Maternal and Perinatal Outcomes of Pregnancies Delivered at 23 Weeks' Gestation

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Abstract

Objective: To evaluate the maternal and perinatal outcomes of pregnancies delivered at 23+0 to 23+6 weeks' gestation.

Methods: This prospective cohort study included women in the Canadian Perinatal Network who were admitted to one of 16 Canadian tertiary perinatal units between August 1, 2005, and March 31, 2011, and who delivered at 23+0 to 23+6 weeks' gestation. Women were included in the network if they were admitted with spontaneous preterm labour with contractions, a short cervix without contractions, prolapsing membranes with membranes at or beyond the external os or a dilated cervix, preterm premature rupture of membranes, intrauterine growth restriction, gestational hypertension, or antepartum hemorrhage. Maternal outcomes included Caesarean section, placental abruption, and serious complication. Perinatal outcomes were mortality and serious morbidity.

Results: A total of 248 women and 287 infants were included in the study. The rate of Caesarean section was 10.5% (26/248) and 40.3% of women (100/248) had a serious complication, the most common being chorioamnionitis (38.6%), followed by blood transfusion (4.5%). Of infants with known outcomes, perinatal mortality was 89.9% (223/248) (stillbirth 23.3% [67/287] and neonatal death 62.9% [156/248]). Of live born neonates with known outcomes (n = 181), 38.1% (69/181) were admitted to NICU. Of those admitted to NICU, neonatal death occurred in 63.8% (44/69). Among survivors at discharge, the rate of severe brain injury was 44.0% (11/25), of retinopathy of prematurity 58.3% (14/24), and of any serious neonatal morbidity 100% (25/25). Two subgroup analyses were performed: in one, antepartum stillbirths were excluded, and in the other only centres that indicated they offered fetal monitoring at 23 weeks' gestation were included and antepartum stillbirths were excluded. In each of these, perinatal outcomes similar to the overall group were found.

Conclusion: Pregnant women delivering at 23 weeks' gestation are at risk of morbidity. Their infants have high rates of serious morbidity and mortality. Further research is needed to identify strategies and forms of management that not only increase perinatal survival but also reduce morbidities in these extremely low gestational age infants and reduce maternal morbidity.

Key Words: Extreme preterm birth, periviable birth, maternal, perinatal

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Résumé

Objectif : Évaluer les issues maternelles et périnatales des grossesses donnant lieu à un accouchement entre 23+0 et 23+6 semaines de gestation.

Méthodes : Cette étude de cohorte prospective portait sur des femmes du Réseau périnatal canadien qui ont été admises à l'une des 16 unités périnatales tertiaires canadiennes participantes entre le 1er août 2005 et le 31 mars 2011, et qui ont accouché entre 23+0 et 23+6 semaines de gestation. Les femmes ont été admises dans le réseau si elles avaient été hospitalisées en raison d'un travail préterme spontané (s'accompagnant de contractions), d'un col court (sans contractions), d'un prolapsus des membranes (s'accompagnant d'une dilatation du col ou dans le cadre duquel les membranes se situaient au niveau de l'orifice externe ou faisaient saillie au-delà de ce dernier), d'une rupture prématurée des membranes préterme, d'un retard de croissance intra-utérin, d'une hypertension gestationnelle ou d'une hémorragie antepartum. Parmi les issues maternelles, on trouvait la césarienne, le décollement placentaire et la manifestation d'une complication grave. La morbidité grave et la mortalité constituaient les issues périnatales.

Résultats : En tout, 248 femmes et 287 nouveau-nés ont été inclus dans l'étude. Le taux de césarienne était de 10,5 % (26/248) et 40,3 % des femmes (100/248) ont connu une complication grave (la plus courante étant la chorioamnionite [38,6 %], suivie de la transfusion sanguine [4,5 %]). Parmi les nouveau-nés pour lesquels les issues étaient connues, le taux de mortalité périnatale était de 89,9 % (223/248) (taux de mortinaissance : 23,3 % [67/287] et taux de décès néonatal : 62,9 % [156/248]). Une admission à l'UNSI a été requise pour 38,1 % (69/181) des enfants nés vivants pour lesquels les issues étaient connues (n = 181). Parmi ces enfants ayant dû être admis à l'UNSI, un décès néonatal a été constaté dans 63,8 % (44/69) des cas. Chez les survivants (au moment de l'obtention de leur congé de l'UNSI), le taux de lésion cérébrale grave était de 44,0 % (11/25), le taux de rétinopathie des prématurés était de 58,3 % (14/24) et le taux de quelque morbidité néonatale grave que ce soit était de 100 % (25/25). Deux analyses de sous-groupe ont été menées : dans le cadre de l'une d'entre elles, les mortinaissances pendant la période antepartum ont été exclues; dans le cadre de l'autre, seuls les centres ayant indiqué qu'ils offraient le monitorage fœtal à 23 semaines de gestation ont été inclus et les mortinaissances pendant la période antepartum ont également été exclues. Des issues périnatales semblables à celles du groupe général ont été constatées dans chacune de ces analyses.

