Painless childbirth? Epidural and spinal techniques in obstetric anesthesia

Schyns-van den Berg, A.M.J.V.

Chapter 4

Association between postpartum depression and chronic postsurgical pain after Cesarean delivery: a secondary analysis of a randomized trial

Asish Subedi,
Sharon Orbach-Zinger,
Alexandra M.J.V. Schyns van den Berg

Published: Canadian Journal of Anaesthesia 2025 Aug; 72(8): 1314-1323

ABSTRACT

Purpose

Psychological factors such as anxiety, depression, and catastrophizing, may increase the risk of chronic postsurgical pain (CPSP) following Cesarean delivery (CD). We sought to evaluate whether postpartum depression (PPD) after CD is associated with CPSP and to assess the potential mediating effect of PPD on the relationship between acute severe postoperative pain and CPSP.

Methods

We conducted a secondary analysis of a previous randomized trial. In the original trial, 290 patients undergoing CD in Nepal were randomized to receive either 100 μg of intrathecal morphine or normal saline in addition to their spinal anesthesia with the goal to investigate the relationship between intrathecal morphine use and CPSP development. Eight weeks after CD, we used the Edinburgh Postnatal Depression Scale to identify patients with a provisional diagnosis of PPD (scores ≥12). The study outcomes were the occurrence of CPSP at three and six months.

Results

Out of 276 patients analyzed, 20 (7%) experienced PPD. The incidences of CPSP at three and six months were 18% (52/276) and 15% (42/276), respectively. A multivariable model revealed that the odds of experiencing CPSP at three months postpartum were significantly higher in patients with depression (odds ratio [OR], 4.24; 95% confidence interval [CI], 1.53 to 11.74; P = 0.005) than in those without depression. Similarly, PPD was independently associated with an increased incidence of CPSP incidence at six months post CD (OR, 4.05; 95% CI, 1.42 to 11.54; P = 0.009). Causal mediation analysis showed no mediating effect of PPD between acute severe postoperative pain and CPSP.

Conclusion

In this secondary analysis of a previous randomized trial, we found a significant association between PPD and CPSP following CD.

INTRODUCTION

Chronic postsurgical pain (CPSP), defined as pain persisting for at least three months after surgery, poses significant health challenges after Cesarean delivery (CD).[1] A meta-analysis of 15 studies showed that the incidence of CPSP at three and six months post CD was 15.4% (95% confidence interval [CI], 9.9 to 20.9%) and 11.5% (95% CI, 8.1 to 15.0%), respectively,[2] with one-third of these patients reporting moderate to severe pain. Most studies to date on CPSP after CD have focused on preoperative or immediate postpartum predictors such as preoperative demographics, perioperative psychological issues, surgical techniques, mode of anesthesia, and acute postoperative pain severity.[3,4] Few studies, however, have examined factors in the longer recovery period, such as pain trajectories and mood, and their relationship to CPSP development.

According to the International Classification of Diseases 11th Revision, postpartum depression (PPD) is defined as a major depressive disorder occurring within six weeks after childbirth.[5] The Edinburgh Postnatal Depression Scale (EPDS) is a widely accepted screening tool for assessing PPD, as it has demonstrated good psychometric properties.[6] Postpartum depression (PPD) affects approximately 17% (95% CI, 16 to 18) of women globally, indicating that 1 in every 5 women experiences PPD (95% CI; 16.00 to 18.51).[7] Postpartum depression profoundly impacts the maternal wellbeing and influences offspring outcome as well as family functioning.[8] Immediate postpartum pain has been linked to PPD development, with one study showing that acute postoperative pain severity independently contributes to persistent pain and depression at 8 weeks after Cesarean delivery.[9,10] A recent study also showed that worsened postpartum quality of recovery, including more severe pain, was an independent risk factor for the development of PPD.[11] While the relationship between pain and depression is well-established in patients with chronic pain, fewer data exist on the intersection of PPD and chronic pain in the obstetric population. Preoperative depression is significantly associated with CPSP following CD.[12] Additionally, postoperative depression assessed at four months following CD strongly correlates with CPSP.[13]

In a previously conducted randomized clinical trial, we compared the impact of intrathecal morphine *vs* placebo on CPSP following elective CD.[14] The results showed that administering intrathecal morphine did not effectively reduce the incidence of CPSP at three and six months after CD. In this secondary analysis of the previous trial, our primary objective was to investigate the relationship between provisional diagnosis of PPD at 8 weeks (EPDS scores ≥12) and the incidence of CPSP three and six months post-Cesarean delivery. We hypothesized that the development of PPD at 8 weeks postpartum would be a predictor for the development of CPSP both at three and six months. We also explored the mediating effect of PPD on the relationship between acute severe postoperative pain and CPSP.

