Rotavirus and Severe Childhood Diarrhea

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Studies published between 1986 and 1999 indicated that rotavirus causes ≈22% (range 17%–28%) of childhood diarrhea hospitalizations. From 2000 to 2004, this proportion increased to 39% (range 29%–45%). Application of this proportion to the recent World Health Organization estimates of diarrhea-related childhood deaths gave an estimated 611,000 (range 454,000–705,000) rotavirus-related deaths.

Rotavirus is the leading cause of diarrhea hospitalization among children worldwide (1). In 2003, we published an estimate of rotavirus-related deaths worldwide based on a review of the literature published from 1986 through 1999 on deaths caused by diarrhea and rotavirus hospitalizations in children (2). This review indicated that rotavirus accounted for ≈22% of hospitalizations for childhood diarrhea. By applying this fraction to an estimate of 2.1 million annual deaths from diarrhea, we calculated that rotavirus causes 440,000 annual deaths in children <5 years of age worldwide. This estimate was ≈50% of the 1985 estimate of 873,000 rotavirus deaths per year (3), and the decrease in estimated rotavirus-related deaths paralleled the decrease in deaths from diarrhea of all causes from an estimated 4.6 million deaths in 1982 to 1.6–2.5 million deaths in 2000 (4–6).

Recent studies suggest that as global deaths from childhood diarrhea decreased during the past 2 decades, the proportion of diarrhea hospitalizations attributable to rotavirus may have increased. For example, prospective, sentinel hospital–based surveillance of rotavirus disease in 9 Asian countries demonstrated a median rotavirus detection of 45% among children hospitalized with diarrhea (7), a figure that was considerably greater than the detection rates in previous studies from the same countries. Similarly, a more extensive study of 5,768 children hospitalized from 1998 through 2000 in 6 centers in Vietnam identified rotavirus in 56% of patients (8), a proportion that was more than twice the 21% detection rate reported among children hospitalized with diarrhea in a hospital in Hanoi, Vietnam, from 1981 to 1984 (9).

To systematically evaluate whether these recent reports are isolated observations or reflect a changing trend in the etiology of childhood diarrhea hospitalizations, we reviewed studies of rotavirus detection among children hospitalized with diarrhea published from 2000 through 2004 and compared the data with those of the previous review of studies published from 1986 through 1999.

The Study

Similar to the approach used in our previous review, we performed a computer search of the scientific literature (in English and other languages) published from January 2000 through June 2004 using the words rotavirus and the truncated stem rota-. We restricted the analysis to studies that met the following criteria: 1) were initiated after 1993; 2) were conducted for at least 1 full calendar year; and 3) examined rotavirus among at least 100 children <5 years of age hospitalized with diarrhea.

For each study, we determined the proportion of cases positive for rotavirus among children hospitalized with diarrhea. We plotted this proportion against the per capita gross national product (GNP) for the country in which the study was conducted. We then classified countries by per capita GNP into World Bank income groups (low, <US $756; low-middle, US $756–$2,995; high-middle, US $2,996–$9,265; and high, >US $9,265) (10), and calculated the median (interquartile range [IQR]) proportion of diarrhea hospitalizations attributable to rotavirus for each income group.

We next calculated an overall median detection rate by taking a weighted average of the median detection rates for each of the income groups. The weights assigned to each income group corresponded to the proportion of deaths from childhood diarrhea among countries in that income group as determined on the basis of our previous analysis (2): 85% in low-income countries, 13% in low-middle–income countries, 2% in high-middle–income countries, and <1% in high-income countries. To estimate deaths from rotavirus disease among children, we multiplied the overall median detection rate of rotavirus among children hospitalized with diarrhea by a recent World Health Organization estimate of deaths from diarrhea among children worldwide (5).

We abstracted information from 41 studies that met all the inclusion criteria (online Appendix Table, available from http://www.cdc.gov/ncidod/EID/vol12no02/05-0006_app.htm). Unlike the previous review of studies conducted for the period 1986–1999, in which the proportion of diarrhea-related hospitalizations attributable to rotavirus showed a distinct increasing trend with increasing income level, we found that the median detection rates increased only slightly with increasing income level (Figure 1). The median detection rate for rotavirus among children hospi-

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talized with diarrhea was 39% in studies conducted in low-income countries, 40% for low-middle–income countries, 38% for high-middle–income countries, and 44% for high-income countries, for an overall weighted median estimate of 39% (Table).

