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REPORTS OF ORIGINAL INVESTIGATIONS

The association between labour epidural analgesia and postpartum depressive symptoms: a longitudinal cohort study

L'association entre l'analgésie péridurale obstétricale et les symptômes de dépression post-partum : une étude de cohorte longitudinale

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Abstract

Background *Pain is a risk factor for postpartum depression (PPD) and labour epidural analgesia (LEA) may lower the incidence of PPD. We evaluated depressive symptoms risk at three, six, and 12 months postpartum in women with LEA compared with women without LEA.*

Methods *With ethics approval, hypotheses were tested using data from a longitudinal prospective observational cohort study between January 2015 and January 2019 in nulliparous women aged ≥ 18 yr with uncomplicated, singleton pregnancies. Email surveys were completed at baseline (18–20 weeks' gestation) and at three-, six- and 12 months postpartum, including the Edinburgh Postpartum Depression Scale (EPDS). Maternal, infant, and anesthesia characteristics were abstracted from electronic databases. The EPDS scores at three, six, and 12 months postpartum were analyzed using generalized estimating equations with and without covariates.*

Results *Of the 909 women who consented to participate, 709 women were included in the study. Antenatal EPDS scores, not LEA, predicted postpartum depressive symptom risk ($P < 0.001$). The adjusted 95% confidence intervals suggest mean EPDS scores differ from 1.0 point lower in the LEA group at 12 months to 1.5 points higher in the no LEA group at three months on its 0–30 scale. All the confidence intervals included zero at three, six, and 12 months, so were considered non-significant ($P > 0.05$).*

Conclusion *This study did not identify an association between LEA and risk of depressive symptoms postpartum, although small mean differences between groups cannot be ruled out. Future studies should focus on other modifiable variables that influence the development of PPD.*

Résumé

Contexte *La douleur constitue un facteur de risque de dépression post-partum (DPP) et l'analgésie péridurale obstétricale (APO) pourrait réduire l'incidence de DPP. Nous avons évalué le risque de symptômes de dépression à trois, six, et 12 mois post-partum chez les femmes ayant reçu une APO comparativement aux femmes sans APO.*

Méthode *Après avoir obtenu l'approbation du comité d'éthique, l'hypothèse a été testée en se fondant sur les données d'une étude de cohorte observationnelle prospective longitudinale réalisée entre janvier 2015 et janvier 2019 auprès des femmes nullipares âgées de ≥ 18 ans avec des grossesses simples et sans complication. Des*

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sondages électroniques ont été complétés au début de l'étude (données de base, 18 à 20 semaines de grossesse), puis à trois, six et douze mois post-partum, et incluaient l'Échelle de dépression postnatale d'Édimbourg (EPDS). Les caractéristiques maternelles, infantiles et anesthésiques ont été extraites des bases de données électroniques. Les scores sur l'EPDS à trois, six, et 12 mois post-partum ont été analysés utilisant des équations d'estimation généralisées avec et sans covariables.

Résultats *Parmi les 909 femmes qui ont consenti à participer, 709 femmes ont été incluses dans l'étude. Les scores prénataux sur l'EPDS, et non l'APO, ont prédit le risque de symptômes de dépression post-partum ($P < 0,001$). Les intervalles de confiance ajustés de 95 % suggèrent que les scores moyens sur l'EPDS différaient de 1,0 point de moins dans le groupe APO à 12 mois à 1,5 point de plus dans le groupe sans APO à trois mois sur l'échelle de 0 à 30. Tous les intervalles de confiance englobaient le zéro à trois, six et 12 mois, et ont donc été considérés comme non significatifs ($P > 0,05$).*

Conclusion *Cette étude n'a pas identifié d'association entre l'APO et le risque de symptômes dépressifs post-partum, bien que de petites différences moyennes entre les groupes ne puissent être exclues. Les études futures devraient se concentrer sur d'autres variables modifiables qui influencent l'apparition de la DPP.*

Keywords Edinburgh postpartum depression scale · epidural · labour · pain · postpartum depression