Conclusion : Les femmes enceintes qui accouchent à 23 semaines de gestation sont exposées à des risques de morbidité. Leurs nouveau-nés présentent des taux élevés de morbidité grave et de mortalité. La poursuite de la recherche s'avère requise pour permettre l'identification de stratégies et de formes de prise en charge qui entraînent non seulement une amélioration du taux de survie périnatale, mais également une baisse des taux de morbidité que connaissent ces nouveau-nés d'âge gestationnel extrêmement faible et les mères.

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INTRODUCTION

In Canada, preterm birth (less than 37 weeks' gestation) complicates 7.9 % of pregnancies, with 1.2% of all births occurring at less than 32 weeks' gestation.[1] Preterm birth can result in significant perinatal morbidity, both in the short term and long term, particularly in infants born at earlier gestational ages.[1–5] Multiple studies have evaluated perinatal outcomes of infants born in the periviable period (23 weeks' gestation).[3–39] Many of these studies, however, have excluded infants that were stillborn or that died before admission to NICU.[3,4,15,21–24,27,34] In addition, some studies present data based on birth weight and not gestational age.[29,40–44] Finally, a number of studies present data from populations that may differ from the Canadian population with respect to ethnicity and access to health care.[3,7–14,16–23,34,45] Few studies have evaluated maternal outcomes of women delivering at a periviable gestation.

It is important to consider maternal and perinatal outcomes, including stillbirth and neonatal death before NICU admission, when counselling and planning management of women admitted at 23 weeks' gestation with risk of preterm delivery. The objective of this study was to summarize the maternal and perinatal outcomes of pregnancies delivered at 23 weeks' gestation in tertiary perinatal care centres in Canada.

METHODS

The details of the Canadian Perinatal Network (CPN) have been published previously.[46] The mandate of the CPN is to focus on the maternal and perinatal outcomes and the optimal management of threatened very preterm birth at 22+0 weeks to 28+6 weeks of gestation. The CPN includes admissions to 16 of 23 tertiary perinatal units across Canada from August 1, 2005, to March 31, 2011.

Inclusion criteria for the CPN were women admitted between 22+0 weeks and 28+6 weeks of gestation inclusive to a participating tertiary perinatal unit, between August 1, 2005, and March 31, 2011, with at least one of the following indications: spontaneous preterm labour with contractions, short cervix without contractions (defined as a cervical length < 2.0 cm on endovaginal ultrasound without regular contractions), prolapsing membranes with membranes at or beyond the external os, or any cervical dilatation (on endovaginal ultrasound examination) without regular contractions, preterm premature rupture of membranes, intrauterine growth restriction (less than the 10th centile for gestational age), gestational hypertension (systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg on two occasions at least 4 hours apart after 20 weeks), or antepartum hemorrhage (> 15 mL of vaginal bleeding before the onset of labour). In this study we included women who delivered at 23+0 weeks to 23+6 weeks' gestation. Dating of the pregnancy was based on the clinician's best estimate using a combination of last menstrual period and ultrasound.

Data collected included maternal demographic factors (age, parity, weight, BMI, ethnicity, and socioeconomic status as determined by census enumerator data of neighbourhood income levels). Other maternal data included past obstetric, medical, and surgical history; aspects of the current pregnancy including the indication for enrolment in the CPN (preterm labour, prolapsing membranes, short cervix, growth restriction, antepartum hemorrhage, gestational hypertension), smoking, alcohol use, and illicit drug use during pregnancy; and interventions used during the pregnancy (including antibiotics, corticosteroids, tocolytics, and cervical cerclage). Other information regarding admission included gestational age at enrolment in CPN (admission), gestational age at delivery, latency from admission to delivery, route of delivery, and perinatal

Table 1. Maternal characteristics of women who delivered infants at 23+0 to 23+6 weeks' gestation (N = 248)

