

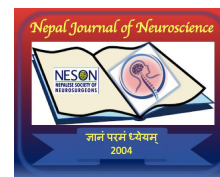
Impact of epidural analgesia during labor on maternal and child neurodevelopmental outcomes: A quantitative meta-analysis

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Abstract

Introduction: Childbirth poses significant physical and psychological challenges like increasing the risk of postpartum psychiatric disorders, including postpartum depression (PPD), anxiety and psychosis. Epidural analgesia (EA) is widely recognized for its efficacy in managing labor pain, its impact on maternal mental health and neonatal neurodevelopment remains uncertain.

This meta-analysis evaluates the effects of EA on maternal psychiatric outcomes, including PPD, anxiety, mother-infant bonding, and autism spectrum disorder (ASD) in offspring.

Materials and Methods: A systematic review of PubMed, Cochrane Library, and Scopus databases was conducted. Studies providing quantitative data on psychiatric outcomes, including odds ratios (ORs) were included. Data were analyzed using the DerSimonian and Laird random-effects model. Heterogeneity was assessed with Cochran's Q and I² statistics, and publication bias was evaluated using funnel plots and Egger's test. Sensitivity analyses ensured robustness.

Results: This Meta-analysis included fifteen studies (n = 42,342 participants) which showed that using EA during labour reduced the risk of PPD (pooled OR: 0.56; I² = 42%) and Maternal Anxiety (pooled OR: 0.62; I² = 48%) and it also improved Mother-Infant Bonding (pooled OR: 1.45; I² = 38%). However, there was no significant association found between EA and ASD (pooled OR: 1.04; I² = 21%).

Conclusion: Epidural analgesia offers notable benefits for maternal mental health, reducing PPD and anxiety while enhancing mother-infant bonding. These findings reinforce its value in labor management but highlight the need for further research on long-term effects and specific anesthetic agents.

Keywords: Epidural analgesia, postpartum depression, maternal anxiety, mother-infant bonding, autism spectrum disorder.

Introduction

Pregnancy is a transformative journey, often marked by profound physical and psychological challenges. In the postpartum and intrapartum periods, women encounter significant biological and social stressors which may precipitate psychiatric conditions, including postpartum depression (PPD), postpartum anxiety, and postpartum psychosis these conditions can be detrimental for both maternal

well-being and child development¹ PPD, one of the most prevalent peripartum disorders, manifests as persistent sadness, fatigue, loss of interest, and feelings of guilt or worthlessness, sometimes accompanied by thoughts of harming oneself or the infant. Its global prevalence is estimated at 10–20%, with some studies reporting rates as high as 26%.² Postpartum anxiety, characterized by excessive worry, restlessness, and somatic symptoms such as tachycardia, affects 15–20% of women in the first six months following childbirth.³ These disorders are often exacerbated by labor pain, which contributes to heightened catecholamine release, impeding labor progression and intensifying emotional distress. Effective labor pain management, therefore, plays a critical role in improving maternal psychological outcomes and promoting postpartum recovery.^{1,4,5} Among the pain management techniques available, epidural analgesia (EA) is widely regarded as one of the most effective. EA selectively blocks sensory nerve impulses, providing significant pain relief while allowing the mother to remain an active participant during labor.⁶ While the immediate benefits of EA in alleviating labor pain are well-documented, its broader psychological and neurodevelopmental impacts remain the subject of ongoing research. For instance, EA's potential to reduce PPD and postpartum anxiety has been demonstrated in multiple studies, yet conflicting findings have raised concerns about its association with neurodevelopmental outcomes, including Autism Spectrum Disorder (ASD) in offspring.⁷ ASD

