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REVIEW ARTICLE/BRIEF REVIEW

Pharmacologic labour analgesia and its relationship to postpartum psychiatric disorders: a scoping review

L'analgésie pharmacologique pour le travail obstétrical et sa relation aux troubles psychiatriques postpartum: une étude exploratoire

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Abstract

Purpose *This scoping review aimed to summarize the current literature on postpartum psychiatric disorders (e.g., postpartum depression, postpartum anxiety, postpartum post-traumatic stress disorder) and the possible relationship of these disorders to the use of pharmacologic labour analgesia (e.g., epidural analgesia, nitrous oxide, parenteral opioids) to identify knowledge gaps that may aid in the planning of future research.*

Sources *PubMed, PsycINFO, CINAHL, and EMBASE were searched from inception to November 9, 2018 for studies that included both labour analgesia and the postpartum psychiatric disorders specified above.*

Principal findings *Two reviewers assessed the studies and extracted the data. Of the 990 identified citations, 17 studies were included for analysis. Existing studies have small sample sizes and are observational cohorts in design. Patient psychiatric risk factors, method of delivery, and type of labour analgesia received were inconsistent among studies. Most studies relied on screening tests for diagnosing postpartum psychiatric illness and did not assess the impact of labour analgesia on postpartum psychiatric illness as the primary study objective.*

Conclusions *Future studies should correlate screen-positive findings with clinical diagnosis; consider adjusting the timing of screening to include the antepartum period, early postpartum, and late postpartum periods; and consider the degree of labour pain relief and the specific pharmacologic labour analgesia used when evaluating postpartum psychiatric disorders.*

Résumé

Objectif *Cette étude exploratoire avait pour objectif de résumer la littérature actuelle portant sur les troubles psychiatriques postpartum (par ex., dépression postpartum, anxiété postpartum, état de stress post-traumatique postpartum) et la relation possible de ces troubles avec l'utilisation d'une analgésie pharmacologique pour le travail obstétrical (par ex., analgésie péridurale, protoxyde d'azote, opioïdes parentéraux) afin d'identifier les lacunes dans nos connaissances qui pourraient aiguiller la planification de futures recherches.*

Sources *Des recherches ont été effectuées dans les bases de données PubMed, PsycINFO, CINAHL et EMBASE de leur création jusqu'au 9 novembre 2018 afin d'en extraire les études incluant des informations concernant l'analgésie du travail et les troubles psychiatriques postpartum spécifiés ci-dessus.*

Constatations principales *Deux évaluateurs ont passé en revue les études et extrait les données. Parmi les 990*

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citations identifiées, 17 études ont été incluses pour analyse. Les études existantes ont de petites tailles d'échantillon et sont conçues comme des cohortes observationnelles. Les facteurs de risque psychiatrique des patientes, le mode d'accouchement et le type d'analgésie reçue pour le travail n'étaient pas uniformes d'une étude à l'autre. La plupart des études s'appuyaient sur des tests de dépistage pour poser un diagnostic de maladie psychiatrique postpartum et n'évaluaient pas l'impact de l'analgésie du travail sur la maladie psychiatrique postpartum comme critère d'évaluation principal.

Conclusion *Les études futures devraient corréler les résultats positifs au dépistage à un diagnostic clinique; envisager d'ajuster le moment de dépistage afin d'inclure la période antepartum ainsi que les périodes du postpartum initial et tardif; et tenir compte du degré de soulagement de la douleur du travail ainsi que de l'analgésie pharmacologique spécifique utilisée pour le travail lors de l'évaluation des troubles psychiatriques postpartum.*

Childbirth is one of the most painful experiences a woman will endure and is associated with an increased risk of first-time episodes of psychiatric disorders.[1] The demands of pregnancy and childbirth make patients vulnerable to psychiatric disorders such as postpartum depression (PPD), anxiety, and stress disorders.[2] Women with postpartum psychiatric disorders have high mortality rates, with the highest risk in the first year after diagnosis.[3,4] The most common postpartum psychiatric disorder is PPD, which is defined by the Diagnostic and Statistical Manual of Mental Disorders, fifth edition, as depression (e.g., sadness, loss of interest, insomnia, impaired concentration) that occurs any time in pregnancy or in the first four weeks after delivery.[5] It can lead to complications such as emotional lability in the mother[6] and pervasive emotional, cognitive, and behavioural effects on the child.[6,7]

In recent years, the association between pain during childbirth and postpartum psychiatric disorders has been investigated.[8–11] The pain of childbirth has been correlated with postpartum blues, which is characterized as transient mood changes within the first few days after delivery and is rarely associated with complications.[12–14] Also, the severity of acute postpartum pain may be an independent risk factor for the development of persistent pain and PPD.[6,13,15] Postpartum anxiety was found in 16.2% of women six weeks after delivery[16] and may coincide with PPD.[17] While the association between labour pain and anxiety has not been specifically evaluated, the co-relationship between PPD and postpartum anxiety makes the association plausible.[18] The pain of childbirth has been linked with postpartum post-traumatic stress disorder (PTSD) symptoms.[19]

This scoping review aimed to identify the extent, range, and nature of literature on postpartum psychiatric disorders (PPD, postpartum anxiety, PTSD) and their possible relationship to the use of pharmacologic labour analgesia (epidural analgesia, nitrous oxide, parenteral opioids) to identify knowledge gaps that may help plan future research.

Methods

Search strategy

The electronic databases (PubMed, EMBASE, CINAHL, and PsycINFO) were systematically searched from inception until November 9, 2018. A search strategy (Appendix A) was developed using selected Medical Subject Headings (MeSH), as well as free text variations on terms related to birth, analgesia, and postpartum psychiatric disorders. Reference lists and hand searching of relevant literature, including commentaries, letters to the editor, and review articles, was also completed.

Inclusion criteria

Inclusion criteria were original research published in English or French. Articles with only neonates or infants as subjects were excluded. Eligible studies had to include at least one of the following terms in the abstract or title: "parturient", "labour", "analgesia", and one or more of "PPD", "postpartum anxiety", "postpartum PTSD symptoms", or related terms for postpartum psychiatric disorders (Appendix A). Labour analgesia was limited to pharmacologic techniques, including nitrous oxide, parenteral opioids, or neuraxial analgesia. The study title did not have to link or evaluate the use of labour analgesia on postpartum psychiatric disorders. Study results must have reported an outcome related to postpartum psychiatric diagnoses occurring $>$ 24 hr postpartum.

