

Based on original research findings:

## Identification of Non-rotavirus associated gastroenteritis pathogens among children with diarrhea in Nepal

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**Introduction:** Diarrheal diseases caused by viruses predominantly rotavirus are still one of the major health problem world wide<sup>1,2</sup>, which infect all age group but mainly children by the age of five years regardless of socioeconomic status or environmental conditions<sup>3</sup>. The disease burden associated with virus and other pathogens in spite of improvements in hygiene and sanitation have not decreased the incidence of gastroenteritis in Nepal<sup>4</sup>.

Viruses are considered to be the major cause of acute diarrhea in young children. Four categories of viruses are considered to be important agents of viral diarrhoea: group A rotavirus (RVA) (Reoviridae family), norovirus (NoV) (Caliciviridae family), adenovirus (AdV) (Adenoviridae family), mainly serotype 40/41 (species F) and astrovirus (AstV) (Astroviridae family)<sup>5,6</sup>. In Nepal infection of rotavirus causing gastroenteritis have been published in several papers, which identified that rotavirus is one of major causative agent for diarrheal disease in Nepal<sup>7,8,9,10</sup> and more than 40% children under 5 years are infected and several hundred children were death due to severe viral infection<sup>11</sup>. Although there are number of data have been generated for rotavirus disease burden, till date no rotavirus vaccine has been introduced in Nepal under National Immunization Program of Ministry of Health<sup>12</sup>.

There is negligible information available in Nepal on diarrheal disease caused by non-rotavirus, therefore, making it difficult for the clinicians to diagnosis and treat during an outbreak of diarrheal diseases in different parts of Nepal. Hence, we initiated and conducted a preliminary study and identified the burden of disease caused by non-rotavirus associated diarrhea in children of Nepal.

**Methods:** From October 2014 to April 2016, randomly selected negative stool samples for rotavirus were performed to identify specific antigens for norovirus, adenovirus and astrovirus using commercially available enzyme immunosorbent assay (EIA). For samples detected as positive for norovirus, enteric adenovirus and astrovirus, real time polymerase chain reaction (RT-PCR)<sup>13</sup> was carried out as confirmatory test.

**Results:** A total of 308 rotavirus negative acute diarrheal samples from children less than 3 years of age were included and examined using EIA tests kit. Enteric adenovirus was detected in 19.8% (61/308), norovirus positive was in 11.03% (34/308) and 6.2% (19/308) of astrovirus. There were 5.8% (18/308) cases of mixed infection. All EIA-positive cases were confirmed by RT-PCR<sup>13</sup>.

Clinical history of the sample population among children had typical symptoms associated with viral infection, including diarrhea, vomiting and fever. Bloody diarrhea was observed in 8.5% of the cases, mainly in co-infections with dual viral infection or viral and bacterial infection, especially when enteropathogenic *Escherichia coli* was the implicated agent, which was observed in 11.1% (4/36) of the cases. Majority of the viral infections were seasonal, as they were mainly detected from November to March, which is the dry winter season of Nepal.

**Conclusions:** The study identified that enteric adenovirus is the most frequent cause of acute gastroenteritis after rotavirus followed by norovirus and astrovirus in children with diarrhea in Nepal. Identification of these findings indicates that there is a need to continue extensive epidemiological study of enteric virus as well as unusual non-rotavirus strain,

which are responsible for causing severe diarrhea. The findings may also contribute to a better understanding of the role that gastrointestinal viruses play in childhood gastroenteritis and may aid in strategic planning for controlling diarrheal diseases in Nepal.

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