EDITORIAL

PLACENTAL MALARIA- INSIGHT INTO VACCINE DEVELOPMENT

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Malaria in pregnancy, a life-threatening situation for both mother and developing fetus, results in multiple complications, from low birth weight to still birth or abortion. Usually a healthy person after the parasitic infection, develop some immunity, but the pregnant status of a female lowers the protective immunity against Plasmodium falciparum which is worldwide considered as the most dangerous specie of all four human infecting malarial parasites. It is estimated that 125 million women worldwide, are threatened with malarial catastrophes which includes around 10,000 maternal and 200,000 neonatal deaths every year[1]. According to a study conducted in Pakistan in 2004, it was observed that mostly the pregnant patients get infected with Plasmodium vivax, but the majority of complications of malaria are associated with Plasmodium falciparum[2]. In Pakistan, Malarial infections are endemic, commonly caused by Plasmodium vivax, but now around 35-40% of cases are being reported with Plasmodium falciparum.[3]

The drop in protective immunity which makes the woman and fetus vulnerable is due to sequestration of Plasmodium falciparum-infected RBCs in the placenta which obstruct in the placental transmission of essential nutrients leading to complications. Infected RBCs infiltrate the intervillous spaces of placenta and adhere to chondroitin sulfate A (CSA) on placental proteoglycans. This helps the parasite to escape safely without detection by filtering through spleen and also blocks the maternal nutrients flow to the fetus which is extremely crucial for its survival[4]. This leads to an extreme inflammatory response increasing cytokines and inflammatory cell which results in oxidative stress-induced placental cell death. This change in immune status from antibody-mediated to cell-mediated immune response is the major cause of fatal morbidities.

Currently, researchers are working on vaccine targeting Variant Surface antigen 2-CSA (var2csa), protein specific of Plasmodium falciparum parasite. Previous studies showed that Parasite clones with disrupted var2csa gene blocked the binding ability of erythrocytes to adhere to CSA.[5] The protein, var2csa, is specific of Plasmodium falciparum's erythrocyte membrane protein 1 (PfEMP1) family, containing 6 domains called Duffy binding-like (DBL1 to DBL6) domains. Among these domains DBL2, DBL3, and DBL6 with highest CSA binding affinity have been identified to target for vaccine development. Antibodies once developed for these domains, would prevent parasite-infected erythrocytes to adhere to the placenta.[6]

For developing this vaccine, the researchers are studying the global diversity of the target var2csa gene, since this could influence the efficacy of vaccine. A recent study published in October 2018[7] studied genetic diversity of the var2csa gene across more than 23 countries. The phylogenetics of the sequences revealed that frequency of SNPs and Insertions and deletions are high at this locus, generating significant haplotype diversity. Among the 23 strains studied the diversity was found highest across parasites of African populations with greater fraction of unique haplotypes which indicate higher transmission intensity in them. The researchers on the basis of diversity patterns hypothesized that a vaccine designed and introduced on the single haplotype or a few heterologous haplotypes might be beneficial for endemic area in South East Asia but it might not be that effective in Africa where it is needed most. However, these findings can be exceedingly helpful not only in developing new preventive tools, but also in designing new vaccines against placental malaria.

In Pakistan, the cause of morbidity and mortality during pregnancy sometimes goes unidentified especially in the rural areas, where malaria is highly endemic. Generally, during pregnancy the patients do not demonstrate apparent malarial signs and symptoms and therefore, go undiagnosed for malaria. The reason for this condition is the above mentioned complications and maternal death due to build up and sequestration of the malarial parasites in the placenta hence are unavailable in the peripheral blood for diagnosis. Antenatal should be enforced in remote areas through midwives or health workers for preventive healthcare where the parasite is endemic.

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