Maternal and paternal contribution to intergenerational recurrence of breech delivery: population based cohort study

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ABSTRACT

Objective To investigate intergenerational recurrence of breech delivery, with a hypothesis that both women and men delivered in breech presentation contribute to increased risk of breech delivery in their offspring.

Design Population based cohort study for two generations.

Setting Data from the medical birth registry of Norway, based on all births in Norway 1967-2004 (2.2 million births).

Participants Generational data were provided through linkage by national identification numbers, forming 451 393 mother-offspring units and 295 253 father-offspring units. We included units where both parents and offspring were singletons and offspring were first born, forming 232 704 mother-offspring units and 154 851 father-offspring units for our analyses.

Main outcome measure Breech delivery in the second generation.

Results Men and women who themselves were delivered in breech presentation had more than twice the risk of breech delivery in their own first pregnancies compared with men and women who had been cephalic presentations (odds ratios 2.2, 95% confidence interval 1.8 to 2.7, and 2.2, 1.9 to 2.5, for men and women, respectively). The strongest risks of recurrence were found for vaginally delivered offspring and were equally strong for men and women. Increased risk of recurrence of breech delivery in offspring was present only for parents delivered at term.

Conclusion Intergenerational recurrence risk of breech delivery in offspring was equally high when transmitted through fathers and mothers. It seems reasonable to attribute the observed pattern of familial predisposition to term breech delivery to genetic inheritance, predominantly through the fetus.

INTRODUCTION

The aetiology of breech delivery is not clear, but several factors are associated with an increased risk of breech delivery, such as first baby, older mother, and low gestational age and low birth weight.[1-4] Mechanical factors, such as uterine malformations, site of placental attachment, and low volume of amniotic fluid, also increase the risk of breech delivery.[4-7] Furthermore, infants with congenital anomalies more often present in breech at delivery.[2 3 5 6 8] Such aetiological factors, however, are identified in only 7-15% of breech deliveries.[4 6 9]

Though recurrence of breech delivery in successive siblings is high,[4 6 9 10] knowledge of recurrence between generations is lacking. Cartledge and Hancock first proposed a genetic predisposition to breech delivery in 1942, using a family inheritance chart.[11] Intergenerational recurrence is plausible if genes are aetiologically important to its occurrence.

We investigated intergenerational recurrence of breech delivery, with a hypothesis that women and men who themselves were delivered in breech presentation contribute to increased risk of breech delivery in their offspring.

METHODS

Population based generational data

We used data up to 2004 from the medical birth registry of Norway, a population based, compulsory registry of all births in Norway since 1967. All live births and stillbirths of at least 16 weeks of gestation are registered, which in 2003 amounted to 2.2 million births.

Births were linked to the birth records of the mother and father by the national identification numbers, providing generation files with birth records on mothers and their offspring (451 393 records) and fathers and their offspring (295 253 records). We considered all births delivered in breech presentation as breech delivery, irrespective of mode of delivery. We excluded multiple pregnancies and births of infants less than 500 g in both generations. For all analyses, we restricted the study to first born offspring in the second generation, which left us with a population of 232 704 mother-offspring units and 154 851 father-offspring units. We also linked records of mother, father, and offspring, yielding 148 692 study units to study the effect on occurrence of breech delivery in offspring if both parents had been delivered in breech presentation.

As possible confounders we evaluated gestational age, birth order, mode of delivery, birth weight by gestational age, period of birth, maternal age, and maternal education. Gestational age was estimated from the reported last menstrual period, and preterm birth was defined as delivery before 37 completed weeks of gestation. We classified birth weight for gestational age as small (<10th centile), appropriate (10th-90th centile), and large (>90th centile).[12 13] Congenital anomalies were registered according to ICD-8 and later ICD-10 (international classification of diseases). We obtained data on maternal educational level as an index of socioeconomic level from Statistics Norway.[14]

Statistical analysis

We calculated odds ratios, which approximated relative risk. Logistic regression was used to estimate

