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Whole exome sequencing improves the genetic diagnosis in fetuses with increased nuchal translucency

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Objective

The purpose of this study was to investigate the value of whole exome sequencing (WES) in fetuses with increased nuchal translucency（NT）.

Methods

The study comprised 249 singleton pregnancies with increased fetal NT and microarray results. 6 of them have done fetus–mother–father trio exome sequencing. The pregnant women and their partners had given written informed consent to take their bloods and use chorionic villi or amniocentesis for subsequent analysis.

Results

The mean maternal age was 31. 1 years (SD, 5. 1). The median fetal NT thickness was 4. 3 mm. The number of normal CMA results decreased from 73(85. 9%) in NT between 2. 5-3. 4 mm to 18 (45. 0%) in NT ≥5. 5 mm. There were seven cases of pathogenic microdeletion or microduplication. In two of them (2. 1%) NT were 3. 5 - 4. 4 mm, in three cases(10. 7%) NT were 4. 5-5. 4mm, in two (5. 0%) cases NT were ≥5. 5 mm. Total number of VOUS CNV were seven, in five(5. 9%) of them, NT were 2. 5-3. 4 mm, one was 3. 5-4. 4mm and another was ≥5. 5 mm, respectively. In fetuses with NT≥5. 5mm, 2 cases (2/40, 5%) with pathgenic CNV could be detected by CMA while 2 more cases (2/40, 5%) with pathogenic mutations could be detected by WES.

Conclusion

The incidence of the fetal abnormalities increases exponentially with increasing NT. And the application of WES can increase the diagnostic yield. Thus, in the investigation of fetuses with increased NT, use of WES should be considered in combination with other technologies like karyotyping or CMA. The limitation of this study is the small sample size. A largest prospective study is needed.