Indian National Rotavirus Surveillance Network

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Indian Council of Medical Research
Introduction of Rotavirus vaccine in National Programme in India:

GOI has introduced Rotavirus Vaccine into the National Immunization Programme. India’s first indigenous rotavirus vaccine developed under a public-private partnership by the Ministry of Science and the Ministry of Health and Family Welfare has been licensed.
Epidemiology of Rotavirus Diarrhoea in India

- Several studies, different settings and methods to estimate proportion of children admitted with diarrhoea:
  - Hospital settings - RV + 34% (19-50%)
  - Community based up to 15% and Outpatients -16%

- Neonatal Infections - RV in neonates ranged (22% - 79%) 
  RV infection in neonates with diarrhoea more than without (55.5% vs 44.4% (P < 0.001)
Epidemiology of Rotavirus Diarrhoea in India

  showed proportionate increase in disease severity

*(Ref  G. Khan, S Fitzwater, J Tate et al. Epidemiology and prospects for prevention of Rotavirus Diseases in India. Indian Paediatrics 2012;49: 467-474)*
Admission and Deaths of hospitalized diarrhoea cases at ID Hospital
Common enteric pathogens in IDH (Nov 2007-Jun 2010)

- **No pathogen**: 12.7% (Age <5 years), 27.5% (All Age group)
- **Mixed Pathogen**: 5.9% (Age <5 years), 30.3% (All Age group)
- **Cryptosporidium spp.**: 10.3% (Age <5 years)
- **Giardia lamblia**: 12.8% (All Age group)
- **Entamaeba histolytica**: 3.4% (Age <5 years), 2.9% (All Age group)
- **Adenovirus**: 7.2% (Age <5 years), 14.8% (All Age group)
- **Rotavirus**: 6.5% (Age <5 years), 11.9% (All Age group)
- **EAEC**: 3.4% (Age <5 years)
- **ETEC group**: 4.5% (Age <5 years)
- **EPEC**: 3.5% (Age <5 years)
- **Salmonella**: 0.8% (Age <5 years), 0.5% (All Age group)
- **Shigella**: 7.4% (Age <5 years), 0.4% (All Age group)
- **C. coli**: 6.5% (Age <5 years), 0.4% (All Age group)
- **Campylobacter jejuni**: 5.2% (Age <5 years), 0.9% (All Age group)
- **V. cholerae Non O1 Non O139**: 9.7% (Age <5 years), 0.5% (All Age group)
- **Vibrio cholerae O139**: 2.1% (Age <5 years), 0.1% (All Age group)
- **Vibrio cholerae O1**: 13.6% (Age <5 years), 23.8% (All Age group)

*Note: The chart illustrates the percentage distribution of common enteric pathogens among different age groups.*
Genesis

• The Indian Rotavirus Strain Surveillance Network was established by ICMR in December 2005
  – To generate timely and geographically representative information on the clinical, epidemiological, and virological features of severe rotavirus disease in Indian children, with use of standardized protocols for enrollment and diagnostic evaluation.
Collection and testing sites in the Indian Rotavirus Strain Surveillance Network.

ICMR and CDC
Administrative and technical coordination

NIE
Data management

Objectives

- To establish a national hospital based surveillance to examine long term trends and pattern of diarrhea attributable to rotavirus among children < 5 years of age seen at in-patient facilities.

- To determine the age, seasonal distribution and outcomes of rotavirus-associated disease among the population under surveillance, including monitoring trends over time.

- To investigate the molecular epidemiology of rotavirus in India by typing the G and P type and characterization of untypeable strains by sequencing.