METHODS

We conducted a secondary analysis of a previously conducted randomized clinical trial approved by the institutional review committee (IRC) of the BP Koirala Institute of Health Sciences (BPKIHS; Dharan, Nepal) with the IRC number 1183/017. All patients had provided written informed consent before enrolment in the study. The original trial evaluated the effects of intrathecal *morphine vs* placebo on the incidences of CPSP at three and six months after CD and found no significant difference in the incidence of CPSP between parturients who received intrathecal *morphine vs* those who did not, with detailed trial methodology published elsewhere.[14] This secondary analysis study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

The study enrolled full-term singleton parturients aged > 18 years, classified as American Society of Anesthesiologists Physical Status II, who were scheduled for planned CD under spinal anesthesia. The exclusion criteria were preeclampsia, height < 150 cm, a body mass index (BMI) > 40 kgm^{-2}, recent opioid use, substance use disorder, significant cardiovascular, renal, or hepatic conditions, known fetal abnormalities, allergies to any study drug, or contraindications to spinal anesthesia. Baseline patient characteristics, such as age, BMI, gestational age, socio-economic status (assessed with Kuppuswamy's scale),[15] previous CD history, and pre-existing chronic pain, were documented. We also recorded preoperative anxiety and depression scores (assessed with the hospital anxiety and depression scale),[16] pain catastrophizing scores,[17] and preoperative pain pressure threshold and tolerance (assessed with a handheld algometer; details of which have been previously reported[14]).

In the trial, 290 patients underwent randomization to receive 100 µg of intrathecal morphine or normal saline as a component of spinal anesthesia. We standardized the perioperative anesthesia and surgical management for all patients. After surgery, we recorded postoperative pain severity at different time points up to 48 hr (using an 11-point numeric rating scale [NRS] score; 0 = no pain and 10 = the worst possible pain), the area of secondary hyperalgesia (in cm^2) around the surgical incision at 48 hr (details explained elsewhere),[14] rescue intravenous morphine (in mg) needed up to 48 hr, and patient satisfaction regarding postoperative analgesia at 48 hr (assessed using a 5-point scale: 1 = highly satisfied, 2 = satisfied, 3 = neutral, 4 = not satisfied, and 5 = strongly dissatisfied).

After discharge from the hospital, we contacted patients via telephone for PPD assessment at 8 weeks and CPSP evaluation at three and six months after surgery. For the provisional diagnosis of PPD, we used the validated Nepali version of the EPDS, which is the most widely used and validated tool for this purpose.[18] The EPDS includes 10 items, each scored from 0–3, resulting in a total score of 0-30. In this study, we identified the presence of PPD with EPDS scores of 12 or higher, as this cutoff point in the Nepalese version of the EPDS demonstrated an accuracy of 98.2%.[18] Chronic postsurgical pain is defined by the presence of 3 criteria: pain at the incision site that developed following surgery, pain that persists for

at least three months, and pain that differs from any pre-existing pain conditions present before the surgery.[1]

The primary outcome of the original study was the incidence of CPSP at three months after surgery, with the secondary outcome being the occurrence of CPSP at six months post-CD. In the present study, we aimed to test the hypothesis that participants reporting EPDS scores ≥ 12, indicating a provisional diagnosis of PPD at 8 weeks, would have a higher likelihood of experiencing CPSP at three and six months after surgery than those with lower EPDS scores. The sample size was based on the data available from our previous study.

Statistical analysis

We used the Shapiro–Wilk test to evaluate the normality of the continuous variables. We expressed all continuous data that were normally distributed as mean (standard deviation [SD]) and analysed the data using two-tailed independent Student's *t* tests; we expressed all non-normally distributed data as median [interquartile range (IQR)] and analyzed the data using Mann–Whitney *U* tests. We used Chi-square tests for categorical variables and applied Fisher's exact tests when the expected cell counts were < 5.

We conducted logistic regression analyses to identify the associations between PPD and CPSP. For building the multivariable regression model, we included variables on the basis of existing knowledge and clinical judgment. We report the results as odds ratios (ORs), with corresponding 95% CIs. We evaluated the goodness of fit of the logistic regression models for the multivariable analysis using the Hosmer–Lemeshow test. We assessed collinearity among the covariates using the variance inflation factor (VIF), with variables exceeding a VIF > 5 regarded as collinear and consequently excluded from the regression model. We also investigated the mediating role of PPD (a binary variable) in the relationship between acute severe postoperative pain (a binary variable) and CPSP (a binary outcome), as illustrated in Fig. 1. To test our hypothesis, we conducted a statistical causal mediation analysis, both with and without adding other covariates (confounders), using the "mediate" package in STATA® version 18 (StataCorp. LP, College Station, TX, USA). This analysis estimates the total effect of acute severe postoperative pain on CPSP and decomposes it into direct and indirect effects (via a mediator) on the odds-ratio scale. We deemed all *P* values < 0.05 were deemed statistically significant. Data were analyzed using Stata 18.0 software.

