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Motor vehicle crashes during pregnancy and cerebral palsy during infancy: a longitudinal cohort analysis

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ABSTRACT

Objectives: To assess the incidence of cerebral palsy among children born to mothers who had their pregnancy complicated by a motor vehicle crash.

Design: Retrospective longitudinal cohort analysis of children born from 1 April 2002 to 31 March 2012 in Ontario, Canada.

Participants: Cases defined as pregnancies complicated by a motor vehicle crash and controls as remaining pregnancies with no crash.

Main outcome: Subsequent diagnosis of cerebral palsy by age 3 years.

Results: A total of 1 325 660 newborns were analysed, of whom 7933 were involved in a motor vehicle crash during pregnancy. A total of 2328 were subsequently diagnosed with cerebral palsy, equal to an absolute risk of 1.8 per 1000 newborns. For the entire cohort, motor vehicle crashes correlated with a 29% increased risk of subsequent cerebral palsy that was not statistically significant (95% CI −16 to +110, p=0.274). The increased risk was only significant for those with preterm birth who showed an 89% increased risk of subsequent cerebral palsy associated with a motor vehicle crash (95% CI +7 to +266, p=0.037). No significant increase was apparent for those with a term delivery (95% CI −62 to +79, p=0.510). A propensity score-matched analysis of preterm births (n=4384) yielded a 138% increased relative risk of cerebral palsy associated with a motor vehicle crash (95% CI +27 to +349, p=0.007), equal to an absolute increase of about 10.9 additional cases per 1000 newborns (18.2 vs 7.3, p=0.010).

Conclusions: Motor vehicle crashes during pregnancy may be associated with an increased risk of cerebral palsy among the subgroup of cases with preterm birth. The increase highlights a specific role for traffic safety advice in prenatal care.

Strengths and limitations of this study

- Motor vehicle crashes in pregnancy were identified in a large comprehensive population cohort of women who subsequently gave birth.
- Long-term outcomes among children were tracked longitudinally for 3 years to examine a subsequent diagnosis of cerebral palsy after delivery.
- The non-randomised design means that an association of motor vehicle crashes in pregnancy with an increased relative risk of cerebral palsy may not be causal.
- Children born at term despite a motor vehicle crash have no statistically significant increase in the absolute risk of cerebral palsy.
- Children born preterm following a motor vehicle crash do not have a large increase in the absolute risk of cerebral palsy.

BACKGROUND

Cerebral palsy is a leading cause of disability during childhood, with about 25 children diagnosed with cerebral palsy each day in the USA.[1] The severity spectrum spans from individuals living independently in the community to those needing comprehensive care in an institution. The average lifetime cost of cerebral palsy amounts to about $1 million in the USA.[2] Several risk factors for cerebral palsy have been identified including prematurity,[3–6] abnormal genetics,[7] multiple pregnancy,[8] maternal infections[9 10] and birth asphyxia.[11 12] However, most cases of cerebral palsy are unexplained and considered due to an unidentified injury to the young developing brain.[13–15]

Motor vehicle crashes are a common cause of maternal trauma,[16–18] complicating over 2000 per 100 000 pregnancies.[19 20] The consequences include maternal death (1 per 100 000 pregnancies) and fetal death (4 per 100 000 pregnancies).[18] The non-fatal short-term consequences of a motor vehicle crash include placental abruption, premature rupture of membranes, uterine disruption or early delivery.[21–23] Fetal injury following a motor vehicle crash correlates imperfectly with the severity of maternal injury, can occur without direct uterine injury and may have a delayed presentation.[24] Maternal trauma from a motor vehicle crash, therefore, might cause injury to a young developing brain.

Several mechanisms could contribute to a possible association between a motor vehicle crash during pregnancy and subsequent cerebral palsy during infancy. The most direct mechanism is acute trauma leading to preterm birth.[25] Less direct mechanisms include fetal cerebral hypoxia caused by maternal hypotension.[26 27] Other possibilities include a stress response involving the maternal autonomic vascular or metabolic systems that compromises uterine perfusion.[28 29] A further mechanism relates to chronic placental insufficiency from clot formation or traumatic shear forces.[30 31] These mechanisms, however, are speculative and no population-based study has tested whether cerebral palsy during infancy might be linked to a motor vehicle crash during pregnancy.