- To estimate the economic burden of rotavirus gastro-enteritis seen at hospitals by standardized costing studies.
Study Protocol

- Hospital based prospective surveillance
- Children *admitted* for Acute Diarrhoea and required hospitalization with rehydration for at least 6 hr were enrolled, clinical assessment and Vesikari score.
- Record of samples submitted and tested
- **Screening by Dako Rota IDEIA**
- **Genotyping by RT-PCR** for VP7 and VP4
- Quality control of screening and genotyping by blinded evaluation.
Results

Total enrolled children = 7643

Total stool specimens = 7285 (95%)

Rotavirus Positive = 2899 (40%)
## Distribution of G & P types Dec 2005 to June 2009

<table>
<thead>
<tr>
<th>Strains</th>
<th>Imphal</th>
<th>Pune</th>
<th>Vellore</th>
<th>Delhi</th>
<th>Trichy</th>
<th>Mumbai</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1P8</td>
<td>45</td>
<td>94</td>
<td>62</td>
<td>70</td>
<td>73</td>
<td>152</td>
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<tr>
<td>G2P4</td>
<td>44</td>
<td>64</td>
<td>105</td>
<td>66</td>
<td>89</td>
<td>121</td>
</tr>
<tr>
<td>G2P6</td>
<td>2</td>
<td>7</td>
<td>1</td>
<td>7</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>G9P6</td>
<td>6</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>G9P8</td>
<td>12</td>
<td>17</td>
<td>54</td>
<td>33</td>
<td>44</td>
<td>16</td>
</tr>
<tr>
<td>G12P6</td>
<td>21</td>
<td>18</td>
<td>2</td>
<td>51</td>
<td>7</td>
<td>64</td>
</tr>
<tr>
<td>G12P8</td>
<td>4</td>
<td>5</td>
<td>10</td>
<td>19</td>
<td>26</td>
<td>29</td>
</tr>
<tr>
<td>Both NT</td>
<td>285</td>
<td>16</td>
<td>103</td>
<td>86</td>
<td>39</td>
<td>7</td>
</tr>
<tr>
<td>G NT</td>
<td>309</td>
<td>72</td>
<td>113</td>
<td>92</td>
<td>48</td>
<td>11</td>
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<tr>
<td>P NT</td>
<td>419</td>
<td>37</td>
<td>156</td>
<td>118</td>
<td>67</td>
<td>34</td>
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<tr>
<td>G Mixed</td>
<td>96</td>
<td>33</td>
<td>26</td>
<td>33</td>
<td>14</td>
<td>38</td>
</tr>
<tr>
<td>P Mixed</td>
<td>13</td>
<td>23</td>
<td>6</td>
<td>15</td>
<td>5</td>
<td>22</td>
</tr>
<tr>
<td>Total</td>
<td>773</td>
<td>403</td>
<td>444</td>
<td>417</td>
<td>345</td>
<td>517</td>
</tr>
</tbody>
</table>
Strain distribution over time in different regions of India

East Zone

2006
2007
2008
2009

N=96
N=76
N=300
N=301

Mixed
Unknown
G12
G10
G9
G4
G3
G2
G1
Strain distribution over time in different regions of India

West Zone
Strain distribution over time in different regions of India
Strain distribution over time in different regions of India

South Zone
Rota-positive stool samples = 2899

G-type determined = 2237 (77%)

Untypable= 662 (23%)

Single G-type = 1997 (69%)

Multiple G-types = 240 (8%)

G 1 (25%)
G 2 (21%)
G 9 (13%)
G 12 (10%)
Rota-positive stool samples = 2899

- P-type determined = 1957 (68%)
  - Single P-type = 1873 (65%)
    - P8 = 631 (33%)
    - P6 = 172 (10%)
    - Others = 12 (10%)
  - Multiple P-types = 84 (3%)
    - P4 = 18 (21%)
    - Others = 66 (78%)
- Untypable = 942 (32%)
Age of children admitted for gastroenteritis in India

[Graph showing the percentage of children admitted for gastroenteritis in different age groups, with cities labeled as Kolkatta, Pune, Vellore+Trichy, Delhi, and Mumbai.]
Temporal distribution between Dec 2005-June 2009

Clear seasonality in Delhi, Pune, Kolkata but not in Vellore and Trichy
Conclusion

• The rigorous surveillance network using standardised protocol for case definition and laboratory evaluation generated geographically representative data and has shown that burden of Rotavirus is much more i.e 39.8% than earlier estimated 20.4%.

