

Association of macrosomia with perinatal and postneonatal mortality among First Nations people in Quebec

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See related commentary by Gray-Donald

ABSTRACT

Background: High prevalence of infant macrosomia (up to 36%, the highest in the world) has been reported in some First Nations communities in the Canadian province of Quebec and the eastern area of the province of Ontario. We aimed to assess whether infant macrosomia was associated with elevated risks of perinatal and postneonatal mortality among First Nations people in Quebec.

Methods: We calculated risk ratios (RRs) of perinatal and postneonatal mortality by birthweight for gestational age, comparing births to First Nations women ($n = 5193$) versus women whose mother tongue is French ($n = 653\,424$, the majority reference group) in Quebec 1991–2000.

Results: The prevalence of infant macrosomia (birthweight for gestational age > 90th percentile) was 27.5% among births to First Nations women, which was 3.3 times (confi-

dence interval [CI] 3.2–3.5) higher than the prevalence (8.3%) among births to women whose mother tongue is French. Risk ratios for perinatal mortality among births to First Nations women were 1.8 (95% CI 1.3–2.5) for births with weight appropriate for gestational age, 4.1 (95% CI 2.4–7.0) for small-for-gestational-age (< 10th percentile) births and < 1 (not significant) for macrosomic births compared to births among women whose mother tongue is French. The RRs for postneonatal mortality were 4.3 (95% CI 2.7–6.7) for infants with appropriate-for-gestational-age birthweight and 8.3 (95% CI 4.0–17.0) for infants with macrosomia.

Interpretation: Macrosomia was associated with a generally protective effect against perinatal death, but substantially greater risks of postneonatal death among births to First Nations women in Quebec versus women whose mother tongue is French.

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A trend toward higher birthweights has emerged in recent decades.^{1–3} Reflected in this trend is a rise in the prevalence of infant macrosomia, commonly defined as either a birthweight greater than 4000 g or a birthweight for gestational age greater than the 90th percentile relative to a fetal growth standard.^{4–8} Maternal obesity, impaired glucose tolerance and gestational diabetes mellitus are important risk factors for infant macrosomia^{9,10} and are known to afflict a much higher proportion of people in Aboriginal populations than in the general population.^{11–14} This is true especially for Aboriginal populations in which a traditional lifestyle has changed to a less physically active, modern lifestyle in recent decades. A high prevalence of infant macrosomia (up to 36%, which, to the best of our knowledge, is the highest in the world) has been reported in some First Nations communities of Quebec and eastern Ontario in Canada.^{15–17} However, little is

known about the implications of this high prevalence for perinatal and infant health of First Nations people in these regions. We examined whether infant macrosomia was associated with increased risk for perinatal and postneonatal death among First Nations infants in Quebec.

Methods

Data source and inclusion criteria

We conducted an analysis of perinatal and infant mortality by birthweight for gestational age in a cohort of births to women with a First Nations mother tongue ($n = 5193$) and a majority reference group of women whose mother tongue is French ($n = 653\,424$) in the province of Quebec from 1991 to 2000.

We used linked data from Statistics Canada on birth and infant deaths. We restricted our analysis to births that occurred at a gestational age of 20

weeks or later and birthweights of 500 g or more. Births for which data on birthweight or gestational age were missing (0.8%) were excluded because fetal growth could not be assessed.

We used maternal mother tongue as recorded on birth registrations to identify births to First Nations women. This method is thought to identify about 50%–60% of all births to First Nations women in Quebec.¹⁸ By design, the study excluded births to women with an Inuit mother tongue (92% of self-identified Inuit in Quebec reported Inuktitut or Inuit language as their mother tongue, according to the 2001 census), a population known to have much higher perinatal and postneonatal mortality compared to non-Aboriginal populations.^{18,19}

We used data for the period of 1991 to 2000 because they were the most recent linked data available at the time the study protocol was approved by the research ethics board and because the linked vital records of more recent years do not allow for identification of First Nations women reporting multiple mother tongues (i.e., French or English plus an Aboriginal language becomes French or English plus other).

