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Research Letter

Risk of Postpartum Opioid Use Disorder or Opioid Overdose After Prenatal Opioid Analgesic Use

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INTRODUCTION

Four percent of women use opioids for pain in pregnancy in the United States and Canada.[1,2] An increased risk of postpartum opioid overdose among women with opioid use disorder (OUD) has been observed; however, the risk of opioid-related harm among women with prenatal opioid analgesic use and no prior OUD is unknown.[3–5] We used administrative health data to estimate the risk of and factors associated with postpartum OUD or opioid overdose in prenatally exposed women.

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METHODS

We followed a population-based cohort in the single-payer health care system in Ontario, Canada, accessed through linked health administrative data at ICES, an independent, nonprofit research institute whose legal status under Ontario's health information privacy law allows collection and analysis of data, without consent, for health system evaluation. We included women with an estimated due date after April 7, 2013, which corresponded to data availability, through March 31, 2018, with prescription opioid analgesic fills during pregnancy.[1] Opioid prescriptions were identified from the linked Narcotics Monitoring System, which records all community pharmacy–dispensed narcotic prescriptions irrespective of payment type. Women with OUD or an opioid overdose 2 years before delivery were excluded. The Queen's University Health Sciences Research Ethics Board approved this study [#6026353].

A priori risk factors included[5,6] prenatal opioid analgesic duration, average daily dose dispensed (morphine equivalents), prescribed prenatal benzodiazepines, age, parity, neighborhood-level income quintile, rural residence, social disadvantage, Elixhauser comorbidity score, pain diagnosis, mental health diagnosis, substance use disorder other than OUD, opioid analgesic use 1 year before conception, neonatal abstinence syndrome, and cesarean delivery.

Study outcomes were OUD or opioid overdose within 365 days of delivery, defined as 1) opioid agonist therapy prescription, 2) outpatient opioid agonist therapy visit, 3) emergency department visits or hospitalizations for OUD or opioid overdose, or 4) opioid-related death. Logistic regression models were used to estimate crude and adjusted odds ratios and 95% CIs. Analyses were performed using SAS 9.4.

Table 1. Factors Associated With Opioid Use Disorder or Opioid Overdose* Between Delivery and 365 Days Postpartum Among Women With Prenatal Prescription Opioid Analgesic Use†

Variable	OUD or Opioid Overdose Between Delivery and 365 d Postpartum*		Unadjusted OR (95% CI)	Adjusted OR (95% CI)‡
	Yes (n=224)	No (n=26,968)		
Age (y)				
12–24	59 (26.3)	4,157 (15.4)	1.74 (1.28–2.37)	1.76 (1.26–2.44)
25–34	133 (59.4)	16,308 (60.5)	1.00 (ref)	1.00 (ref)
35–50	32 (14.3)	6,503 (24.1)	0.60 (0.41–0.89)	0.58 (0.39–0.86)
Neighborhood-level income quintile				
1 (lowest income)	99 (44.2)	7,011 (26.0)	2.25 (1.73–2.94)	1.80 (1.37–2.37)
2–5	125 (55.8)	19,957 (74.0)	1.00 (ref)	1.00 (ref)
Rural residence				
Rural	46 (20.5)	2,981 (11.1)	2.08 (1.50–2.88)	1.81 (1.29–2.54)
Urban	178 (79.5)	23,987 (88.9)	1.00 (ref)	1.00 (ref)
Prior live birth				
No	183 (81.7)	22,114 (82.0)	1.00 (ref)	1.00 (ref)
Yes	41 (18.3)	4,854 (18.0)	1.02 (0.73–1.44)	1.03 (0.72–1.45)
History of social risk factors§				
No	212 (94.6)	26,540 (98.4)	1.00 (ref)	1.00 (ref)
Yes	12 (5.4)	428 (1.6)	3.51 (1.95–6.33)	1.73 (0.91–3.32)
Elixhauser comorbidity score				
0	210 (93.8)	26,374 (97.8)	1.00 (ref)	1.00 (ref)
1 or higher	14 (6.3)	594 (2.2)	2.96 (1.71–5.11)	1.23 (0.69–2.21)
History of maternal pain diagnosis‖				
Absent	137 (61.2)	22,485 (83.4)	1.00 (ref)	1.00 (ref)
Present	87 (38.8)	4,483 (16.6)	3.18 (2.43–4.17)	1.79 (1.33–2.41)
History of mental health diagnosis				
Absent	197 (87.9)	26,219 (97.2)	1.00 (ref)	1.00 (ref)
Present	27 (12.1)	749 (2.8)	4.80 (3.19–7.22)	2.11 (1.31–3.41)
History of nonopioid substance use disorder				
Absent	214 (95.5)	26,803 (99.4)	1.00 (ref)	1.00 (ref)
Present	10 (4.5)	165 (0.6)	7.59 (3.95–14.57)	2.91 (1.34–6.32)
Opioid analgesic use 1 y before conception				
Absent	88 (39.3)	18,410 (68.3)	1.00 (ref)	1.00 (ref)
Present	136 (60.7)	8,558 (31.7)	3.32 (2.54–4.35)	1.20 (0.87–1.66)
Duration of prenatal opioid analgesic use (d)				
1–29	105 (46.9)	24,126 (89.5)	1.00 (ref)	1.00 (ref)
30 or more	119 (53.1)	2,842 (10.5)	9.61 (7.37–12.54)	7.12 (5.14–9.86)
Average daily dose of opioid analgesics (MEQ)				
50 or less	11 (4.9)	3,596 (13.3)	1.00 (ref)	1.00 (ref)
51–90	16 (7.1)	5,648 (20.9)	0.93 (0.43–2.00)	0.86 (0.40–1.87)
More than 90	197 (87.9)	17,709 (65.7)	3.64 (1.98–6.68)	1.63 (0.87–3.07)
Prescribed benzodiazepines				
Absent	167 (74.6)	24,253 (89.9)	1.00 (ref)	1.00 (ref)
Present	57 (25.4)	2,715 (10.1)	3.05 (2.25–4.13)	1.24 (0.88–1.75)
Diagnosis of NAS				
Absent	215 (96.0)	26,914 (99.8)	1.00 (ref)	—
Present	9 (4.0)	54 (0.2)	20.85 (10.17–42.77)	—
Mode of delivery				
Vaginal	145 (64.7)	17,509 (64.9)	1.00 (ref)	1.00 (ref)
Cesarean	79 (35.3)	9,459 (35.1)	1.01 (0.77–1.33)	0.97 (0.73–1.29)

