Insight into the abnormal cardiotocographic patterns following neuraxial analgesia for pain management in labor

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BACKGROUND: Neuraxial analgesia (NA) is widely used for pain management in labor but may be associated with abnormal fetal heart rate patterns, including prolonged decelerations.

OBJECTIVE: To investigate decelerations and fetal bradycardia following neuraxial analgesia (NA; epidural, combined spinal-epidural, or spinal) in labor, in terms of frequency, associated factors, and outcomes. The primary objective was to determine whether maternal hypotension (SBP<100 mmHg or DBP<60 mmHg), uterine hyperstimulation (ie, exaggerated response to uterine stimulants presenting as a prolonged contractions for over 2 minutes), or other potentially implicated factors are associated with prolonged deceleration (lasting more than 3 minutes) after NA (PDAA).

STUDY DESIGN: We retrospectively analyzed data of 898 singletons term pregnant women who underwent NA during labor. Data were retrieved from a prospectively collected database and medical records. All cardiotocographic tracings were manually reviewed from at least 10 minutes before NA to delivery. Univariate and multivariable logistic regression analyses were used to explore the associations between demographic, obstetric, and clinical characteristics and the occurrence of PDAA within 30 minutes after NA.

RESULTS: PDAA occurred in 6.57% (59/898; 95% CI 5.08%−8.44%) of women within 30 minutes after NA. Uterine hyperstimulation was significantly more frequent in those with PDAA [39% (23/59) vs 5.4% (45/839); *P*<.001], who also reported higher preanalgesia pain scores [9.7 (0.94) vs 8.9 (2.04); *P*=.003]. No significant differences were found between groups in systolic/diastolic blood pressure or the prevalence of maternal hypotension. Nulliparity (OR 2.27, 95% CI 1.01−1.06; *P*=.048), uterine hyperstimulation (OR 11.4, 95% CI 5.48−23.7; *P*<.001), and higher pain intensity at time 0 (OR 1.50, 95% CI 1.10−2.30; *P*=.007) were independently associated with PDAA.

CONCLUSION: Uterine hyperstimulation appeared to be the strongest factor associated with PDAA. The role of uterine hyperstimulation due to a rapid drop in catecholamines in the occurrence of PDAA may be further supported by the association with higher preanalgesia pain intensity and nulliparity. Conversely, postanalgesia hypotension did not appear to be a key factor.

Key words: adrenaline, blood pressure, combined spinal-epidural, epidural, epinephrine, mechanism, noradrenaline, spinal, tachysystole

Introduction

The intensity of labor pain varies significantly among women, ranging from mild to extreme or intolerable. Pain is known to trigger physiological changes, which may lead to emotional distress and suffering.[1] Consequently, pain relief during labor has become a crucial aspect of labor management, and leaving severe pain untreated is considered unacceptable when safe options are available.[2]

Various methods exist for managing labor pain, including nonpharmacological approaches, systemic analgesics, and regional techniques.[3] Among the latter, neuraxial analgesia (NA) offers the most effective relief and is the preferred first-line option for women in labor.[4] NA encompasses several techniques, with continuous epidural and combined spinal-epidural (CSE) being the most commonly used.[5] These methods differ in application, analgesia onset, and medication dosage.[6,7] The choice is usually determined by the clinical situation, institutional norms, available equipment, and clinician preferences.

While NA is generally safe, it is sometimes associated with adverse effects or complications for both the mother and the fetus. Fetal heart rate abnormalities, such as prolonged deceleration or bradycardia, are known events that can follow the administration of NA during labor.[7−10] These abnormalities may be interpreted as signs of fetal compromise with possible impact on labor management, such as the choice to expedite delivery via operative vaginal birth or cesarean section.[11,12]

Prolonged decelerations or fetal bradycardia following NA are traditionally believed to be caused by placental hypoperfusion consequent to analgesia-induced hypotension.[13,14] However, the exact mechanism underlying prolonged fetal decelerations following NA and related outcomes remains debated. Indeed, other mechanisms have been proposed, such as uterine hyperstimulation caused by the reduced maternal catecholamine levels after pain relief.[15−20]

On that basis, this study aimed to further investigate decelerations and fetal bradycardia following NA, determining their frequency, exploring associated factors, and clarifying their outcomes. The primary objective was to determine whether maternal hypotension, uterine hyperstimulation, or other potentially implicated factors are associated with

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AJOG MFM at a Glance

Why was this study conducted?

To determine the frequency, associated factors, and outcomes of prolonged fetal decelerations after neuraxial analgesia (NA) in labor.

Key findings

Uterine hyperstimulation, rather than maternal hypotension, is the strongest factor associated with prolonged decelerations after NA.

What does this add to what is known?

The study clarifies the mechanisms underlying abnormal fetal heart rate patterns after NA and suggests preventive strategies focused on uterine activity.

these cardiotocographic abnormalities. We hypothesized that uterine hyperstimulation due to a sudden catecholamine drop after NA, rather than maternal hypotension, was the main factor determining prolonged decelerations.

Materials and methods

We conducted a case-control study in a cohort of consecutive patients representing the entire population of women who delivered in 2019 and 2022 at the labor and delivery unit of our center. We focused on deliveries that occurred in two different years because two different NA protocols were used: high dosage in 2019 and low dosage in 2022, as explained in the Supplementary material.

We retrospectively reviewed the prospectively maintained databases of all consecutive deliveries that occurred in 2019 and 2022. We identified all women with singleton term (≥ 37 gestational weeks) pregnancy who underwent NA during labor. Given the time-intensive nature of reviewing cardiotocographic tracings — which was essential to assess our primary outcome of interest, prolonged deceleration following NA — we decided to evaluate 50% of the total eligible cases for each year by blindly selecting one every two consecutive eligible deliveries.[21–23] Cases with unavailable cardiotocographic trace for review were excluded. Data on maternal demographics, obstetric and clinical characteristics, intrapartum details, and maternal and neonatal outcomes were retrieved from the prospectively maintained delivery room database. Medical records, anesthesiologic documentation, and cardiotocographic tracers were also retrieved and reviewed.