Informed consent was not sought from individual participants because the study was based on anonymized, linked birth data. The study was approved by the research ethics board of Sainte-Justine Hospital, University of Montreal, and by the First Nations of Quebec and Labrador Health and Social Services Commission.

Outcomes

Primary outcomes were perinatal and postneonatal death. Perinatal death included stillbirths

(fetal deaths at ≥ 20 weeks of gestation or later with weight of greater than 500 g) plus neonatal deaths (0–27 days postnatally). Postneonatal death included any death between 28 days of postnatal life and the child's first birthday. We chose perinatal death as a primary outcome because it would not have been affected by variability in the registration of births at the borderline of viability (i.e., variable judgments by individual physicians could have resulted in such deaths being registered as either stillbirths or neonatal deaths).²⁰

Statistical analysis

Two dimensions of comparisons were made. First, we calculated the risk ratio (RR) and 95% confidence intervals (CIs) for perinatal and postneonatal death, comparing births to First Nations women versus women whose mother tongue was French by birthweight for gestational age according to the Canadian sex-specific fetal growth standards²¹ (small for gestational age = < 10th percentile, appropriate for gestational age = 10th–90th percentile, and large for gestational age = > 90th percentile, or macrosomic). Second, we calculated the RRs (95%) for perinatal and postneonatal death comparing macrosomic versus weight appropriate-for-gestational-age infants within the First Nations and French-as-mother-tongue groups. We also calculated the RRs for postneonatal mortality due to sudden infant death syndrome (SIDS). Other cause-specific death risks were not calculated because the numbers were too small for First Nations births. Crude RRs by birthweight for gestational age categories were presented because our objective

Table 1: Perinatal and postneonatal mortality† by birthweight for gestational age among births in Quebec to First Nations women and women whose mother tongue is French, 1991–2000

Birthweight for gestational age, percentile	First Nations* per 1000 (n/total)	French mother tongue* per 1000 (n/total)	First Nations v. French mother tongue RR (95% CI)
Perinatal death			
< 10th	69.5 (13/187)	16.9 (1193/70 736)	4.12 (2.43–6.98)
10th–90th	9.2 (33/3575)	5.2 (2759/528 517)	1.77 (1.26–2.49)
> 90th	4.9 (7/1431)	8.0 (435/54 179)	0.61 (0.29–1.28)
Postneonatal death			
10th–90th	5.4 (19/3542)	1.3 (659/525 758)	4.28 (2.72–6.74)
> 90th	6.3 (9/1424)	0.8 (41/53 744)	8.28 (4.03–17.01)
Postneonatal SIDS			
10th–90th	1.7 (6/3542)	0.4 (198/525 758)	4.50 (2.00–10.13)
> 90th	2.1 (3/1424)	0.2 (9/53 744)	12.58 (3.41–46.42)

Note: CI = confidence interval, RR = risk ratio, SIDS = sudden infant death syndrome.
 *Data for outcome rates are per 1000 total births for perinatal death and per 1000 postneonatal survivors for postneonatal death. Results in the category of birthweight for gestational age < 10th percentile were not presented for postneonatal death because values for the First Nations group were too small (one death) for meaningful comparisons.

was to describe the effects of fetal growth on perinatal and postneonatal mortality. Various risk factors could have affected the risks of death through affecting fetal growth (on the causal pathway). No information was available on medical risk factors such as diabetes in pregnancy in the Canadian linked birth data. Because remoteness may affect timely access to high-quality tertiary care and hence the risks of perinatal and postneonatal death,²² we further assessed the risk differences restricted to remote areas. We defined remote areas as any rural area with a workforce-commuting flow into urban centres (population $\geq 10\,000$ in the 1996 census) of less than 5% based on maternal residential postal codes as recorded on birth registrations.²²

Two-tailed p values < 0.05 were considered significant.

