Neighbourhood Income Level and Outcomes of Extremely Preterm Neonates: Protection Conferred by a Universal Health Care System

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ABSTRACT

Objectives: To determine the impact of neighbourhood income and maternal residence population density on mortality and various morbidities at discharge or transfer from the NICU among extremely preterm neonates (<27 weeks gestation) in Canada.

Methods: Neighbourhood income level and residential status was derived using a postal code conversion file and census data. Multivariable logistic regression analysis was used to estimate the risk-adjusted odds ratio (AOR) of mortality and survival without major morbidities (chronic lung disease, necrotizing enterocolitis, severe intraventricular hemorrhage, and retinopathy of prematurity) among 2,752 extremely preterm infants admitted to 25 tertiary level neonatal intensive care units in Canada between 2007 and 2008.

Results: There were no significant differences between mothers from different neighbourhood income quintiles (Q1 = low; Q5 = high) and neonatal mortality AOR (95% confidence interval): Q1: 1.10 (0.74-1.62), Q2: 1.00 (0.67-1.49), Q3: 1.39 (0.93-2.07), Q4: 1.01 (0.67-1.52), Q5: 1 (reference); or survival without major morbidity: Q1: 1.01 (0.70-1.44), Q2: 0.84 (0.58-1.23), Q3: 0.85 (0.58-1.24), Q4: 0.92 (0.63-1.35), Q5: 1 (reference). There were no significant differences in mortality (AOR 1.14 [0.83-1.57]) or in survival without major morbidity (AOR 0.92 [0.67-1.26]) between infants of mothers residing in sparsely populated areas compared to densely populated areas.

Conclusion: Maternal residence in a low-income neighbourhood or sparsely populated area was not associated with higher odds of mortality or survival free of major morbidities in extremely preterm infants.

Key words: Neonatal mortality; morbidity; preterm birth; neonatal intensive care unit; socioeconomic status

La traduction du résumé se trouve à la fin de l'article.

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The Canada Health Act of 1984 guarantees free and universal access to publicly insured health care for all Canadian citizens. Despite such an advantageous position, significant health disparities exist between people of low socio-economic status (SES) and those of higher SES.¹ In particular, a number of population- and facility-based studies in industrialized countries have documented the relationship between low SES and an increased risk of preterm labour.²⁻⁷ Although, the effects of low SES on the outcomes of infants born preterm are uncertain, mothers of low SES are speculated to have higher adverse outcomes due to delayed/no prenatal care, higher rates of unintended pregnancy, and higher rates of smoking during pregnancy.⁸ The population-based studies of neonatal outcomes in Canada reported thus far have involved infants born over a long time period and restricted to one provincial boundary, thus limiting the generalizability of findings in the context of a universal health care system.⁹⁻¹¹ Additionally, it has been speculated that residing in a rural area impacts neonatal mortality and morbidities independent of SES. However, results from studies conducted both in Canada^{10,12,13} and in other countries¹⁴⁻¹⁸ have been inconsistent, with reports of protective, null, or adverse effects of rural residence on neonatal outcomes.

Our primary objective was to determine the impact of neighbourhood income level on mortality and survival free of major morbidity among extremely preterm neonates (<27 weeks gestation) admitted to tertiary level neonatal intensive care units (NICUs) in Canada. Our secondary objective was to evaluate the impact of maternal residence in either sparsely populated or dense-

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Conflict of Interest: None to declare.

Table 1. Maternal and Infant Characteristics of Infants Included in the Analysis Distributed According to Income Quintiles

