Incidence of Rubella / Congenital Rubella Syndrome cases at Port Moresby General Hospital. Retrospective – Prospective Study

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Introduction

• Mild disease in adults and children.

• Maternal infection in early pregnancy leads to CRS [ophthalmic, auditory, cardiac, & craniofacial defects].

• Incidence rubella 1.78 per 100,000 population. Western Pacific region 4.08 per 100,000 population. [WHO-2009]

• Est. >100,000 infants are born with CRS annually.

• Recent epidemics - Japan 42.5 / 100,000 population & Poland 26,000 cases (80% are male 29-30). [CDCP-2013]
Introduction

• About 131 (68%) [40% of birth cohort] have introduced rubella vaccine.

• Rubella vaccines is live attenuated RA 27/3 strain, highly effective & produce life long immunity with a single dose of vaccine.
  • Clinical trials have shown that > 95% of vaccinees age 1 year or more develop immunity from a single dose & > 90% have clinical protection against acute rubella for up to 15 yrs.

• PNG incidence is unknown.

• More cases – lack of awareness – under recognition and under-reporting of cases.
Aim

1. Retrospectively report on Incidence over 6 year period:
   - Clinical Confirmed Congenital Rubella Syndrome Cases (according to WHO CRS criteria) and
   - Acute Rubella Infection

2. Prospectively over 1 year period:
   - Confirm Clinically Suspected Congenital Rubella Syndrome cases at Special Care Nursery and their serology.
   - Children with Acute Fever & Rash and their serology.
Methodology

Design/Site

Descriptive retrospective- prospective study at Port Moresby General Hospital

Time

Part A
- Retrospective study - 2006-2011 (June –December  2012)

Part B
- Prospective study (March  2012- May 2013)

Data Collection
- Admission registry
- Patient files for extra information
- Medical records
Retrospective- Inclusive Criteria

- Special Care Nursery
- Ear Nose Throat,
- Ophthalmology,
- Cardiac,
- Central Public Health Laboratory

- Age – 0 – 12 years
- Time - 2006-2011

- CRS
  Clinically confirmed cases - Any 2 signs according to WHO Classification.

- Acute Rubella
  All positive rubella IgM
Case Definition for Retrospective CRS Study.

Clinically confirmed cases with least 2 of the complications listed below.

A. Cataract, congenital glaucoma, congenital heart disease, loss of hearing, pigmentry retinopathy

B. Purpura, radiolucent bone disease, jaundice that begin within 24 hours of birth.

C. Other – Microcephaly, Micrognathia , nystagmus, diminished vision, squint, mental retardations, microphthalmia, heptosplenomegaly, menigoencephalities
Prospective Study - Inclusive Criteria

**Acute Rubella**
Children between 1-12 years with AFR with serology (rubella IgM).

COPD, Cons clinic, General Wards

**CRS**
An infant born with any suspected sign of CRS admitted to SCN with their serology.
Prospective – Data & Sample Collection

• Awareness

• Identification of cases

• Verbal consent

• Sample collection (~ 1 ml of serum in a plain bottle).

• AFR surveillance form (detailed clinical notes for all patient presenting with CRS).

• Rubella IgG/IgM antibody ELISHA test.
Data Management & Analysis

- Ethical approval – UPNG research committee.
- Data entering - Microsoft Excel 2010.
- Further analysis- SPSS Version 19.
- Incidence rate - new cases over the total population within the given period.
Retrospective study
Overall retrospective study results.

Total number of patient seen
13 431

PMGH 3 Clinics attendees & SCN admission
13 231

Excluded
Suspected – 128
Syndromic - 27

Any one CRS sign documented
200 (1.5%)

Clinically confirmed CRS (WHO classification)
41 (0.3%)

Acute Febrile Rash
200

Acute Rubella
50 (25%)
• WHO clinically confirmed Congenital Rubella Syndrome cases accounted for 0.3% (3.05 per 1,000) population of PMGH clinic attendees/SCN admission.

