Highlights of data on rotavirus vaccine impact in a densely populated country in Africa: Rwanda

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Introduction

- Rwanda introduced pentavalent rotavirus vaccine (RV5; RotaTeq) May 2012
  - 3 oral doses at 6, 10, 14 weeks of age

- As first sub-Saharan GAVI-eligible country to introduce RV5, unique opportunity to generate data on vaccine impact and performance in high mortality, low income setting
Objectives

- To examine rotavirus vaccine uptake following introduction into national immunization program
- To monitor trends in rotavirus and acute watery diarrhea hospitalizations pre- and post-rotavirus vaccine introduction
- To describe changes in the epidemiology of rotavirus disease following vaccine introduction
- To determine the field effectiveness of RV5 under conditions of routine use
Methods

- **Rotavirus vaccine coverage and timing**
  - Obtained administrative coverage data from Ministry of Health
  - Compared with vaccine coverage from active surveillance platform
    - Determined coverage rotavirus negative children with card confirmed vaccination history
    - Calculated age at administration for each dose
  - Compared coverage of rotavirus vaccine with pentavalent vaccine
## Vaccine coverage among age-eligible children by year

<table>
<thead>
<tr>
<th></th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Surveillance Data</td>
<td>Administrative Data</td>
</tr>
<tr>
<td>Rotavirus vaccine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age-eligible to be</td>
<td></td>
<td></td>
</tr>
<tr>
<td>fully vaccinated*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=434)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 dose</td>
<td>99.5%</td>
<td>97.3%</td>
</tr>
<tr>
<td>2 doses</td>
<td>99.1%</td>
<td>97.3%</td>
</tr>
<tr>
<td>3 doses</td>
<td>98.4%</td>
<td>96.0%</td>
</tr>
<tr>
<td>Pentavalent vaccine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 doses</td>
<td>99.1%</td>
<td>96.2%</td>
</tr>
</tbody>
</table>

*Children >3 months of age*
Age at Rotavirus and Pentavalent Vaccination among All Vaccinated Children <5 Years of Age

Timeliness of Rotavirus Vaccination

<table>
<thead>
<tr>
<th>Dose 1: 6 weeks</th>
<th>± 1 week</th>
<th>± 2 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose 2: 10 weeks</td>
<td>70%</td>
<td>83%</td>
</tr>
<tr>
<td>Dose 3: 14 weeks</td>
<td>61%</td>
<td>77%</td>
</tr>
</tbody>
</table>
Methods

- Trends in rotavirus & acute watery diarrhea hospitalizations

  - Rotavirus hospitalizations
    - Active surveillance at a sentinel hospital from Jan 2011-Dec 2015
      - WHO generic protocol for rotavirus surveillance
  
  - Acute watery diarrhea hospitalizations
    - Review of admission registers for acute gastroenteritis admissions at 6 sentinel hospitals from Jan 2009 – Dec 2015
    - Review of Health Management Information System (HMIS) data for diarrhea hospitalizations at 24 district hospitals from Jan 2009 - Dec 2014
Rotavirus Detection by Month among Hospitalized Children <5 Year of Age at a District Hospital, January 2011-December 2015

Rotavirus vaccine introduction, May 2012

61%-70% reduction in rotavirus hospitalizations following vaccine introduction.
Total hospital and acute gastroenteritis (AGE) admissions and proportion of total hospitalizations due to diarrhea among children <5 years of age at 6 hospitals, 2009-2015

AGE admissions fell by 45%-49% from 19%-20% of all admissions among children <5 yrs of age to 12%-13%
Number of AGE hospitalizations by month among children <5 years of age, 6 hospitals, 2009-2015
Diarrhea hospitalizations by month among children <5 years of age at 24 district hospitals, HMIS, 2009-2014

Annual reductions of 17%-23% in diarrhea hospitalizations following rotavirus vaccination introduction, May 2012.
Diarrhea hospitalizations by pre (2009-2011) and post-rotavirus (2013 and 2014) vaccine introduction among children <5 years of age at 24 district hospitals, HMIS