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Table 1 | Risk of breech delivery in first born offspring (2nd generation) of mothers and fathers (1st generation) by their own presentation at birth. Norway, 1967-2004

Gestation and birth order (1st generation)	No of offspring	No (%) of breech offspring	Odds ratio (95%CI)	
			Crude	Adjusted*
Mother's own presentation at birth				
≥37 weeks, first:				
Breech	2797	237 (8.5)	2.2 (1.9 to 2.5)	2.2 (1.9 to 2.5)
Cephalic	82 569	3376 (4.1)	1.0§	1.0§
≥37 weeks, subsequent:				
Breech	2 336	163 (7.0)	1.7 (1.5 to 2.1)	1.7 (1.5 to 2.0)
Cephalic	127 923	5271 (4.1)	1.0§	1.0§
<37 weeks, first:				
Breech	274	16 (5.8)	1.3 (0.8 to 2.2)	1.4 (0.8 to 2.4)
Cephalic	3690	167 (4.5)	1.0§	1.0§
<37 weeks, subsequent:				
Breech	231	10 (4.3)	1.1 (0.6 to 2.2)	1.1 (0.6 to 2.2)
Cephalic	4559	175 (3.8)	1.0§	1.0§
Total†:				
Breech	5881	449 (7.6)	1.9 (1.8 to 2.1)	1.9 (1.8 to 2.1)
Cephalic	226 823	9265 (4.1)	1.0§	1.0§
Father's own presentation at birth				
≥37 weeks, first:				
Breech	1351	119 (8.8)	2.2 (1.8 to 2.7)	2.2 (1.8 to 2.7)
Cephalic	54 742	2308 (4.2)	1.0§	1.0§
≥37 weeks, subsequent:				
Breech	1234	82 (6.6)	1.6 (1.3 to 2.0)	1.6 (1.3 to 2.1)
Cephalic	85 408	3594 (4.2)	1.0§	1.0§
<37 weeks, first:				
Breech	167	3 (1.8)	0.5 (0.2 to 1.5)	0.5 (0.2 to 1.6)
Cephalic	2849	104 (3.7)	1.0§	1.0§
<37 weeks, subsequent:				
Breech	157	8 (5.1)	1.1 (0.6 to 2.4)	1.2 (0.6 to 2.5)
Cephalic	3624	162 (4.5)	1.0§	1.0§
Total†:				
Breech	3020	221 (7.3)	1.8 (1.6 to 2.1)	1.8 (1.6 to 2.1)
Cephalic	151 831	6370 (4.2)	1.0§	1.0§
Presentation at birth in both parents‡				
Total†:				
Breech	96	12 (12.5)	3.3 (1.8 to 6.1)	3.1 (1.6 to 6.0)
Cephalic	148 596	6121 (4.1)	1.0§	1.0§

*Adjusted with logistic regression for birth weight by gestational age in 1st generation: small, appropriate, or large; period of birth 1st generation: 1967-71, 1972-6, 1977-81, 1982-6; maternal age 1st generation (years): <20, 20-24, 25-29, 30-34, ≥35; maternal education 1st generation: no high school, high school, beyond high school.
†Includes 8325 (3.6%) mothers and 5319 (3.4%) fathers with missing data on gestational age.
‡These are also counted in upper part of table.
§Reference category.

effects, adjust for confounding, and evaluate interaction between factors. Relative risk modelling was used for the frequent outcomes.

RESULTS

The proportion of breech delivery registered in the birth registry was 2.5% in 1967-76, 3.0% in 1977-86, 3.2% in 1987-96, and 3.5% in 1997-2004. Among 318 855 boys and 301 438 girls born in 1967-76, 96.8% and 97.6%, respectively, survived to the age of 18. The mortality among those delivered in breech presentation was four times as high as among those delivered in cephalic presentation. For females and males in the first generation, breech delivery was associated with primiparity, prematurity, major congenital anomalies, and caesarean section (see bmj.com).

