Rotavirus vaccine impact on diarrhea associated child mortality, hospital admissions & clinical visits in Bolivia

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Bolivian Ministry of Health-EPI:UMSA-IBMB:PAHO

12 Rotavirus Symposium: Melbourne, September 2016
Overview

• Background
• Bolivian Rotavirus Surveillance Network
• Rotavirus Vaccine Effectiveness Study
• Trend rates of diarrhea associated child mortality, hospital admissions: Pre-vaccine & post-vaccine period.
• NIDI study: Outpatient diarrhea.
• Summary of findings
## Bolivia: Basic Health & Population Indicators

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Bolivia</th>
<th>Low &amp; middle income countries</th>
<th>Latin America</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant mortality</td>
<td>50</td>
<td>44</td>
<td>18</td>
</tr>
<tr>
<td>Child mortality (under 5 years of age)</td>
<td>63</td>
<td>61</td>
<td>22</td>
</tr>
<tr>
<td>GNI per capita (US)</td>
<td>1460</td>
<td>2544</td>
<td>7057</td>
</tr>
<tr>
<td>Annual rate of population growth</td>
<td>2</td>
<td>1.3</td>
<td>1.2</td>
</tr>
</tbody>
</table>

ENDSA, 2006
World Bank Statistics
**Surveillance Protocol: 2005-2008**

### Surveillance of Diarrhea caused by Rotavirus among children hospitalized with diarrhea

- Expanded Immunization Program: Ministry of Health and Sports of Bolivia
- Pan American Health Organization
- Universidad Mayor de San Andrés
- Institute of Molecular Biology & Biotechnology
- National Bioethics Committee

### Suspected Case Definition:

All children under five years old hospitalized for diarrhea:

Presence of vomits and 3 or more loose stools in 24-h period.
National Rotavirus Surveillance Network

RV Surveillance

RV Epidemiology & Disease Burden

Evaluation of potential vaccine introduction

PAHO-EPI-IBMB
Rotavirus Disease Burden in Bolivia

**Event**

- **Death**: 534-913
- **Hospitalization**: 9484
- **Medical Visits**: 47570

**Cumulative Risk**

- 1:277 - 1:476
- 1:26
- 1:5

2007
Clinical and epidemiological characteristics: Burden of disease

Cost-effectiveness analysis

Sharing of results

Motion before the Treasury Department

Preparation of Operational Requirements

Vaccine introduction: August 2008

SEDES, local EPIs
Hospitals
Pediatric Society
National Immunization Committee

Ministry of Health and Sports

Government of Bolivia

EPI: Preparation of Operational Requirements

Implementation of Rotavirus Surveillance 2005

Implementation of Epidemiological Surveillance of ADD caused by rotavirus 2006

Ministry of Health and Sports

Government of Bolivia

Vaccine introduction: 2008
### Effectiveness of Rotavirus Vaccine against Rotavirus Disease

<table>
<thead>
<tr>
<th>Group</th>
<th>1 dose No/total (%)</th>
<th>2 doses No/total (%)</th>
<th>VE% (95% CI)</th>
<th>VE% (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Crude</td>
<td>Adjusted</td>
<td>Crude</td>
<td>Adjusted</td>
</tr>
<tr>
<td><strong>Rotavirus disease requiring hospital admission</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases</td>
<td>100/192 (52)</td>
<td>208/300 (69)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospital controls</td>
<td>226/343 (66)</td>
<td>857/954 (88)</td>
<td>57 (35-71)</td>
<td>80 (70-86)</td>
</tr>
<tr>
<td></td>
<td>56 (32-72)</td>
<td>77 (65-84)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test (-) controls</td>
<td>131/208 (63)</td>
<td>510/587 (87)</td>
<td>39 (8-60)</td>
<td>70 (56-79)</td>
</tr>
<tr>
<td></td>
<td>36 (0-59)</td>
<td>69 (54-79)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

March 2010 - June 2011
6 hospitals

Patel et al, 2013;
General Objective

To assess the impact of RV1 vaccine in diarrhea-associated deaths and hospital admissions in Bolivia.
Interrupted time-series analysis: children < than 5 years of age.

