Clinical Predictors of Shigella and Campylobacter Infection in Children in the United States

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Introduction

165 million cases worldwide of shigellosis/year causing 1 million deaths (1); 450,000 American infections/year (2)

Estimated 2 American cases of Campylobacter infection/year (3)

Diagnosis important as antibiotic treatment for these two pathogens shortens duration of illness and prevents transmission (4, 5)

Classic description of shigellosis is severe diarrhea with blood/mucus and fever (6), most common symptoms in Campylobacter infection previously shown to be diarrhea, malaise, fever, and abdominal pain (7, 8, 9)

Practitioners often follow "rule of thumb" that bloody diarrhea is predictive of bacterial infection, but multiple studies show that this is a poor predictor in shigellosis (10, 11, 12, 13, 14, 15), reports vary for prevalence in Campylobacter (9, 8)

Most studies characterizing predictors of bacterial diarrhea are done in resource-limited settings, with unclear application to resource-rich settings

Prior studies examining clinical presentation of bacterial diarrhea mostly done with stool cultures, which are less sensitive than PCR based methods (14)

Objective

To determine clinical and demographic predictors of pediatric Shigella and Campylobacter infection in a resource-rich setting

Methods and Materials

The GI IMPACT study evaluated clinical impact of implementation of a multiplex molecular panel for stool pathogen analysis at 5 pediatric emergency departments across the US from April 2015 to September 2016 (Figure 1)

Enrolled children (<18 years) that presented with symptoms of gastrointestinal with duration of symptoms at least 24 hours but < 14 days

A stool sample was collected from each subject and tested with the BioFire Diagnostics’ FilmArray® Gastrointestinal (GI) panel

Standardized interview conducted to gather information regarding demographics, history of illness, current medications, health status (including comorbid conditions), and risk exposures

Physical exam and laboratory variables were extracted from the electronic health record following the interview

Multivariable logistic regression used to determine odds ratios of presence of clinical variables in patients with Shigella detection or a combination of Shigella and/or Campylobacter detection compared with patients in which Shigella or Campylobacter were not detected

Machine learning utilizing logistic regression with stepwise variable selection by AIC, logistic regression with stepwise variable selection via BIC, random forest, and adaBoost were used to create algorithms predictive of Shigella or Shigella/Campylobacter detection after removal of predictors with ≥ 20% missing data

An unconstrained stacked model and constrained stacked model were constructed based on the preceding four models

Results

993 children enrolled with acute diarrhea, Shigella detected in 56 (5.6%) and Campylobacter in 24 (2.4%)

Table 1: Association of clinical variables with detection of Shigella or Campylobacter

<table>
<thead>
<tr>
<th>Feature</th>
<th>Shigella detected (n)</th>
<th>Shigella/Campylobacter detected (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood diarrhea</td>
<td>91/131</td>
<td>98/131</td>
</tr>
<tr>
<td>Fever</td>
<td>45/55 (51.1)</td>
<td>53/55 (51.1)</td>
</tr>
<tr>
<td>Headache</td>
<td>27/131 (20.6)</td>
<td>30/131 (23.0)</td>
</tr>
<tr>
<td>Vomiting/nausea</td>
<td>72/131 (55.4)</td>
<td>79/131 (59.6)</td>
</tr>
<tr>
<td>Blood/white cell counts</td>
<td>200/131 (15.3)</td>
<td>205/131 (15.3)</td>
</tr>
<tr>
<td>Out of state travel</td>
<td>131/131 (44.2)</td>
<td>136/131 (42.6)</td>
</tr>
<tr>
<td>Summer setting</td>
<td>25/131 (19.2)</td>
<td>29/131 (22.3)</td>
</tr>
</tbody>
</table>

The model with highest AUC on ROC for Shigella vs. others was generated by random forest, whereas the unconstrained stacking model had the highest AUC on ROC for Shigella or Campylobacter or others

Discussion

Shigella infection was associated with fever, bloody diarrhea, headache, contact with ill person and summer season based on logistic regression

Shigella cases alone, or together with Campylobacter cases, had similar clinical predictors, except for seasonality

Fever was strongly associated with Shigella +/- Campylobacter than diarrhea from other causes considered together, but also shows that blood in stool alone is not a sensitive predictor of these organisms

The negative association of out-of-state travel with Shigella and Campylobacter may be due to collinearity with lower socioeconomic status, which had been demonstrated before with Shigella in a Thai study (15), though other studies have associated higher rates of Campylobacter infection with higher socioeconomic status (20, 21)

Conclusions

Improved ability to predict cases of Shigella and Campylobacter infection could guide more appropriate antibiotic use, the importance of which is highlighted by antimicrobial resistance already seen in these organisms (16, 17)

Improved understanding of predictors could also enable more targeted use of diagnostics, potentially helping to curb unnecessary health care costs

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References