OUD, opioid use disorder; OR, odds ratio; ref, referent; MEQ, morphine equivalents; NAS, neonatal abstinence syndrome.

* Opioid use disorder or opioid overdose includes 1) filled prescription for methadone or buprenorphine for opioid agonist therapy; 2) outpatient visit for opioid agonist therapy; or 3) diagnostic codes (International Classification of Diseases, Tenth Revision [ICD-10]) in health care records from emergency department visits or hospitalizations related to opioid use disorder (ICD-10 F11 or DSM-5 304.00 or 305.50), opioid overdose (ICD-10 T40.0-T40.4, T40.6), or opioid-related death (ICD-10 T40.0-T40.4, T40.6 and X40-44, X60-64, X85, or Y10-Y14).

† Prescription opioid analgesic use includes butorphanol, buprenorphine for pain, codeine, fentanyl, hydrocodone, meperidine, methadone for pain, morphine, opium, oxycodone, pentazocine, tapentadol, and tramadol.

‡ Includes maternal age, neighborhood-level income quintile, rurality, prior live birth, history of social risk factors, Elixhauser comorbidity score, history of maternal pain diagnosis, history of mental illness, history of substance use disorder, opioid analgesic use 1 y before conception, duration of prenatal opioid analgesic use, average daily dose of prenatal opioid analgesics, prescribed benzodiazepines, and mode of delivery. Neonatal abstinence syndrome was excluded from the adjusted analysis because low prevalence.

§ Social disadvantage composite includes medical care while involved in the criminal justice system recorded on health care records, homelessness recorded on health care records, violence-related health care, or neonatal discharge to social services at birth hospitalization.

‖ Pain conditions include low back pain, joint pain, migraine or headache, rheumatoid arthritis, fibromyalgia, joint pain, chronic pancreatitis, peripheral neuropathy, sickle cell disease, and renal calculus.

RESULTS

Of 27,192 women with prenatal analgesic opioid use and no OUD history, 224 (0.8%) experienced OUD or opioid overdose between delivery and 365 days postpartum. Most events were OUD-related (outpatient visit or opioid agonist therapy prescription; n=209) and opioid overdose (n=19); there were no overdose deaths. Women with these outcomes differed from women without on most characteristics (Table 1). In the adjusted model, risk factors included longer prenatal opioid analgesic use, pain diagnosis, mental illness, non-OUD substance use before conception, younger age, and residing in low-income and rural areas.

DISCUSSION

In this large cohort study of women exposed to opioid analgesics during pregnancy, the risk of postpartum OUD or opioid overdose was low (less than 1%). However, the odds of such outcomes were increased among women younger than age 25 years, those in low income or rural areas, and those with mental health and addiction diagnoses and 30 or more days of prenatal opioid analgesic use, albeit with modest increases in absolute risk. Outside of pregnancy, longer initial opioid prescription duration, mental illness, substance use, and younger age have been associated with opioid overdose, long-term opioid use, and OUD.[6,7] Although neonatal abstinence syndrome risk was too low to explore in adjusted analyses, neonatal abstinence syndrome was a risk factor of postpartum opioid overdose and mortality in Massachusetts, Ontario, and the United Kingdom, presumably due to maternal OUD.[5,8] In our cohort, mothers of newborns with neonatal abstinence syndrome used prenatal opioid analgesics for longer durations. Our data suggest that these identifiable clinical factors may also be markers of risk in women without OUD. Study strengths include the comprehensive population-based data, including opioid prescriptions; however, findings may be limited to health care system users and reflect diagnostic code accuracy. These new findings may be useful for physicians treating pregnant and postpartum women for pain. Shorter opioid prescribing and prenatal screening for mental health diagnoses and substance use are recommended.

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