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REVIEW
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Poor Birth Outcomes in Malaria in Pregnancy: Recent Insights Into Mechanisms and Prevention Approaches

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Pregnant women in malaria-endemic regions are susceptible to malaria in pregnancy, which has adverse consequences on birth outcomes, including having small for gestational age and preterm babies. These babies are likely to have low birthweights, which predisposes to infant mortality and lifelong morbidities. During malaria in pregnancy, *Plasmodium falciparum*-infected erythrocytes express a unique variant surface antigen, VAR2CSA, that mediates sequestration in the placenta. This process may initiate a range of host responses that contribute to placental inflammation and dysregulated placental development, which affects placental vasculogenesis, angiogenesis and nutrient transport. Collectively, these result in the impairment of placental functions, affecting fetal development. In this review, we provide an overview of malaria in pregnancy and the different pathological pathways leading to malaria in pregnancy-associated low birthweight. We also discuss current prevention and management strategies for malaria in pregnancy, and some potential therapeutic interventions that may improve birth outcomes. Lastly, we outline some priorities for future research that could bring us one step closer to reducing this health burden.

Keywords: low birthweight, preterm birth, small for gestational age, malaria, pregnancy, VAR2CSA

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INTRODUCTION

Global efforts to combat malaria have resulted in declining malaria transmission in many regions over the last decade. Unfortunately, young children and pregnant women remain vulnerable, especially in areas with sustained transmission. Malaria, a disease caused by the *Plasmodium* spp. parasite, can result in severe morbidity and mortality. Worldwide, infection with *Plasmodium falciparum* contributes to the highest burden, and it will be the main focus of this review (1). Despite childhood exposure that leads to acquisition of immunity against malaria, first time pregnant mothers or primigravidas are again susceptible to the disease due to a combination of host and parasitic factors (2, 3). Malaria in pregnancy (MiP) results in placental infection, termed placental malaria (PM), which predisposes to placental injury and insufficiency. Placental insufficiency refers to poor placental function and is commonly observed in PM. It is also hypothesized to be a leading cause of low birthweight (LBW). A baby with LBW is defined as a live born who is <2,500 g regardless of gestational age (4). LBW deliveries can be due to preterm birth (live birth < 37 gestational weeks) or small for gestational age (SGA) (birthweight < 10th percentile for its