Common test for detecting liver problems in children is often interpreted incorrectly

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New research led by physician-scientists at University of California, San Diego School of Medicine shows that the test most commonly used to screen pediatric patients for chronic liver disease is often incorrectly interpreted in many children's hospitals throughout the United States.

The SAFETY study (Screening ALT For Elevation in Today's Youth) will be published in the April issue of *Gastroenterology* and is available online now.

Currently, screening for chronic liver disease is most commonly done using serum alanine aminotransferease (ALT) activity and is intended to determine which children:

- have liver disease associated with obesity
- should be treated if they have viral hepatitis
- take medications that are harming their livers
- should not participate in clinical trials because of their livers

However, the appropriate ALT threshold value to use for detecting liver disease in children is unknown.

"Our first step was to find out what value was being used in the nation's

children's hospitals," said Jeffrey Schwimmer, MD, associate professor of pediatrics, UCSD School of Medicine and Director of the Fatty Liver Clinic at Rady Children's Hospital, San Diego. "We found such a broad range between hospitals for ALT values that they could not possibly be biologically appropriate. This means that a child identified with liver disease at one hospital would go undetected in another."

These variations are not based on biology or the particular machine used for testing at the hospital or lab, but rather the characteristics of the populations used by individual labs to determine their own specific ranges.

To find a biologically correct method, Schwimmer and his team developed sex-specific, biology-based, pediatric ALT thresholds using data from the Centers for Disease Control and Prevention's National Health and Examination Survey. The investigators assessed ALT in nearly a 1,000 children who had no detectable liver disease or risk factors for it. Based upon this group of healthy metabolically normal children, the upper limit of normal for ALT would be set at 22 for girls and 25 for boys. This is less than half of what is used in the typical children's hospital in the United States.

In order to determine how useful these new values would be for identification, four groups of children were assembled for further testing - children with normal livers, with non-alcoholic fatty liver disease, with chronic Hepatitis B virus, and with Hepatitis C virus. These children were used to compare the new biologically-based thresholds to those currently used by acute care children's hospitals nationwide. Based on the current values, only one-third to one-half of children with chronic liver disease would be detected. The new values would improve the rate of detection to 70 to 80 percent.

"These findings are relevant to over 25 million children in the United

States," said Schwimmer. "Imagine a pediatrician who screens a child for liver disease based on current guidelines, but never knows that the child has it because the electronic medical system at the lab does not flag the results with an 'H' due to an incorrect threshold value."

Likewise, investigators conducting clinical trials for the development of new drugs rely on ALT to screen out children with liver disease, typically those with an ALT that is three times higher than normal. If the threshold value is set too high, the strategy used by pharmaceutical companies magnifies this error by a factor of three which can create safety problems for some children.

In an effort to solve this problem, researchers propose a three-fold plan that includes:

- Re-examination of laboratory thresholds used for children
- Modification of exclusion criteria for clinical trials to properly identify children with liver disease
- Encouraging physicians to consider using the threshold values derived from the UCSD study to identify children with possible liver disease

Provided by University of California - San Diego