Study selection

Two reviewers (A.M. and H.M.) independently screened titles and abstracts using the pre-determined inclusion criteria. Full-text of manuscripts that appeared to meet inclusion criteria based on abstract review were further reviewed. Discrepancies were resolved through discussion, with third-party consensus when needed.

Data extraction and analysis

Two reviewers (A.M. and A.S.) independently extracted data from the relevant articles using a pre-determined data extraction form (Appendix B). Study characteristics, participant demographic information, obstetric outcomes, psychiatric risk factors, and outcome measures of interest were established *a priori* and data were extracted using a standardized form.

Results

Search and screening

The search strategy yielded 1,088 articles (PubMed 600, Embase 320, PsycINFO 77, CINAHL 91). Citations were managed with the review manager Covidence (systematic review software, Veritas Health Innovation, Melbourne, Australia), and 98 duplicates were removed leaving 990 unique citations. Following title and abstract screening, 909 citations did not match study inclusion, leaving 81 citations for full-text review. Sixty-three citations were excluded during the second screening phase for inappropriate outcomes, non-pharmacologic analgesic interventions, or inappropriate study methodology. The number of articles excluded during each screening phase, and the reasons for exclusion during the second screening phase were recorded using a flow diagram following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement[20] (Figure 1). A total of 17 articles were included in the final review. The available literature reviewed postpartum psychiatric disorders and the use of pharmacologic labour analgesia in two major ways—studies that linked pharmacologic labour analgesia to postpartum psychiatric disorders, and studies that linked labour pain to postpartum psychiatric disorders.

A description of study characteristics, including type of labour analgesia is available in Table 1. Patient demographics and risk factors for postpartum psychiatric disorders included in the studies are listed in Table 2. The most commonly utilized form of labour analgesia was labour epidural analgesia (LEA) but details of the epidural technique were not described in all studies (Table 1). Three studies described the LEA technique as a manual bolus of low concentration local anesthetic, with or without opioid, followed by a continuous infusion of local anesthetic solution, with or without opioid.[8,10,21] One study described manually administered boluses of a local anesthetic and opioid solution to maintain labour analgesia.[22] Only one study specified that the labour analgesia may have included a combined spinal-epidural, but the details of the technique were not provided.[23]

Types of postpartum psychiatric disorders

The primary objective of most studies (11/17)[8–11,14,21–29] focused on identifying depressed mood and a positive PPD screen. Five of the 17 studies[25,26,28,30,31] evaluated

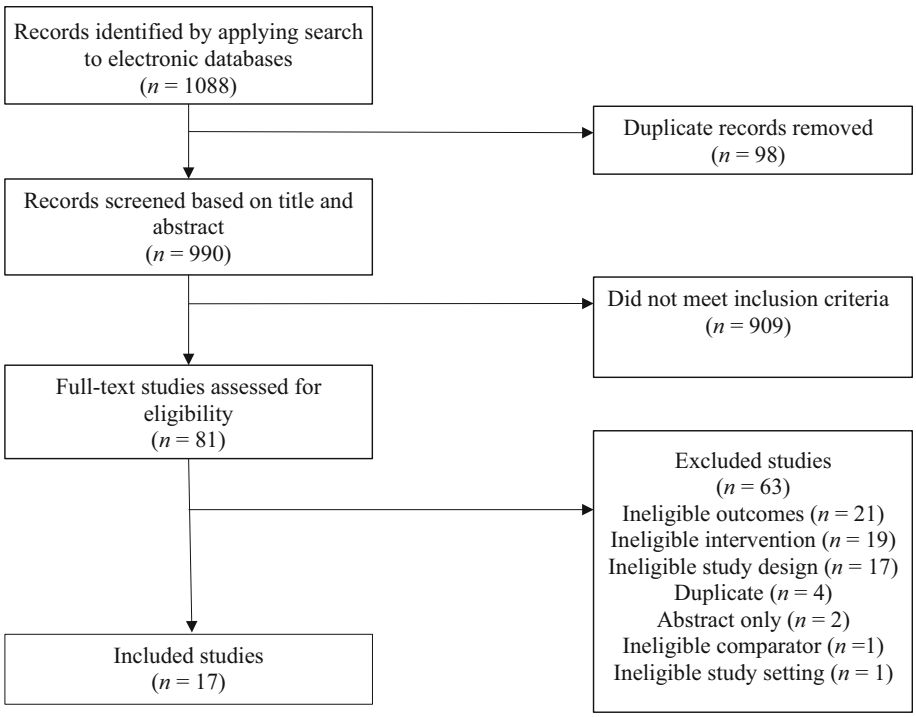

Figure 1 PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) diagram for scoping review of pharmacological labour analgesia and the relationship to postpartum psychiatric disorders

