

Estimated deaths due to rotavirus in Bangladesh

We estimated the number of childhood deaths from rotavirus in Bangladesh. We used the under 5 mortality rate and proportion of deaths due to diarrhoea from the Bangladesh Demographic and Health Survey 2004 to derive diarrhoea death figures, and multiplied these figures with the proportion of diarrhoea that was due to rotavirus in two ICDDR,B hospital surveillance systems in Dhaka and Matlab. We estimate that between 5,756 and 13,430 children died each year in Bangladesh between 2001 and 2004 from severe rotavirus gastroenteritis. An effective, affordable rotavirus vaccine could save thousands of lives each year in Bangladesh.

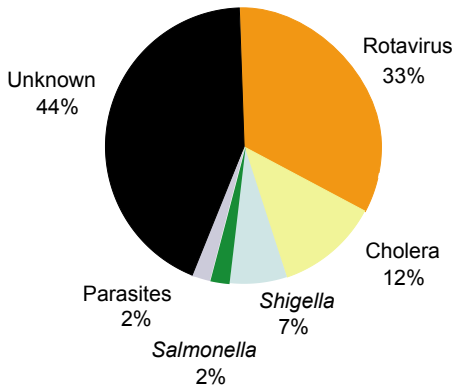
Rotavirus is the leading cause of severe gastroenteritis among young children. Globally, rotavirus is estimated to cause over 500,000 deaths among children aged under 5 years each year (1). Two new vaccines against rotavirus have been demonstrated in large studies to be safe and effective in preventing severe rotavirus disease (2,3). These studies were conducted among well-nourished patients, but additional evaluation is expected in lower income settings with higher levels of malnutrition, including ongoing studies in Bangladesh. Data on the number of deaths from rotavirus disease will help policy makers evaluate the value of these vaccines for their country.

A previous evaluation conducted by Unicomb and colleagues, based on data from 1990-1993 concluded that between 14,850 and 27,000 of the 3 million Bangladeshi children born in 1994 would die of rotavirus by the age of 5 years, equivalent to 1 rotavirus death per 111 to 203 children (4). Since the early 1990s, however, the proportion of all childhood deaths due to diarrhoea has decreased (5). An updated estimate of rotavirus associated deaths will be an important element of the decision on whether or not to introduce new rotavirus vaccines in Bangladesh. Thus, we reassessed the number of deaths from rotavirus in Bangladesh using more recent sources of data on child mortality from diarrhoea and the proportion of severe diarrhoea cases attributable to rotavirus.

ICDDR,B has two hospitals, one in Dhaka and one in Matlab, which treat patients for diarrhoea. Most patients presenting to these facilities are treated as outpatients, but those with more severe illness are admitted. Thus, hospitalized inpatients are a reasonable sample of persons with severe diarrhoea. From 1990 to 1995 a 4% systematic sample of patients admitted to the Dhaka hospital had their stool evaluated for rotavirus and other pathogens; after 1995 the sample was reduced to 2%. All patients from the community that is under active surveillance in Matlab (220,000 persons) who presented to the Matlab hospital with diarrhea since 2000 have had stool evaluation performed.

Faecal samples collected from patients enrolled in the surveillance at both hospitals were tested in the Laboratory Sciences Division of the ICDDR,B for rotavirus antigen using an enzyme-linked immunosorbent assay (ELISA). This

Figure 1: Etiologic agents detected in faecal specimens from 18,544 children <5 years of age admitted with diarrhoea to Dhaka hospital during 1993 to 2004.



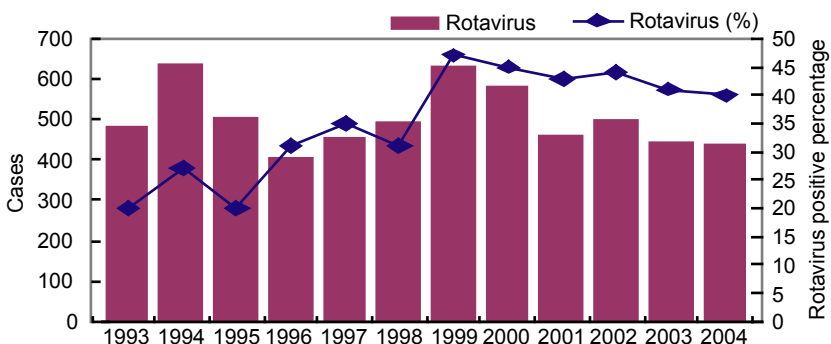
method has not changed since the early 1990s. The same specimens are also tested routinely for *Salmonella* (enteric media), *Shigella* (MacConkey agar), *Vibrio cholerae* O1 and O139 (TCBS agar), *Giardia lamblia*, *Entamoeba histolytica*, and *Cryptosporidium* (microscopic assay and ELISA).

From 1993 to 2004, a total of 18,544 children <5 years of age admitted with diarrhoea to the Dhaka hospital were included in the surveillance. Of these, 33% tested positive for rotavirus, 21% tested positive for bacterial agents including *V. cholerae*, *Shigella*, and *Salmonella*, and 2% tested positive for parasites, and no

agent was identified in 44% of cases (Figure 1).