The physical and emotional demands of pregnancy and childbirth[1] in addition to the stressors of the postpartum period, such as sleep deprivation[2] and child care,[3] make women vulnerable to postpartum depression (PPD). Although childbirth is usually considered a positive milestone, depression is one of the most common postpartum complications.[4] Defined as major depression beginning within four weeks of giving birth,[5] clinical studies estimate the prevalence of PPD is approximately 17% among mothers without a prior history of depression.[6] Clinical observation suggests that PPD may occur up to 12 months or longer after childbirth.[7] Declining hormone levels postpartum may contribute to depression in susceptible women.[4,8] A history of mood and anxiety disorders and untreated depression as well as anxiety during pregnancy are the strongest risk factors for PPD.[9] Other proposed contributors to PPD are genetic predisposition [10] and social factors, including low social support, relationship difficulties, relationship violence, previous abuse, and negative life events.[4,11] Maternal suffering and reduced functioning associated with PPD increases risks of marital conflict,[12] impairs infant bonding,[13] and in rare cases can lead to suicide.[14] Canadian data suggest that suicide is the fourth leading cause of postpartum mortality.[15] Additionally, the pervasive effects of PPD can affect the emotional, cognitive, and behavioural development of the child.[16,17]

While the association between chronic pain and depression is well established,[18] the relationship between labour pain and PPD has been less well studied. The severity of acute postpartum pain has been identified as an independent risk factor for the development of persistent pain and depression.[19] To illustrate the physiologic relationship between labour pain management and risk of PPD, cortisol concentration has been investigated in the peripartum period.[20] While labour epidural analgesia (LEA) reduces pain intensity and cortisol levels in the early postpartum period, adequate pain relief had a small impact on PPD risk six weeks postpartum.[20] It is possible that LEA directly mitigates stress hormones or that intrapartum pain is a mediator or effect modifier of the known association between antenatal depression and PPD.[21] Women who report a greater improvement in pain relief after labour analgesia appear to have a lower risk of PPD.[22] The association between labour pain and the development of postpartum psychiatric disorders, particularly PPD, has been the target of recent labour analgesia research.[23]As epidural analgesia remains the most effective modality for ameliorating labour pain,[24] investigators have examined the relationship between PPD and LEA.[7,25,26] This clinical inquiry has yielded mixed results.[20,22,23,25–33] The contrasting results exemplify the need for the present large prospective study, which controls for demographic and clinical variables known to influence the risk of PPD. There is a need to identify common and easily modifiable risk factors for PPD to target preventive efforts. Additionally, most studies evaluate PPD risk a short time after delivery, usually between four to eight weeks, so the long-term effects of LEA on PPD risk are not known—a knowledge gap that we will address in the current study.

The primary objective of this study was to determine if women that receive LEA have a lower incidence of postpartum depressive symptoms up to 12 months postpartum than women without LEA do. We hypothesized that, while controlling for established demographic and clinical variables,[34] LEA would be associated with a decreased risk of postpartum depressive symptoms at three months postpartum and have a similar effect, but of less magnitude, at six and 12 months postpartum.

Methods

This was a longitudinal study of nulliparous women recruited during pregnancy, between 18- and 22-weeks gestational age, from January 2015 to January 2019. The current analysis is a secondary analysis of a pre-existing data set designed to examine postpartum genito-pelvic pain.

With approval of the IWK Research Ethics Board (22 December 2014), women were recruited for the primary study from the diagnostic imaging clinic of a tertiary care obstetrical hospital during routine antenatal ultrasonography. The inclusion criteria were older than 18 yr; nulliparous; uncomplicated, singleton pregnancy; fluent in English; and access to a personal email account. Women with depression that was well-managed (self-reported) were included. Women were only excluded if they self-reported a major medical or psychiatric illness that was not well-managed. All members of the study cohort must have completed at least one postpartum survey and not had any additional pregnancies or deliveries during the study period. Participation retention strategies included email and phone call reminders using an established protocol.[35] Women received gift certificates for completion of each postpartum survey.

Potential participants were identified by research staff prior to their 20-week appointment. At their appointment, a research assistant described the study and obtained informed written consent from eligible participants. All surveys were completed online via an e-mailed link using Qualtrics Research Suite survey software. Surveys were completed at baseline (18–22 weeks gestational age) and at three, six, and 12 months postpartum. Medical information related to labour and delivery was collected by chart review of birth records. Anesthetic characteristics were accessed in the web-based information management system Innovian (Draeger, Inc. Telford, PA, USA). Data from the baseline, three-, six-, and 12-month postpartum questionnaires were used for the descriptive and clinical predictors of postpartum depressive symptoms risk.