Table 1 Study characteristics

PPD	Country of origin	Year	Study methodology	Sample size	Primary objective	Labour analgesia	Findings	Psychiatric evaluation tool	Psychiatric evaluation period
Boudou *et al.*[14]	France	2007	Prospective observational cohort	$n = 43$	To examine the association between pain intensity during childbirth and mood three days postpartum	Epidural $n = 34$ (79%)	A significant positive correlation was identified between pain intensity during childbirth and depressed mood postpartum.	EPDS ≥ 10	3 days postpartum
Ding *et al.*[8]	China	2014	Prospective observational cohort	$n = 214$	To identify whether LEA was associated with PPD development.	Epidural $n = 107$ (50%)	Results indicated that PPD occurred in 14% of women who received LEA. PPD occurred in 35% of women who did not receive LEA.	EPDS ≥ 10	3 days and 6 wks postpartum
Ferber *et al.*[24]	Israel	2005	Prospective observational cohort	$n = 82$	To investigate whether labour pain catastrophizing is associated with social functioning and maternity blues postpartum.	Epidural $n = 47$ (57%) Pethidine or Entonox $n = 35$ (43%)	When controlling for maternal age, parity, analgesia type, and labour pain intensity, pain catastrophizing during labour positively predicted maternity blues and social functioning postpartum	EPDS ≥ 14	2 days and 6 wks postpartum
Hiltunen *et al.*[9]	Finland	2004	Prospective observational cohort	$n = 185$	To evaluate whether LEA or paracervical blockade performed during delivery influences the incidence of PPD.	Epidural or paracervical block $n = 103$ (56%) Nitrous oxide and/or acupuncture $n = 16$ (9%) Pudendal nerve block $n = 4$ (2%)	Results indicated that postnatal depression scores one week following delivery decreased in the epidural/paracervical group compared with the no analgesia group.	EPDS ≥ 13	2–7 days and 4 months postpartum
Lim *et al.*[10]	United States	2018	Retrospective, observational cohort	$n = 201$	To examine whether effective LEA is associated with reduced PPD symptomatology.	Epidural $n = 201$ (100%)	Women showing greater improvements in pain presented with lower postnatal depression scores.	EPDS ≥ 10	6 wks postpartum
Nahirney *et al.*[11]	Canada	2017	Prospective observational cohort	$n = 206$	To evaluate whether LEA is associated with reduced PPD risk at 6 weeks or 6 months postpartum among a sample of mothers with no pre-existing depression.	Epidural $n = 118$ (58%)	PPD occurred in 13.3% of the sample. However, there was no statistically significant relationship between LEA use and PPD development.	EPDS ≥ 10	6 wks and 6 months postpartum
Orbach-Zinger *et al.*[27]	Israel	2018	Prospective observational cohort	$n = 1,326$	To examine the influence of delivering without analgesia on PPD development among mothers who planned to receive LEA.	Epidural $n = 1058$ (70%)	The PPD rate among women who did not receive LEA, despite that being their intended plan, was not statistically different from women who received LEA for delivery.	EPDS ≥ 10	6 wks postpartum

Table 1 continued

PPD	Country of origin	Year	Study methodology	Sample size	Primary objective	Labour analgesia	Findings	Psychiatric evaluation tool	Psychiatric evaluation period
Riazanova *et al.*[21]	Russia	2018	Prospective observational cohort	$n = 210$	To evaluate the influence of LEA for spontaneous delivery on mothers' stress levels during labour and PDD development.	Epidural $n = 107$ (51%)	Use of LEA significantly reduced pain and stress during spontaneous delivery, There was no significant difference in the frequency of PPD development among women who received LEA and women who did not.	EPDS	6 hr, 3 days, and 6 wks postpartum
Suhitharan *et al.*[29]	Singapore	2016	Case control	$n = 479$	To examine peripartum analgesics and other psychologic variables that may be associated with clinically confirmed PPD.	Epidural $n = 329$ (69%) Nitrous oxide $n = 203$ (42%) Opioids $n = 32$ (9%)	PPD was significantly lower in women who received LEA compared with women who chose non-epidural pain control methods. Absence of LEA, increased age, history of depression, and history of PPD were risk factors for PPD development.	EPDS ≥ 7 and DSM criteria	4–8 wks postpartum
Wu *et al.*[23]	Canada	2018	Retrospective observational cohort	$n =$ 80,606	To investigate whether LEA use is related to maternal PPD among women seeking medical care.	Epidural $n =$ 40,303 (26%) Nitrous oxide $n =$ 10,668 (27%) Opioids $n =$ 18,034 (45%)	LEA was not related to maternal PPD in women presenting to the healthcare system.	Administrative coding for depressive disorder at hospital admission, outpatient psychiatry visit, or outpatient general practitioner	Within 12 months postpartum
Zanardo *et al.*[22]	Italy	2017	Case control	$n = 186$	To investigate the role of nitrous oxide on labour pain, satisfaction with the childbirth experience, and maternal feelings toward lactation.	Epidural $n = 81$ (44%) Nitrous oxide $n = 62$ (33%)	Nitrous oxide use was not associated with postnatal depression scores upon discharge.	EPDS ≥ 9	2 days postpartum

Table 1 continued

PTSD	Country of origin	Year	Study methodology	Sample size	Primary objective	Labour analgesia	Findings	Psychiatric evaluation tool	Psychiatric evaluation period
Boudou *et al.*[30]	France	2007	Prospective observational cohort	$n = 117$	To identify whether childbirth pain and perinatal distress/ dissociation impacts the development of PTSD postpartum.	Epidural $n = 113$ (97%)	Perinatal distress best predicted PTSD development postpartum. Emotional reactions to pain played a vital role in PTSD development. Epidural satisfaction was not predictive of PTSD symptoms postpartum.	EPDS ≥ 11 and IES-R, PDI, PDEQ	6 wks postpartum
Gosselin *et al.*[31]	Canada	2016	Prospective observational cohort	$n = 176$	To investigate whether: (i) fear of childbirth is associated with the process of delivery (i.e., perception of pain, use of anesthesia, and Cesarean delivery); (ii) higher fear of childbirth is associated with more negative postpartum outcomes (e.g., PPD/PTS symptoms); (iii) pain and process of delivery is associated with post-delivery symptoms.	Epidural or spinal anesthesia $n = 94$ (74.6%) (Epidural $n = 84$, spinal $n = 4$, missing data $n = 6$) Pudendal nerve block $n = 13$ (10%)	In the absence of anesthesia, fear of childbirth was associated with perceived pain. Irrespective of anesthesia use, fear was related to the development of PTSD and PPD symptoms.	EPDS, TES	During pregnancy and 5 wks postpartum
Gürber *et al.*[25]	Switzerland	2017	Prospective observational cohort	$n = 140$	To investigate the association between depressive symptoms during pregnancy and childbirth experiences for mothers and fathers with regard to PPD and ASR development postpartum.	Epidural $n = 38$ (27%)	When controlling for demographic covariates, mothers had more depressive symptoms, greater negative birth experiences, and higher stress reactions, compared with fathers. Depressive symptoms throughout pregnancy, in addition to negative birth experiences, epidural anesthesia, infant gender, and birth weight predicted PDS and ASR postpartum.	EPDS, IES-R	Third trimester and 4 wks postpartum

