

Born too soon: Is it a family affair? Preterm delivery in sisters

Jeanene Johnson BA, Carla I. Mercado MS, Angela S. Tang BS

Background

- Preterm delivery (PTD), defined as delivery prior to 37 weeks' gestation, is the leading cause of perinatal morbidity and mortality worldwide.
- PTD is associated with newborn health complications, mortality, lifelong medical conditions, developmental delays, and serious disabilities.
- In the US, 12-13% of all deliveries are preterm.
- We assessed risk of PTD in women whose sister had PTD and attempted to identify factors that may modify that risk.

Methods

- *Study Design:* Population-based retrospective cohort
- *Data Source:* Maternally-linked birth certificate and hospital discharge data for sister pairs in Washington State
- *Subjects:* Sister pairs who delivered singleton babies in Washington State from 1987-2007. In each pair, the first sister to deliver is referred to as the "exposure sister"; the second to deliver is the "index sister".
- *Main Exposure:* PTD in the exposure sister
- *Main Outcome:* PTD in the index sister
- *Analysis:* Mantel-Haenszel stratified analysis was used to calculate relative risks (RRs) and 95% confidence intervals (CIs). Maternal age, parity, and other factors were considered for their potential effects but did not change RR estimates. Therefore, crude RRs are presented.

Results

- Women had an increased risk of PTD if their sister had a prior PTD (RR=1.66, 95% CI: 1.46, 1.88; Table 1).
- Among women whose sister had an early PTD (<32 weeks' gestation), both an increased risk of early PTD (RR=3.81, 95% CI: 2.29, 6.33) and of moderate PTD (32-36 weeks; RR=1.93, 95% CI: 1.36, 2.74) were observed (Table 1).
- There is a suggestion that non-overweight/obese women achieving recommended pregnancy weight gain (15-30 lbs) and overweight/obese women who gain <15 lbs may not have a significantly increased risk of PTD, even if their sister experienced PTD (Table 2). None of the other factors examined appeared to modify the risk.
- Even when restricted to healthy exposure sisters (first delivery, no diabetes or hypertension), the risk of PTD in index sisters remained increased (data not shown).

Table 1. Risk of preterm delivery associated with having a sister who had a preterm delivery, Washington State, 1987-2007

Gestational age (wks) of exposure sister's prior delivery	N	Index sisters with deliveries at different gestational age (wks) n (%)			Relative risk of index sisters delivering at different gestational age (wks) RR (95%CI)		
		<32	32-36	37+	<37 vs. 37+	<32 vs. 37+	32-36 vs. 37+
<37	2849	64 (2.3)	271 (9.5)	2514 (88.2)	1.66 (1.46, 1.88)	2.22 (1.61, 3.05)	1.60 (1.39, 1.84)
<32	438	17 (3.8)	39 (8.9)	382 (87.2)	1.80 (1.40, 2.33)	3.81 (2.29, 6.33)	1.52 (1.11, 2.07)
32-36	2411	47 (1.9)	232 (9.6)	2132 (88.4)	1.63 (1.43, 1.87)	1.93 (1.36, 2.74)	1.61 (1.39, 1.87)
37+	8366	88 (1.1)	505 (6.0)	7773 (92.9)	1.0 (ref)	1.0 (ref)	1.0 (ref)

Table 2. Risk of preterm delivery associated with having a sister with preterm delivery (<37 weeks), by potentially modifiable characteristics of the Index sister, Washington State, 1987-2007

Risk Factors in the Index Sister	RR ^a	95% CI
Smoking during pregnancy		
Yes	1.61	1.22, 2.13
No	1.65	1.42, 1.91
Hypertension/Preeclampsia		
Yes	1.48	1.08, 2.03
No	1.69	1.47, 1.96
Prenatal care		
No or late	1.60	1.14, 2.24
Early	1.60	1.37, 1.86
Pre-pregnancy BMI		
14.9 to <18.5	1.49	0.65, 3.41
18.5 to <25	1.58	1.25, 1.99
25 to <30	1.52	1.06, 2.17
30+	1.43	0.97, 2.11
Weight gain (pounds)		
<15	1.48	1.03, 2.12
15 to 30	1.57	1.25, 1.97
>30	1.54	1.19, 1.98
Interaction between pre-pregnancy BMI and weight gain		
BMI <25		
Weight gain <15	2.24	1.32, 3.79
Weight gain 15 to 30	1.30	0.92, 1.82
Weight gain >30	1.57	1.10, 2.24
BMI ≥25		
Weight gain <15	0.83	0.46, 1.50
Weight gain 15 to 30	2.09	1.42, 3.09
Weight gain >30	1.32	0.83, 2.09

^a Risk relative to women whose sisters delivered 37+ weeks



Discussion

- Women whose sister had a prior PTD were at increased risk for PTD; this was consistent in nearly all subgroups examined.
- These results are consistent with the only two published studies that have investigated PTD in sisters.
- These findings suggest that genetic and/or environmental factors may be associated with risk of PTD, regardless of most modifiable risk factors.
- Although preliminary, these results suggest that women identified as being at increased risk of PTD due to their sisters' history of PTD may potentially decrease their risk through weight control.
- Limitations to this study include large proportions of missing data, possible errors in self-reported variables, and inaccuracies in gestational age calculations.
- These analyses are exploratory, and further research is needed to investigate the risk of PTD in sisters as well as possible risk factors that may modify this association.

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