An Outbreak of Necrotising Enterocolitis of Unknown Aetiology in Newborns Admitted to a Neonatal Unit in Gauteng Province, March – August 2018

Andronica Moipone Shonhiwa
Division of Public Health Surveillance and Response, Outbreak Response Unit, NICD

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Background

- Necrotizing enterocolitis (NEC)
  - Common and serious gastrointestinal disease among newborn babies, requiring emergency treatment
  - Is an acute inflammatory disease with a multifactorial and controversial aetiology
    - Attributable to both infective (bacteria, virus and fungi)
    - Non-infective factors (e.g. low birth weight, low gestational age, formula milk feeding, etc.)
Background

- National Institute for Communicable Diseases notified on 4 April 2018 by neonatal unit paediatrician
  - 12 premature babies diagnosed (on imaging) with NEC
  - All patients had low serum C-reactive protein levels and no diarrhoea
  - A viral aetiology was suspected but no testing was done
Aims and objectives

• Suspected NEC outbreak at neonatal unit investigated in order to:
  – Verify the diagnosis
  – Ascertain the existence of an NEC outbreak
  – Determine the possible causes and sources of NEC
  – Implement prevention and control measures in order to contain the outbreak
  – Make recommendations on prevention and control measures to prevent future outbreaks
Methodology

1. Study design
   • We conducted a cross-sectional study
     – To describe the characteristics and possible source/causes of the outbreak

2. Case definition
   – Modified Bell’s staging criteria for NEC and reported stages 2 & 3
   – Outbreak included cases with NEC onset from 01 March-29 Aug 2018, born and admitted at hospital’s neonatal unit (ward 16B)
Methodology

3. Data sources

• **Retrospective baseline data**: Number of NEC cases diagnosed over the last year (Jan – Dec 2017) to March 2018, provided by hospital

• **Clinical and epidemiological data from 1 March to 29 August 2018**
  • From case-patient record reviews
  • Lab results obtained from the lab information system
  • **Healthcare worker interviews, IPC audits, environmental health assessment**
4. Laboratory investigations

• **Clinical samples (blood and stool)** were collected
  – Blood and stool cultures testing at local NHLS laboratory
  – Stool enteric pathogen testing at NICD (Real-time PCR, FTD for bacteria, parasites, viruses, fungi)

• **Environmental samples** (surface swabs and milk)
  – Formula and breast milk samples tested at NHLS ICLS (bacteria)
  – Some milk and swabs samples tested at NICD
Findings

Neonatal unit map - 17 May 2018
Findings

Epidemic curve showing number of NEC cases by month of disease onset, ward 16B, Jan-Dec 2017/Jan-Aug 2018
Findings

Epidemic curve showing number of NEC cases by date of disease onset, Ward 16B, March – Aug 2018
Findings

- A total number of 42 cases reported (as of 29 August 2018)
  - 38 (90.5%) premature and four (9.5%) full-term babies
  - Birth weight: 79% (33) were <1500 g, 21% >1500 g
  - HIV exposure history was known in 64.3% (n=27) cases
    - HIV exposed: 40.7% (n=11) cases
    - HIV unexposed: 59.3% cases
Findings

Gestational age of NEC cases at birth, March – August 2018

- The gestational age (GA) at birth ranged from 26 to 40 weeks (median: 32; IQR: 29-35)
  - 24% of cases born at 32 weeks GA.
  - 20% born at 28 weeks GA
Age distribution of NEC cases, March – August 2018.

- Age ranged from 2 to 59 days (median: 13; IQR: 7-21)
- Children under 1-month old accounted for 90.5% of the cases (n = 38),
- 9.5% (n = 4) were cases aged between 1 – 2 months old
Findings

Clinical staging of the cases, March – August 2018

<table>
<thead>
<tr>
<th>NEC Stage</th>
<th>Number of cases</th>
<th>Proportion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NEC IIA</td>
<td>22</td>
<td>52.4</td>
</tr>
<tr>
<td>NEC IIB</td>
<td>9</td>
<td>21.4</td>
</tr>
<tr>
<td>NEC IIIA</td>
<td>3</td>
<td>7.1</td>
</tr>
<tr>
<td>NEC IIIB</td>
<td>8</td>
<td>19</td>
</tr>
<tr>
<td>Total</td>
<td>42</td>
<td>100</td>
</tr>
</tbody>
</table>

The cases were definite NEC stage IIA-B (mildly to moderately ill) and stage IIIA-B (severely ill). Most cases were NEC stage II (~74%)
Findings

Outcomes for NEC cases, March – August 2018

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number of cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Died</td>
<td>9 (21.4)</td>
</tr>
<tr>
<td>Discharged</td>
<td>28 (66.7)</td>
</tr>
<tr>
<td>Transferred</td>
<td>4 (9.5)</td>
</tr>
<tr>
<td>Still admitted*</td>
<td>1 (2.4)</td>
</tr>
<tr>
<td>Total</td>
<td>42 (100%)</td>
</tr>
</tbody>
</table>

