Epidemiology of Rotavirus Diarrhea in Egyptian Children and Implications for Disease Control

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Reliable epidemiologic data are essential for formulating effective policy to control rotavirus disease through immunization. The objective of this study was to describe the epidemiology of rotavirus diarrhea in a population-based cohort of children under 3 years of age residing in Abu Homos, Egypt, in 1995–1996. Rotavirus diarrhea incidence rates (episodes per person-year) were 0.13 for infants aged <6 months, 0.61 for those aged 6–11 months, 0.17 for those aged 12–23 months, and 0.15 for those aged 24–35 months. Fifty-six percent of children with rotavirus diarrhea had clinical dehydration; 90% of rotavirus diarrheal episodes occurred between July and November. In infants under 1 year of age, receipt of breast milk was associated with a lower incidence of rotavirus diarrhea. No other sociodemographic or environmental factor was found to be significantly associated with rotavirus diarrhea. Of 46 rotavirus isolates with strains identified, 41 (89%) were G serotypes 1 and 2. Rotavirus diarrhea was a major cause of morbidity in this cohort. Promotion of breastfeeding may exert a protective effect in young infants in this setting, but improvements in water and sanitation are unlikely to be effective preventive measures. The use of effective immunization against rotavirus in early infancy should be considered a public health priority. Am J Epidemiol 1999; 150:770–7.

Rotavirus is reported to be the most common cause of severe childhood diarrhea worldwide (1, 2). Despite the recognized efficacy of oral rehydration therapy in treating dehydrating diarrhea, each year in developing nations rotavirus infections are estimated to result in 600,000–800,000 deaths in children under 5 years of age (2). By the age of 3, almost every child in the world has been infected by rotavirus (3). In the United States, where fewer than 40 children die each year from rotavirus infection, the disease is estimated to cost over 1 billion dollars per year (4). Since rotavirus disease remains widely prevalent in developed nations, it is unlikely that improving hygienic and sanitary conditions alone will have a dramatic impact on the disease in developing countries. Therefore, effective immunization against rotavirus has been considered a public health priority for developing nations.

The World Health Organization has stated that in considering routine immunization against rotavirus, countries will need sound epidemiologic data to assess the burden of disease, to examine trends in seasonality and age patterns of incidence, and to determine the serotypes of strains currently in circulation (5). Advances in molecular characterization of rotavirus strains, particularly the genes encoding the outer capsid proteins VP4 (the protease cleaved protein) and VP7 (the glycoprotein), have increased our ability to P- and G-type rotavirus strains. While G types 1–4, the targets for current vaccines, are the most common types worldwide, in some countries other G types predominate, which may challenge the vaccines’ efficacy (6).

In this study, we have addressed these issues in a population-based cohort of Egyptian children under 2 years of age who were monitored for a period of 1 year. The specific objectives of this study were to determine age-specific and season-specific incidence rates of diarrhea caused by rotaviruses, to describe the clinical features of rotavirus infection, to determine the association between excretion of rotaviruses and the occurrence of diarrheal symptoms (patho-
genicity), to identify sociodemographic and environmental factors associated with the risk of rotavirus diarrhea, to identify factors associated with severe disease following infection with rotaviruses (virulence), and to determine the P and G types of rotavirus strains in circulation.

MATERIALS AND METHODS

Study population

The study population consisted of a cohort of children under the age of 24 months assembled from two villages in the vicinity of Abu Homos, a rural district located in the Nile Delta in northern Egypt, approximately 40 km from Alexandria. In January 1995, following a house-to-house census, enrollment of neonates and children under 24 months of age commenced. Thereafter, newborns in households within the censused area were continuously enrolled in the cohort. Since the children in the cohort were to be considered as potential candidates for future enteric vaccine trials, children with major congenital abnormalities or severe chronic illnesses were not eligible for participation. During the study period, there was no child who met the ineligibility criteria. Baseline sociodemographic and household hygiene information was collected during the census. Prior to enrollment, written informed consent was obtained from each child's parent or guardian, and the human use guidelines of the US Departments of Defense and Health and Human Services were followed throughout the study.