Characteristics	Income Quintiles					p-value
	Q1 N = 720	Q2 N = 569	Q3 N = 579	Q4 N = 516	Q5 N = 368	
Male (n = 2750)	379 (52.6)	297 (52.2)	317 (54.8)	280 (54.3)	201 (54.6)	0.87
Birth weight (g)	851 ± 197	838 ± 193	835 ± 198	836 ± 190	846 ± 179	0.52
Gestational age (wks)	25.6 ± 1.2	25.6 ± 1.3	25.6 ± 1.2	25.6 ± 1.2	25.6 ± 1.2	0.69
SNAP-II score						
0-9	250 (34.7)	197 (34.7)	220 (38.0)	182 (35.3)	140 (38.3)	0.64
10-19	210 (29.2)	159 (28.0)	148 (25.6)	157 (30.4)	99 (27.1)	
20-29	127 (17.6)	94 (16.6)	98 (16.9)	70 (13.6)	53 (14.5)	
≥30	133 (18.5)	117 (20.6)	113 (19.5)	107 (20.7)	74 (20.2)	
Median SNAP-II score (n = 2748)	14 (9-25)	14 (9-26)	14 (9-25)	14 (9-25)	14 (9-25)	0.70
Apgar at 5 minutes <7 (n = 2696)	284 (40.4)	233 (41.7)	235 (41.5)	196 (39.0)	139 (38.1)	0.75
Outborn (n = 2750)	181 (25.1)	128 (22.5)	137 (23.7)	109 (21.1)	59 (16.0)	0.01
Maternal hypertension (n = 2688)	87 (12.5)	79 (14.1)	76 (13.4)	57 (11.3)	41 (11.4)	0.59
Diabetes (n = 2748)	65 (9.0)	53 (9.3)	60 (10.4)	51 (9.9)	34 (9.3)	0.94
Completed antenatal steroids (n = 2655)	284 (41.5)	216 (39.2)	222 (39.6)	224 (44.8)	159 (44.2)	0.22
Small for gestational age (n = 2743)	61 (8.5)	42 (7.4)	55 (9.5)	46 (9.0)	24 (6.5)	0.47
Chorioamnionitis (n = 2328)	174 (28.1)	106 (20.7)	103 (20.6)	119 (25.5)	66 (20.2)	0.01
Caesarean birth (n = 2651)	366 (50.8)	320 (56.3)	335 (57.9)	279 (54.1)	207 (56.3)	0.10
Teenage mother (n = 2666)	50 (7.3)	31 (5.6)	20 (3.6)	28 (5.6)	14 (3.9)	0.04
Lone parent (n = 2455)	55 (8.7)	27 (5.5)	21 (4.0)	20 (4.4)	16 (4.7)	<0.01
Primigravida (n = 2743)	209 (29.1)	201 (35.5)	193 (33.4)	209 (40.7)	144 (39.2)	<0.01
Multiple births (n = 2751)	149 (20.7)	112 (19.7)	164 (28.4)	160 (31.0)	126 (34.2)	<0.01

* SNAP-II: score of neonatal acute physiology.

Outborn status: preterm infants born in a non-tertiary care centre and then transferred to a tertiary care centre for further treatment.

ly populated areas on mortality and survival free of major morbidities among extremely preterm neonates admitted to tertiary level NICUs in Canada.

METHODS

Study population

The study cohort consisted of extremely preterm infants admitted to tertiary level NICUs in Canada that participated in the Canadian Neonatal Network between January 1, 2007 and December 31, 2008. Of the 28 tertiary NICUs in Canada, a total of 25 participated in the network during this time, comprising greater than 95% of admissions to NICUs in Canada. This cohort can therefore be considered population-based, as all extremely preterm infants are admitted to NICUs due to the intensive nature of the care they require.

Data collection

Trained abstractors retrospectively collected information on neonates and mothers from patient charts using standardized definitions provided in the Canadian Neonatal Network™ Data Abstractor's Manual.¹⁹ The database has built-in checks and final validation was performed prior to analyses at the central coordination centre. Patient information collected included demographic information, perinatal risk factors, admission illness severity, and outcomes. This study was a retrospective secondary analysis of previously collected data. Data were collected with institutional approval from either a local Research Ethics Board or an institutional quality improvement process.

Exposure definitions

Neighbourhood income quintile and population density were defined according to definitions in the Statistics Canada Postal Code Conversion File (PCCF+) Version 5F, a SAS control program that merges the Statistics Canada PCCF with the 2006 postal code population weight field (WCF) in a logical and consistent way to assign geographic identifiers.²⁰ A mother's residence was classified based on the income quintile of the enumeration area in which she

Figure 1. Adjusted odds ratios of survival without major morbidity for each neighbourhood income quintile compared to Q5

resided, on a scale of low (Q1) to high (Q5). Maternal residence was classified as sparsely populated if the postal code matched to an enumeration area that did not correspond to a census agglomeration (CA) or census metropolitan area (CMA). The 2006 Canadian census defines a CA as a cluster of census subdivisions with a total population between 10,000 and 100,000, and a CMA as a cluster of census subdivisions with a total population greater than or equal to 100,000.²⁰

