Diabetes During Pregnancy Modifies the Association Between Birth Weight and Education: A Whole-of-Population Study

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Higher birth weights usually reflect better intrauterine health, nutrition, and growth. Higher birth weights are also associated with better cognitive outcomes for children (1). However, among pregnancies complicated by diabetes, being born large for gestational age may reflect different intrauterine disease processes, and it is unclear whether this carries the same benefits for education. Our objective is to examine whether diabetes during pregnancy modifies the association between birth weight and school achievement.

This whole-of-population study was conducted using deidentified administrative data that linked perinatal data to children's school assessments. School assessments were obtained from the National Assessment Program – Literacy and Numeracy (NAPLAN), which involves assessments of reading, writing, spelling, grammar, and numeracy in grade three (age ~8 years). Scores were dichotomized at performing above the national minimum standard or not. Children who perform at or below the standard typically require classroom learning support. *Z* scores of birth weight for gestational age (BWGA) were calculated using Australian norms. Diabetes was recorded as either preexisting (i.e., prior to pregnancy, including all types of diabetes) or gestational diabetes mellitus. Preexisting and gestational diabetes mellitus were combined for analyses due to small numbers.

The analysis explored whether the effect of BWGA on NAPLAN was modified by maternal diabetes. BWGA was categorized into the lowest (<20th), middle (20–79th), and highest (≥80th) quintiles. Risk ratios (RR) were calculated from log-Poisson regression models with robust errors and adjustment for confounding by stabilized inverse probability of treatment weights. We tested for effect measure modification by maternal diabetes on the additive scale using the relative excess risk due to interaction (RERI) (2) because the additive scale is important for public health outcomes. We also report the multiplicative scale using the ratio of relative risks (RRR). Potential confounders were identified based on evidence and content knowledge of common causes of birth weight and educational achievement. Analyses were conducted using Stata SE, version 14.0 (Stata Corp, College Station, Texas).

The total sample included 73,642 children. Birth weight in grams (mean ± SD) was 3,419 ± 572 and 3,376 ± 572 for infants born to mothers with and without diabetes, respectively. Table 1 shows that, in the absence of diabetes, $BWGA_{<20}$ had higher and $BWGA_{\geq 80}$ had lower risks of poor school outcomes compared with $BWGA_{20–79}$. For example, the risks of poor spelling scores were 17% higher for $BWGA_{<20}$ (RR 1.17 [95% CI 1.13, 1.22]) and 6% lower for $BWGA_{\geq 80}$ (0.94 [0.90, 0.98]). In the presence of diabetes, risks of poor scores were higher for $BWGA_{\geq 80}$ than $BWGA_{20–79}$, which was reflected in the RERI. For example, risk of poor scores on spelling was 38% higher than that for $BWGA_{20–79}$ (1.38 [1.15, 1.67]); RERI 0.49 [95% CI 0.15, 0.83]).

Among women who had diabetes during pregnancy, infants with birth weights in the heaviest quintile for their gestational age had poorer school assessments. The evidence is less clear for mothers with diabetes whose infants are born in the lowest quintile due to smaller numbers and wide confidence intervals. Among women who do not have diabetes, lower birth weights for gestational age were linked to poorer assessments and higher birth weights were linked to better assessments. Our use of a population-based data set is less susceptible to recall and selection biases than cohort studies, and the large size is well powered for looking

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Table 1—Associations between BWGA and meeting the national minimum standard score for NAPLAN assessments, according to the presence of maternal diabetes*

