Exploring the Relationship Between Pregnancy Loss and Genetic Factors: An Examination of Fetal Chromosomal Abnormalities

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Abstract

Recurrent pregnancy loss (RPL), commonly defined as the occurrence of two or more consecutive miscarriages, is a multifactorial condition that affects 5-10% of couples of reproductive age. Genetic abnormalities, particularly chromosomal aneuploidies, represent one of the leading causes of early miscarriage, yet their frequency and patterns remain strongly influenced by maternal age and other biological factors. Pregnancy loss in the first trimester (≤12 weeks) is a frequent and distressing complication, with genetic abnormalities playing a central role in its pathogenesis. In this study, we examined uncontaminated early pregnancy loss specimens to determine the frequency and spectrum of fetal chromosomal abnormalities and associated genetic factors. Overall, 51.7% of cases demonstrated chromosomal aneuploidies or mutations in genes linked to coagulation, immune regulation, and embryonic development. Age-stratified analysis revealed an abnormality rate of 43.4% in women <30 years, with trisomies (48.7%), triploidy (26.1%), and monosomy (16.5%) as predominant findings. Among women aged 31–35 years, the abnormality rate increased to 53.9%, with trisomies being most frequent. In women ≥36 years, abnormalities were observed in 71.4% of cases, overwhelmingly represented by trisomies (79.7%), while triploidy (6.4%) and monosomy (6.4%) were less common. Specific recurrent abnormalities included trisomy 16 (32.8%) and trisomy 22 (6.9%), while structural chromosomal rearrangements were detected in 3.6% of recurrent miscarriage cases.

Our findings demonstrate that chromosomal aneuploidies are the leading contributors to early pregnancy loss, with a clear age-related increase in frequency, particularly for trisomies. The co-occurrence of mutations in coagulation, immune, and developmental pathways underscores the multifactorial etiology of miscarriage and highlights the importance of integrated genetic testing for risk assessment, counseling, and potential preventive strategies. While chromosomal aneuploidies remain the leading cause of early and recurrent pregnancy loss, our findings also highlight the importance of non-chromosomal biomarkers in understanding and managing this condition. Mutations in genes regulating coagulation, immune tolerance, and embryonic development indicate that recurrent miscarriage is not solely a genetic-chromosomal problem, but rather a multifactorial disorder with contributions from maternal, fetal, and environmental factors. The incorporation of additional biomarkers, such as those related to inflammation, vascular function, and metabolic regulation, may improve risk stratification and provide earlier, more personalized interventions for affected women. This broader perspective underscores the need for integrated multi-omics approaches in both research and clinical practice, paving the way for novel diagnostic tools and potential therapeutic strategies to reduce the burden of pregnancy loss.

Reference

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