Landscape of Sex Chromosome Aneuploidies in Pregnancy Loss: A Prenatal Data-Based Study

Yuanhang Zhu
Department of Medical Genetics and Prenatal Diagnostics, The Third Affiliated Hospital of Zhengzhou University, Zhengzhou, P.R. China

Haoqian Zhang
Department of Obstetrics and Gynecology, The Third Affiliated Hospital of Zhengzhou University, Zhengzhou, P.R. China

Ling Liu
Department of Medical Genetics and Prenatal Diagnostics, The Third Affiliated Hospital of Zhengzhou University, Zhengzhou, P.R. China

Chenchen Ren
Department of Obstetrics and Gynecology, The Third Affiliated Hospital of Zhengzhou University, Zhengzhou, P.R. China

Abstract:

Background: Pregnancy loss, a common pregnancy complication, is conclusively linked to embryonic chromosomal abnormalities. Given the rising proportion of pregnancies at advanced maternal age, a contemporary re-examination of the relationships among pregnancy loss, chromosomal anomalies, and maternal age is imperative to optimize clinical counseling strategies.

Objective: To characterize the population prevalence of sex chromosome aneuploidies (SCAs) and examine associations between pregnancy loss, SCAs, and maternal age, thereby improving clinical counseling frameworks.

Study Design: This study included fetal samples (amniotic fluid, embryonic/fetal tissue, fetal blood (intracardiac or cordocentesis-derived), and chorionic villus sampling) undergoing chromosomal analysis at the Department of Medical Genetics and Prenatal Diagnosis, Third Affiliated Hospital of Zhengzhou University, between 2022 and 2024. Inclusion criteria required fetal samples (amniotic fluid, chorionic villi, or embryonic tissue) with <10% maternal cell contamination confirmed by fluorescent PCR-capillary electrophoresis. Exclusion criteria included absence of CNV-seq/CMA testing results, discordant results, incomplete documentation, or donor oocyte pregnancies. Samples were divided into a pregnancy loss group and a non-pregnancy loss group. Chromosomal abnormalities (aneuploidies, triploidy/tetraploidy, and uniparental disomy involving chromosomes 21, 18, 13, X, and Y), and maternal age were characterized within the miscarriage group.

Results: The study comprised 2,452 cases of pregnancy loss and 18,859 non-pregnancy loss cases. Chromosomal abnormalities were identified in 569 cases, while 19,855 cases showed no abnormalities. Within the pregnancy loss group (n=2,452), 1,883 cases had no detectable chromosomal abnormalities, and 569 cases had abnormalities. These included: 78 cases of Trisomy 21/mosaic Trisomy 21, 23 cases of Trisomy 18, 61 cases of Trisomy 13/mosaic Trisomy 13, 171 cases of sex chromosome abnormalities (164 cases of 45, X; 1 case of 47, XXX; 4 cases of 47, XXY; 2 cases of 47, XYY), 196 cases of triploidy, 8 cases of uniparental disomy, and 32 cases of other chromosomal abnormalities. The incidence of 45, X was significantly higher in the pregnancy loss group (164/2,452) compared to the non- pregnancy loss group (67/18,859; χ^2=811.71, p<0.001). Conversely, the incidence of sex chromosome trisomies was significantly lower in pregnancy loss tissues (7/2,452) compared to non- pregnancy loss tissues (182/18,859; χ^2=11.40, p=0.001). The mean maternal age in the pregnancy loss group (31.74 ± 4.40 years) was significantly higher than in the non- pregnancy loss group (31.37 ± 5.06 years; t=3.42, p=0.001).

Conclusion: In pregnancy loss cases, sex chromosome abnormalities accounted for 6.97% of cases. Among these chromosomal abnormalities, 45, X constituted 28.82%, and sex chromosome trisomies constituted 1.23%. The incidence rate of 45, X was significantly higher in the pregnancy loss group compared to the non-pregnancy loss group, while the incidence rate of sex chromosome trisomies was significantly lower in the pregnancy loss group. Maternal age was also significantly higher in the pregnancy loss group than in the non-pregnancy loss group.

Keywords:

Pregnancy loss, Sex chromosome abnormalities, Genetic testing, Advanced maternal age, Fluorescence polymerase chain reaction