*Still admitted for other premature-related medical conditions by 29 August 2018
Findings

Type of feeding for NEC cases, March – August 2018

<table>
<thead>
<tr>
<th>Feeding type</th>
<th>Number of cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast milk (EBM/DEBM)</td>
<td>14 (33.3)</td>
</tr>
<tr>
<td>Mixed feeding</td>
<td>13 (31)</td>
</tr>
<tr>
<td>Formula milk</td>
<td>11 (26.2)</td>
</tr>
<tr>
<td>Unknown</td>
<td>4 (9.5)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>42 (100%)</strong></td>
</tr>
</tbody>
</table>

**EBM:** Expressed breast milk. **DEBM:** Donated EBM.
## Findings

### Blood cultures performed for 36 cases (86%)

<table>
<thead>
<tr>
<th>Blood culture results</th>
<th>Number of cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No growth</td>
<td>17 (47.2%)</td>
</tr>
<tr>
<td>Coagulase-negative <em>Staphylococcus</em></td>
<td>9 (25.0%)</td>
</tr>
<tr>
<td><em>Candida albicans</em></td>
<td>4 (11.1%)</td>
</tr>
<tr>
<td><em>Acinetobacter baumannii</em></td>
<td>1 (2.8%)</td>
</tr>
<tr>
<td><em>Candida parapsilosis</em></td>
<td>1 (2.8%)</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td>1 (2.8%)</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>1 (2.8%)</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em> and <em>Staphylococcus aureus</em></td>
<td>1 (2.8%)</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>1 (2.8%)</td>
</tr>
</tbody>
</table>

- No specific pathogen isolated.
Findings

• **Stool samples** were collected for 19/42 cases (45%)
  - **Enteric bacteria were tested in 12 cases (12/19, 63%)**
    • 9 (75%) stool cultures were negative
      - For any of the bacteria tested: *Salmonella*, *Shigella*, *Campylobacter*, *Listeria*, *Vibrio cholerae*, *enterohaemorrhagic Escherichia coli*, *Clostridium perfringens*, *Bacillus cereus*, *Vibrio spp*, *Staphylococcus aureus*, or *Yersinia enterocolitica*
    • 3 (25%) stool samples rejected: not tested
  - **Enteric viruses were tested in 10 cases (10/19, 53%)**
    • All 10 were negative for rotavirus, astrovirus, sapovirus, norovirus and adenovirus.
Findings

• Environmental sample testing:
  - 50 milk samples (n = 48 formula; n = 2 EBM) collected & tested
    • Milk contamination found in 39 (78%) samples (n = 38 formula; n = 1 EBM)
      - *Bacillus* species/*Streptococcus* species isolated
        » In both mixed and dry powder milk (opened and unopened containers)
    - All surface swabs were negative
Findings

IPC audits, HCW interviews (n=25), environmental health assessment

• Highlighted sub-optimal IPC practices
  • By both HCW, mothers, cleaners and students

• Overcrowding: of babies and due to students on rotation

• Staff shortages: only 1 nurse per cubicle

• Shortage of equipment: cubicles sharing equipment

• Poor monitoring: IPC championship
Discussion and limitations

• No specific pathogen identified as possible cause of NEC
  – Several pathogens were isolated from blood culture,
  – No enteric pathogen isolated in stool samples

• Results should be interpreted with caution as antibiotic treatment was initiated when samples were collected
Discussion and limitations

• Isolation of *Bacillus* and *Streptococcus* spp in formula milk and one EBM may indicate possible contamination

• Risk factors such as HIV exposure and underlying medical conditions not well recorded
Discussion and conclusions

- The decline of cases since June could be attributed to the interventions measures implemented

**IPC audits. environmental health assessment: 21-22 May**
- Education on hand hygiene and adherence to IPC
- Reduced no of student on rotation at a time
- Provided hand hygiene resources
Discussion and conclusions

- Outbreak was declared over as case numbers have returned to baseline level
Recommendations

• We recommended:
  – Heightened surveillance to detect and report outbreaks
  – Education and strict adherence to IPC practices
    – Hand hygiene and case isolation
  – Clinical sample collection before treatment initiation
Recommendations

• We further recommend in the long term to
  – Address long-standing problems
    – Overcrowding: More patients admitted than beds available
    – Staff shortages: Patient to professional nurse ratios
    – Shortage and sharing of equipment

• Outbreak created research opportunities
  – Further analytical studies (e.g. a case control study) might be necessary to further understand the NEC risk factors
ACKNOWLEDGEMENTS

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• NICD: DPHSR-Outbreak Response Unit, CHARM and CED

• Local academic hospital management

• Local academic hospital neonatal unit team and management

• EHP at local academic hospital

• NHLS HJH microbiology lab

• NHLS Wits ICLS
THANK YOU

Infant with necrotizing enterocolitis.