

Searching for cause of alarming increase in acute severe hepatitis in children

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Gülsen Özkaya Sahin. Credit: Tove Smeds

At the end of March, the first cases of acute severe hepatitis of unknown origin in children were reported in the U.K. Since then, the number has increased to more than 300 in around 20 countries; there are now reports of nine suspected cases in Sweden. The acute liver infection mainly affects otherwise completely healthy children under the age of 16, which puzzles researchers who are now searching for answers as to why these

children are affected.

By early May, 18 [children](#) had undergone liver transplants and at least five children had died. The illness is discovered when the children's skin and the whites of their eyes turn yellow. The patient's urine turns dark, their feces are light in color, and they often vomit and get loose bowel movements or diarrhea.

"We don't yet know whether this is a new form of hepatitis. For example, it is quite strange that only one-third of the children develop a fever, which is otherwise a common symptom in cases of hepatitis," says Gülsen Özkaya Sahin, a researcher at Lund University and consultant physician in Region Skåne, where she is the medical director for HIV and hepatitis diagnostics in clinical microbiology, Skåne Laboratory Medicine.

She also chairs the Viral Hepatitis Group in ESCMID (the European Society for Clinical Microbiology and Infectious Diseases), a European network gathering around 45 hepatitis researchers from 22 different countries. Due to the situation, the Viral Hepatitis Group remains in close contact with the public health authorities in the UK and is collaborating with the European Centre for Disease Prevention and Control, ECDC. The group is carefully monitoring the acute, severe hepatitis now affecting children around the world.

"We are seeing an increase, but we must remember that still only a few children have become ill. Now we need further studies on samples from affected patients."

Different theories

There are a couple of theories as to potential causes of this hepatitis. One is that adenovirus is involved in some way. Adenovirus has been found

in 75% of affected children.

"It is very rare for adenoviruses to cause what is known as acute fulminant hepatitis and this only happens in immunosuppressed patients with compromised immune defenses. Moreover, in nine cases in Alabama, adenovirus was found in the blood, but not in the liver. We are still in doubt as to whether the adenovirus is causing the hepatitis in these children."

Instead, according to Gülsen Özkaya Sahin, the adenovirus is more likely to be what is known as a co-factor (i.e. a component which helps another substance to convey a biological effect) contributing to the disease attacking the children's liver. Such factors could also be other viruses, including SARS-CoV-2, increased sensitivity to infection, environmental toxins, infectious agents from food or something new and completely unknown.

"Another theory is that because children stayed home during the pandemic, they were not exposed to viruses and bacteria in the same everyday way. This could result in some of them now having an increased sensitivity to microorganisms."

Speculation

None of the early cases affected by acute hepatitis had been vaccinated against COVID-19. However, according to Gülsen Özkaya Sahin, SARS-CoV-2 was confirmed in 10–15% of the affected children. An ongoing infection could potentially make the children more vulnerable to [hepatitis](#), according to the researchers. Another possible cause could be an outbreak from contaminated food.

"This is still speculation, but there are [toxic substances](#) produced by fungi, such as aflatoxin or amatoxin, which can contaminate food and

thus cause poisoning. Food production today is a centralized process, in which it is not unusual for a single producer to distribute to suppliers all over the world. Think of a [food product](#) that children like and eat more of compared to adults; if contaminated, it could result in children being more affected. This also needs to be investigated," observes Gülsen Özkaya Sahin.

Continued research

As the cause of the cases is currently unclear, there is no specific treatment. However, treatment is offered to alleviate symptoms and the only intervention that helps in cases of acute liver failure is transplantation.

"Discussions are now underway about how best to continue researching this. Should samples from all over Europe be sent to a single laboratory, or should each country process its own samples? There are advantages and disadvantages to both paths. Unfortunately, a lot of bureaucratic obstacles need to be overcome, while we want to determine the causes behind this as fast as possible."

What can parents do?

"It is rare for a child to be affected. Monitor the whites of the child's eyes. Contact your doctor if you think the whites of the child's eyes appear to be yellow, if the child's urine is dark and their feces are light in color. As usual, it is important to ensure that children wash their hands properly, as this helps to prevent the spread of viral infections."

Potential causes behind the increase in hepatitis in children

- The adenovirus hypothesis
- Increased sensitivity to viruses/bacteria after the pandemic
- Compromised immune system due to another infection (e.g. SARS-CoV-2)
- Food-borne outbreak
- Reaction to medication
- Toxic substances in the environment

Provided by Lund University

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