Breech delivery in offspring of men and women delivered in breech presentation

The highest risk of recurrence of breech delivery was observed in babies of first born men and women delivered in breech presentation at term (odds ratio 2.2,

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Table 2 | Risk of breech delivery in first born offspring (2nd generation) by presentation at birth of mother* and father* (1st generation) and mode of delivery and gestational age of offspring, Norway, 1967-2004

	Offspring of mothers				Offspring of fathers			
	No of offspring‡	No (%) of breech offspring‡	Relative risk (95% CI)		No of offspring‡	No (%) of breech offspring‡	Relative risk (95% CI)	
			Crude	Adjusted†			Crude	Adjusted†
Mode of delivery offspring:								
Vaginal								
Breech mother/father	2330	91 (3.9)	2.3 (1.9 to 2.9)	2.3 (1.9 to 2.9)	1131	51 (4.5)	2.7 (2.0 to 3.5)	2.7 (2.0 to 3.5)
Cephalic mother/father	70 730	1192 (1.7)	1.0§	1.0§	47520	800 (1.7)	1.0§	1.0§
Elective section:								
Breech mother/father	108	69 (63.9)	1.2 (1.1 to 1.4)	1.2 (1.1 to 1.4)	51	32 (62.7)	1.2 (0.96 to 1.5)	1.2 (0.94 to 1.5)
Cephalic mother/father	1968	1028 (52.2)	1.0§	1.0§	1355	713 (52.6)	1.0§	1.0§
Emergency section:								
Breech mother/father	293	68 (23.2)	1.8 (1.5 to 2.3)	1.8 (1.5 to 2.3)	153	33 (21.6)	1.6 (1.2 to 2.2)	1.7 (1.2 to 2.3)
Cephalic mother/father	7697	975 (12.7)	1.0§	1.0§	5346	701 (13.1)	1.0§	1.0§
Gestational age offspring:								
<37 weeks								
Breech mother/father	189	26 (13.8)	1.6 (1.1 to 2.3)	1.5 (1.1 to 2.2)	99	16 (16.2)	1.7 (1.1 to 2.7)	1.7 (1.1 to 2.7)
Cephalic mother/father	5393	476 (8.8)	1.0§	1.0§	3581	341 (9.5)	1.0§	1.0§
37-38 weeks								
Breech mother/father	453	64 (14.1)	2.0 (1.6 to 2.6)	2.0 (1.6 to 2.5)	191	25 (13.1)	1.8 (1.2 to 2.6)	1.8 (1.2 to 2.6)
Cephalic mother/father	11 258	790 (7.0)	1.0§	1.0§	7905	574 (7.3)	1.0§	1.0§
39-40 weeks								
Breech mother/father	1199	89 (7.4)	2.0 (1.6 to 2.5)	2.0 (1.6 to 2.5)	610	50 (8.2)	2.2 (1.7 to 2.9)	2.2 (1.6 to 2.8)
Cephalic mother/father	34 627	1275 (3.7)	1.0§	1.0§	23842	896 (3.8)	1.0§	1.0§
41-42 weeks								
Breech mother/father	715	37 (5.2)	2.2 (1.6 to 3.0)	2.2 (1.6 to 3.0)	343	24 (7.0)	2.8 (1.9 to 4.2)	2.7 (1.8 to 4.0)
Cephalic mother/father	22 643	539 (2.4)	1.0§	1.0§	15372	383 (2.5)	1.0§	1.0§

*Confined to first born mothers and fathers delivered at term.
†Adjusted by logistic regression for birth weight by gestational age 1st generation: small, appropriate, or large; period of birth 1st generation: 1967-71, 1972-6, 1977-81, 1982-6; maternal age 1st generation (years): <20, 20-24, 25-29, 30-34, ≥35; maternal education 1st generation: no high school, high school, beyond high school.
‡Total is lower than in table 2 because of offspring with missing data on mode of delivery and gestational age and exclusion of gestational ages ≥ 43 weeks in lower half of table (2.6% mother-offspring units and 2.1% father-offspring units).
§Reference category.

