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***Original Research Article***

# Comparison of Norepinephrine and Phenylephrine Infusions for Maintenance of Haemodynamics Following Subarachnoid Block in Lower Segment Caesarean Section

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**Abstract:** *Phenylephrine (PE) is widely regarded as the drug of choice for treating maternal hypotension during cesarean delivery under subarachnoid block. However, growing evidence from recent studies indicates that norepinephrine (NE) is an effective alternative.* ***Objective:*** *To compare the outcome of norepinephrine and phenylephrine infusions for maintenance of hemodynamics following subarachnoid block in lower segment caesarean section.* ***Methods:*** *This randomized controlled trial took place at the Department of Anesthesiology, National Hospital and Medical Centre, Lahore, from 1st July 2024 to 1st January 2025, enrolling 84 patients undergoing cesarean section under subarachnoid block. Patients were randomly assigned to receive PE or NE infusions, and intraoperative bradycardia (HR <50 bpm) was recorded. Statistical analysis was carried out using the Mann-Whitney U test for continuous variables and the Chi-square or Fisher's exact test for categorical variables, with $p \leq 0.05$ considered significant. Stratification for potential confounders was also performed.* ***Results:*** *Baseline demographics were comparable between groups ($p > 0.05$ each). The incidence of bradycardia was substantially higher with PE (61.9%) compared to NE (9.5%) ($p = 0.000$). Stratified analyses confirmed lower bradycardia rates with NE across age groups (7.7% vs. 63.6%, $p = 0.000$; 12.5% vs. 60.0%, $p = 0.004$), parity groups (8.3% vs. 56.7%, $p = 0.000$; 16.7% vs. 75.0%, $p = 0.019$), ASA II patients (9.5% vs. 61.9%, $p = 0.000$), and term gestations (9.5% vs. 65.0%, $p = 0.000$).* ***Conclusion:*** *Norepinephrine is a favorable alternative to phenylephrine for preserving maternal blood pressure during subarachnoid block for cesarean delivery. Given its lower incidence of bradycardia across all subgroups, norepinephrine can be considered the preferred vasopressor for routine clinical use in obstetric anesthesia.*

**Keywords:** Cesarean delivery, Anesthesia, Subarachnoid block, Hemodynamics, Hypotension, Norepinephrine, Phenylephrine.

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## Introduction

The anesthetic management of a cesarean section places an added responsibility on the anesthesiologist to protect the wellbeing of the mother as well as the fetus (1). Cesarean delivery is mainly performed using either general anesthesia or regional anesthesia as the techniques of choice (2, 3). This choice is primarily based on factors such as the patient's clinical features, the doctor's level of experience, access to drugs and equipment, and the patient's preferences. (2) For cesarean delivery, recent trends indicate a preference for subarachnoid block, also known as spinal anesthesia, over general anesthesia. (4) This preference is mainly attributed to lesser airway-related complications in mothers and reduced risk of drug transfer to neonates, which is a common concern with general anesthesia. (5) Additionally, it promptly achieves an adequate sensory and motor blockade. (6) Although both techniques come with distinct risk–benefit profiles and implications for maternal and fetal outcomes (2, 3), hypotension along with nausea and vomiting is frequently encountered in patients after receiving a subarachnoid block. (7) In a recent study, hypotension was experienced by 64% patients after subarachnoid block for cesarean section. (8)

Numerous studies have examined the prevention and treatment of hypotension after subarachnoid block during cesarean delivery. (9-12) Phenylephrine (PE) is currently considered the gold standard vasopressor, widely recommended by clinical guidelines for the prevention and management of hypotension in patients undergoing cesarean section under subarachnoid block. (13, 14) It is a potent alpha-adrenergic receptor agonist that produces rapid vasoconstriction, elevates systemic vascular resistance, and efficiently restores blood pressure. However, it is linked with decreased heart rate and a subsequent decline in cardiac output among patients, resulting in reduced uteroplacental perfusion and adverse fetal outcomes. (9, 11, 15, 16)