The primary study outcome was Edinburgh Postnatal Depression Scale (EPDS) scores at three-, six-, and 12 months postpartum in women who received LEA compared with women who did not receive LEA. The secondary outcome was to determine the delivery type (Cesarean, operative, and spontaneous vaginal deliveries) in women who received LEA compared with women who did not receive LEA. The EPDS is a ten-item self-rating scale used to detect PPD risk.[36] Responses to items are scored from 0 to 3, with a maximum score of 30. Summed total scores were used for analysis. The measure shows excellent psychometric properties[37] and is widely accepted as the preferred screening method for PPD risk with a sensitivity of $> 90\%$ and a specificity of $> 80\%$.[38,39] Four demographic[40–42] and three clinical factors[34,40,43] were chosen *a priori* from available literature as possible confounders for the development of postpartum depressive symptoms. The chosen covariates included age, average income, level of education, and marital status. Clinical covariates included the antenatal EPDS score, method of delivery (spontaneous vaginal, Cesarean, or operative vaginal (forceps or vacuum), and gestational age at birth. Women request LEA at their discretion at our centre and are interviewed by the anesthesia provider at the time of request. Both combined spinal epidural and labour epidural bolus techniques are used to initiate LEA. Initiation of LEA occurs typically by a loss of resistance to saline technique and then either a bolus of epidural ropivacaine 0.2% with fentanyl 100 μg in divided doses or bupivacaine 0.25% (0.8 mL) with fentanyl 10 μg administered intrathecally. The LEA is maintained using programmed intermittent boluses of ropivacaine 0.1% μg with fentanyl 2 $\mu g \cdot mL^{-1}$ (8 mL) every 45 min with patient-controlled epidural analgesia.

The current analyses represent secondary analysis of a larger data set and were not pre-registered and should be considered exploratory. The research question and theory-driven covariates and predictors were selected prior to examining the data. Only once these variables were decided was the data analyzed. One exception was the use of labour induction, which was added as a covariate post-hoc, based on reviewer recommendation. The sample size was determined by the primary outcome of the original study to examine the trajectories and predictors of postpartum genito-pelvic pain. Descriptive statistics were calculated with the Statistical Package for the Social Sciences (SPSS V. 25.0., SPSS Inc, Chicago, IL, USA). Demographics were summarized with means and standard deviations or counts and percentages. Data were analyzed using generalized estimating equations. Missing data were handled using a maximum likelihood approach. Alpha for hypothesis testing was set at 0.05. A negative binomial distribution was assumed for our primary outcome, EPDS scores (i.e., a right-skewed distribution of count data) with a natural logarithm link. Robust estimates of standard errors were used to account for violations of the homogeneity of variance assumption. Given known problems with dichotomizing numerical data, the EPDS scores were analyzed as numerical dimensions, rather than clinical categories.[44] Both adjusted and unadjusted analyses were completed. The unadjusted analysis included only time (baseline, three, six, and 12 months postpartum), LEA (yes *vs* no), and the time*LEA interaction as predictors. The interaction effect allowed the model to test whether the effect of epidural varied over time. The adjusted analysis added in antenatal EPDS scores

(log-transformed), maternal education (dichotomized as no post-secondary *vs* post-secondary), gestational age, delivery type, maternal age (a numerical variable in years), and income (an ordinal variable ranging from 1 to 11) as covariates. This analysis controlled for potential confounding variables.

Results

A total of 909 women consented to participate in the study and 822 completed the baseline survey, indicating enrolment. Of the enrolled sample, 58 women were excluded because they subsequently became pregnant or gave birth again during the data collection period. Additionally, 54 women were excluded because only the baseline survey in pregnancy was completed, one was excluded because epidural status was missing, leaving 709 women who were included in the current analysis (Fig. 1).

In the present data, 54 datapoints or 7.2% of postpartum EPDS scores were missing. Missing data for EPDS scores increased as the study progressed: 3.2% at three months, 8.7% at six months, and 9.7% at 12 months. Higher antenatal EPDS scores predicted missingness at six months (odds ratio [OR], 1.08; $P = 0.008$) and 12 months (OR, 1.09; $P = 0.003$), but not at three months (OR, 1.05; $P = 0.35$). For induction of labour, 27 participants had a planned Cesarean delivery; these cases were treated as missing data for the adjusted hypothesis test. When using scores of 13 or higher on the EPDS as an indicator of PPD risk,[45] the prevalence of postpartum depressive symptoms was: baseline: 6.5%, three months: 6.4%, six months: 6.5%, and 12 months: 8.6%. These rates are comparable with the national prevalence rates of 7.4%.[46] Women who received LEA had more operative vaginal deliveries ($P < 0.001$) and more spontaneous vaginal deliveries ($P < 0.001$) than women without LEA did. Women who received LEA had higher gestational age infants than women without LEA did (mean difference, 0.6 weeks; $P < 0.001$). Women with LEA were also more likely to have induced births ($P < 0.001$). Descriptive information for patient demographic variables is presented in Table 1.