METHODS

Study setting

We conducted a retrospective longitudinal population-based cohort study using data sets from the Institute for Clinical Evaluative Sciences (ICES).[32] These data sets integrate information from medical encounters by patients throughout the Ontario healthcare system as covered by the universal health insurance plan.[33] This plan provided all-inclusive access to care with no cost to patients for emergency or prenatal treatments, thereby providing comprehensive longitudinal patient data for analysis. Patients were not involved in setting the research agenda.

Pregnancy identification

We identified women (age 14–50 years) who gave birth between 1 April 2002 and 31 March 2012 by screening physician codes for a newborn delivery (codes P006, P018, P020) using the MOM-BABY database at ICES.[34 35] Abortions were excluded and repeat pregnancies were counted as separate events.[36] One woman, therefore, was counted for each birth and twins were counted as separate observations. Each pregnancy was categorised as complicated or not complicated by a motor vehicle crash, defined as a traffic event sending the woman to an emergency department.[37] Regardless of crashes, we also distinguished each pregnancy followed by a preterm delivery (International Statistical Classification of Diseases (ICD) V.10 codes O60) or followed by an at-term or post-term delivery.

Newborn identification

Children were identified using the MOM-BABY database at ICES that linked maternal and birth records with 98% completeness.[38 39] The database has been used extensively.[40–43] We excluded individuals with faulty medical records, living outside Ontario or high-order multiple births; otherwise, the sampling was comprehensive and complete. Limitations of the database include the lack of direct information on sibling relationships, paternal connections and home environment. The database also lacked information about multiple lifestyle behaviours including smoking, alcohol, substance abuse, domestic violence, dietary intake, toxin exposure, marital status and other social determinants of health.

Identification of crashes

We identified motor vehicle crashes using validated diagnostic codes from all emergency departments throughout Ontario (ICD V.10 codes V00-V69).[44] This definition reflected motor vehicle crashes that sent the woman as a patient to an emergency department, including events as drivers, passengers, or other road users and excluding events related to aircraft or watercraft. Additional crash characteristics included day, season, clock-time (morning, afternoon, night), position (driver, passenger, other), enrolment interval (first 5 years, second 5 years), ambulance involvement (yes, no) and triage urgency (higher, lower). For each case, we also determined whether subsequent newborn delivery occurred within 48 hours of the crash.

Identification of cerebral palsy

Newborns were followed for 3 years to determine survival and subsequent diagnosis since most cerebral palsy is diagnosed by age 3 years.[45 46] Diagnostic codes were used to search for a physician diagnosis of cerebral palsy (ICD V.9 code 343, V.10 code G80).[42] We further distinguished cerebral palsy cases as explained or unexplained according to known antecedents, namely congenital abnormalities, maternal infection, birth asphyxia, illicit drug use and bleeding complication[10–12 47] (ICD V.10 codes Q00 to Q99; P02 to P04; P10-P15; P20-P21; P36 to P39). We did not define prematurity as a direct explanation because it might be an intermediate mechanism (explored in secondary analysis).

Identification of additional predictors

The demographic registry was used to obtain maternal data on age, socioeconomic status and home location (urban, rural).[48] Prenatal care, pregnancy duration, mode of delivery, twin gestations and length of hospital stay were determined based on linked identifiers.[49–51] Primiparity and multiparity were based on birth records from the previous 20 years. Neonatal variables included prematurity (binary), sex (binary), day of delivery (weekend vs weekday) and enrolment interval (first 5 years, second 5 years).[3 5 6 52] The databases did not contain driving history, roadway infractions, chosen destinations, license status, travel diaries, vehicle distances, injury severity or impact velocity.

Statistical analysis

The primary study outcome was the risk of a subsequent diagnosis of cerebral palsy by age 3 years. The main analysis used proportional hazards analysis to compare children born after a pregnancy complicated by a motor vehicle crash to children born after a pregnancy not complicated by a motor vehicle crash. HRs were used for relative risk estimates and interval deaths were censored in the primary analysis (considered in secondary analysis). Stratified analyses assessed differences according to individual characteristics with special attention to preterm births.[49 53] We also used propensity-matched analysis to re-examine preterm births and re-evaluate the risk of cerebral palsy after accounting for other baseline characteristics. More extensive regressions with interaction terms were not conducted due to small numerators in some groups.

