

Multiple pregnancies in Norway, 1967-2008

The influence of assisted reproductive technologies

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Abstract:

Aims: The incidence of twin pregnancies has been rising in industrialized countries during the last twenty years. Poor pregnancy outcome is more common in multiple pregnancies. Our aim was to investigate the incidence, causes and several consequences (alternative: outcome) of multiple pregnancies. Using generational data, we also looked into specific issues as maternal birth characteristics trying to understand the underlying mechanisms behind the higher mortality in twins.

Methods: All three studies are population based cohort studies with data from the Medical Birth Registry of Norway 1967-2008. Pregnancies from assisted reproductive technologies (ART) were available from 1988. We used cross-sectional-, sibship- and generational data files provided by linkage of the mothers unique identification number and the infants day of birth. Outcomes for twins and triplets were compared with those for singletons and relative risks were estimated between the time periods(1967-1987 and 1988-2006). Contingency tables, stratification, generalized linear models and multiple regressions were used to calculate statistical associations.

Results: *Incidence:* The twin birth rate in Norway increased from 1.1% in 1967 to 1.9 % in 2004. Excluding pregnancies from ART, the twin birth rate increased from 1.1% to 1.6 %, same period. The triplet rate increased epidemically from the late eighties and through the nineties, followed by a decline from year 2000. After excluding ART pregnancies, the triplet rate increased more modestly to a maximum of 2.6 per 10,000 births in 1997-2001, followed by a slightly decline. In spontaneous conceptions, the chance to be pregnant with twins increased up to age 38, followed by a strong downward trend. In ART pregnancies, the highest risk was among women 25-30 years and a steep decline thereafter. The likelihood to conceive with twins was also studied in relation to maternal birth characteristics. The relative risk to conceive with twins in the study population was dependent on the mother's birth weight, but not on her gestational age at birth.

Perinatal outcome: The gestational age declined and the cesarean section rate increased considerably in both twin- and triplet pregnancies from the first to the second period. Risk of

perinatal mortality in twins improved slightly, but was unchanged in triplets relative to singletons over time, although the overall perinatal mortality rates improved significantly. We calculated the 10th percentile for gestational age at delivery for singletons, twins and triplets and explored the risk of mortality below versus above these thresholds. For triplets, RR for a perinatal death was 13.9 (95% CI 9.9-13.4) below 29 gestational weeks compared to 29-40 weeks. In twins, RR 16.0 (14.7-17.3) below 34 weeks compared to 34-42 weeks and for singletons RR 20.7 (20.1-21.3) below 39 weeks compared to 39-43 weeks. A mother's birth characteristics have significant impact on the outcome of her reproduction, especially if she is pregnant with twins. Mothers born at 27-31 weeks had four times higher risk of losing one or both of her twins compared to term born mothers (RR 3.82; 1.56-9.36). Term mothers with birthweight-by-gestational age z score <-2 experienced the highest mortality in twin offspring [RR 2.42 (1.37-4.29)] relative to the most favourable z-score (1-1.99).

ART?

Conclusions: The twin birth rate in Norway increased significantly in all age groups during the last decades, even when pregnancies from ART were excluded. The perinatal mortality rate for triplets and twins has declined considerably during the last 40 years, but the improvement was not so favourable for triplets compared to singletons. We found no difference in perinatal death between multiples from ART and non-ART pregnancies. A twin pregnancy is a high-risk pregnancy in general, but even more so if the mother herself was born preterm or was growth restricted at birth.