• Rubella accounted for 25% of children presenting with AFR.
### Characteristics of clinically confirmed CRS cases in the retrospective study

<table>
<thead>
<tr>
<th></th>
<th>Number (n)</th>
<th>Percent (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>25</td>
<td>58</td>
</tr>
<tr>
<td>Female</td>
<td>16</td>
<td>37</td>
</tr>
<tr>
<td><strong>Origin</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Southern</td>
<td>24</td>
<td>56</td>
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<tr>
<td>Highlands</td>
<td>5</td>
<td>12</td>
</tr>
<tr>
<td>Momase</td>
<td>4</td>
<td>9</td>
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<tr>
<td>Islands</td>
<td>6</td>
<td>14</td>
</tr>
<tr>
<td><strong>Gestational Age †</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GA 37- &lt;42 weeks</td>
<td>11</td>
<td>27</td>
</tr>
<tr>
<td>GA 32- &lt;37 weeks</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>GA 28- &lt;32 weeks</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>GA 20- &lt;28 weeks</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><strong>Classification of † Birth Weights</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bt. Wt. 2.5-4kg</td>
<td>7</td>
<td>16</td>
</tr>
<tr>
<td>Bt. Wt. 0.5-&lt;2.5kg</td>
<td>9</td>
<td>21</td>
</tr>
</tbody>
</table>

†Missing datas – analyzed only available datas.
Number of clinically confirmed CRS cases in the 3 clinics & SCN - retrospective study.
### Characteristics of children presenting with Acute Rubella - Retrospective Study

<table>
<thead>
<tr>
<th></th>
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<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
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<td>25</td>
<td>50</td>
</tr>
<tr>
<td>Female</td>
<td>25</td>
<td>50</td>
</tr>
<tr>
<td><strong>Origin</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Southern Highlands</td>
<td>20</td>
<td>39</td>
</tr>
<tr>
<td>Highlands</td>
<td>16</td>
<td>30</td>
</tr>
<tr>
<td>Momase Islands</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Islands</td>
<td>9</td>
<td>17</td>
</tr>
<tr>
<td><strong>Year of Presentation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2006</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>2007</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2008</td>
<td>7</td>
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<td>2009</td>
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<td>33</td>
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<td>2010</td>
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<td>10</td>
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<tr>
<td>2011</td>
<td>19</td>
<td>17</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>5.68 (1-12)</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>5.00</td>
<td></td>
</tr>
<tr>
<td>SD</td>
<td>3.34</td>
<td></td>
</tr>
<tr>
<td>IQR</td>
<td>3-8</td>
<td></td>
</tr>
</tbody>
</table>
Relationship between the Acute Rubella and CRS cases in the Retrospective study
Prospective Study
Overall Prospective Study Results

Total Number of patient tested 77

- 31 patient had suspected CRS
  - No Laboratory Confirmed CRS
  - 5 Probable cases of CRS (Positive IgG)
- 11 patient with Acute Febrile Rash
  - 1 confirmed - Acute Rubella
- 3 – other syndrome
- 32 - Did not meet criteria
Results

About 1.7% of the total infants admitted to PMGH SCN were suspected to have CRS.

- Non Laboratory Confirmed CRS
- 5 Probable CRS cases – Rubella IgG positive

One case of Acute Rubella with AFR
### Characteristics of children presenting with CRS
#### Prospective Study

<table>
<thead>
<tr>
<th></th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>22</td>
<td>71</td>
</tr>
<tr>
<td>Female</td>
<td>8</td>
<td>26</td>
</tr>
<tr>
<td>Unknown</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td><strong>Origin</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Southern</td>
<td>23</td>
<td>74</td>
</tr>
<tr>
<td>Highlands</td>
<td>5</td>
<td>16</td>
</tr>
<tr>
<td>Momase</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Islands</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>
# Age, G.A & Bt. Wts of infants admitted to SCN-PMGH in Prospective Study.

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Median</th>
<th>SD</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age when seen (days)</strong></td>
<td>6</td>
<td>3</td>
<td>7.7</td>
<td>2- 7</td>
</tr>
<tr>
<td></td>
<td>(0- 34)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Gestational Age (weeks)</strong></td>
<td>36</td>
<td>37</td>
<td>3.5</td>
<td>35-39</td>
</tr>
<tr>
<td></td>
<td>(28-40)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Birth Weights (kg)</strong></td>
<td>1.97</td>
<td>2.00</td>
<td>0.66</td>
<td>1.4- 2.4</td>
</tr>
<tr>
<td></td>
<td>(0.85-3.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
CRS Signs of infants admitted to SCN

- CHD, Deformed Ears
- CHD, Talipes
- Cleft Lip & Palate, TEF, Micrognathia
- Cleft Lip & Palate, Rt eye agenesis
- LBW, Cleft Lip & palate
- CHD, Cleft Lip & Palate/Imperforated Anus
- Microcephaly, Encephalitis, Micrognathia
- CHD, Tracheosophageal Fistula
- Microcephaly, Micronathia, Glaucoma
- CHD, LBW, Jaundice
- CHD, LBW, Micrognathia
- CHD, LBW
- CHD, Cleft palate
- Jaundice, LBW
- Microcephaly, Jaundice, Talipes
### CRS signs of patients with positive Rubella IgG in the Prospective study.