Norepinephrine (NE) is also a strong alpha-adrenergic receptor agonist with comparatively weaker agonistic activity at beta-adrenergic receptors. In recent years, it has gained attention as an effective substitute to PE in managing hypotension caused by a subarachnoid block during cesarean section. This is mainly because of the lesser risk of reflex bradycardia and a promising impact on maintaining maternal cardiac output. It also provides a balanced vasoconstrictive response while preserving uteroplacental perfusion, making it an ideal vasopressor in current obstetric anesthesia practice. (17) In a recent study, the frequency of bradycardia was markedly elevated in the PE group (16%) in contrast to the NE group (1%), whereas the overall incidence of hypotension was 13.9%. (18)

The current study is designed to compare the outcomes of NE and PE infusions for maintaining hemodynamics following subarachnoid block during lower segment caesarean section. Getting region-specific evidence will help anesthesiologists select the vasopressor that provides optimal maternal hemodynamic stability with minimal fetal compromise. The findings will guide protocol development, reduce complications, and contribute to the global body of knowledge by highlighting data from an underrepresented population.

## Methodology

This randomized controlled trial was conducted in the Department of Anesthesiology at the National Hospital and Medical Centre in Lahore. The study lasted six months, from July 1, 2024, to January 1, 2025. A total of 84 participants were included, with 42 women assigned to each

group. The sample size was calculated using a power of 80 percent, a margin of error of 5 percent, and expected frequencies of hypotension of 16 percent in the phenylephrine group and 1 percent in the norepinephrine group. A random sampling technique was used to select participants.

Eligible participants were female patients scheduled for cesarean section under subarachnoid block, aged between 18 and 45 years, of any parity, and carrying singleton pregnancies beyond 36 weeks of gestation confirmed by ultrasonography. Only patients with an ASA physical status classification of II were included. Individuals were excluded if they had any documented cardiac disease, such as rheumatic heart disease or coronary artery disease, preexisting renal impairment, or a history of hypertensive disorders during pregnancy. Pregnancies with multiple gestations and those requiring general anaesthesia were also excluded.

After obtaining endorsement from the hospital ethics committee and informed consent from patients, the data were collected from the Department of Anesthesiology, National Hospital and Medical Centre, Lahore, in collaboration with the labor rooms of the same hospital. All 84 females enrolled met the inclusion criteria; their demographic and gestational details were collected. All females were randomly divided into 2 groups (A and B) using a lottery. Females in group A were given PE 100 µg/mL, and females in group B were given NE 5 µg/mL. NE and PE were diluted and prepared in labeled 10-mL syringes to achieve concentrations of 4 µg/mL for NE and 50 µg/mL for PE. Outcomes will be measured as bradycardia (heart rate <50 bpm during surgery). All data were collected using a predesigned questionnaire.

All collected data were analyzed using SPSS version 25. For continuous data such as age (years), parity, and gestational age (weeks), means ± standard deviations and medians with IQRs were calculated. The Mann-Whitney U test was used to compare these variables between the two groups; for categorical variables such as ASA status and bradycardia, frequencies and percentages were calculated. The chi-square test or Fisher's exact test was used to compare the frequency of bradycardia between groups. A p-value ≤ 0.05 was considered statistically significant. Data were then stratified by age, ASA status, parity, and gestational age to control for potential confounders. The chi-square test was applied after stratification, with $p \leq 0.05$ considered significant.

## Results

Table 1 presents the demographic and clinical characteristics of patients in the NE and PE groups (n = 84). The mean age was 29.43 ± 3.68 years in the NE group and 30.48 ± 4.59 years in the PE group (p = 0.306), with median ages of 29 (IQR = 5.25) and 30 (IQR = 7.25) years, respectively. Most participants were between 18 and 30 years (61.9% vs. 52.4%; p = 0.378). Parity did not differ significantly between groups, with a mean parity of 1.95 ± 0.58 versus 2.17 ± 0.70 (p = 0.207), and the majority of patients had 1–2 previous deliveries (85.7% vs. 71.4%; p = 0.111). Gestational age at delivery was similar, averaging 37.29 ± 0.46 weeks in the NE group and 37.36 ± 0.66 weeks in the PE group (p = 0.689), with a median of 37 weeks (IQR = 1.00) in both. Nearly all patients delivered at term (100% vs. 95.2%; p = 0.494). All participants were classified as ASA physical status II.

