Role of Viruses in Acute Gastroenteritis in Infants and Young Children at Vellore, South India

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Summary

The aetiological contribution of viral agents in the causation of acute diarrhoea was studied prospectively in 915 infants and young children aged 1-35 months. This was a hospital-based study, selection being carried out by proportionate random sampling; 587 matched controls were also investigated simultaneously. Methods of detection included direct electron microscopy, ELISA for rotaviruses and immune electron microscopy. Rotaviruses emerged as the single most important cause with highest prevalence in the 6-11-month age group. The contribution of other agents was negligible. Electron microscopy, though a ‘catch-all’ technique, is not a cost-effective diagnostic method for developing countries.

Acute infectious diarrhoea is a global health problem. It continues to be a leading cause of morbidity and mortality in young children in developing countries. However, the role of viral agents other than rotaviruses in the causation of diarrhoea in children in India is virtually unknown.

This paper presents a detailed analysis of the viral agents that were detected during the course of a detailed study of aetiological agents in acute diarrhoea of children.

Subjects Studied and Methods

Fecal specimens were collected from children between 1 and 35 months of age who presented with diarrhoea at the Child Health out-patient department of the Christian Medical College Hospital, Vellore, South India. Patients were selected by proportionate random sampling from all patients who had diarrhoea of less than 72 hours duration. A total of 916 patients and 587 matched controls were included in the study over a period of 2 years.

Viral studies performed on the stool samples included electron microscopy (EM), immune electron microscopy (IEM), and enzyme-linked immunosorbent assay (ELISA) for rotaviruses.

Results

The viruses detected included rotaviruses, adenoviruses, caliciviruses, astroviruses, coronavirus-like particles (CVLP) and small round viruses (SRV). Their rates of detection in patients and controls is shown in Table 1. Rotaviruses were detected in 163 of the patients by either EM or ELISA for the group antigen.

There were 27 cases of rotavirus diarrhoea detected only by EM and not picked up by ELISA, and six cases only detected by ELISA and not by EM. Table 2 shows the detection of rotaviruses in the different age groups and also compares its detection by EM and ELISA for the group antigen. Table 3 shows the distribution of rotaviruses and other viruses when found as the sole pathogen or in association with other bacterial or parasitic agents.

Discussion

Several prospective studies from developing countries looked for viruses as agents of diarrhoea using ELISA for rotaviruses and conventional methods of tissue culture for other viruses. Using the EM for detecting agents is cumbersome, time-consuming and a method not easily available to laboratories in developing countries. The role of rotaviruses as important causative agents of acute diarrhoea in infants and young children has been reported from this area previously and is once again reiterated in this study. This is also in keeping with reports from several other parts of India. The highest prevalence
TABLE 1
Percentage detection of viruses by electron microscopy

| Category       | Total no. of children | Rota viruses | Adeno viruses | Calici | Astro | Corona virus-like particles | Small round viruses (SRV's) |
|----------------|-----------------------|--------------|---------------|--------|-------|-----------------------------|-----------------------------|
| Patients       | 916                   | 16.9         | 4.3           | 1.2    | 0.1   | 2.5                         | 2.2                         |
| Controls       | 587                   | 1.2          | 1.4           | 0.2    | 0.3   | 4.6                         | 1.4                         |

TABLE 2
Detection of rotaviruses by EM and ELISA in the different age groups

| Category       | No. studied | Age (months) |
|----------------|-------------|--------------|
|                |             | 1-5 | 6-11 | 12-23 | 24-35 |
| Patients       | 916         | 13.8 | 21.1 | 15.6 | 14.1 |
|                |             | 10.9 | 19.6 | 13.8 | 10.2 |
| Controls       | 587         | 1.4  | 1.8  | 0.8  | 0.0  |
|                |             | 0.9  | 1.8  | 0.8  | 0.0  |

TABLE 3
Detection of pathogens in patients and controls

| Age groups in months | Patients | Controls |
|----------------------|----------|----------|
|                      | 1-11 | 12-35 | 1-11 | 12-35 |
| Rotavirus (RV) only  | 11.7  | 8.5    | 1.1  | 0.5   |
| Other viruses (singly) | 4.8  | 2.3    | 1.9  | 5.6   |
| RV + bacteria        | 5.5   | 4.3    | 0.3  | 0.5   |
| Other viruses + bacteria | 3.6 | 5.4    | 1.3  | 3.2   |
| RV + parasite        | 0.9   | 0.9    | 0.3  | 0.0   |
| Other virus + parasite | 0.4 | 1.1    | 0.3  | 3.2   |
| RV + other virus     | 0.2   | 0.6    | 0.0  | 0.0   |
| RV + bacteria + parasite | 0.9 | 0.9    | 0.0  | 0.0   |
| Other virus + bacteria + parasite | 0.5 | 0.9    | 0.8  | 0.9   |

in our study is between 6 and 11 months of age when it accounts for 20 per cent of all diarrhoeal cases. There are regional differences of rotavirus detection in India which may be related to climate, and other environmental or social factors. These differences could also depend on whether the study is community- or hospital-based.

Adenoviruses were the second most frequently detected viruses. However, our rates of detection are on the lower side as compared to reports from temperate countries. These findings are however compatible with the only other report from India, wherein ELISA was used for detection of enteric adenoviruses (EAD) and a clear association between adenoviruses and diarrhoea could not be ascertained.

Caliciviruses, astroviruses, and small round viruses were detected at a very low frequency and did not contribute significantly as aetiological agents. All these viruses have been detected in control children as well. Bacterial pathogens being excreted in the absence of any disease has been reported from this region before and shedding of rotaviruses and caliciviruses is unknown elsewhere.8 It is therefore very unlikely that calici, astro and other small round (SRV) viruses play any major role in diarrhoea in this part of India.

The role of coronaviruses like particles (CVLP) in acute diarrhoea in children is remote in the face of these findings. CVLP have been observed in several epidemiological studies in normal indi-
individuals, but interestingly in this study they were found in even higher frequencies in the asymptomatic children as compared to those with diarrhoea.

The absence of the Norwalk group conforms to their known pattern of primarily causing disease in older children and adults.

In conclusion, this study reiterates that rotaviruses continue to be the single most important viral agent of diarrhoea in this region. A clear causal role for adenoviruses was not found and perhaps needs to be defined. The role if any of the other viruses in acute gastroenteritis, viz calici, astro, and SRV is negligible because of their low levels of detection in both patients and their presence in the stools of healthy children. CVLP clearly do not have a causal role in acute gastroenteritis in children in this region.

Many reports indicate that viruses play an important role in diarrhoea in children. However, other than RV, this aspect has been little studied in India because of the cost and expertise involved in using an electron microscope for diagnosis. Since rotaviruses and enteric adenoviruses can be detected by ELISA, the EM as a diagnostic tool is not a feasible cost-effective method for diagnostic laboratories in developing countries. However, it still holds the advantage of being the 'catch all' method and holds the key to the discovery of new enteric viruses as also viruses not directly sought.

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