#267 Efficacy and Tolerability of Artemisinin- and Quinine-based Treatments for Uncomplicated Falciparum Malaria During Pregnancy: A WWARN Individual Patient Data Meta-analysis

**Background**

- Treatment of uncomplicated falciparum malaria in pregnancy has been neglected: paucity of efficacy studies particularly RCTs and lack of standard methodology make aggregated data meta-analysis difficult.
- Risk factors for treatment failure (PCR-confirmed recrudescence) not fully understood.

**Objectives**

- To summarise the available evidence on the efficacy and tolerability of antimalarials for pregnant women in the world.
- To investigate risk factors for PCR-corrected treatment failure in pregnancy.

**Methods**

- Literature search to identify relevant articles assessing efficacy of artemisinin-based (ABT) or quinine-based treatment (QBT).
- Principal investigators invited to join and contribute individual patient data.
- Random effects Cox's regression model (for treatment failure) or logistic regression (for other outcomes).

**Find out more**

- info@iddo.org
- info@wwarn.org
- @IDDOnews @WWARN

**Results**

- Data shared from 19 studies out of 28 trials identified (Fig 1)
  - 4968 episodes included (92% of total data - 4968/5360)
  - 10 antimalarial treatments

- PCR-corrected treatment failure compared with artemether-lumefantrine (AL) (Table):
  - Lower in artesunate-amodiaquine (ASAQ), artesunate-mefloquine (ASMQ), dihydroartemisinin-piperaquine (DP) and artesunate-clindamycin (AC).
  - Higher in quinine monotherapy (Q).
  - Higher baseline asexual parasitaemia load and nulliparous women (in moderate and high malaria transmission areas) associated with higher risk of failure.

**Table. Risk factors associated with PCR-corrected treatment failure**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Number of failure / all</th>
<th>Multivariable Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>HR (95% CI)</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AAP</td>
<td>2/91</td>
<td>0.31 (0.06-1.61)</td>
</tr>
<tr>
<td>AC</td>
<td>6/142</td>
<td>0.37 (0.15-0.91)</td>
</tr>
<tr>
<td>AS</td>
<td>15/230</td>
<td>0.64 (0.34-1.23)</td>
</tr>
<tr>
<td>ASSP</td>
<td>4/173</td>
<td>2.05 (0.38-11.03)</td>
</tr>
<tr>
<td>ASAQ</td>
<td>12/841</td>
<td>0.27 (0.14-0.52)</td>
</tr>
<tr>
<td>ASMQ</td>
<td>25/1,028</td>
<td>0.56 (0.34-0.94)</td>
</tr>
<tr>
<td>DP</td>
<td>14/874</td>
<td>0.35 (0.18-0.68)</td>
</tr>
<tr>
<td>Q</td>
<td>31/244</td>
<td>6.11 (2.57-14.54)</td>
</tr>
<tr>
<td>QC</td>
<td>1/67</td>
<td>0.46 (0.04-5.24)</td>
</tr>
<tr>
<td>Parity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>892/130</td>
<td>Reference</td>
</tr>
<tr>
<td>1</td>
<td>31/1,040</td>
<td>0.59 (0.39-0.89)</td>
</tr>
<tr>
<td>≥2</td>
<td>56/1,733</td>
<td>0.62 (0.44-0.89)</td>
</tr>
</tbody>
</table>

AAP: artesunate-ratoavagoon-proguanil, AS: artesunate monotherapy, ASSP: artesunate-sulfadoxine-pyrimetamine

**Conclusions**

- Performance of ACTs over quinine:
  - Higher adjusted efficacy (equivalent for supervised QC).
  - Longer post-treatment prophyaxis.
  - Lower adjusted risk of adverse symptoms.
  - Faster parasite clearance.
  - Impact on transmission: lower risk of gametocyte development.

- Risk factors for treatment failure:
  - Nulliparous women and higher baseline parasitaemia.
  - ACTs:
    - Higher adjusted efficacy of ASAQ, ASMQ and DP compared with AL.
    - Higher risk of adverse symptoms after ASAQ/ASMQ compared with AL.

**Figure 1. Geographical locations of the included 19 studies conducted between 1995 and 2014**

**Figure 2. Adverse symptoms developed after the treatment**

- Abdominal pain
- Anorexia
- Dizziness
- Headache
- Muscle/skeletal pain
- Nausea
- Tinnitus
- Vomiting
- Fatigue

- Adjusted odds ratio compared with AL.