The design, analysis, interpretation of data, drafting, and revisions conform to the Helsinki Declaration, the Committee on Publication Ethics guidelines, and the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement. Each patient signed the informed consent to allow anonymized data collection and analysis for research purposes. The study was not advertised, and the patients were not remunerated. This study is retrospective in nature and involves analysis of existing data that were previously collected and de-identified prior to the initiation of this research. It was determined to be exempt from the Institutional Review Board (IRB).

Neuraxial analgesia

Per institutional protocol, NA is offered for pain control to every woman upon request or medical indication and initiated either during labor induction or after labor onset. Data regarding the NA were manually extracted from the anesthesiologic records, which collected the NA technique, cervical dilatation at the time of analgesia, pain intensity before and 20 minutes after analgesia, and patient systolic (SBP) and diastolic blood pressure (DBP) 20 minutes after analgesia. NA was recorded as epidural, spinal, or CSE according to the adopted technique. Technical details and dosage (high vs low) of each approach are reported as Supplementary Material. Pain intensity was assessed using the Numerical Rating Scale (NRS), with the two endpoints representing 0 ("no pain") and 10 ("pain as bad as it could be"), both before and after analgesia onset as per clinical practice. Additionally, anesthesiologic records recorded the total number of boluses administered during the entire duration of analgesia and the time interval between them.

Clinical definitions

Labor was diagnosed in the presence of regular uterine contractions (four in 20 minutes for a minimum of 1 hour) and cervical modifications.[24] Pregestational and gestational diabetes were defined according to the American Diabetes Association (ADA) guidelines.[25] The classification of fetuses as small for gestational age (SGA) and with growth restriction [fetal growth restriction (FGR)] was performed according to Gordijn et al.[26] and confirmed according to neonatal birth weight. Hypertensive disorders of pregnancy were classified according to the American College of Obstetricians and Gynecologists (ACOG) criteria.[27] Neonatal outcomes were evaluated regarding admission to the neonatal intensive care unit, umbilical artery pH and base excess at birth, and the 5' APGAR score. Maternal hypotension was defined by a SBP <100 mmHg or DBP <60 mmHg, representing the 3rd centile of blood pressure at term.[28]

Cardiotocographic parameters

We carefully and manually evaluated the cardiotocographic tracings of all included women from at least 10 minutes before starting the analgesia until delivery. Cardiotocographic features were defined according to the Intrapartum Fetal Monitoring Guidelines.[29] Tracings were carefully evaluated by a trained obstetrician (BDB) and subsequently checked by a senior one for interpretation correctness (MB). In the case of discordance or unclear interpretation, a third investigator was involved (SG). We recorded the

presence or absence of prolonged decelerations (decelerations lasting more than 3 minutes), fetal bradycardia (a baseline value below 110 bpm lasting more than 10 minutes), uterine hyperstimulation (ie, exaggerated response to uterine stimulants presenting as a prolonged contractions for over 2 minutes), or uterine tachysystole (ie, excessive frequency of contractions and is defined as the occurrence of more than five contractions in 10 minutes, in two successive 10-minute periods or averaged over 30 minutes) within 30 minutes of the first bolus of NA.[29–32] When a prolonged deceleration was recorded, cardiotocographic variability was assessed within the first three minutes of deceleration. Immediate outcomes of prolonged decelerations were recorded and classified as "resolution with labor continuation," "delivery by vacuum extraction," or "delivery by cesarean section." The diagnosis of possible irreversible causes of fetal prolonged decelerations/bradycardia (ie, uterine rupture, placental abruption, and umbilical cord prolapse) was also retrieved from cardiotocographic and medical records.

Statistical analysis

Categorical data were summarized as proportions, whereas continuous variables were summarized by medians and interquartile ranges (IQR) or mean and standard deviation (SD) based on distribution. The Kolmogorov-Smirnov test and visual plot inspection assessed the normality of continuous data distributions. Demographic, obstetric, clinical characteristics, intrapartum details, and maternal and neonatal outcomes were compared between two groups defined by the presence (cases) versus absence (controls) of a prolonged deceleration after NA (PDAA). As appropriate, the Chi-square or Fisher's exact test was used for categorical data, and the Mann-Whitney U test or t-test for continuous variables.

Univariate and multivariable logistic regression analyses were used to investigate the association between demographic, obstetric, and clinical characteristics and intrapartum details before NA and the occurrence of PDAA. Independent variables with a $P<.1$ at the univariate analysis were included in the multivariable logistic regression analysis. Multivariable logistic regression analyses were conducted following Akaike's information criterion (AIC) minimization starting from the full model. A two-tailed P value $<.05$ was considered statistically significant. R for Mac (version 2024.04.0 +735) was used for statistical analysis.

Results

A total of 5941 women delivered at the University Hospital of Verona in 2019 and 2022 (3285 and 2656, respectively). Of the 2006 (33.77%) who received NA (1082 in 2019 and 924 in 2022), we blindly selected one every two consecutive deliveries for reviewing cardiotocographic trace: 541 and 462 consecutive women from 2019 and 2022, respectively. After excluding women without cardiotocographic trace available for review (71 in 2019 and 34 in 2022), we finally included a total of 898 pregnant women with singleton-term pregnancy who underwent NA during labor: 470 in 2019 and 428 in 2022 (Figure). At least a PDAA was registered within 30' after the first bolus of NA in 6.57% (59/898; 95% CI 5.08%–8.44%) of women.