- **National Health Data Base Information System:**
- **Data from Rotavirus Bolivian Surveillance network for hospitalized children**

- **Regression analysis:** a generalized linear model: Poisson distribution.
- **Data adjusted for seasonality & for secular trends**
Rotavirus Trends: Reduction in Rotavirus Hospitalizations with increasing vaccine coverage in children < 5 years of age

EPI, Ministry of Health Bolivia

(Percent decline (95%CI)

47 (43-49)
Decline in diarrhea related hospital admissions in children <5 years of age in Bolivia after vaccine introduction

<table>
<thead>
<tr>
<th>Year</th>
<th>Observed</th>
<th>Expected</th>
<th>Percent decline (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2001</td>
<td>19140</td>
<td>27430</td>
<td>30 (6-32)</td>
</tr>
</tbody>
</table>
Decline in Diarrhea related mortality rate in children <5 years of age in Bolivia after vaccine introduction

Observed rates vs. Expected rates

No. of diarrhea deaths
- Observed: 699
- Expected: 1179

Rates of diarrhea deaths
- Observed: 6,7
- Expected: 14,1

Percent decline (95%CI): 52 (42-58)
Decline in RV- diarrhea hospital admissions rate in children<5 years of age in Bolivia

Decline in RV-diarrhea hospital admissions rate in children<5 years of age in Bolivia

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<th>Year</th>
<th>Observed</th>
<th>Expected</th>
<th>Percent decline (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2001</td>
<td>30.1</td>
<td>43.3</td>
<td>30 (21-55)</td>
</tr>
</tbody>
</table>
Rotavirus & Age Distribution

2005-2008

No. RV(+) cases

Cumulative % of RV infections

P<0.001

2009-2015

No. RV(+) cases

Cumulative % of RV infections

IBMB: LI
<table>
<thead>
<tr>
<th>Age group (months)</th>
<th>N (%)</th>
<th>Modified Vesikari Index*</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-2</td>
<td>38 (8)</td>
<td>13,8± 2,95</td>
</tr>
<tr>
<td>3-5</td>
<td>50 (10,5)</td>
<td>14,8± 3,03</td>
</tr>
<tr>
<td>6-8</td>
<td>63 (13,3)</td>
<td>14,4± 3,03</td>
</tr>
<tr>
<td>9-11</td>
<td>105 (22,2)</td>
<td>13,8±3,03</td>
</tr>
<tr>
<td>12-23</td>
<td>200 (42,2)</td>
<td>13,5±3,03</td>
</tr>
<tr>
<td>24-35</td>
<td>14 (3,0)</td>
<td>11,3± 2,67</td>
</tr>
<tr>
<td>&gt;35</td>
<td>4 (0,8)</td>
<td>11,5 ±2,71</td>
</tr>
</tbody>
</table>

Modified Vesikari Index: severity score (14 – 18)

*p= 0,031 (ANOVA)
Prospective community cohort (June 2013 – December 2014) at El Alto, Bolivia

- 341 children (2-4 weeks old) from low socioeconomic level, were enrolled while healthy & followed prospectively for 16-18 months.
NIDI: ADDs & Pathogens

Diarrheal episodes: Total of 135 in 122 children
Cases of clinical visits associated to diarrhea: 40%

Total of 3 Rotavirus (+) Cases: 2.45%
Pre-vaccine period 2002-2005: 15–25%

Importance of high vaccine coverage!
## IMPACT of RV1 Vaccine: Outpatient Diarrhea

<table>
<thead>
<tr>
<th>Age (Months)</th>
<th>Onset of Diarrhea Date</th>
<th>1st RV1 DOSE</th>
<th>2º RV1 DOSE</th>
<th>CU</th>
<th>Anemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3,17</td>
<td>09/10/2013</td>
<td>03/09/2013</td>
<td>04/11/2013</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>2,13</td>
<td>21/03/2014</td>
<td>03/09/2013</td>
<td>30/05/2014</td>
<td>+</td>
</tr>
<tr>
<td>3</td>
<td>9,73</td>
<td>30/06/2014</td>
<td>23/10/2013</td>
<td>13/01/2014</td>
<td>--</td>
</tr>
</tbody>
</table>
Conclusions

In a low-middle income country, under routine use of RV1 in the post vaccine period, among children <5 years of age:

- Decline in the number of diarrhea associated:
  - hospital admissions
  - deaths

- Decline in the number of rotavirus diarrhea associated:
  - hospital admissions
  - ambulatory cases
These results encourage broader introduction of the rotavirus vaccine in developing countries to reduce childhood mortality due to diarrhea.
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