The unadjusted and adjusted analysis of the effect of LEA on postpartum depressive symptoms risk are presented in Table 2. The unadjusted model included postpartum time points (three-, six-, and 12 months), LEA, and the postpartum time*LEA interaction, and all effects were non-significant. There was no statistically significant main effect of LEA when collapsing across all three postpartum timepoints and no statistically significant postpartum time*LEA interaction effect. Thus, we did not find that epidural usage had a conditional effect on EPDS scores at certain postpartum time points. In the adjusted analysis (Table 2), only antenatal EPDS scores predicted postpartum depressive symptoms risk ($P < 0.001$). After correction for covariates, the 95% confidence intervals suggest mean EPDS scores differ from 1.0 point lower in the LEA group at 12 months to 1.5 points higher in the no LEA group at three months on its 0–30 scale. As all of the confidence intervals included zero at three-, six-, and 12 months, they are non-significant ($P > 0.05$). Mean EPDS scores and 95% confidence intervals are presented in Table 3 and Fig. 2.

Discussion

This study did not detect a relationship between LEA use and the risk of developing postpartum depressive symptoms up to 12 months postpartum. Our results are consistent with results from other studies in the literature.[20,25,28,29,33] A population based longitudinal cohort study of 1,503 primiparous women found LEA was not associated with the risk of PPD at six weeks postpartum after adjusting for sociodemographic, psychosocial, and obstetric variables.[27] A recent study of 565 women found LEA was actually associated with higher PPD risk up to four weeks postpartum compared with transcutaneous electrical nerve stimulation and doula therapy.[47]

It is important to note that our study findings contrast other studies examining LEA and PPD risk.[7,22,26,30] These studies, however, have been criticized for subject selection bias, not appropriately controlling for measured confounding variables, excluding obese patients, and having a differential loss to follow-up.[26,48] In both retrospective and prospective observational studies, it is difficult to determine whether LEA use predicts PPD risk, as depressed women may simply be more likely to request epidural analgesia.[25] The contrast in findings of these studies compared with those of the current study warrants evaluation of study methodology and timeline of clinical evaluation as well as consideration of PPD risk factors. Our study contributes to moving the mixed literature forward. This study is one of few observational cohort studies with more than 500 participants[7,27,29,33,47] examining the use of LEA and the risk of developing PPD, based on EPDS screening.[7,27,29,47] Three of these large prospective studies also found that LEA use did not reduce the occurrence of potential PPD.[27,29,47]

This study is one of three other longitudinal studies that have followed patients longer than eight weeks postpartum.[7,33] Postpartum depression generally peaks four to six weeks after childbirth and resolves by three to six months,[9,49] but it can last for years.[7,50,51] Studies assessing depression early in the postpartum period risk