Characteristic	
Maternal age, years*	30.1 ± 6.3 30 [25.8 to 34]
Parity	
Nulliparous	53.6% (133/248)
Parous	46.4% (115/248)
Multiple pregnancy	18.6% (46/247)
Pre-pregnancy weight, kg (n =128)	71.9 ± 17.7 68 [58 to 81.7]
Pre-pregnancy BMI (kg/m^2) (n= 113)	26.9 ± 6.67 25 [22.3 to 31]
Underweight (BMI < 20.0 kg/m^2)	15.9% (18/113)
Normal weight (BMI 20.0 to 24.9 kg/m^2)	35.4% (40/113)
Overweight (BMI 25.0 to 29.9 kg/m^2)	20.4% (23/113)
Obese (BMI ≥ 30.0 kg/m^2)	28.3% (32/113)
Ethnicity (n = 158)	
Caucasian	62.0% (98/158)
Asian or Indo-Canadian	4.4% (7/158)
African-Canadian	13.3% (21/158)
Aboriginal	3.2% (5/158)
Other	17.1% (27/158)
Socioeconomic status (n = 219)†	$67 968 ± $14 916 $65 243 [$56 089 to $77 216]
Past obstetric history (parous women) (n = 115)	
Previous preterm birth < 37 weeks	33.0% (38/115)
Previous preterm birth < 34 weeks	23.5% (27/115)
Previous second trimester dilatation and evacuation	3.5% (4/115)
Previous stillbirth	11.3% (13/115)
Pre-existing medical conditions	
Pre-existing hypertension	4.0% (10/248)
Uterine structural abnormality	4.8% (12/248)

Results are mean ± standard deviation, % (n), or median [quartiles]

*Maternal age at estimated due date

†Expressed as median neighbourhood income levels, derived from postal codes and census enumerator data obtained from Statistics Canada

morbidity and mortality including stillbirth, neonatal death, birth weight, NICU admission, and serious morbidities (bronchopulmonary dysplasia, retinopathy of prematurity, severe brain injury, necrotizing enterocolitis, and sepsis). For neonates admitted to an NICU for at least 24 hours, probabilistic linkage was used to obtain data from the Canadian Neonatal Network, a sister network of CPN in the Maternal Infant Care Network. For babies admitted to NICU for less than 24 hours, or not admitted to NICU, data were obtained directly from the neonatal hospital record. Bronchopulmonary dysplasia was recorded as present if the infant required continuous supplemental oxygen at a postnatal gestational age of 36 weeks. Retinopathy of prematurity was recorded as present if stage 3, 4, or 5 retinopathy of prematurity was noted in the discharge summary. Severe brain injury was defined as any of intraventricular hemorrhage grade III or IV, ventricular enlargement with or without germinal matrix or intraventricular hemorrhage, parenchymal echodensities/lucencies in the white or grey matter, periventricular leucomalacia, evidence of diffuse brain lesions in the white matter (white matter injury) or multiple cysts in the white matter on ultrasound (cystic periventricular leucomalacia). Necrotizing enterocolitis was recorded as present if necrotizing enterocolitis, pneumatosis, or pneumatosis intestinalis, diagnosed by X-ray, at surgery, or at autopsy,

was recorded in the discharge summary. Neonatal sepsis was defined as having a positive blood or cerebrospinal fluid culture. Major congenital anomaly was recorded as present if the neonatal chart indicated a confirmed anomaly.

Maternal morbidity included placental abruption, intensive care unit admission, receipt of blood products, chorioamnionitis, and infection. Placental abruption was diagnosed clinically by the presence of abdominal pain or uterine contractions with vaginal bleeding or intrauterine death. Chorioamnionitis was diagnosed clinically (for example, by the presence of fetal tachycardia and abdominal tenderness with or without fever), by placental pathology (on the pathology report), or by culture of the maternal genital tract, placenta, or blood showing growth of Gram-negative bacteria or anaerobes. Infection included sepsis (definite evidence of infection with a systemic response to infection such as lactic acidosis, oliguria, or acute alteration in mental status) or endometritis (as indicated in the medical chart clinically or in the pathology report).

Descriptive statistics were calculated for maternal characteristics, obstetric complications, obstetric interventions, and maternal and perinatal outcomes. Categorical data were described as n (%) and continuous data as mean (standard deviation) or median (interquartile range), as appropriate. Two subgroup analyses were performed: in the first, antepartum stillbirths were excluded, and in the second antepartum stillbirths were excluded and only women who delivered at centres that offered fetal heart rate monitoring at 23 weeks' gestation (according to a survey of participating centres) and their infants were included.

The study was approved by the research ethics committees at each of the participating centres.

RESULTS

The tertiary centres in the study included all geographic regions (6 Western centres, 8 Ontario/Quebec centres, 2 Atlantic centres), with annual delivery rates of ≥ 5000 deliveries/year in six centres, 4000 to 4999 deliveries/year in two centres, 3000 to 3999 deliveries/year in five centres, and 2000 to 2999 deliveries/year in three centres. A total of 248 women and 287 infants were included in this study. The maternal characteristics of these women are summarized in Table 1. Almost one in five had multiple pregnancies, and approximately one half were nulliparous. Of those with BMI recorded, one quarter were obese. Of parous women, one third had a history of preterm birth, and over 10% had a history of a previous stillbirth.