FIGURE
Flow chart of the subject selection process

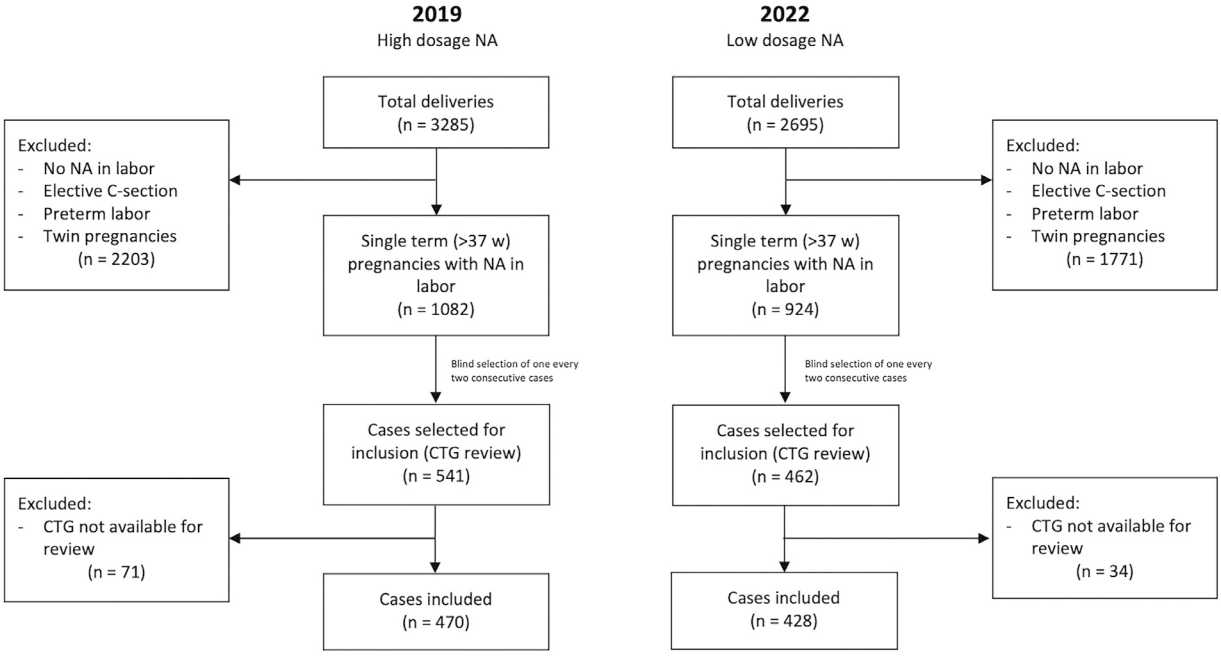

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TABLE 1
Demographic, anesthesiologic, and obstetric characteristics and maternal and fetal outcomes of women undergoing labor analgesia

	Overall (N=898)[a]	No PDAA (N=839)[a]	PDAA (N=59)[a]	*P* value[b]
Year				.283
2019	470 (52%)	435 (52%)	35 (59%)	
2022	428 (48%)	404 (48%)	24 (41%)	
Low/high dosage of analgesia	470 (52%)	435 (52%)	35 (59%)	.283
Cervical dilatation at NA (cm)	4.66 (1.79)	4.64 (1.78)	4.95 (2.00)	.291
Total NA duration (min)	377.83 (252.44)	382.06 (252.13)	317.61 (251.27)	**.030**
NA technique				.157
Peridural	148 (16%)	143 (17%)	5 (8.5%)	
CSE	737 (82%)	683 (81%)	54 (92%)	
Spinal	13 (1.4%)	13 (1.5%)	0 (0%)	
Nulliparity	631 (70%)	584 (70%)	47 (80%)	.107
Gestational age at NA	39.71 (1.40)	39.72 (1.39)	39.60 (1.57)	.814
Maternal age at NA	32.16 (5.14)	32.13 (5.20)	32.54 (4.31)	.606
BMI	22.84 (4.37)	22.92 (4.44)	21.71 (3.08)	.105
FGR	34 (3.8%)	29 (3.5%)	5 (8.5%)	.066
SGA	22 (2.4%)	19 (2.3%)	3 (5.1%)	.171
Diabetes mellitus				.485
No diabetes	773 (86%)	720 (86%)	53 (90%)	
Diet-controlled GDM	87 (9.7%)	81 (9.7%)	6 (10%)	
Insulin-treated GDM	34 (3.8%)	34 (4.1%)	0 (0%)	
Pregestational DM	4 (0.4%)	4 (0.5%)	0 (0%)	
Hypertensive disorders of pregnancy				.094
No hypertension	827 (92%)	773 (92%)	54 (92%)	
Gestational hypertension	33 (3.7%)	33 (3.9%)	0 (0%)	
Preeclampsia	34 (3.8%)	30 (3.6%)	4 (6.8%)	
Chronic Hypertension	3 (0.3%)	2 (0.2%)	1 (1.7%)	
Superimposed preeclampsia	1 (0.1%)	1 (0.1%)	0 (0%)	
Induction of labor	423 (47%)	399 (48%)	24 (41%)	.346
Oxytocin administration				**.002**
Not administered	431 (48%)	397 (47%)	34 (58%)	
For labor induction	219 (24%)	215 (26%)	4 (6.8%)	
For labor augmentation	248 (28%)	227 (27%)	21 (36%)	
High-risk labor	652 (73%)	608 (72%)	44 (75%)	.880
Duration of PDAA (min)	4.42 (1.58)	NA (NA)	4.42 (1.58)	
First 3' PDAA variability	51 (93%)	0 (NA%)	51 (93%)	>.999
Deceleration outcome				>.999
Labor continuation	54 (91.5%)	0 (NA%)	54 (91.5%)	
Vacuum delivery	0 (0%)	0 (NA%)	0 (0%)	

(continued)

TABLE 1
Demographic, anesthesiologic, and obstetric characteristics and maternal and fetal outcomes of women undergoing labor analgesia *(continued)*