If we multiply the greater median rotavirus detection rate of 39% (IQR 29%–45%) from this analysis by 1,566,000 recently estimated childhood diarrhea deaths \(^{(5)}\), we find that rotavirus causes \(\approx 611,000\) childhood deaths (IQR 454,000–705,000). More than 80% of all rotavirus-related deaths were estimated to occur in low-income countries of south Asia and sub-Saharan Africa (Figure 2).

### Conclusions

Compared with results from studies published from 1986 to 1999, the proportion of diarrhea hospitalizations attributable to rotavirus appears to have increased between 2000 and 2004. This phenomenon likely reflects a relatively slower rate of decrease in hospitalizations for rotavirus compared with other causes of severe childhood diarrhea. This finding could be accounted for by several factors. First, interventions to improve hygiene and sanitation are likely to have a greater impact on diarrhea caused by bacterial and parasitic agents, which are transmitted primarily through contaminated food or water, unlike rotavirus, which is often spread from person-to-person. This hypothesis is supported by data from the United States \(^{(11)}\) and Mexico \(^{(12)}\), which showed that as diarrhea-related childhood deaths decreased dramatically in both countries; the decrease was greatest during the summer months when diarrheal diseases caused by bacteria are more prevalent. In both countries, diarrhea-related deaths in recent years have exhibited peaks only in the winter when rotavirus infections are common. Second, oral hydration therapy to replace loss of body fluids, which many regard as a major factor responsible for the decrease in diarrhea deaths \(^{(13)}\), is often more difficult to successfully administer in children with severe vomiting \(^{(14)}\), a common manifestation attributable to rotavirus.

| Income group | 1986–1999 Median % (IQR) | 2000–2004 Median % (IQR) |
|--------------|---------------------------|---------------------------|
| Low          | 20 (16–27)                | 39 (28–45)                |
| Low middle   | 25 (20–33)                | 40 (32–43)                |
| High middle  | 31 (25–42)                | 38 (35–45)                |
| High         | 34 (28–38)                | 44 (40–50)                |
| Total*       | 21 (17–28)                | 39 (29–45)                |

*The overall median was calculated by taking a weighted average of the median rotavirus detection rate for each income group. The weights applied to each group corresponded to that group’s proportion of global diarrheal deaths: 85% for low-income countries, 13% for low-middle–income countries, 2% for high-middle–income countries, and <1% for high-income countries.
of rotavirus disease. Third, unlike antimicrobial therapies
that are effective against some bacterial and parasitic
agents, no specific treatment for rotavirus infection is
available.

We have derived preliminary updated estimates of
rotavirus-related childhood deaths on the basis of the find-
ings of our review. Because we wanted to assess the most
recent trends in rotavirus incidence, we examined a rela-
tively limited number of studies published in the last 5
years, particularly from upper-middle– and high-income
countries. However, these 2 income groups account for
only a small fraction (<5%) of all deaths from rotavirus
disease, and the 28 studies available from low- and low-
middle–income countries allowed for a reasonably robust
analysis. Nevertheless, our findings should be updated as
new data on rotavirus hospitalizations and updated esti-
mates of childhood diarrhea deaths become available. In
2002, the World Health Organization published a generic
protocol for hospital-based surveillance of rotavirus (15),
and studies using this protocol are currently being conduct-
ed or planned in >30 countries in Asia, Africa, the Middle
East, and Latin America. Data from these and other stud-
ies, particularly from countries such as India and China,
which account for a large fraction of global rotavirus
deaths, should be used to update our estimate of rotavirus-
related deaths and further refine it to develop country-spe-
cific figures. These data, together with information on
effects and costs of rotavirus disease, will allow policy-
makers to assess the magnitude of the problem of rotavirus
and the value of new vaccines that may soon be available.

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