

# Diagnostic yield of genetic testing in a local cohort of isolated fetal growth restriction



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**OBJECTIVE:** To evaluate the clinical relevance and diagnostic yield of chromosomal microarray analysis (CMA) and exome sequencing (ES) in a local cohort of fetuses diagnosed with isolated intrauterine growth restriction (IUGR).

**METHODS:** A retrospective analysis was conducted on a local cohort of fetuses with isolated IUGR diagnosed prenatally along 2019-2025, at Hadassah Medical Center, Jerusalem. The genetic evaluation protocol included CMA as the first-tier test for 78 cases, followed by ES for 70 cases where CMA results were normal. Isolated IUGR was defined as growth restriction in the absence of other structural malformations.

**RESULTS:** CMA identified pathogenic or likely pathogenic findings in 3/78 (3.8%) cases, including a 15q11-q13 deletion, a 1q21.1 microdeletion, and triploidy. The first two are not essentially related to IUGR. In other cases, large regions of homozygosity (ROH) were identified on chromosomes 5 and 6, not necessarily related to the diagnosis. In the ES subgroup (n=70), definitive genetic diagnoses were achieved in 4 cases (5.7%), identifying pathogenic/likely pathogenic variants in the YY1, ANKRD11, DDX3X, and NSD2 genes. All four diagnoses are related IUGR but also to developmental delays. The combined diagnostic yield for this cohort reached approximately 9-10%.

**CONCLUSION:** IUGR is a non-specific anatomical finding that can stem from placental dysfunction or range from a constitutional state to a manifestation of a severe genetic syndrome. A combined diagnostic yield of approximately 10% in this cohort highlights that even in apparently isolated cases without structural malformations, serious underlying genetic diseases may exist. These findings underscore the importance of a comprehensive genetic workup and timely referral to ensure appropriate patient counseling and expectation management.