Fig. 1. Outline of causal mediation analysis model

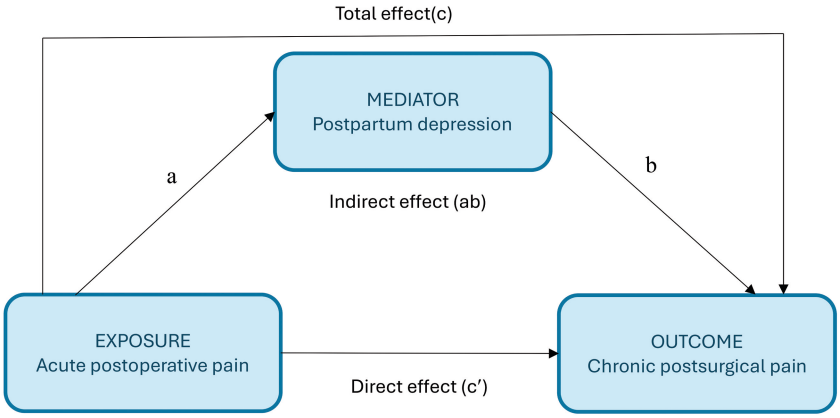
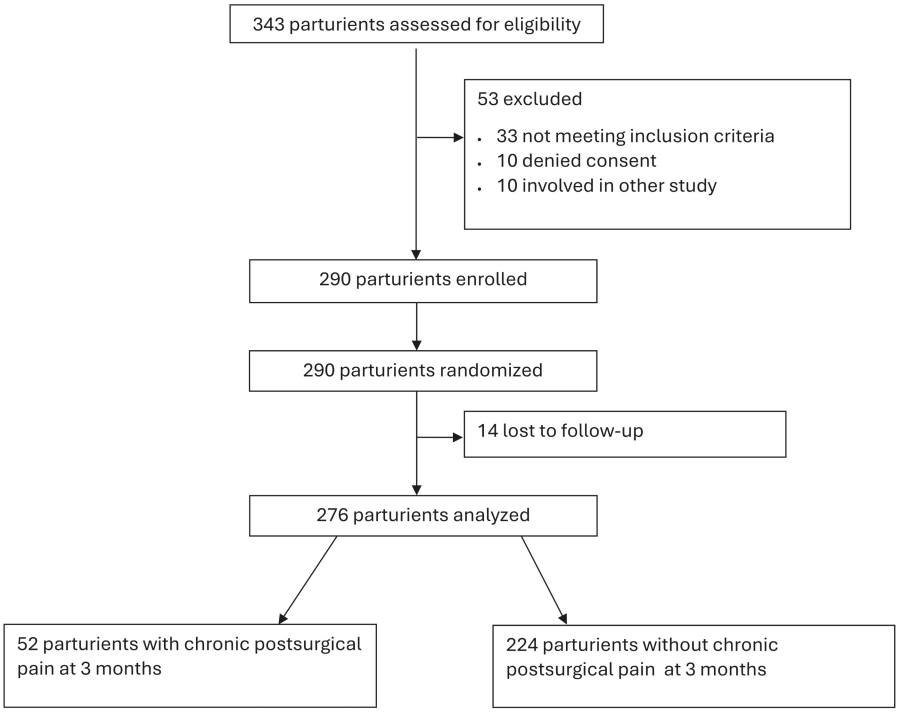


Fig. 2. Flowchart of the study



RESULTS

Of the 290 patients initially randomized in the original study, we included 276 in the final analysis, as 14 patients (5%) were lost to telephone follow-up (Fig. 2). At the 8-week follow-up after surgery, 20 patients (7%) reported a provisional diagnosis of PPD according to EPDS scores. Out of 276 women, 52 (18%) reported chronic postsurgical pain (CPSP) at three months following Cesarean delivery, while 42 (15%) experienced it at six months. Table 1 presents the baseline and clinical characteristics of patients who developed PPD and those who did not. Forty-three out of 256 patients (17%) in the non-PPD group and 9/20 patients (45%) in the PPD group reported CPSP at three months (P = 0.002) (Table 1). Likewise, within the PPD group, 8/20 patients (40%) reported CPSP at 6 months, while in the nonPPD group, 34/256 patients (13%) experienced CPSP (P = 0.001) (Table 1).