	Overall (N=898)[a]	No PDAA (N=839)[a]	PDAA (N=59)[a]	*P* value[b]
Cesarean delivery	5 (8.5%)	0 (NA%)	5 (8.5%)	
Uterine hyperstimulation	68 (7.6%)	45 (5.4%)	23 (39%)	**<.001**
Uterine tachysystole	24 (2.7%)	21 (2.5%)	3 (5.1%)	.205
SBP <100 and DBP <60 mmHg	53 (9.0%)	50 (9.1%)	3 (7.1%)	>.999
SBP<100 mmHg	77 (13%)	73 (13%)	4 (9.5%)	.637
DBP <60 mmHg	148 (25%)	140 (26%)	8 (19%)	.460
SBP (mmHg)	113.04 (12.99)	112.95 (12.99)	114.14 (13.01)	.734
DBP (mmHg)	66.64 (11.08)	66.59 (11.06)	67.29 (11.37)	.616
Maternal heart rate (bpm)	82.63 (12.98)	82.66 (12.82)	82.16 (15.15)	.642
NRS at 0'	8.99 (1.99)	8.94 (2.04)	9.67 (0.94)	**.003**
NRS at 20'	1.97 (2.37)	1.95 (2.34)	2.21 (2.63)	.771
Delta NRS (20-0')	−6.82 (2.84)	−6.76 (2.84)	−7.41 (2.81)	.141
Total number of boluses	3.31 (2.09)	3.34 (2.11)	2.83 (1.72)	.113
Labor length (min)	297.74 (213.59)	297.47 (212.06)	301.94 (237.81)	.850
I–II bolus interval (min)	103.13 (76.64)	104.48 (76.79)	82.67 (71.86)	.064
Emergency Cesarean delivery	10 (1.1%)	8 (1.0%)	2 (3.4%)	.136
II stage duration (min)	60.90 (60.25)	61.37 (60.32)	54.17 (59.20)	.173
Delivery (mode)				.052
Vaginal delivery	684 (76%)	643 (77%)	41 (69%)	
Vacuum delivery	51 (5.7%)	50 (6.0%)	1 (1.7%)	
Cesarean delivery	163 (18%)	146 (17%)	17 (29%)	
Umbilical artery pH	7.23 (0.09)	7.23 (0.09)	7.24 (0.07)	.608
Arterial base excess	−5.23 (3.54)	−5.24 (3.53)	−4.94 (3.67)	.596
5' Apgar score <7	21 (2.3%)	20 (2.4%)	1 (1.7%)	>.999
Neonatal weight (g)	3359.76 (444.39)	3370.39 (440.03)	3209.86 (481.47)	**.020**
NICU admission	57 (6.4%)	51 (6.1%)	6 (10%)	.260
Abruptio placentae	4 (0.4%)	4 (0.5%)	0 (0%)	>.999
Cord prolapses	1 (0.1%)	1 (0.1%)	0 (0%)	>.999
Uterine rupture	3 (0.3%)	3 (0.4%)	0 (0%)	>.999

Bold values highlight statistical significance (p <0.05).

[a] n (%); Mean (SD); [b] Fisher's exact test; Fisher's Exact Test for Count Data with simulated *P* value (based on 5000 replicates); Wilcoxon rank sum test.

BMI, body mass index; DBP, diastolic blood pressure; FGR, fetal growth restriction; GDM, gestational diabetes mellitus; NICU, neonatal intensive care unit; NRS, Numerical Rating Scale; SBP, systolic blood pressure; SGA, small for gestational age.

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Demographic, obstetric, and clinical characteristics, intrapartum details, and maternal and neonatal outcomes are summarized overall and stratified by the occurrence of PDAA in Table 1.

In 82% (737/898) of cases, CSE was the adopted NA technique, without differences between those who experienced a PDAA versus those who had not. In the group of women who experienced a PDAA, we observed a lower neonatal birth weight [3209 (481.47) g vs 3370 (440.03) g, *P*=.02], a shorter duration of NA [317.6 minutes (251.3) vs 383.1 minutes (252.1); *P*=.03], and a lower use of oxytocin [42.4% (25/59) vs 52.6 (442/839); *P*=.002]. The evaluation of cardiotocographic tracings showed that the prevalence of uterine hyperstimulation was significantly higher among women who experienced a

deceleration after labor analgesia [39% (23/59) vs 5.4% (45/839); *P*<.001]. Pain records reported a higher pain intensity before analgesia initiation [9.7 (0.94) vs 8.9 (2.04); *P*=.003] in the group of women who experienced a PDAA. No significant differences were observed between the two groups regarding the other investigated variables, including mean SBP, DBP, and the prevalence of maternal hypotension after labor analgesia (Table 1).

Table 2 shows factors independently associated with PDAA at univariate logistic regression analysis.

Factors independently associated with PDAA in the final multivariable logistic regression model were nulliparity (OR 2.27, 95% CI 1.01−1.06; *P*=.048), uterine hyperstimulation (OR 11.4, 95% CI 5.48−23.7; *P*<.001) and reporting higher pain before NA (OR 1.50, 95% CI 1.10−2.30; *P*=.007) (Table 3).

