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Maternal-Child Health

Interdisciplinary Aspects Within the Perspective of Global Health



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16. Malaria in Pregnancy: The Parasite Infection Mechanism

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Plasmodium vivax (P.vivax) malaria is the most widely distributed species of human malaria, threatening nearly 3 billion people in 95 countries ranging from temperate to tropical in the Americas, Africa, Asia. In Indonesia, it is estimated that nearly 129,6 million people lived at risk of P.vivax transmission in 2010 (Elyazar et al., 2012). The number of patients with P.vivax malaria annually reaches 72-80 million cases per year, and the highest rate is in Asia (Luxemburger et al., 2001). By contrast, in Africa the number of people with P.vivax malaria is low, due to low prevalence of Duffy antigen which serves as receptor for the invasion of merozoites of P. vivax into red blood cells (Mendis et al., 2001). Malaria in pregnancy can be caused by all human-pathogenic species of Plasmodium, but P.vivax and P.falciparum are the most common parasites that cause infection in pregnant wom-

en. *Plasmodium falciparum* as the predominant parasite has the most severe impact on morbidity and mortality of mother and foetus (Mc Gregor, 1984).

In order to invade host erythrocytes, *P. vivax* requires a cell receptor, for example the Duffy antigen. Unlike *P. falciparum* that can invade red blood cells of all ages, *P. vivax* only invades reticulocytes. *Plasmodium vivax* also has a longer incubation period (12 days to several months) with the erythrocyte cycle of 42-48 hours and the production of 12-24 merozoites per schizont (Collins et al., 2004). The ability of *P. falciparum* to adhere to the endothelium of blood vessels causes the occurrence of severe malaria in *P. falciparum*-infected patients (Rogerson et al., 2004). In contrast, *P. vivax*-infected erythrocytes change their shape cannot attach to the endothelium of blood vessels and thus, rarely progresses to severe malaria (Suwanarusk et al., 2004).

Pregnant women in malaria-endemic areas are highly susceptible, especially in primigravidae. The main factors are related to low cellular immunity and the placenta which unfortunately favors the parasite to multiply (Espinosa et al., 2004). Malaria has an impact on the mother and foetus causing maternal anemia and low birth weight (LBW).

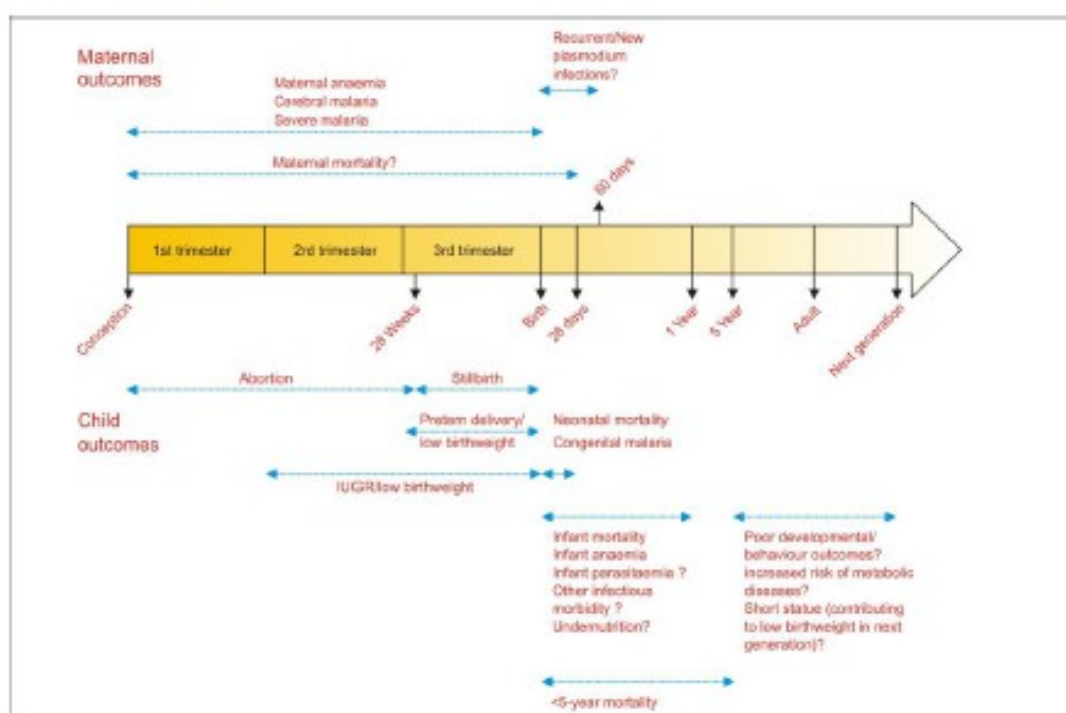


Figure 1: Effect of malaria in pregnancy on maternal, newborn, infant, and child health (Desai M, et al., 2007), own presentation.

