Introduction

Malaria prevention, control, and ultimately, elimination feature one of the most important public health challenges nowadays. Malaria-associated maternal illness and low birth weight is mostly the result of *Plasmodium falciparum* infection of pregnant women and occurs predominantly in Africa[1].

**OBJECTIVE** The aim of this review is to elucidate the current situation of the immunopathogenesis of malaria on pregnant women and which area requires further investigation.

Methods: search strategy

A systematic literature search in PubMed database was conducted between January and March 2015 using the combination of keywords including: “Malaria” AND “Pregnancy” OR “Immunity” OR “VAR2CSA” OR “Placenta”.

DIFERENCES BETWEEN INFECTED ERYTHROCYTES (IEs)[2]

<table>
<thead>
<tr>
<th>Parameter</th>
<th>IEs from the placenta of pregnant women</th>
<th>IEs from non-pregnant individuals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adhesion to CSA</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Adhesion to CD36, ICAM-1</td>
<td>No</td>
<td>Common</td>
</tr>
<tr>
<td>Rosetting</td>
<td>No</td>
<td>Common</td>
</tr>
<tr>
<td>Agglutination</td>
<td>Variable</td>
<td>Common</td>
</tr>
<tr>
<td>Non-specific binding of IgM to IEs</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Sex-specific IgG recognition of variant surface antigens</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Parity-dependent IgG recognition of variant surface antigens</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

Cytokine balance

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>Pregnant healthy women</th>
<th>Malaria pregnant women</th>
<th>Maternal anaemia, spontaneous abortions, low birth weight and pre-term delivery[3]</th>
<th>Susceptibility to malaria may spread into later gravities, and among the infants who are infected[3]</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑Tn12</td>
<td>IL-10</td>
<td>IL-12</td>
<td>TNF-α IFN-γ IL-18 IL-2</td>
<td></td>
</tr>
<tr>
<td>↓Tn1</td>
<td>IL-4●</td>
<td>IL-6●</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Malaria control implications in natural acquired immunity

- Exposure to malaria may fall
- Antibody to placental-binding IEs may be less developed
- Susceptibility to malaria may spread into later gravities, and among the infants who are infected[3]
- How long does immunity in pregnant women last?

Humoral immunity

Chondroitin Sulphate A (CSA)-binding IEs

No immunity to pregnancy associated malaria (PAM)

VAR2CSA protein in IEs surface

Immunity to PAM

Antibodies block placenta adhesion and/or trigger removal by monocytes

Cytoadherence and multigraftae protection

Adhesion to the CSA of the placenta

Several expositions along successive pregnancies

Highly variable and complex structure

→ Cross-reactive epitopes have been recently identified[4], which represent a key element to develop a VAR2CSA-based vaccine

Conclusion

The greatest difficulty of the malaria immune response is the complex, multistage, multiantigen life cycle of *Plasmodium*, that adheres to the placenta mediating the VAR2CSA protein. There is a reduction of IgG transference from mother to foetus and the cytokine balance is directed towards a strong Tn1 response.

**RESEARCH NEEDS:**

- A novel VAR2CSA-based vaccine
- The role of protective maternal antibodies in the newborn
- Evaluation of intermittent preventive treatment regimens, the emerging resistance outcomes and new rapid diagnosis techniques
- Studies with *Plasmodium vivax* and *Plasmodium knowlesi*
- Co-infection with other pathogens such as HIV and Dengue

References


Fig. 1. Countries with ongoing transmission of malaria, 2013[3]

Fig. 2. Binding of infected erythrocytes to the placenta[4]

Fig. 3. VAR2CSA mediated IE binding to placental CSA[7]

Fig. 4. Adhesion to CSA of the placenta

Fig. 5. No immunity to pregnancy associated malaria (PAM)

Fig. 6. Var2CSA protein in IEs surface

Fig. 7. Immunity to PAM

Fig. 8. Antibodies block placenta adhesion and/or trigger removal by monocytes