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PATERNAL AND MATERNAL BIRTHWEIGHTS AND THE RISK OF INFANT PRETERM BIRTH

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Abstract

OBJECTIVE—Increasing paternal birthweight has been associated with increased risk of fathering a preterm infant, causing speculation that a fetus programmed to grow rapidly can trigger preterm labor.

METHODS—Pregnancies occurring from 1974 to 1989 among women themselves born in the Danish Perinatal Study (1959–61) were identified through the Population Register; obstetrical records were abstracted. Paternal birthweight was obtained by linking Personal Identification Numbers of the fathers to archived midwifery records.

RESULTS—Paternal birthweight was not associated with preterm infants overall. However, there was a significant interaction between paternal and maternal birthweights ($p=0.003$). When the mother weighed <3 kg at birth, increasing paternal birthweight was associated with increased occurrence of preterm birth (p for trend $=0.02$); paternal birthweight was unassociated with preterm birth for mothers weighing ≥ 3 kg at birth ($p=0.34$).

CONCLUSION—When the mother was born small, increasing paternal birthweight was associated with increased risk of preterm birth, suggesting that a fetus growing faster than its mother can accommodate might trigger preterm birth.

Keywords

Birthweight; genetics; paternal effects

INTRODUCTION

A woman's own weight at birth is associated with the birthweight of her offspring,^{1,2} but the association between maternal gestational age at birth and infant gestational age is less consistent.^{1,3} Independently of maternal birthweight, paternal birthweight appears to be associated with infant birthweight, although the magnitude of this association is less for fathers than for mothers.⁴ Less is known about the association between paternal birthweight or

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CONDENSATION:

When the mother was small at birth, increasing paternal birthweight is associated with an increased risk of giving birth to a preterm infant.

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gestational age and infant gestational age.⁵ Lie, et al.⁶ recently reported that while paternal and infant delivery gestational ages were positively correlated, fathers who had high birthweights were at increased risk of having a preterm infant compared with fathers with lower birthweights. This result was unexpected, and therefore requires confirmation. The purpose of this report is to evaluate whether, compared to men who were smaller at birth, men who were larger are at increased risk of fathering a preterm infant.

MATERIALS AND METHODS

Data for this report are from a study of birthweight across generations in Denmark. Study methods have been described in detail previously.^{1,4} In brief, pregnancies occurring during 1974–89 to women who were themselves born as subjects in the Danish Perinatal Study (1959–61) were identified through the Danish Population Register, from which the Personal Identification Numbers of the fathers of the pregnancies were obtained. This Personal Identification Number was used to obtain the father's birthweight from archived midwifery records; the father's gestational age at birth was deemed unreliable in these old records and was not abstracted. Gestational age of the infants, born from 1974 to 1989, was based on LMP supplemented by physical examination and sonography when done. Preterm was defined as a gestational age of less than 37 completed weeks. This study was approved by the Institutional Review Board of the University of Copenhagen, and permission to access population records was obtained from the Danish Ministry of Health.

Women in this study may have had up to four children, and therefore the pregnancy outcomes were not independent. To address non-independence, we utilized Generalized Estimating Equations⁷ and robust standard errors: logistic regression to evaluate the association between paternal birthweight and preterm birth, and linear regression to evaluate mean gestational age. To model trends and interactions, maternal and paternal birthweights were entered as continuous variables and unless otherwise indicated, reported p-values are from these models. However, for clarity, maternal birthweight is presented dichotomized at 3 kg, and paternal birthweight is presented <3 kg, 3–3.9 kg and ≥4 kg. The maternal dichotomy was derived from evaluation of the data following discovery of a statistically significant interaction between maternal and paternal birthweights; paternal categorization was derived from a previous report.⁴

RESULTS

As previously described^{1,4} the original study population included 1298 women; records from the births to 10 of these women could not be located. The 1288 remaining women had 2103 births; and after excluding twins (n=30), births with missing records (n=27) or missing data on gestational age (n=16), and late fetal deaths (n=13, which were included in the previous publication⁴), 2017 liveborn children remained. Paternal birthweight was available for 1258 of these children. Characteristics of fathers with and without available data on birthweight have been described previously.⁴

Overall, paternal birthweight was not associated with gestational age of children. The probability that an infant was born at <37 weeks' gestation for fathers who weighed <3, 3–3.9 and ≥4 kg at birth was 6.3, 7.3 and 7.9 percent, respectively (overall preterm birth rate=6.7%, p for trend = 0.83); the corresponding mean infant gestational age was 279, 278 and 278 days (p for trend=0.66). However, the association between paternal weight at birth and infant gestational age differed significantly according to the birthweight of the mother; for infant gestational age <37 weeks the p-value for interaction between maternal and paternal birthweights was 0.003, and for mean infant gestational age it was 0.005.