Outcome definitions

Survival without major morbidity was defined as being discharged home or being transferred out of an NICU and not having any of the four major morbidities:

- Chronic lung disease (CLD), defined as need for supplemental oxygen at 36 weeks post-menstrual age or at discharge;²¹
- Severe neurological injury, defined as grade 3 or 4 intraventricular hemorrhage (IVH)²² or periventricular lesions (PVL);
- Severe retinopathy of prematurity (ROP), classified as stage 3 to 5 retinopathy;²³ or
- Necrotizing enterocolitis (NEC) stage 2 or 3.²⁴

Table 2. Rates and Adjusted Odds Ratios With 95% Confidence Intervals of Multivariable Models Comparing Income Quintiles and Outcomes

Outcome	Rates					Adjusted Odds Ratios*				
	Neighbourhood Income Quintile					Neighbourhood Income Quintile				
	Q1 (lowest) n (%)	Q2 n (%)	Q3 n (%)	Q4 n (%)	Q5 (highest) n (%)	Q1 (lowest)	Q2	Q3	Q4	Q5 (highest)
Survival without major morbidity	148 (22.2)	96 (18.8)	103 (19.1)	102 (21.1)	80 (23.5)	1.01 (0.70-1.44)	0.84 (0.58-1.23)	0.85 (0.58-1.24)	0.92 (0.63-1.35)	1
Mortality	143 (19.9)	121 (21.3)	142 (24.5)	103 (20.0)	71 (19.3)	1.10 (0.74-1.62)	1.00 (0.67-1.49)	1.39 (0.93-2.07)	1.01 (0.67-1.52)	1
Severe neurological injury	173 (27.0)	122 (24.9)	135 (26.8)	112 (24.4)	91 (27.8)	0.89 (0.63-1.27)	0.83 (0.58-1.19)	0.86 (0.59-1.24)	0.78 (0.53-1.13)	1
Chronic lung disease	298 (51.6)	232 (51.3)	243 (55.4)	212 (51.6)	151 (50.1)	0.96 (0.70-1.33)	0.92 (0.67-1.28)	1.16 (0.83-1.62)	0.96 (0.68-1.34)	1
Severe retinopathy of prematurity	100 (21.4)	81 (23.3)	82 (22.5)	78 (22.9)	45 (18.4)	1.29 (0.81-2.05)	1.38 (0.86-2.22)	1.35 (0.83-2.19)	1.55 (0.96-2.50)	1
Necrotizing enterocolitis	82 (11.5)	63 (11.3)	66 (11.6)	54 (10.6)	24 (6.6)	1.83 (1.09-3.06)	1.78 (1.05-3.02)	1.81 (1.06-3.07)	1.62 (0.94-2.80)	1

* Results adjusted for birth weight, teenage mother, sex, SNAP-II score group, Apgar score at 5 minutes, chorioamnionitis, outborn status, completed antenatal steroids, small for gestational age and Caesarean birth.

Data analysis

All data analyses were conducted using SAS v9.2 (SAS Institute, Cary, NC). Univariate analyses were conducted to describe the characteristics of mothers and various perinatal risk factors in each income quintile. Multivariable logistic regression analysis was used to create a risk-adjusted model comparing survival without major morbidity, mortality, and each of the major morbidities in infants of mothers in lower income quintiles (Q1-4) to infants of mothers in the highest income quintile (Q5). The full model was developed after controlling for birth weight, teenage mother, sex, Apgar score at 5 minutes, chorioamnionitis, outborn status, completed antenatal steroids, small for gestational age, Caesarean birth and severity of illness group based on Score of Neonatal Acute Physiology-II (SNAP-II).²⁵ A second multivariable logistic regression analysis was used to develop a risk-adjusted model comparing survival without major morbidity, mortality, and each of the major morbidities in infants of mothers residing in sparsely populated areas to infants of mothers residing in densely populated areas.

