



Severe acute hepatitis cases of unknown aetiology in Ireland

Prepared by HPSC on 08/09/2022, data as of 9:30 08/09/2022

Background

An increase in severe acute hepatitis cases of unknown aetiology among previously healthy children was first reported by the United Kingdom (UK) to the World Health Organization's International Health Regulations (IHR) notification system on 5 April 2022 (testing had excluded viral hepatitis types A, B, C, D and E and other known causes of acute hepatitis). Following this alert, the United States and several European Union, European Economic Area (EU/EEA) and other countries have reported suspected cases.

According to the [latest Update](#) from the European Centre for Disease Prevention and Control (ECDC), the aetiology and pathogenetic mechanisms of disease are still under investigation. A possible association with current adenovirus infection has been identified, but other hypotheses and possible co-factors are under investigation. Most cases continue to be reported as sporadic, unrelated cases.

The most recent update from the World Health Organization (WHO) is available from:

<https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON400>

The most recent update from the UK Health Security Agency (UKHSA) - Technical briefing 4: investigation into acute hepatitis of unknown aetiology in children in England - is available from:

[Acute hepatitis: technical briefing - GOV.UK \(www.gov.uk\)](https://www.gov.uk/government/consultations/acute-hepatitis-technical-briefing-4)

Irish response

Following the initial international alert of paediatric cases of hepatitis of unknown aetiology and subsequent identification of suspect Irish cases meeting the same clinical profile, a multidisciplinary Incident Management Team was established by the HSE in early April 2022. Cases are notified under Infectious Diseases (Amendment) (No. 3) Regulations 2003 (regulation 14) whereby doctors and directors of diagnostic laboratories are required to notify unusual clusters or changing patterns of any illness, and individual cases, that may be of public health concern.

Data on cases, collected by clinical teams in paediatric hospitals, laboratories and public health, have been collated and analysed in order to understand the aetiology and risk factors for the disease. Anonymous data are shared with ECDC and WHO as part of the international efforts to understand this event.

The IMT continues to monitor the national and international situation relating to this event, collecting and analysing data on Irish cases meeting the case definition (described below).

This report summarises the epidemiological situation in relation to cases meeting the case definition in Ireland. These data are provisional and subject to change as results from investigations become available over time.

The following working case definition matches that used by WHO/ECDC with the exception of the 'Possible' case category, which is unique to Ireland. This additional classification was agreed by the national IMT to ensure that all suspect cases could be identified and investigated appropriately.

Cases meeting this case definition are reported to the Departments of Public Health and the HPSC.

Working case definition in Ireland

For the purposes of case identification, the national IMT agreed to adopt the following case definition:

- **Confirmed:** N/A at present
- **Probable:** A person presenting with an acute hepatitis (non hepA-E*) with serum transaminase >500 IU/L (AST or ALT), who is 16 years and younger, since 1 October 2021
- **Possible:** A person presenting with an acute hepatitis (non hepA-E*) with serum transaminase between 200 and 500 IU/L (AST or ALT), and cholestatic who is 16 years and younger, since 1 October 2021
- **Epi-linked:** A person presenting with an acute hepatitis (non hepA-E*) of any age who is a close contact of a probable case, since 1 October 2021.

*If hepatitis A-E serology results are awaited, but other criteria met, these can be reported and will be classified as "pending classification". Cases with other explanations for their clinical presentation are discarded.

Persons under investigation (PUI): When potential cases, who have some features of this disease, are notified by clinicians, they are first called 'persons under investigation', until clinical history and laboratory tests (specifically hepatitis A-E serology) are available, at which time they are either categorised as cases, or discarded, if another cause for their hepatitis has been found.

Summary of probable cases identified in Ireland

As of 8th September 9:30, **twenty eight probable cases of severe acute hepatitis** of unknown aetiology have been identified in Ireland: **two probable cases underwent liver transplantation; one probable case (non-transplant) died. Three possible cases** of severe acute hepatitis of unknown aetiology have also been identified. A small number of further potential cases are currently classified as PUIs.

Twenty seven of the twenty eight probable cases had at least one test for adenovirus (blood, stool, respiratory, serum or other specimen type). Of these fourteen (52%) tested positive. Eleven of the cases who tested positive or weak positive for adenovirus were also tested for adeno-associated virus type 2 (AAV2). AAV2 was detected in 73% (n=8) of specimens for these cases. Twenty five probable cases had a SARS-CoV-2 PCR or antibody test. No cases tested positive on PCR test (tests for current infection) and 15 (60%) tested positive for SARS-CoV-2 antibodies (current or past infection). The other most commonly detected organism was human herpesvirus 7 (HHV-7), but the number of cases tested was low; 12 cases tested, 6 positive (50%). Eight cases also tested positive for rhinovirus or enterovirus and small numbers tested positive for other pathogens.

