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# Assessment of prevalence and outcome of rotaviral diarrhoea among children from Bihar region

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**Abstract**
Rotavirus is a highly contagious virus, almost every child worldwide would be exposed to the virus by 5 years of age, causing acute gastroenteritis (AGE) often associated with severe dehydration and rarely even convulsion. While it is primarily transmitted via fecal–oral route by person-to-person contact, it has been postulated that spread also occurs through respiratory secretions and contaminated environmental surfaces, which can explain the rapid acquisition of anti-rotavirus antibody in the first 3 years of life regardless of hygiene and sanitary conditions. Hence based on above condition the present study was planned for Assessment of Prevalence and Outcome of Rotaviral Diarrhoea among children from Bihar Region.
The present study was planned in Department of Pediatrics, Darbhanga Medical College and Hospital Darbhanga (DMCH), Bihar, India. In the present 50 childrens suffered from the children suffering from acute gastroenteritis were enrolled and evaluated. Those children admitted with acute diarrhoea their parents were interviewed for duration, fever, vomiting and any other signs of dehydration. The severity of dehydration was assessed according to the WHO Integrated Management of Childhood Illness Model Handbook guidelines and was categorized into severe, some or no dehydration. The standard proforma based on WHO protocol was prepared and used to collect all details and data.
The data generated from the present study concludes that the highest incidence of rota viral diarrhea is seen in children in age group of 0-12 months. The male predominance was obtained in incidence of rota viral diarrhea during this study. All vaccinated children with rota virus vaccine were protected from rota viral infection.

**Keywords:** prevalence, outcome, rotaviral diarrhoea, children, Bihar, etc.

## 1. Introduction
Rotavirus gastroenteritis is the most common cause of severe diarrhoea among infants and young children. It is caused by Rotavirus, a genus of double-stranded RNA virus in the family Reoviridae. By the age of five, nearly every child in the world has been infected with rotavirus at least once. However, with each infection, immunity develops, and subsequent infections are less severe; adults are rarely affected. There are five species of this virus, referred to as A, B, C, D, and E. Rotavirus A, the most common, causes more than 90% of infections in humans. [1].
The virus is transmitted by the faecal-oral route. It infects and damages the cells that line the small intestine and causes gastroenteritis (which is often called "stomach flu" despite having no relation to influenza). Although rotavirus was discovered in 1973 and accounts for up to 50% of hospitalisations for severe diarrhoea in infants and children, its importance is still not widely known within the public health community, particularly in developing countries. In addition to its impact on human health, rotavirus also infects animals, and is a pathogen of livestock. [2].
Rotavirus is usually an easily managed disease of childhood, but worldwide nearly 500,000 children under five years of age still die from rotavirus infection each year and almost two million more become severely ill. In the United States, before initiation of the rotavirus vaccination programme, rotavirus caused about 2.7 million cases of severe gastroenteritis in children, almost 60,000 hospitalisations, and around 37 deaths each year. Public health campaigns to combat rotavirus focus on providing oral rehydration therapy for infected children and vaccination to prevent the disease. The incidence and severity of rotavirus infections has declined significantly in countries that have added rotavirus vaccine to their routine childhood immunisation policies. [3].
Rotavirus gastroenteritis is a mild to severe disease characterised by vomiting, watery diarrhoea, and low-grade fever. Once a child is infected by the virus, there is an incubation period of about two days before symptoms appear. Symptoms often start with vomiting followed by four to eight days of profuse diarrhoea. Dehydration is more common in rotavirus infection than in most of those caused by bacterial pathogens, and is the most common cause of death related to rotavirus infection. [4].
Rotavirus A infections can occur throughout life: the first usually produces symptoms, but subsequent infections are typically mild or asymptomatic, as the immune system provides some protection. Consequently, symptomatic infection rates are highest in children under two years of age and decrease progressively towards 45 years of age. Infection in newborn children, although common, is often associated with mild or asymptomatic disease; the most severe symptoms tend to occur in children six months to two years of age, the elderly, and those with compromised or absent immune system functions. Due to immunity acquired in childhood, most adults are not susceptible to rotavirus; gastroenteritis in adults usually has a cause other than rotavirus, but asymptomatic infections in adults may

maintain the transmission of infection in the community. [5].

Rotavirus is transmitted by the faecal-oral route, via contact with contaminated hands, surfaces and objects, and possibly by the respiratory route. The faeces of an infected person can contain more than 10 trillion infectious particles per gram; fewer than 100 of these are required to transmit infection to another person.