Table 2. Obstetric complications and interventions of women who delivered infants at 23+0 to 23+6 weeks' gestation (N = 248)

Complication	
Smoking during pregnancy	17.3% (42/243)
Alcohol use during pregnancy	2.9% (7/243)
Illicit drug use during pregnancy	3.7% (9/243)
Polyhydramnios	2.9% (6/207)
Indicator conditions (occurrence any time)	
Preterm labour on enrolment	38.7% (96/248)
Short cervix*	10.1% (25/248)
Prolapsing membranes†	23.8% (59/248)
PPROM	41.1% (102/248)
IUGR	2.8% (7/248)
Gestational hypertension	5.2% (13/248)
APH	23.4% (58/248)
Interventions/investigations	
Fetal fibronectin testing	0.9% (1/116)
Corticosteroids for fetal lung maturation	34.3% (85/248)
Tocolytic use	23.8% (59/248)
Antibiotic use	72.2% (179/248)
Cerclage placement	14.9% (37/248)
Maternal transfer from another hospital	52.0% (128/246)

Results are % (n)

*Short cervix: cervical shortening < 2.0 cm by endovaginal ultrasound without regular contractions

†Prolapsing membranes: prolapsing membranes at or beyond the external as visualized on speculum examination, or any cervical dilatation of external os by endovaginal ultrasound, without regular contractions

PPROM: preterm premature rupture of membranes; IUGR: intrauterine growth restriction; APH: antepartum hemorrhage

The obstetric complications and interventions in these women are summarized in Table 2. Approximately one in six women smoked during their pregnancy, 2.9% used alcohol, and 3.7% used illicit drugs. The most common indication for inclusion that occurred either before or during admission was preterm premature ruptured membranes (41.1%); this was followed by preterm labour (38.7%), prolapsing membranes or cervical dilatation (23.8%), and antepartum hemorrhage (23.4%). Approximately one third of women received antenatal corticosteroids for fetal lung maturation (34.3%), approximately one quarter received a tocolytic agent (23.8%), and 72.2% received antibiotics. Cervical cerclage placement occurred in 14.9% of women. Of the 85 women who received corticosteroids, 18 (21.1%) received them at another institution.

Maternal outcomes of these women are presented in Table 3. The mean time from admission to delivery was two days, with 35.5% of women delivering on the day of admission. Approximately 10% of women delivered by Caesarean section. At least one serious maternal outcome

Table 3. Maternal outcomes of women who delivered infants at 23+0 to 23+6 weeks' gestation

Outcome	All women N = 248	Excluding women with antepartum stillbirth n = 234	Women delivering at centres that offer fetal monitoring at 23 weeks' gestation (excluding women with antepartum stillbirth) n = 50
Gestational age at enrolment, week	23.2 ± 0.4 23.2 [23 to 23.6]	23.2 ± 0.4 23.1 [23.0 to 23.6]	23.2 ± 0.4 23.2 [23.0 to 23.6]
Gestational age at delivery, week	23.5 ± 0.3 23.6 [23.1 to 23.7]	23.5 ± 0.4 23.4 [23.1 to 23.7]	23.5 ± 0.3 23.6 [23.2 to 23.7]
Latency from enrolment to delivery, days	2.0 ± 2.5 1 [0 to 3]	1.8 ± 2.4 1 [0 to 3]	1.8 ± 2.5 1 [0 to 2.8]
Delivery on day of admission	35.5% (88/248)	36.3% (85/234)	38.0% (19/50)
Caesarean section	10.5% (26/248)	10.7% (25/234)	22.0% (11/50)
Abruption	6.5% (16/247)	6.4% (15/233)	10.0% (5/50)
Serious maternal outcome	40.3% (100/248)	41.0% (96/234)	42.0% (21/50)
1 serious outcome	37.5% (93/248)	38.0% (89/234)	38.0% (19/50)
> 1 serious outcome	2.8% (7/248)	3.0% (7/234)	4.0% (2/50)
Chorioamnionitis	38.6% (91/236)	39.0% 87/223)	45.7% (21/46)
Blood product transfusion	4.5% (11/247)	4.3% (10/223)	4.0% (2/50)
ICU admission	0.4% (1/247)	0.4% (1/233)	0% (0/50)
Death	0% (0/247)	0% (0/233)	0% (0/50)
Severe maternal morbidity			
Infection	0% (0/247)	0% (0/233)	0% (0/50)
Respiratory complication	1.2% (3/248)	1.3% (3/234)	0% (0/50)
Hematologic complication	0.4% (1/248)	0.4% (1/234)	0% (0/50)
Other*	0.8% (2/248)	0.9% (2/234)	0% (0/50)

Results are % (n), mean ± standard deviation, or median [quartiles]

*Other = neurologic, cardiac, renal, hepatic

occurred in 40.3% of women; the most common of these was chorioamnionitis (38.6%), followed by blood product transfusion (4.5%). One woman required ICU admission, and there were no maternal deaths. Of the 91 cases of chorioamnionitis, 32 (35.2%) were based on clinical findings, 55 (60.4%) on placental pathology, and four (4.4%) on a positive culture. The maternal outcomes of the two subgroups were similar to the overall group, except that the Caesarean section rate was 22.0% in centres that indicated they offered fetal heart rate monitoring at 23 weeks' gestation (excluding antepartum stillbirths).