Table 1 continued

PTSD	Country of origin	Year	Study methodology	Sample size	Primary objective	Labour analgesia	Findings	Psychiatric evaluation tool	Psychiatric evaluation period
Lyons[26]	United Kingdom	1998	Prospective observational cohort	n = 42	To compare feelings about childbirth experiences after delivery, with reported PTSD symptoms 1 month postpartum among a sample of first-time mothers.	Epidural n = n/a	A sub-group of women reported PTSD symptoms, with medium to high levels of distress. Reported PTSD and PPD symptoms were found to both coincide and present independently.	EPDS ≥ 13, IES	1 month postpartum
Séjourné *et al.*[28]	France	2018	Prospective observational cohort	n =109	To identify whether pain intensity during childbirth and the postpartum period was associated with PPD and PTSD development 6 weeks postpartum.	Epidural n = 91 (83%)	Pain during childbirth and the immediate postpartum period was positively associated with PPD (r = 0.27 and r = 0.31 respectively) and PTSD symptomology (r = 0.30 and r = 0.34 respectively).	EPDS = 9–11 (intense blues) EPDS ≥ 12 (PPD) IES-R	2 and 4 days postpartum and 6 wks postpartum

Anxiety	Country of origin	Year	Study methodology	Sample size	Primary objective	Labour analgesia	Findings	Psychiatric evaluation tool	Psychiatric evaluation period
Floris *et al.*[32]	Switzerland	2017	Prospective observational cohort	n = 79	To examine anxiety and satisfaction with childbirth based on expectations prior to childbirth (i.e., upon admission) and actual experiences following childbirth.	Epidural n = 73 (92%)	The mean STAI score was higher upon admission, compared with following delivery. Postnatal anxiety was not related to mode of delivery, LEA, or pain.	EPDS ≥ 13 and STAI	2 hr and 4 months postpartum

EPDS =Edinburgh Postnatal Depression Scale (the most widely used screening instrument for PPD, with scores above 10 on the 30-point scale generally accepted to predict PPD risk;[33] PTSD = post-traumatic stress disorder; IES-R = Impact of Event Scale-Revised (22-item self-report measure that assesses subjective distress caused by traumatic events. Items are rated on a five-point scale and yield a total score ranging from 0 to 88. The IES-R provides cut-off scores for a preliminary diagnosis of PTSD;[28] PDI = Peritraumatic Distress Inventory (13-item self-report quantitative measure of the level of distress experienced during and immediately after a traumatic event. Studies suggest that peritraumatic distress increases the risk of developing post-traumatic stress disorder);[30] PDEQ = Peritraumatic Dissociative Experiences Questionnaire (each item is scored from 1 to 5 and a score above 15 indicates significant dissociation);[30] STAI = State-Trait Anxiety Inventory (includes 20 items for assessing trait anxiety and 20 items for assessing state anxiety. All items are rated on a four-point scale. Range of scores for each subtest is 20–80, the higher score indicating greater anxiety. A cut-off point of 39–40 has been suggested as clinically significant symptoms for the S-Anxiety scale);[32] TES = traumatic events scale (comprises the stressor criterion (criterion A) and the 17 DSM-IV PTSD symptoms that follow (criteria B, C, and D);[31]

ASR = acute stress reactions; DSM = Diagnostic and Statistical Manual of Mental Disorders; LEA = labour epidural analgesia; PPD = postpartum depression; wks = weeks.

Table 2 Patient characteristics

	Parity	Age [mean (SD)]	SES	Education	Ethnicity & language	Marital status	Medical comorbidities	Included risk factors for postpartum psychiatric disorders	Method of delivery
Boudou *et al.*[14]	Nulliparous *n* = 20 (47%) Multiparous *n* = 23 (54%)	30 (5)	n/a	n/a	n/a	n/a	n/a	Breastfeeding rates	SVD *n* = 34 (79%) AVD *n* = 9 (21%)
Boudou *et al.*[30]	Nulliparous *n* = 63 (54%) Multiparous *n* = 54 (46%)	30 (5)	n/a	n/a	n/a	n/a	Unspecific conditions *n* = 6 (5%)	History of trauma/abuse Planned pregnancy /prenatal classes	SVD *n* = 82 (70%) AVD *n* = 35 (30%)
Ding *et al.*[8]	Nulliparous *n* = 214 (100%)	29 (3)	Total income of husband and wife (¥ = Chinese Yuan)	> 12 years *n* = 194 (91%)	n/a	n/a	Obstetric disease *n* = 17 (8%) Internal medical disease *n* =18 (8%)	Planned pregnancy Prenatal classes Fear of childbirth Neonatal outcomes/ hospital admissions Breastfeeding rates	SVD *n* = 129 (60%) AVD *n* = 30 (14%) CD *n* = 55 (26%)
Ferber *et al.*[24]	Nulliparous *n* = n/a Multiparous *n* = n/a	30 (5)	n/a	Elementary *n* = 15 (18%) High school *n* = 27 (33%) Academic education *n* = 40 (49%)	n/a	Married *n* = 75 (92%) Other *n* = 7 (8%)	n/a		SVD *n* = 82 (100%)
Floris *et al.*[32]	Nulliparous *n* = 79 (100%)	30 (5)	Annual household income	< 15 years *n* = 33 (44%) > 15 years *n* = 42 (56%)	European *n* = 62 (78%) Other *n* = 17 (22%)	Married *n* = 53 (67%) Other *n* = 26 (33%)	n/a	Personal history of depression/ psychiatric disorders Breastfeeding rates	SVD *n* = 39 (49%) AVD *n* = 24 (30%) CD *n* = 16 (20%)
Gosselin *et al.*[31]	Nulliparous *n* = 176 (100%)	28 (4)	n/a	n/a	n/a	n/a	n/a	Personal history of depression/ psychiatric disorders Prenatal classes Fear of childbirth	SVD *n* = 130 (74%) CD *n* = 45 (26%)
Gürber *et al.*[25]	Nulliparous *n* = 62 (44%) Multiparous *n* = 76 (54%)	34 (5)	n/a	n/a	n/a	Couples *n* = 140 (100%)	n/a		SVD *n* = 74 (52%) AVD *n* = 17 (12%) CD *n* = 36 (26%)