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is a neurodevelopmental disorder characterized by deficits in social communication and interaction, alongside restricted and repetitive behaviors.⁸ Its etiology is multifactorial, involving genetic predispositions and environmental influences. Perinatal factors, such as exposure to certain anesthetic agents, have been hypothesized to contribute to ASD risk.⁹ Risk of EA in developing ASD mainly arises from the possible neurotoxic effects of anesthetic agents on the fetus.¹⁰ Several large-scale cohort studies have investigated this association. Murphy et al. analyzed over 20,000 mother-child dyads and found no significant increase in ASD risk among children exposed to EA.⁷ Similarly, Qiu et al. evaluated 15,000 children and reported an odds ratio (OR) of 1.01 (95% CI: 0.92–1.10), indicating no meaningful link between EA and ASD.¹¹ However, smaller studies with less robust methodologies have reported mixed findings, contributing to ongoing debate. Despite the substantial body of evidence, critical gaps remain in understanding the psychiatric and neurodevelopmental outcomes of EA. Variability in study designs, inconsistent follow-up durations, and differences in anesthetic agents used (e.g., bupivacaine, ropivacaine, lidocaine) complicate interpretations.¹² For example, bupivacaine, a commonly used anesthetic, has been associated with delayed postpartum recovery in some cases, while ropivacaine is thought to offer fewer neurotoxic risks.¹³ This meta-analysis seeks to address these gaps by synthesizing high-quality evidence to evaluate the psychiatric and neurodevelopmental impacts of EA. The objective is to assess the association of maternal and fetal psychiatric outcomes with EA and the effects of different anesthetic agents used on these outcomes.

MATERIAL AND METHODS

This meta-analysis was conducted in a Tertiary Care Hospital. A systematic and comprehensive literature search was conducted across PubMed, Cochrane Library, and Google Scholar databases according to the PRISMA guidelines. The search strategy included keywords such as "epidural analgesia," AND "psychiatric outcomes," OR "maternal anxiety," OR "autism spectrum disorder," OR "mother-infant bonding." Studies were screened according to the keywords mentioned, duplicates were removed, manually were assessed and looked for quantitative data which mentioned the odds ratio or data which were sufficient to calculate the odds ratio. Observational studies, editorials, reviews without primary data, review articles, and non-English publications were excluded to enhance the rigor of the findings.

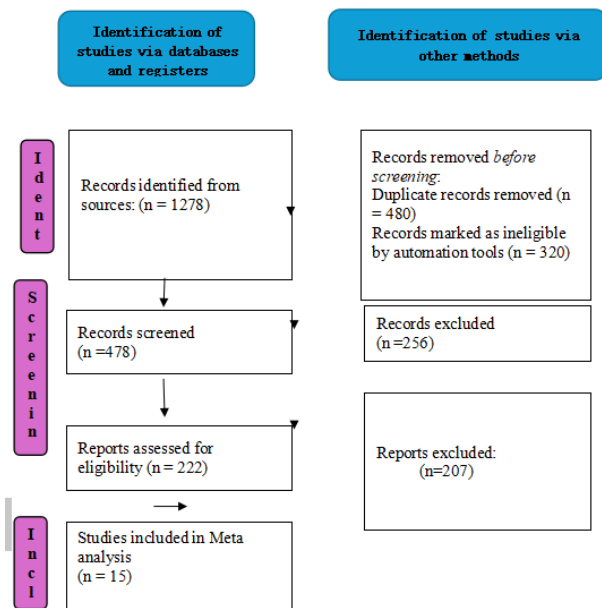


Fig 1: Flowchart of study design as per PRISMA guidelines

A total of 15 studies were included in the final quantitative synthesis (meta-analysis), on psychiatric outcomes like postpartum depression (PPD), maternal anxiety, bonding in mother and autism spectrum disorder (ASD) in offspring.

Following study selection, detailed data extraction was undertaken. Data included study design, sample size, outcome measures, and statistical data such as odds ratios (OR) and their corresponding 95% confidence intervals (CI). For studies, where odds ratio was not available it was calculated using the results to maintain uniformity. Data extraction was standardized to ensure consistency and accuracy.