The association between paternal birthweight and percent of infants born before 37 weeks' gestation, stratified by maternal birthweight, is presented in Table 1. When the mother weighed less than 3 kg at birth, increasing paternal birthweight was associated with an increased risk of preterm birth. However, paternal birthweight was unassociated with the probability of preterm birth when the mother weighed at least 3 kg at birth. The corresponding results for mean infant gestational age at birth are presented in Table 2. Although the association between paternal birthweight and mean infant gestational age was not significant when the mother was either <3 kg or at least 3 kg at birth, the direction of the association paralleled that for preterm birth. However, when the mother weighed <2 kg at birth, a 1 kg increase in paternal birthweight was associated with a 1.1 week shortened mean infant gestation ($p=0.03$). Inclusion of maternal gestational age at her own birth did not change any of these results, but the small number of births to extreme combinations of maternal and paternal birthweights precluded statistical adjustment for other potentially confounding factors.

When late fetal deaths were included in the analysis, the interaction between paternal and maternal birthweights remained statistically significant for infant preterm birth ($p=0.002$) and for infant gestational age as a continuous variable ($p=0.006$). In addition, the interaction between maternal and paternal birthweights remained statistically significant for infant preterm birth ($p=0.0007$) and mean infant gestational age ($p=0.015$) when infants born after indicated preterm births were excluded.

COMMENT

This study partially confirms the results of Lie, et al.⁶ While there was no overall association between paternal birthweight and infant gestational age, a couple where the father was large at birth and the mother was small was at elevated risk of having a preterm infant. While the mechanism for this association is uncertain, a possible explanation is that a father who was large at birth and a mother who was small might result in a fetus that will grow faster than the mother can accommodate, thereby triggering preterm birth. Such a phenomenon has been described in beef cattle.⁸

To test this proposed mechanism directly, it will be necessary to measure fetal growth with serial sonograms in a large population with available data on both maternal and paternal size and gestational age at birth. The mechanism might be assessed indirectly by evaluating the size at birth of infants of birthweight-discordant couples. If a fetus growing faster than its mother can accommodate triggers labor, then one might expect that the slower-growing fetuses of large fathers and small mothers are the ones that preferentially remain *in utero*. If this is the case then one might evaluate the relative size at different gestational ages at birth of the children of birthweight-discordant couples. The relative size for gestational age of these children might be expected to decline as pregnancy progresses, because the larger fetuses will be the ones born early, while the relatively smaller ones continue undelivered. Although the number of infants would need to be large and the design is cross-sectional rather than longitudinal, such a study would require only data on size and gestational age at birth of the infant and both parents.

There are several limitations to the present study. First, father's gestational age at birth was not assessed. Therefore we can neither confirm the positive association between paternal and infant gestational ages⁶ nor determine whether small paternal size at birth resulted from shortened gestation or reduced growth. Second, the number of couples studied was small, particularly for extreme combinations of paternal and maternal size. Third, the small sample size precluded evaluation of births at gestational ages more preterm than 37 weeks. It precluded adjustment for potentially confounding factors such as maternal smoking, and also precluded evaluation of potentially mediating factors such as pregnancy complications or paternal and

maternal adult size. Fourth, the decrease in mean gestational age was on the order of five days (Table 2). Therefore, while these results may be of etiologic interest, their immediate clinical importance is unclear. Additional large, record-linkage studies are required to confirm and extend these results.

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Table I

Percent of infants born preterm by paternal and maternal birthweights

	Number of preterm infants/total number of infants (percent preterm)	
	Maternal birthweight	
Paternal Birthweight	<3 kg	≥3 kg
<3 kg	4/90 (4.4%)	8/146 (5.5%)
3–3.9 kg	24/301 (8.0%)	35/533 (6.6%)
≥ 4 kg	11/68 (16.2%)	2/120 (1.7%)
p-value for trend	0.02	0.34
p-value for interaction between maternal and paternal birthweights*	0.003	

* P-value for interaction based on maternal and paternal birthweights as continuous terms; logistic coefficients for a 100 gram increase in maternal and paternal birthweights 0.28 and 0.28, respectively. Coefficient for interaction term=0.0093.

Table II

Mean infant gestational age at birth by paternal and maternal birthweights

	Mean infant gestational age (days)	
	Maternal Birthweight	
Paternal Birthweight	< 3 kg	≥3 kg
< 3 kg	278.7	279.0
3–3.9 kg	277.8	280.0
≥ 4 kg	273.7	280.5
p-value for trend	0.30	0.23
p-value for interaction between maternal and paternal birthweights*	0.005	

* P-value for interaction based on maternal and paternal birthweights as continuous terms; coefficients for a 100 gram increase in maternal and paternal birthweights -1.0 days and -1.0 days, respectively. Coefficient for interaction term=+0.033.