Rotaviruses are stable in the environment and have been found in estuary samples at levels as high as 1–5 infectious particles per US gallon. Sanitary measures adequate for eliminating bacteria and parasites seem to be ineffective in control of rotavirus, as the incidence of rotavirus infection in countries with high and low health standards is similar. [1].

There are five species of rotavirus, referred to as A, B, C, D and E. Humans are primarily infected by species A, B and C, most commonly by species A. All five species cause disease in other animals. Within rotavirus A there are different strains, called serotypes. As with influenza virus, a dual classification system is used based on two proteins on the surface of the virus. The glycoprotein VP7 defines the G serotypes and the protease-sensitive protein VP4 defines P serotypes. Because the two genes that determine G-types and P-types can be passed on separately to progeny viruses, different combinations are found [6].

Rotaviruses replicate mainly in the gut, and infect enterocytes of the villi of the small intestine, leading to structural and functional changes of the epithelium. The triple protein coats make them resistant to the acidic pH of the stomach and the digestive enzymes in the gut.

The virus enter cells by receptor mediated endocytosis and form a vesicle known as an endosome. Proteins in the third layer (VP7 and the VP4 spike) disrupt the membrane of the endosome, creating a difference in the calcium concentration. This causes the breakdown of VP7 trimers into single protein subunits, leaving the VP2 and VP6 protein coats around the viral dsRNA, forming a double-layered particle (DLP) [7].

The eleven dsRNA strands remain within the protection of the two protein shells and the viral RNA-dependent RNA polymerasecreates mRNA transcripts of the double-stranded viral genome. By remaining in the core, the viral RNA evades innate host immune responses called RNA interference that are triggered by the presence of double-stranded RNA.

During the infection, rotavirus produces mRNA for both protein biosynthesis and gene replication. Most of the rotavirus proteins accumulate in viroplasm, where the RNA is replicated and the DLPs are assembled. Viroplasm is formed around the cell nucleus as early as two hours after virus infection, and consists of viral factories thought to be made by two viral nonstructural proteins: NSP5 and NSP2. Inhibition of NSP5 by RNA interference results in a sharp decrease in rotavirus replication. The DLPs migrate to the endoplasmic reticulum where they obtain their third, outer layer (formed by VP7 and VP4). The progeny viruses are released from the cell by lysis [8].

The diarrhoea is caused by multiple activities of the virus. Malabsorption occurs because of the destruction of gut cells called enterocytes. The toxic rotavirus protein NSP4 induces age- and calcium ion-dependent chloride secretion, disrupts SGLT1 transporter-mediated reabsorption of water, apparently reduces activity of brush-border membrane disaccharidases, and possibly activates the calcium ion-dependent secretory reflexes of the enteric nervous system. Healthy enterocytes secrete lactase into the small intestine; milk intolerance due to lactase deficiency is a symptom of rotavirus infection, which can persist for weeks. A recurrence of mild diarrhoea often follows the reintroduction of milk into the child's diet, due to bacterial fermentation of the disaccharide lactose in the gut [9].

Diagnosis of infection with rotavirus normally follows diagnosis of gastroenteritis as the cause of severe diarrhoea. Most children admitted to hospital with gastroenteritis are tested for rotavirus A. [38, 39]. Specific diagnosis of infection with rotavirus A is made by finding the virus in the child's stool by enzyme immunoassay. There are several licensed test kits on the market which are sensitive, specific and detect all serotypes of rotavirus A. Other methods, such as electron microscopy and PCR, are used in research laboratories. Reverse transcription-polymerase chain reaction (RT-PCR) can detect and identify all species and serotypes of human rotavirus [10].

Because improved sanitation does not decrease the prevalence of rotaviral disease, and the rate of hospitalisations remains high, despite the use of oral rehydrating medicines, the primary public health intervention is vaccination. Two rotavirus vaccines against Rotavirus A infection are safe and effective in children: Rotarix by GlaxoSmithKline [11]. and RotaTeq by Merck. [12]. Both are taken orally and contain attenuated live virus.