TABLE 2
Factors associated with PDAA at univariate logistic regression analysis

	N	OR	95% CI	*P* value
Year	898	0.90	0.75, 1.08	.26
Low/high dosage analgesia	898	1.35	0.80, 2.34	.26
Cervical dilatation at NA	898	1.09	0.95, 1.25	.22
Total duration of NA	898	1.00	1.00, 1.00	**.049**
NA technique	898	1.64	0.81, 3.59	.17
Nulliparity	898	1.71	0.92, 3.43	**.091**
Gestational age at NA	897	0.94	0.79, 1.14	.53
Maternal age at NA	898	1.02	0.96, 1.07	.55
BMI	896	0.93	0.86, 0.99	**.028**
FGR	898	2.59	0.85, 6.42	**.088**
SGA	898	2.31	0.53, 7.04	.23
Diabetes mellitus	898	0.62	0.26, 1.15	.14
HDP	898	1.27	0.75, 1.94	.35
Induction of labor	898	0.76	0.44, 1.29	.30
Use of oxytocin	898	0.98	0.71, 1.33	.88
High-risk labor	898	1.11	0.62, 2.11	.72
Duration of PDAA	55	1.00	0.00, Inf	>.99
First 3' PDAA variability	55	1.00	0.00, Inf	>.99
Deceleration outcome	55	1.00	0.00, Inf	>.99
Uterine hyperstimulation	898	11.3	6.12, 20.6	**<.001**
Uterine tachysystole	898	2.09	0.48, 6.29	.28
SBP <100 and DBP <60 mmHg	589	0.76	0.18, 2.21	.65
SBP <100 mmHg	589	0.68	0.20, 1.76	.46
DBP <60 mmHg	589	0.68	0.29, 1.44	.33
SBP	589	1.01	0.98, 1.03	.57
DBP	589	1.01	0.98, 1.03	.70
Maternal heart rate (bpm)	836	1.00	0.98, 1.02	.78
NRS at 0 min	679	1.53	1.13, 2.34	**.002**
NRS at 20 min	459	1.04	0.91, 1.19	.53
Delta NRS	459	0.92	0.81, 1.03	.16
Total number of boluses	837	0.87	0.74, 1.01	**.071**
Labor length	839	1.00	1.00, 1.00	.88
I–II bolus interval	836	1.00	0.99, 1.00	**.036**
Emergent cesarean section	898	3.64	0.54, 15.0	.16
II stage length	898	1.00	0.99, 1.00	.36
Delivery mode	**898**	**1.31**	**0.96, 1.76**	**.090**
Umbilical Artery pH	834	2.21	0.09, 60.0	.63
Arterial Base Excess	833	1.02	0.95, 1.11	.55
5'Apgar score<7	897	0.71	0.04, 3.48	.72

(continued)

Discussion

Principal findings

The main findings of this work are the following: 1) the occurrence of prolonged deceleration after neuraxial analgesia is a relatively common event (6.57% after NA in labor) that does not appear associated with cesarean section or worse perinatal outcomes; 2) factors preceding NA and related to the occurrence of PDAA were nulliparity and pain intensity; 3) the prevalence of uterine hyperstimulation was significantly higher in the group of women who experienced a prolonged deceleration while no differences were observed in maternal blood pressure or in the prevalence of hypotension between the two groups.

Results in the context of what is known

NA is widely adopted for pain control in labor, being considered effective and safe. However, NA can influence the fetus both directly and indirectly.[33] Direct effects might be linked to the transplacental transfer of the drug, which can affect fetal heart rate in terms of variability and periodic decelerations and may result in neonatal respiratory

TABLE 2
Factors associated with PDAA at univariate logistic regression analysis
(continued)

	N	OR	95% CI	*P* value
Neonatal weight	**846**	**1.00**	**1.00, 1.00**	**.009**
NICU admission	897	1.75	0.65, 3.97	.25
Abruptio placentae	898	0.00		.46
Cord prolapse	898	0.00		.71
Uterine rupture	898	0.00		.52

OR, odds ratio; *CI*, confidence interval; *BMI*, body mass index; *DBP*, diastolic blood pressure; *FGR*, fetal growth restriction; *GDM*, gestational diabetes mellitus; *HDP*, hypertensive disorders of pregnancy; *NICU*, neonatal intensive care unit; *NRS*, Numerical Rating Scale; *SBP*, systolic blood pressure; *SGA*, small for gestational age.

Bold value refer to independent variables with a p <0.1 which were included in the multivariable logistic regression analyisis.

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TABLE 3
Factors independently associated with PDAA at final multivariable logistic regression analysis

	OR	95% CI	*P* value
Nulliparity	**2.27**	**1.01, 5.89**	**.048**
BMI	0.97	0.88, 1.06	.57
FGR	3.01	0.67, 9.80	.14
Uterine hyperstimulation	**11.4**	**5.48, 23.7**	**<.001**
NRS at 0'	**1.50**	**1.10, 2.30**	**.007**

OR, odds ratio; *CI*, confidence interval; *BMI*, body mass index; *FGR*, fetal growth restriction; *NRS*, numerical rating scale.

Bold values highlight statistical significance (p <0.05).

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depression or neonatal behavioral changes (though rarely described in association with NA).[6] Indirect effects are more common, with the most frequently reported being prolonged decelerations or fetal bradycardia following the initiation of NA.[6] In this regard, our results consistently report PDAA as a relatively common effect of NA administration in labor.

Understanding the pathophysiology of such indirect effects on the fetus is key to identifying potentially effective interventions. Generally, the main mechanism reported underlying cardiotocographic alterations after NA is a reduction in uteroplacental perfusion in the context of maternal hypotension caused by the sympathetic block induced by the analgesia.[34] However, other mechanisms determining placental hypoperfusion have been proposed, such as uterine hyperstimulation. The sudden drop in maternal epinephrine associated with the initiation of analgesia can result in decreased beta2-adrenergic receptor activation (ie, reduced tocolytic activity), with a secondary "rebound" effect of increased uterine activity.[6,8,16,34,35] Consistent with the latter hypothesis, our results reported uterine hyperstimulation after NA as the strongest factor associated with PDAA. In contrast, we did not observe any difference in maternal blood pressure or the proportion of women with NA-induced hypotension, supporting the fact that, although accounted among the possible mechanisms of PDAA,[13,14,36] this does not appear to represent the leading mechanism. Of note, in addition to the direct observation of a higher rate of uterine hyperstimulation among those women who experienced a PDAA, our results support the proposed pathophysiology.[6,8,16,34,35]

Indeed, the reported pain intensity before NA was significantly higher in women who developed a PDAA. For every one-point increase in the NRS pain score, there was a 50% higher likelihood of developing a PDAA. Higher pain before NA may suggest stronger pain reduction among those who experienced a PDAA, although we did not find a significant difference in delta NRS between the two groups, possibly because we missed NRS at 20 minutes in a relevant proportion of patients. Additionally, the identification of nulliparity as an additional independent risk factor for PDAA further supports the possible role of maternal epinephrine.[37,38]

Contrary to what was expected, we observed that the use of oxytocin was significantly less common in the group of women with PDAA. In our center, labor analgesia is often offered to women with an indication for oxytocin either for labor induction or augmentation, and it is performed before starting oxytocin infusion. Physicians might have been less prone to administer oxytocin in instances where a prolonged deceleration was recorded after NA. Alternatively, this finding may reflect underlying differences in uterine activity. Indeed, oxytocin is often initiated in cases of incoordinate uterine activity or uterine inertia—situations where contractions are insufficient or poorly coordinated. In such cases, the uterus is less likely to develop hyperstimulation given the sympathetic blockade.

