199 ACOG and SMFM recommendations for prenatal diagnosis: is karyotyping really sufficient?

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OBJECTIVE: ACOG and SMFM recommend the use of chromosomal microarray analysis (CMA) in prenatal diagnosis for cases with one or more structural abnormality detected by ultrasound. For patients with a structurally normal fetus, invasive testing by either microarray or karyotype is recommended. We evaluated CMA results for cases that could be clinically grouped into the two recommended categories and aimed to specifically determine how many clinically significant chromosome abnormalities would not have been detected if evaluated solely by karyotype analysis following the recommendations.

STUDY DESIGN: A total of 3225 prenatal samples evaluated over a three year period by single nucleotide polymorphism (SNP) array were analyzed. Cases were categorized into two groups: those that met ACOG guidelines for array testing versus those that met ACOG guidelines for karyotype *or* array. CMA results for each group were classified as: normal, abnormal or VOUS.

RESULTS: Of the 3225 cases analyzed, 1476 (45.8%) met ACOG recommendations for CMA and 1749 (54.2%) for either CMA or karyotype. For the CMA group, 258 (17.5%) had abnormal results, 1149 (77.8%) normal results and 69 (4.7%) VOUS results. Notably, of the 258 with abnormal results, 78 (5.28% of the total cases) would not been detected by karyotype. In the CMA or karyotype group, 156 (8.9%) had abnormal results, 1498 (85.7%) normal results and 95 (5.4%) VOUS results. Of the 156 abnormal CMA cases, 45 (2.6% of the total cases) would not have been detected solely by karyotype analysis.

CONCLUSION: This study suggests that at least 2.6% of cases with abnormal CMA results including microduplications/deletions, uniparental isodisomy and mosaic abnormalities would have been missed by karyotype analysis following ACOG recommendations. This is significant and reinforces the profound value and diagnostic utility in performing microarray in place of karyotype for pregnancies undergoing invasive testing regardless of the presence of a structural fetal abnormality.

200 The changing face of invasive diagnostic testing in the era of cell free fetal DNA

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OBJECTIVE: Screening for fetal chromosomal anomalies using cell-free fetal DNA (cffDNA) in maternal serum became clinically available in 2012, and has since been widely adopted by pregnant women with or without risk factors for fetal aneuploidy. Concomitantly, the use of invasive diagnostic testing, amniocentesis (amnio) or chorionic villus sampling (CVS) has been steadily declining. The purpose of this study was to determine the magnitude of decline and the changes in indications for invasive testing over the past 6 years.

STUDY DESIGN: This was an IRB approved retrospective cohort study that included all women who were referred to our genetic division for consultation between January 2010 and December 2015 and decided to have diagnostic testing (amnio or CVS). The total number of patients choosing either option was determined for each year over the entire period and grouped by indication for the procedure: advanced maternal age (AMA), abnormal maternal serum screening (MS), abnormal ultrasound finding (US), personal or family history of a chromosomal or genetic anomaly (FH), or other. Statistical analysis included logistic regression and chi-square to examine trends over time.

RESULTS: While our total obstetric patient population remained unchanged over the study period (5900±300), the number of invasive procedures declined steadily from 429 amnio and 154 CVS procedures in 2010 to 72 amnio and 60 CVS procedures in 2015 ($p<.001$ for trend for both). Over the same period, the distribution of indications for diagnostic testing changed significantly. The proportion of procedures performed due to AMA or MS declined significantly over time ($p<.001$, for both): the proportion of procedures done for AMA declined at an average yearly rate of 24% (95% confidence interval 19%, 29%), and those done for MS declined at a yearly rate of 13% (6%, 20%). Over the same period, the proportion of procedures performed due to US, FH, and other indications combined increased ($p<.001$) at an average rate of 45% (36%, 55%).

CONCLUSION: The use of invasive procedures to diagnose fetal chromosomal and genetic anomalies has declined over the past years, primarily due to the availability of cffDNA testing for AMA and abnormal serum screening. The new reality is that fewer women opt for invasive procedures, and do so primarily following abnormal ultrasound findings or due to a history of chromosomal or genetic anomalies.