Table 1. Baseline patient characteristics and perioperative profiles

Variable	All patients (N=276)	PPD group (N=20)	Non-PPD group (N=256)	*P*-value
Age (yr), mean (SD)	28.2 (4.8)	26.8 (4.8)	28.3 (4.7)	0.16*
Body mass index (kg. m-2), mean (SD)	27.4 (3.6)	26.8 (3.2)	27.4 (3.7)	0.48*
Gestational age (weeks), mean (SD)	38.7 (1.2)	39 (1.2)	38.7 (1.2)	0.36*
Indo-Aryan origin, n/total N (%)	167/276(61%)	14/20 (70%)	153/256 (60%)	0.36**
Previous cesarean delivery, n/total N (%)	185/276 (67%)	15/20 (75%)	170/256 (66%)	0.43**
Pre-existing chronic pain, n/total N (%)	6/276 (2%)	2/20 (10%)	4/256 (1%)	0.06***
Socio-economic status, n/total N (%)				0.55***
Upper class	18/276 (7%)	2/20 (10%)	16/256 (6%)	
Upper middle class	131/276 (47%)	7/20 (35%)	124/256 (49%)	
Lower middle class	82/276 (30%)	7/20 (35%)	75/256 (29%)	
Upper lower class	45/276 (16%)	4/20 (20%)	41/256 (16%)	
HADS scores (0-21)				
Anxiety, median [IQR]	4 [3-6]	5 [4-6]	4 [3-6]	0.25****
Depression, median [IQR]	3 [2-5]	4 [2-5]	3 [2-5]	0.91****
Pain catastrophizing scores, median [IQR]	8 [5-12]	7 [5-9]	8 [5-12]	0.32****
Pain pressure threshold (kg), mean (SD)	4.3 (1.2)	4.5 (1.2)	4.3 (1.2)	0.46*
Pain pressure tolerance (kg), mean (SD)	6.6 (1.4)	6.8 (1.1)	6.6 (1.4)	0.71*
Received spinal morphine, n/total N (%)	139/276 (50%)	7/20 (35%)	132/256 (51%)	0.15**
Duration of surgery (min), mean (SD)	56 (14)	58.7 (14.6)	56.4 (14.1)	0.49*
Severe pain up to 48 h (NRS scores ≥ 7), n/total N (%)	29/276 (11%)	3/20 (15%)	26/256 (10%)	0.45***

Table 1. Continued

Variable	All patients (N=276)	PPD group (N=20)	Non-PPD group (N=256)	P-value
Secondary hyperalgesia at 48 h (cm2), median [IQR]	42.5 [18-76]	68 [21-115]	42 [18-74]	0.14****
IV morphine used up to 48 h (mg), median [IQR]	6 [4-8]	7 [4-10]	6 [4-8]	0.60****
Satisfaction, post-operative analgesia, n/ total N (%)				0.08***
Highly satisfied	36/276 (13%)	3/20 (15%)	33/256 (13%)	
Satisfied	158/276 (57%)	7/20 (35%)	151/256 (59%)	
Neutral	63/276 (23%)	7/20 (35%)	56/256 (22%)	
Dissatisfied	14/276 (5%)	3/20 (15%)	11/256 (4%)	
Strongly dissatisfied	5/276 (2%)	0/20 (0%)	5/256 (2%)	
CPSP, after 3 months, n/total N (%)	52/276 (19%)	9/20 (45%)	43/256 (17%)	0.002**
CPSP, after 6 months, n/total N (%)	42/276 (15%)	8/20 (40%)	34/256 (13%)	0.001**

Abbreviations: CPSP, Chronic postsurgical pain; HADS, Hospital anxiety and depression scale; IQR, interquartile range; NRS, Numeric rating pain scale scores; PPD, Postpartum depression; SD, standard deviation
*Student's *t* test
**Chi square test
***Fisher's exact test
****Mann-Whitney *U* test

The only statistically significant univariable predictor for CPSP after three months was the presence of PPD (OR, 4.05; 95% CI, 1.58 to 10.4; $P = 0.004$) (Table 2). In the multivariable analysis, patients who developed PPD had higher odds of developing CPSP after three months than patients who did not develop PPD (OR, 4.24; 95% CI, 1.53 to 11.7; $P = 0.005$) (Table 2). At six months following surgery, in the univariable analysis the odds of experiencing CPSP was increased by 4.3 times in patients with PPD (OR, 4.35; 95% CI, 1.65 to 11.4; $P = 0.003$) (Table 3). Likewise, an increased requirement of intravenous morphine within the initial 48 hr postoperatively was associated with a statistically significant increased risk of CPSP at 6 months (OR, 1.15; 95% CI, 1.01 to 1.32; $P = 0.03$). Nevertheless, after adjustment for confounding factors in the multivariable logistic regression model, only the presence of PPD was independently associated with a higher risk of CPSP (OR, 4.05; 95% CI, 1.42 to 11.54; $P = 0.009$) (Table 3).

Table 2. Univariable and multivariable analysis of risk factors associated with chronic post-surgical pain after 3 months.