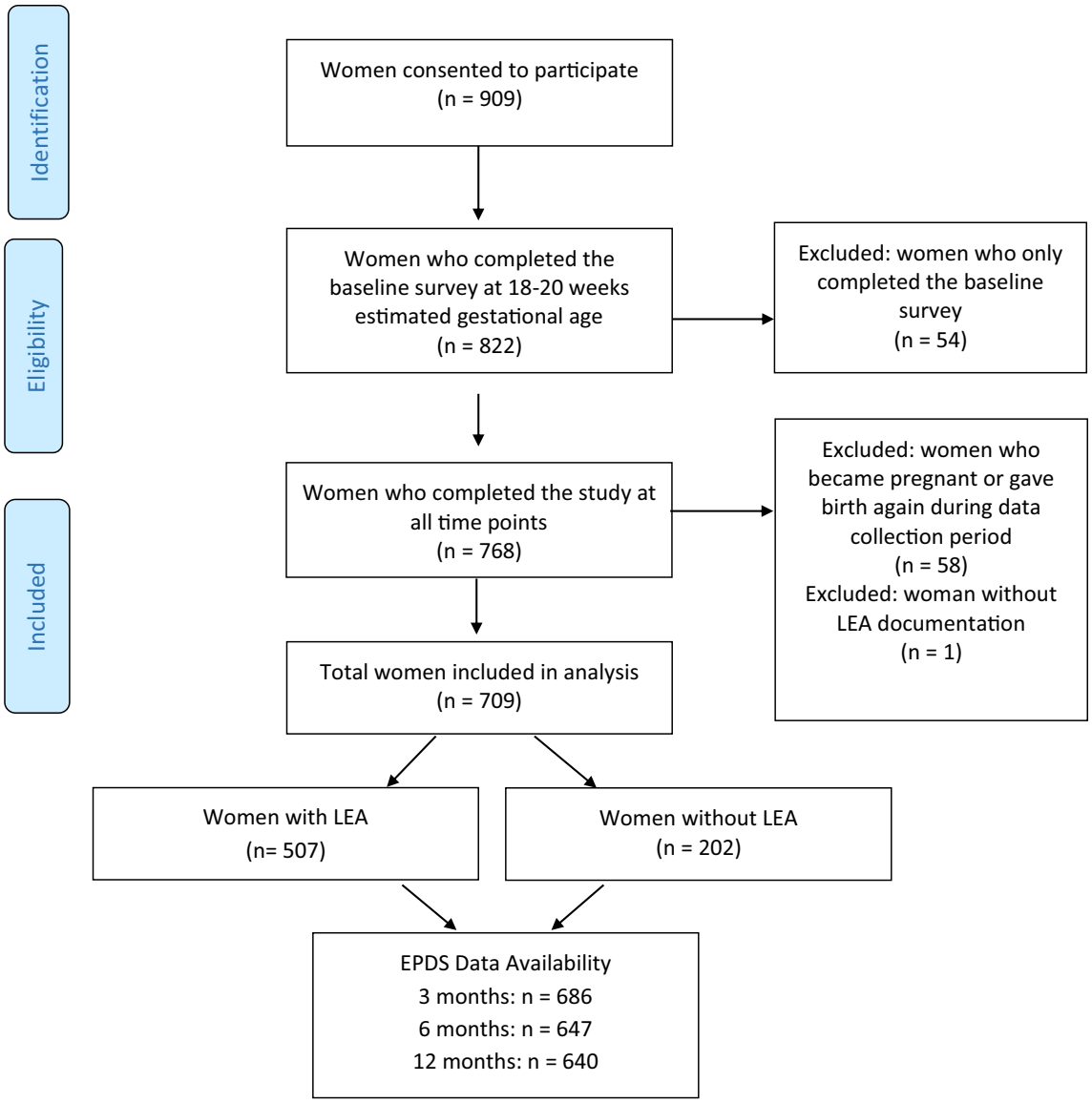

Fig. 1 Patient flow diagram. EPDS = Edinburgh Postpartum Depression Score; LEA = labour epidural analgesia

capturing women with persistent antenatal depression making it unclear whether LEA truly affects the risk of developing PPD. Nevertheless, addressing PPD risk in the late postpartum period might overlook a possible impact of LEA as many women with moderate depressive symptoms recover spontaneously.[52] Our study mitigates this uncertainty by capturing antenatal EPDS scores as well as following the risk of postpartum depressive symptoms during early-, mid-, and late postpartum periods. Our study is unique in that it also examines an epidural*time interaction. It is important to note that our study indicated that the only predictor of postpartum depressive symptoms risk was the presence of antenatal depressive symptoms. Early screening could provide an opportunity for consultation with an anesthesiologist to discuss labour analgesia for patients who screen positive for postpartum depressive symptoms, who are deemed high risk of developing PPD, or who have had prior PPD. Depression during pregnancy is an established risk factor for the development of PPD[53] but is often not accounted for as a potential covariate when assessing the relationship between LEA and PPD risk.