Since 1993 the proportion of children <5 years of age admitted to the ICDDR,B Dhaka hospital with diarrhoea who tested positive for rotavirus increased steadily from 20% in 1993 to over 40% in 2004 (Figure 2). The number of patients with rotavirus did not appear to increase over this time period, suggesting that the increasing proportion of cases attributable to rotavirus likely reflected a decline in total diarrhoea admissions of non-rotavirus aetiology.

Figure 2: Number and percent of children <5 years of age with rotavirus diarrhoea admitted to ICDDR,B Dhaka hospital, 1993-2004.



Data from Matlab hospital on diarrhoea admissions showed an aetiological pattern similar to that from Dhaka hospital. Between 2000 and 2004, around

35% of children <5 years of age living in the demographic surveillance area and presenting to the Matlab hospital had positive stool ELISA for rotavirus.

The estimated population of Bangladesh in 2005 was 142 million persons, and the crude birth rate was 26.4/1000 (6). Thus, an estimated 3.7 million infants were born in Bangladesh in 2005. The mortality rate for children <5 years of age estimated by the Bangladesh Demographic and Health Survey is 88 deaths per 1000 children per year (7), and so we estimated that the total number of children <5 years of age in 2005 was 17,100,000. The Bangladesh Demographic and Health Survey used a new method to classify cause of death in 2004. The objective of the reclassification was to reduce the number of children assigned an unknown cause of death. Using this new method, 5.1% of deaths of children <5 years of age were attributed to diarrhoea and 6.8% were attributed to a combination of acute respiratory tract infection, diarrhoea and possible serious infection (5). For the low estimate of rotavirus burden we assumed that only a fraction of the 5.1% of deaths attributed solely to diarrhoea could be attributed to rotavirus. For the upper estimate we assumed that rotavirus could be responsible for the same fraction of deaths due solely to diarrhoea and those due to a combination of acute respiratory tract infection. We assumed that the fraction of rotavirus gastroenteritis among the diarrhoea deaths in Bangladesh were similar to the fraction of rotavirus gastroenteritis cases among diarrhoea patients at the ICDDR,B hospitals in Matlab and Dhaka between 2000 and 2004. Since rotavirus disproportionately causes severe diarrhoea (8,9) this is a conservative assumption.

Taken together, this model estimates that between 5,756 and 13,430 children died each year in Bangladesh between 2001 and 2004 from severe rotavirus gastroenteritis (Table 1). This is equivalent to 1 child death from rotavirus per 275 to 642 Bangladeshi children born each year by age 5.

Table 1: Model for estimating rotavirus burden of deaths among children <5 years of age in Bangladesh.

	Low estimate	Upper estimate
Bangladesh Population <5 year	17,100,000	17,100,000
Death rate among children <5 year	0.088	0.088
Annualizing 5-year death rate	0.2	0.2
Proportion of deaths attributable to diarrhoea	0.051	0.119
Proportion of diarrhoea attributable to rotavirus	0.375	0.375
Deaths attributable to rotavirus	5,756	13,430

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Comment

This analysis confirms that rotavirus remains an important cause of childhood death in Bangladesh, responsible for between 5,700 and 13,400 deaths per year. These estimates are lower than the figure of 14,850-27,000 rotavirus deaths from Unicomb's analysis in the early 1990s. Nevertheless, our data indicate that the introduction of a safe and effective rotavirus vaccine in Bangladesh could prevent several thousand childhood deaths and hospitalizations from diarrhoea each year.

Compared with Unicomb's figures, the lower estimate of rotavirus mortality in the current study largely reflects the decline in the proportion of childhood deaths in Bangladesh attributable to diarrhoea. Unicomb derived her figures based on the assumption that 25% of childhood deaths in Bangladesh were attributable to diarrhoea, whereas we used substantially lower estimates of 5%-10% from recent data. In fact, our data show that while overall deaths from diarrhoea have declined in Bangladeshi children, the proportion of diarrhoea deaths due to rotavirus have actually increased and this pathogen now alone accounts for about 40% of all diarrhoea deaths.

Our findings indicate that increase in the proportion of diarrhoea hospitalizations in Bangladeshi children that are attributable to rotavirus likely reflects a decline in hospitalizations for other causes of childhood diarrhoea rather than an increase in absolute number of rotavirus hospitalizations. This is not surprising, since interventions to improve hygiene and sanitation are likely to have a greater impact on diarrhoea caused by bacterial and parasitic agents, which are transmitted primarily through contaminated food or water, than on rotavirus which is often spread from person-to-person. In addition, oral rehydration therapy is often more difficult to successfully administer to children with rotavirus diarrhoea because of severe vomiting and no effective antimicrobial therapies against rotavirus are available. A recent review of global data reported a similar trend of increasing detection rates of rotavirus in children with severe diarrhoea (10).

An important limitation to this analysis is the uncertainty over attribution of cause of death by verbal autopsy in the Bangladesh Demographic and Health Survey, however we included both a conservative low estimate as well as an upper estimate based on different assumptions.

If the new rotavirus vaccines prove effective in low-income settings with high levels of malnutrition and poor sanitation, and if they are available at an affordable price, then inclusion of rotavirus into the routine childhood vaccination programme in Bangladesh would be expected to save thousands of lives each year. The lack of a decline in rotavirus hospitalizations despite substantial overall reductions in diarrhoea mortality between 1993 and 2004 further underscores the need for targeted interventions against rotavirus, such as vaccines, to sustain the progress in reducing severe morbidity and mortality from diarrhoea in Bangladeshi children.

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