SNP array to identify pathogenic copy number variations in fetuses with defects and women with adverse reproductive history

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Objective
Applying the single nucleotide polymorphisms microarray (SNP array), to detect genome-wide copy number variation in fetuses with malformations and women with an adverse reproductive history. Through analysis the relationship of rare CNVs and the clinical manifestations, to prevent the birth of children with birth defects.

Methods
Samples (amniotic fluid and umbilical cord blood) from 314 women with singleton pregnancy who referred for prenatal diagnosis to our center between Jan 2013 and December 2014. The samples were divided into two groups: 1. ultrasound showed at least one major malformation (VSD/ASD/F4/VM/IUGR/NT,NT abnormal); 2. women with an adverse reproductive history. SNP array was performed after excluding G-banded chromosomal abnormalities to analysis the pathogenicity of the detected CNVs with its clinical manifestations.

Results
Positive CNVs were detected in 8.91% (28/314) samples, among which were 11 duplications, 9 deletions, 4 LOH, and 4 deletion combine with duplication. The sizes of duplications are between 0.47Mb and 16.7Mb, deletions are between 0.16Mb and 13.3Mb. 15 CNVs are located within the regions of microdeletion or microduplication syndromes /diseases or regions associated with clinical manifestations, but other 13 are considered to be benign or variant of uncertain significance.

Conclusion
In this research we applied SNP array to definite etiological diagnosis of 4.78%(15/314) in fetuses with malformations and women with an adverse reproductive history with a normal karyotype, 53% (8/1) pCNVs are within the regions of well known syndromes, but the other 47% are not. In the field of prenatal diagnosis, SNP array provides clues to the discovery of the new syndrome, and the theoretical basis for genetic counseling, risk assessment and prenatal diagnosis.