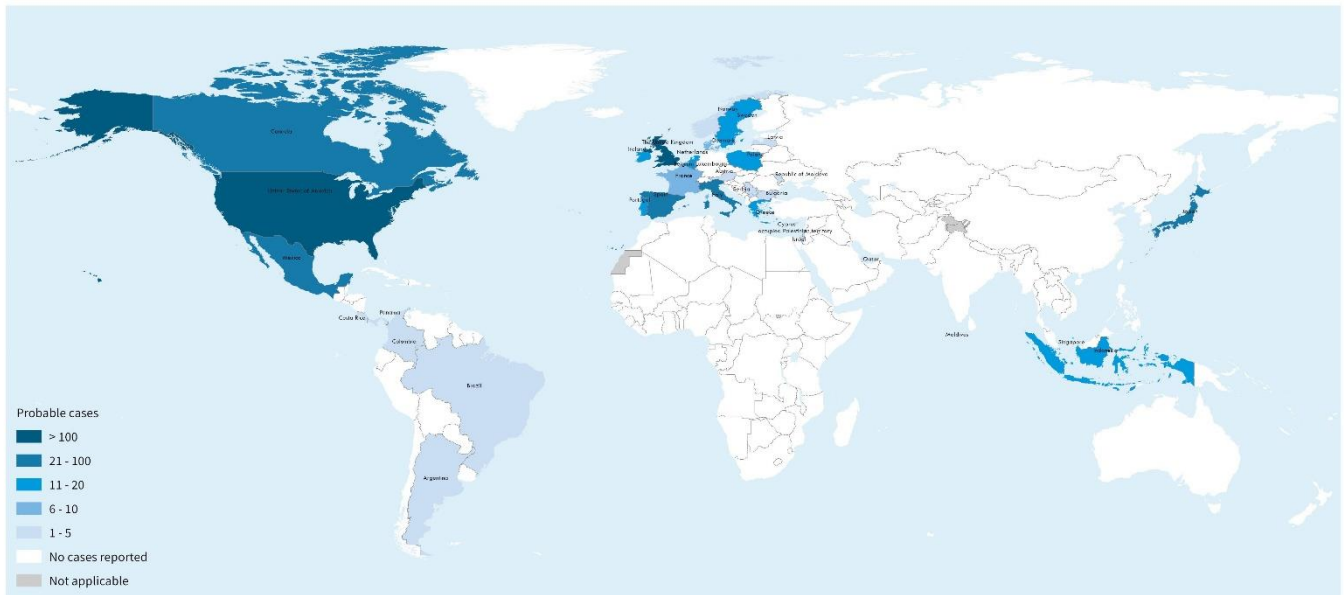


BACKGROUND

In early April 2022, the World Health Organization (WHO) released an emergency outbreak notice regarding an acute hepatitis of unknown origin in the United Kingdom of Great Britain and Northern Ireland that affected young children. In a matter of days, cases increased from ten to 74 in otherwise well children with acute hepatitis without detection of hepatitis viruses (A-E). The earliest cases occurred in January 2022. There is no known association with travel, SARS-CoV-2 infection or vaccination. Adenovirus (Type 41 and 44) was identified in up to one-third of the cases. Currently (12 July, 2022), there are 1010 probable cases in 35 countries (Figure 1) with 22 deaths (2%) and 46 (5%) requiring liver transplant. As of 12 July 2022, of 571 cases with information on gender and age, 48% of cases are male (n=232), and the majority of cases (76%, n=384) are under 6 years of age.

Figure 1. Distribution of cases of acute severe hepatitis in children (WHO July 12, 2022)



The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
Map Production: WHO Health Emergencies Programme
Map Date: 12 July 2022



Acute hepatitis is characterised by an acute onset of discrete symptoms including fever, jaundice, abdominal pain, nausea and vomiting, which rarely may progress to fulminant hepatic failure and the need for liver transplantation.