Table 1 summarises the probable cases. Figure 1a and 1b show the number of probable cases, possible cases and PUIs by week of onset and week of hospitalisation. Figure 2 shows the % of probable cases with each clinical symptom, where information on symptoms was reported. Figure 3 shows available laboratory results for probable cases as of 9:30 8th September. The percentage positive for some organisms should be treated with caution due to low numbers tested.

Table 1. Summary table of probable cases as of Thursday 1st September 9:30

Characteristics	Number	%
Age		
<1	2	7.1
1-4 yrs	15	53.6
5-11 yrs	10	35.7
12-16 yrs	1	3.6
Median age	4	
Age range	0 - 12	
Sex		
Male	13	46.4
Female	15	53.6
Ethicity		
White Irish	27	96.4
Other	1	3.6
International travel		
Yes	6	21.4
No	18	64.3
Unknown	4	14.3
SARS-CoV-2 vaccination status		
Vaccinated	2	7.1
Not vaccinated	19	67.9
Unknown	7	25.0
Clinical		
Hospitalised - Non ICU	21	75.0
Hospitalised - ICU	6	21.4
Not hospitalised	1	3.6
Transplant		
Had liver transplant	2	7.1
Total	28	

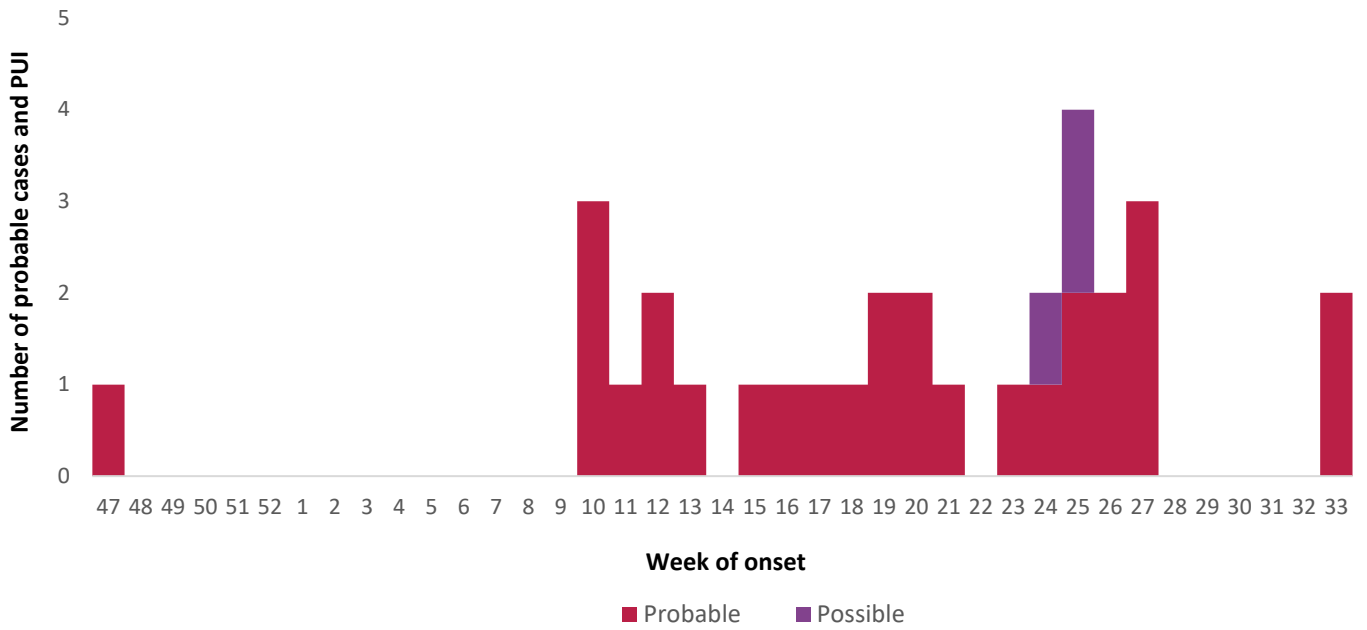


Figure 1a. Number of probable and possible cases by week of onset of symptoms

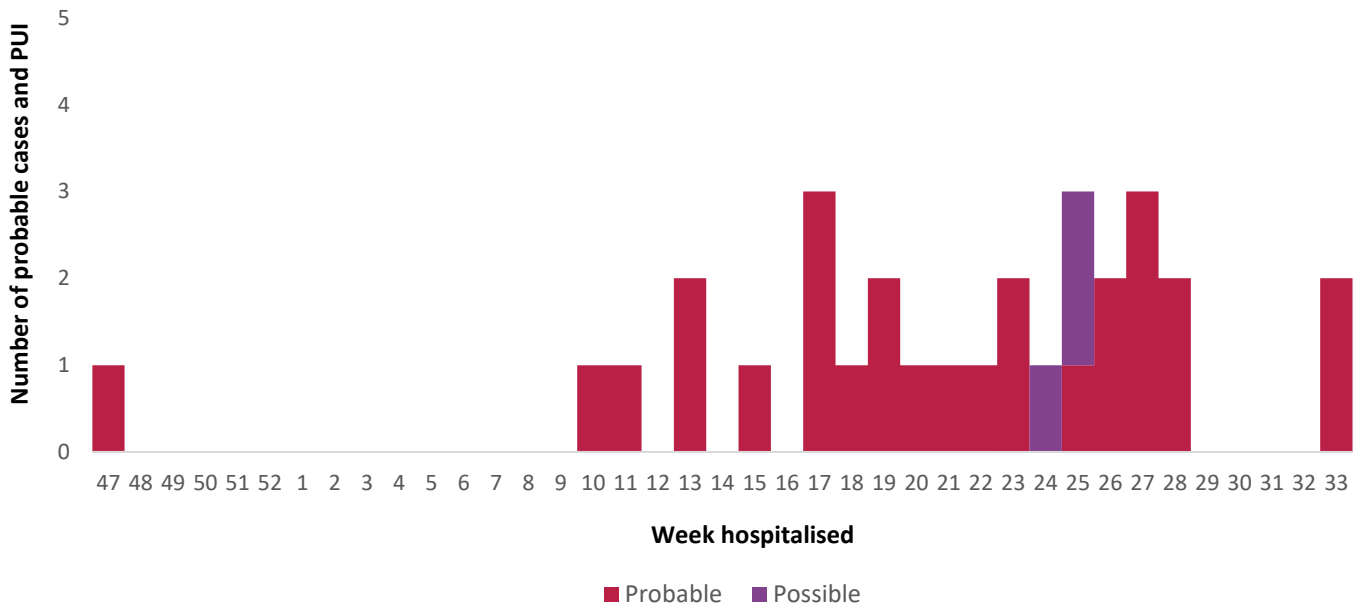


Figure 1b. Number of probable and possible cases by week of hospitalisation*

*One probable case was not admitted to hospital.

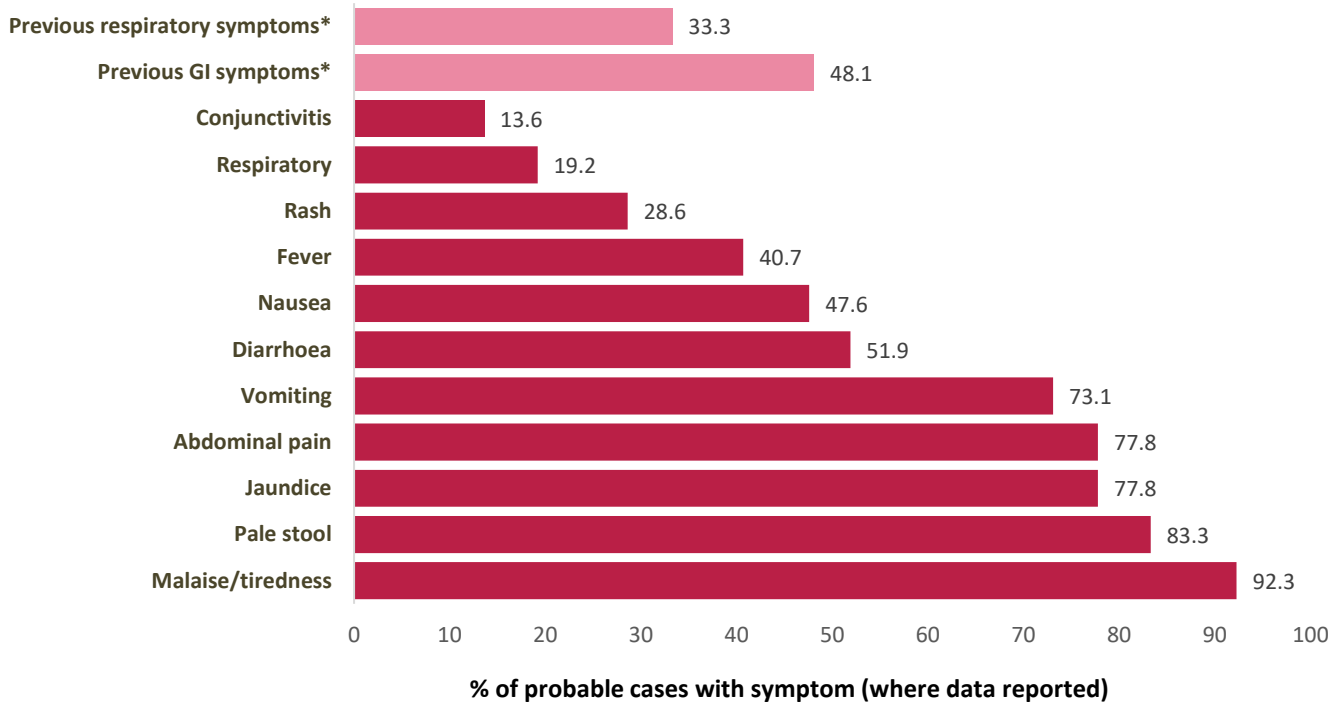


Figure 2. Frequency of each clinical symptom for probable cases where information on symptom was reported (varied by symptom, n=21 to 27)

