Household transmission of rotavirus in Malawian children with acute gastroenteritis is associated with disease severity

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Introduction

Rotavirus vaccine effectiveness is reduced in low income settings. Any additional effect of vaccine on transmission may improve overall impact

RVV: reduction in severe RVGE

Disease severity may relate to viral shedding density

Symptoms associated with risk of transmission

Potential for RVV to impact on infectiousness of rotavirus case
Study aims

Investigate risk factors for household rotavirus transmission in Blantyre, Malawi

• What is the SAR of rotavirus infection from a symptomatic index child to household contacts in Blantyre?
• What is the SAR of rotavirus disease from a symptomatic index child to household contacts in Blantyre?
• Is disease severity associated with rotavirus transmission to household contacts?
Study Design

**Age eligible RV +ve child**
- Questionnaire
- Severity scoring (Vesikari score)
- Vaccine status (Health passports)
- Stool sample: qRT-PCR for rotavirus viral load
- Blood sample: Serum IgA, HIV testing

**Household recruitment**
- Surveillance for clinical disease
- 2 stool samples from HH members
  - Real-time qRT-PCR for rotavirus

**Intensive cohort**
- 9 stool samples per HH member
- 28 days follow up

**Control households**
- Random location
- Contain child frequency age matched to index children
- Clinical data
- Stool sample for rotavirus testing (qRT-PCR)

**Diarrhoeal surveillance**
- Children under 5 years with AGE at QECH
- Clinical data
- Stool sample for rotavirus testing (EIA)

20 months
Methods: analytical

Secondary attack rate
- Infection: proportion of household contacts with >100 copies rotavirus on qRT-PCR
- Disease: proportion of household contacts with >100 copies rotavirus on qRT-PCR and symptoms of gastroenteritis
- Comparisons between proportions – chi squared tests

Predictive factors for transmission for infection and disease
- Hierarchical conceptual framework
- Poisson models with an exchangeable correlation matrix (GEE)
Distal susceptibility factors (household level)

- Household size
- Toilet type
- Shared toilet
- Distance to water
- Source of water
- Maternal education
- Household head education
- Number of people in household with a salary
- Has an adult in the house skipped a meal in the last month due to insufficient food?
- How often does the household have difficulty obtaining the food it needs?
- Wealth

Proximal susceptibility factors (individual contacts)

- Relationship to child
- Share room with child
- Share bed with child
- Share toilet with child
- Age of household contact
- Time spent with child
- Time spent in house
- HIV status
- Primary care giver for child
- Responsibility for changing nappy
- Under 5 household contacts only:
  - Rotavirus vaccine status
  - Prematurity
  - Birth weight
  - WHZ
  - WAZ
  - HAZ
  - MUAC

Infectiousness Factors (index child)

- Age
- Sex
- HIV exposure
- HIV infection
- Prematurity
- Birth weight
- Breast feeding
- Rotavirus vaccine status
- WHZ
- WAZ
- HAZ
- MUAC
- Vesikari score
- Diarrhoea duration (days)
- Diarrhoea frequency (per day)
- Vomiting
- Vomiting frequency
- Vomiting duration
- Dehydration
- Thirst
- Temperature
- Outcome
- Admission
- Viral load
- Genotype of rotavirus
Results: Index children

Recruitment from Jan 2015 to November 2016
196 symptomatic index children with 705 contacts
55 asymptomatic control children with 144 contacts

Characteristics of index children
• Median age 11.5 months (IQR 8.7, 15.5)
• 55% males (108/196)
• 13% HIV exposed (25/196)
• 99% vaccinated (194/196)
• Severe disease - median vesikari score of 14 (IQR 12, 16)

No significant difference between characteristics of index children and control children
## Secondary attack rates

<table>
<thead>
<tr>
<th>Infection</th>
<th>Clinical disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;= 100 copy numbers</td>
<td>Rotavirus positive clinical disease</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Study</th>
<th>Control</th>
<th>$\chi^2$ P**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>434/664 (65.4%)</td>
<td>40/144 (27.8%)</td>
<td>&lt;0.001 †</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Study</th>
<th>Control</th>
<th>$\chi^2$ P**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>37/701 (5.28%)</td>
<td>0/153 (0.0)</td>
<td>0.004 †</td>
</tr>
</tbody>
</table>
Risk factors for infection in household contacts

<table>
<thead>
<tr>
<th>Variable</th>
<th>RR</th>
<th>P Value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vesikari</td>
<td>1.04</td>
<td>0.007</td>
<td>1.01, 1.07</td>
</tr>
<tr>
<td>Age in months</td>
<td>1.00</td>
<td>0.821</td>
<td>1.00, 1.01</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>0.98</td>
<td>0.788</td>
<td>0.85, 1.13</td>
</tr>
<tr>
<td>Log viral copy number</td>
<td>1.01</td>
<td>0.360</td>
<td>0.99, 1.04</td>
</tr>
<tr>
<td>Number of adults with salary in household</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥1</td>
<td>0.82</td>
<td>0.002</td>
<td>0.72, 0.93</td>
</tr>
<tr>
<td>Problems getting food in the past month (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sometimes/often</td>
<td>0.90</td>
<td>0.192</td>
<td>0.76, 1.06</td>
</tr>
<tr>
<td>Relationship with child</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mother</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other adult relative</td>
<td>0.74</td>
<td>0.000</td>
<td>0.64, 0.85</td>
</tr>
<tr>
<td>Child contact</td>
<td>0.82</td>
<td>0.000</td>
<td>0.73, 0.91</td>
</tr>
<tr>
<td>Muac</td>
<td>1.07</td>
<td>0.006</td>
<td>1.02, 1.14</td>
</tr>
</tbody>
</table>
# Risk factors for disease in household contacts

<table>
<thead>
<tr>
<th>Disease</th>
<th>IRR</th>
<th>P value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vesikari score</td>
<td>1.27</td>
<td>0.001</td>
<td>1.09, 1.48</td>
</tr>
<tr>
<td>Age in months</td>
<td>1.02</td>
<td>0.396</td>
<td>0.98, 1.06</td>
</tr>
<tr>
<td>Log viral copy numbers</td>
<td>1.00</td>
<td>0.897</td>
<td>0.92, 1.10</td>
</tr>
<tr>
<td>Toilet type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simple pit/VIP</td>
<td>0.62</td>
<td>0.310</td>
<td>0.24, 1.57</td>
</tr>
<tr>
<td>Water toilet</td>
<td>0.34</td>
<td>0.341</td>
<td>0.04, 3.12</td>
</tr>
<tr>
<td>Skin pinch</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Goes back slowly</td>
<td>0.51</td>
<td>0.265</td>
<td>0.16, 1.66</td>
</tr>
<tr>
<td>Goes back very slowly</td>
<td>0.93</td>
<td>0.907</td>
<td>0.26, 3.14</td>
</tr>
<tr>
<td>Household member age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5 years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-15 years</td>
<td>0.15</td>
<td>0.001</td>
<td>0.05, 0.48</td>
</tr>
<tr>
<td>15-45 years</td>
<td>0.38</td>
<td>0.005</td>
<td>0.19, 0.75</td>
</tr>
<tr>
<td>45+ years</td>
<td>0.42</td>
<td>0.400</td>
<td>0.06, 3.13</td>
</tr>
</tbody>
</table>
Conclusions

Secondary attack rates for rotavirus infection are high (65%)
Attack rates for clinical disease are lower (5%)
Increasing disease severity in index children increases the risk of infection and disease in household contacts

Vaccination has potential to reduce infectiousness of a vaccinated index child and contribute to herd protection.
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