Most childhood cases of acute hepatitis are infection-related, with Hepatitis A (HAV) and B (HBV) being the commonest causes. Other viruses (e.g. Hepatitis E, Epstein-Barr, cytomegalovirus, adenovirus) and non-viral infections (e.g. toxoplasma, leptospirosis) may also cause hepatitis in children. Countries such as the United States that have introduced routine HAV and HBV vaccination into their national childhood immunisation programmes have observed dramatic reductions in the incidence of acute HAV (92%) and HBV (82%), respectively, across all age-groups [Daniels et al., 2009]. The UK, Ireland, Australia and New Zealand do not routinely immunise against HAV but have included HBV vaccination in their infant immunisation schedule.

In response to the emergence of severe acute hepatitis of unknown origin internationally, members of the International Network of Paediatric Surveillance Units (INOPSU) initiated a collaborative surveillance study. In line with the BPSU and the NZPSU we will conduct national surveillance for severe acute hepatitis in children and adolescents. This APSU study protocol and CRF has been developed based on the INOPSU protocols and informed

by international data on severe acute hepatitis of any cause to prospectively collect information from Australian paediatricians about children who have developed severe acute hepatitis since 01 July 2022.

OBJECTIVES

1. To identify cases of severe acute hepatitis of any cause in Australian children aged under 17 years and seen by paediatricians.
2. To describe severe acute hepatitis of any cause in children, including demographics, clinical features and severity, treatment; and short-term outcomes.
3. To document outcomes at 6-12 months in terms of morbidity and mortality and requirement for liver transplantation.

CASE DEFINITION

Please report any newly diagnosed case of severe acute hepatitis of any aetiology in any child aged under 17 years of age with:

- 1) acute onset of symptoms consistent with hepatitis (e.g. fever, jaundice, abdominal pain, fatigue, loss of appetite, rash, itch, joint or muscle ache, dark urine, pale coloured stools, nausea or vomiting); **AND**
- 2) elevated serum alanine aminotransferase (ALT) **OR** aspartate aminotransferase (AST) levels (>500 IU/L); **AND**
- 3) hepatitis of known or unknown cause (see below), including infections, drugs, metabolic or autoimmune causes.

Causes of Severe Acute Hepatitis may include:

Unknown

All of the below have been excluded or test results are still pending.

Please report probable cases as unknown if test results are still pending

Confirmed virus-specific acute hepatitis infection – fulfils case definition and laboratory confirmation for specific virus markers (antigen, antibody, DNA, RNA, etc. depending on the causative agent)

- for Hepatitis B, this will include Hepatitis B surface antigen (HBsAg)-positive or IgM antibody to hepatitis B core antigen (HBcAb-IgM) or HBV DNA PCR positive
- for Hepatitis A, this will include HAV IgM-positive or HAV RNA PCR positive
- for Hepatitis C, this will include HCV IgG antibody positive or HCV DNA positive
- for Hepatitis E, this will include HEV IgM-positive or HEV RNA PCR positive
- or other viruses (e.g. EBV, CMV, Adenovirus, HSV, VZV, etc.), this will involve laboratory confirmation of specific markers of viral infection (e.g. PCR, IgM antibody, etc.) at different sites (blood, respiratory, stools)
- For Hepatitis D; (PCR or serology)
- For Sars-CoV-2: antigen or PCR

Other infectious agents

Laboratory confirmed acute hepatitis associated with other viral, bacterial, and other infectious agents – e.g. Salmonella, toxoplasma, etc. identified by through culture, PCR, antigen/antibody testing, etc.

Autoimmune conditions

Diagnosis with assessment of liver function tests, auto-antibody levels (i.e., ANA, SMA, LKMA1) and biopsy results.

Drugs

Diagnosis may include the drugs: antibiotics (i.e., flucloxacillin, augmentin), antiepileptics, anti-tuberculosis drugs (uncommonly given) and paracetamol.

FURTHER INFORMATION

For further information related to this study or assistance completing the Case Report Form, please contact the APSU by either:

- email: SCHN-APSU@health.nsw.gov.au or
- phone: (02) 9845 300

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