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High rate of abnormal findings in prenatal trio exome in low risk pregnancies

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Objective

Many patients perform amniocentesis without any indication. Even if the ultrasound anomaly scan and the CMA results in amniotic fluid are normal there are patients that ask for prenatal exome sequencing. Data on the value of exome sequencing in such pregnancies are limited, especially in the early stages of pregnancy and in low-risk pregnancies. We investigated the yield of targeted clinical prenatal trio exome sequencing in pregnancies with and without fetal structural anomalies.

Methods

We performed prenatal exome sequencing in 703 pregnancies: Group 1 included 256 pregnancies with high clinical suspicion for a genetic disease: pregnancies with increased nuchal translucency/nuchal edema, ultrasound structural defects, IUGR, polyhydramnios. Group 2 included 447 pregnancies with no notable abnormal fetal ultrasound findings. 2a. low risk pregnancies with minor ultrasound findings (50); and 2b. normal pregnancy surveillance (397). In all cases the CMA results in amniotic fluid were normal.

Results

Overall, 41 (7.36%) fetal analyses had pathogenic/likely pathogenic variants. In group 1, 31/256 (12.1%) cases had pathogenic/ likely pathogenic variants. In group 2a, 5/50 (10%) cases were found to have pathogenic/likely pathogenic variants and in group 2b, 5/397 (1.2%). In 10 cases a revision and expansion of the exome analysis was needed (after normal CMA and normal targeted exome trio), because of new ultrasound findings diagnosed later in pregnancy. We are now analyzing 300 more cases and the results will be presented as well.

Conclusion

These results show a high rate of abnormal findings on prenatal exome sequencing even in apparently normal pregnancies.