

Severe acute hepatitis of unknown cause in children

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1 Public health agencies worldwide have raised concern over cases of severe acute hepatitis of unknown cause in children

As of July 8, 2022, 1010 probable cases have been reported to the World Health Organization (WHO),¹ including 21 in Canada.² Whether this represents an increase from baseline remains uncertain. The cause is also unclear; however, it may be triggered by SARS-CoV-2 or adenovirus infection.³

2 Presentation varies from mild symptoms to acute liver failure

Children may present with signs or symptoms that are specific (e.g., jaundice, scleral icterus, dark urine, pale stools, hepatic encephalopathy), nonspecific (e.g., nausea, vomiting, loss of appetite) or systemic (e.g., myalgia, lethargy, fever).⁴

3 The WHO defines a probable case as a child (age ≤ 16 yr) with acute hepatitis with an aspartate aminotransferase (AST) or alanine aminotransferase (ALT) level of more than 500 IU/L, excluding cases caused by hepatitis A–E or other explanations

First-line investigations include complete blood count, markers of liver cell injury (AST, ALT, alkaline phosphatase, γ -glutamyltransferase) and liver function (conjugated bilirubin, albumin, international normalized ratio [INR]). Probable cases should be tested for SARS-CoV-2 (polymerase chain reaction and antibody testing) and adenovirus infection.⁴ Differential diagnoses include infectious (hepatotropic and nonhepatotropic viruses) and non-infectious (drug-induced liver injury, autoimmune, metabolic) conditions.⁵

4 Children with an ALT level of more than 500 IU/L or an INR of 1.5 or higher require referral

Input from a pediatric gastroenterologist should be obtained to prioritize investigations, provide anticipatory guidance and discuss management (including use of vitamin K and acetaminophen).⁴ Rarely, children may progress to aplastic anemia, which requires consultation with a hematologist. Clinicians should immediately consult a pediatric liver transplantation program for children with suspected encephalopathy, or with an INR above 2.0 that is not corrected with a single dose of intravenous vitamin K (0.3 mg/kg, maximum daily dosage 10 mg).

5 Most children recover fully with supportive care, although liver transplantation has been reported

In the United States, hepatitis-associated emergency department visits, hospital admissions and transplantations have not increased compared with pre-COVID-19 pandemic levels.⁶ However, at least 46 children have required transplantation and 22 have died since Oct. 1, 2021.¹

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