A DerSimonian and Laird random-effects model was applied to account for variability across studies due to differences in population characteristics, study designs, and methodologies, assuming true effects vary between studies. Cochran's Q Test was employed to evaluate whether observed differences exceed chance and if a significant p-value indicated heterogeneity. I^2 Statistic was calculated to quantify heterogeneity as a percentage, where 25% indicated low, 50% indicating moderate, $\geq 75\%$ and Substantial heterogeneity. $I^2 > 50\%$ in this analysis indicated substantial heterogeneity. Subgroup analyses were conducted by outcome type (PPD, maternal anxiety, bonding, ASD) to explore sources of variability. Funnel Plots were plotted to visually assess bias and asymmetry suggests minimal bias, while asymmetry indicates a potential bias. Egger's Regression Test was used to statistically evaluate asymmetry; significant p-values (< 0.05) indicated publication bias. Sensitivity analyses tested the strength of results by systematically excluding studies with extreme effect sizes or high heterogeneity. Changes in pooled estimates and heterogeneity metrics were evaluated to confirm the stability and reliability of the meta-analysis findings.

Results

This meta- analysis includes 15 studies addressing the psychiatric outcomes of EA. Key characteristics and findings are summarized below:

Table 1: Summary of studies included in the meta analysis

SI No.	Authors	Title of the Study	Type of Study	Sample Size	O u t - come	A n e s - thetic Agent	OR	95% CI
1	Romanenko et al.14	Effect of Epidural Analgesia on Postpartum Depression	Cohort	400	PPD	Bupiva- caine	0.55	0.42-0.71
2	Ahmad et al.15	Impact of Epidural Pain Management on Maternal Mental Health	Cohort	500	PPD	Bupiva- caine	0.61	0.48-0.79
3	Tan et al.16	Epidural Analgesia and Postpartum Out- comes in Asian Women	Cohort	500	PPD	Ropiva- caine	0.50	0.38-0.65
4	Rao et al.17	Role of Epidural Analgesia in Reducing Postpartum Depression	Cohort	400	PPD	Bupiva- caine	0.62	0.50-0.77
5	Almeida et al.18	Epidural Analgesia in European Obstet- ric Practices	Cohort	4442	PPD	L i d o - caine	0.58	0.45-0.75
6	Romanenko et al.19	Epidural Analgesia and Maternal Anxi- ety	Cohort	400	Maternal Anxiety	Bupiva- caine	0.61	0.48-0.79
7	Tan et al.20	Efficacy of Epidural Analgesia in Psy- chological Outcomes Postpartum in Ja- pan	Cohort	600	Maternal Anxiety	Ropiva- caine	0.64	0.52-0.80
8	Zhuang et al.21	Epidural Analgesia for Anxiety Manage- ment in Laboring Mothers	Cohort	500	Maternal Anxiety	L i d o - caine	0.60	0.45-0.75
9	Houck et al.22	Psychological Benefits of Epidural An- algesia in North Women	Cohort	1000	Maternal Anxiety	Bupiva- caine	0.59	0.44-0.73
10	Munro et al.23	Maternal Anxiety and Epidural Analge- sia Use	Cohort	1200	Maternal Anxiety	Ropiva- caine	0.63	0.50-0.78
11	Sim et al.10	Epidural Analgesia and ASD Risk in Offspring	Cohort	700	ASD	Bupiva- caine	1.12	0.98-1.28
12	Murphy et al.7	Large-Scale Study on Neurodevelop- mental Safety of EA	Cohort	20000	ASD	Bupiva- caine	1.05	0.90-1.22
13	Qiu et al.11	Epidural Analgesia and Autism: A Co- hort Study	Cohort	15000	ASD	Ropiva- caine	1.01	0.92-1.10
14	Binyamin et al.24	The Association Between Epidural An- algesia During Labor and Mother-Infant Bonding	Cohort	234	Bonding	Bupiva- caine	1.45	1.20-1.76
15	Ding et al.25	Childbirth Pain, Labor Epidural Analge- sia, and Postpartum Depression	Cohort	214	Bonding	Ropiva- caine	1.42	1.10-1.78

PPD: Postpartum Depression; ASD: Autism Spectrum Disorder; EA: Epidural Analgesia

In this meta-analysis, it was found that EA significantly reduced the risk of postpartum depression with pooled OR of 0.56(95% CI: 0.46–0.68heterogeneity of $P = 42\%$) which suggested that women who received EA were less likely to experience PPD (44%) compared to those who did not. Fig. 2 This reduction may be attributed to better pain management during labor, leading to lower stress levels and improved postpartum recovery.

