Utility of a Multiplex Molecular Gastrointestinal Panel in Rapid Identification and Control of a Norovirus Outbreak in a Pediatric Tertiary Care Centre

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Introduction
Norovirus is one of the most common viral pathogens implicated in gastroenteritis outbreaks, both in community and healthcare settings. The virus’ short incubation period and high attack rate allow its rapid spread through inpatient wards to patients, staff and visitors. Early identification and appropriate implementation of infection prevention and control measures is essential to interrupt transmission.

Objectives
1/ To describe a single-ward norovirus outbreak in a pediatric tertiary care centre.
2/ To study and describe the implications of a newly acquired molecular laboratory method: FilmArray Gastrointestinal Panel.

Methods
Setting: The IWK Health Centre is a 250-bed tertiary care pediatric and women’s hospital serving the Maritime Provinces in Canada. The Pediatric Medical Unit (PMU) is a 24-bed, single room ward with private en suite bathrooms for patients and families. Families are permitted to stay in overnight and visitors may visit at any time as per the family’s discretion.

Definitions:
• Outbreak: increase in the number of cases above baseline for a given area (ward) in a given time
• Case Definition: Hospital-acquired norovirus: Patients admitted ≥ 48 hrs with lab-confirmed norovirus AND ≥ 1 of:
  1/ Acute onset diarrhea with no likely non-infectious cause identified
  2/ of the following signs or symptoms:
    • nausea, vomiting, abdominal pain, fever (>38°C), or headache
  3/ Day 0: first date of symptom onset in first patient

Laboratory Methods:
In September 2017 the FilmArray Gastrointestinal GI (Panel BioFire Diagnostics, LLC, SLC, Utah) was introduced in the Clinical Microbiology Laboratory as part of a preventive infectious causes of enteritis. Given then, stool samples sent for viral, bacterial, or parasitic testing are evaluated by PCR as the standard of the diagnosis. The panel tests for 22 GI analytes (Table 3), including 5 viruses, with a mean 2-hr turnaround time from sample arrival in the lab to result reporting. Previously, in-house stool viral testing was limited to adenov- and rotavirus antigen.

Outbreak Investigation and Analysis:
Patient clinical characteristics and laboratory investigations were collected. Potential timing and location of transmission were evaluated.

Ethics
Ethics approval to evaluate the FilmArray GI Panel as a non-interventional study was obtained through the IWK Health Centre Research Ethics Board.

Results: Outbreak
On day 0, Patient 1 developed new onset diarrhea and emesis. The following day, Patients 2 and 3 developed multiple episodes of watery diarrhea and emesis. At this time, Infection Prevention and Control (IPAC) were alerted to the cluster of diarrheal illness. Stool specimens from Patients 1,2, and 3 were sent for testing, all resulting positive for norovirus and an outbreak was declared (Figure 1).

Four caregivers and a 1 medical resident were also symptomatic although stool was not tested. Patient 3’s patients (likely source) had had diarrhea and emesis on days -3 and -2, and had used common spaces such as the ward kitchen. Patient 2’s parent and grandparent had diarrhoea and emesis on days 3 and 1. The medical resident developed diarrhoea and emesis on day 2 and remained off work until two days post symptom resolution. The outbreak was declared over on day 6 (5 days without new cases).

On days 2-3, 8 other patients (Patients 4-9) developed in-hospital new-onset loose stools and none were positive for norovirus (Table 3). No patients on other wards developed symptoms. Of note, norovirus was highly prevalent in the community during this time.

Results: Infection Prevention and Control (IPAC)
All symptomatic patients were immediately placed on contact precautions (gown and glove use while in the room), room/ward cleaning frequency increased and proper hand hygiene was reinforced both with staff and patients’ families. Common areas (playroom/kitchen) were closed until the outbreak was declared over. The unit was not closed due to rapid containment of the outbreak.

IPAC outbreak investigation included establishment of a case definition for hospital-acquired infection (HAI) and line list (Table 2). Current practices with respect to communicable illness in families (including recommendations to stay home while unwell), families’ use of shared equipment and common spaces, hand hygiene education to families, and screening visitors for communicable illnesses were reviewed. Most notably it was found that sharing of bottle warmers was necessary due to a limited number of equipment. Frequent use in the common kitchen area likely resulted in exposure and subsequent infection transmission.

