ROTAVIRUS INFECTION IN INFANTS AND YOUNG CHILDREN

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ABSTRACT

Rotaviruses are the major cause of severe gastroenteritis in infants and young children worldwide. The aim of the present study was to determine (1) the involvement of rotavirus in acute gastroenteritis (AGE) in children up to 3 years of age in geographical region of the study area, (2) the seasonal prevalence of rotavirus-related AGE and (3) the presence of asymptomatic rotavirus infection in children attending day care centers. A two-year retrospective study was carried out on 250 children with AGE aged 6 months to 3 years. Ninety children were hospitalized with pronounced disease symptoms, and 160 children with milder symptoms received ambulatory treatment. The investigation included 860 healthy children attending day care centers in Nis as well. A single stool sample was taken from each child for analysis. The samples were identified as rotavirus positive by antigen detection strategies, including latex agglutination (LA) tests. Out of 250 episodes of acute gastroenteritis 68 (27.20%) were associated with rotavirus antigen detection. Of 160 children with episodes of AGE treated ambulatory, rotavirus antigen was detected in 30 (18.75%). Of 90 children hospitalized with more severe AGE, higher percentage of rotavirus antigen-positive was recorded in 38 (42.22%). In the group of 860 healthy children attending day care centers in Nis, asymptomatic rotavirus infection was confirmed in 48 children (5.58%). The highest prevalence of rotavirus infection was observed in the period October-December (41.17%), and the lowest in the summer months July-September (14.71%). Rotaviruses are involved in a high percentage in the etiology of AGE in geographical region of the study area.

Introduction

Rotaviruses belong to a family of Reoviridae, the genus Rotavirus.

Rotavirus was first identified by electron microscopy in 1973 from duodenal biopsies of children with diarrhea. Human and animal rotaviruses are known.

Rotaviruses are non-enveloped, icosahedral, with double capsid. Their electron microscopic appearance shows a 60-80nm wheel with radiating spokes (Latin, rota = wheel). The rotavirus genome contains double stranded (ds) RNA in 11 segments.

Outer structural proteins are VP7 and VP4. VP4 is the viral hemagglutinin and forms spikes from the surface. Inner core structural proteins are VP 1, 2, 3, and 6. VP6 is an important antigenic determinant.

*Abbreviations: AGE- acute gastroenteritis, LA- latex agglutination.
There are at least 15 different serotypes of rotaviruses. Six are based on antibodies to VP7 (P type) while nine serotypes, based on VP4 (G type), are known.

Group A viruses are the most common, with subgroups that are defined by antigenic differences in VP6 and with 4 different serotypes that affect humans.

Affected host cells are mature enterocytes lining the middle and upper end of the intestinal villi.

Rotaviruses infect children at a young age. Older infants and young children (4 months - 2 years) tend to be more symptomatic with diarrhea. Young infants may be protected due to trans-placental transfer of antibody. Vomiting, nausea and diarrhea are dominant symptoms. Diarrhea is usually watery, lasting 3-9 days, but longer in malnourished and immune deficient individuals. Necrotizing enterocolitis and hemorrhagic gastroenteritis are seen in neonates. Dehydration is the main contributor to mortality. Secondary malabsorption of lactose and fat, and chronic diarrhea are possible.

The aim of the present study was to determine (1) the involvement of rotavirus in AGE in children up to 3 years of age in geographical region of the study area, (2) the seasonal prevalence of rotavirus-related AGE and (3) the presence of asymptomatic rotavirus infection in children attending day care centers.

Materials and Methods
A two-year retrospective study was conducted on 250 children aged 6 months to 3 years with the symptoms of acute gastroenteritis (AGE). Ninety children were hospitalized in the Clinic of Pediatrics in Nis for pronounced disease symptoms (vomiting, diarrhea, dehydration), and 160 children with milder symptoms received ambulatory treatment. A stool sample was taken right after the observation. Rectal swab specimens were excluded from the procedure. Stool samples were examined macroscopically and microscopically, and afterwards stored at -20 degrees C for a longer period. Stool samples containing blood and leucocytes were not examined. The investigation was carried out on 860 healthy children attending day care centers in Nis as well. A single stool sample was taken from each child for analysis. The investigation was carried out in the period September-December. The samples were identified as rotavirus positive by antigen detection strategies, including latex agglutination tests (Orion Diagnostics, Finland) used according to the instructions of the manufacturer. Statistical analysis of the data was performed using Chi square test with Yates correction.