	BWGA percentiles across the whole population						Within stratum of diabetes	
	<20th		20–79th		≥80th		<20th vs. 20–79th	≥80th vs. 20–79th
	n ≤ NMS/total *N* (%)	RR (95% CI)*	*n* ≤ NMS/total *N* (%)	RR (95% CI)*	*n* ≤ NMS/total *N* (%)	RR (95% CI)*	RR/RERI/RRR (95% CI)	RR/RERI/RRR (95% CI)
Grammar								
No diabetes	3,545/14,515 (24.4%)	1.17 (1.12, 1.21)	8,181/42,256 (19.4%)	Reference	2,348/13,368 (17.6%)	0.93 (0.89, 0.97)	RR 1.17 (1.12, 1.21)	RR 0.93 (0.89, 0.97)
Diabetes	89/383 (23.2%)	1.05 (0.83, 1.32)	262/1,387 (18.9%)	0.98 (0.88, 1.10)	171/737 (23.2%)	1.40 (1.17, 1.70)	RR 1.22 (0.97, 1.53)	RR 1.30 (1.08, 1.57)
							RERI −0.10 (−0.42, 0.22)	RERI 0.49 (0.13, 0.84)
							RRR 0.91 (0.63, 1.20)	RRR 1.53 (1.10, 1.97)
Reading								
No diabetes	3,655/14,502 (25.2%)	1.19 (1.14, 1.23)	8,346/42,122 (19.8%)	Reference	2,420/13,348 (18.1%)	0.95 (0.90, 0.99)	RR 1.19 (1.14, 1.23)	RR 0.95 (0.90, 0.99)
Diabetes	79/382 (20.7%)	0.91 (0.71, 1.16)	272/1,381 (19.7%)	1.00 (0.90, 1.11)	159/723 (22.0%)	1.19 (0.98, 1.45)	RR 1.08 (0.85, 1.37)	RR 1.13 (0.93, 1.37)
							RERI −0.27 (−0.57, 0.02)	RERI 0.25 (−0.08, 0.57)
							RRR 0.77 (0.53, 1.01)	RRR 1.26 (0.90, 1.62)
Spelling								
No diabetes	3,733/14,515 (25.7%)	1.17 (1.13, 1.22)	8,698/42,256 (20.6%)	Reference	2,532/13,368 (18.9%)	0.94 (0.90, 0.98)	RR 1.17 (1.13, 1.22)	RR 0.94 (0.90, 0.98)
Diabetes	94/383 (24.5%)	1.10 (0.88, 1.38)	273/1,387 (19.7%)	0.95 (0.86, 1.06)	177/737 (24.0%)	1.38 (1.15, 1.67)	RR 1.29 (1.04, 1.61)	RR 1.30 (1.08, 1.55)
							RERI −0.03 (−0.34, 0.29)	RERI 0.49 (0.15, 0.83)
							RRR 0.98 (0.69, 1.28)	RRR 1.54 (1.12, 1.97)
Writing								
No diabetes	2,266/14,413 (15.7%)	1.16 (1.10, 1.22)	5,191/42,069 (12.3%)	Reference	1,460/13,295 (11.0%)	0.91 (0.86, 0.97)	RR 1.16 (1.10, 1.22)	RR 0.91 (0.86, 0.97)
Diabetes	50/379 (13.2%)	0.94 (0.68, 1.29)	168/1,380 (12.2%)	0.98 (0.85, 1.14)	122/731 (16.7%)	1.60 (1.25, 2.05)	RR 1.08 (0.79, 1.50)	RR 1.46 (1.15, 1.86)
							RERI −0.21 (−0.61, 0.19)	RERI 0.71 (0.20, 1.22)
							RRR 0.82 (0.48, 1.12)	RRR 1.79 (1.13, 2.44)
Numeracy								
No diabetes	4,152/14,481 (28.7%)	1.20 (1.16, 1.24)	9,395/42,035 (22.4%)	Reference	2,635/13,302 (19.8%)	0.92 (0.88, 0.96)	RR 1.20 (1.16, 1.24)	RR 0.92 (0.88, 0.96)
Diabetes	115/387 (29.7%)	1.10 (0.90, 1.33)	316/1,373 (23.0%)	1.03 (0.94, 1.14)	190/728 (26.1%)	1.27 (1.06, 1.51)	RR 1.32 (1.08, 1.60)	RR 1.16 (0.98, 1.38)
							RERI −0.14 (−0.43, 0.15)	RERI 0.32 (0.02, 0.62)
							RRR 0.88 (0.65, 1.12)	RRR 1.34 (1.00, 1.69)

*RRs and 95% CI were calculated from a generalized linear model with log-Poisson links and inverse probability of treatment weighting to adjust for the following potential confounders: maternal age, smoking in pregnancy, ethnicity, occupation, birthing in private hospital, index of relative socioeconomic advantage and disadvantage, living in a remote area, maternal asthma, high blood pressure, singleton, parity, gestational age, and child's sex. NMS, national minimum standard score for age.

within subgroups of infants with higher/lower birth weights and presence/absence of diabetes. The analysis included adjustments for a wide range of confounders but not maternal BMI, as it was not collected. However, others have shown little change to point estimates after adjusting for BMI (3). Furthermore, adjusting for maternal BMI is more important for studies where child weight is an outcome, than education.

The current study may have implications for clinical management of pregnant women with diabetes. Large fetal size can reflect overnutrition due to hyperglycemia or healthy fetuses who are constitutionally large and not at risk for poor academic outcomes. The perinatal database does not include information on diabetes control, and women who have poorer control and larger babies may have children who have poorer school assessments. Births at 40–41 weeks' gestation are optimal for school achievement (4). Ultrasound monitoring of fetal size during pregnancy in addition to diet and insulin (if required) may help reduce large-for-gestational age births (5). Optimization of blood glucose levels for pregnant women with diabetes is key, and prevention of obesity, while difficult, might theoretically represent the best approach. However, studies involving dietary interventions for overweight or obese women have been largely unsuccessful; thus, preventing prepregnancy obesity is likely to be important but not achievable at the population level.

To summarize, on average, being born in the highest quintile of BWGA is linked to poorer school achievement if mothers have diabetes during pregnancy.

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