95% confidence interval 1.8 to 2.7, and 2.2, 1.9 to 2.5, respectively) (table 1). We found no recurrence between generations for men and women born preterm. Adjustment for birth weight by gestational age, maternal age, maternal education, and period of birth, all in the first generation, only slightly affected the results (table 1).

When we stratified the analysis by mode of delivery of the offspring within the group of parents who were term and first born, we found the highest recurrence of breech delivery among those delivered vaginally. The recurrence through both men and women was lowest when offspring were delivered by elective caesarean section. When we stratified by gestational age of the offspring, there was a tendency of higher recurrence with increasing gestational age (table 2).

The combination of both parents delivered in breech did not occur often but still gave a high risk of breech delivery in the next generation with a crude odds ratio of 3.3 (1.8 to 6.1), with the reference being both parents delivered in cephalic presentation (table 1).

We calculated the attributable risk for the offspring and found that 3% of the cases of breech delivery were attributable to breech delivery in the father and 3% were attributable to breech delivery in the mother. Thus 6% of the breech deliveries in the population offspring were accounted for by parental influence.

Low birth weight is associated with breech delivery.[1-3] Recurrence of breech delivery in children of men and women themselves born with low birth weight was found only among those parents delivered at term. Recurrence was not influenced by whether the

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WHAT IS ALREADY KNOWN ON THIS TOPIC

Breech delivery is associated with significantly increased perinatal mortality and morbidity

Recurrence of breech delivery in successive siblings is high, but knowledge on recurrence between generations is lacking

WHAT THIS STUDY ADDS

Both men and women delivered in breech presentation at term contribute to increased risk of breech delivery in their offspring

Recurrence through the father is as strong as recurrence through the mother

Genes passed on from the father or the mother seem to be closely related to breech delivery

offspring in the second generation was registered with a major congenital anomaly. Women delivered at term in breech presentation and with a major anomaly, however, had an odds ratio of 4.1 (2.5 to 6.6) of delivering offspring in breech compared with women delivered at term in cephalic presentation without a major anomaly. The highest recurrence was found when the anomaly was a congenital hip dislocation (4.8, 2.6 to 9.0). The corresponding odds ratio for women delivered at term in breech presentation without a major anomaly was 1.9 (1.7 to 2.1). For men with a major anomaly, we did not find a significantly increased risk of recurrence compared with men without a major anomaly.

DISCUSSION

Principal findings and interpretation

Both women and men delivered in breech presentation contribute to increased risk of breech delivery in their own offspring. As the recurrence associated with the father's delivery was as strong as the recurrence from the mother's, we infer that fetal genes from either the mother or the father are strongly related to breech delivery in the next generation.

The effect of maternal genes seems to be low as recurrence from mother to offspring, being a sum of the effect of fetal genes passed on from the mother plus maternal genes, is similar to the effect of fetal genes passed on from the father.[15] Intergenerational recurrence of different birth outcomes could also be explained by environmental conditions that persist in a family over generations. We are not aware of any such environmental factors, however, that might explain the magnitude of our results.

Our results could be explained by a higher proportion of caesarean sections at lower gestational ages for offspring of individuals who themselves were delivered in breech. If so, the highest risk of recurrence should be among offspring delivered by elective caesarean section. However, we found the highest risk among vaginally delivered births. This supports our hypothesis of a genetic component in the aetiology of breech delivery.

The familial association was mainly confined to breech delivery at term for both parents and offspring. This is in agreement with breech delivery in preterm pregnancies being a consequence of the preterm delivery itself and not genetic susceptibility to breech delivery.

Preterm infants naturally have low birth weight, whereas term infants with low birth weight are more likely growth restricted. Again, for men and women delivered in breech with low birth weight, the risk of breech delivery in their offspring was found among those parents delivered at term. Being small for gestational age is a risk factor for breech delivery.[6] There are acknowledged intergenerational associations in fetal growth rate,[16] so recurrence of fetal growth might confound our results. Adjustment for the mother's and the father's growth did not significantly change the results.