The choice of screening tool presents another area of discrepancy between existing studies. While clinical evaluation remains the gold standard for diagnosis of PPD, the most widely used instrument to screen postpartum women for major depression is the self-reported EPDS.[54] Scores $\geq$ 10 on the 30-point scale are usually used as a cut-off to predict risk of PPD[9,37,55] and were used to reflect PPD risk with LEA use in several studies.[20,25,28,29] In

Table 1 Descriptive statistics*

Variable	Epidural (*n*=507)	No epidural (*n*=202)	*P* value	Combined (*n*=709)
Antenatal EPDS score	5.9 (3.8)	5.6 (3.9)	0.31	5.8 (3.8)
Gestational age (weeks)	39.8 (1.5)	39.2 (1.9)	< 0.001	39.7 (1.7)
Maternal age (yr)	29 (4.4)	30 (4.1)	0.19	30 (4.3)
Income	8.5 (2.8)	8.7 (2.6)	0.39	8.6 (2.8)
Education			0.06	
No post-secondary	77 (15.2%)	20 (9.9%)		97 (13.7%)
Post-secondary	430 (84.8%)	182 (90.1%)		612 (86.3%)
Ethnicity			0.16	
Euro-Canadian	450 (88.7%)	168 (83.2%)		618 (87.1%)
African Canadian	6 (1.2%)	5 (2.5%)		11 (1.6%)
First Nations	4 (0.8%)	1 (0.5%)		5 (0.7%)
Other	47 (9.4%)	28 (12.8%)		75 (10.5%)
Relationship status			0.17	
Married	311 (61.3%)	132 (65.3%)		443 (62.5%)
Engaged	28 (5.5%)	16 (7.9%)		44 (6.2%)
Common-law	48 (9.5%)	20 (9.9%)		68 (9.6%)
Living with partner	95 (18.7%)	25 (12.4%)		120 (16.9%)
Dating one partner	17 (3.4%)	7 (3.5%)		24 (3.4%)
No regular partner	8 (1.6%	1 (0.5%)		9 (1.3%)
Other	0 (0%)	1 (0.5%)		1 (0.1%)
Sexual orientation			0.59	
Heterosexual	470 (92.9%)	184 (91.1%)		654 (92.4%)
Lesbian	3 (0.6%)	1 (0.5%)		4 (0.6%)
Bisexual	24 (4.7%)	10 (5.0%)		34 (4.8%)
Other	9 (1.8%)	7 (3.5%)		16 (2.3%)
Delivery type			< 0.001	
Spontaneous vaginal	292 (57.6%)	144 (71.3%)		436 (61.5%)
Operative vaginal	98 (19.3%)	9 (4.5%)		107 (15.1%)
Cesarean	117 (23.1%)	49 (24.3%)		166 (23.4%)
Induction of labour				
Yes	229 (45.4%)	43 (23.4%)	< .001	272 (39.5%)
No	275 (54.6%)	114 (62.0%)		389 (56.5%)
Cesarean delivery	0 (0%)	27 (14.7%)		27 (3.9%)

Mean (standard deviation) or *n* (%). For numerical outcomes, means were compared with Welch *t* tests. For categorical outcomes, means were compared using Pearson Chi squares. Income was measured using an 11-point ordinal scale where 1 = CAD 0–9,999 and 11 = CAD 100,000 and over, with each number in between increasing in increments of CAD 10,000. Thus, a mean of 8.6 corresponds roughly to an income between CAD 70,000 and CAD 89,999. *P* values refer to comparisons between epidural and no-epidural groups. EPDS = Edinburgh Postnatal Depression Scale

* The de-identified data and syntax are available upon request

contrast, other observational studies examining LEA have used EPDS scores > 12 to predict PPD risk.[27,53,56] The lack of standardization of the screening cut-offs makes generalizing the study results difficult, as some studies risk over- or underestimating the effect of labour analgesia on PPD. The EPDS has been scrutinized as a screening tool for comparing research results because of the various methods of assessment (different cultural context), dichotomized cut-off criteria, and timing of assessments. Nonetheless, in the present study, the two groups differed by less than one point on the EPDS; this result suggests that differences are not liable to be clinically significant. It is also important to note that our sample had low EPDS scores throughout the study period. This study examined LEA use and the risk of PPD while adjusting for potential demographic and clinical confounders. The risk factors for

Table 2 Unadjusted and adjusted analysis of covariates predicting risk of PPD

Variable	Unadjusted		Adjusted	
	Wald χ^2	*P* value	Wald χ^2	*P* value
Time	0.96	0.62	1.21	0.55
Epidural	0.85	0.36	0.70	0.40
Time * epidural	2.48	0.29	4.14	0.13
Antenatal EPDS score	–	–	303.38	<0.001
Education	–	–	0.05	0.83
Gestational age	–	–	0.47	0.49
Delivery type	–	–	1.68	0.43
Maternal age	–	–	0.35	0.55
Income	–	–	1.15	0.28
Induction of labour	–	–	0.23	0.63