Reductions in diarrhea hospitalizations of 27%-40% during the rotavirus season
Methods

- Changes in the epidemiology of rotavirus disease

  - Data from 8 hospitals conducting active surveillance
  - Changes in rotavirus detections by age group
  - Changes in rotavirus positivity including in age groups not directly protected by vaccination

55%-62% reduction in proportion of hosps due to rotavirus in children <5 years

Largest reductions observed in children age-eligible to receive rotavirus vaccine (3-11 months in 2013 and 3-23 months in 2014 and 2015)

Reductions were also observed in age groups not directly protected by the vaccine

Median age
Pre-vaccine: 11 months
Post-vaccine: 14 months
Methods

Effectiveness of rotavirus vaccination

- Case-control design built upon active surveillance platform

- **Cases**: vaccine age-eligible children with acute diarrhea (≥3 loose stools in 24 hrs) who are hospitalized at an active surveillance facility and test **positive** for rotavirus by enzyme immunoassay (EIA)

- **Test-negative controls**: vaccine age-eligible children with acute diarrhea (≥ 3 loose stools in 24 hrs) who are hospitalized at an active surveillance facility and test **negative** for rotavirus by EIA

- **Vaccination status** confirmed by vaccine card or clinic registry
  - Note: Rotavirus vaccine coverage was high and timely so few unvaccinated children in the comparison group
  - Examined children 7-18 weeks of age at time of vaccine introduction (born immediately prior to vaccine introduction 15 Jan-15 Apr 2012)

- Vaccine effectiveness = (1-Odds Ratio)*100
Rotavirus vaccine effectiveness among children born between 15 January and 15 April 2012

<table>
<thead>
<tr>
<th></th>
<th>Rota+ n (%)</th>
<th>Rota- n (%)</th>
<th>Unadjusted VE (95% CI)</th>
<th>Adjusted VE* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Children</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 doses</td>
<td>33 (87%)</td>
<td>76 (61%)</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>3 doses</td>
<td>5 (13%)</td>
<td>49 (39%)</td>
<td>76% (36%, 91%)</td>
<td>75% (31%, 91%)</td>
</tr>
<tr>
<td>Hospitalized Children</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 doses</td>
<td>26 (90%)</td>
<td>54 (60%)</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>3 doses</td>
<td>3 (10%)</td>
<td>36 (40%)</td>
<td>83% (38%, 95%)</td>
<td>80% (28%, 94%)</td>
</tr>
<tr>
<td>Children ≥6 and &lt;12 mths</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 doses</td>
<td>8 (80%)</td>
<td>41 (56%)</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>3 doses</td>
<td>2 (20%)</td>
<td>32 (44%)</td>
<td>68% (-61%, 94%)</td>
<td>65% (-80%, 93%)</td>
</tr>
<tr>
<td>Children ≥12 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 doses</td>
<td>25 (89%)</td>
<td>35 (67%)</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>3 doses</td>
<td>3 (11%)</td>
<td>17 (33%)</td>
<td>75% (6%, 93%)</td>
<td>81% (25%, 95%)</td>
</tr>
</tbody>
</table>
Conclusions

• Rotavirus vaccine coverage is high and vaccination is timely
  – 3 dose coverage is >99%
  – 77%-87% of children receive rotavirus vaccine within 2 weeks of recommended schedule

• Rotavirus positive decreased in all age groups pre- (2011) and post- (2013-2015) vaccine introduction
  – Greatest decrease occurred among children 3-23 months of age

• Proportion of total hospital admissions due to diarrhea decreased from ~20% pre-vaccine introduction to 13% post-vaccine introduction

• Annual peak in diarrheal hospitalizations, which corresponds to a peak in rotavirus disease, was substantially blunted in 2013 and 2014 compared to 2009-2011 baseline

• Vaccine is ~80% effective in preventing rotavirus hospitalizations and did not appear to wane
  – Analysis limited due to high vaccine coverage in vaccine eligible children
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