

## VIRAL DIARRHEA IN YOUNG CHILDREN

Khalafli H. N.

Abduganieva A. E.

Azerbaijan Medical University, Department of Epidemiology Fergana Medical Institute of Public Health, Department of Epidemiology and Infectious Diseases

### Abstract

Every year, millions of children become infected with viruses that affect the gastrointestinal tract and cause acute gastroenteritis, that is, viral damage to the stomach, small or large intestine. Children under five experience about a billion episodes of diarrhea every year. Symptoms accompanying acute gastroenteritis include malaise, abdominal pain and cramps, nausea, vomiting and diarrhea, which usually last from 1 to 5 days, but sometimes up to 14 days.

RNA viruses, including rotavirus, norovirus, sapovirus, astrovirus and enteroviruses, which are transmitted by the fecal-oral route, as well as DNA viruses, including enteric adenoviruses, are associated with age in immunocompetent and immunocompromised individuals of all age groups [1, 2]. Enteric viral co-infections, infections involving more than one virus, have been reported for various groups of etiologic agents, including rotavirus, norovirus, astrovirus, adenovirus, and enteroviruses.

These pathogens are the causative agents of acute gastroenteritis and diarrheal diseases in immunocompetent and immunocompromised people of all ages throughout the world [2, 4]. Although cases of viral-viral co-infection in the intestine are increasingly being identified, little is known about their impact on disease outcome or human health.

In the past, acute gastroenteritis was usually attributed to a single pathogen known to be associated with clinical symptoms. However, due to their high prevalence, exposure to multiple viruses at the same time can potentially occur in the same host, and these viruses can infect simultaneously or within a short period of time [3, 4].

Enteric pathogens, including enteric viruses, are extremely common in early life, and virus-virus interactions, in addition to being synergistically pathogenic, may play an important role in the development of homeostatic host-virus relationships as well as in shaping the immune system. Risk factors for contracting intestinal co-infections include early childhood, attending kindergartens and having more than



three children in the family, as well as the use of contaminated drinking water and poor sanitary living conditions.

Children from high-income areas often have lower rates of co-infection than children from low-income areas [1, 3].

Adenoviruses are non-enveloped DNA viruses that are known to cause conjunctivitis, upper and lower respiratory tract diseases, and acute gastroenteritis. Adenovirus can be transmitted by airborne droplets and the fecal-oral route and primarily affects the respiratory and gastrointestinal epithelium.

Epidemiological data indicate that most adenovirus infections occur in children under 5 years of age, but epidemics are also common among adults. Adenovirus genotypes are commonly associated with acute gastroenteritis in pediatric populations worldwide. The intestinal tract also appears to be a common site of adenovirus reactivation in immunosuppressed settings.

Although adenovirus infection in the respiratory tract is well characterized, gastrointestinal infection is less well understood in terms of cellular tropism, mechanism of entry, and intestinal immune responses.

Previously, coronaviruses were considered as possible rare causes of acute gastroenteritis in infants.

However, the ongoing global pandemic of the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) began in late 2019. The infection is often associated with gastrointestinal symptoms, including diarrhea, and SARS-CoV-2 viral RNA can be detected in fecal samples and viral antigens found in the intestinal tissues of COVID-19 patients.

In addition, there is growing evidence for the presence of SARS-CoV-2 antigen in the intestines of model animals such as macaques and ferrets. Although SARS-CoV-2 infection exhibits milder clinical symptoms in children compared to adults, prolonged shedding of these viruses has been observed in pediatric practice. The pandemic has raised important questions about this new pathogen in the gut and whether it may become an important factor in enteric viral coinfections in the future. With the increasing ability to efficiently analyze samples for multiple putative pathogens using quantitative real-time PCR approaches, our understanding that more than one virus may be present in an infected individual has increased. Concomitant enteric virus infections are commonly identified for all viruses associated with acute gastroenteritis.



However, although we are increasingly aware of the prevalence of enteric viral coinfections, the mechanisms underlying viral coinfection are not yet understood. There are significant gaps in our knowledge regarding the dynamics between co-infectious agents and how they influence disease severity, immune responses, or vaccine efficacy.

Many features of the mechanisms of viral coinfection in the intestine remain unclear, and further research will be critical.

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