Variable	Univariable		Multivariable	
	OR (95% CI)	***P*-value**	**OR (95%CI)**	***P*-value**
Previous cesarean section	0.60 (0.32 to 1.12)	0.11	0.56 (0.29 to 1.07)	0.08
Preexisting chronic pain	2.20(0.39 to12.34)	0.37	1.40 (0.21 to 9.22)	0.72
Preoperative HADS anxiety scores	0.95 (0.83 to 1.08)	0.46	0.90 (0.77 to 1.06)	0.23
Preoperative HADS depression scores	0.99 (0.86 to 1.13)	0.88	1.03 (0.88 to 1.21)	0.68
Preoperative PCS scores	1 (0.95 to1.04)	0.94	1.01 (0.96 to 1.07)	0.49
Secondary hyperalgesia at 48 h (cm^2)	1 (0.99 to 1.01)	0.1	1 (0.99 to 1.01)	0.21
Severe pain up to 48 h (NRS ≥ 7)	2.13 (0.91 to 5)	0.08	1.85 (0.72 to 4.77)	0.19
IV morphine used up to 48 h (mg)	1.09 (0.96 to 1.23)	0.14	1.06 (0.93 to 1.21)	0.33
EPDS scores ≥ 12	4.05(1.58 to10.37)	0.004	4.24 (1.53 to 11.74)	0.005

Abbreviations: CI, confidence interval; EPDS, Edinburgh postnatal depression scale; HADS, hospital anxiety and depression scale; IV, intravenous; NRS, numeric rating scale; OR, odds ratio; PCS, pain catastrophizing scale

Table 3. Univariable and multivariable analysis of risk factors associated with chronic post-surgical pain after 6 months.

Variable	Univariable		Multivariable	
	OR (95% CI)	***P*-value**	**OR (95%CI)**	***P*-value**
Previous cesarean delivery	0.86 (0.43 to 1.72)	0.68	0.85 (0.41 to 1.76)	0.66
Preexisting chronic pain	2.87(0.50 to 16.22)	0.23	2.05 (0.31 to 13.35)	0.45
Preoperative HADS anxiety scores	0.93 (0.80 to 1.08)	0.36	0.86 (0.73 to 1.02)	0.08
Preoperative HADS depression scores	0.96 (0.83 to 1.12)	0.65	1.01 (0.85 to 1.20)	0.88
Preoperative PCS scores	0.98 (0.93 to 1.04)	0.62	1 (0.94 to 1.07)	0.8
Severe pain up to 48 h (NRS ≥ 7)	1.92 (0.76 to 4.84)	0.16	1.37 (0.49 to 3.80)	0.53
Secondary hyperalgesia at 48 h (cm^2)	1 (0.99 to 1.01)	0.11	1(0.99 to 1.01)	0.2
IV morphine used up to 48 h (mg)	1.15 (1.01 to 1.32)	0.03	1.14 (0.99 to 1.32)	0.05
EPDS scores ≥ 12	4.35 (1.65 to 11.42)	0.003	4.05 (1.42 to 11.54)	0.009

Abbreviations: CI, confidence interval; EPDS, Edinburgh postnatal depression scale; HADS, hospital anxiety and depression scale; IV, intravenous; NRS, numeric rating scale; OR, odds ratio; PCS, pain catastrophizing scale

We did not observe any collinearity among the covariates before inclusion in the multivariable models for CPSP at three and at six months following CD. The multivariable models for CPSP at three and six months had a Hosmer–Lemeshow goodness-of-fit statistic test with $P = 0.15$ and $P = 0.69$, respectively. Table 4 presents the mediation effect of PPD on CPSP. The results indicate that both the direct impact of acute severe postoperative pain and the indirect effect via PPD on CPSP were statistically insignificant.

DISCUSSION

In this secondary analysis of a previously reported randomized trial, we explored several peri- and postpartum patient characteristics aiming to identify those at heightened risk for CPSP following elective CD. Our findings show that a provisional diagnosis of PPD at 8 weeks after CD was strongly associated with CPSP at three and six months.

Chronic postsurgical pain after CD is not infrequent, with a reported incidence ranging from 7% to 30%.[4] A recent meta-analysis and a narrative review highlighted the presence of the preoperative pain and the severity of acute postoperative pain as factors associated with CPSP following CD.[3,4] In contrast, the link between pre-existing psychological vulnerability—i.e., the presence of anxiety, depression, or catastrophizing—with CPSP following CD was inconsistent. One study found that preoperative depression assessed with the EPDS scale was a reliable predictor for chronic pain at three months and at six months after CD.[12] Nevertheless, the studies on CPSP that have explored the risk factors after CD are limited to the early postoperative period.[3,4] Because the transition from acute to chronic pain may be influenced by postsurgical psychological factors it is necessary to identify these modifiable variables beyond the healing phase of the wound scar. In this context, PPD may be a significant contributing factor influencing the occurrence of CPSP.