RESULTS

Maternal characteristics

A total of 884 897 women gave birth to 1 325 660 newborn children, of whom 7933 newborns (1 in 170) had the pregnancy complicated by a motor vehicle crash. As expected, motor vehicle crashes involved women across a wide spectrum of age, socioeconomic status and experience (table 1). The mean maternal age was 29.9 years and slightly lower for those pregnancies complicated by a motor vehicle crash compared with those pregnancies not complicated by a motor vehicle crash. Otherwise, the distributions of socioeconomic status, home location, prenatal care visits, parity, pregnancy duration, mode of delivery and hospital length of stay were similar for the two groups. A total of 38 women had more than one crash during pregnancy. A total of 52 women delivered within 48 hours of a crash.

Table 1 Maternal and newborn characteristics (n=1 325 660)

Characteristic	Motor vehicle crash Present (n=7933)	Motor vehicle crash Absent (n=1 317 727)
Age		
<25	2112 (27)	225 742 (17)
25–35	4887 (62)	884 878 (67)
>35	934 (12)	207 107 (16)
Socioeconomic status*		
Higher	2757 (35)	488 943 (37)
Middle	1610 (20)	266 435 (20)
Lower	3566 (45)	562 349 (43)
Home location		
Urban	6891 (87)	1 182 313 (90)
Rural	1042 (13)	135 414 (10)
Enrolment interval		
First 5 years	4011 (51)	645 370 (49)
Second 5 years	3922 (49)	672 357 (51)
Prenatal care†		
≥13 clinic encounters	7422 (94)	1 147 405 (87)
≥1 hospital admission	3253 (41)	438 570 (33)
Parity		
Primiparous	3968 (50)	597 344 (45)
Multiparous	3965 (50)	720 383 (55)
Pregnancy duration		
Preterm‡	548 (7)	86 887 (7)
At-term	6481 (82)	1 080 323 (82)
Post-term §	904 (11)	150 517 (11)
Mode of delivery		
Vaginal	5657 (71)	952 375 (72)
Caesarean	2276 (29)	365 352 (28)
Newborn child		
Male	3973 (50)	669 801 (51)
Female	3870 (49)	635 266 (48)
Not recorded	90 (1)	12 660 (1)
Length of hospital stay		
≤3 days	4739 (60)	826 711 (63)
≥4 days	3194 (40)	491 016 (37)

Values are count (percentage) of each group.
Each pregnancy counted as a separate event.
*Based on median neighbourhood income quintile.
†In previous year.
‡Maternal ICD-10 code O60.
§Maternal ICD-10 code O48.
ICD, International Statistical Classification of Diseases.

Subsequent child outcomes

A total of 2328 children were diagnosed with cerebral palsy by age 3 years (1 325 660 identified newborns, 5425 interval deaths). The median age at cerebral palsy diagnosis was 586 days and median age at death was 7 days. The most common identified reasons linked to cerebral palsy were perinatal disorders and congenital abnormalities, collectively accounting for 1225 children (53%). The remaining 1103 children (47%) were classified as having unexplained cerebral palsy. The median age for diagnosing unexplained cerebral palsy was 610 days. The overall rate of cerebral palsy per 1000 pregnancies was about the same in the first 5 years of the study and the second 5 years of the study (1.82 vs 1.70, respectively).

Motor vehicle crashes and cerebral palsy risk

A total of 18 children diagnosed with cerebral palsy were born following 7933 pregnancies complicated by a motor vehicle crash. In contrast, 2310 children with cerebral palsy were born following 1 317 727 pregnancies with no motor vehicle crash. The difference in risk equalled a marginally increased incidence of cerebral palsy associated with motor vehicle crashes per 1000 pregnancies (2.27 vs 1.75, p=0.274), equal to a 29% relative increase in risk (95% CI −16 to +110). The absolute difference amounted to 685 fewer cases of cerebral palsy among those who did not have a crash during pregnancy. The increased risk was most apparent before age 2 years (see online supplementary appendix).