• Rotavirus infection and disease occur early in life, up to 13% before the age of 6 months.

• Children with rotavirus diarrhea had more severe disease than did those with rotavirus-negative disease (mean severity scores, 11.7 vs. 11.2; )
Contd:

- Circulation of a diverse range of rotavirus strains, including several uncommon with high proportion of untypables in the East region in 2009

- Proportion of G12 infections rose from 8% to 39% in Northern region and 8% to 24% in Western region

- In Southern region the proportion G1 infections rose from 10% to 60% with corresponding decline in the proportion of strains that were type G2.

- G9 strains were detected in each of the four regions each year with some temporal and regional variations in prevalence.
Multicenter, Hospital-Based Surveillance of Rotavirus Disease and Strains among Indian Children Aged <5 Years


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0022-1899/2009/20009S1-0019$15.00
DOI: 10.1086/605031
Diversity of circulating rotavirus strains in children hospitalized with diarrhea in India, 2005–2009∗


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l Regional Medical Research Centre for Tribals, Jabalpur, India
m Enterovirus Research Centre, Mumbai, India
n Lohana rwa Tidik Municipal General Hospital, Mumbai, India
o Topiwala National Medical College, Mumbai, India
p Division of Virology, National Institute of Cholera and Enteric Diseases, Kolkata, India
q Department of Microbiology, Regional Institute of Medical Sciences, Imphal, India
Table 1
Samples tested by EIA and positive for rotavirus by region between November 2005 and June 2009.

<table>
<thead>
<tr>
<th>Region</th>
<th>2006(^a)</th>
<th>2007(^b)</th>
<th>2008(^b)</th>
<th>2009(^b)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Samples tested</td>
<td>Rotavirus positive samples (%)</td>
<td>Samples tested</td>
<td>Rotavirus positive samples (%)</td>
<td>Samples tested</td>
</tr>
<tr>
<td>East</td>
<td>166</td>
<td>96 (58%)</td>
<td>197</td>
<td>76 (39%)</td>
<td>744</td>
</tr>
<tr>
<td>West</td>
<td>553</td>
<td>178 (32%)</td>
<td>794</td>
<td>274 (35%)</td>
<td>736</td>
</tr>
<tr>
<td>South</td>
<td>607</td>
<td>279 (46%)</td>
<td>485</td>
<td>178 (37%)</td>
<td>452</td>
</tr>
<tr>
<td>North</td>
<td>292</td>
<td>107 (37%)</td>
<td>310</td>
<td>107 (35%)</td>
<td>298</td>
</tr>
<tr>
<td>Total</td>
<td>1618</td>
<td>660 (41%)</td>
<td>1786</td>
<td>635 (36%)</td>
<td>2230</td>
</tr>
</tbody>
</table>

\(^a\) Represents November of the preceding calendar year to October of the listed calendar year.
\(^b\) Represents November of the preceding calendar year to June of the listed calendar year.
Need for the expansion

Based on data collected by MOH, proposed to expand and extend surveillance activities in different geographical zones across the country:

- Generate adequate nationally representative baseline data from different parts of India including high mortality states
- 30 Participants: ICMR Institutes – Medical Colleges – Hospitals with facilities (Public and Private).
- Ensuring Nationwide coverage
Objectives

• To establish a national hospital based surveillance to examine long term trends and pattern of diarrhea attributable to rotavirus among children < 5 years of age seen at in-patient facilities.

• To determine the age, seasonal distribution and outcomes of rotavirus-associated disease among the population under surveillance, including monitoring trends over time.

• To investigate the molecular epidemiology of rotavirus in India by typing the G and P type and characterization of untypeable strains by sequencing.

