4771: Indication based sampling in fetuses with marker(s) and defects found on prenatal ultrasound – Conventional Karyotype (KT) or Chromosomal Microarray (CMA)?

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Introduction: Chromosomal microarray analysis is an emerging molecular genetic technology that has enabled the accurate detection of small chromosomal alterations such as microdeletions and microduplications . Conventional karyotyping has been the traditional genetic test of choice if any marker or defect was identified on prenatal ultrasound. The advent of chromosomal microarray analysis has enabled the accurate detection of additional microdeletions and microduplications associated with ultrasound markers or defects.

Objective: To study the diagnostic yield of Conventional Karyotype (KT) and Chromosomal Microarray in fetuses with markers and structural defects found on prenatal ultrasound from 12 – 24 weeks of pregnancy.

Methodology:

- Retrospective study of prospectively collected data from a tertiary centre from June 2008 to Dec 2022
- 1,411 CVS, amniocenteses and cordocenteses performed in view of ultrasound markers and defects between 12-24 weeks of gestation
- Parental samples obtained to exclude maternal cell contamination, when indicated
- Invasive procedures were performed by FMF certified operators and records maintained on Astraia software

Table 1 – Fetuses with markers

Abnormal KT - 59/890 (6.63%)		Abnormal CMA - 17/255 (6.66%)	
Aneuploidies – 51/890 (5.7%)	Translocations, mosaics and inversions – 8/890 (0.89 %)	Aneuploidies – 11/255 (4.31%)	Pathogenic– 6 /255 (2.35%)
Normal KT - 823/890 (92.47%)		Normal CMA - 213/255 (83.52%)	
Culture failure – 8/890 (0.89%)		VOUS – 25/255 (9.8%)	

Table 2 – Fetuses with Defects

Abnormal KT - 28/188 (14.89 %)		Abnormal CMA - 5/78 (6.41%)	
Aneuploidies – 24/188 (12.76%)	Translocations, mosaics and inversions – 4/188 (2.12%)	Aneuploidies – 2/78 (2.56%)	Pathogenic– 3/78 (3.84%).
Normal KT - 158/188 (82.44%)		Normal KT - 158/188 (82.44%)	
Culture failure – 2/188 (1.1%)		VOUS - 5/78 (6.41%)	

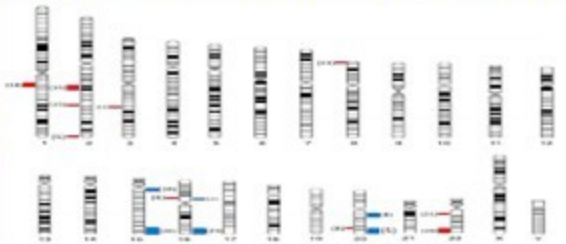

Fig 1: Chromosomal Microarray

Fig 2 : Conventional Karyotype

Results:

- 890 and 255 fetuses with markers had KT and CMA respectively. The KT was abnormal in 59/890 (6.63%) fetuses; 51 (5.7%) were aneuploidies and 8 (0.89 %) were translocations, mosaics and inversions. CMA showed chromosomal aberrations in 17/255 (6.66%), with 11(4.31%) being aneuploidies and 6 pathogenic CNVs (2.35%). KT was normal in 823/890 (92.47%) fetuses and no CNVs were detected in 213/255 (83.52%). The rate of culture failure was 0.89%. 25/255 (9.8%) had VOUS.
- 188 and 78 fetuses with defects had KT and CMA respectively. The KT was abnormal in 28/188 (14.89 %) fetuses with defects; 24 (12.76%) were aneuploidies and 4 (2.12%) were translocations, mosaics and inversions. Chromosomal aberrations were detected in 5/78 (6.41%) fetuses with 2 (2.56%) being aneuploidies and 3 pathogenic CNVs (3.84%). KT was normal in 158/188 (82.44%) fetuses and no CNVs were detected in 68/78 (87.17%). The rate of culture failure was 1.1%. 5/78 (6.41%) had VOUS.

Conclusions:

- The diagnostic yield of KT was 0.9% above CMA and that of CMA was 2.35% over KT in the presence of ultrasound markers
- The diagnostic yield of KT was 2.12% above CMA and that of CMA was 3.84% over KT in the presence of ultrasound defects
- Detection of translocations, mosaics and inversions are not possible on CMA whereas not all pathogenic CNVs will present antenatally as a Fetal defect(s)
- However the detection of variants of uncertain clinical significance present a challenge for counseling when a microarray is done.

Reference : Wapner RJ, Martin CL, Levy B et al. Chromosomal microarray versus karyotyping for prenatal diagnosis. N Engl J Med. 2012 Dec 6;367(23):2175-84. doi: 10.1056/NEJMoa1203382. PMID: 23215555; PMCID: PMC3549418.

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