Seroepidemiology of Human Group C Rotavirus in South Africa

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Sera from three separate healthy population cohorts were used to determine the incidence of group C rotavirus infections in 1,356 South Africans. Using an enzyme-linked immunosorbent assay based on a recombinant group C rotavirus VP6 protein, the total percent positivity was found to be 34.4% (range, 33 to 38%), with almost half of the population infected after the age of 20 years.

Rotaviruses are well known as important agents of acute infantile gastroenteritis. The group A rotaviruses are considered the most important cause of severe dehydrating diarrheal illness in infants and young children worldwide and are estimated to result in approximately 870,000 deaths in young children in the developing world each year (15). However, rotaviruses are classified into at least seven serogroups (A to G) on the basis of distinctive antigenic and genetic properties (23). Members of at least two of these rotavirus serogroups (serogroups B and C) have been reported to occur in humans. Large outbreaks of group B rotavirus-associated illness in adults in China were reported (9). Group C rotaviruses, on the other hand, have been associated with either sporadic diarrheal illness or limited outbreaks of illness in various settings.

The group C rotaviruses were detected initially in the feces of young pigs with diarrhea (22). This finding was soon followed by the identification of these porcine viruses in Europe and Australia (1, 17). Viruses of this serogroup in humans were soon being reported as well. The human group C rotaviruses have been identified in several developed countries, including Australia (21), the United States (12), England (2, 11), Finland (27), and Japan (14, 26). In addition, the group C rotaviruses have been identified in developing countries such as those in Latin America (6), India (3), China (5), and Malaysia (19). In South Africa, group C rotaviruses in diarrheal feces from young pigs were initially identified (8), followed by the detection of the virus in human stool by polyclonal antibody gel electrophoresis in Pretoria (23a).

Several seroepidemiological studies have been undertaken with reagents derived from a porcine group C rotavirus and have demonstrated that antibodies to group C rotaviruses are present in 3 to 45% of the human sera tested (3, 20, 25). Generally, group C antibody was believed to be present only in children over three years of age. More recently, the cloned VP6 gene of a human group C rotavirus has been expressed in a baculovirus system and utilized to generate recombinant reagents for serological assays (11). In this latter study, antibodies to the group C rotaviruses were detected in 43% of serum samples tested, with the maximum levels present in samples from septuagenarians.

In this study, we utilized collections of sera from various local indigenous populations in South Africa to conduct a seroepidemiological survey of antibodies to group C rotavirus with recombinant reagents developed against the cloned and expressed human group C rotavirus VP6. Sera were available from three separate population cohorts in South Africa that had participated in hepatitis B virus vaccine trials. First, sera were available from 396 individuals of a healthy family-based cohort in an urban setting in Ga-Rankuwa (15). Second, 248 sera from a healthy family-based cohort of San Bushmen living in a rural situation in Schmidtsdrift were analyzed (7). Finally, 350 sera were available from school children between 6 and 20 years of age in VendaLand in the northern tip of South Africa; a further 365 sera were available from Venda adults over 20 years of age (24).

A solid-phase enzyme-linked immunosorbent assay (ELISA) was previously developed to detect serum antibodies to human group C rotaviruses (11). All serum samples were analyzed for the presence of antibodies to group C rotavirus antibodies at a dilution of 1:100 by the enzyme immunoassay techniques previously described (11). The wells of 96-well polyvinyl chloride flat-bottom microtiter plates (ICN Flow, Immunol-2) were coated with baculovirus-expressed recombinant group C rotavirus VP6 protein. A direct ELISA with a horseradish peroxidase-conjugated goat anti-human immunoglobulin G (Dako Diagnostic, Ltd.) and tetramethylbenzidine as the substrate was performed on all serum samples. After development of the enzymatic reaction, the absorbance was read at 450 nm on an automated spectrophotometer (Anthos Labotec). An optical density value of greater than four times the value of a nonreactive human serum sample was used as a cutoff for a positive result.

In total, 466 (34.4%) of the 1,356 sera tested were positive for group C rotavirus antibodies (Table 1). The seroprevalence rate found in this study is similar to the levels found in women of childbearing age in western New York state (20) and in random blood donors in a small study in Bristol, United Kingdom (4). However, it is slightly lower than the levels found in a study utilizing the same recombinant reagents in Southampton, United Kingdom (10). The reagents have previously been shown to be specific for group C human virus and not to cross-react with group A antibody (10).