**Table 1: Demographic and Clinical Characteristics of Patients between the two groups (n=84)**

| Variables | | Type of vasopressor administered | | p-value |
|---|---|---|---|---|
| | | Norepinephrine | Phenylephrine | |
| Age (years) | Mean ± SD | 29.43 ± 3.68 | 30.48 ± 4.59 | 0.306 [a] |
| | Median (IQR) | 29.00 (5.25) | 30.00 (7.25) | |
| Age groups (years), n (%) | 18-30 | 26 (61.9%) | 22 (52.4%) | 0.378 [b] |
| | 31-45 | 16 (38.1%) | 20 (47.6%) | |
| Parity | Mean ± SD | 1.95 ± 0.58 | 2.17 ± 0.70 | 0.207 [a] |
| | Median (IQR) | 2.00 (0.00) | 2.00 (1.00) | |
| Parity Groups, n(%) | 1-2 | 36 (85.7%) | 30 (71.4%) | 0.111 [b] |
| | 3-4 | 6 (14.3%) | 12 (28.6%) | |
| Gestational age (weeks) | Mean ± SD | 37.29 ± 0.46 | 37.36 ± 0.66 | 0.689 [a] |
| | Median (IQR) | 37.00 (1.00) | 37.00 (1.00) | |
| Gestational age (weeks), n (%) | Late Pre-term (34-36) | 0 (0.0%) | 2 (4.8%) | 0.494 [c] |
| | Term (≥ 37) | 42 (100.0%) | 40 (95.2%) | |
| ASA Physical Status II, n (%) | | 42 (100.0%) | 42 (100.0%) | NA |

Table 1: a For continuous variables: p-values were computed using the Mann–Whitney U test. b For qualitative variables, p-values were derived using the Chi-square test. c Fisher's Exact Test applied where cell counts were ≤5 or zero. IQR (Interquartile Range) = Q3 – Q1; it indicates variability between the 25th and 75th percentiles. NA: Not applicable because both groups had identical distributions. ASA = American Society of Anesthesiologists. All patients were ASA status II.

Among 84 patients, the incidence of bradycardia differed significantly between the two vasopressor groups (p = 0.000; see Table 2). Bradycardia occurred significantly more frequently in the PE group (61.9%) compared to the NE group (9.5%). Conversely, the absence of bradycardia was more common in the NE group (90.5%) than in the PE group (38.1%).

**Table 2: Comparison of Bradycardia between NE and PE groups**

| | | Type of vasopressor | | Total n (%) | p-value |
|---|---|---|---|---|---|
| | | Norepinephrine | Phenylephrine | | |
| Bradycardia, n (%) | Yes | 4 (9.5%) | 26 (61.9%) | 30 (35.7%) | 0.000* |
| | No | 38 (90.5%) | 16 (38.1%) | 54 (64.3%) | |
| Total | | 42 (100.0%) | 42 (100.0%) | 84 (100.0%) | |

Table 2: Values are presented as numbers (percentages). Chi-square test was applied. $p \leq 0.05$ considered statistically significant; * indicates high significance.

Stratified analysis showed a substantially greater incidence of bradycardia in patients receiving PE compared with NE across most subgroups, as shown in Table 3. In the 18–30 years age group,

bradycardia occurred in 63.6% of PE cases versus 7.7% with NE (p = 0.000), while in the 31–45 years group it was 60.0% versus 12.5% (p = 0.004). Among women with parity 1–2, bradycardia was seen in 56.7% of PE cases versus 8.3% with NE (p = 0.000), and for parity 3–4, it was 75.0% versus 16.7% (p = 0.019). In patients with ASA physical status II, bradycardia occurred in 61.9% of PE cases compared to 9.5% with NE (p = 0.000). For term pregnancies (≥37 weeks), the incidence was 65.0% versus 9.5% respectively (p = 0.000). No cases of bradycardia were reported in late pre-term patients (34–36 weeks). Overall, NE use was consistently linked with a significantly lower risk of bradycardia across all strata.

