Placental lesions and key obstetric outcomes: a unique linked cohort study using PALGA national pathology and Perined pregnancy registries

M.C. Marijnen[1,2,3], C.J.M. Oudejans[3], A.A. Freedman[4], L.M. Ernst[5], W. Ganzevoort[1,2], M.H. Schoots[6], L.E. van der Meeren[7,8], S.J. Gordijn[3]

1. Department of Obstetrics and Gynecology, Amsterdam University Medical Centers, University of Amsterdam, The Netherlands.
2. Amsterdam Reproduction & Development Research Institute, Amsterdam, The Netherlands.
3. Department of Obstetrics and Gynecology, University Medical Center Groningen, University of Groningen, The Netherlands.
4. Department of Preventive Medicine, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA.
5. Department of Pathology and Laboratory Medicine, NorthShore University HealthSystem, University of Chicago Pritzker School of Medicine, Evanston, Illinois, USA.
6. Department of Pathology, University Medical Center Groningen, University of Groningen, The Netherlands.
7. Department of Pathology, Leiden University Medical Center Leiden, The Netherlands.
8. Department of Pathology, Erasmus Medical Center, University Medical Center, Rotterdam, The Netherlands.

Background

The placenta is essential for fetal growth and development. However, placental lesions can result in placental dysfunction and are linked to adverse conditions such as fetal growth restriction (FGR) and preterm birth (PTB).

Objectives

Analyze the association of placental lesion patterns with pregnancy characteristics and short-term perinatal outcomes stratified for small for gestational age (SGA) and non-SGA infants and gestational age (GA) at birth.

Methods

A unique dataset was created by linking registries incorporating pathology (PALGA) and pregnancy data (Perined) from 2005 to 2022. Placental lesions were categorized based on the Amsterdam criteria: maternal vascular malperfusion (MVM), fetal vascular malperfusion (FVM), chronic inflammation (CI), and acute inflammation (AI). SGA was used as a proxy for FGR. Lesion patterns were studied for SGA (birthweight <3rd percentile (p3), p3-p10) and non-SGA (≥p10) and GA at birth (<32, 32-33, 34-37, ≥37 weeks). Multinomial logistic regression was used to analyze associations,

providing odds ratios (ORs) with 95% confidence intervals (CI). Inverse probability weighting was applied to reduce selection bias; adjusted ORs were calculated.

Results

Of 2,774,975 eligible cases, 112,418 cases (4.4%) had placental pathology data available. The subsample with pathology data available had a higher proportion of infants in lowest birthweight percentiles compared to the sample without placenta data. MVM, FVM, and CI were more frequent in SGA while AI was more frequent in non-SGA. MVM, FVM and CI combined were associated with the greatest odds of an SGA infant, with adjusted ORs of 6.0 (95% CI: 5.5-6.5) for <p3 and 4.7 (95% CI: 4.5-5.0) for p3-p10. MVM and FVM combined were associated with the greatest odds of birth <32 weeks (adjusted OR: 3.0, 95% CI: 2.8-3.4).

Conclusion

Combined placental lesions significantly increase the odds of an SGA infant and PTB <32 weeks. Multiplicity of lesions identifies fetuses at risk of adverse outcomes.