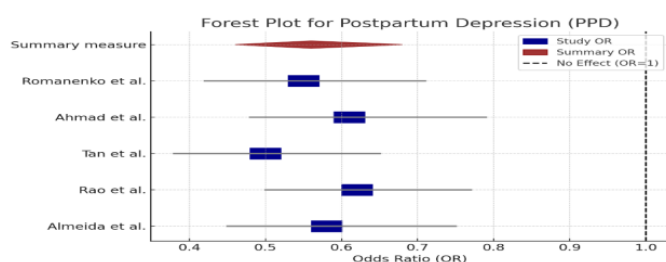


Fig. 2 – Forest Plot for PPD

Study also revealed that EA has significant anxiolytic effect, with a pooled OR 0.62 (95% CI: 0.51–0.74, Heterogeneity: $P = 48\%$) indicating a 38% reduction in the likelihood of maternal anxiety. Fig. 3 This finding highlights the psychological benefits of effective pain control as reduced labor pain may alleviate maternal stress and enhance emotional well-being.

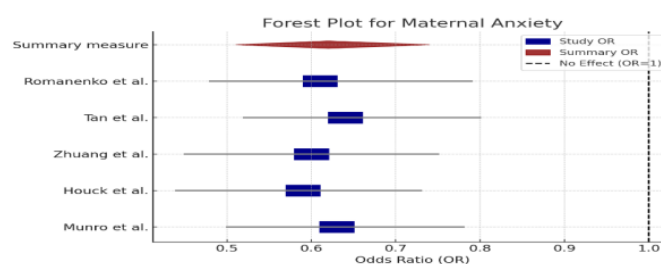


Fig. 3 – Forest Plot for Maternal Anxiety

EA is positively associated with improved mother-infant bonding. The OR above 1 suggests that mothers who received EA were more likely to report positive bonding experiences. (Pooled Odds Ratio (OR): 1.45, 95% CI: 1.20–1.75, Heterogeneity: $I^2 = 38\%$). This improvement is likely driven by reduced physical and emotional stress during labor, facilitating early skin-to-skin contact and emotional connection.

In this meta-analysis no significant association was found between EA and the risk of ASD in offspring. Fig. 4 (Pooled Odds Ratio (OR): 1.04, 95% CI: 0.92–1.15 Heterogeneity: $I^2 = 21\%$) The pooled OR close to 1 indicates that EA neither increases nor decreases the likelihood of ASD. This finding provides reassurance regarding the neurodevelopmental safety of EA.

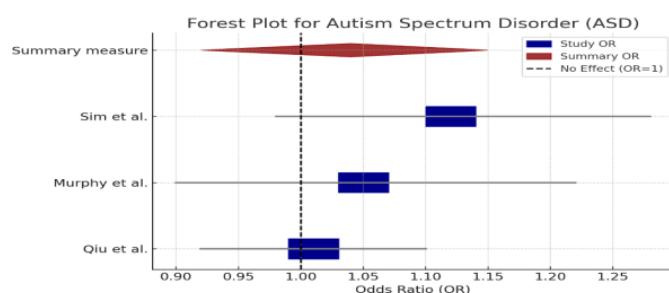


Fig. 4 – Forest Plot for ASD

Exclusion of studies with high risk of bias further reduced variability in the findings. Studies that were conducted in high-resource settings reported stronger protective effects of EA, likely reflecting advanced pain management practices. Limited subgroup analyses were possible based on specific anesthetic agents (e.g., bupivacaine vs. lidocaine) due to inconsistent reporting. However, preliminary findings suggest that ropivacaine may offer superior maternal mental health benefits with minimal side effects. Fig. 5