The mechanisms by which depression increases the risk of chronic pain are not fully understood. One proposed explanation is that depression leads to the depletion of serotonin and norepinephrine in the central nervous system.[19] This depletion alters the descending modulatory pathways, resulting in the amplification of pain. Studies in nonobstetric populations have shown the ability of pre-existing depression to predict the development of chronic pain.[20,21] Nevertheless, we did not find a significant association between pre-existing depression before surgery and CPSP. Since depression and chronic pain share common neuroplastic changes, their interaction is often bidirectional, suggesting that persistent pain may plausibly contribute to depression. Nevertheless, we did not evaluate subacute postpartum pain, such as pain at 2- or 4-weeks following CD. Therefore, our findings only show an association between PPD and CPSP, without establishing causality. A longitudinal assessment of pain trajectories and depression throughout the perinatal period would provide a more comprehensive understanding of the interaction between depression and persistent pain. A key strength of our study was the assessment of the mediating role of PPD in the relationship between acute severe postoperative pain and CPSP. Nevertheless,

the indirect effect was insignificant, indicating that the ability of PPD to predict CPSP was not driven by an association with greater pain intensity in the immediate postoperative period.

Table 4. Total, direct, and indirect association of acute severe postoperative pain with chronic postsurgical pain mediated through postpartum depression.

Effect	Estimates OR (95% CI)	P value	Proportion mediated % (95% CI)
CPSP at 3 months			
Model without confounders			0.08 (-0.18 to 0.34)
Direct effect	2.02 (0.91 to 4.49)	0.08	
Indirect effect	1.05 (0.87 to 1.27)	0.57	
Total effect	2.13 (0.91 to 5)	0.08	
Model with confounders*			0.10 (-0.22 to 0.40)
Direct effect	1.78 (0.75 to 4.23)	0.18	
Indirect effect	1.05 (0.87 to 1.28)	0.57	
Total effect	1.88 (0.75 to 4.71)	0.17	
CPSP at 6 months			
Model without confounders			0.16 (-0.38 to 0.71)
Direct effect	1.75 (0.70 to 4.35)	0.22	
Indirect effect	1.09 (0.79 to 1.51)	0.57	
Total effect	1.92 (0.76 to 4.84)	0.16	
Model with confounders*			0.27 (-0.73 to 1.28)
Direct effect	1.33 (0.51 to 3.42)	0.54	
Indirect effect	1.10 (0.77 to 1.56)	0.58	
Total effect	1.47 (0.56 to 3.84)	0.43	

Abbreviations: CI, confidence interval; CPSP, chronic postsurgical pain; OR, odds ratio
**Adjusted for previous Cesarean delivery, pre-existing chronic pain, preoperative anxiety, depression and pain catastrophizing, secondary hyperalgesia, postoperative intravenous morphine up to 48 hr.*

A systematic review has highlighted the potential negative effects of maternal PPD on both maternal and child health.[22] Among the consequences of untreated maternal PPD are a diminished quality of life, heightened risk behaviours, and disruptions in social relationships. Interestingly, a few studies have explored the relationship between depression and the presence of chronic pain conditions, such as pelvic pain disorders and dyspareunia, in nonpregnant populations.[23-25] Nevertheless, research on the association between PPD and CPSP remains scarce. A prospective cohort study found a significant correlation between PPD and CPSP at four months following CD.[13] However, the simultaneous assessment of

PPD and CPSP within the same timeframe in that study suggests a bidirectional relationship, making it challenging to establish causation.

Postpartum depression is one of the most common mental disorders of pregnancy. While maternal care primarily emphasizes pregnancy and the early postpartum period, the psychological wellness of mothers in later phases should not be overlooked, as the recent MBRRACE-report covering 2018-2020 identified that mental health-related causes were responsible for nearly 40% of maternal deaths occurring within the first year after pregnancy in the UK.[26] Early identification of PPD holds the potential for implementing psychosocial interventions that could mitigate the severity and consequences of PPD. Indirectly, this may also contribute to a reduction in the incidence of CPSP. Hence, there is a crucial need for future prospective studies to investigate whether preventing or treating PPD in the early postpartum phase can, apart from improving maternal health, diminish the occurrence of CPSP.

It is intriguing that in our univariable analysis, we found a significant correlation between postoperative opioid requirements and the likelihood of CPSP after six months following CD. Nevertheless, after accounting for confounding factors, this association became insignificant. Current evidence has been increasingly highlighting the link between perioperative opioid consumption and CPSP. Studies have elucidated that preoperative chronic opioid usage is associated with a higher incidence of CPSP.[27,28] The probable explanation lies in the neuroadaptive changes that occur owing to chronic opioid administration, leading to allodynia and hyperalgesia.[29] The question of whether acute or excessive use of opioids in the early postoperative period contributes to the development of CPSP remains a topic of debate. Notably, a study found that high-dose remifentanil infusions during cardiac surgery were linked to chronic thoracic pain 1 year after sternotomy.[30] In contrast, a retrospective cohort study reported that increased intraoperative opioid doses were associated with lower incidences of CPSP at three months.[31] The higher opioid requirement in the intraoperative and postoperative period may be attributed to either the intense pain experienced or opioid-induced hyperalgesia (OIH). Given that both the worsening of acute postoperative pain and OIH following surgery are risk factors for CPSP, it becomes crucial to differentiate between these two entities. Consequently, there is a need for further, larger trials with robust methodologies to thoroughly explore the relationship between perioperative opioids and CPSP.