Results and Discussion
The frequency of detection of rotavirus in faeces in children with AGE less than three years of age is shown in Table 1. Out of 250 episodes of acute gastroenteritis, 68 (27.20%) were associated with rotavirus antigen detection.

<table>
<thead>
<tr>
<th>Investigated groups</th>
<th>No. of Subjects</th>
<th>No. Positive</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalized children with AGE</td>
<td>90</td>
<td>38</td>
<td>42.22</td>
</tr>
<tr>
<td>Children with AGE treated ambulatory</td>
<td>160</td>
<td>30</td>
<td>18.75</td>
</tr>
<tr>
<td>Healthy children in day care centers</td>
<td>860</td>
<td>48</td>
<td>5.58</td>
</tr>
</tbody>
</table>

Out of 160 children with episodes of AGE, who received ambulatory treatment, rotavirus antigen was detected in 30 (18.75%). Out of 90 children hospitalized with more severe AGE, higher percentage of rotavirus antigen-positive was recorded in 38 (42.22%). A significant difference was found in the frequency of rotavirus antigen detection between hospitalized children and those who received ambula-
In the group of 860 healthy children attending day care centers in Nis, asymptomatic rotavirus infection in a stool sample was confirmed in 48 children (5.58%).

In the present study, the occurrence of rotavirus infection in relation to season was analyzed. The results are shown in Table 2.

The highest prevalence of rotavirus infection was observed in the period October-December (41.17%), and the lowest in the summer months July-September (14.71%). A statistically significant difference was found in the occurrence of rotavirus infection between autumn and summer months (p<0.01).

Rotaviruses are the major cause of severe gastroenteritis in infants and young children worldwide. Group A rotaviruses are the single most important cause of severe acute diarrhea in young children throughout the world (1).

Each year, rotavirus causes an estimated 111 million episodes of diarrhoea requiring only home care, 25 million clinic visits, and 2 million hospitalizations. The prevalence of rotavirus disease is similar in children in both developed and developing countries. Surveillance studies and serum antibody studies indicate that all young children are likely to have had at least one rotavirus infection by the time they are 3 years of age. Worldwide, approximately 400 000-600 000 children in developing countries die of rotavirus-associated dehydration each year (2). However, children in developing nations die more frequently, possibly because of several factors, including poorer access to hydration therapy, and a greater prevalence of malnutrition. An estimated 1.205 children die from rotavirus disease each day, and 82% of these deaths occur in children in the poorest countries.

Rotaviruses account for about 10% of diarrhoea episodes that cause a child to receive medical treatment but are associated with about 40% of diarrhea episodes in young children who require hospitalization. Many children are infected more than once. First infections with rotavirus usually are the most severe; however, some severe second infections occur. The protective immunity acquired from infection is incomplete and the efficacy of that immunity varies according to the severity of symptoms. However, rotavirus was detected in 11-71% of children with diarrhea; the median rate of detection (33%) was independent of the level of economic development or geographical region of the study area (3). In the United States, rotaviruses cause about 5% to 10% of all diarrheal episodes in infants and children less than 5 years of age; however, these viruses account for 30% to 50% of severe diarrheal episodes (4).

In the present study, the latex agglutination (LA) test detecting Group A rotaviruses with high sensitivity was used for rotavirus detection (5). Of the total of 250 children aged up to 3 years with AGE, in 68 (27.20%) rotavirus antigen was confirmed in a stool sample. The results of the present investigation conducted in geographical region of the study area correspond to most results obtained from the investigations performed in developing