The outcomes for all infants are summarized in Figure 1. A total of 108 infants were admitted to NICU, but outcomes for 39 of these infants were not known because they were transferred to NICUs in pediatric hospitals that were not participating in CPN. Of all infants with known outcomes (N = 248), 23.3% (67/287) were stillborn and 62.9% (156/248) had a neonatal death; 71.8% (112/156) of neonatal deaths occurred before admission to NICU. Of all infants with a known outcome, only 10.1% (25/248) survived to be discharged from NICU. All survivors had at least one serious form of neonatal morbidity. The temporal trends in outcomes of infants during the time period of the study are shown in Figure 2. There were no significant differences in these outcomes over time (using Mann-Kendall test for trend). Details of the perinatal outcomes are shown in Table 4. Of all babies surviving to discharge (n = 25), approximately two thirds had bronchopulmonary dysplasia, over 50% had retinopathy of prematurity, and 44% had severe brain injury. The perinatal outcomes of the two subgroups were similar to the entire group, including similar rates of survival to discharge (25/232 [10.8%] in the subgroup excluding antepartum stillbirths and 5/39 [12.8%] in the subgroup excluding antepartum stillbirths and including infants born in centres that offered fetal heart rate monitoring at 23 weeks' gestation).

DISCUSSION

Previous research on extreme preterm birth has focused on perinatal outcomes and not maternal outcomes.[3–45] We found a high rate of chorioamnionitis in our study