Surveillance

Active surveillance of the cohort with twice-weekly home visits began in February 1995. If the child had diarrhea, he or she was examined by a study physician. The physician obtained a rectal swab, which was placed in Cary-Blair transport medium, and a fecal specimen. Upon clinical examination, dehydration was classified according to the World Health Organization criteria as "none," "some," or "severe" (7). When it was deemed necessary by the physician, symptomatic children were referred to a village clinic for further evaluation and rehydration therapy. Deaths and other losses to follow-up were recorded at the twice-weekly visits. All individuals in the cohort, irrespective of symptoms, were surveyed once every 2 months (bimonthly), at which time a rectal swab placed in Cary-Blair medium and a new fecal specimen were collected. At each home visit, information regarding the child's diet and breastfeeding status was obtained.

Definitions

A "diarrheal day" was defined as the occurrence of at least three nonformed stools (or at least one, if bloody) in a 24-hour period. In addition, if the child was being breastfed and the stool was not bloody, the mother had to report an increase in frequency or a reduction in consistency of the stools compared with what she considered to be normal. A "diarrheal episode" was defined as beginning on the first diarrheal day after at least 3 consecutive nondiarrheal days and ending on the first diarrheal day to be followed by at least 3 consecutive nondiarrheal days. A "rotavirus diarrheal episode" was defined as a diarrheal episode in which rotavirus was detected in a fecal specimen collected during the episode. Breastfeeding was defined as the receipt of any breast milk, irrespective of other components of the diet.

Laboratory evaluations

All rectal swabs and fecal specimens were transported in ice packs to the Abu Homos field laboratory, where they were refrigerated. Twice weekly, the rectal swabs and fecal specimens were transported in ice packs to the laboratories of US Naval Medical Research Unit 3 in Cairo, where the rectal swabs were evaluated with standard microbiologic methods to isolate Salmonella, Shigella, Campylobacter, and Vibrionaceae (8). In addition, the rectal swabs were plated on McConkey's media, and five lactose-positive colonies were evaluated for both heat-labile enterotoxin-positive and heat-stable enterotoxin-positive enterotoxigenic Escherichia coli (ETEC), using GM1-ganglioside enzyme-linked immunosorbent assays (9, 10).

The fecal specimens were kept frozen at −70°C and subsequently transported on dry ice from the Naval Medical Research Unit 3 laboratories to the gastrointestinal virology laboratories at the Centers for Disease Control and Prevention in Atlanta, Georgia. Stool suspensions were prepared as 10 percent (weight/volume) phosphate-buffered saline (pH 7.2) extracts and were tested for rotavirus using a commercial enzyme-linked immunosorbent assay kit (Rotaclone; Meridian Diagnostics, Inc., Cincinnati, Ohio). All rotavirus strains were then P- and G-typed by reverse-transcription polymerase chain reaction (11–13).

Analyses

The study period was February 11, 1995, through February 10, 1996. Crude diarrhea incidence rates and age-specific incidence rates were calculated by dividing the number of episodes by the number of person-
years at risk (total person-years of follow-up minus the
duration of diarrheal episodes after the first day of
each episode). The independent associations between
variables under study and incidence of rotavirus diar-
rhea (first episodes) were estimated by multivariate
analyses, using proportional hazards models (14).
Associations, expressed as hazards ratios, were
derived from the model coefficients. The variables
evaluated as potential predictors of rotavirus incidence
were gender, season (warm vs. cool), maternal educa-
tion (any vs. none), household size (number of persons
in household), crowding (number of persons in house-
hold/number of rooms in house), water sources for
drinking, washing, and bathing (municipal vs. other),
presence of a household latrine, presence of a house-
hold garbage container, presence of household elec-
tricity, and breastfeeding (any vs. none). Bivariate
analyses, adjusting for age, were carried out for all
exploratory variables. A statistical significance level of
0.05 was selected for inclusion of variables in multi-
variate modeling. Analyses evaluating breastfeeding as
a potential predictor of rotavirus incidence were
repeated separately for the <1-year and ≥1-year age
groups.