Recurrence of breech delivery was not influenced by whether or not the offspring was registered with a major congenital anomaly. When women with a major anomaly such as congenital hip dislocation were delivered in breech presentation, however, the risk of breech delivery in their offspring was significantly higher than for women delivered in breech presentation without a major anomaly. These associations were not similarly observed among men. One hypothesis might be that the morphological characteristics of the pelvis in women with congenital hip dislocation differ from those in women with normal hips, which in turn poses the potential risk of breech delivery in their offspring.

Strengths and limitations of the study

Our cohort data were based on mandatory reporting to a population based registry over a 37 year period. The cohort design comprising the whole population reduces the possibility that selection bias can explain our results. The large study size and standardised collection of data provide high precision in the effect estimates.

Our data indicate a time trend in breech delivery, from 2.5% in the first generation to 3-4% in the offspring generation. Changes in the notification and registration of breech delivery in the birth registry could account for this, together with demographic changes in terms of increasing proportion of births with low birth order, caesarean section, and high maternal age.[1]

The parental cohort includes only survivors and those reproducing, while the offspring cohort is complete. Breech delivery was associated with increased mortality up to the age of 18. Among individuals who survived to 18, the proportion who reproduced was lower for those delivered in breech than cephalic presentation, possibly linked to the excess of congenital anomalies among infants delivered in breech presentation.[2 3 5 6 8 17 18]

Conclusions and implications for clinicians

Genes passed on from either the mother or the father to the fetus seem to be closely related to breech delivery. A considerable number of breech presentations are not detected before labour.[19] To avoid undiagnosed breech

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deliveries, information about the mother's and the father's own presentation at birth will be valuable in the evaluation of fetal presentation in the third trimester.

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Internal and external validity of cluster randomised trials: systematic review of recent trials

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ABSTRACT

Objectives To assess aspects of the internal validity of recently published cluster randomised trials and explore the reporting of information useful in assessing the external validity of these trials.

Design Review of 34 cluster randomised trials in primary care published in 2004 and 2005 in seven journals (*British Medical Journal*, *British Journal of General Practice*, *Family Practice*, *Preventive Medicine*, *Annals of Internal Medicine*, *Journal of General Internal Medicine*, *Pediatrics*).

Data sources National Library of Medicine (Medline) via PubMed.

Data extraction To assess aspects of internal validity we extracted data on appropriateness of sample size calculations and analyses, methods of identifying and recruiting individual participants, and blinding. To explore reporting of information useful in assessing external validity we extracted data on cluster eligibility, cluster inclusion and retention, cluster generalisability, and the feasibility and acceptability of the intervention to health providers in clusters.

Results 21 (62%) trials accounted for clustering in sample size calculations and 30 (88%) in the analysis; about a quarter were potentially biased because of procedures surrounding recruitment and identification of patients; individual participants were blind to allocation status in 19 (56%) and outcome assessors were blind in 15 (44%). In almost half the reports, information relating to generalisability of clusters was poorly reported, and in two fifths there was no information about the feasibility and acceptability of the intervention.

Conclusions Cluster randomised trials are essential for evaluating certain types of interventions. Issues affecting their internal validity, such as appropriate sample size calculations and analysis, have been widely disseminated and are now better addressed by researchers. Blinding of those identifying and recruiting patients to allocation status is recommended but is not always carried out. There may be fewer barriers to internal validity in trials in which individual participants are not recruited. External validity seems poorly addressed in many trials, yet is arguably as important as internal validity in judging quality as a basis for healthcare intervention.

INTRODUCTION

In cluster randomised trials, groups or clusters of individuals are randomised. These trials are increasingly used in health services research for evaluating interventions aimed at changing behaviour in patients or practitioners or changing organisation of services. Cluster randomised trials are pragmatic,

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