RAPID WHOLE EXOME SEQUENCING AS A DIAGNOSTIC TEST FOR FETAL MULTIPLE CONGENITAL ANOMALIES ON ULTRASOUND

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IntroductionIdentifying the cause of fetal anomalies provides important information to improve perinatal management. Microarray leads to a diagnosis in approximately 40% of fetuses with multiple congenital anomalies (MCA). Whole Exome Sequencing (WES) is a promising technique to improve diagnostic yield. Implementing WES in the prenatal setting is challenging due to uncertainties around fetal phenotyping, variant interpretation, ethical issues of incidental findings, and the requirement of short turnaround times.In this study, we implement WES in prenatal care to increase the number of genetic diagnoses and provide parents and healthcare providers with more information for the benefit of medical decision-making. MethodsProspective study of rapid trio WES analysis in addition to conventional genetic tests for twenty-five fetuses with abnormalities detected through ultrasound. Inclusion criteria are at least the presence of two congenital malformations or one congenital malformation in addition to a previous pregnancy with a fetus with a similar phenotype. Questionnaires and interviews with patients about the test are conducted to study patient's perspective. ResultsFourteen fetuses have been included (August 2018), resulting in a genetic diagnosis in four (two cases still ongoing), including a de novo mutation in SAMD9 (MIRAGE syndrome) and in COL1A1 (Osteogenesis Imperfecta), compound heterozygous mutations in PEX1 (Zellweger syndrome), homozygous mutations in POMGNT1 (Walker Warburg syndrome). The turnaround time was 9-10 working days. Analysis of the first results of the interviews and questionnaires is in progress. ConclusionThe preliminary results from our prospective study show that implementing WES as a routine test in the prenatal setting is challenging, but technically feasible and has a promising diagnostic yield.