A narrative review in 2020 reported that patients with pre-existing chronic pain are at an increased risk of developing CPSP after CD.[4] Nevertheless, some studies have not observed preoperative pain as a significant risk factor for CPSP following CD.[12,13,32] In our study, although the odds of developing CPSP were higher in patients with preoperative chronic pain, the association was not statistically significant. One possible reason for this finding could be the small number of patients with pre-existing chronic pain included in our study.

LIMITATIONS

This study has several limitations. First, this study was a secondary analysis of previously published study; therefore, the sample size and statistical power were not specifically calculated. It has been argued that *post-hoc* power calculations can be misleading and flawed, particularly in retrospective studies where additional data cannot be collected. [33] Therefore, given the *post-hoc* nature of our study, the results should be interpreted with caution. Second, the rate of PPD in our study was lower than the 17% reported in a previous study conducted in Nepal,[18] which might be the result of follow-up data being collected by phone and cultural stigma surrounding mental health. In our setting, telephone-based screening was feasible as most participants were unlikely to attend follow-up visits in person. Moreover, a study has shown that EPDS, when administered via telephone, retains its psychometric properties.[34] Nonetheless, the small number of patients with PPD may limit the generalizability of our findings. Therefore, a larger cohort with better representation of patients experiencing PPD would strengthen the robustness of our study's findings. Lastly, our primary focus was solely on persistent wound pain, and we did not assess other sources of persistent painful postpartum conditions (such as back pain, pelvic pain, or persistent headache) which might be associated with PPD. In addition, pre-existing depression was assessed using the HADS rather than the EPDS, which may have led to inconsistencies in reporting pre-existing depression. Likewise, we did not specify if patients received any treatment for depression before delivery or after the diagnosis of PPD.

CONCLUSION

In this secondary analysis of a previous randomized trial, we found that a provisional PPD diagnosis at 8 weeks was associated with an increased risk of CPSP at three and six months after CD. Further research is warranted to explore the dynamic relationship between PPD and the development of CPSP following CD.

REFERENCES

1. Treede RD, Rief W, Barke A, et al. A classification of chronic pain for ICD-11. Pain 2015; 156: 1003-7.
2. Weibel S, Neubert K, Jelting Y, et al. Incidence and severity of chronic pain after caesarean section: A systematic review with meta-analysis. Eur J Anaesthesiol 2016; 33:853-65.
3. Sharma LR, Schaldemose EL, Alaverdyan H, et al. Perioperative factors associated with persistent postsurgical pain after hysterectomy, cesarean section, prostatectomy, and donor nephrectomy: a systematic review and meta-analysis. Pain 2022; 163:425-35.
4. Komatsu R, Ando K, Flood PD. Factors associated with persistent pain after childbirth: a narrative review. Br J Anaesth 2020; 124:e117-e130.
5. Radoš SN, Akik BK, Žutić M, et al. Diagnosis of peripartum depression disorder: A state-of-the-art approach from the COST Action Riseup-PPD. Compr Psychiatry 2024;130:152456.
6. Sultan P, Ando K, Elkhateb R, et al. Assessment of patient-reported outcome measures for maternal postpartum depression using the consensus-based standards for the selection of health measurement instruments guideline: a systematic review. JAMA Netw Open 2022; 5:e2214885.
7. Wang Z, Liu J, Shuai H, et al. Correction: Mapping global prevalence of depression among postpartum women. Transl Psychiatry 2021;11:640.
8. Heesen P, Orbach-Zinger S, Grigoriadis S, Halpern S, Eidelman LA. The Effect of Analgesia and Anesthesia on Postpartum Depression. Adv Anesth 2020;38:157-165.
9. Eisenach JC, Pan PH, Smiley R, Lavand'homme P, Landau R, Houle TT. Severity of acute pain after childbirth, but not type of delivery, predicts persistent pain and postpartum depression. Pain 2008; 140:87-94.
10. Bijl RC, Freeman LM, Weijenborg PT, et al. A retrospective study on persistent pain after childbirth in the Netherlands. J Pain Res 2016; 9:1-8.
11. Ben Hayoun DH, Sultan P, Rozeznic J, et al. Association of inpatient postpartum quality of recovery with postpartum depression: A prospective observational study. J Clin Anesth 2023; 91:111263.
12. Jin J, Peng L, Chen Q, et al. Prevalence and risk factors for chronic pain following cesarean section: a prospective study. BMC Anesthesiol 2016; 16:99.
13. Daly B, Young S, Marla R, et al. Persistent pain after caesarean section and its association with maternal anxiety and socioeconomic background. Int J Obstet Anesth 2017; 29:57--63.
14. Subedi A, Schyns-van den Berg AMJV, Thapa P, et al. Intrathecal morphine does not prevent chronic postsurgical pain after elective Caesarean delivery: a randomised controlled trial. Br J Anaesth 2022; 128:700-7.
15. Ghosh A, Ghosh T. Modification of Kuppuswamys socioeconomic status scale in context to Nepal. Indian Pediatr 2009; 46: 1104-5.
16. Risal A, Manandhar K, Linde M, Koju R, Steiner TJ, Holen A. Reliability and validity of a Nepali-language version of the hospital anxiety and depression scale (HADS). Kathmandu Univ Med J (KUMJ) 2015; 13:115-124.