Figure 1. Outcomes of all infants born at 23 weeks' gestation

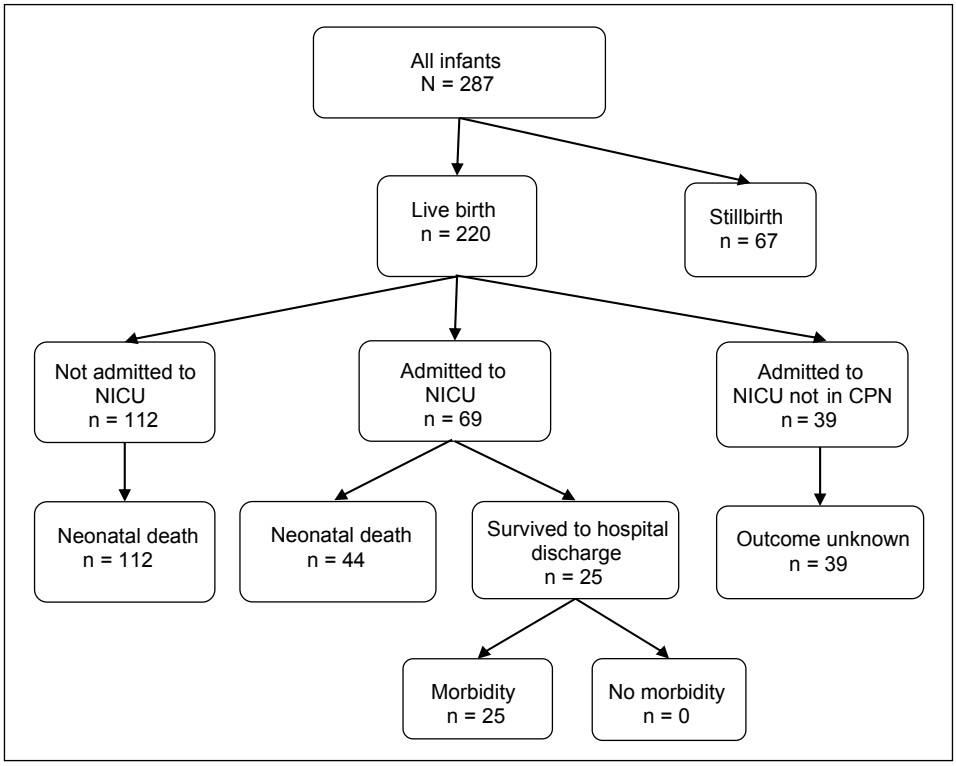
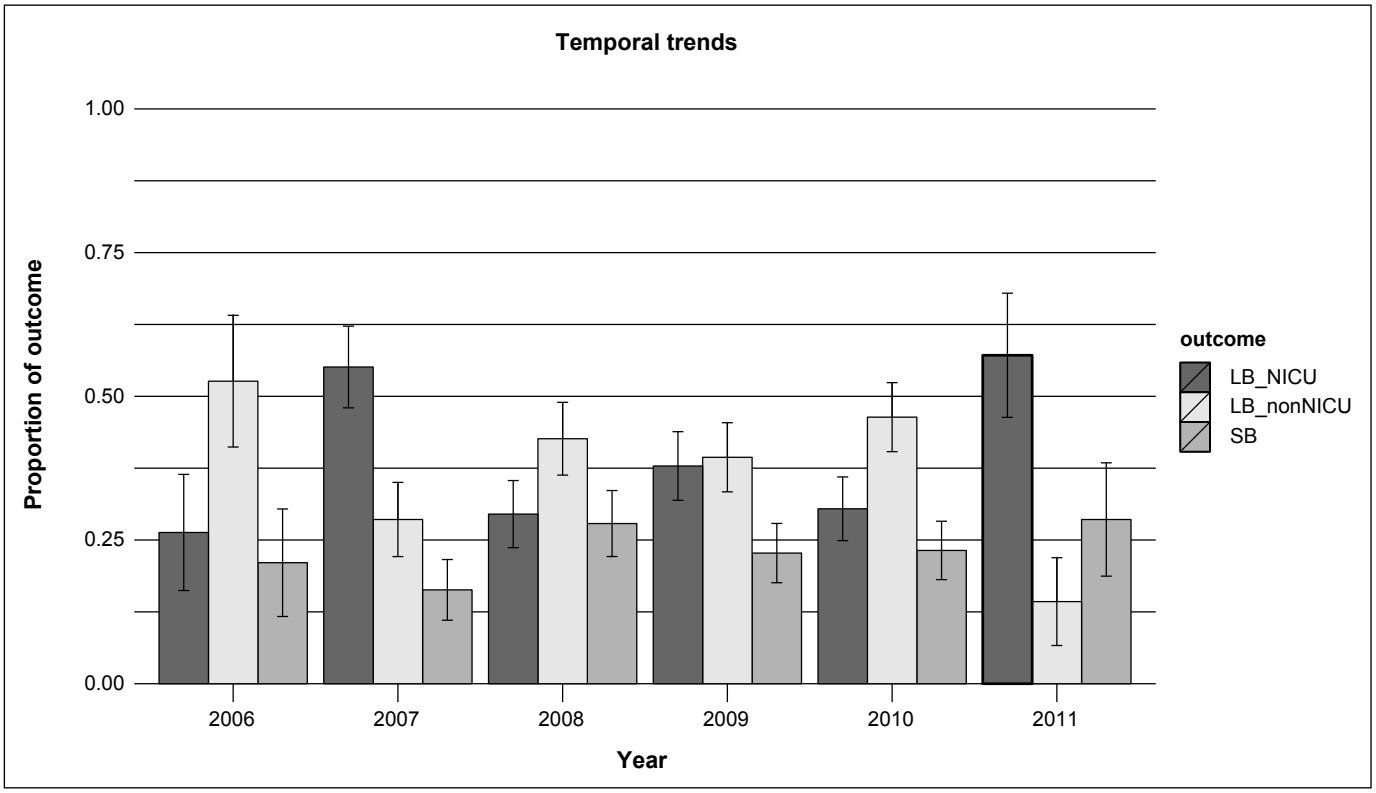


Figure 2. Temporal trends of neonatal outcomes by year of delivery



LB_NICU: live birth admitted to NICU; LB_nonNICU: live birth not admitted to NICU; SB: stillbirth

Table 4. Interventions and outcomes of infants born 23+0 to 23+6 weeks' gestation (N = 287)

