

Hepatitis of unknown origin in children: Why and how to create an open access database



Hepatitis of unknown origin in previously healthy children, from one month old to 16 years old, were reported in early 2022 to the IHR-International Health Regulation System of WHO [1,2].

Between 5 April and 8 July 2022, 35 countries have reported 1010 probable cases and 22 deaths. amongst the probable cases, 46 (5%) children have required transplants and 22 (2%) deaths have been reported to WHO [3]. In Europe according to ECDC (European Centre for Disease Prevention and Control) up to June 30, 473 cases are reported from 21 countries [4] (see Fig. 1), of which 328 were hospitalized, 87 required admissions to an intensive care unit and 20 have received a liver transplant, as shown in Fig. 2.

The aetiology and pathogenetic mechanisms of the disease are still unknown and under deep investigation. All known panels of Hepatitis virus A-E were excluded. A possible association with several viruses and especially with a current Adenovirus infection has been suspected and reported in high prevalence for some of them: in agreement with the most updated WHO report [3], in the European region Adenovirus was detected by PCR in 52% of cases (193/368). Other hypotheses and possible co-factors involvement are under investigation. Most cases continue to be reported as sporadic and non-related cases.

The clinical presentation of severe acute hepatitis requires hospitalization with jaundice and markedly elevated liver transaminases. Usually, the onset of jaundice was preceded by a gastrointestinal illness with vomiting, diarrhoea, and nausea. The majority of the patients (whose information is available) did recover, but some of them progressed to acute liver failure and required liver transplantation [5].

The outcome of acute liver failure, with some cases requiring liver transplantation, implies that "the potential impact for the affected paediatric population is considered high" [5]. Affected children require assistance in highly specialised paediatric intensive care units and trans-

plantation services. As stated by ECDC itself, "considering the unknown aetiology, the affected paediatric population, and the potential severe outcome, this currently constitutes a public health event of concern" [5].

To provide insight into the spread of the disease and support global response efforts with epidemiological data in real-time, we created an open-access database available on a GitHub repository [6], which reports the daily new and cumulative cases. Moreover, where available, the cases are stratified by age, gender, locations (aggregated to the country level), and clinical outcome (i.e., hospitalization, admission to an intensive care unit, and need for liver transplantation).

Data are extracted from verified sources, such as the "Disease Outbreak News" published by the WHO and the ECDC bulletins, which provide an overview of the cases of hepatitis of unknown origin in children reported by the five WHO Regions (i.e., Americas, Eastern Mediterranean, Europe,

South-East Asia, Western Pacific) and to ECDC and the WHO Regional Office for Europe through The European Surveillance System (TESSy), respectively.

The main goals of our work are: i) to facilitate the epidemiological investigations of the transmission dynamics of this outbreak; ii) to inform the citizens and make the collected data available; iii) to support clinical and public health decisions. These data can allow predictive analysis of the evolving infection situation and identifying areas where the disease is most likely to spread. However, it is necessary to strengthen data governance with regard to data collection, data partnership, data analysis, and data dissemination, to provide effective, timely, and inclusive responses to manage the outbreak.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

