Developing an algorithm to diagnose biliary atresia in infants

When an infant is sick, doctors and parents are faced with difficult decisions. Should the infant undergo surgery, or are there less invasive ways to determine what's wrong? A recent study of infants with neonatal cholestasis gives us new information about the best way to diagnose the cause of the problem.

Neonatal cholestasis is an umbrella term for any condition that stops or slows the flow of bile from the liver. Cholestasis can have a number of causes, which makes it difficult to diagnose the specific underlying cause in each case.

One of the most important and relatively common causes of neonatal cholestasis is biliary atresia (BA). Ensuring the best outcome for babies with BA requires timely diagnosis, which currently means exploratory surgery. Deciding which infants should undergo surgical exploration is critical. Ideally, one would like to minimize the number of infants who undergo unnecessary surgery, while not missing or delaying the diagnosis of BA. However, there is no consensus on the steps to determine whether BA is the cause and whether surgery is necessary.

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Dr. Benjamin Shneider

Using data from the Childhood Liver Disease Research Network (ChiLDReN), a National Institutes of Health-funded consortium, researchers attempted to develop a diagnostic algorithm using non-invasive parameters to guide clinicians' decisions about the need for invasive procedures. They used two approaches to build models for diagnosis prediction: a hierarchical classification and regression decision tree (CART) and a logistic regression model using a stepwise selection strategy.

Using the CART predictive model, 12% of BA infants were misclassified as Non-BA. The stepwise logistic regression model similarly yielded an 11% false negative rate. In addition, a significant number of infants could not be classified as either BA or Non-BA using this model. In both of these models, diagnosis of BA would be delayed or missed for a significant number of infants if clinicians relied solely on these non-invasive tests.

"In light of the importance of timely diagnosis of biliary atresia and the findings of this study, clinicians should be very cautious in postponing or deferring definitive testing to either exclude or diagnose biliary atresia in infants with neonatal cholestasis simply on the basis of presenting clinical features," said lead author Dr. Benjamin Shneider. "Further investigations will be required to optimize subsequent diagnostic approaches for neonatal cholestasis."

Despite this rigorous large-scale, multi-center prospective analysis, the investigators were unable to generate a diagnostic algorithm to differentiate BA from Non-BA in all patients. It is clear from the current detailed analysis that clinicians should be very cautious about either diagnosing or excluding BA on the basis of presenting clinical features in infants with cholestasis. Early referral to a specialist for possible liver biopsy or surgical exploration needs to be considered as soon as cholestasis is identified.

CITATION:

Shneider BL, Moore J, Kerkar N, Magee JC, Ye W, Karpen SJ, Kamath BM, Molleston JP, Bezerra JA, Murray KF, Loomes KM, Whitington PF, Rosenthal P, Squires RH, Guthery SL, Arnon R, Schwarz KB, Turmelle YP, Sherker AH, Sokol RJ. Initial assessment of the infant with neonatal cholestasis – Is this biliary atresia? PLOS ONE 12(5)-e0176275, 2017.