We also did not find any significant difference in the rate of PDAA according to the analgesic dosage adopted; however, the prevalence of PDAA decreased from 7.4% in 2019 (high dosage) to 5.6% in 2022 (low dosage), supporting the fact that a lower analgesic dosage might be associated with a more gradual reduction of pain intensity and therefore a lower incidence of PDAA. This observation is consistent with Abrão and colleagues, who demonstrated in 2009 that CSE analgesia, compared to traditional epidural analgesia,

was associated with a higher incidence of fetal heart rate abnormalities related to uterine hyperstimulation, concluding that the faster the pain is relieved, the more likely uterine hyperstimulation and cardiotocographic alterations are.[16]

Concerning maternal and neonatal outcomes, we did not observe a higher rate of cesarean section or adverse neonatal outcomes in the group of women with PDAA. Notably, the cardiotocographic variability within the first three minutes of PDAA (a sign of an intact fetal autonomic nervous system and a positive prognostic factor of spontaneous resolution of deceleration)[14] was preserved in the vast majority of cases with PDAA (93%). All these aspects, in line with previous reports,[16,39–41] support that fetal heart rate changes after NA usually resolve spontaneously, do not need urgent operative deliveries, and do not adversely affect neonatal outcomes.

Clinical implications

Understanding the mechanisms underlying PDAA and their risk factors is key to prevention and management. A more gradual reduction of pain in labor, especially in nulliparous women, might provide a more gradual decrease in epinephrine levels and reduce the occurrence of PDAA. Finally, although a preserved variability within the first three minutes of deceleration is a sign of an intact autonomic fetal nervous system and is predictive of deceleration resolution, when cardiotocographic abnormalities persist, an urgent intervention to improve fetal oxygenation is required. If uterine hyperstimulation is the cause, administering acute tocolysis may be effective. Depending on the clinical circumstances and experience, various pharmacological options can be used: β-agonists such as ritodrine and terbutaline, nitric acid donors such as nitroglycerin, selective oxytocin antagonists such as atosiban, and magnesium sulfate.[42] The choice of drug may depend on several factors, including local availability, safety profile, and mechanism of action. For example, in Europe, approved options for acute tocolysis include oxytocin receptor antagonists and beta-2 adrenergic agonists. Nitric oxide donors, although sometimes used off-label, are generally considered second-line agents due to their association with maternal hypotension. Additionally, the mechanism of action should be considered: for instance, atosiban, an oxytocin receptor antagonist, may have limited effectiveness in established labor where most oxytocin receptors are already occupied, reducing its competitive binding capacity.[43]

Research implication

The results of this study highlight the need for further research to elucidate the precise mechanisms underlying the fetal heart rate changes observed after neuraxial analgesia. Prospective studies with detailed monitoring of maternal and fetal parameters, including uterine activity, maternal catecholamine levels, and uteroplacental perfusion, could provide valuable insights into the pathophysiology of PDAA.

Strengths and limitations

The main limitation of this study is the retrospective design. However, strengths include data from a prospectively collected registry and manual review of medical records and cardiotocographic tracers by trained staff following standardized guidelines. Evaluating tracings from NA administration to delivery helped establish temporal relationships between events. Some limitations remain. The study's sample size may have limited the detection of differences, especially for low-prevalence factors like delta NRS (0−20 minutes) or fetal growth. While neonatal birth weight was lower in the PDAA group, FGR[44–46] was not an independent risk factor, likely due to the small sample size. We acknowledge that some cardiotocographic tracings were not included as not available for review. However, there was no systematic pattern in which cases had missing cardiotocographic (eg, not clustered by time of the day or severity), reinforcing that exclusion was noninformative. Lastly, this monocentric study ensured uniform protocols, enhancing population homogeneity. However, larger multicentric studies with multiparametric pain assessments are needed to validate these findings.

Conclusion

Cardiotocographic abnormalities are common after NA initiation in labor, often linked to uterine hyperstimulation. Higher preanalgesia pain and nulliparity are risk factors, while hypotension seems less relevant. Understanding PDAA's pathophysiology is crucial for prevention and management. If hyperstimulation from epinephrine withdrawal is confirmed as a cause, fast-acting tocolytics may be a viable treatment when decelerations persist. ■

CRediT authorship contribution statement

Mariachiara Bosco: Writing − review & editing, Writing − original draft, Supervision, Methodology, Formal analysis, Data curation, Conceptualization. **Stefano Uccella:** Writing − review & editing, Validation, Supervision, Resources. **Beatrice De Bellis:** Writing − original draft, Investigation, Data curation. **Roberto D'Alessandro:** Writing − review & editing, Supervision, Methodology, Investigation, Conceptualization. **Rosa Laterza:** Writing − review & editing, Supervision. **Simone Garzon:** Writing − review & editing, Supervision, Formal analysis, Conceptualization. ■

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.ajogmf.2025.101747.

References

1. Brownridge P. The nature and consequences of childbirth pain. Eur J Obstet Gynecol Reprod Biol 1995;59(Suppl:S9-15). https://doi.org/10.1016/0028-2243(95)02058-z.

2. ACOG Committee Opinion #295: pain relief during labor. Obstet Gynecol 2004;104(1):213.

3. Zuarez-Easton S, Erez O, Zafran N, Carmeli J, Garmi G, Salim R. Pharmacologic and nonpharmacologic options for pain relief during labor: an expert review. Am J Obstet Gynecol 2023;228(5S):S1246–59. https://doi.org/10.1016/j.ajog.2023.03.003.