17. Shakya S, Thapa K, Mahotra S, Kandel KP, Rutkkowski JT, Thomson I. Relationship between pain catastrophizing with postoperative pain after lower limb trauma surgery. J Psychosom Res 2021; 149: 110575.
18. Bhusal BR, Bhandari N, Chapagai M, Gavidia T. Validating the Edinburgh postnatal depression scale as a screening tool for postpartum depression in Kathmandu, Nepal. Int J Ment Health Syst 2016; 10:71.
19. Sheng J, Liu S, Wang Y, Cui R, Zhang X. The link between depression and chronic Pain: neural mechanisms in the brain. Neural Plast 2017; 2017:9724371.
20. Leino P, Magni G. Depressive and distress symptoms as predictors of low back pain, neck-shoulder pain, and other musculoskeletal morbidity: a 10-year follow-up of metal industry employees. Pain 1993; 53:89-94.
21. Dworkin RH, Hartstein G, Rosner HL, Walther RR, Sweeney EW, Brand L. A high-risk method for studying psychosocial antecedents of chronic pain: the prospective investigation of herpes zoster. J Abnorm Psychol 1992; 101:200-205.
22. Slomian J, Honvo G, Emonts P, Reginster JY, Bruyère O. Consequences of maternal postpartum depression: A systematic review of maternal and infant outcomes [published correction appears in Womens Health (Lond). 2019 Jan-Dec;15:1745506519854864]. Womens Health (Lond) 2019; 15:1745506519844044.
23. Bryant C, Cockburn R, Plante AF, Chia A. The psychological profile of women presenting to a multidisciplinary clinic for chronic pelvic pain: high levels of psychological dysfunction and implications for practice. J Pain Res 2016; 9:1049-56.
24. Sackett S, Gates E, Heckman-Stone C, Kobus AM, Galask R. Psychosexual aspects of vulvar vestibulitis. J Reprod Med 2001; 46:593-598.
25. Burri A, Hilpert P, Spector T. Longitudinal evaluation of sexual function in a cohort of pre- and postmenopausal women in the context of psychopathology, personality traits, and coping resources: results from a prospective longitudinal cohort study from age 30 to 50. Arch Sex Behav 2015; 44:1551-60.
26. Knight M, Bunch K, Felker A, et al (Eds.) on behalf of MBRRACE-UK. Saving Lives, Improving Mothers' Care Core Report - Lessons learned to inform maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2019-21. Oxford: National Perinatal Epidemiology Unit, University of Oxford 2023
27. VanDenKerkhof EG, Hopman WM, Goldstein DH, et al. Impact of perioperative pain intensity, pain qualities, and opioid use on chronic pain after surgery: a prospective cohort study. Reg Anesth Pain Med 2012; 37:19-27.
28. Glare P, Aubrey KR, Myles PS. Transition from acute to chronic pain after surgery. Lancet 2019; 393:1537-46.
29. Colvin LA, Bull F, Hales TG. Perioperative opioid analgesia-when is enough too much? A review of opioid-induced tolerance and hyperalgesia. Lancet 2019 13; 393:1558-68.
30. van Gulik L, Ahlers SJ, van de Garde EM, et al. Remifentanil during cardiac surgery is associated with chronic thoracic pain 1 yr after sternotomy. Br J Anaesth 2012; 109:616-22.
31. Santa Cruz Mercado LA, Liu R, Bharadwaj KM, et al. Association of intraoperative opioid administration with postoperative pain and opioid use. JAMA Surg 2023; 158:854-864.
32. Borges NC, de Deus JM, Guimarães RA, et al. The incidence of chronic pain following Cesarean section and associated risk factors: A cohort of women followed up for three months. PLoS One 2020; 15:e0238634.

33. Dziak JJ, Dierker LC, Abar B. The interpretation of statistical power after the data have been gathered. Curr Psychol 2020; 39:870--77.

34. Figueiredo FP, Parada AP, Cardoso VC, et al. Postpartum depression screening by telephone: a good alternative for public health and research. Arch Womens Ment Health 2015;18:547-553.