

WHO warns of severe hepatitis among children across several countries, possibly tied to spread of COVID-19

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The World Health Organization (WHO) has advised countries that there has recently been a sudden rise in cases of acute hepatitis of unknown origin among children. Hepatitis is an inflammation of the liver that can lead to jaundice (the yellowing discoloration of the skin and whites of the eyes), poor appetite, fatigue, abdominal pain, vomiting and diarrhea. Blood work usually reveals very elevated liver enzymes.

Typically, acute hepatitis resolves on its own, but it can progress to acute liver failure in some. In such instances, liver transplantation becomes a life-saving surgery. Long-term concerns include progression to scarring of the liver (cirrhosis), chronic liver failure, and liver cancer.

As of April 21, 2022, at least 169 of these rare cases have been reported to the WHO across 12 countries. The age of the patients has ranged from one month to 16 years old. The United Kingdom, with 114, has reported the majority of cases. Ten of these children have required liver transplants, of which seven were in England. Spain has documented 13 such cases and Israel 12. The US has reported at least 14 severe hepatitis cases: nine in Alabama, two in North Carolina, and three in Illinois.

The other countries include Denmark (six), Ireland (less than five), the Netherlands (four), Italy (four), Norway (two), France (two), Romania (one), and Belgium (one). In total, 17 children (10 percent) have undergone liver transplantation, and one child has died.

The Scottish National Health Service first broke the news of these cases of acute hepatitis among children to the WHO in early April. A rapid communication to *Eurosurveillance* on their experience was published on April 14.

They wrote in their report that “five children aged 3-5 years [presented] to the Royal Hospital for Children, Glasgow with severe hepatitis of unknown etiology within a three-week period. The typical number of cases of hepatitis of unknown etiology across Scotland would be fewer than four per year.” Of the first 10 cases in children under the age of 10 requiring hospitalization, nine of these cases had symptom onset in March and the first one was in January.

By April 8, an additional 64 cases were identified, raising the total to 74 who met the case definition specified by the UN health authority. Several children were transferred to pediatric centers specializing in liver disorders, and six children had undergone liver transplants by then.

All tested cases excluded hepatitis type A, B, C and E viruses (and D where applicable.) However, the SARS-CoV-2 and/or adenovirus infections were documented in several cases. Health authorities caring for these children are also investigating epidemiological risk factors such as recent international travel and exposure to chemicals or toxins.

An additional five cases were then reported from Ireland, prompting the WHO to release a Disease Outbreak News alert on April 15 regarding these developments and calling for diligence in identifying, investigating, and reporting such cases in the UK and internationally.

They wrote, “The priority is to determine the etiology of these cases to guide further clinical and public health actions. Any epidemiological links between or among the cases might provide indications for tracking the source of illness. Temporal and geographical information of the cases, as well as their contacts

should be reviewed for potential risk factors. While some cases tested positive for SARS-CoV-2 and/or adenovirus, genetic characterization of viruses should be undertaken to determine any potential associations between cases.”

Since that initial report, cases have grown more than expected. The WHO said, “Given the increase in cases reported over the past one month and enhanced case search activities, more cases are likely to be reported in the coming days.”

During an emergency session at the European Congress of Clinical Microbiology and Infectious Diseases in Lisbon on Monday, Dr. Meera Chand, who is the incident director for the UK Health Security Agency investigating these outbreaks, said, “The cases in England are not known to be connected to each other and are dispersed all over the country,” meaning there is no epidemiological linkage like with the transmission of the SARS-CoV-2 virus, implying the disease is not being transmitted.

Chand explained, “I think our leading hypothesis, given the data we’ve seen, is that we probably have a normal adenovirus circulating, but we have a co-factor affecting a particular age group of young children which is either rendering that infection more severe, or causing it to trigger some kind of inappropriate immune response.”

In their April 23 report, the WHO noted that in 74 cases, an adenovirus infection was detected, of which 18 on molecular testing were identified as type 41. Though adenoviruses have been implicated in rare cases of acute hepatitis, most of these cases occur in immunocompromised children, and such complications have not been documented among previously healthy children. Additionally, 20 of these cases were positive for the SARS-CoV-2 virus, and 19 were co-infected with both viruses.

Adenoviruses are respiratory viral infections that generally cause symptoms analogous to the common cold or flu, presenting with fever, cough and sore throat. Other characteristics of the infection can include conjunctivitis, bronchitis and diarrhea. Individuals with weakened immune systems can suffer more severe complications.

After dropping to unusually low levels during the pandemic, the complete social relaxation and return to in-class instructions have meant a surge in adenovirus

infections. At the same time, the incidence of COVID infection among children in the US has risen to 75 percent, according to data recently published by the Centers for Disease Control and Prevention (CDC).

One of the working theories being proposed is that recent COVID infections could sufficiently alter the immune response, making children susceptible to severe side effects from relatively harmless viruses. Genotyping of adenoviruses in these cases has not revealed that there might be a more virulent strain of adenovirus circulating in communities.

Still, Jim McMenamin, Scotland’s director of public health, told Reuters that “work was underway to establish if the adenovirus involved had mutated to cause more severe disease.” He added, however, “Or [possibly the adenovirus] could be causing the problems ‘in tandem’ with another virus, including possibly SARS-CoV-2, the virus that causes COVID.”

Dr. Yael Mozer-Glassberg, head of the pediatric liver transplant unit at Schneider Children’s Medical center in Petah Tikva, speaking on the cases from Israel, said, “After we ruled out all the various possibilities, the common denominator in all the cases we found was that all had come down with the coronavirus around three and a half months before the infection appeared. This certainly raises the question. But I don’t think it’s possible to say yet that all these cases are a post-COVID phenomenon.”

All authorities agree that there is no link to the COVID vaccines. None of the cases in the UK in the under-10-years of age are known to have been vaccinated. However, vaccination rates among the youngest are the lowest in any age category. Should the linkage between seasonal viruses and SARS-CoV-2 prove to trigger the development of severe acute hepatitis among the most vulnerable, it only further confirms the importance of eliminating COVID and the criminal negligence in allowing it to spread throughout the world’s population.



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