Because enrollment included children under 2 years
of age, the cohort contained many children initially
assembled at more than 6 months of age. This older
age group had an increased likelihood of having had
episodes of rotavirus diarrhea that had occurred before
enrollment and could not be documented. Hence, to
reduce the likelihood of children with undocumented
pre-enrollment episodes of rotavirus diarrhea being
included in the analyses, the calculations were
repeated using only the children who were under 6
months of age at the time of enrollment in the cohort
(defined as the "inception cohort").

To identify factors associated with severe disease in
children with episodes of rotavirus diarrhea (vira-
lence), we compared children who had clinical evi-
dence of at least "some" dehydration with children
who had no clinical evidence of dehydration. Com-
parisons were statistically appraised with the \(\chi^2\) test,
or with Fisher's exact test if the population was
sparsely distributed.

A case-control analysis was used to evaluate the
association between excretion of rotaviruses and the
occurrence of diarrheal symptoms (pathogenicity).
The sampling frame for cases was any individual with
an episode of diarrhea, and the sampling frame for
controls was all individuals without diarrhea in each
bimonthly stool survey. Both cases and controls with a
prior history of having rotavirus detected in their stools
were excluded (either as a case or as a control). To
avoid bias from repeated fecal sampling during a sin-
gle diarrheal episode, only the first fecal specimen
obtained during each episode was included in these
analyses. The independent association between the ini-
tial detection of rotavirus in fecal specimens and diar-
rheal episodes was evaluated using a multiple logistic
regression model, taking case/control status as the
dependent variable and fitting the detection of
rotavirus in fecal specimens and potentially confound-
ing variables as the independent variables. The coeffi-
cient for detection of rotavirus in fecal specimens was
exponentiated to estimate the adjusted odds ratio. In all
multivariate analyses, standard errors of the coeffi-
cients were used to derive 95 percent confidence inter-
vals, and statistical significance was defined as a \(p\)
value of <0.05 (two-tailed).

**RESULTS**

Prior to the start of surveillance, 178 children were
enrolled in the cohort. During the 1-year study period,
another 94 newborns were accrued. At the time of
enrollment in the cohort, 134 children were under 6
months of age. During the study period, 97 percent (\(n =
22,116\)) of the 22,849 twice-weekly scheduled visits
were completed and 98 percent (\(n = 1,301\)) of the 1,333
bimonthly scheduled surveys were completed. A stool
specimen was obtained from 98 percent (\(n = 1,280\)) of
the 1,301 visits during the bimonthly surveys, and at
least one stool specimen was collected from 80 percent
(\(n = 1,013\)) of the 1,270 diarrheal episodes. A rectal
swab was obtained from every diarrheal episode. In
multiple logistic regression models, obtaining a stool
specimen during a diarrheal episode was associated
with a diarrheal episode of longer duration (\(p = 0.03\)),
with higher levels of maternal education (\(p = 0.04\)), and
with having electricity in the household (\(p = 0.04\)).
The higher collection rate during the bimonthly surveys
was due to the longer period of time available for revisits
and specimen collection.

During the study period, 46 children had one
episode of rotavirus diarrhea and two children had two
episodes. Of these episodes, mixed infections occurred
with ETEC (\(n = 5\)), *Campylobacter* (\(n = 7\)), both
*Campylobacter* and ETEC (\(n = 3\)), and both
*Campylobacter* and *Shigella* (\(n = 1\)). During the study
period, the overall incidence rates of all diarrheal
episodes and of rotavirus, ETEC, *Campylobacter,* and
*Shigella* diarrheal episodes were 6.25, 0.24, 1.48, 0.84,
and 0.47 episodes per person-year, respectively (table
1). *Salmonella* was isolated from a single diarrheal
episode. For comparative purposes, we analyzed a sub-
ext of diarrheal episodes in which both a rectal swab and
a stool specimen were collected, since only these
episodes were evaluated for the presence of rotavirus.
In this subset, the overall incidence rates of rotavirus,
TABLE 1. Annual age-specific incidence rates of all-cause diarrhea and cause-specific diarrhea, Abu Homos, Egypt, 1995–1996

