Sequential screening provides better test performance than cell free DNA

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In a study to be presented on Feb. 5 in an oral plenary session at 8 a.m. PST, at the Society for Maternal-Fetal Medicine's annual meeting, The Pregnancy Meeting, in San Diego, researchers will report that cell free DNA analysis is less effective than sequential screening as primary testing for fetal chromosomal abnormalities.

The study, titled Cell free DNA Analysis vs. Sequential Screening as Primary Testing Considering Chromosomal Abnormalities, compared sequential screening to cell free DNA for detection of all fetal chromosomal abnormalities in a general prenatal cohort.

The study discusses some of the complexities of cell free DNA screening when implemented in large populations. Although cell free DNA can very precisely detect Down syndrome and a few other serious chromosome abnormalities (as well as fetal sex), there are two limitations that are important. One is that cell free DNA screens for a very limited panel of abnormalities, as compared to current screening, which is able to determine that there is an increase in risk in the presence of a very broad array of fetal abnormalities, including many different chromosome problems in addition to the common conditions.

Secondly, sequencing of fetal DNA is complex, and requires that a minimum amount of fetal DNA be present in the mother's blood. In those patients with low fetal DNA or failed sequencing interpretation, the risk of aneuploidy (chromosome abnormality) is higher, so some cases of aneuploidy will remain undetected. In this study, the investigators considered these two characteristics in analyzing cell free DNA testing in comparison to the current screen as implemented in the California Prenatal Screening Program.

In a cohort of 450,000 women, the California PNS detected 82 percent of chromosome abnormalities at a 4.9 percent screen positive rate. It was calculated that cell free DNA would have detected approximately 68 percent at a one percent screen positive rate. If all the patients with failed cell free DNA tests were flagged as "high risk," the detection rate would increase to 78 percent but the false positive rate would be 5.5 percent.

"Overall, when considering all chromosome abnormalities and including those cases with no test result, sequential screening has better test performance than cell free DNA," stated Mary Norton, M.D. with the University of California, San Francisco, Division of Maternal Fetal Medicine, Department of Obstetrics, Gynecology and Reproductive Sciences. Norton will present the study.

Provided by Society for Maternal-Fetal Medicine