Group C rotaviruses have been described as being more common in an older population than are the group A rotaviruses (11), a finding which was supported in this study. Approximately half of the exposures to the group C rotavirus must have occurred after the age of 20 years. In total, only 24.9% (167 of 669) of the children and young adults under 20 years of age had antibodies to the group C virus, whereas in the adult cohort over 20 years of age, this figure reached 44.8% (265 of 582) (Table 1). This is a picture very similar to that reported for the United Kingdom (10).
When analyzing the separate population groups in this study, several observations could be made. For instance, in the San, a family-based group of Bushmen who were relocated from Namibia, Africa, in 1991 and who live in a refugee camp near Schmidtsdrift (7), the levels of group C antibody are similar in the two age groups (i.e., subjects <20 and >20 years old). In addition, the relative optical density values were higher in this population than in the other two population groups. This may be due to a more recent exposure of the entire community to group C rotavirus; this is likely to have occurred after their relocation, when water had to be shipped into the camp. In the Ga-Rankuwa cohort, which is the most urban of the three groups (15), almost half of the total seropositive population had acquired their antibodies by the age of 10 years.

The role of group C rotavirus infection in humans has been considered to be insignificant in the global picture of diarrheal illness, due to the apparent sporadic nature of the virus’s occurrence. However, there has been a lack of sensitive techniques for the detection of these viruses or for large-scale seroepidemiological surveys. The development of more sensitive techniques, such as recombinant-based ELISAs, both for the detection of group C rotavirus antigen in stools (11, 12) and for the determination of exposure to the virus by sero-prevalence studies (10, 25) will help to describe the epidemiology and importance of this virus.

Further studies of the distribution and epidemiology of the group C human rotaviruses with newly developed recombinant reagents for ELISA-based tests are indicated in developing countries for a number of reasons. First, group C rotaviruses have been associated with outbreaks of diarrheal illness, demonstrating their epidemic potential (16, 18). Second, group C rotaviruses have been associated with fatalities in a family-based outbreak of group C rotavirus-associated illness, demonstrating their potential virulence (4). Third, the distribution of group C rotaviruses has been shown to be more common than previously believed, according to a number of seroepidemiological surveys of the presence of group C rotavirus antibody in humans (references 10, 14, and 20 and this study).

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REFERENCES

### TABLE 1. Serological survey for antibodies to group C rotavirus in South African populations with a recombinant ELISA

<table>
<thead>
<tr>
<th>Age range (yrs)</th>
<th>Ga-Rankuwa</th>
<th>Schmidtsdrift</th>
<th>Vendaland</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. subjects</td>
<td>No. positive</td>
<td>No. subjects</td>
<td>No. positive</td>
</tr>
<tr>
<td>1–5</td>
<td>6</td>
<td>1 (16.7)</td>
<td>25</td>
<td>8 (32)</td>
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<tr>
<td>6–10</td>
<td>55</td>
<td>9 (16.4)</td>
<td>71</td>
<td>27 (38.0)</td>
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<tr>
<td>11–15</td>
<td>60</td>
<td>13 (21.7)</td>
<td>31</td>
<td>11 (35.5)</td>
</tr>
<tr>
<td>16–20</td>
<td>67</td>
<td>18 (26.9)</td>
<td>7</td>
<td>2 (28.6)</td>
</tr>
<tr>
<td>Subtotal</td>
<td>188</td>
<td>41 (21.8)</td>
<td>134</td>
<td>48 (35.8)</td>
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<td>80</td>
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<td>29</td>
<td>14 (48.3)</td>
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<td>31–40</td>
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<td>15 (34.9)</td>
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<td>11 (40.7)</td>
<td>20</td>
<td>11 (55)</td>
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<td>7</td>
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<td>2 (25)</td>
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<td>&gt;70</td>
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<td>6 (40)</td>
<td>4</td>
<td>1 (25)</td>
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<tr>
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<td>93 (44.7)</td>
<td>111</td>
<td>47 (42.3)</td>
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<tr>
<td>Total</td>
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<td>134 (34)</td>
<td>245</td>
<td>95 (38.8)</td>
</tr>
</tbody>
</table>

Not all ages for all individuals were recorded.