RESULTS

During the study period, 3,018 extremely preterm infants were admitted to participating NICUs. A total of 266 infants (8.8% of admitted infants) were excluded for the following reasons: 48 infants were moribund on admission (where an explicit decision was made not to initiate life support at the time of birth) and 218 infants did not have postal code information. The basic characteristics of the excluded infants did not differ from those of the included infants. The remaining 2,752 infants (91.2% of admitted infants) comprised the study population. Of these, 720 (26.2%) infants were born to mothers residing in Q1 (lowest), 569 (20.7%) in Q2, 579 (21.0%) in Q3, 516 (18.8%) in Q4, and 368 (13.4%) to mothers in income quintile Q5 (highest).

The characteristics of infants born to mothers in each neighbourhood income quintile are reported in Table 1. There were significant differences in the proportion of infants who were outborn (defined as those infants not born at a tertiary care perinatal centre), or born to mothers with chorioamnionitis, teenage mothers, lone parents, primigravida mothers, and mothers who had multiple births. The rates of mortality and each of the major morbidities (severe neurological injury, CLD, severe ROP and NEC) for infants in each income quintile of maternal residence are shown in Table 2, along with the results of the multivariable logistic regression comparing income quintile and outcomes. There were no significant differences between income quintiles for survival without major morbidity (Figure 1), mortality, severe neurological injury, CLD, and severe ROP. Infants born to mothers in Q1, Q2 and Q3 were more likely to develop NEC compared with infants born to mothers in Q5.

Densely populated vs. sparsely populated areas

In this study population, 397 (14.4%) infants were born to mothers residing in sparsely populated areas and 2,355 (85.6%) were born to mothers residing in densely populated areas. The characteristics of infants born to mothers in sparsely and densely populated areas are reported in Table 3. There were significant differences in the proportion of infants who: had an Apgar score of less than 7; were outborn; were born to teenage mothers; were born to mothers who had multiple births. The rates of mortality and each of the major morbidities for infants in densely and sparsely populated areas are shown in Table 4, along with the results of the multivariable logistic regression comparing population density of maternal residence and outcomes. There were no significant differences between population density of maternal residence for survival without major morbidity, mortality, severe neurological injury, CLD, and severe ROP. Infants born to mothers in sparsely populated areas were more likely to develop NEC compared with infants born to mothers in densely populated areas.

DISCUSSION

In this study, we demonstrated that extremely preterm infants born to mothers in lower income quintiles and admitted to tertiary NICUs in Canada, were as likely to survive without most of the major morbidities as infants born to mothers in the highest income quintile. There was also no significant difference in survival without most of the major morbidities when comparing outcomes between infants of mothers residing in sparsely populated areas and infants of mothers residing in densely populated areas. Necrotizing enterocolitis was the only exception to this, as its incidence was higher in infants born to women from lower income quintiles and from sparsely populated areas.

Previous studies comparing neonatal outcomes in Canada with respect to SES have yielded conflicting results. Joseph et al.¹¹ demonstrated higher rates of composite perinatal mortality and serious morbidity among infants of mothers in lower income quintiles in Nova Scotia. On the other hand, Luo et al.⁹ demonstrated that significant differences in neonatal death between income quintiles only existed in urban areas of British Columbia. By contrast, no significant differences in neonatal death were demonstrated between high income quintiles and low income quintiles after incorporating individual SES factors in the province of Quebec.¹⁰ These studies were performed using population-based administrative databases, which are known to provide only limited information regarding the exact nature of severe morbidities and capabilities of adjusting for known confounders (e.g., Apgar score, severity of illness). The study described here is the first to focus on extremely preterm infants in NICUs, who are at the highest risk of adverse outcomes, as previous studies consisted of all infants (preterm and term) born in a province. This study also differed from other studies by including mortality and morbidities in the outcomes, as at extremes of gestational ages one can substitute for the other depending on the practices adopted at a particular centre.