Table 2 continued

	Parity	Age[mean (SD)]	SES	Education	Ethnicity& language	Marital status	Medical comorbidities	Included risk factors for postpartum psychiatric disorders	Method of delivery
Hiltunen *et al.*[9]	Nulliparous *n* = 86 (46%) Multiparous *n* = 99 (54%)	29 (5)	n/a	Basic education *n* = 7 (4%) Middle education *n* = 117 (63%) University education *n* = 61 (33%)	n/a	Partner *n* = 176 (94%) Other *n* = 9 (6%)	Gestational diabetes *n* =3 (16%) Hypertension *n* = 2 (11%) Other *n* = 3 (16%)	Season of delivery Neonatal hospital admissions	SVD *n* = 136 (73%) AVD *n* = 6 (3%) CD *n* = 43 (23%)
Lim *et al.*[10]	Nulliparous *n* = n/a Multiparous *n* = n/a	28 (6)	n/a	n/a	n/a	n/a	Hypertension *n* = 25 (16%) Anemia *n* = 15 (9%) Chronic pain *n* = 4 (2%) Other *n* = 32 (20%)	Personal history of depression/ psychiatric disorders History of trauma/abuse or domestic abuse	SVD *n* = 167 (83%) AVD *n* = 3 (2%) CD *n* = 31 (15%)
Lyons[26]	Nulliparous *n* = 42 (100%)	29 (Range 20–39)	UK Registrar General's six socio-economic categories	n/a	100% Caucasian	n/a	n/a		SVD *n* = 19 (45%) AVD *n* = 15 (36%) CD *n* = 8 (19%)
Nahirney *et al.*[11]	Nulliparous *n* = 108 (52%) Multiparous *n* = 98 (48%)	30 (5)	Annual household income & home ownership	High school or less *n*= 34 (16%) Post-secondary education *n* = 172 (84%)	English *n* = 181 (88%) other *n*= 25 (22%)	Married *n* = 201(98%) Other n = 5 (92%)	n/a		SVD *n* = 206 (100%)
Orbach-Zinger *et al.*[27]	Nulliparous *n* = 477 (31%) Multiparous *n* = 1019 (69%)	Group 1 32 (5) Group 2 29 (5) Group 3 31 (5) Group 4 32 (5)	n/a	n/a	Israel born *n* = 1,348 (91%) non-immigrant *n* = 140 (9%)	Married *n* = 1,444 (95%) Other *n* = 52 (5%)	Hypertension *n* = 80 (5%) Diabetes *n* = 97 (6%) Hypothyroidism *N* = 72 (5%) Other chronic disease *n*=128 (9%)	Personal history of depression/ psychiatric disorders	SVD *n* = 1,152 (88%) AVD *n* = 174 (12%)

Table 2 continued

	Parity	Age[mean (SD)]	SES	Education	Ethnicity& language	Marital status	Medical comorbidities	Included risk factors for postpartum psychiatric disorders	Method of delivery
Riazanova *et al.*[21]	n/a	Epidural 29 [IQR 26–31] No epidural 30 [IQR 27–32]	n/a	n/a	n/a	n/a	n/a	Neonatal outcomes	SVD *n* = 210 (100%)
Séjourné *et al.*[28]	Nulliparous *n* = 54 (50%) Multiparous *n* = 55 (50%)	30 (5)	n/a	n/a	n/a	In a relationship n = 107 (98%) Other *n* = 2 (2%)	n/a		SVD *n* = 109 (100%)
Suhitharan *et al.*[29]	Nulliparous *n* = n/a Multiparous *n* = n/a	31 (5)	n/a	Basic education *n* = 7 (2%) Middle education *n* = 114 (24%) University education n = 359 (75%)	Chinese *n* = 472 (98%)	Married *n* = 478 (99%) Other *n* =1 (1%)	Case group Gestational diabetes *n* = 4 (7%) Gestational hypertension *n* = 4 (7%) Chronic medical condition *n*= 6 (10%) Control group Gestational diabetes *n* = 29 (7%) Gestational hypertension *n* = 10 (2%) Chronic medical condition *n* = 6 (1%)	Personal and family history of depression/ psychiatric disorders History of PPD Planned pregnancy	SVD *n* = 382 (80%) AVD *n* = 59 (12%) CD *n* = 92 (19%)

Table 2 continued

	Parity	Age[mean (SD)]	SES	Education	Ethnicity& language	Marital status	Medical comorbidities	Included risk factors for postpartum psychiatric disorders	Method of delivery
Wu *et al.*[23]	Nulliparous *n* = 80,606 (100%)	Epidural 27 (5) No epidural 27 (5)	SES determined using the Ontario Marginalization Index	n/a	No epidural group English *n* = 31,611 (78%) other *n* = 8,692 (22%) Epidural group English *n* = 31,475 (78%) other *n* = 8,828 (22%)	n/a	No epidural group Any medical condition *n* = 6,072 (15%) Infectious diseases *n* = 209 (0.5%) Cardiac and pulmonary disease *n* = 138 (0.3%) Hypertension-related *n* = 148 (0.4%) Diabetes and metabolic *n* = 942 (2%) Other *n* = 2,734 (7%) Epidural group Any medical condition *n* = 6,040 (15%) Infectious diseases *n* = 199 (0.5%) Cardiac and pulmonary disease *n* = 136 (0.3%) Hypertension-related *n* = 134 (0.3%) Diabetes and metabolic *n* = 903 (2%) Other *n* = 2,735 (7%)	Breastfeeding rates	SVD No epidural group *n* = 31,887 (79%) Epidural group *n* = 31,779 (79%) No epidural group *n* = 6,179 (15%) Epidural group *n* = 6,399 (16%)

Table 2 continued

	Parity	Age[mean (SD)]	SES	Education	Ethnicity& language	Marital status	Medical comorbidities	Included risk factors for postpartum psychiatric disorders	Method of delivery
Zanardo *et al.*[22]	Nulliparous *n* = 138 (74%) Multiparous *n* = 48 (27%)	Nitrous oxide group 33 (4) Control group 33 (4)	n/a	Nitrous oxide group Primary education *n* = 4 (6%) Secondary education *n* = 28 (45%) University degree *n* = 27 (44%) Control group Primary education *n* = 14 (11%) Secondary education *n*= 64 (52%) University degree *n* = 42 (34%)	n/a	n/a	n/a	Personal history of depression/psychiatric disorders Breastfeeding rates	SVD *n* = 156 (84%) CD *n* = 30 (16%)

AVD = assisted vaginal delivery; CD = Cesarean delivery; IQR = interquartile range; SD = standard deviation; SES = socioeconomic status; SVD = spontaneous vaginal delivery; wks = weeks.

postpartum PTSD symptoms, and one study[32] focused on postpartum anxiety (Table 1). Risk factors for these included postpartum psychiatric disorders are summarized in Table 2.

