Key Summary of Conference Abstract

Frequency of Incidental Maternal Mosaic and Variant Turner Syndrome Detected by NIPT in a Pregnant Cohort

Background

- About 40% to 50% of individuals with Turner syndrome (TS) have monosomy X (a completely missing X chromosome); the rest have either mosaic monosomy X or variant TS (partial deletion of an X chromosome).[1]
- TS can cause short stature, heart and kidney issues, cognitive function/learning disabilities, and infertility.[1] However, some patients with TS exhibit few signs, which is often associated with mosaic or variant TS.[2,3]
- The variability of symptoms leads to underdiagnosis or delayed diagnosis of mosaic and variant TS. Missed or delayed diagnoses are concerning because lifelong surveillance for multiple conditions is recommended and pregnancy is high risk for all women with TS.[2]
- The current estimated prevalence of TS is 1 in 2,000 live female births. However, this estimate does not account for underdiagnosis of TS and may not adequately represent prevalence among pregnant women or the general female population.
- **Objective:** To increase understanding of the prevalence of TS in the United States, the investigators of this study estimated the frequency of incidental mosaic/variant TS in a general population of pregnant women undergoing routine prenatal cell-free DNA (cfDNA) screening.

Methods

- As part of routine obstetric care, maternal blood specimens from a general population of pregnant women (>10 weeks pregnant) were submitted to Quest Diagnostics for cfDNA screening and analyzed using the prenatal QNatal® Advanced assay. Prenatal cfDNA screening can detect maternal TS as an incidental finding, which can trigger follow-up with the mother.
- If a screening result suggested a completely or partially missing maternal X chromosome, the referring clinician was contacted by a laboratory genetic counselor (GC).
- Confirmatory laboratory testing was conducted by fluorescence in situ hybridization (FISH) or chromosomal microarray (CMA) on the original specimen remnant or by FISH, karyotype, and/or CMA on another follow-up maternal blood specimen.
- Investigators assessed concordance of follow-up test results with the QNatal Advanced assay results and estimated the frequency of incidental mosaic/variant TS.

Results

- Of the 279,658 specimens screened with the QNatal Advanced test, 129 (0.046%) had screening results indicating a completely or partially missing maternal X chromosome.
  - One specimen was from a patient with a second pregnancy, 7 were from patients with confirmed TS diagnoses at the time of results, and 1 was from a patient with an unspecified diagnosis who used a donor egg to achieve pregnancy.
- Among the 120 remaining patient specimens, confirmatory laboratory testing was performed for 79.
  - Mosaic/variant TS was confirmed for 62 (79%): 56 had mosaicism for 45X; 6 had an X deletion consistent with variant TS.
  - Of the 17 other specimens, 7 had an X chromosome deletion unrelated to variant TS, 5 had normal results, and 5 had inconsistent FISH and karyotype results.
- The estimated frequency of incidental mosaic/variant TS was 1 in 4,510 (0.022%).

Conclusions

- This study provides an estimate of mosaic/variant TS in a general population of pregnant women.
- Such data may provide insight into the phenotypic variance among women born with mosaic/variant TS and help improve clinical management.

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