Patient characteristics

The increased risk of cerebral palsy associated with a motor vehicle crash was evident for subgroups with different characteristics (table 2). The highest observed relative risks were among pregnancies followed by a preterm delivery that showed an 89% relative increase in risk (95% CI +7 to +266, p=0.037). No significant

Table 2 Subsequent cerebral palsy diagnosis

	Total cases of cerebral palsy	Relative risk after crash	CI
Full cohort	2328	1.29	0.84 to 2.10
Age			
<25	451	1.20	0.57 to 3.06
25–35	1479	1.48	0.88 to 2.69
>35	398	0.56	0.17 to 4.16
Socioeconomic			
Higher	794	1.58	0.82 to 3.47
Middle	478	0.35	0.10 to 2.58
Lower	1056	1.51	0.86 to 2.91
Home location			
Urban	2087	1.41	0.91 to 2.32
Rural	241	0.54	0.16 to 4.04
Enrolment interval			
First 5 years	1179	1.65	0.99 to 3.01
Second 5 years	1149	0.90	0.45 to 2.11
Prenatal care			
≥13 clinic visits	1982	1.26	0.80 to 2.11
≥1 admissions	1069	1.14	0.64 to 2.29
Parity			
Primiparous	1179	1.16	0.64 to 2.32
Multiparous	1149	1.43	0.80 to 2.87
Pregnancy duration			
Preterm	850	1.89	1.07 to 3.66
At-term	1314	0.76	0.38 to 1.79
Post-term	164	2.06	0.73 to 8.94
Mode of delivery			
Vaginal	1285	1.05	0.57 to 2.20
Caesarean	1043	1.55	0.89 to 3.00
Newborn child			
Male	1339	1.52	0.91 to 2.77
Female	989	1.00	0.50 to 2.34
Length of stay			
≤3 days	1026	1.37	0.74 to 2.86
≥4 days	1302	1.19	0.68 to 2.29

Estimates provide results from subgroup analyses (full cohort listed at top).
Referent based on pregnancies with no motor vehicle crash.
Relative risk estimate from proportional hazards analysis (Cox regression).
CI based on 95% limits using normal approximation (Wald statistic).

increase was apparent among the large number of pregnancies followed by a term delivery or among the small number of pregnancies followed by post-term delivery. All CIs were wide, almost all upper bounds overlapped a 100% relative increase in risk, and no subgroup showed a statistically significant contrary pattern.

Additional predictors in cases with preterm birth

Several baseline characteristics were also associated with cerebral palsy following a preterm birth (table 3). Older age predicted lower risk, whereas socioeconomic status and home location were not significant predictors. Those born in recent years had a lower risk. Prenatal care visits were associated with lower risk. Conversely, past hospitalisations predicted higher risk (perhaps as a proxy for underlying patient illnesses). As expected, cerebral palsy was more frequent in boys. The absolute rate of cerebral palsy averaged about 9.7 per 1000 pregnancies among all newborns with preterm birth (estimate essentially unchanged in analyses that excluded interval deaths or analyses that excluded the 12 cases with preterm birth who delivered within 48 hours of a crash).

Propensity-matched analysis in preterm birth

Propensity score matching yielded a cohort of 4384 newborns with preterm birth, of whom 548 had the pregnancy complicated by a motor vehicle crash and the remaining 3836 had no complicating motor vehicle crash (matching ratio 1 in 7 by design). As expected, the distribution of maternal characteristics was similar for the two groups (table 4). A total of 38 children were subsequently diagnosed with cerebral palsy, equal to a 138% increased relative risk of cerebral palsy associated with a

Table 3 Additional predictors of cerebral palsy risk in preterm newborns

	Univariate analysis*		Multivariable analysis†	
Predictor	Relative risk	CI	Relative risk	CI
Age (per year older)	0.82	0.73 to 0.93	0.86	0.76 to 0.97
Socioeconomic (low)	0.98	0.84 to 1.14	–	–
Home (rural)	1.22	0.98 to 1.51	–	–
Enrolment (recent)	0.82	0.72 to 0.94	0.84	0.73 to 0.96
Prenatal care ≥13 encounters ‡	0.83	0.69 to 0.99	0.80	0.66 to 0.95
Hospital care ≥1 admission ‡	1.25	1.09 to 1.43	1.24	1.08 to 1.43
Parity (multiparous)	0.85	0.74 to 0.97	0.89	0.78 to 1.03
Newborn (male)	1.32	1.15 to 1.52	1.32	1.15 to 1.52