4. Jones L, Othman M, Dowswell T, et al. Pain management for women in labour: an overview of systematic reviews. Cochrane Database Syst Rev 2012;2012(3):CD009234. https://doi.org/10.1002/14651858.CD009234.pub2.

5. Landau R. Combined spinal-epidural analgesia for labor: breakthrough or unjustified invasion? Semin Perinatol 2002;26(2):109–21. https://doi.org/10.1053/sper.2002.32204.

6. Chestnut DH. Editor. Epidural and Spinal Analgesia/Anaesthesia for Labour and Vaginal Delivery. 5th Ed. Philadelphia: Chestnut's Obstetric Anaesthesia: Principles and Practice; 2016.

7. Bucklin BA, Chestnut DH, Hawkins JL. Intrathecal opioids versus epidural local anesthetics for labor analgesia: a meta-analysis. Reg Anesth Pain Med 2002;27(1):23–30. https://doi.org/10.1053/rapm.2002.29111.

8. Van de Velde M, Vercauteren M, Vandermeersch E. Fetal heart rate abnormalities after regional analgesia for labor pain: the effect of intrathecal opioids. Reg Anesth Pain Med 2001;26(3):257–62. https://doi.org/10.1053/rapm.2001.22258.

9. Cohen SE, Cherry CM, Holbrook RH, el-Sayed YY, Gibson RN, Jaffe RA. Intrathecal sufentanil for labor analgesia—sensory changes, side effects, and fetal heart rate changes. Anesth Analg 1993;77(6):1155–60. https://doi.org/10.1213/00000539-199312000-00013.

10. Eberle RL, Norris MC, Eberle AM, Naulty JS, Arkoosh VA. The effect of maternal position on fetal heart rate during epidural or intrathecal labor analgesia. Am J Obstet Gynecol 1998;179(1):150–5. https://doi.org/10.1016/s0002-9378(98)70266-2.

11. Anim-Somuah M, Smyth RM, Cyna AM, Cuthbert A. Epidural versus non-epidural or no analgesia for pain management in labour. Cochrane Database Syst Rev 2018;5(5):CD000331. https://doi.org/10.1002/14651858.CD000331.pub4.

12. Damhuis SE, Groen H, Thilaganathan B, Ganzevoort W, Gordijn SJ. Effect of intrapartum epidural analgesia on rate of emergency delivery for presumed fetal compromise: nationwide registry-based cohort study. Ultrasound Obstet Gynecol Off J Int Soc Ultrasound Obstet Gynecol 2023;62(5):668–74. https://doi.org/10.1002/uog.26309.

13. Heijtmeijer ESET, Damhuis SE, Thilaganathan B, et al. Intrapartum epidural analgesia and emergency delivery for presumed fetal compromise: association or causation? Hypothesized mechanism explored. Ultrasound Obstet Gynecol Off J Int Soc Ultrasound Obstet Gynecol 2023;62(5):757–60. https://doi.org/10.1002/uog.27495.

14. Chandraharan E, Ghi T, Fieni S, Jia YJ. Optimizing the management of acute, prolonged decelerations and fetal bradycardia based on the understanding of fetal pathophysiology. Am J Obstet Gynecol 2023;228(6):645–56. https://doi.org/10.1016/j.ajog.2022.05.014.

15. Steiger RM, Nageotte MP. Effect of uterine contractility and maternal hypotension on prolonged decelerations after bupivacaine epidural anesthesia. Am J Obstet Gynecol 1990;163(3):808–12. https://doi.org/10.1016/0002-9378(90)91073-l.

16. Abrão KC, Francisco RPV, Miyadahira S, Cicarelli DD, Zugaib M. Elevation of uterine basal tone and fetal heart rate abnormalities after labor analgesia: a randomized controlled trial. Obstet Gynecol 2009;113(1):41–7. https://doi.org/10.1097/AOG.0b013e31818f5eb6.

17. Yang L, Wan L, Huang H, Qi X. Uterine hypertonus and fetal bradycardia occurred after combined spinal-epidural analgesia during induction of labor with oxytocin infusion: A case report. Medicine (Baltimore) 2019;98(28):e16282. https://doi.org/10.1097/MD.0000000000016282.

18. Cambic CR, Wong CA. Labour analgesia and obstetric outcomes. Br J Anaesth 2010;105(Suppl 1):i50–60. https://doi.org/10.1093/bja/aeq311.

19. Papazova DA, Schyns-van den Berg AMJV, Beenakkers ICM, van den Bosch OFC. Can national registry data be used to assess effects of epidural analgesia during labor? Ultrasound Obstet Gynecol Off J Int Soc Ultrasound Obstet Gynecol 2023;62(5):753–4. https://doi.org/10.1002/uog.27483.

20. Cavoretto PI, Silvani P, Farina A. Does intrapartum epidural analgesia influence rate of emergency delivery for fetal compromise? Ultrasound Obstet Gynecol Off J Int Soc Ultrasound Obstet Gynecol 2023;62(5):621–3. https://doi.org/10.1002/uog.27494.

21. Rothman KJ, Greenland S, Lash TL. Modern Epidemiology 2008.

22. Zhang J, Troendle J, Reddy UM, et al. Contemporary cesarean delivery practice in the United States. Am J Obstet Gynecol 2010;203(4):326.e1–326.e10. https://doi.org/10.1016/j.ajog.2010.06.058.

23. Lakens D. Sample size justification. Collabra: psychology 2022;8(1):33267.

24. American College of Obstetrics and Gynecology Committee on Practice Bulletins-Obstetrics. ACOG Practice Bulletin Number 49, December 2003: Dystocia and augmentation of labor. Obstet Gynecol 2003;102(6):1445–54. https://doi.org/10.1016/j.obstetgynecol.2003.10.011.

25. American Diabetes Association. Classification and diagnosis of diabetes: standards of medical care in diabetes-2020. Diabetes Care 2020;43(Suppl 1):S14–31. https://doi.org/10.2337/dc20-S002.