Rotavirus vaccines are licensed in more than 100 countries, but only 17 countries have introduced routine rotavirus vaccination. Following the introduction of routine rotavirus vaccination in the US in 2006, the health burden of rotavirus gastroenteritis "rapidly and dramatically reduced" despite lower coverage levels compared to other routine infant immunizations. Clinical trials of the Rotarix rotavirus vaccine in South Africa and Malawi, found that the vaccine significantly reduced severe diarrhoea episodes caused by rotavirus, and that the infection was preventable by vaccination. [13]. A 2019 Cochrane systematic review of 55 clinical trials that included 216,480 participants concluded RV1 (Rotarix), RV5 (RotaTeq), and Rotavac and are effective vaccines. [14]. Additional rotavirus vaccines are under development. The World Health Organization (WHO) recommends that rotavirus vaccine be included in all national immunisation programmes. [15]. The incidence and severity of rotavirus infections has declined significantly in countries that have acted on this recommendation.

The Rotavirus Vaccine Program is a collaboration between PATH, the (WHO), and the U.S. Centers for Disease Control and Prevention, and is funded by the GAVI Alliance. The Program aims to reduce child morbidity and mortality from diarrhoeal disease by making a vaccine against rotavirus available for use in developing countries. [16]. Rotavirus is a highly contagious virus, almost every child worldwide would be exposed to the virus by 5 years of age, causing acute gastroenteritis (AGE) often associated with severe dehydration and rarely even convulsion. While it is primarily transmitted via fecal–oral route by person-to-person contact, it has been postulated that spread also occurs through respiratory secretions and contaminated environmental surfaces, which can explain the rapid acquisition of anti-rotavirus antibody in the first 3 years of life regardless of hygiene and sanitary conditions. Hence based on above condition the present study was planned for Assessment of Prevalence and Outcome of Rotaviral

Diarrhoea among children from Bihar Region.

## Methodology

The present study was planned in Department of Pediatrics, Darbhanga Medical College and Hospital Darbhanga (DMCH), Bihar, India. In the present 50 childrens suffered from the children suffering from acute gastroenteritis were enrolled and evaluated. Those children admitted with acute diarrhoea their parents were interviewed for duration, fever, vomiting and any other signs of dehydration. The severity of dehydration was assessed according to the WHO Integrated Management of Childhood Illness Model Handbook guidelines and was categorized into severe, some or no dehydration [17]. The standard proforma based on WHO protocol was prepared and used to collect all details and data [18]. The samples were collected from the pediatric ward and collected in Universal sterile container. Fecal rotavirus antigen detection ELISA kit (Epitope diagnostics Inc., USA) All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Following was the inclusion and exclusion criteria for the present study.

## Inclusion criteria

Children under five years with acute gastroenteritis. Children below five years with diarrhoea alone.

## Exclusion criteria

Children under five years with bloody diarrhoea, Children less than five years who acquired diarrhoea during, hospitalization (Healthcare Associated Infection/ Nosocomial infection), Children below five years with chronic diarrhoea (diarrhoea >14 days), Children under five years with immuno compromised state.

## Results & Discussion

According to Global Burden of Disease Study 2010, Diarrhoea stands on fourth place in terms of maximum Disability Adjusted Life Years (DALY) lost. Globally, rotavirus is the most common cause of severe gastroenteritis in early childhood. Almost all children have been infected by the time they reach five years of age. In developing countries rotavirus is responsible for approximately half a million deaths per year. In India, approximately 30% of hospitalised diarrhoea cases are caused by rotaviruses. Of India's more than 2.3 million annual deaths among children, about 334 000 are attributable to diarrhoeal diseases. Rotavirus is the leading cause of severe diarrhoea in children in developed and developing countries. [19-21]. Treatment of acute rotavirus infection is nonspecific and involves management of symptoms and, most importantly, maintenance of hydration. In 2004, the WHO and UNICEF recommended the use of low osmolarity oral rehydration solution and zinc supplementation as a two-pronged treatment of acute diarrhoea. Therapy is symptomatic, often treated with fluid and salt replacement and oral zinc, but the lack of access to parenteral therapy/health care in developing countries results in a high rotavirus gastroenteritis (RVGE)-associated mortality. Further, the high incidence of severe vomiting in rotaviral diarrhea reduces the efficacy of oral rehydration salts, resulting in hospitalization for parental therapy. Hence, the most efficient option to protect children currently is to prevent the disease [22]. Natural rotavirus infection is associated with protection against severe rotavirus disease, though infection still occurs. While both cell-mediated and humoral immunities are important, it has been seen that the first infection with rotavirus elicits a predominantly homotypic and serum neutralizing antibody response to the virus while subsequent infections elicit a broader and heterotypic response [23]. Protection is greatest against the moderate-to-severe disease after the first two infections, and severity of the disease is reduced in subsequent infections [24]. Velázquez *et al*. have previously shown complete protection against moderate-to-severe RVGE after two infections [24].