• To estimate the economic burden of rotavirus gastro-enteritis seen at hospitals by standardized costing studies.
National Rotavirus Surveillance Network (NRSN)

Sponsor and Overall Coordination
Indian Council of Medical Research (ECD Division)

Coordinating Center
National Institute of Epidemiology

Coordinating Laboratory
CMC, Vellore

Referral Centers
NICED  NIV  CMC  AIIMS

Regional Centers
RMRCs - Port Blair, Belgaum, Dibrugarh, Bhubaneswar; RMRCT Jabalpur, RMRIMS Patna, NIE Chennai

Peripheral Centers
~30 CRS
Surveillance Methodology

**Enrolment**
- 0-59 months Children *admitted* for Acute Diarrhoea and required hospitalization with rehydration for at least 6 h were enrolled
- Completion of CRF and Collection of Stool Samples

**Rotavirus Positivity**
- By ELISA (Rotaclone)

**G & P Typing**
- For every 3rd positive
Sample & Data Flow

**ICMR**

**NIE**

**Referral Lab**

- FORM 1 (CRF) – Monthly
- FORM 4 – Monthly
- FORM 5 – Quarterly

**Regional Lab**

- G & P typing results – Quarterly
- Positive samples for G & P typing* – Monthly

**Data entry through online portal**

- FORM 1 (CRF) – Monthly
- FORM 4 – Monthly
- FORM 5 – Quarterly

**Data analysis report after data validation** – Half yearly / Annual

**Original CRF; Stool specimens** – Fortnightly / Monthly

* For Year 1
Data Management

- Data captured on CRFs entered Online
- Original CRFs sent to NIE for Double Data Entry
- Data Validation and analysis
RESULTS
### Distribution of Rotavirus Diarrheal cases (%) [Sep 12 – Jun 14]*

(Consolidated data from Monthly reports)

<table>
<thead>
<tr>
<th>Referral Centre</th>
<th>No. of children admitted with diarrhea</th>
<th>No. of Children Enrolled</th>
<th>No. of Stool Specimens Collected (%)</th>
<th>No. Tested Positive for Rotavirus (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NICED</td>
<td>1476</td>
<td>1076</td>
<td>1076 (100)</td>
<td>619 (58)</td>
</tr>
<tr>
<td>NIV</td>
<td>1488</td>
<td>1409</td>
<td>1224 (87)</td>
<td>465 (38)</td>
</tr>
<tr>
<td>CMC</td>
<td>4414</td>
<td>3899</td>
<td>3749 (96)</td>
<td>1455 (39)</td>
</tr>
<tr>
<td>Jamia Hamdard#</td>
<td>1189</td>
<td>767</td>
<td>743 (97)</td>
<td>391 (53)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>8563</strong></td>
<td><strong>7151</strong></td>
<td><strong>6792 (95)</strong></td>
<td><strong>2930 (43)</strong></td>
</tr>
</tbody>
</table>

# Formerly at AIIMS
Analysis based on Validated Data
# Annual Distribution of Rotavirus Diarrheal cases

**NRSN2 (Sept 2012 - April 2014)**

<table>
<thead>
<tr>
<th>Year</th>
<th>RV Negative</th>
<th>RV Positive (%)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>263</td>
<td>170 (39.3)</td>
<td>433</td>
</tr>
<tr>
<td>2013</td>
<td>1533</td>
<td>1144 (42.7)</td>
<td>2677</td>
</tr>
<tr>
<td>2014</td>
<td>464</td>
<td>498 (51.8)</td>
<td>962</td>
</tr>
<tr>
<td>Total</td>
<td>2260</td>
<td>1812# (44.5)</td>
<td>4072</td>
</tr>
</tbody>
</table>

