Topic: Prenatal Genetic Diagnosis

Title: CHROMOSOMAL MICROARRAY HAS ONLY A MODERATE CONTRIBUTION OVER STANDARD KARYOTYPING IN FETUSES WITH ISOLATED INCREASED NUCHAL TRANSLUCENSY

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Objective: to assess the yield of chromosomal microarray (CMA) in detecting clinically significant copy number variants (CNVs) in cases of isolated increased nuchal translucency (NT).

Methods: from January 2014 to December 2015, 57 CMA analyses were performed due to isolated increased NT (defined as ≥3 mm). Cases with additional major malformation detected by ultrasonography were excluded from this study. Cases were compared with 280 CMA analyses performed during the same time period for patient choice, all with documented NT

Results: 47/57 (82.46%) of CMA tests performed for the indication of isolated increased NT were found normal, in comparison with 255/280 (91.07%) of CMA tests in controls. In the increased NT group, clinically significant findings were mostly due to the diagnosis of gross chromosomal imbalances which would have been detected by a conventional karyotype, with OR of 8.88 (P value=0.0005). Clinically significant CNVs, which would not have been detected by conventional karyotyping were found in 1/57 (1.75%) of CMA tests in the increased NT group vs. 2/280 (0.36%) in controls (OR-4.98, P value=0.21). Those were: Xp22.31`duplication (increased NT) Xp11.4 deletion and 15q11.2 deletion (controls). The results of CMA for the indication of isolated NT3 versus controls are summarized in table No. 1. Gross chromosomal imbalances became more common as NT increased, while clinically significant CNVs did not, as shown in diagram No.1.

Conclusion: CMA added clinically significant information of likely pathologic/pathologic CNVs in 1.75% of cases performed for isolated increased NT. As NT increase, most of the chromosomal imbalances detected were gross. A similar trend was not noted for submicroscopic CNVs. Our results suggest CMA has only a moderate contribution over standard karyotyping in fetuses with isolated increased NT.

Diagram No. 1: Distribution of CMA result according to increasing severity of NT thickness

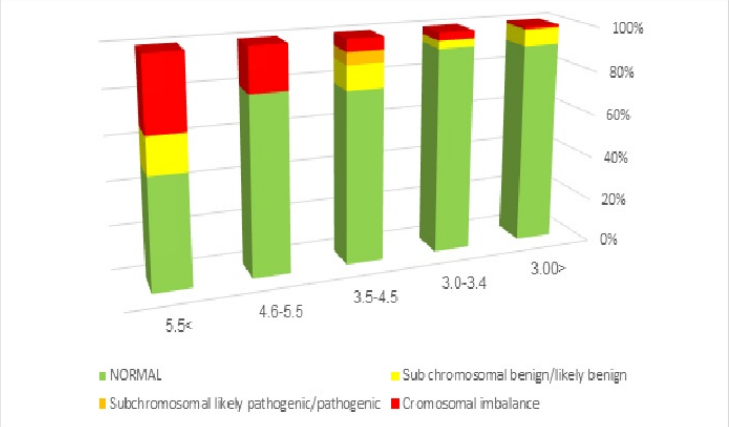

Table no. 1: Results of CMA for the indication of isolated increased NT versus non-medically indicated CMA.

CMA Result	NT= 3 mm		NT< 3 mm	
	n	%	N	%
Normal	47	82.46	255	91.07
Benign and likely benign VOUS	4	7.02	21	7.50
Likely pathogenic VOUS and known pathogenic CNVs	1	1.75	1	0.36
Gross chromosomal imbalances	5	8.77	3	1.07
Total	57	100	280	100