Epidemiology of Viral Gastroenteritis in Iran

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When comparing BMD with Vitek 2, only 44 (21%) had different MIC values with the vast majority (95%) different by only 1-well dilution. Overall, Vitek 2 results were more consistent with BMD, while standard Etest appeared to overestimate MICs when compared with the standard method of BMD.

Clinical patient data were available for 187 patients (63 MRSA and 124 MSSA). There were no differences in median length of hospital stay, median hospital cost or all-cause mortality when comparing patients infected with a staphylococcal isolate with an MIC <1 µg/mL compared with those with an MIC ≥ 1 µg/mL or when comparing patients with MSSA versus MRSA bacteremia.

**DISCUSSION**

In the adult population, the trend during 2000–2005 toward increasing vancomycin MIC values for *S. aureus*, so-called “MIC creep,” has led to the concern that vancomycin may no longer be appropriate to treat invasive staphylococcal infection in adults where the MIC is ≥ 2 µg/mL. Furthermore, the increase in vancomycin MICs has been associated with worse outcomes in adults with invasive *S. aureus* disease. We did not observe a similar trend in our pediatric population during the study period. Our data are consistent with other reports in which a significant vancomycin MIC increase in pediatric populations was not demonstrated. There is not a clear explanation for the difference in MIC trends between children and adults. However, it may be related to differences in vancomycin usage (both frequency of use and dosing strategies) in children and adults leading to differences in resistance patterns of *S. aureus*. Our study is the first to specifically evaluate all blood isolates during a specified period.

We also evaluated the prevalence of heterogeneous vancomycin-intermediate *S. aureus* in our pediatric population with invasive MRSA. Evaluation of the presence of vancomycin heteroresistance is challenging as there is a lack of standardized methodology for identification and the gold standard, population analysis profile to vancomycin exposure curve ratio (PAP-AUC), can be labor-intensive and is typically unavailable in clinical laboratory settings. We used the Etest GRD method as a screening test to detect vancomycin heteroresistance for all MRSA isolates in our population. This method has demonstrated relatively high specificity and sensitivity when compared with PAP-AUC, suggesting that it may be an adequate screening test. However, confirmation of positive tests by PAP-AUC is warranted. Although no vancomycin heteroresistance was identified among our isolates, observations should be confirmed in other pediatric populations because of the potentially associated clinical complications and poor outcomes reported in adult cases.

Storage of *S. aureus* isolates can potentially impact vancomycin susceptibility results and is a recognized limitation of this study. Furthermore, results over a more extensive study period may potentially demonstrate an increasing trend in vancomycin MICs. Finally, a larger sample size may be required to detect heteroresistance.

In our study, vancomycin MIC results varied across testing methods, with the standard Etest resulting in a higher value 94% of the time when compared with BMD. This could be problematic in clinical care as a falsely elevated vancomycin MIC may deter a clinician from using vancomycin in a scenario in which it would otherwise be the preferred first-line therapy. Therefore, it is essential for clinicians to be aware of the testing method used for susceptibility testing in their institution and consider MIC results in light of the method when selecting vancomycin as the preferred antimicrobial agent.

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**REFERENCES**


**EPIDEMIOLOGY OF VIRAL GASTROENTERITIS IN IRAN**

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**Abstract:** Viruses are prominent causative agents of acute gastroenteritis in children <5 years of age per year. In the present review, all viral gastroenteritis studies in Iran were assessed, and the mean prevalences of rotaviruses, noroviruses, enteric adenoviruses, sapoviruses and astroviruses associated with acute gastroenteritis were 39.9%, 6%, 5.7%, 4.2% and 2.7%, respectively. In 2 studies, human bocavirus and human parechovirus were detected in 21.8% and 23.7% of children with acute gastroenteritis, respectively.

**Key Words:** viral gastroenteritis, prevalence, Iran

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**TABLE 1.** Detection Rates of RVs, NoVs, EAdVs, SaVs and AstVs in Children With Acute Gastroenteritis in Iran Between 1986 and 2011

<table>
<thead>
<tr>
<th>Viral Agents</th>
<th>Number of Samples Tested</th>
<th>Positivity Rate, n (%)</th>
<th>Number of Studies</th>
<th>Year</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>RVs</td>
<td>13,383</td>
<td>5335 (39.9)</td>
<td>22</td>
<td>1986–2011</td>
<td>4–7</td>
</tr>
<tr>
<td>EAdVs</td>
<td>3559</td>
<td>200 (5.7)</td>
<td>9</td>
<td>1999–2010</td>
<td>4,8–15</td>
</tr>
<tr>
<td>NoVs</td>
<td>9028</td>
<td>182 (6.0)</td>
<td>5</td>
<td>2006–2010</td>
<td>4,15–18</td>
</tr>
<tr>
<td>SaVs</td>
<td>289</td>
<td>12 (4.2)</td>
<td>3</td>
<td>2006–2009</td>
<td>16,19,20</td>
</tr>
<tr>
<td>AstVs</td>
<td>3629</td>
<td>98 (2.7)</td>
<td>5</td>
<td>2002–2010</td>
<td>4,14,21–23</td>
</tr>
</tbody>
</table>

RVs indicates rotaviruses; EAdVs, enteric adenoviruses; NoVs, noroviruses; SaVs, sapoviruses; AstVs, astroviruses.