# 1486 Genotyped
Regional distribution of Rotavirus Positivity (%) according to season

<table>
<thead>
<tr>
<th>Region</th>
<th>Season</th>
<th>RV NEG</th>
<th>RV POS</th>
<th>Total</th>
<th>% RVPOS</th>
</tr>
</thead>
<tbody>
<tr>
<td>East</td>
<td>Dec - Feb</td>
<td>50</td>
<td>145</td>
<td>195</td>
<td>74</td>
</tr>
<tr>
<td></td>
<td>Mar - May</td>
<td>24</td>
<td>89</td>
<td>113</td>
<td>79</td>
</tr>
<tr>
<td></td>
<td>Sep - Nov</td>
<td>3</td>
<td>50</td>
<td>53</td>
<td>94</td>
</tr>
<tr>
<td>West</td>
<td>Dec - Feb</td>
<td>150</td>
<td>209</td>
<td>359</td>
<td>58</td>
</tr>
<tr>
<td></td>
<td>Mar - May</td>
<td>112</td>
<td>39</td>
<td>151</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>Sep - Nov</td>
<td>124</td>
<td>90</td>
<td>214</td>
<td>42</td>
</tr>
<tr>
<td>South</td>
<td>Dec - Feb</td>
<td>328</td>
<td>271</td>
<td>599</td>
<td>45</td>
</tr>
<tr>
<td></td>
<td>Mar - May</td>
<td>308</td>
<td>154</td>
<td>462</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td>Jun - Aug</td>
<td>285</td>
<td>83</td>
<td>368</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>Sep - Nov</td>
<td>373</td>
<td>261</td>
<td>634</td>
<td>41</td>
</tr>
<tr>
<td>North</td>
<td>Dec - Feb</td>
<td>110</td>
<td>182</td>
<td>292</td>
<td>62</td>
</tr>
<tr>
<td></td>
<td>Mar - May</td>
<td>129</td>
<td>61</td>
<td>190</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>Jun - Aug</td>
<td>108</td>
<td>30</td>
<td>138</td>
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<tr>
<td></td>
<td>Sep - Nov</td>
<td>156</td>
<td>148</td>
<td>304</td>
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<td></td>
<td></td>
<td>2260</td>
<td>1812</td>
<td>4072</td>
<td>44</td>
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</table>
# Genotype profile of RV strains

<table>
<thead>
<tr>
<th>G-Strains</th>
<th>No of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Samples Tested</td>
<td>1486</td>
</tr>
<tr>
<td>G-P Typed</td>
<td>1443</td>
</tr>
<tr>
<td>G- Typed</td>
<td>1480</td>
</tr>
<tr>
<td>P- Typed</td>
<td>1477</td>
</tr>
<tr>
<td>G or P Untyped</td>
<td>28</td>
</tr>
<tr>
<td>Both Untyped</td>
<td>15</td>
</tr>
</tbody>
</table>
### Distribution of G-P strains

<table>
<thead>
<tr>
<th>RV Strains</th>
<th>No of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1 P[8]</td>
<td>880</td>
<td>59.2</td>
</tr>
<tr>
<td>G9 P[8]</td>
<td>59</td>
<td>4.0</td>
</tr>
<tr>
<td>G12 P[6]</td>
<td>72</td>
<td>4.8</td>
</tr>
<tr>
<td>G12 P[8]</td>
<td>47</td>
<td>3.2</td>
</tr>
<tr>
<td>Other G-P</td>
<td>155</td>
<td>10.4</td>
</tr>
<tr>
<td>GT P[Mix]</td>
<td>36</td>
<td>2.4</td>
</tr>
<tr>
<td>G[Mix] PT</td>
<td>47</td>
<td>3.2</td>
</tr>
<tr>
<td>Both Mixed</td>
<td>14</td>
<td>0.9</td>
</tr>
<tr>
<td>GT P[UT]</td>
<td>15</td>
<td>1.0</td>
</tr>
<tr>
<td>GUT P[T]</td>
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<td>0.9</td>
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<tr>
<td>Both UT</td>
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<td>1.0</td>
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<tr>
<td><strong>Total Tested</strong></td>
<td><strong>1486</strong></td>
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Monitoring and Evaluation

• Independent Monitoring Committee
• Clinical and Laboratory assessment tools/checklists developed