In terms of the infant outcomes according to population density, in a study from Australia, a country that also has a universal health care system and a regionalized perinatal care model, mortality was higher among preterm infants born to mothers from rural areas compared with those from urban areas among all infants admitted to NICUs.¹⁶ Our results may differ from these findings because of a slightly different method of defining rural–urban contrast. We assessed population density rather than rural–urban contrast, because in a large country like Canada, several suburbs are designated as villages and may lead to misclassification. One outcome that showed an association with being in the low income quintile and residing in a sparsely populated area was NEC. We speculate this may be due to lower rates of breastfeeding or breast milk ingestion among such infants as there are barriers to pumping and/or breastfeeding in women from low SES. These include reduced support for pumping, reduced access to support from lactation consultants, lack of support from family members, need to restart work and inability to pump at workplaces.^{26,27} This is also an issue for mothers residing in rural areas, as they generally have to travel longer distances to attend their infant, which leads to a lower success rate for breastfeeding. Further studies from different countries are needed to assess this association in detail.

The major strength of this study is the use of a large nearly population-based clinical database, which allows the inclusion of important perinatal risk factors such as illness severity scores, and

Table 3. Maternal and Infant Characteristics of Infants Included in the Analysis Distributed According to Population Density

Characteristics	Population Density		p-value
	Sparsely Populated N = 397	Densely Populated N = 2355	
Male (n = 2750)	216 (54.4)	1258 (53.5)	0.72
Birth weight (g)	856 ± 204	839 ± 191	0.10
Gestational age (wks)	25.6 ± 1.3	25.6 ± 1.2	0.90
SNAP-II score			
0-9	134 (33.8)	855 (36.4)	0.10
10-19	107 (27.0)	666 (28.3)	
20-29	59 (14.9)	383 (16.3)	
≥30	97 (24.4)	447 (19.0)	
Median SNAP-II score (n = 2748)	14 (9-29)	14 (9-25)	0.07
Apgar at 5 minutes <7 (n = 2696)	176 (45.0)	911 (39.5)	0.04
Outborn (n = 2750)	71 (17.9)	543 (23.1)	0.02
Maternal hypertension (n = 2688)	46 (12.0)	294 (12.8)	0.70
Diabetes (n = 2748)	41 (10.4)	222 (9.4)	0.57
Completed antenatal steroids (n = 2655)	172 (45.0)	933 (41.1)	0.14
Small for gestational age (n = 2743)	33 (8.3)	195 (8.3)	0.99
Chorioamnionitis (n = 2328)	70 (20.4)	498 (23.9)	0.16
Caesarean birth (n = 2651)	226 (56.9)	1281 (54.4)	0.35
Teenage mother (n = 2666)	120 (30.2)	591 (25.1)	0.03
Lone parent (n = 2455)	27 (6.9)	116 (5.1)	0.15
Primigravida (n = 2743)	19 (5.3)	120 (5.7)	0.72
Multiple births (n = 2751)	155 (39.1)	801 (34.1)	0.05

* SNAP-II: score of neonatal acute physiology.

Outborn status: preterm infants born in a non-tertiary care centre and then transferred to a tertiary care centre for further treatment.

maternal characteristics including medical conditions. Limitations of this study include the use of population-level parameters for assessing SES and missing individual socio-economic information. In addition, our classification regarding population density may not exactly fit with a clear rural–urban contrast. The usual caveats of unmeasured confounders also apply to our study, although a large number of covariates were used to adjust our models, which strengthens our findings.

Our study demonstrates that the income level and rurality of maternal residence has no impact on survival without major morbidity and most neonatal outcomes. However, our results showing horizontal “equity” of care across different SES groups need to be interpreted with caution. We did identify several “upstream” differences in the baseline characteristics of mothers from different income quintile groups. There were more outborn infants, teenage mothers, and infants born to single mothers in the lowest income (Q1) group. The presence of more outborn infants in the lowest SES group may be indicative of issues with availability/access to health services. From the literature, we know that the rates of preterm births are higher among lower SES groups²⁻⁷ and, if more of these births are outborn infants, this indicates that providers of prenatal services may need to take this into consideration, as survival at lower GA is improving in developed countries. Our study also supports the hypothesis of a pos-

Table 4. Rates and Adjusted Odds Ratios With 95% Confidence Intervals Comparing Population Density and Outcomes