<table>
<thead>
<tr>
<th>Age group (months)</th>
<th>Days of follow-up</th>
<th>No. of episodes</th>
<th>Incidence rate*</th>
<th>No. of episodes</th>
<th>Incidence rate</th>
<th>No. of episodes</th>
<th>Incidence rate</th>
<th>No. of episodes</th>
<th>Incidence rate</th>
<th>No. of episodes</th>
<th>Incidence rate</th>
</tr>
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<tbody>
<tr>
<td>&lt;6</td>
<td>13,810</td>
<td>293</td>
<td>7.47</td>
<td>5</td>
<td>0.13</td>
<td>59</td>
<td>1.56</td>
<td>40</td>
<td>1.06</td>
<td>6</td>
<td>0.16</td>
</tr>
<tr>
<td>6–11</td>
<td>13,219</td>
<td>314</td>
<td>8.67</td>
<td>22</td>
<td>0.61</td>
<td>59</td>
<td>1.63</td>
<td>53</td>
<td>1.46</td>
<td>19</td>
<td>0.52</td>
</tr>
<tr>
<td>12–23</td>
<td>30,690</td>
<td>501</td>
<td>5.96</td>
<td>14</td>
<td>0.17</td>
<td>143</td>
<td>1.70</td>
<td>58</td>
<td>0.69</td>
<td>55</td>
<td>0.65</td>
</tr>
<tr>
<td>24–35</td>
<td>16,487</td>
<td>162</td>
<td>3.59</td>
<td>7</td>
<td>0.15</td>
<td>40</td>
<td>0.89</td>
<td>20</td>
<td>0.44</td>
<td>16</td>
<td>0.35</td>
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<tr>
<td>Total</td>
<td>74,206</td>
<td>1,270</td>
<td>6.25</td>
<td>48</td>
<td>0.24</td>
<td>301</td>
<td>1.48</td>
<td>171</td>
<td>0.84</td>
<td>96</td>
<td>0.47</td>
</tr>
</tbody>
</table>

* Episodes/person-year.

ETEC, Campylobacter, and Shigella were 0.24, 1.19, 0.67, and 0.39 episodes per person-year, respectively; and of the 165 episodes accompanied by severe dehydration, rotavirus alone, ETEC alone, Campylobacter alone, Shigella alone, and more than one pathogen were isolated from 7 (4 percent), 31 (19 percent), 14 (8 percent), 8 (5 percent), and 16 (10 percent) episodes, respectively. The age-specific incidence rates of rotavirus diarrheal episodes per person-year were 0.13 for infants aged <6 months, 0.61 for those aged 6–11 months, 0.17 for those aged 12–23 months, and 0.15 for those aged 24–35 months (table 1). No rotavirus diarrheal episodes occurred in infants under 20 weeks of age. The monthly incidence rates of rotavirus diarrhea demonstrate that 90 percent of the disease episodes occurred during the warmer months of July–November, with a peak incidence in August (figure 1). Diarrheal episodes associated with rotavirus were characterized by fever (54 percent), vomiting (50 percent), or some degree of dehydration (56 percent) in at least half of the children (table 2). Of the rotavirus, ETEC, Campylobacter, and Shigella diarrheal episodes in which both a rectal swab and a stool specimen were collected, severe dehydration was noted in 12 (25 percent), 44 (18 percent), 23 (17 percent), and 14 (18 percent) episodes, respectively. After adjustment for age, the only sociodemographic or environmental factor found to have a statistically significant association with the incidence of rotavirus diarrheal episodes was season. When we repeated the evaluation of breastfeeding separately for infants aged <1 year and those aged ≥1 year, breastfeeding was significantly associated with the incidence of rotavirus diarrheal episodes only in the <1-year age group. Therefore, both season and breastfeeding were added to the multivariate model to obtain hazards ratios adjusted for age, season, and breastfeeding. Crude relative rates and adjusted hazards ratios with 95 percent confidence intervals for the associations between selected sociodemographic or environmental factors and the incidence of rotavirus diarrheal episodes are shown in table 3. The adjusted hazards ratio for episodes of rotavirus diarrhea occurring in the warm season (May–October) compared with the cool season (November–April) was 3.1 (95 percent confidence interval (CI): 1.5, 6.5; \( p = 0.003 \)). The adjusted hazards ratio during the first year of life in infants receiving any breast milk compared with infants receiving no breast milk was 0.35 (95 percent CI: 0.13, 0.94; \( p = 0.04 \)).