Results

The prevalence of infant macrosomia was 27.5% (1431/5193) for births to First Nations women, or 3.3 times the prevalence of 8.3% (54 192/653 424) for macrosomic births to women whose mother tongue is French ($p < 0.001$). The prevalence of preterm birth (< 37 completed weeks of gestation) was similar for all births (6.6% v. 7.3%) and for macrosomic births (6.4% v. 6.6%) to First Nations women versus women whose mother tongue is French (all $p > 0.05$). Perinatal mortality (7.3 v. 6.1 per 1000) and postneonatal mortality (1.7 v. 1.2 per 1000) were significantly higher for male versus female infants ($p < 0.001$), with a similar proportion of male infants for births to First Nations women (50%) versus women whose mother tongue is French (51%).

Perinatal mortality among births to First Nations women was 1.5 times higher than among births to women whose mother tongue is French (10.2 per 1000 [53/5193] v. 6.7 per 1000 [4387/653 424], $p < 0.001$), and postneonatal mortality was 3.9 times higher (5.6 per 1000 [29/5193] v. 1.4 per 1000 [940/653 424]). Perinatal mortality was 1.8 times higher for births with appropriate-for-gestational-age birthweight and 4.1 times higher for those with small-for-gestational-age birthweight (all $p < 0.001$), but not significantly lower for macrosomic births (Table 1). The RR for postneonatal death among infants of First Nations women versus women whose mother tongue is French was about 4.3 for infants with appropriate-for-gestational-age birthweight and was much greater (RR = 8.3) for macrosomic infants (all $p < 0.001$). The RR for postneonatal SIDS was 4.5 among infants with appropriate-for-gestational-age birthweight and

was much greater (RR = 12.6) among macrosomic infants (all $p < 0.001$).

When compared to appropriate-for-gestational-age births, perinatal mortality among macrosomic births was significantly higher for women whose mother tongue is French ($p < 0.001$), but nonsignificantly lower for First Nations women (Table 2). Postneonatal mortality among macrosomic births versus weight-appropriate-for-gestational-age births was significantly lower for women whose mother tongue is French (RR = 0.61, $p < 0.001$), but a significant difference was not observed (RR = 1.2, $p > 0.68$) among infants of First Nations women.

The proportion of births to mothers residing in remote areas was substantially higher for First Nations women (69%, 3607/5193) versus women whose mother tongue is French (5%, 35 705/653 424). Comparing births to First Nations women versus women whose mother tongue is French living in remote areas, perinatal mortality was substantially higher for small-for-gestational-age infants (81.8 v. 18.7 per 1000, RR = 4.4, $p < 0.001$), and postneonatal mortality was substantially higher for macrosomic infants (66.2 v. 7.2 per 1000, RR = 9.0, $p < 0.01$). The RRs for both comparisons were similar to those observed in the overall analyses.

Interpretation

Main findings

We found that macrosomia was not associated with increased risk of perinatal death among births to First Nations women in Quebec, although its prevalence was three times higher than among births to women whose mother tongue is French. Macrosomia was associated with a much greater risk of postneonatal death among infants of First Nations women versus women whose mother tongue is French.

Our data confirmed the high prevalence of infant macrosomia among births to First Nations women,^{15,23} and the higher perinatal and postneonatal mortality among births to First Nations

Table 2: Risk ratios of perinatal and postneonatal mortality comparing large- versus appropriate-for-gestational-age birthweight births in Quebec to First Nations women and women whose mother tongue is French, 1991–2000

Variable	First Nations, RR (95% CI)	French mother tongue, RR (95% CI)
Perinatal death	0.53 (0.24–1.20)	1.54 (1.39–1.70)
Postneonatal death	1.18 (0.53–2.60)	0.61 (0.44–0.83)
Postneonatal SIDS	1.24 (0.31–4.97)	0.44 (0.23–0.87)

Note: CI = confidence interval, RR = risk ratio, SIDS = sudden infant death syndrome.