**TABLE 2**

<table>
<thead>
<tr>
<th>Month</th>
<th>No. of Subjects</th>
<th>Positive No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>January</td>
<td>10</td>
<td>4</td>
<td>5.88</td>
</tr>
<tr>
<td>February</td>
<td>18</td>
<td>6</td>
<td>8.82</td>
</tr>
<tr>
<td>March</td>
<td>17</td>
<td>8</td>
<td>11.76</td>
</tr>
<tr>
<td>April</td>
<td>19</td>
<td>5</td>
<td>7.35</td>
</tr>
<tr>
<td>May</td>
<td>11</td>
<td>4</td>
<td>5.88</td>
</tr>
<tr>
<td>June</td>
<td>26</td>
<td>3</td>
<td>4.42</td>
</tr>
<tr>
<td>July</td>
<td>29</td>
<td>2</td>
<td>2.94</td>
</tr>
<tr>
<td>August</td>
<td>18</td>
<td>2</td>
<td>2.94</td>
</tr>
<tr>
<td>September</td>
<td>28</td>
<td>6</td>
<td>8.82</td>
</tr>
<tr>
<td>October</td>
<td>36</td>
<td>16</td>
<td>23.53</td>
</tr>
<tr>
<td>November</td>
<td>18</td>
<td>7</td>
<td>10.29</td>
</tr>
<tr>
<td>December</td>
<td>20</td>
<td>5</td>
<td>7.35</td>
</tr>
<tr>
<td>Total</td>
<td>250</td>
<td>68</td>
<td></td>
</tr>
</tbody>
</table>

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countries.

Saravanan P, et al. in their study showed an overall infection rate of 22.55% in children with acute diarrhea (1). Shahrazad M, et al. showed that the overall rate of rotavirus infection was 15.3% in children with diarrhea (6). Similar results were obtained from other investigations as well (3, 6). These results correspond to those obtained by other authors in developing countries (China, Pakistan), which record a prevalence of >16% in infection cases (3, 7). As documented by other studies, most of the cases of rotaviral diarrhea occur in children less than two years of age (8, 9, 10).

In children with milder symptoms of AGE who received ambulatory treatment (160), rotaviruses in stools were identified by using the LA test in 18.75%. In the group of children with more severe symptoms of AGE, with pronounced dehydration (hospitalized children) the finding of rotavirus was significantly higher and amounted to 42.22%. A statistically significant difference was observed in the finding of rotavirus between ambulatory treated and hospitalized patients (p<0.001).

During a period of over 8 years, in 34.5% of infants and young children admitted with diarrhea to Washington, D.C., Hospital, rotavirus was detected in their feces on admission (11). In addition, the investigation of the involvement of rotavirus in AGE in hospitalized children in Myanmar have documented a high percentage of involvement (53%) (12).

Given the possibility of endemic occurrence of rotavirus-related AGE, asymptomatic rotavirus infection was investigated in different geographical regions. Contradictory results varying from negative to a very high percentage (>50%) of the presence of rotavirus antigen in feces were documented (6, 13).

Burke et al. have demonstrated asymptomatic infection of rotavirus in 11% (14), Keswick et al. in 12.4% of children (15). The investigation carried out on healthy soldiers revealed the presence of rotavirus in 4.32% of their stool samples (16). The investigation conducted in Iran documented asymptomatic rotavirus infection in 1.1% of healthy children (6).

In the present investigation carried out on healthy children (860) attending day care centers in the City of Nis, asymptomatic virus infection was confirmed in (5.58%).

Rotaviruses display a seasonal pattern of infection in developed countries, with epidemic peaks occurring in cooler months of each year (17, 18).

This is similar to the prevalence in other developing countries where rotavirus is a significant pathogen among infants aged less than 12 months (8). In most parts of the world, rotavirus is present throughout the year (3).

In our investigation, the prevalence of rotavirus-related AGE was highest in the period October-December (41.17%) with the greatest number of cases in October 23.53%. In the summer months, July-September, the lowest percentage of rotavirus-related AGE (14.71%) was recorded. A statistically significant difference was found in the occurrence of rotavirus infection between autumn and summer months (p<0.01). The lowest frequency of rotavirus-related AGE was recorded in July and August (2.49%).

An investigation conducted in the USA documented the absence of rotavirus infection from July to October in contrast to 67% of rotavirus-related AGE in January and February (11). Similar results have been reported by other authors as well (3.19).

Conclusions

The overall involvement of rotavirus in AGE in children aged up to 3 years in geographical region of the study area amounted to 27.20%. In hospitalized children with more severe AGE, rotaviruses were identified in 42.22%. In ambulatory treated children, the percentage of LA
positive was 18.75%. The highest prevalence of rotavirus-related AGE was recorded in the period October-December (41.17%), and the lowest in July-September (14.71%). Asymptomatic rotavirus infection in children attending day care centers was confirmed in 5.58%. Rotaviruses are involved in a high percentage in the etiology of AGE in geographical region of the study area.

REFERENCES