When we limited the analyses to the inception cohort, again season and breastfeeding (in infants
TABLE 3. Crude relative rates and adjusted hazards ratios for the associations between selected sociodemographic or environmental factors and the incidence of rotavirus diarrhea, Abu Homos, Egypt, 1995–1996

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. of episodes (n = 46)</th>
<th>Incidence (episodes per person-year)</th>
<th>Crude RR*</th>
<th>Hazards ratio†</th>
<th>95% CI*</th>
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</thead>
<tbody>
<tr>
<td><strong>Season</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warm</td>
<td>37</td>
<td>0.39</td>
<td>4.0</td>
<td>3.1†</td>
<td>1.5, 6.5</td>
</tr>
<tr>
<td>Cold</td>
<td>9</td>
<td>0.10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Breastfeeding</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>27</td>
<td>0.27</td>
<td>1.2</td>
<td>0.57</td>
<td>0.25, 1.3</td>
</tr>
<tr>
<td>No</td>
<td>19</td>
<td>0.22</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>No. of persons in household</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥12</td>
<td>24</td>
<td>0.29</td>
<td>1.3</td>
<td>1.5</td>
<td>0.81, 2.6</td>
</tr>
<tr>
<td>&lt;12</td>
<td>22</td>
<td>0.21</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>No. of persons in household/ no. of rooms in house</strong></td>
<td></td>
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</tr>
<tr>
<td>≥3</td>
<td>24</td>
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<td>1.2</td>
<td>1.2</td>
<td>0.65, 2.1</td>
</tr>
<tr>
<td>&lt;3</td>
<td>22</td>
<td>0.22</td>
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<td></td>
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<tr>
<td><strong>Gender</strong></td>
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<td></td>
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<td></td>
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<tr>
<td>Male</td>
<td>21</td>
<td>0.21</td>
<td>0.70</td>
<td>0.74</td>
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<tr>
<td>Female</td>
<td>25</td>
<td>0.30</td>
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<td><strong>Electricity</strong></td>
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<td>Yes</td>
<td>42</td>
<td>0.26</td>
<td>1.4</td>
<td>1.9</td>
<td>0.68, 5.4</td>
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<td>No</td>
<td>4</td>
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<td><strong>Latrine</strong></td>
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</tr>
<tr>
<td>Yes</td>
<td>27</td>
<td>0.28</td>
<td>1.3</td>
<td>1.3</td>
<td>0.70, 2.3</td>
</tr>
<tr>
<td>No</td>
<td>19</td>
<td>0.22</td>
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<td><strong>Garbage container</strong></td>
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<tr>
<td>Yes</td>
<td>7</td>
<td>0.28</td>
<td>1.2</td>
<td>0.94</td>
<td>0.42, 2.1</td>
</tr>
<tr>
<td>No</td>
<td>39</td>
<td>0.24</td>
<td></td>
<td></td>
<td></td>
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<td><strong>Drinking water source</strong></td>
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<tr>
<td>Municipal</td>
<td>44</td>
<td>0.25</td>
<td>1.4</td>
<td>2.2</td>
<td>0.52, 9.1</td>
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<td>Other</td>
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<tr>
<td>Municipal</td>
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<td>0.24</td>
<td>0.63</td>
<td>0.90</td>
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<td>0.38</td>
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<td><strong>Bathing water source</strong></td>
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<tr>
<td>Municipal</td>
<td>43</td>
<td>0.25</td>
<td>1.3</td>
<td>1.7</td>
<td>0.52, 5.5</td>
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<tr>
<td>Other</td>
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<td>0.20</td>
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<td></td>
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<td><strong>Maternal education</strong></td>
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<td>Any</td>
<td>3</td>
<td>0.24</td>
<td>0.98</td>
<td>1.0</td>
<td>0.32, 3.3</td>
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<tr>
<td>None</td>
<td>43</td>
<td>0.25</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* RR, relative rate; CI, confidence interval.
† Adjusted for age, season, and breastfeeding.
‡ p = 0.003.