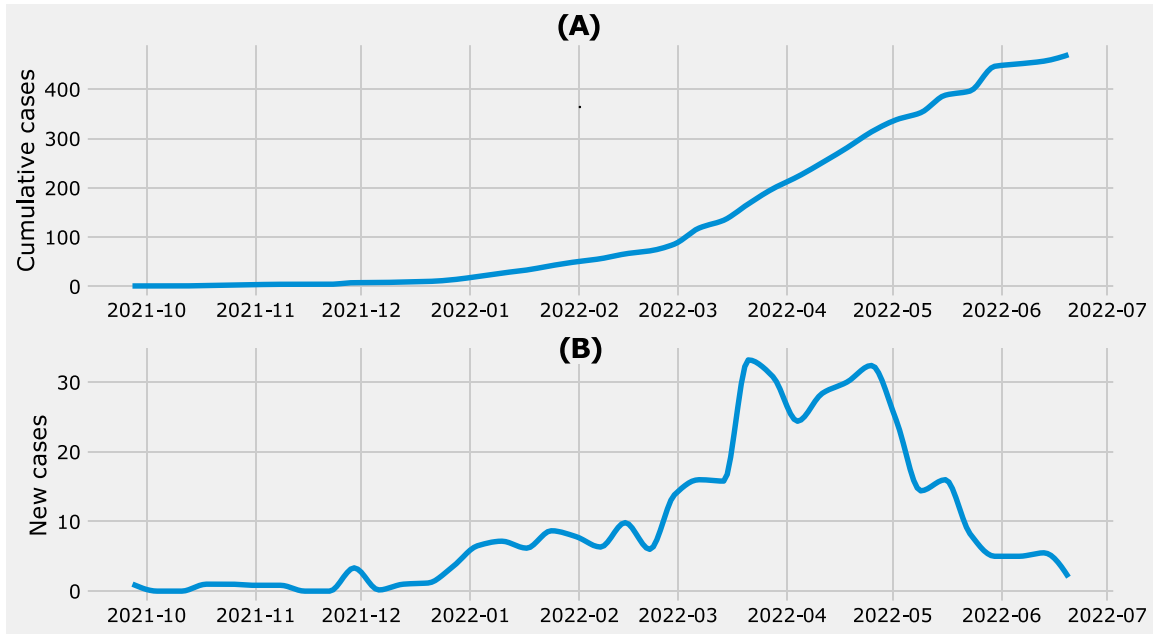


Fig. 1. (A) Cumulative number of confirmed cases since the first reported case in September 2021, and (B) daily number of new confirmed cases in EU/EEA countries.

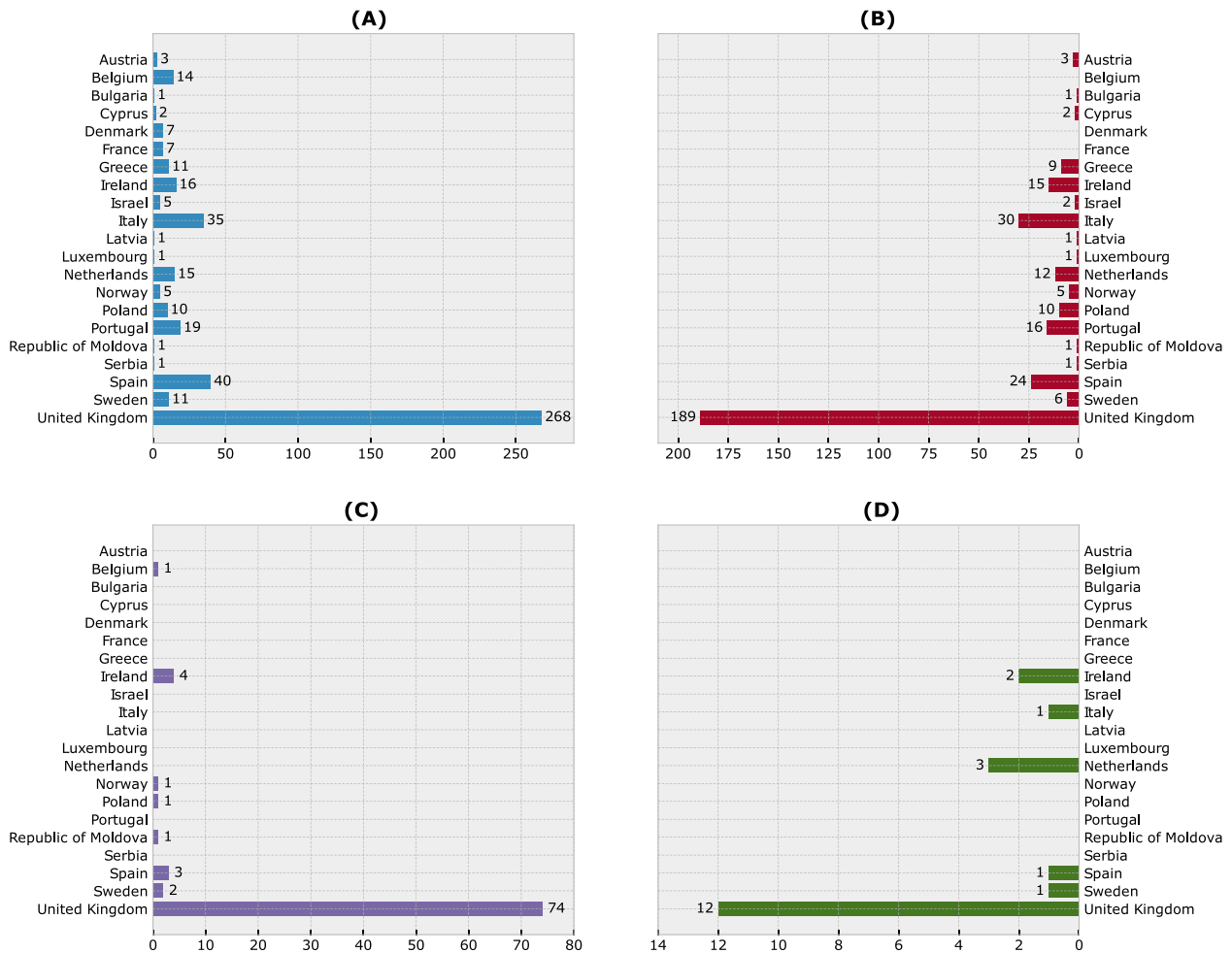


Fig. 2. (A) Number of cases by disease onset, (B) hospitalization, (C) admission to an intensive care unit and (D) required transplants per EU/EEA country.

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