Discussion
At a time when norovirus was prevalent in the community, a small, contained single-ward outbreak occurred in our institution. Based on investigation and analysis, we hypothesize that parents rooming in with their child (patient 3), who were ill with gastroenteritis in the days prior to the hospital associated cases, were the likely source of this outbreak.

The use of the FilmArray GI panel permitted same-day identification of the pathogen in all affected patients. Prior to use of this molecular method, our laboratory did not have in-house ability to identify norovirus, nor rapidly exclude other infectious causes of enteritis. For infected number of other children with diarrheal illness at the time, it is likely that the outbreak would have appeared more wide-spread and longer. Timely identification of the pathogen permitted accurate knowledge of the outbreak activity and allowed prompt return to usual practices once terminated.

The investigation of infection prevention and control practices on the unit highlighted areas of improvement with 1) communication and management of families rooming in who are ill, and 2) increasing inventory of shared equipment (bottle warmers), with steps implemented in both respects to avoid future outbreaks.

Conclusion
The syndromic FilmArray GI panel enabled same-day identification of a norovirus outbreak, exclusion of other infectious causes and permitted real-time identification of the outbreak termination. While IPAC measures, including vigilant hand hygiene, remain mainstays of outbreak avoidance, this technology facilitates real-time laboratory testing, data acquisition and guiding of appropriate infection control practices, should one occur.

Table 3: GI pathogens detected by FilmArray GI Panel

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Sources</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Campylobacter jejuni</td>
<td>Enteric gram-negative</td>
<td>YES</td>
</tr>
<tr>
<td>E. coli 0157</td>
<td>Enterohemorrhagic</td>
<td>YES</td>
</tr>
<tr>
<td>Enteroaggregative E. coli (EAEC)</td>
<td>Enterosporogenic</td>
<td>YES</td>
</tr>
<tr>
<td>Enteroaggregative E. coli (EPEC)</td>
<td>Enterotoxigenic</td>
<td>YES</td>
</tr>
<tr>
<td>Plesiomonas shigelloides</td>
<td>Enteroinvasive</td>
<td>YES</td>
</tr>
<tr>
<td>Salmonella</td>
<td>Shigella flexneri</td>
<td>YES</td>
</tr>
<tr>
<td>Shigella dysenteriae</td>
<td>Vibrio cholerae</td>
<td>YES</td>
</tr>
<tr>
<td>Vibrio vulnificus</td>
<td>Vibrio parahaemolyticus</td>
<td>YES</td>
</tr>
<tr>
<td>Yersinia enterocolitica</td>
<td>Yersinia pseudotuberculosis</td>
<td>YES</td>
</tr>
</tbody>
</table>

Table 4: Line list developed by IPAC including patient characteristics and assessment. Day 1 = day outbreak declared.

<table>
<thead>
<tr>
<th>AGE/GENDER</th>
<th>ADMISSION DIAGNOSIS</th>
<th>DAY OF ADMISSION</th>
<th>DAY OF SYMPTOM ONSET</th>
<th>DAY OF INITIATION OF PRECAUTIONS</th>
<th>DAY OF POSITIVE SPECIMENS</th>
<th>DISCHARGE DAY</th>
<th>HAI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 4 yr M</td>
<td>Pneumonia (influenza)</td>
<td>-11</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>4</td>
<td>No family illness</td>
</tr>
<tr>
<td>2 3 mo M</td>
<td>Biliary atresia, Failure to thrive</td>
<td>-5</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>5</td>
<td>Parent and Grandparent had vomiting and diarrhea on same day</td>
</tr>
<tr>
<td>3 3 mo M</td>
<td>Hypopyonemia</td>
<td>-11</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>Both parents had vomiting and diarrhea on days 3 and 2</td>
</tr>
</tbody>
</table>

Figure 1: Outbreak curve: day of symptom onset for each affected person.

Contact Information
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