Outcome	All infants N = 287	Excluding infants with antepartum stillbirth n = 271	Infants delivering at centres that offer fetal monitoring at 23 weeks' gestation (excluding infants with antepartum stillbirth) n = 54
Caesarean section	10.8% (31/287)	11.1% (30/271)	20.4% (11/54)
Male	52.3% (150/287)	50.9% (138/271)	57.4% (31/54)
Live births	79.5% (221/287)	81.2% (220/271)	87.0% (47/54)
Perinatal mortality*	89.9% (223/248)	89.2% (207/232)	87.2% (34/39)
Stillbirth	23.3% (67/287)	18.8% (51/271)	13.0% (7/54)
Neonatal death*	62.9% (156/248)	67.2% (156/232)	69.2% (27/39)
Perinatal mortality or severe morbidity*	100% (248/248)	100% (232/232)	100% (39/39)
Perinatal mortality or severe brain injury*	94.4% (234/248)	94.0% (218/232)	92.3% (36/39)
Congenital anomaly	9.3% (23/247)	9.1% (21/231)	7.9% (3/38)
Birthweight, grams	577 ± 101	581 ± 95	608 ± 84
Small for gestational age*			
< 10%	11.2% (32/287)	9.2% (25/271)	1.9% (1/54)
< 3%	4.5% (13/287)	3.3% (9/271)	0% (0/54)
NICU admission*	37.6% (108/287)	39.9% (108/271)	46.3% (25/54)
Perinatal morbidities for survivors	100% (25/25)	100% (25/25)	100% (5/5)
Bronchopulmonary dysplasia	64.0% (16/25)	64.0% (16/25)	60.0% (3/5)
Retinopathy of prematurity	58.3% (14/24)	58.3% (14/24)	40.0% (2/5)
Severe brain injury	44.0% (11/25)	44.0% (11/25)	40.0% (2/5)
Necrotizing enterocolitis	24.0% (6/25)	24.0% (6/25)	20.0% (1/5)
Neonatal sepsis	44.0% (11/25)	44.0% (11/25)	80.0% (4/5)
SNAPII score	11.8 ± 18.7 0 [0 to 21.8]	11.8 ± 18.7 0 [0 to 21.8]	9.5 ± 15.8 0 [0 to 19.5]

Results are % (n), mean ± standard deviation, median [quartiles]

*Includes all infants with follow up to death or hospital discharge

SNAPII: Score for Neonatal Acute Physiology 2nd version

cohort, based either on clinical diagnosis or on pathologic findings. In addition, we identified other serious maternal outcomes including blood product transfusion, respiratory complications, and ICU admission. It is important to recognize that these extreme preterm deliveries can result in significant maternal morbidity as well as perinatal morbidity and mortality. The rate of maternal morbidity may vary by the indication for admission; however, sample sizes for each indication were not large enough to allow comparison of maternal morbidity by indication. The Caesarean section rate of 10.8% may seem lower than expected, but likely reflects a decision by some women and health care providers not to intervene. When only centres that offered fetal heart rate monitoring at 23 weeks' gestation were included (and antepartum stillbirths were excluded), the Caesarean section rate increased to 22.0%, representing a higher rate of intrapartum intervention.

We found a high perinatal mortality rate in infants born at 23 weeks' gestation, with only 10.1% of all infants with known outcomes surviving to discharge. There were similar survival rates for the subgroups. The rate of survival was 10.8% (25/232) when antepartum stillbirths were excluded and 12.8% (5/39) in centres that offered fetal heart rate monitoring at 23 weeks' gestation. Previous studies have noted a wide range of survival rates for all births (including stillbirths) at this gestation, ranging from 0% to 37%.[5–7,9–12,14,17–19,36,37] Some studies present survival rates for live births only, ranging from 0% to 53%.[5,7,10,11,14,16–18,20,36,37,47] Other studies include only infants admitted to the NICU, with survival rates ranging from 0% to 66%.[4,9,11–15,17,18,20,21,23,24,34] Previous Canadian studies that did not include stillbirth noted survival rates in infants admitted to the NICU of 35.2% to 41.7%.[4,15,24] The survival rate was lower in our study. We included infants delivering at 23 weeks' gestation in participating centres, including stillbirths and neonatal deaths before admission to NICU, thus reducing selection bias. Different centres may have different resources and criteria for admission to NICU. In

the current study, 23.0% of all infants were stillborn and 39.4% died before admission to NICU. If we had included only infants admitted to the NICU with follow-up to discharge or death in NICU, the survival rate would have been 36.2% (25/69), thus overestimating the true perinatal survival rate.[5,45,48,49] The information on perinatal survival from our study allows us to counsel women admitted at 23 weeks' gestation more accurately regarding all possible outcomes of delivery in this gestational week.

A very high morbidity rate was noted among infants surviving to discharge, and all survivors had at least one serious morbid condition. This high rate is similar to those in other reports, which describe rates of survival without morbidity ranging from 7% to 28%.[3,4,9,14,15,24,42] Previous Canadian research has also noted rates of morbidity in survivors after admission to the NICU of 71.6% to 92.9%.[4,15,24] In the current study, morbidity included bronchopulmonary dysplasia, retinopathy of prematurity, severe brain injury, necrotizing enterocolitis, and sepsis. Some other studies did not include sepsis among morbidities.[4,15,24] Even excluding sepsis, the rate of morbidity in survivors was 96.0% for infants with known outcomes (24/25).

We found that approximately one third of women in our cohort received corticosteroids for fetal lung maturation. No randomized trials have evaluated corticosteroids at this gestational age,[50] although some cohort studies have suggested that they may be of benefit in reducing mortality and possibly intraventricular hemorrhage.[9,28,51–54] Further research is needed to determine if interventions such as administration of corticosteroids in this population does indeed reduce perinatal morbidity or mortality.