<table>
<thead>
<tr>
<th>Clinical sign</th>
<th>Maternal Hx.</th>
<th>Age (days)</th>
<th>IgM</th>
<th>IgG</th>
</tr>
</thead>
<tbody>
<tr>
<td>LBW, Jaundice, PDA</td>
<td>No</td>
<td>13</td>
<td>Negative</td>
<td>Positive</td>
</tr>
<tr>
<td>Tracheosophageal Fistula / PDA</td>
<td>No</td>
<td>7</td>
<td>Negative</td>
<td>Positive</td>
</tr>
<tr>
<td>Cleft lip/palate/LBW</td>
<td>No</td>
<td>0</td>
<td>Negative</td>
<td>Positive</td>
</tr>
<tr>
<td>Cleft lip/palate</td>
<td>No</td>
<td>8</td>
<td>Negative</td>
<td>Positive</td>
</tr>
<tr>
<td>Malformed ears/Complex CHD/Talipes</td>
<td>No</td>
<td>4</td>
<td>Negative</td>
<td>Positive</td>
</tr>
</tbody>
</table>
• Retrospectively WHO clinically confirmed diagnosis of CRS accounted for 0.3% with an incidence rate of 3.05 per 1000 population of PMGH clinic attendees & SCN admission.

• World wide incidences varies (range 0.4- 2.2 /1000 live birth).

• There were more male than female and 21% were LBW and 27% were SFD.

• Majority of the CRS patients presented with deafness & mental retardation from ENT clinic.
  • *Bloom et al* (Lancert 2005- Morocco) showed of the 225 cases of clinically confirmed rubella cases, 129 cases had deafness and metal retardation.
Discussion

- Acute Rubella accounted for 25% of patients presenting with AFR.

- There was an equal number of M:F ratio with a median age of 5.6 years (IQR of 3-8 years).

- No significant relationship noted between the number of rubella & CRS cases in the retrospective arm of the study.
Discussion

• Prospectively the study showed that 1.7 % of total infants admitted to PMGH SCN were suspected to have CRS.

• More M>F and the mean age which they presented was 6 days (IQR 2-7 days) with bt. Wt. 1.97kg (IQR 1.4-2.4 kg)

• Non of this infants that were admitted to SCN over 1 year period had Laboratory confirmed CRS.
Discussion

• Five probable cases of CRS who had positive IgG with a suspected CRS sign.

• Non of their mothers had rubella vaccine or had signs of AFR during pregnancy.

  • Lab. Confirmed CRS= Positive IgM (IgM is detectable in 100% of CRS cases at birth & declines by 50% at 12mnths & rarely detectable by 18 mnths)
  • Positive IgG indicates maternal infection.

• Only one case of Acute Rubella with AFR.
Study Limitations

Poor Data Management

- Poor recording systems
- Non availability of AFR Surveillance forms
- AFR forms not completely filled out.
  - (80% incomplete, 3% blank) (J.Kumbu)

Low awareness on Disease

- Missing out on cases

Small sample size in the prospective study.

Study limited to Port Moresby
Conclusion

- Possible probable CRS cases noted.

- Acute Rubella is a major contributor to AFR at PMGH – (?)- vaccine.

- Using retrospective approach the study showed higher incidence rate however this might not reflect true CRS burden.

- Increase awareness, surveillance & Serology confirmation to identify the true burden of rubella in PNG.

- Improving Data Management (congenital defect registry data/ neonatal check list).

- Similar study in other provinces, increase sample size.
Acknowledgement

- Dr Siddartta Datta
- Prof Nekapi Tefuarani
- Prof Trevor Duke
- Dr Paulus Ripa
- Dr Evelyn Lavu
- Dr Simon Malenges
- Dr Paki Molumi
- Clerks & SIC (clinics /Wards)
- CPHL team
- Pediatric Team (PMGH)
- My family
Reference


• Nationwide rubella epidemic, Japan 2013, Centre of Disease Control and Prevention.