Outcome	Rates		Adjusted Odds Ratios*	
	Population Density		Population Density	
	Sparsely Populated n (%)	Densely Populated n (%)	Sparsely Populated	Densely Populated
Survival without major morbidity	73 (19.4)	456 (21.1)	0.92 (0.67-1.26)	1
Mortality	100 (25.2)	480 (20.4)	1.14 (0.83-1.57)	1
Severe neurological injury	95 (27.3)	538 (26.0)	1.05 (0.77-1.42)	1
Chronic lung disease	164 (54.5)	984 (51.7)	1.21 (0.91-1.61)	1
Severe retinopathy of prematurity	57 (21.9)	329 (21.9)	0.95 (0.65-1.39)	1
Necrotizing enterocolitis	53 (13.7)	236 (10.2)	1.57 (1.11-2.22)	1

* Results adjusted for birth weight, teenage mother, sex, SNAP-II score group, Apgar score at 5 minutes, chorioamnionitis, outborn status, completed antenatal steroids, small for gestational age and Caesarean birth.

sible protective effect of breast milk for NEC. The finding that there is no disparity in the majority of morbidities in extremely preterm infants based on maternal SES or area of residence, despite having higher rates of adverse pregnancy outcomes for women residing in low SES areas, is reassuring. It is possible that Canada's universal health care and welfare system mitigates the adverse effects of socioeconomic status on the health of extremely preterm infants while they are in hospital. However, a cautionary note is warranted to reflect the fact that we have only evaluated outcomes prior to discharge from an NICU. It may be argued that, theoretically, parental SES should not have much impact on neonatal outcomes in the NICU because parents are not involved in the care of infants during that time, except for provision of breast milk. However, in modern NICUs, this is not the case as all NICUs positively seek parental participation in care provision and management from day one, starting with skin-to-skin contact in the resuscitation room and then involvement during clinical decision making at each step in the care pathway. On the other hand, the impact of socio-economic status on childhood neurodevelopmental outcomes is evident in several studies.²⁸⁻³⁰ This indicates that preventive efforts should be strongly encouraged for at-risk infants discharged into an adverse socio-economic environment. In particular, future studies should assess the follow-up of preterm infants discharged from NICUs with a similar risk of adverse outcomes and assess the impact based on their neighbourhood income level to tease out the timing of onset of adversity in at-risk infants.

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RÉSUMÉ

Objectifs : Déterminer l'impact du revenu du quartier et de la densité de population du lieu de résidence maternel sur la mortalité et sur diverses morbidités lors du congé ou du transfert des unités néonatales de soins intensifs chez les grands prématurés (<27 semaines de gestation) au Canada.

Méthode : Le niveau de revenu du quartier et le statut résidentiel ont été dérivés à l'aide d'un fichier de conversion du code postal et des données du Recensement. Au moyen d'une analyse de régression logistique multivariée, nous avons estimé le rapport de cotes ajusté selon le risque (RCA) pour la mortalité et pour la survie sans morbidité grave (pneumopathie chronique, entérocolite nécrosante néonatale, hémorragie intraventriculaire grave, rétinopathie des prématurés) chez 2 752 grands prématurés hospitalisés dans 25 unités de soins néonataux intensifs de niveau tertiaire au Canada entre 2007 et 2008.

Résultats : Nous n'avons constaté aucun écart significatif entre les mères de différents quintiles de revenu du quartier (Q1=faible; Q5=élevé) dans la mortalité néonatale (intervalle de confiance de 95 %) : Q1 : 1,10 (0,74-1,62), Q2 : 1,00 (0,67-1,49), Q3 : 1,39 (0,93-2,07), Q4 : 1,01 (0,67-1,52), Q5 : 1 (référence), ni dans la survie sans morbidité grave : Q1 : 1,01 (0,70-1,44), Q2 : 0,84 (0,58-1,23), Q3 : 0,85 (0,58-1,24), Q4 : 0,92 (0,63-1,35), Q5 : 1 (référence). Nous n'avons constaté aucun écart significatif non plus dans la mortalité (RCA 1,14 [0,83-1,57]) ou dans la survie sans morbidité grave (RCA 0,92 [0,67-1,26]) entre les nourrissons de mères habitant des zones à faible densité de population comparativement aux zones urbaines.

Conclusion : La résidence maternelle dans un quartier à faible revenu ou à faible densité de population n'était pas associée à une probabilité plus élevée de mortalité ou de survie sans morbidité grave chez les grands prématurés.

Mots clés : mortalité néonatale; morbidité; naissance prématurée; unité soins intensifs nouveau-né; statut socioéconomique