



ACOG and SMFM Guidelines for Prenatal Diagnosis: Is Karyotyping Really Sufficient?



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Poster #199

ABSTRACT

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; 30.2% of abnormal cases*) would not be 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; 28.8% of abnormal 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/microdeletions, 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.

* Updated data

TABLE 1 Prenatal CombiSNP Array Data sorted by ACOG Recommendations

Result Details	Met ACOG Recommendations for CMA		Did Not Meet ACOG Recommendations for CMA	
	Number of Cases	% of Total (N=1476)	Number of Cases	% of Total (N=1749)
SNP ARRAY RESULTS				
NORMAL	1149	77.85%	1498	85.65%
VOUS	69	4.67%	95	5.43%
ABNORMAL	258	17.48%	156	8.92%
FOR ABNORMAL RESULTS: Was the abnormality detectable by karyotype?				
<i>YES – DETECTABLE</i>	172	11.65%	111	6.35%
<i>POSSIBLY DETECTABLE</i>	8	0.54%	0	0.00%
<i>NO – NOT DETECTABLE</i>	78	5.28%	45	2.57%

FIGURE 1 Breakdown of Results That Met ACOG Recommendations for CMA

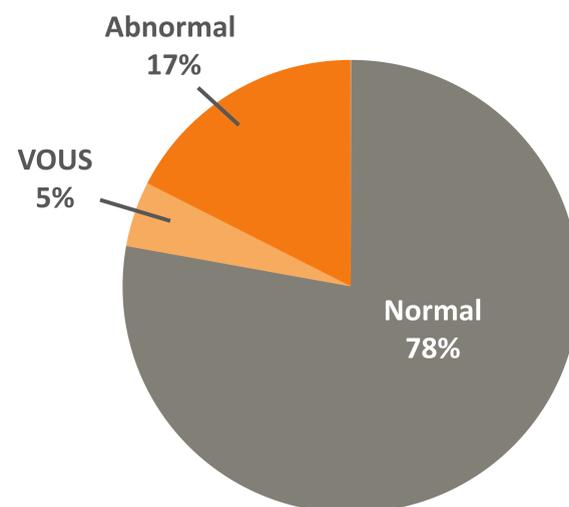


FIGURE 2 Breakdown of Results That Did Not Meet ACOG Recommendations for CMA

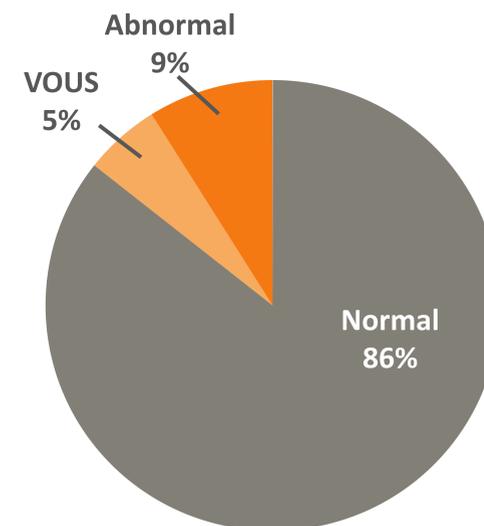
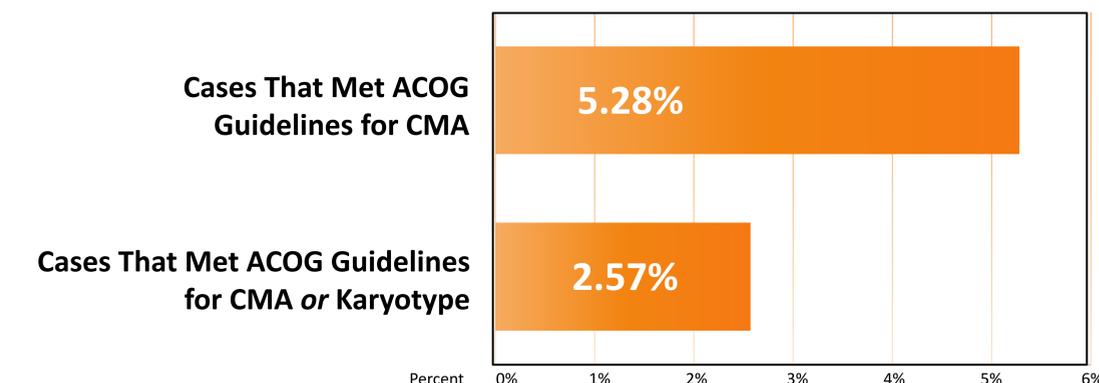


FIGURE 3 Comparison of Abnormal Cases That Would Have Been Missed With a Karyotype-Only Strategy by ACOG Recommendations Classification



CONCLUSIONS

- Current recommendations by ACOG include the option of karyotyping OR CMA for pregnancies with no structural fetal abnormalities.
- Our data demonstrates that karyotyping alone in such situations will fail to identify 2.57% of patients with a fetal chromosome abnormality.
- Previously published data suggests that 1.7% of patients with a fetal chromosome abnormality would be missed by karyotyping alone when the indication for testing did not include a fetal structural abnormality (Wapner et al., 2012). Our data indicates a 51% increase compared to previous estimates with respect to the projected number of cases that would be missed.
- This data reinforces the diagnostic utility of performing CMA in lieu of karyotyping for all women undergoing prenatal diagnostic testing, regardless of the presence of a structural fetal abnormality.

REFERENCES

American College of Obstetricians and Gynecologists Committee on Genetics. Committee Opinion No. 581: the use of chromosomal microarray analysis in prenatal diagnosis. *Obstet Gynecol.* 2013; 122(6):1374-7.

Wapner RJ et al. Chromosomal microarray versus karyotyping for prenatal diagnosis. *NEJM.* 2012; 367(23): 2175-84.

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