Analyses based on 850 events in 87 435 children (absolute risk=9.7 per 1000).
Relative risk estimate from proportional hazards analysis (Cox regression).
CI based on 95% limits using normal approximation (Wald statistic).
*Basic univariate comparison with no adjustments for other baseline differences.
†Adjusted multivariable comparison accounting for significant univariate predictors.
‡In previous year.

motor vehicle crash (95% CI +27 to +349, p=0.007). The absolute risk of cerebral palsy equalled 10.9 additional cases per 1000 pregnancies complicated by a motor vehicle crash (18.2 vs 7.3, p=0.010). Repeating the analysis after excluding twins yielded a similar absolute increase (17.7 vs 7.9, p=0.034).

Crash features

The increased overall risk of cerebral palsy associated with a motor vehicle crash was evident for crashes with different features (table 5). The most frequent time for a crash was a weekday and no large seasonal variation was apparent. The second trimester accounted for a disproportionate number of crashes and afternoon hours accounted for more than half of the crashes. All secondary estimates overlapped the primary analysis, most showed a nominal increase in relative risk, and most were not statistically significant in isolation. Afternoon crashes were a high outlier and associated with a 91% increased relative risk of cerebral palsy (95% CI +19 to +225, p=0.011). About half of the crashes received subsequent ambulance transport and most were assigned high triage urgency.

DISCUSSION

We studied over a million newborn children and found that a motor vehicle crash during pregnancy was associated with an increased subsequent risk of cerebral palsy among cases with preterm birth. The baseline rate of cerebral palsy was similar to past reports and the most frequent predictor was preterm birth (observed in 1 in 15 newborns and 1 in 3 cases of cerebral palsy, equal to a fivefold increased cerebral palsy risk).[1 54] The relative risk of cerebral palsy associated with a motor vehicle crash was particularly large for those with preterm birth after propensity score adjustment for imbalances in measured baseline characteristics. The most vulnerable interval was afternoon traffic that explained more than half the crashes.

Our research supports past reports describing an increased risk of cerebral palsy following a motor vehicle crash. A case series of 10 children with cerebral palsy following pregnancies complicated by a motor vehicle crash found brain lesions on MRI consistent with cerebral vascular damage from trauma.[30] Individual case reports have also described maternal injury causing fetal intracranial haemorrhage.[55–60] Direct injury to fetal brain tissue or diffuse axonal injury without brain deformation may be other possible mechanisms described in animal models.[61 62] In contrast, no study, to the best of our knowledge, suggests that a motor vehicle crash in pregnancy might decrease the risk of cerebral palsy.

A different set of possible mechanisms involves indirect injury to the fetus from placental compromise. Blunt trauma may cause the placenta to shear from the uterus resulting in placental blood flow insufficiency.[63] The extreme case is placental abruption and preterm birth; however, less severe trauma might result in small degrees of shearing and losses in perfusion that chronically deprive the fetus of nutrients needed for brain development.[21] A related speculative mechanism is transient placental underperfusion due to maternal catecholamine surges from acute stress that shunt blood flow away from uterine arteries.[64 65] Regardless of potential mechanisms, our study also indicates that the fetus is resilient because the vast majority of motor vehicle crashes during pregnancy do not result in cerebral palsy.

An important limitation of our research relates to random chance and statistical imprecision (since a high number of term births can mask a significant difference among the preterm group). Collectively, the observed frequency of motor vehicle crashes exceeded 1 per 200 pregnant women and the sample size for the whole cohort amounted to about four million patient-years of follow-up. However, the estimated relative risks of cerebral palsy associated with a motor vehicle crash were wide, overlapped the null and ranged to more than a