Measures of psychiatric disorders

Ten of the studies that evaluated PPD symptoms used the Edinburgh Postnatal Depression Scale (EPDS) screening tool.[8–11,14,21,22,24,27,29] The EPDS is a ten-item self-rating scale used to screen for symptoms that are common in women with PPD.[33] Responses to items are scored from 0 to 3, with a maximum score of 30. This measure shows excellent psychometric properties and is widely accepted as the preferred screening method for PPD. A cut-off score ≥ 10 identifies a major depressive disorder with sensitivity of $> 90\%$ and specificity of $> 80\%$.[34,35] One study[29] combined this screening tool with a clinical interview that evaluated symptoms using the Diagnostic and Statistical Manual for Mental Disorders, fifth edition (DSM-5).[5] One study[23] used administrative coding for depressive disorder at hospital admission to determine the presence of PPD screen-positive patients. The EPDS cut-off score, which determined if the patient may be at risk for PPD, varied between studies, ranging from seven to 14. The time at which the EPDS was evaluated ranged between two days and six months postpartum. More than half of screening evaluations (6/10)[8,10,11,21,24,25,27–29,31] were completed between four and six weeks postpartum.

Four of the studies that evaluated postpartum PTSD symptoms used the revised Impact of Event Scale (IES-R) screening tool.[25,26,28,30] One study[30] used the Peritraumatic Distress Inventory and the Peritraumatic Dissociative Experiences Questionnaire screening tools in addition to the IES-R to estimate the risk of postpartum PTSD symptoms. Another study[31] used the Traumatic Events Scale and the IES-R to evaluate postpartum PTSD symptoms. The one study[32] that examined postpartum anxiety used the State-Trait Anxiety Inventory. Threshold values of the screening tools outlined above are listed in Table 1.

Studies assessing the link between pharmacologic labour analgesia to postpartum psychiatric disorders

Nine studies[8–11,21–23,27,29] had a primary objective of evaluating the association of pharmacologic labour analgesia with postpartum psychiatric disorders. Of the six studies with the primary objective of linking LEA and PPD,[8–11,27,29] two studies found that fewer patients screened positive for PPD with LEA compared with patients who chose non-epidural labour analgesia.[8,29] In one study, all patients received LEA, and the extent of

labour pain relief by LEA predicted lower PPD scores.[10] Two studies found no difference between patients who screened positive for PPD with LEA compared with women who did not choose LEA.[11,27] One study found no difference in positive PPD screening between patients who received LEA or paracervical blockade and patients who received nitrous oxide, acupuncture, or no pain relief.[9] Studies that did not see a difference in the prevalence of PDD based on the use of labour analgesia were adequately powered to detect this outcome.

Zanardo *et al.* found that EPDS subscales were not different upon discharge in a nitrous oxide group and a matched control group.[22] Studies by both Ferber *et al*. and Gürber *et al.* controlled for use of labour analgesia in positive PPD screening, but did not look for a relationship between labour analgesia intervention and the outcome.[24,25] While all of these studies involved the use of LEA, one study combined LEA with a paracervical block[9] and another study evaluated the effect of nitrous oxide on postpartum mental illness.[22] One study specifically evaluated postpartum anxiety in patients who received labour analgesia and concluded that postnatal anxiety was not associated with mode of delivery, epidural analgesia, or pain.[32]

Four studies[25,26,30,31] examined the relationship between postpartum PTSD symptoms and labour analgesia. Gosselin *et al*. concluded that childbirth was related to PTSD symptoms regardless of whether analgesia was used or not.[31] Similarly, Gürber *et al.* noted that depressive symptoms and a negative birth experience were independently predictive of risk for PTSD symptoms when controlling for labour analgesia.[25] Boudou *et al.* found that satisfaction with LEA was predictive of PTSD symptoms.[30] Interestingly, Lyons found that higher scores on the Impact of Event Scale (IES), a subjective measure of distress caused by traumatic events, correlated positively with having LEA.[26]

Studies assessing the link between labour pain and postpartum psychiatric disorders

The link between labour pain and postpartum psychiatric disorders, regardless of analgesia mode, was explored in four studies.[14,28,30,31] Boudou *et al*. found a significant positive correlation between the intensity of childbirth pain and depressed mood postpartum in parturients.[14] Emotional reactions caused by pain played an important role in the development of PTSD symptoms postpartum in a subsequent study.[30] Séjourne *et al.* found that pain of childbirth did not show a relationship with postpartum mood in a study where 83% of the cohort received LEA.[28] Nevertheless, the pain of delivery and pain immediately postpartum correlated with PTSD symptomatology.[28] Similarly, Gosselin *et al.* found a link between the intensity of childbirth pain, PPD intensity, and the presence of PTSD symptoms, regardless of the use of LEA.[31]

Discussion

This scoping review, which summarized the possible relationship between labour analgesia, childbirth pain, and postpartum psychiatric disorders reported in the current literature, identified significant variability among existing studies. While some studies were designed to specifically observe the association between pharmacologic labour analgesia and the development of postpartum psychiatric disorders, others determined associations through secondary regression analysis. As it was not the primary objective of some studies to evaluate the effect of labour analgesia on the development of a postpartum psychiatric disorder, caution is required when interpreting the findings.

Study design

In studies examining the linkage between LEA and postpartum psychiatric disorders, the disagreement among study conclusions must be taken in the context of the high rate of LEA use as the use of LEA was not always controlled for in the analysis. Even if LEA was found to be significantly related to any of the postpartum psychiatric outcomes, it may be spurious, with other confounders proving to be more meaningful.[10] Most studies were cross-sectional and could not evaluate the true development of postpartum psychiatric disorders, rather only comment on the presence of psychiatric symptoms at the time of assessment. Longitudinal studies examining symptom levels at different time points are required to examine the development of postpartum psychiatric disorders over time.

