The performance of Alere Malaria Ag P.f®, a highly sensitive malaria RDT (hsRDT) for screening, against PCR in Cambodia

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Background

• Médecins Sans Frontières (MSF) implements passive and active case detection of malaria in the Chey Saen district of Preah Vihear, an area of documented partial artesinin resistance and low P.f incidence.
• Since 2015, MSF teams run (bi)monthly screening rounds in the villages for asymptomatic forest and plantation workers at highest risk for malaria.
• In 2017, the HRP-2 based hsRDT (Alere Malaria Ag P.f®) replaced qPCR as screening tool for Plasmodium falciparum, aiming at a more replicable and cost-efficient strategy.

Study objectives

• to determine the performance of the hsRDT against PCR in this context
• to link the performance to the parasite density
• to investigate HRP2/3 deletions as potential reason of false negative hsRDT

Methodology

Context

• study implemented at the pro-active screening rounds targeting asymptomatic forest & plantation workers
• period: 5 October 2017 - 6 March 2018
• location: 11 screening locations in Chey Saen district (Preah Vihear, Cambodia)
• low yearly incidence 12.4/1000 (2017)

Procedure:

• standard procedure plus double reading hsRDT (maximum 1-2 minutes interval)
• dry blood spot for qPCR including estimation of parasite density and sequencing for HRP2/3 deletions (at the Institut Pasteur du Cambodge)
• criteria for exclusion from screening:
  • malaria treatment preceding 4 weeks
  • symptomatic patients (were referred to the village malaria worker)

The study has approval from the MSF and the Cambodian ERB

Results

• from the 2008 persons screened, 38 have a positive PCR (table 1).
• The hsRDT shows a good sensitivity for these asymptomatic persons and a high specificity (table 2).
• The qPCR based estimated parasite density, done only for P.f mono-infections (n=26), shows a low median level for the false negative hsRDT (table 3)
• only 1 discordant reading (1st reader negative, 2nd reader positive)
• no HRP2 deletions were identified among the 5 samples with sufficient DNA (including the sample with 369 p/µl).

Conclusions

• screening of persons at risk with hsRDT identifies a high proportion of the P.f carriers, including persons with significant parasite density, and misses mainly carriers with very low parasite density.
• the hsRDT can be a useful tool for screening in elimination setting to reduce the parasite reservoir, especially relevant in an area of artesinin resistance where more aggressive strategies to accelerate elimination of P.f malaria are indicated.

References


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Table 1. Screening results

<table>
<thead>
<tr>
<th>PCR</th>
<th>Positive</th>
<th>Negative</th>
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<tbody>
<tr>
<td>hs RDT Postive</td>
<td>25</td>
<td>2</td>
</tr>
<tr>
<td>Negative</td>
<td>13</td>
<td>1968</td>
</tr>
</tbody>
</table>

Sensitivity (with 95%CI): 66.6% (49-80%)
Specificity: 99.9% (99.6-99.9%)
Positive predictive value: 92.5% (75.7-99%)
Negative predictive value: 99.3% (98.9-99.6%)

Table 2. Performance indicators hsRDT compared to PCR (95 % CI)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Median estimated parasite density p/µl</th>
<th>Range</th>
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<tbody>
<tr>
<td>all (n=26)</td>
<td>204</td>
<td>(1-132236)</td>
</tr>
<tr>
<td>true positive hsRDT (n=17)</td>
<td>861</td>
<td>(8-132236)</td>
</tr>
<tr>
<td>false negative hsRDT (n=9)</td>
<td>2</td>
<td>(&lt;1-369)</td>
</tr>
</tbody>
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Table 3. Estimated P.f densities for true positive and false negative hsRDT

We recommend further investigation of discordant results before declaring persons as negative.

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