Models are predicting EPDS score. Antenatal EPDS scores were natural log-transformed. The unadjusted model includes postpartum time points 3-,6-, and 12 months, LEA use, and the postpartum time*LEA interaction. The adjusted model adds in numerical EPDS scores, maternal education, gestational age, delivery type, maternal age, income, and labour induction as covariates. The unadjusted analysis incorporated 1,973 observations (n = 709 participants after missing data). The adjusted analysis incorporated 1,805 observations (n = 649 participants after missing data). Antenatal EPDS (between 18 and 20 weeks' gestation) score refers to an EPDS score prior to delivery. We assessed linearity in the log scale for numerical predictors using scatterplots faceted by time and epidural status with loess regression lines. All relationships seemed approximately linear in a log scale

EPDS = Edinburgh Postnatal Depression Scale; LEA = labour epidural analgesia; PPD = postpartum depression

Table 3 Means and confidence intervals of EPDS scores at 3-, 6-, and 12 months postpartum between women who used LEA and those who did not use LEA

Timepoint	Epidural	Mean	SE	Mean difference (No LEA – LEA) (95% CI)
Unadjusted				
EPDS 3 months	No LEA	5.5	0.3	
	LEA	5.6	0.2	-0.1 (-0.8 to 0.7)
EDPS 6 months	No LEA	5.4	0.3	
	LEA	5.5	0.2	-0.1 (-0.9 to 0.6)
EDPS 12 months	No LEA	5.0	0.3	
	LEA	5.7	0.2	-0.6 (-1.4 to 0.1)
Adjusted				
EPDS 3 months	No LEA	5.5	0.4	
	LEA	4.8	0.2	0.7 (-0.1 to 1.5)
EDPS 6 months	No LEA	5.2	0.4	
	LEA	4.9	0.2	0.3 (-0.5 to 1.1)
EDPS 12 months	No LEA	4.8	0.3	
	LEA	5.1	0.2	-0.3 (-1.0 to 0.5)

Adjusted means are controlling for antenatal EPDS score, education level, gestational age, delivery type, total household income, age, and labour induction

CI = confidence interval; EPDS = Edinburgh Postnatal Depression Scale; LEA = labour epidural analgesia; SE = standard error

the development of PPD are multifactorial, including psychological, physical, social, and obstetric factors and genetic susceptibility[57,58] making adjusting for all confounders difficult. Analyses in existing studies have been criticized for disregarding the interrelationships between pain, analgesia efficacy, social support, and fear of childbirth and pre-existing depression.[59] A recent longitudinal cohort study by Eckerdal *et al.*, attempted to

