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REVIEW
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Malaria in Pregnancy: From Placental Infection to Its Abnormal Development and Damage

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Malaria remains a global health burden with *Plasmodium falciparum* accounting for the highest mortality and morbidity. Malaria in pregnancy can lead to the development of placental malaria, where *P. falciparum*-infected erythrocytes adhere to placental receptors, triggering placental inflammation and subsequent damage, causing harm to both mother and her infant. Histopathological studies of *P. falciparum*-infected placentas revealed various placental abnormalities such as excessive perivillous fibrinoid deposits, breakdown of syncytiotrophoblast integrity, trophoblast basal lamina thickening, increased syncytial knotting, and accumulation of mononuclear immune cells within intervillous spaces. These events in turn, are likely to impair placental development and function, ultimately causing placental insufficiency, intrauterine growth restriction, preterm delivery and low birth weight. Hence, a better understanding of the mechanisms behind placental alterations and damage during placental malaria is needed for the design of effective interventions. In this review, using evidence from human studies and murine models, an integrated view on the potential mechanisms underlying placental pathologies in malaria in pregnancy is provided. The molecular, immunological and metabolic changes in infected placentas that reflect their responses to the parasitic infection and injury are discussed. Finally, potential models that can be used by researchers to improve our understanding on the pathogenesis of malaria in pregnancy and placental pathologies are presented.

Keywords: low birth weight, preterm birth, malaria, pregnancy, *Plasmodium falciparum*, syncytiotrophoblast, placental insufficiency, fetal growth restriction

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INTRODUCTION

Malaria is a blood-borne disease caused by *Plasmodium* spp., with *Plasmodium falciparum* (*P. falciparum*) being the most deadly species (World Health Organization [WHO], 2020). Pregnant women, especially first-time mothers, are at high risk of severe malaria due to *P. falciparum*, hence *P. falciparum*-related malaria in pregnancy (MiP) will be the focus of this review. Long-term childhood exposure to the parasites can result in the development of protective antibodies; however,