The studies included in this review were predominantly observational cohorts as randomized-controlled trials are not plausible. Notably, LEA remains the gold standard for pain relief and ethical implications become apparent by attempting to deny this modality of labour analgesia in a randomized-controlled trial. Additionally, randomizing LEA compared with other pharmacologic labour analgesia may result in high cross-over rates reducing the interpretability of results even in the context of intent-to-treat analysis and make it challenging to recruit and retain participants.

Several studies explored the link between labour pain and postpartum psychiatric disorders, regardless of analgesia mode. Labour pain has been correlated with postpartum blues,[14] and the severity of acute postpartum

pain has been cited as an independent risk factor for the development of persistent pain and depression.[6] Recent meta-analysis have also identified an association between level of pain during delivery and postpartum PTSD symptoms.[19] Change in pain with therapy has been shown to be more important to patients than pain itself, and percentage of pain improvement has been correlated with improved patient outcomes.[10] Only one of the included studies addressed analgesia quality in detail by evaluating pain improvement.[10] Therefore, it remains uncertain if analgesia that provides comfort during labour, but is inadequate during delivery, could be a source of postpartum psychiatric disorders. The degree to which labour pain improves with intervention rather than the utilization of pharmacologic labour analgesia needs to be examined with respect to postpartum psychiatric disorders. Additionally, the included studies did not specify the length of time that pain was present prior to initiating LEA, which may relate to the intensity of the experience of labour pain. Future studies could examine if there is a link between duration of unrelieved pain and perceived pain intensity.

By explicitly assessing the relationship between changes in labour pain intensity or pharmacologic labour analgesia and risk of postpartum psychiatric disorders, previously noted associations can be further clarified in future studies.

Controlling for confounders

Antepartum psychiatric risk factors and risk factors for psychiatric illness in the postpartum period varied between studies and were not always controlled. The relationship between LEA and reduced PPD risk may be better explained by mechanisms other than labour analgesia.[10] Patient risk factors, such as the role of adverse life events, environmental factors, and a family history of depression should be accounted for to fully understand the development of PPD.[36] Future studies evaluating the effect of labour analgesia on postpartum psychiatric outcomes should account for these confounding psychosocial risk factors.

There is evidence that maternal satisfaction with childbirth is influenced by mode of delivery, with less satisfaction associated with assisted and operative deliveries.[37] It is plausible that women unsatisfied with their mode of delivery may be more prone to PPD, which was not accounted for in the included studies. Similarly, most of the included studies failed to examine the link between perceived loss of control during delivery and pain intensity. Only one study attempted to address unmatched expectations during labour.[27] There is evidence of a negative interaction between unmatched expectations (in terms of women desiring and actually receiving labour analgesia) and the development of PPD.[27] Patient expectations for labour analgesia were not accounted for in the remaining studies, so it is uncertain whether this negative interaction plays a role in the risk of PPD. An assessment of mother's expectations for delivery and labour analgesia would be advantageous in future studies.

Method of postpartum psychiatric assessment

The method of psychiatric evaluation varied among the available studies. The EPDS was the most commonly employed method of screening for PPD, but the threshold score used to identify possible presence of PPD (dichotomous outcome) varied among studies. The available studies evaluating postpartum PTSD symptoms used different screening scales. The lack of a standardized screening threshold makes generalizability of the results difficult, as some studies risk under- or overestimating the effect of labour analgesia on postpartum psychiatric disorders.[38] Though screening tools are not intended to make a formal diagnosis, they may be reasonable endpoints because tests are highly sensitive and specific, and positive screening and diagnosis are fairly concordant.[39] Studies that use tools to diagnose postpartum psychiatric disease as an endpoint should clearly indicate the findings as positive screens rather than a clinical diagnosis. Application of the DSM-5 criteria combined with clinical examination of the patient would ultimately be the gold standard for diagnosis in future studies.

Time of postpartum psychiatric assessment

The timing in which screening for PPD was completed varied between the studies. It has been suggested that postpartum screening for depression should occur six to 12 weeks after birth and be repeated at least once in the first postnatal year.[40] As early as postpartum day two, the EPDS is considered a reliable screening tool for predicting a positive screen later postpartum and determining which patients need close follow-up.[41] Depressive symptoms were not detected before epidural analgesia in any of the included studies. Future studies may want to include screening at time points up to one year postpartum to better understand the relationship between labour analgesia and the timing of PPD development.

Conclusions

This scoping review showed that the relationship between pharmacologic labour analgesia and postpartum psychiatric disorders remains uncertain. Existing studies have small sample sizes and are observational cohorts in design.

Patient psychiatric risk factors, type of labour analgesia received, and the use of tools to diagnose postpartum psychiatric disease are inconsistent among studies. While some studies were designed to specifically observe the association between labour analgesia and the development of postpartum psychiatric disorders, others have inferred an association through secondary analysis. The ideal study would correlate positive screening with clinical diagnosis, include screening in the antepartum period in addition to early and late in the postpartum period, and consider improvement in pain in addition to pharmacologic labour analgesia when evaluating postpartum psychiatric disorders.

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Appendix A Search Strategy for labour analgesia and postpartum psychiatric disorders

Embase

((‘postpartum-depression’:ti,ab OR ‘postnatal-depression’:ti,ab OR ‘postpartum-blues’:ti,ab OR ‘postnatal-blues’:ti,ab OR ‘postnatal depression’/exp) AND (epidural*:ti,ab OR analges*:ti,ab OR anesthe*:ti,ab OR anaesthe*:ti,ab OR pain*:ti OR ‘epidural analgesia’/exp OR ‘epidural anesthesia’/exp OR ‘obstetric analgesia’/exp OR ‘analgesia’/exp)) OR ((labor*:ti OR labour*:ti OR deliver*:ti OR ‘labor’/exp OR childbirth:ti OR birth*:ti) AND (epidural*:ti,ab OR analges*:ti,ab OR anesthe*:ti,ab OR anaesthe*:ti,ab OR pain*:ti OR ‘epidural analgesia’/exp OR ‘epidural anesthesia’/exp OR ‘obstetric analgesia’/exp OR ‘analgesia’/exp) AND (ptsd:ti,ab OR ‘post-traumatic-stress’:ti,ab OR ‘posttraumatic-stress’:ti,ab OR anxiety:ti,ab OR ‘postpartum-depression’:ti,ab OR ‘postnatal-depression’:ti,ab OR ‘postpartum-blues’:ti,ab OR ‘postnatal-blues’)