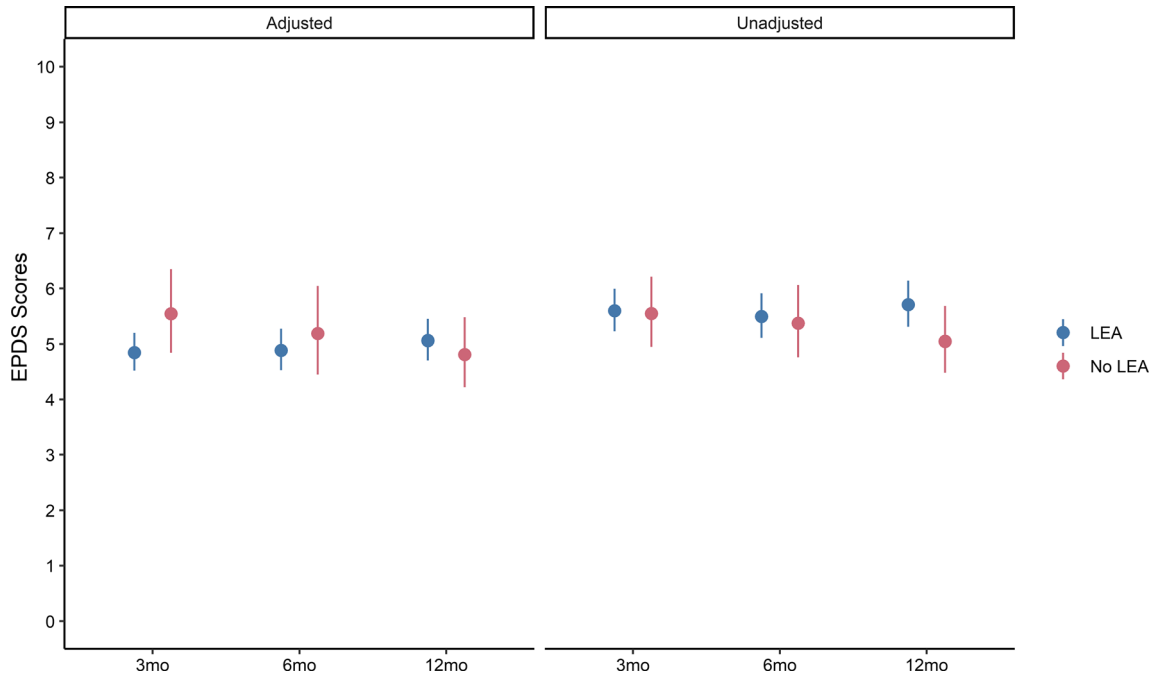

Fig. 2 Means and 95% confidence intervals for depression split by time and epidural. The left panel presents means and confidence intervals from the adjusted analysis, and the right panel presents means and confidence intervals from the unadjusted analysis. Scores are presented in their original metric, not in a log-transformed metric

account for factors that may explain the influence of LEA on PPD risk using conceptual path analysis.[27] Nevertheless, the authors only adjusted for three variables (fear of childbirth, antenatal depressive symptoms, and age) in the multivariable logistic regression, once again leaving open the question as to whether confounding was adequately addressed.[59] Additionally, there is evidence of a negative interaction between unmatched expectations compared with matched expectations in terms of women desiring and actually receiving LEA and the development of PPD.[29] With patient expectations for LEA not accounted for in our study, it is uncertain whether this negative interaction could be playing a role in the risk of PPD.

Our study showed higher operative vaginal deliveries in women with LEA than in women without LEA, which contrasts current literature suggesting LEA is not associated with delivery method.[24] The women in our study who received LEA also had infants with a higher gestational age, so it is possible that the larger infant size could account for this difference. It is also possible that labour induction or labour characteristics not captured by our study, such as labour length and dystocia, may impact delivery outcome. Ultimately, women with LEA in our sample were still most likely to deliver vaginally, which matches the current literature evaluating delivery outcomes while using low concentration local anesthetics for LEA.[24]

There are limitations to the present study that may influence the ability to determine the true risk association of LEA on postpartum depressive symptom development. Only nulliparous women were included, limiting the generalizability to parous women and participants were largely Caucasian and Eurocentric, limiting the diversity of the cohort. While our cohort may not be generalizable to all centres providing obstetrical care, it may share similar demographics to two other Canadian studies, which also showed no influence of LEA on PPD risk.[25,33] Our study population had high rates of LEA use, which may not mimic the practice of other obstetrical care centres. Additionally, the two study groups differed significantly in size, which may have biased the study results. This study did not measure whether expectations for LEA were matched with delivery, which has been established as a predictor of PPD development.[29] Additionally, there is a wide range of interindividual variability in labour pain relief for women using LEA. The degree to which improvement of labour pain relief influences the risk for PPD among women who use LEA needs to be further clarified.[22] In our study, LEA was used as a surrogate marker for labour pain, but the absence of a specific labour pain assessment is a limitation of our study. Finally, because these analyses were exploratory, they may have higher error rates than pre-registered analyses, which discuss the limitations of using the EPDS. Since our margin of error on the mean differences on the 30-point

scale of the EPDS was roughly ± 0.75 points, we cannot rule out small differences between groups in either direction. Participants were more likely to have missing data over time if they had higher antenatal EPDS scores at baseline, which limits generalizability.

Conclusion

This prospective observational cohort study showed that the use of LEA was not associated with postpartum depressive symptom risk at three-, six- and 12 months postpartum. After adjusting for covariates, the only predictor of postpartum depressive symptoms was antenatal EPDS scores. In summary, the current findings suggest that use of LEA is not associated with postpartum depressive symptoms in the year after birth, underscoring the importance of investigating other potential predictors of PPD risk to better identify and prevent the development of PPD.

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