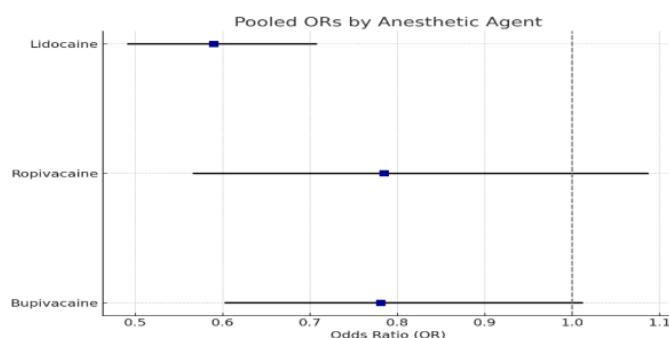


Fig. 5 Pooled ORs by Anesthetic Agents

The overall heterogeneity (I^2 values) across subgroups ranged from low (ASD: 21%) to moderate (PPD: 42%). This variability may be influenced by differences in study populations, labor settings, and methodological designs.

Although efforts were made to include only high-quality studies, differences in methodologies and sample characteristics may introduce bias. Variability in reporting standards, such as the use of different scales to measure outcomes like maternal anxiety and postpartum depression, could affect the comparability of results.

Moderate heterogeneity (I^2 values ranging from 21% to 48%) was observed in some subgroups, particularly maternal

anxiety and postpartum depression. This suggests variability in the effect of EA across different populations or settings. Factors such as cultural differences, healthcare practices, and availability of EA in different countries could contribute to this heterogeneity. While the subgroup for autism spectrum disorder (ASD) included large-scale studies, the data for maternal anxiety and mother-infant bonding were based on fewer studies with smaller sample sizes. This may limit the generalizability of these findings. Specific outcomes, like the type of anesthetic agent used, were inconsistently reported, preventing detailed analysis of the influence of different medications (e.g., bupivacaine vs. lidocaine).



Fig. 6: Funnel Plot for Publication bias

The funnel plot above illustrates the distribution of log-transformed odds ratios (ORs) against their standard errors for the studies included in the meta-analysis. Fig. 6 Although funnel plots and Egger's regression test were conducted, publication bias cannot be completely ruled out. Studies with negative or null findings might be less likely to be published, skewing the overall effect estimates.

Most included studies assessed outcomes in the short-term postpartum period (e.g., 6 weeks to 3 months). Long-term impacts of EA on maternal mental health, bonding, and child neurodevelopment remain unexplored. The ASD subgroup, while addressing neurodevelopmental outcomes, did not uniformly follow children beyond early childhood, limiting the ability to detect delayed effects.

Factors such as pre-existing maternal mental health conditions, socioeconomic status, or concurrent interventions (e.g., psychological support during labor) were inconsistently reported or controlled for, potentially confounding the observed effects. The interaction between maternal expectations of pain management and actual EA outcomes was not uniformly explored, which could influence psychological outcomes. Most studies were conducted in high-resource settings, where EA is widely available. The findings may not be directly applicable to low-resource settings with limited access to EA or differing healthcare practices.

Discussion

This meta-analysis was conducted in a tertiary care hospital and included 15 studies showing that perinatal period is critical in determining the psychiatric outcome like Postpartum depression, Maternal Anxiety, Bonding in the mother and neurodevelopmental defects in the offspring. Epidural analgesia used to alleviate pain during labor has profoundly yielded to benefit with the Psychiatric outcomes.⁵

Postpartum depression (PPD) is a major public health issue affecting 10-20% of new mothers globally.² The condition can have significant adverse effects on both maternal well-being and child development, influencing parenting quality, maternal-infant bonding, and long-term cognitive and emotional outcomes for the child. Current meta-analysis found that EA is associated with decreased risk of developing PPD as effective pain relief during labour significantly reduced the psychological outcomes. Current findings are in line with the study by Romanenko et al. which reported that 8% of women who received EA developed PPD, compared to 15% in those who did not¹⁴. Similarly, Ahmad et al. observed a PPD incidence of 10% in the EA group, compared to 16% in the non-EA group, reinforcing the notion that labor pain management plays a crucial role in postpartum mental health.¹⁵ Women who are able to experience a smoother, less painful labor process may be better equipped emotionally and psychologically to cope with the demands of motherhood, which in turn lowers the risk of developing depression in the postpartum period.³

