

Situation Summary

This technical note is in follow-up to the communication published by the World Health Organization (WHO) on 23 April 2022 and updated on 25 April 2022 on the Event Information Site for the International Health Regulations (IHR) National Focal Points (EIS) and the information published in the Disease Outbreak News website on 23 April 2022¹.

On 5 April 2022, the first report was received from the United Kingdom (UK) reporting an increase in cases of acute hepatitis of unknown origin in previously healthy children under 10 years of age, all residents of Scotland. A week later, additional cases under investigation were reported from England, Wales, and Northern Ireland.

To date, a total of 169 cases of acute, severe hepatitis of unknown origin have been reported among children aged 1 month to 16 years in 12 countries², including one death. Of the 169 cases reported, 85 cases were tested for adenovirus, of which 74 were positive. Adenovirus type 41 was identified in 18 cases.

Most of the reported cases were classified considering the current working case definition, which are based on the clinical-epidemiological characterization of the cases identified to date.

Clinical manifestations among identified cases correspond to acute hepatitis with elevated transaminases, many presenting with jaundice and gastrointestinal symptoms (including abdominal pain, diarrhea, and vomiting) and none presenting with fever. Infections caused by hepatitis A, B, C, D, and E viruses were not identified among any of the affected children. Clinical outcomes thus far have varied, with 10% requiring liver transplantation.

Hepatitis and adenovirus

Hepatitis is an inflammation of the liver that can cause several health problems and can be deadly. Several factors can cause inflammation of the liver. The five main viruses involved in liver inflammation are the hepatitis A, B, C, D, and E viruses. Viral hepatitis represents a high burden of disease and mortality worldwide with an estimated 1.1 million deaths each year. It is estimated that 57% of cases of liver cirrhosis and 78% of cases of primary liver cancer are due to hepatitis B or C virus infections.

Adenoviruses are double-stranded DNA viruses that are spread by close personal contact, respiratory droplets, and fomites. There are more than 50 immunologically distinct types of adenoviruses that can cause infections in humans. Adenoviruses usually cause respiratory diseases but depending on the type of adenovirus they can cause other diseases such as gastroenteritis, conjunctivitis, cystitis and, less commonly, neurological diseases. There is no specific treatment for adenovirus infections.

Adenovirus type 41 commonly causes acute pediatric gastroenteritis, which typically presents with diarrhea, vomiting, and fever; it can often be accompanied by respiratory symptoms. Rare cases of hepatitis caused by adenoviruses have been reported in immunocompromised children, but so far **there is no available evidence indicating that adenovirus type 41 is a cause of hepatitis in otherwise healthy children.**

¹ Multi-Country – Acute, severe hepatitis of unknown origin in children. Available at: <https://bit.ly/3Ko1xu0>

² Belgium, Denmark, France, Ireland, Israel, Italy, Netherlands, Norway, Romania, Spain, the United Kingdom, and the United States of America.

On 18 April 2022, the United States of America IHR National Focal Point (NFP) reported a total of 9 cases of acute hepatitis among children aged 1 to 6 years to the Pan American Health Organization/World Health Organization (PAHO/WHO); the cases were identified between 2 October 2021 and 21 February 2022. Among the 9 cases, 7 were female, and all 9 cases presented with signs and symptoms compatible with different stages of hepatitis (scleral jaundice, jaundice, hepatomegaly, encephalopathy, and elevated transaminases). Two children required liver transplantation, whereas the rest of the cases were managed clinically. Adenovirus type 41 was identified in whole blood samples by RT-PCR in 5 of the 9 cases. A possible association between cases of severe acute hepatitis in the pediatric population and adenovirus infection is currently being investigated.

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The etiology of the cases remains under investigation. Laboratory tests are ongoing to understand the underlying mechanism and the potential association of the cases to infectious agents, chemicals, and toxins. The cases have no obvious epidemiological risk factors, including recent international travel. Most of the reported cases have not received the COVID-19 vaccine.

The investigation remains ongoing, and a priority on determining the disease etiology to better inform prevention and control measures. This requires identifying additional cases and conducting further tests.

PAHO/WHO shares this technical note to maintain Member States' awareness. Information will be shared as it becomes available.

In the Region of the Americas, considering the circulation of the yellow fever virus in several areas, as well as the presence of endemic areas for malaria, testing for these diseases in addition to hepatitis A-E testing should be considered.

References and sources of additional information

1. WHO. Disease Outbreak News. Multi-Country – Acute, severe hepatitis of unknown origin in children. April 23, 2022. Available at: <https://bit.ly/3xVolFd>
2. U.S. Centers for Disease Control (US-CDC). Recommendations for the reporting of adenovirus in children with acute hepatitis of unknown etiology. April 21, 2022. Available at: <https://bit.ly/3LmRR49>
3. U.S. Centers for Disease Control (US-CDC). CDC alerts health care providers to cases of hepatitis of unknown origin. April 21, 2022. Available at: <https://bit.ly/3rV1n6R>
4. European Centre for Disease Prevention and Control (ECDC). Update: Hepatitis of unknown origin in children. 19 April 2022. Available at: <https://bit.ly/3xRpgjH>
5. European Centre for Disease Prevention and Control (ECDC). Increase in acute hepatitis of unknown origin among children – United Kingdom. 12 April 2022. Available at: <https://bit.ly/3MCM3nz>
6. UK Security Agency. Investigation of acute hepatitis of unknown etiology in children in England. April 25, 2022. Available at: <https://bit.ly/3OGhG10>
7. WHO. Hepatitis. Available at: <https://bit.ly/3Kjo3UE>
8. PAHO/WHO. Hepatitis. Available at: <https://bit.ly/3ODsi0M>