under 1 year of age) were the only variables significantly associated with the incidence of rotavirus diarrheal episodes. The adjusted hazards ratio for episodes of rotavirus diarrhea occurring in the warm season as compared with the cool season was 4.8 (95 percent CI: 1.4, 16.5; p = 0.01), and the adjusted hazards ratio during the first year of life for infants receiving any breast milk as compared with no breast milk was 0.30 (95 percent CI: 0.11, 0.80; p = 0.02). We did not find any statistically significant associations between gender, maternal education, household size, crowding, water sources, presence of latrines, presence of garbage containers, or presence of electricity and the incidence of rotavirus diarrheal episodes. Furthermore, we did not find any sociodemographic or environmental factor to be associated with severe disease in children with episodes of rotavirus diarrhea.

In our case-control analysis evaluating the pathogenicity of rotaviruses, we found a significant association between excretion of rotaviruses and the occurrence of diarrheal symptoms. After controlling for age, calendar time, and breastfeeding, the relative odds of excreting rotaviruses in children having diarrhea compared with children having no diarrhea was 6.7 (95 percent CI: 3.3, 13.3; p = 0.0001). When we restricted the analysis to the inception cohort, the relative odds of excreting rotaviruses in children having diarrhea compared with children having no diarrhea, adjusted
for age, calendar time, and breastfeeding, was 10.0 (95 percent CI: 3.3, 30.1; \( p = 0.0001 \)).

A total of 46 isolates obtained from all first rotavirus diarrheal episodes were subjected to P- and G-typing (table 4). The majority (67 percent) of the isolates were of the same strain (P[4]G2), and G serotypes 1 and 2 comprised 89 percent of the isolates. Mixed infections constituted 7 percent of the episodes and were of the G1 and G2 serotypes.

**DISCUSSION**

Our results, similar to those obtained in other less-developed settings worldwide, confirm diarrheal illnesses, including those caused by rotaviruses, to be major causes of morbidity in children under 3 years of age in Abu Homos. A previous cohort study in Bilbeis, Egypt, found rotavirus diarrheal episode incidence rates of 0.17 per person-year in children aged <6 months, 0.37 per person-year in those aged 6−11 months, 0.14 per person-year in those aged 1−2 years, and 0.03 per person-year in those aged 2−3 years (15). After exclusion of the children aged <6 months, the rotavirus diarrheal incidence rates observed in our study were higher for all age groups. In the 6- to 11-month age group, the age group that experienced the highest incidence of rotavirus diarrheal episodes, rotavirus accounted for 7 percent of all diarrheal episodes.

Our observation that in a population-based cohort, 56 percent of the children with rotavirus diarrhea had clinical evidence of dehydration attests to the significant burden of disease caused by this pathogen. Most hospital-based studies have shown rotavirus to be the most common identifiable cause of acute diarrhea (1, 16). Hospital-based studies in Egypt have identified rotaviruses in 20–40 percent of children presenting with diarrhea (17, 18). Previous population-based studies support our findings that, in comparison with treatment center-based studies, rotaviruses are a less frequently identified cause of acute diarrhea and they become more significant pathogens when analyses are restricted to clinically severe cases of diarrhea as opposed to mild cases (19–22). The true pathogenic potential of rotaviruses may be underestimated, since, as the results of several studies have suggested (15, 21–23), the isolation of ETEC, *Campylobacter*, or *Shigella* from stool specimens more frequently represents colonization than does the isolation of rotavirus.

The previous cohort study conducted in Bilbeis found rotavirus identification rates among cases compared with controls to be 3.3 percent versus 0.8 percent (\( p < 0.001 \)) and the seasonal isolation of rotavirus to be twice as frequent during the colder season of November–April (15). The seasonality in the cooler months observed in Bilbeis is similar to observations made in comparable temperate zones (19). We also observed a significant difference in the relative odds of excreting rotaviruses among children having diarrhea compared with children having no diarrhea and a strong seasonal peak in the incidence of rotavirus diarrhea. However, in our study, 90 percent of rotavirus diarrheal incidence occurred during the warmer months of July–November. Since Bilbeis and Abu Homos are both located in the Nile Delta, it does not appear that there is a consistent seasonal pattern of rotavirus outbreaks in this area, despite consistent pathogenicity.