Diarrrhea is an important symptom of most enteric infections that are most frequent in children <5 years of age. In 1992, Bern et al. published a review manuscript of studies from 1980s and reported 3.3 million deaths. They estimated 2–3 episodes of diarrhea per child of <5 years of age every year in developing countries. In 2003, Kosek et al. published a review of the burden of diarrheal disease from reports between 1992 and 2000. They reported 3.2 episodes per child <5 years of age per year in developing countries and also estimated 2.5 million deaths (range: 2.1–4.7 million), which was less than that in previous studies. In addition, the mortality rate of diarrhea disease was 4.9 per 1000 per year in the 1990s, which was decreased compared with reported previous studies. Bern et al. reported 13.6 and 5.6 per 1000.

Agents that were recognized to cause diarrheal disease include bacteria, parasites and viruses. In developing countries, rotavirus (RVs) are responsible of approximately 20% of diarrhea-related deaths in children <5 years of age. Noroviruses (NoVs) and Sapoviruses (SaVs) of the Caliciviridae family also cause acute gastroenteritis (AGE). Currently, NoVs as emerging viruses are the most important cause of AGE, particularly in countries after introduction of universal RV vaccination. Many studies have shown that SaVs are important in outbreaks of sporadic gastroenteritis in children <5 years of age. Enteric adenoviruses (EAdVs), serotypes 40 and 41, are also associated with AGE. The frequency of EAdV-associated gastroenteritis varies considerably in the various studies and locations. Astroviruses (AstVs) also increasingly detected as another viral causing of gastroenteritis which reported in up to 10% of sporadic gastroenteritis. Moreover, toroviruses and coronaviruses of the Coronaviridae family, human parechoviruses and Aichivirus of the Picornaviridae family, and human bocavirus (HBoVs) of the Parvoviridae family are other viruses, which have been found to be associated with AGE.

Through improvement of the safety of drinking water and the disposal of sewage, the rate of nonviral gastroenteritis infections has decreased. Detection and management of viral AGE are considered high priority for the healthcare system, including Iran. In this review, all viral gastroenteritis studies in Iran were assessed to analyze the infection rate and association with enteric viruses.

**METHODS**

For this review, all published viral gastroenteritis studies from Iran were obtained by searches of Medline, PubMed and National databases. Search key words included: Viral gastroenteritis, diarrhea, Iran, rotavirus, norovirus, adenovirus, astrovirus, sapovirus, parechovirus and bocavirus. Overlapping data were excluded.

**RESULTS**

Data analysis of 22 gastroenteritis studies attributable to rotavirus estimated that prevalence of RV infection was 39.9% (Table 1). EAd40 and AAd41 viruses were detected in 5.7% of the stool samples in 9 published studies (Table 1). For NoVs and SaVs, positivity rates were on average 6.0% and 4.2% from 5 studies and 3 studies, respectively. The prevalence of AstVs was 2.7% on average (5 studies) (Table 1). Another observation was that age and seasonal patterns of AGE due to virus infections in Iran were similar to each other. Viral infection occurred most often in children <2 years of age and during the cooler months.

In 2010, Nadji et al. reported HBoVs isolation from 21.8% children with AGE. In 2012, Ghazi et al. also showed that the incidence of human parechovirus 1 in children with AGE in Iran was 23.7%.

**DISCUSSION**

Considering that there have been few reports about burden of viral AGE in Iran, this review provides helpful information about frequency and circulation of viruses causing childhood AGE. RVs, NoVs, AdVs, SaVs and AstVs were all found to be involved as causes of AGE as well as human parechoviruses and HBoVs.

Rotaviruses were the most prevalent viral agent causing AGE, consistent with findings in other regions in the world before the introduction of the RV vaccine. NoVs have been shown to be responsible for 70–90% of AGE outbreaks in Europe and the United States, respectively. The prevalence of NoV in Iran was 6.0% which is close to data reported from neighboring countries such as Pakistan. However, the prevalence of NoV in some countries such as India, Iraq, Taiwan, Nicaragua, Brazil and Italy was 12–48%, i.e higher than in Iran. The detection rate of SaVs was not as high as that of NoVs in Iran, but it was consistent with rates in studies of other parts of the world. EAdVs were responsible for 5.7% of AGE in children which is much lower than in Nigeria and close to that of epidemiologic reports of adenovirus detection in Brazil, Indonesia, Singapore and China. AstVs as cause of AGE in children which have a prevalence rate of 1.4–8.6% in different reports, but higher rates in Japan and Central America. In Iran, the prevalence of AstV was estimated to be 2.7%, similar to recent reports from Venezuela and Taiwan. In summary, this data analysis suggests that SaVs and AstVs are minor causes of AGE in children compared with RVs, NoVs and EAdVs.

In 2 studies, HBoV and human parechovirus 1 were detected in 21.8% and 23.7% of children with AGE, respectively. These reports were accordance to previous studies, but they need to confirm by further studies.

Overall, most studies assessed in this review have investigated for only a single virus or a limited range of viruses. Therefore, the true prevalence of viruses as cause of AGE and the real burden of viral AGE in Iran remain to be identified in carefully planned prospective studies with appropriate control groups. Furthermore, genotyping should be carried out in such a study to identify the most frequent types of the different viruses responsible for the clinical burden of AGE in children in Iran.