Parents, MDs agree: genome sequencing as first-tier diagnostic benefits infants in ICU

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A vast majority of doctors and parents of babies in intensive care, with diseases of unknown origin, believe genomic sequencing is beneficial in managing care, according to two new papers published by Rady

Children's Institute for Genomic Medicine.

The study examined the attitudes of parents and physicians of infants admitted to neonatal intensive care at Rady Children's Hospital-San Diego about their perceptions of the usefulness of applying genomic testing in search of a diagnosis.

"In the case of babies who received genomic sequencing, we surveyed their physicians and parents and found that both groups overwhelmingly felt that genetic testing was beneficial," said Stephen Kingsmore, MD, DSc, President & CEO of Rady Children's Institute for Genomic Medicine (RCIGM). "When results are positive, sequencing reveals the genetic variation responsible for the child's disease. But what astounded us was the high proportion of both doctors and parents who perceived that this testing had life-changing utility, even in cases when results were negative for genetic disease."

Doctors reported genomic sequencing was medically useful 93% of the time in the 23% of cases where the test was positive and 72% of the time when the test was negative. Physicians reported the genome wide sequencing improved the outcomes of 32 infants in this study. The likelihood of changes in management increased when test results were returned faster.

Similarly 97% of parents whose children were tested reported that genomic sequencing was useful. Only 2 parents reported that having testing performed in the ICU setting increased stress or confusion.

"These studies clearly show that genomic sequencing can be done safely in the NICU, leading to improved communication between families and their healthcare teams," said David Dimmock, MD, Senior Medical Director for RCIGM. "These results underscore the importance of rapid test results in changing care"

The research was done as part of an NIH initiative called the second Newborn Sequencing in Genomic Medicine and Public Health (NSIGHT). The specific study was called NSIGHT2, a randomized controlled trial comparing two different methods of genomic sequencing as a means for diagnosing the cause of rare disease in babies admitted to intensive care (ClinicalTrials.gov Identifier: NCT03211039).

A total of 213 infants were offered a genome wide sequencing test within four days of being admitted to intensive care. Two dozen of those babies were too seriously ill to be randomized and instead received ultra-rapid whole genome sequencing to return results to attending physicians as soon as possible—a median of 2.3 days. The rest of the infants, who were more stable, were randomized for rapid whole exome sequencing or rapid whole genome sequencing with results returned in an average of 12 days.

The current work produced two papers published Nov. 5 in The *American Journal of Human Genetics*. The first, "An RCT of Rapid Whole Genome and Exome Sequencing in exome sequencing among seriously ill infants results in high clinical utility, changes in management, and low perceived harm" was written by RCIGM investigators led by Dr. Dimmock.

The second paper, "A prospective study of parental perceptions of rapid whole genome and exome sequencing among seriously ill infants" was led by RCIGM and UC San Diego investigators Julie Cakici and Cinnamon Bloss with co-authors from RCIGM.

Genetic disease is a leading cause of death in the U.S. among infants admitted to intensive care hospital units. Disease in newborns can progress extremely rapidly making precise, fast diagnosis essential to guide medical intervention that can lessen suffering, reduce lasting disability or in some cases prevent death.

More than 14,000 genetic diseases have been identified with many new genetic variations or code errors discovered daily. The team at Rady Children's Institute of Genomic Medicine has optimized the use of rapid whole genome sequencing to speed answers to attending physicians in time to guide disease-specific intervention.

More information: *American Journal of Human Genetics* (2020). DOI: 10.1016/j.ajhg.2020.10.003

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