The mean latency from admission to delivery in the study cohort was only two days. This may be partly explained by the inclusion criteria of the CPN. The earliest gestational age at admission was 22 weeks. Thus women admitted before 22 weeks with obstetric complications were not included in the study. Also contributing to the short latency period may be the high rate of infection, as evidenced by a high rate of maternal chorioamnionitis. Additionally, the short latency may reflect the fact that patients or health care providers may not recognize early signs or symptoms of obstetric complications (such as preterm labour) that result in periviable birth, or that these early signs and symptoms are not obvious or evident.

Limitations of previous studies include reporting of outcomes by birth weight and not by gestational age.[40,43,44,55] Some studies have reported data from over two decades ago,[6,40,42,55] and survival has improved during this time period.[5,56] Older data may therefore not reflect current rates of morbidity and mortality. In addition, previously published studies evaluating populations without universal access to health care could potentially have different outcomes as a result of this lack of access.

Our study has a number of limitations. The CPN cohort does not include women admitted to hospital for reasons other than one of the indicator conditions, nor does it include women who were admitted before 22 weeks' gestation but who delivered at 23 weeks. Our study cohort likely included infants for whom a decision was made not to resuscitate, but planned palliative care was not a variable recorded in the database. The wishes of parents regarding interventions for infants delivered at 23 weeks' gestation may range from no intervention at all (with comfort care only) to assessment at delivery and resuscitation if the baby appears "vigorous," and to planned resuscitation at delivery.[45] The wishes of parents may also change during the course from admission to delivery.[45] It is not known how many women were not transferred to a tertiary centre because active neonatal resuscitation would not be offered and who consequently delivered in their community centre.

Active management of extremely preterm infants increases survival.[5,36,45,48] A survey of participating CPN centres from September 2011 to January 2012 noted variation among centres regarding the lowest gestational age at which fetal monitoring begins (at 23 weeks in 5 centres, and at 24 weeks in 9 centres), the lowest estimated fetal weight at which interventions for signs of fetal compromise are considered (at 400 g in 1 centre, at 500 g in 11 centres, and at 600 g in 2 centres), and actual birth weight at which active resuscitation occurs (at 400 g in 2 centres, and at 500 g in 11 centres).

Outcome data are missing for a number of infants in our study. A total of 39 infants (13.6% of the perinatal cohort) were transferred to NICUs that were not participating in CPN, and follow-up data are therefore not available for these infants. Because our study included only tertiary care perinatal centres, our findings may not be applicable to deliveries in other Canadian centres. Unfortunately, because of the absence of a shared national data set, we do not have information about the outcomes of mothers and babies delivering in non-CPN centres. Some demographic data, such as maternal BMI and ethnicity, were not available for all mothers and infants. We did not stratify levels of morbidity, and so cannot comment on the severity of morbidity. We did not perform subgroup analyses for perinatal outcomes by indicator condition because of small sample sizes. It might be expected that morbidity and mortality would be higher in some conditions, such as severe intrauterine growth restriction or preterm pre-

labour rupture of membranes with chorioamnionitis. We do not have data for infants after discharge and therefore cannot comment on long-term outcomes such as neurodevelopmental impairment. We did not evaluate regional or between-centre differences in maternal and perinatal morbidities or perinatal mortality. The rates of some maternal outcomes such as chorioamnionitis may vary between centres because of differences in diagnosis (clinical versus pathological).

A strength of our study is that all perinatal outcomes, including stillbirth and neonatal death, were evaluated, providing a more accurate reflection of perinatal outcomes and reducing selection bias. In addition to perinatal outcomes, our study also evaluated maternal outcomes, and included the majority (16 of 23) of tertiary care perinatal centres in Canada with recent data (from 2005 to 2011).

CONCLUSION

Pregnant women delivering at 23 weeks' gestation are at risk of morbidity. Their infants have high rates of serious morbidity and mortality, with only 10.1% in this cohort surviving to discharge from NICU and all survivors having one or more forms of neonatal morbidity. This low rate of survival may reflect a decision by some women and health care providers not to intervene, and does not necessarily reflect perinatal survival if the decision is made to provide active intrapartum intervention and aggressive resuscitation. This information can be used to counsel women and their families and can help in making decisions regarding the care and management of these women. It is also important for counselling to be individualized, based on each centre's experience. Further research is needed to identify strategies and management that will not only increase survival, but also reduce morbidities in these extremely low gestational age infants and reduce maternal morbidity.

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APPENDIX
CANADIAN PERINATAL NETWORK (CPN) COLLABORATIVE GROUP

This includes the CPN Steering Committee Members, CPN Site Investigators, current CPN Coordinator Dane De Silva, CPN Research Analyst Tang Lee, and CPN Database Manager Larry Li.

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