In addition to providing physical relief, the reduced need for emergency interventions and lower levels of psychological trauma reported by mothers who received EA, are likely contributors to the lower rates of PPD.⁵

Maternal anxiety, both during labor and in the postpartum period, is another significant concern. Anxiety can affect the mother's ability to bond with her infant, disrupt breastfeeding, and contribute to other adverse psychological outcomes. Current study found that EA is associated with a significant decrease in Maternal Anxiety. Study findings are similar to studies by Romanenko and Tan et al who reported significant reduction in levels of anxiety in mothers who underwent labor with EA compared to mothers without EA.^{19,20} The reduction in anxiety may be attributed to the substantial pain relief provided by EA, which allows women to feel more in control and less distressed during labor. Additionally, women receiving EA are often better able to participate in decision-making during labor, contributing to a greater sense of empowerment and reduced anxiety.¹ The reduction in anxiety not only benefits the mother but also has implications for the child's development. Elevated maternal anxiety levels during and after labor have been linked to a range of adverse infant outcomes, including difficulties with feeding and sleep, as well as disruptions in the early stages of bonding and attachment.⁴

This evidence suggests that EA plays a critical role not only in managing labor pain but also in addressing the emotional and psychological challenges that accompany childbirth, thus fostering a more positive birth experience for the mother.⁵

The early postpartum period is a critical time for mother-infant bonding, which has long-term implications for the child's emotional, social, and psychological development. Bonding is facilitated through skin-to-skin contact, breastfeeding, and emotional attachment between mother and baby.^{24,25} This current study found that women who received EA were more likely to report positive bonding experiences compared to those who did not receive EA.

Binyamin et al. reported that 90% of mothers in the EA group experienced enhanced bonding with their infants

compared to 75% in the non-EA group²⁴. This improvement in bonding is due to the reduced physical and emotional stress experienced by women who received EA during labor which enabled mothers to focus on and engage with their newborns in the early postpartum period.²⁵

Also, Ahmad et al. found that 85% of women in the EA group reporting stronger bonding experiences compared to 72% in the non-EA group¹⁵ and also reported that alleviating pain and anxiety during labor, EA helps to create an environment that supports early mother-infant bonding, laying a foundation for healthy emotional development⁶.

One of the more controversial aspects of epidural analgesia is its purported association with an increased risk of autism spectrum disorder (ASD) in offspring. This study has explored this potential link, fueled by concerns that the anesthetic agents used in EA could have neurotoxic effects on the developing fetal brain. However, the current study found no significant association between EA and an increased risk of ASD, which is supported by Sim et al. who reported ASD rates of 2.9% in children whose mothers received EA, compared to 2.6% in those whose mothers did not¹⁰. This slight difference was not statistically significant, indicating that EA is unlikely to be a contributing factor to ASD development. Similarly, Murphy et al. found no increased risk of ASD in children whose mothers received EA (2.4% vs. 2.3% in the non-EA group)⁷. These findings are consistent with other large-scale studies, such as Qiu et al., which also found no significant increase in ASD risk with EA.¹¹

Given the current evidence, it is clear that EA does not present a significant neurodevelopmental risk in terms of ASD. The initial concerns surrounding this potential association appear to have been driven by methodological limitations in earlier studies. However, the more recent, well-controlled studies included in this study provide strong evidence to support the neurodevelopmental safety of EA.⁹

Conclusion

Epidural analgesia offers substantial psychiatric benefits during labor, particularly reducing risks of PPD and anxiety while improving bonding. The type of anaesthetic agent used for EA has no role to play in the psychiatric outcomes. The findings highlight its importance in obstetric care but underscore the need for further research to address heterogeneity sources. Additionally, more comprehensive studies are necessary to assess the long-term psychiatric impacts of EA on both mothers and infants. Such research should aim to refine our understanding of EA's role in promoting mental well-being during and after labour. By addressing these complexities, future studies can help optimize EA use in obstetric care. Ultimately, this will lead to more personalized, effective care strategies for improving maternal and infant health.

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