The rotavirus genus belongs to Reoviridae family of viruses. Rotaviruses are highly contagious and the predominant mode of transmission is the fecal-oral route. [25]. It remains stable and infective in human feces for up to one week and can survive for weeks in recreational or drinking water, hence nosocomial infections are also widespread. Person-to-person spread, via contaminated hands, is probably the most important means by which rotaviruses are disseminated in close communities, such as hospitals and homes. Transmission among non-toilet trained children in nurseries and day care centers is facilitated by direct close contact, as well as sharing contaminated food, drinks or toys [26]. Asymptomatic excretion of rotavirus occurs in half of the infected children before the onset of clinical symptoms, and persists in one-third of the children a week after the symptoms end. Rotavirus infection is preceded by an incubation period of 24 - 48 hours. Symptoms range from vomiting and mild watery diarrhea of short duration to severe gastroenteritis with life-threatening dehydration, secondary to gastrointestinal fluid loss, a problem associated with developing countries.

**Table 1:** Basic Detail

| Parameters | No. of Cases |
|---|---|
| Sex: | |
| Males | 38 |
| Females | 12 |
| Age: | |
| 0 – 6 months | 11 |
| 7 – 12 months | 15 |
| 1 – 2 years | 9 |
| 2 – 4 years | 12 |
| 4 – 5 years | 3 |
| Rotavirus Positive | 27 |
| Rotavirus Negative | 23 |
| Total | 50 |

**Table 3:** Outcome of Treatment

| Outcome | Rotavirus Positive | Rotavirus Negative |
|---|---|---|
| Improved & Discharged | 26 | 21 |
| Developed Complications | 1 | 2 |
| Total | 27 | 23 |

**Table 4:** Dehydration Status

| Dehydration Status | Rotavirus Positive | Rotavirus Negative |
|---|---|---|
| No | 16 | 14 |
| Same | 9 | 5 |
| Severe | 2 | 4 |
| Total | 27 | 23 |

Many different agents, including viruses, bacteria, and parasites, of which viruses have been intensively studied in recent years, can cause acute diarrhea. The most notable viral agents causing diarrhea are rotavirus, adenovirus, astrovirus, and Norwalk-like viruses. [27]. Rotavirus is a leading cause of infantile gastroenteritis worldwide and is responsible for approximately 20% of diarrhea-associated deaths in children under 5 years of age. [28]. Bishop *et al*. first identified rotaviruses in humans in 1973. [29]. When they observed characteristic particles in the cytoplasm of duodenal epithelial cells from young children admitted to the hospital for treatment for acute diarrhea. In our study of 100 children presenting with diarrhea, 40% were found to be positive for rotavirus antigen in their stool samples that is relevant to previous studies. [30]. Gender difference of boys are affected than girls which has been stated by Bass *et al*. [31]. which coincides with our study

Rotavirus is transmitted by feco-oral route because of poor personal hygiene, poor sanitary practice and lower socio economic class. Our study was conducted in a tertiary care hospital and mainly patients were coming from rural and other peripheral areas. In previous studies, prevalence rate was high because of lacking awareness about personal hygiene, use of open defecation and other poor sanitary practices. Nowadays people from rural area are also well educated, follow good personal hygiene and proper use of toilets leads to lower infection among themselves and in children also. The government have also increased the awareness regarding the sanitation and improved hygiene through their programs which further lead to decrease in the infection rates. The reason behind the low incidence of the rotavirus may be that there is proper maintenance of personal hygiene, due to which there is overall rise in the immunity of community which decrease the infection chances.

Diarrhea due to rotavirus among children under 5 is an important public health problem in India. Since traditional measures like sanitation, safe water supply, and hygiene have little influence on its prevention, breast feeding provides protection only for a limited period during infancy and oral rehydration therapy is difficult in view of associated vomiting; an effective vaccine is the logical choice for prevention. Serodiversity of rotavirus in India and its regional variation favor either a monovalent vaccine that can induce heterotypic immunity or a polyvalent vaccine incorporating majority of serotypes prevalent in the country. Emergence of newer serotypes over period of time call for continued surveillance as periodically composition of the vaccine may require to be altered. Rotarix trial using two doses of vaccine in India and other developing countries has shown poor immunogenicity.

## Conclusion

The data generated from the present study concludes that the highest incidence of rota viral diarrhea is seen in children in age group of 0-12 months. The male predominance was obtained in incidence of rota viral diarrhea during this study. All vaccinated children with rota virus vaccine were protected from rota viral infection.

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