LBW is related with specific changes in the placenta where parasites mature and accumulate in high density of the placental intervillous space. Sequestration in the placenta is mediated by the receptor chondroitin sulphate A (CSA) and hyaluronic acid (HA), expressed by the syncytiotrophoblast placental intervillous space limit (Matejevic, 2001). To enable the attachment between parasitized erythrocytes with receptors in the placenta, the erythrocytes express variant surface antigens (VSA). The dominant VSA on the surface is *P.falciparum* Erythrocyte Membrane Protein 1 (PfEMP1) encoded by the var multigene family (Newbold et al., 1992, Smith et al., 1995; Noviyanti et al., 2007). Adhesion mediated by VSA results in changes of inflammatory cytokines in the placenta, such as an increase of TNF- α , interleukin (IL) 2 and interferon (IFN)- λ (Fried et al., 1998), which finally is associated with low birth weight and anemia.

The existence of TH1 cytokines as a response to the parasites results in excessive adverse effects. Despite this, IL-10 is important to regulate the inflammatory cytokine effect, foetal trophoblasts and maternal leukocytes. Expressing IL-10 in high concentrations to protect the foetus from the inflammatory reaction will suppress anti-inflammatory responses against parasites and thus, the parasite persists in the placenta. This situation affects the incidence of severe anemia and preterm birth (Suguitan et al., 2003).

Unlike *P.falciparum*, *P.vivax* is not able to cause parasite sequestration in the placenta and placental pathologic changes. In the placenta, hemozoin can only be found slightly which is produced from hemoglobin catabolism within Plasmodium-infected erythrocytes. Its presence is an indication of placental infection and it is associated with decreased foetal weight (Rogerson et al., 2003). Histological pictures of the active form of placental infection show black/gray colour, dense sinusoid with infected erythrocytes. Syncytial knots can occur with fibrinoid necrosis and thickening of the basal membrane and damage of trophoblasts (Suparman, 2005).

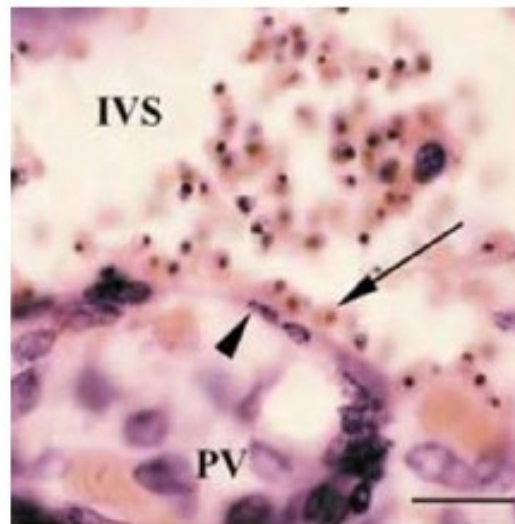


Figure 2: Histopathology of the infected placental tissue.

Some *Plasmodium falciparum*-infected erythrocytes (arrow) in the intervillous space (IVS) appear to be directly adherent to the surface of the syncytiotrophoblast cell layer (arrowhead) of a placental villus (PV). Scale bar = ~20 μm . (Beeson et al. 2001).

