at least one month apart [13]. Despite widespread adoption, coverage remains uneven due to factors such as late antenatal attendance, drug stockouts, and limited health worker training. These implementation challenges directly influence the effectiveness of the intervention.

Impact of Malaria and Preventive Therapy on Maternal Health Outcomes

Malaria during pregnancy is a major contributor to maternal anemia, which increases the risk of maternal morbidity, hemorrhage, and mortality [14]. Anemia arises from hemolysis of infected erythrocytes, suppressed erythropoiesis, and inflammatory-mediated iron sequestration. Intermittent preventive therapy has been shown to significantly reduce the prevalence and severity of maternal anemia by preventing recurrent infections.

In addition to anemia, malaria infection increases the risk of febrile illness and hospitalization during pregnancy [15]. Preventive therapy reduces parasitemia and inflammatory burden, contributing to improved maternal well-being and reduced health system utilization. Biochemically, reduced parasite load limits oxidative stress and preserves red blood cell integrity, supporting improved hematological parameters.

However, the effectiveness of preventive therapy is influenced by drug resistance, particularly resistance to sulfadoxine-pyrimethamine. Although partial resistance reduces parasitological efficacy, studies indicate that the drug retains sufficient activity to confer clinical benefits, especially when administered consistently throughout pregnancy.

Effects of Intermittent Preventive Therapy on Malaria-Related Birth Outcomes

Low birth weight is the most consistently reported adverse outcome of malaria in pregnancy and is a major determinant of infant morbidity and mortality [16]. Placental malaria interferes with fetal growth through impaired nutrient transfer and chronic inflammation. Intermittent preventive therapy significantly reduces the incidence of low birth weight by preventing placental infection and improving placental function.

Preterm delivery and stillbirth are also associated with malaria-related placental pathology [17, 18]. By reducing parasite burden and inflammatory responses, preventive therapy lowers the risk of premature labor and fetal loss. Several large-scale studies have demonstrated improved mean birth weight and reduced neonatal mortality among infants born to mothers who received adequate preventive therapy doses.

The magnitude of benefit varies depending on transmission intensity, gravidity, and adherence to dosing schedules. Importantly, the protective effects extend beyond parasite clearance, suggesting that even in areas of reduced drug sensitivity, intermittent preventive therapy continues to provide meaningful improvements in birth outcomes.

Public Health Challenges and Future Directions

Despite strong evidence supporting intermittent preventive therapy, several challenges limit its full impact in sub-Saharan Africa. Drug resistance, particularly increasing resistance to sulfadoxine-pyrimethamine, raises concerns regarding long-term sustainability [19, 20]. While alternative drugs are under investigation, safety, cost, and feasibility remain critical considerations [21].

Health system factors such as inadequate antenatal care attendance, supply chain disruptions, and inconsistent policy implementation also undermine coverage [22]. Sociocultural barriers, including limited awareness and misconceptions about medication use during pregnancy, further reduce uptake.

Future strategies should focus on strengthening antenatal care systems, enhancing community engagement, and expanding surveillance of drug resistance markers. From a research perspective, identifying new preventive agents and optimizing combination strategies represent important priorities. Integrating biochemical insights with public health interventions will be essential for advancing malaria prevention in pregnancy.

CONCLUSION

Malaria in pregnancy continues to pose a significant threat to maternal and neonatal health in sub-Saharan Africa, driven by unique biochemical and pathophysiological mechanisms that promote placental infection and adverse birth outcomes. Intermittent preventive therapy has proven to be an effective intervention, reducing maternal anemia, placental parasitemia, low birth weight, and neonatal mortality. Although challenges such as drug resistance and implementation gaps persist, the overall benefits of preventive therapy remain substantial. Sustained commitment to surveillance, health system strengthening, and research innovation is essential to preserve and enhance these gains. It is recommended that sub-Saharan African countries intensify antenatal-based delivery of intermittent preventive therapy while supporting research into safe and effective alternative antimalarial agents for pregnant women.

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