*Respiratory or gastrointestinal symptoms experienced in weeks prior to hospital admission – difficult to determine if due to separate illness or illness leading to hepatitis-related hospitalisation in some cases. Therefore a case may be reported as having had respiratory symptoms, diarrhoea and vomiting and also previous respiratory or gastrointestinal symptoms.

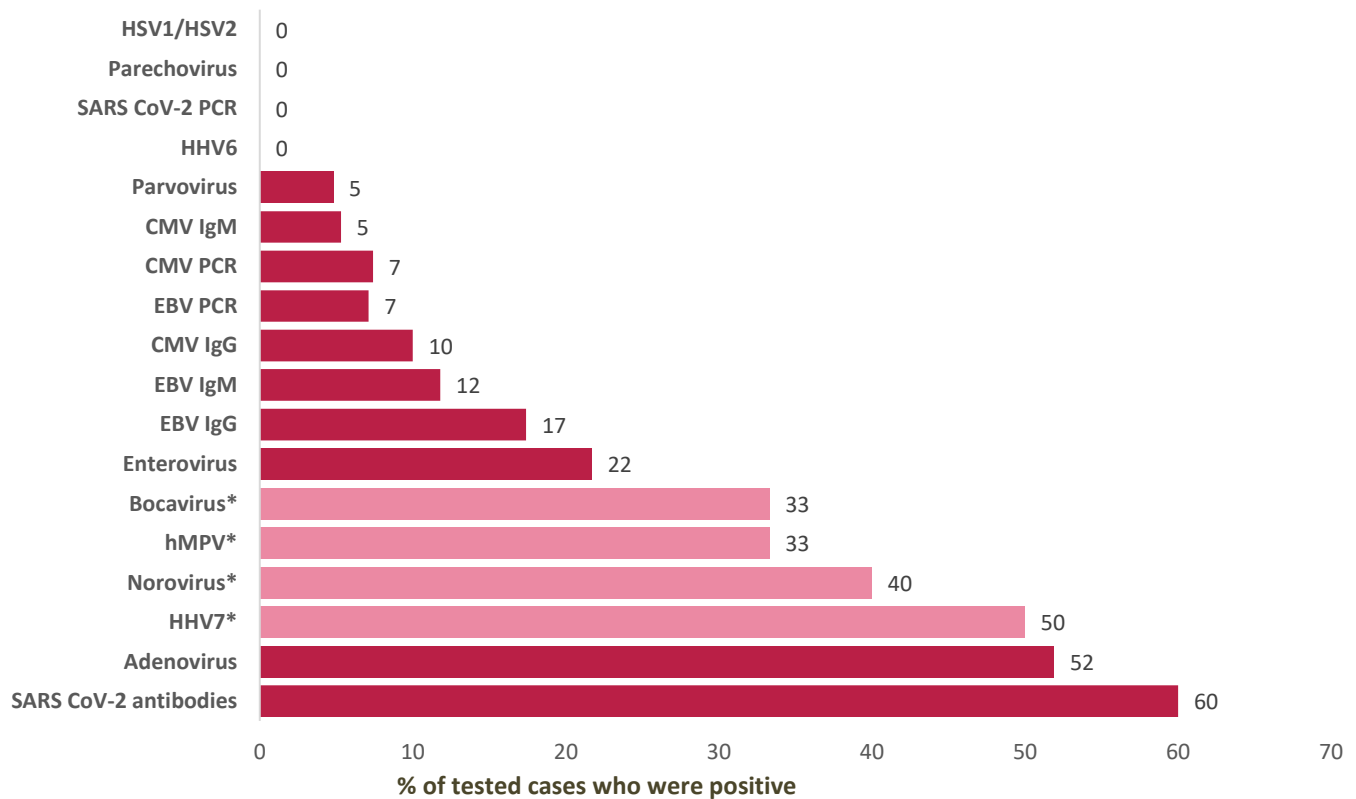


Figure 3. % of probable cases positive for each organism where results reported (varied by pathogen, n=3 to 28)

*The number of cases tested was low for HHV-7 (n=12), hMPV (n=3), Norovirus (n=5) and Bocavirus (n=3)

Acknowledgements

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