26. Gordijn SJ, Beune IM, Thilaganathan B, et al. Consensus definition of fetal growth restriction: a Delphi procedure. Ultrasound Obstet Gynecol Off J Int Soc Ultrasound Obstet Gynecol 2016;48(3):333–9. https://doi.org/10.1002/uog.15884.

27. Gestational Hypertension and Preeclampsia: ACOG Practice Bulletin, Number 222. Obstet Gynecol 2020;135(6):e237–60. https://doi.org/10.1097/AOG.0000000000003891.

28. Green LJ, Mackillop LH, Salvi D, et al. Gestation-Specific Vital Sign Reference Ranges in Pregnancy. Obstet Gynecol 2020;135(3):653–64. https://doi.org/10.1097/AOG.0000000000003721.

29. Chandraharan E, Evans SA, Krueger D, Pereira S, Skivens S, et al. Physiological CTG interpretation. Intrapartum Fetal Monitoring Guideline 2018. https://physiological-ctg.com/guideline.html. Accessed 12 March 2025.

30. Chandraharan E, Pereira S, Ghi T, et al. International expert consensus statement on physiological interpretation of cardiotocograph (CTG): First revision (2024). Eur J Obstet Gynecol Reprod Biol 2024;302:346–55. https://doi.org/10.1016/j.ejogrb.2024.09.034.

31. Jia YJ, Ghi T, Pereira S, Gracia Perez-Bonfils A, Chandraharan E. Pathophysiological interpretation of fetal heart rate tracings in clinical practice. Am J Obstet Gynecol 2023;228(6):622–44. https://doi.org/10.1016/j.ajog.2022.05.023.

32. Sukumaran S, Jia YJ, Uterine Tachysystole Chandraharan E. Hypertonus and hyperstimulation: an urgent need to get the definitions right to avoid intrapartum hypoxic-ischaemic brain injury. Glob J Reprod Med 2021;8(2):5556735.

33. Grangier L, Martinez de Tejada B, Savoldelli GL, Irion O, Haller G. Adverse side effects and route of administration of opioids in combined spinal-epidural analgesia for labour: a meta-analysis of randomised trials. Int J Obstet Anesth 2020;41:83–103. https://doi.org/10.1016/j.ijoa.2019.09.004.

34. Callahan EC, Lee W, Aleshi P, George RB. Modern labor epidural analgesia: implications for labor outcomes and maternal-fetal health. Am J Obstet Gynecol 2023;228(5S):S1260–9. https://doi.org/10.1016/j.ajog.2022.06.017.

35. Lim G, Facco FL, Nathan N, Waters JH, Wong CA, Eltzschig HK. A Review of the Impact of Obstetric Anesthesia on Maternal and Neonatal Outcomes. Anesthesiology 2018;129(1):192–215. https://doi.org/10.1097/ALN.0000000000002182.

36. D'Angelo R, Eisenach JC. Severe maternal hypotension and fetal bradycardia after a combined spinal epidural anesthetic. Anesthesiology 1997;87(1):166–8. https://doi.org/10.1097/00000542-199707000-00023.

37. Gaston-Johansson F, Fridh G, Turner-Norvell K. Progression of labor pain in primiparas and multiparas. Nurs Res 1988;37(2):86–90.

38. Sheiner E, Sheiner EK. Shoham-Vardi I. The relationship between parity and labor pain. Int J Gynaecol Obstet Off Organ Int Fed

Gynaecol Obstet 1998;63(3):287–8. https://doi.org/10.1016/s0020-7292(98)00164-7.
39. Landau R, Carvalho B, Wong C, Smiley R, Tsen L, Van de Velde M. Elevation of uterine basal tone and fetal heart rate abnormalities after labor analgesia: a randomized controlled trial. Obstet Gynecol 2009;113(6):1374. https://doi.org/10.1097/AOG.0b013e3181a8909d.
40. Albright GA, Forster RM. Does combined spinal-epidural analgesia with subarachnoid sufentanil increase the incidence of emergency cesarean delivery? Reg Anesth 1997;22(5):400–5. https://doi.org/10.1016/s1098-7339(97)80025-9.
41. Mardirosoff C, Dumont L, Boulvain M, Tramèr MR. Fetal bradycardia due to intrathecal opioids for labour analgesia: a systematic review. BJOG Int J Obstet Gynaecol 2002;109(3):274–81. https://doi.org/10.1111/j.1471-0528.2002.01380.x.
42. Chandraharan E, Arulkumaran S. Acute tocolysis. Curr Opin Obstet Gynecol 2005;17(2):151–6. https://doi.org/10.1097/01.gco.0000162184.45854.88.
43. Fieni S, Morganelli G, Chandraharan E, Dall'Asta A, Ghi T. Intrauterine fetal resuscitation: from maternal repositioning to the latest pharmacological strategies. J Matern-Fetal Neonatal Med Off J Eur Assoc Perinat Med Fed Asia Ocean Perinat Soc Int Soc Perinat Obstet 2025;38(1):2502977. https://doi.org/10.1080/14767058.2025.2502977.
44. Krishna U, Bhalerao S. Placental insufficiency and fetal growth restriction. J Obstet Gynaecol India 2011;61(5):505–11. https://doi.org/10.1007/s13224-011-0092-x.
45. Dall'asta A, Cagninelli G, Galli L, Frusca T, Ghi T. Monitoring fetal well-being in labor in late fetal growth restriction. Minerva Obstet Gynecol 2021;73(4):453–61. https://doi.org/10.23736/S2724-606X.21.04819-X.
46. Lin CC, Moawad AH, Rosenow PJ, River P. Acid-base characteristics of fetuses with intrauterine growth retardation during labor and delivery. Am J Obstet Gynecol 1980;137(5):553–9. https://doi.org/10.1016/0002-9378(80)90695-x.

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Tweetable Statement: Uterine hyperstimulation, not maternal hypotension, is the main factor associated with prolonged fetal decelerations after neuraxial analgesia in labor, without worsening perinatal outcomes.

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