women in Quebec versus women whose mother tongue is French.¹⁸ However, the elevated risk for postneonatal mortality (RR = 3.9) was smaller than that for births in Inuit-inhabited versus other areas of Canada (RR = 6.2).¹⁹

How such disparities in mortality may differ for infants with poor or excessive fetal growth has not been explored. Our results show that elevation of risk varied substantially by fetal growth. Among births to First Nations women, small-for-gestational-age infants were at much higher risk for perinatal death (RR = 4.1) versus those born to women whose mother tongue is French, indicating a need for improved access to high-quality perinatal care for such high-risk deliveries to First Nations women, especially those living in remote areas. (Most of the First Nations women in our study lived in remote communities.) By contrast, macrosomic births to First Nations women were not at higher risk for perinatal death compared with such births to women whose mother tongue is French or compared with births of infants with appropriate-for-gestational-age birthweight among First Nations women. Macrosomia seemed somewhat protective against perinatal death among births to First Nations women. By contrast, macrosomia was associated with an increased risk of perinatal death among births to women whose mother tongue is French.

Macrosomia was associated with a significantly lower risk of postneonatal death among infants of women whose mother tongue is French but not First Nations women. It is unclear why macrosomia was protective against postneonatal death among infants of women whose mother tongue is French; we are unaware of such an effect reported in other populations. Although the risks for postneonatal death and SIDS were higher for macrosomic infants among First Nations versus French-as-mother-tongue groups, our study's within-group comparisons could not detect a significantly higher risk of postneonatal death and SIDS associated with macrosomia among births to First Nations women. This finding could be explained by the relatively small sample size of First Nations births in our study and hence, its limited power to detect moderate differences in death rates among birthweight subgroups. Alternatively, the observed differences could have been due to chance. Caution is particularly warranted when interpreting the elevated risk of SIDS among First Nations infants with macrosomia, given the small number of events.

The underlying causes of the observed high risk of postneonatal death and SIDS among macrosomic births to First Nations women are unclear. Impaired glucose tolerance and gesta-

tional diabetes are frequent causes of macrosomia.^{15,24} One might speculate that abnormalities in maternal glucose metabolism in pregnancy could be an underlying cause. However, we are unaware of evidence linking postneonatal death or SIDS to diabetes in pregnancy. Type 2 diabetes and gestational diabetes are much more prevalent (two to three times higher than rates for the general population) in some First Nations communities in Quebec.^{25,26} Prevention-based programs to reduce the high prevalence of diabetes may help to decrease the rate of macrosomic births and perhaps also that of postneonatal deaths.

Limitations

We had no data on glucose tolerance and gestational diabetes. It would be worthwhile to explore whether impaired glucose tolerance and gestational diabetes are associated with postneonatal death and SIDS. We used maternal mother tongue to flag First Nations births. However, about 40% of self-identified Aboriginal women in Quebec did not report an Aboriginal language as their mother tongue, according to the 2001 census. Hence, a large number of self-identified Aboriginal women could have reported French as a mother tongue. However, such misclassifications would be unlikely to have affected the outcome rates for the much larger French-as-mother-tongue group in the comparisons.

Conclusion

Parents and caregivers should be vigilant about the substantially elevated risk of postneonatal death among macrosomic infants of First Nations women. Further research is needed to understand the causal mechanisms and develop effective prevention programs.

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Contributors: Spogmai Wassimi, Russell Wilkins and Zhong-Cheng Luo conceived the study. All of the authors contributed to the design of the study and the interpretation of the data. Zhong-Cheng Luo and Russell Wilkins analyzed the data. Spogmai Wassimi, Fabienne Simonet and Lin Xiao were involved in the literature review. Spogmai Wassimi and Zhong-Cheng Luo drafted the manuscript, and Russell Wilkins and Zhong-Cheng Luo revised it. All of the authors critically reviewed the manuscript for important intellectual content and approved the version submitted for publishing.

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