CINAHL:

((TI (“postpartum-depression” OR “postnatal-depression” OR “postpartum-blues” OR “postnatal-blues” OR (MH “Depression, Postpartum”)) OR AB (“postpartum-depression” OR “postnatal-depression” OR “postpartum-blues” OR “postnatal-blues” OR (MH “Depression, Postpartum”))) AND (TI (epidural* OR analges* OR anesthe* OR anaesthe* OR pain* OR (MH “Analgesia, Epidural”) OR (MH “Anesthesia, Epidural”) OR (MH “Analgesia, Obstetrical”) OR (MH “Pain Management”)) OR AB (epidural* OR analges* OR anesthe* OR anaesthe* OR pain* OR (MH “Analgesia, Epidural”) OR (MH “Anesthesia, Epidural”) OR (MH “Analgesia, Obstetrical”) OR (MH “Pain Management”)))) OR (TI (labor* OR labour* OR deliver* OR (MH “Labor”) OR childbirth OR birth*) AND ((TI (epidural* OR analges* OR anesthe* OR anaesthe* OR pain*) OR AB (epidural* OR analges* OR anesthe* OR anaesthe*)) OR (MH “Analgesia, Epidural”) OR (MH “Anesthesia, Epidural”) OR (MH “Analgesia, Obstetrical”) OR (MH “Pain Management”)) AND (TI (PTSD OR “post-traumatic-stress” OR “posttraumatic-stress” OR anxiety OR “postpartum-depression” OR ”postnatal-depression” OR “postpartum-blues” OR “postnatal-blues” OR AB (PTSD OR “post-traumatic-stress” OR “posttraumatic-stress” OR anxiety OR “postpartum-depression” OR ”postnatal-depression” OR “postpartum-blues” OR “postnatal-blues”)

PsycINFO:

((TI (“postpartum-depression” OR “postnatal-depression” OR “postpartum-blues” OR “postnatal-blues” OR (DE “Postpartum Depression”)) OR AB (“postpartum-depression” OR “postnatal-depression” OR “postpartum-blues” OR “postnatal-blues” OR (DE ”Postpartum Depression”))) AND (TI (epidural* OR analges* OR anesthe* OR anaesthe* OR pain* OR (DE “Analgesia”) OR (DE “Anesthesia (Feeling)”) OR (DE “Pain Management”)) OR AB (epidural* OR analges* OR anesthe* OR anaesthe* OR pain* OR (DE “Analgesia”) OR (DE “Anesthesia (Feeling)”) OR (DE “Pain Management”)))) OR (TI (labor* OR labour* OR deliver* OR (DE “Labor (Childbirth)”) OR childbirth OR birth*) AND ((TI (epidural* OR analges* OR anesthe* OR anaesthe* OR pain*) OR AB (epidural* OR analges* OR anesthe* OR anaesthe*)) OR (DE “Analgesia”) OR (DE “Anesthesia (Feeling)”) OR (DE “Pain Management”)) AND (TI (PTSD OR “post-traumatic-stress” OR “posttraumatic-stress” OR anxiety OR “postpartum-depression” OR ”postnatal-depression” OR “postpartum-blues” OR “postnatal-blues” OR AB (PTSD OR “post-traumatic-stress” OR “posttraumatic-stress” OR anxiety OR “postpartum-depression” OR ”postnatal-depression” OR “postpartum-blues” OR “postnatal-blues”)

Pubmed:

(((“postpartum-depression”[Title/Abstract] OR “postnatal-depression”[Title/Abstract] OR “postpartum-blues”[Title/Abstract] OR “mood” [Title/Abstract] “postnatal-blues”[Title/Abstract] OR (“Depression, Postpartum”[Mesh])) AND (((epidural*[Title/Abstract] OR analges*[Title/Abstract] OR anesthe*[Title/Abstract] OR anaesthe*[Title/Abstract])) OR pain*[ti] OR ((((“Analgesia, Epidural”[Mesh]) OR “Anesthesia, Epidural”[Mesh]) OR “Analgesia, Obstetrical”[Mesh]) OR “Pain Management”[Mesh]))) OR ((((labor*[Title] OR labour*[Title] OR deliver*[Title]) OR (“Labor, Obstetric”[Mesh])) OR (childbirth[Title] OR birth*[Title])) AND (((epidural*[Title/Abstract] OR analges*[Title/Abstract] OR anesthe*[Title/Abstract] OR anaesthe*[Title/Abstract])) OR pain*[ti] OR ((((“Analgesia, Epidural”[Mesh]) OR “Anesthesia, Epidural”[Mesh]) OR “Analgesia, Obstetrical”[Mesh]) OR “Pain Management”[Mesh])) AND (PTSD[Title/Abstract] OR “post-traumatic-stress”[Title/Abstract] OR “posttraumatic-stress”[Title/Abstract] OR anxiety[Title/Abstract] OR “postpartum-depression”[Title/Abstract] OR “postnatal-depression”[Title/Abstract] OR “postpartum-blues”[Title/Abstract] OR “postnatal-blues”[Title/Abstract]

Appendix B Extraction tool used for studies that met inclusion criteria

Part A: Study details	
Title	Month, year published
Authors	Journal
Study country	Funding type
Study type	Study exclusion criteria
Hospital type	Sample size
Primary outcome	Multicentre study
Secondary outcomes	Study duration
Study inclusion criteria	Study conclusion
Part B: Demographics	
Average age	Socioeconomic status
Marital status	Education
Ethnicity	Chronic medical conditions
Part C: Psychiatric risk factors	
Psychiatric history	History of postpartum depression
History of depression	Family psychiatric history
History of trauma of abuse	Domestic violence
Prenatal class/preparedness for birth	Illegal drugs or alcohol use
Home support	Fear of childbirth
History of analgesia use	Season of delivery
Preterm delivery	Planned pregnancy
Breastfeeding status	NICU admission
Appearance, pulse, grimace, activity, respiration (score of baby)	
Part D: Obstetric factors	
Parity	Method of delivery
Major obstetrical comorbidities (diabetes, hypertensive diseases of pregnancy etc.)	
Part E: Psychiatric outcome measures	
Screening tool used	Cut-off for screening tool
Assessment timeline	Psychiatric outcome evaluated

NICU = neonatal intensive care unit.

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