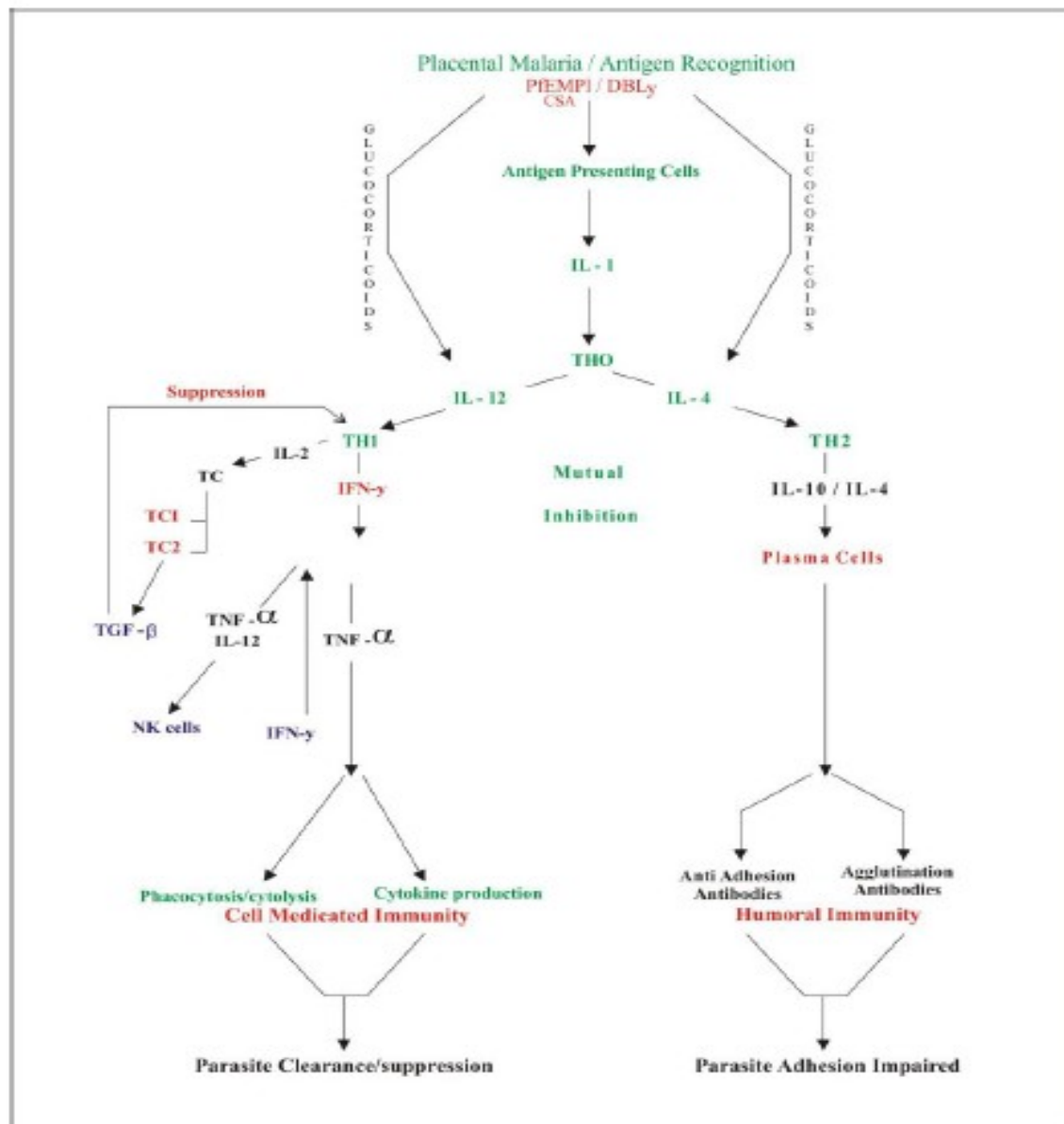


Figure 3: Placenta-related mechanisms of malaria parasite clearance, suppression and adhesion (Brabin BJ, et al., 2004), own presentation.

Abbreviation: *PfEMP*, *P. falciparum* erythrocyte membrane protein; *DBLy*, Duffy binding like domain- γ ; *CSA*, chondroitin sulphate A; NK, natural killer cells; *IFN γ* , interferon γ ; *TGF β* , transforming growth factor β ; TC, cytotoxic T cell; TH0, T helper (precursor).

The placenta has the function as a protective barrier against various pathogens present in the mother's blood, but the accumulation of erythrocytes infected with *P.falciparum* in the placental intervillous space can affect the mother and the foetus. In conclusion, malaria infection in pregnancy can cause severe anemia and low birth weight and increases the risk of death (Khong et al., 2006).

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