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A dangerous and mysterious illness continues to spread among children, and so do questions over what's causing it, including possible links to Covid-19. But it's too soon to tell what is behind the cases, experts say.

More than 600 cases of hepatitis with no known cause have been identified around the globe since October 2021, and many of the cases are in previously healthy children now stricken with severe illness.

The UK has the highest number of identified cases, with 197, while the US has 180 cases, most of which have been severe enough to require hospitalization.

Although more cases are being recognized, the cause is still a medical mystery.

"The playing field is changing on an hour-to-hour basis," said Jason Kindrachuk, an assistant professor in medical microbiology and infectious diseases at the University of Manitoba and coauthor of a new commentary on the status of these cases.

"Inch by inch, we're starting to figure out what this problem is," Kindrachuk said. "But I don't think we have all those pieces of the puzzle yet to say, 'OK, this is what we think is going on.'"

While mild liver inflammation isn't uncommon among children, severe inflammation like this is. Normally the UK has eight to 10 liver transplants each year, but is has already passed those numbers, with 11 in only three months.

Globally, 26 patients – 15 in the US – have required liver transplants. Nearly half of the deaths – five out of 11 so far – have occurred in the US, although the nation accounts for only one-third of identified cases.

The first cases in the US were reported in Alabama, but after the CDC issued a nationwide alert, cases were found in 36 states and territories.

Blood tests reveal the severe liver inflammation isn't caused by the usual culprits, including the hepatitis viruses A, B, C, D and E.

Several possible causes are being investigated. This could be a new virus that hasn't yet been unidentified. Or it could be an existing virus, or existing viruses grouped together, causing new symptoms.

One of the top viruses under consideration is adenovirus, a common family of viruses detected in the bloodstreams of many patients – especially the variant 41, which usually presents as a stomach bug. But the liver tissues that have been examined so far don't show signs of adenovirus, and it's unusual for this virus to cause hepatitis.

It's not unheard-of to discover rare effects from common viruses. In 2012, another common virus, an enterovirus, was found to cause a very rare condition known as acute flaccid myelitis. These very rare conditions emerge when there is a high rate of cases, which could be the case with adenovirus – UK health officials, who track the virus, found a five-year high of cases in young children this winter.

Another cause could be long-term effects from Sars-CoV-2. In some cases, the children with hepatitis tested positive for Covid, but in others, there was no documented history of a Covid infection.

Covid infections have been widespread in children, and many of the patients are too young to be vaccinated against Covid. The CDC estimates that 75% of American children have had the virus.

There are already links between Covid and liver problems. Unusual liver function, including the possibility for hepatitis after Covid infection, has been documented in children and adults throughout the pandemic.

Italian researchers raised the alarm about a possible Covid link to hepatitis in May 2021, after seeing a 10-year-old boy with liver problems during a Covid infection. Brazilian researchers also documented Covid-induced hepatitis in an immune-compromised child in September 2021.

Multisystem inflammatory syndrome in children (MIS-C), a dangerous inflammatory syndrome associated with Covid, may also injure the liver, research shows. Acute hepatitis is a leading sign of MIS-C, researchers found in August 2020.

One three-year-old girl was previously healthy, and she had a mild bout of Covid. But three weeks later, she developed hepatitis and acute liver failure, according to a new study published this month.

New research is building on this possible link with the recent hepatitis cases.

Indian researchers posted a preprint study, which has not been peer-reviewed or published yet, on 9 May highlighting a rise in pediatric hepatitis cases after asymptomatic Covid cases. Out of 475 children who tested positive, 37 had symptoms of hepatitis – and they recovered well with treatment.

Another large new preprint study compared the liver function of thousands of children who tested positive for Covid with kids who had other respiratory illnesses.

“Children with Covid have a significantly higher risk” of abnormal liver function, said Rong Xu, professor of biomedical informatics at the Case Western Reserve University School of Medicine and coauthor of the preprint study.

And, worryingly, these issues persisted for at least six months, she said.

But that doesn’t mean the hepatitis being seen now is linked to Covid. “For this study, we just found the association” of Covid and liver issues, she said. The next step would be seeing whether the children who have abnormal liver function after Covid subsequently experience other negative outcomes.

It could be that weakened immune systems, battered by Covid or other viruses, make the children more susceptible to hepatitis. Another researcher has proposed that Covid could create outsized immune reactions to other pathogens long after the initial infection.

This study, like others, is one link in the chain, experts said, but not a smoking gun.

“We’re always taking pieces of the puzzle and slowly building them together,” Kindrachuk said. “All these things have to be put on to the list of potential causal agents, and now we’ve got to try to do the difficult part, which is to say, ‘What is it?’”

Whether the cause is traced to an adenovirus, the coronavirus, some combination of the two, or another culprit entirely, the research emerging points to possible long-term effects of viruses, especially as they spread widely and reveal rare side effects.

Covid, for instance, has been shown to affect hearts, brains, lungs, livers and kidneys long after the initial infection ceases – and even in mild cases.

“I really worry about the long-term effects of Covid-19 on multiple organ systems of children,” Xu said.

The good news is that we know how to prevent cases of this and many other viruses, by employing masks, improving ventilation, washing hands, providing sick leave, vaccinating everyone who is eligible, and more, Kindrachuk said.

“We don’t have all the answers for what’s going on right now. But what we do have, certainly, is information on mitigation measures and protective measures that can reduce the incidence of infection.”

Source: The Guardian

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