Our inability to find any association between rotavirus diarrheal episodes and any variables reflecting socioeconomic status, household crowding, sanitation, and water sources reaffirms that, unlike many other causes of diarrheal disease, potential improvements in living conditions and standards of sanitation in Egypt are not likely to significantly affect the incidence of rotavirus disease. Our confirmation of a previous observation in Bangladesh that during the first year of life breastfeeding is associated with a lower incidence of rotavirus diarrheal episodes adds to the multitude of benefits that have been associated with breastfeeding (24). Nevertheless, in the absence of any identifiable environmental or behavioral measure with which to effectively control diarrheal disease due to rotavirus infection in Egypt, effective immunization against rotavirus should be considered a public health priority.

The 1-year duration of this study provides an indication of the incidence and severity of rotavirus diarrhea in this population, but clearly it would be desirable to extend these observations with further surveillance, since year-to-year variations are probable. Another limitation of this study was our inability


<table>
<thead>
<tr>
<th>Rotavirus type</th>
<th>Specimens obtained from 46 first episodes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
</tr>
<tr>
<td>P[8]G1</td>
<td>4</td>
</tr>
<tr>
<td>P[4]G1,G2</td>
<td>2</td>
</tr>
<tr>
<td>P[4]G1</td>
<td>1</td>
</tr>
<tr>
<td>P[8]G1,G2</td>
<td>1</td>
</tr>
<tr>
<td>P[14]G8</td>
<td>1</td>
</tr>
<tr>
<td>G1*</td>
<td>1</td>
</tr>
<tr>
<td>G2*</td>
<td>1</td>
</tr>
<tr>
<td>Nontypeable specimen</td>
<td>4</td>
</tr>
</tbody>
</table>

* Partially nontypeable specimen; i.e., only the G type could be determined.
to obtain a stool specimen from 20 percent of all diarrheal episodes, which may have led to an underestimate of the incidence of rotavirus diarrheal episodes in this population. Indeed, when we limit our evaluation of rectal swabs to those diarrheal episodes in which a stool specimen was collected, we observe that the incidence rates of ETEC, *Campylobacter*, and *Shigella* all decrease by approximately 20 percent. Since we did not find a significant association between rotavirus diarrhea and higher levels of maternal education or having electricity in the household, it does not appear that the selection bias in children from whom a stool specimen could be obtained during a diarrheal episode resulted in any false associations.

In Venezuela, a rhesus rotavirus-based quadrivalent vaccine was found to be efficacious against severe rotavirus diarrheal illness (25). However, in view of earlier trials carried out in Peru (26) and Brazil (27) that revealed lesser levels of protection, questions were raised as to whether the results of the Venezuelan study could be generalized to developing countries with higher background rates of diarrheal disease and poorer sanitary conditions (28). In addition, the high prevalence of rotavirus strain P[6]G9 observed in India raised concerns about the widespread utility of candidate rotavirus vaccines targeted against the four major G serotypes (6).

Several observations from Abu Homos lend optimism to the potential incorporation of the rhesus rotavirus-based quadrivalent vaccine into the national Expanded Program on Immunization. We have shown rotavirus to be a major burden of disease in this population. Our characterization of rotavirus strains in circulation showed that 76 percent of these strains are the commonly encountered strains P[4]G2 and P[8]G1 and revealed that infection with unusual or multiple strains of rotavirus is not common in this setting. In addition, the absence of observed rotavirus diarrheal episodes in infants under 20 weeks of age suggests that candidate rotavirus vaccines may be included in the routine Expanded Program on Immunization schedule of diphtheria-tetanus-pertussis vaccine, which is administered at 6, 10, and 14 weeks of life.

A consensus workshop has recommended that the World Health Organization support the conduct of rotavirus vaccine effectiveness trials in very poor developing countries in which immunogenicity can be demonstrated, particularly in Africa and Asia (5). Our study suggests that Abu Homos, Egypt, can be considered a suitable field site for conducting such effectiveness trials, which could not only evaluate the impact of incorporating candidate rotavirus vaccines into the national Expanded Program on Immunization but also allow estimates of cost-effectiveness (29).

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