Table 4 Propensity score-matched analysis of preterm newborns (n=4384)*

Characteristic	Motor vehicle crash Present † (n=548)	Motor vehicle crash Absent ‡ (n=3836)
Age		
<25	132 (24)	933 (24)
25–35	351 (64)	2430 (63)
>35	65 (12)	473 (12)
Socioeconomic status§		
Higher	181 (33)	1230 (32)
Middle	104 (19)	762 (20)
Lower	263 (48)	1844 (48)
Home location		
Urban	485 (89)	3447 (90)
Rural	63 (11)	389 (10)
Enrolment interval		
First 5 years	277 (51)	1970 (51)
Second 5 years	271 (49)	1866 (49)
Prenatal care¶		
≥13 clinic encounters	516 (94)	3620 (94)
≥1 hospital admission	322 (59)	2278 (59)
Parity		
Primiparous	288 (53)	2024 (53)
Multiparous	260 (47)	1812 (47)
Pregnancy duration		
Preterm	548 (100)	3836 (100)
At-term	–	–
Post-term	–	–
Mode of delivery		
Vaginal	321 (59)	2255 (59)
Caesarean	227 (41)	1581 (41)
Newborn child		
Male	287 (52)	2036 (53)
Female	252 (46)	1761 (46)
Not recorded	9 (2)	39 (1)
Length of hospital stay		
≤3 days	173 (32)	1224 (32)
≥4 days	375 (68)	2612 (68)

Values are count (percentage) of each group.
*All data from propensity-matched analysis of original cohort.
†Crash present group includes all cases with preterm birth.
‡Crash absent group includes those from 1:7 matching of cases to controls.
§Based on median neighbourhood income quintile.
¶In previous year.

Table 5 Crash features and cerebral palsy risk

	Total pregnancies with a crash	Relative risk after crash	CI
Full cohort	7933	1.29	0.84 to 2.10
Crash position			
Driver	4358	1.57	0.94 to 2.85
Not driver	3575	0.96	0.48 to 2.24
Crash day			
Weekend	1982	1.73	0.86 to 4.04
Weekday	5951	1.15	0.69 to 2.09
Crash season			
Spring/Summer	3717	1.07	0.56 to 2.36
Autumn/Winter	4216	1.49	0.87 to 2.78
Pregnancy trimester			
First	2457	1.39	0.70 to 3.26
Second	3714	1.08	0.56 to 2.36
Third	1762	1.62	0.77 to 4.11
Vehicle			
Car	7100	1.12	0.69 to 1.95
Other	833	2.74	1.22 to 7.78
Time of day			
Morning	1719	0.66	0.24 to 2.87
Afternoon	4488	1.91	1.19 to 3.25
Night	1726	0.33	0.10 to 2.46
Ambulance arrival			
Yes	3957	1.30	0.72 to 2.59
No	3976	1.29	0.72 to 2.58
Triage urgency			
Higher	5525	1.45	0.89 to 2.51
Lower	2408	0.95	0.42 to 2.69

Estimates provide results from subgroup analyses (full cohort listed at top).
Referent based on pregnancies with no motor vehicle crash.
Relative risks estimate from proportional hazards model.
CI based on 95% limits.

100% increase. Taking into account term births, we estimate that future research may require a sample size exceeding 20 million patient-years of follow-up to confirm or refute our findings. We doubt such data will be available soon.

Our study has several other limitations. Women who have adverse behaviours during pregnancy (eg, alcohol) may have both an increased risk of a motor vehicle crash during pregnancy as well as an increased risk of preterm birth.[66] Maternal and delivery characteristics were unavailable (eg, APGAR scores, differing degrees of prematurity), as were data on biomechanical forces and minor crashes receiving no medical attention.[67] The total number of observed crashes was not enormous and the totality of all-cause maternal trauma would be greater due to injuries from falls, assault and self-harm.[18] Details of the severity of the crashes were also not known and most crashes did not result in cerebral palsy. Subgroup analyses are also prone to chance findings and analyses adjusting for an intermediate feature along a causal pathway can lead to underestimated risks.[68 69] More research is justified examining these and other clinical distinctions.

Previous data suggest that pregnant women have a significant incidence of a motor vehicle crash during pregnancy.[23 70] Few studies describe the long-term consequences of maternal trauma on the surviving children. Our data suggest that a motor vehicle crash during pregnancy might increase the subsequent risk of cerebral palsy in cases of preterm birth. These results highlight an opportunity around prenatal traffic safety counselling for reducing the risks to a developing fetus.[71 72] Injuries due to motor vehicle crashes may be particularly important and relevant since they are often preventable by following standard safety warnings. Avoiding a crash might possibly prevent a wide range of disability.

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