Key Summary of conference abstract

Prenatal Cell-Free DNA Screening for 22q11.2 Deletion Syndrome: Positive Predictive Value Estimates From a Large US Clinical Laboratory

Background

- The most common microdeletion syndrome is chromosome 22q11.2 deletion syndrome, occurring in 1 of every 3,000 to 6,000 live births.[1]
- Diagnosis can be delayed because the phenotype varies, but appropriate care can be provided if the syndrome is detected and diagnosed during pregnancy.
- Data about microdeletion screening efficacy and clinical utility are limited; thus, the American College of Obstetricians and Gynecologists and the American College of Medical Genetics have not fully recommended prenatal cell-free (cf) DNA screening for deletion syndromes.[2,3]
- **Objective:** To address this research gap, investigators assessed the positive predictive value (PPV) of prenatal cfDNA screening for the 22q11.2 deletion at a large US clinical laboratory.

Methods

- As part of routine obstetric care, maternal blood specimens were submitted to Quest Diagnostics for cfDNA screening and analyzed using the QNatal® Advanced assay.
- cfDNA extraction, massively parallel sequencing, and bioinformatics analysis were performed on the submitted specimens using standard laboratory protocols.
- Pregnancy outcomes were acquired from the recorded diagnostic testing results at Quest Diagnostics or from the clinicians who referred the patients for screening.
- Concordance of screening results with pregnancy outcomes was determined for all consecutive specimens positive for 22q11.2 deletion from 2015 to 2018.

Results

- Of the submitted specimens, 26 were positive for a 22q11.2 deletion. In 56, a maternal 22q11.2 deletion was found; these specimens were not included in the analysis because a fetal deletion cannot be detected when a maternal deletion is present.
- Among the 26 pregnancies, 22q11.2 deletion syndrome was confirmed or strongly suspected in 18:
  - Ten had 22q11.2 deletion syndrome confirmed by pre- or postnatal fluorescence in situ hybridization, microarray, or multiplex ligation-dependent probe amplification.
  - In 8 others, 22q11.2 deletion syndrome was suspected based on ultrasound detection of congenital heart defects.
  - Of the 8 remaining specimens, 1 was from a patient who had a spontaneous abortion with a clinical indication of abnormal ultrasound; 3 were from patients who gave birth to infants without available diagnostic testing results; and 4 were from patients lost to follow-up.
- The PPV was 69% (assuming 8 remaining specimens had false-positive results) to 100% (assuming 8 suspected and 8 remaining specimens had true-positive results).

Conclusions

- The QNatal Advanced assay has a high PPV for the detection of 22q11.2 deletion syndrome.
- These findings will help clinicians better understand the performance of this assay and help them counsel their patients.

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