



## Letter to the editor



## Severe hepatitis of unknown etiology in the pediatric population, a new conundrum to solve?

Dear editor,

A severe acute type of hepatitis in the pediatric population has recently been reported in multiple countries. As of May 26, 2022, around 650 probable and 100 suspicious cases have been reported to WHO from the five regional areas. Europe accounts for 58% of the reported cases, with 34% cases from the United Kingdom of Great Britain and Northern Ireland alone. The remaining cases have been reported from the United States of America, South East Asia, Western Pacific Region, and Eastern Mediterranean Region.<sup>1</sup> The actual number of cases may be understated, owing to the limited surveillance capability available in certain regions. This increase in likely cases of unexplained acute hepatitis was also observed in comparison to the preceding five years, according to an online rapid survey conducted by a group of European clinical trial networks and the organizations for pediatric gastroenterology-hepatology and infectious diseases.<sup>2</sup> Even though there have been prior reports of acute hepatitis in children with uncertain etiology, however, these recently reported cases are more clinically severe with a higher proportion of children requiring intensive care and potentially developing acute liver failure, requiring liver transplant. Because of its potential for a severe outcome and the affected pediatric population, this issue deserves our utmost attention.

The majority of the affected population are children aged up to 10 years, with three quarters (75.4%) of cases less than 5 years of age and they all were previously healthy.<sup>1</sup> As per the available data, they presented with symptoms like vomiting (72.8%), diarrhea (49.4%) and lethargy (55.6%) before being diagnosed with severe acute hepatitis, which was accompanied by elevated liver enzymes and jaundice (74.1%).<sup>3</sup> All patients tested negative for hepatitis viruses A, B, and C, and other causes of pediatric hepatitis and infections, including bacteremia, urinary tract infections, were also excluded.<sup>4</sup> The strongest link appears to be with either adenovirus or SARS-Covid 19. Adenovirus particularly subtype 41F was the most common pathogen found in the majority of the cases in England (75.5%) and Scotland (50%), which is the same subtype found in several of the US instances.<sup>5</sup> This subtype typically presents with common gastrointestinal and respiratory symptoms but previously is not known to cause acute hepatitis in otherwise healthy children. Many experts pointed out that the majority of the cases emerged during the surge of the Omicron variant of SARS-Cov-2. One of the leading hypotheses is that Covid-19 superimposed on Adenovirus infection in young children, which is mild in normal circumstances, causes a more serious illness or immune-mediated liver damage. As the etiology is not yet confirmed, detailed investigations regarding additional infectious and non-infectious causes are being carried out.

Keeping in view this public health concern, all countries must be on the same page so that awareness and surveillance can be established at the national and international levels. Various national authorities are conducting investigations that involve more thorough exposure

histories, toxicological testing, and additional virological/microbiological examinations to identify the etiology and any epidemiological links.<sup>1</sup> Countries with limited resources should also make every effort to identify and report any suspicious cases as it will enable us to implement effective control measures and optimal case management. In addition, standard hygiene measures along with contact and droplet precautions must be followed in all public settings. This comprehensive approach will possibly lead to a significant number of cases being identified early and reduce the overall morbidity and mortality.

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## Declarations of competing interest

The authors declare that they have no competing interests.

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