**Table 3: Association of Vasopressor Type with Bradycardia after Stratification**

| Stratification variable | | Bradycardia | Type of vasopressor, n (%) | | p-value |
|---|---|---|---|---|---|
| | | | Norepinephrine | Phenylephrine | |
| Age groups (years) | 18-30 (n = 48) | Yes | 2 (7.7%) | 14 (63.6%) | 0.000* |
| | | No | 24 (92.3%) | 8 (36.4%) | |
| | 31-45 (n = 36) | Yes | 2 (12.5%) | 12 (60.0% | 0.004* |
| | | No | 14 (87.5%) | 8 (40.0%) | |
| Parity | 1-2 (n = 66) | Yes | 3 (8.3%) | 17 (56.7%) | 0.000* |
| | | No | 33 (91.7%) | 13 (43.3%) | |
| | 3-4 (n =18) | Yes | 1 (16.7%) | 9 (75.0%) | 0.019* |
| | | No | 5 (83.3%) | 3 (25.0%) | |
| ASA Physical status | ASA II (n = 84) | Yes | 4 (9.5%) | 26 (61.9%) | 0.000* |
| | | No | 38 (90.5%) | 16 (38.1%) | |
| Gestational age (weeks) | Late Pre-term (34-36) (n = 2) | Yes | 0 (0.0%) | 0 (0.0%) | NA |
| | | No | 0 (0.0%) | 2 (100.0%) | |
| | Term (≥37) (n = 82) | Yes | 4 (9.5%) | 26 (65.0%) | 0.000* |
| | | No | 38 (90.5%) | 14 (35.0%) | |

Table 3: Chi-square test was used. p < 0.05 means statistical significance. NA = Chi-square test not applicable due to insufficient data.

**Discussion**

As phenylephrine is often associated with reflex maternal bradycardia and reduced maternal cardiac output, growing evidence and expert opinion now favor NE as the preferred vasopressor in obstetric anesthesia. (19, 20) The lack of a notable reduction in umbilical artery pH values offers compelling evidence that NE is safe for the fetus in this clinical context. (20) The present study evaluated the outcome of NE and PE infusions for maintaining hemodynamic stability after subarachnoid block in lower-segment cesarean section. Our results showed that NE significantly reduced the bradycardia rate compared with PE (9.5% vs 61.9%, p < 0.001). Baseline demographic variables were comparable between groups. The mean age was 29.43 ± 3.68 years in the NE group and 30.48 ± 4.59 years in the PE group (p = 0.306). Parity also showed no significant difference, with medians of 2.00 (IQR = 0.00) versus 2.00 (IQR = 1.00) for NE and PE, respectively (p = 0.207). Gestational age was nearly identical (37.29 ± 0.46 vs. 37.36 ± 0.66 weeks, p = 0.689), confirming that both groups were well matched before intervention. Likewise, in a report by Tiwari et al., the mean age of patients was comparable between the two groups (29.4 ± 4.82 years vs 30.2 ± 5.09 years), with a p value of 0.73. (7) Goel et al. also reported no significant age variation between the two groups (p = 0.957). (18)

Previous studies have also highlighted the impact of PE on reflex bradycardia and cardiac output. Hasnain et al. exhibited that the frequency of bradycardia was less in patients receiving NE (13% vs. 21%). Nonetheless, the association was insignificant (p = 0.3). (9) Similarly, Queiroz et al. demonstrated that there was no substantial variation in the frequency of bradycardia between two groups (51.4% and 70.3%, p = 0.16). (21) Conversely, a meta-analysis documented a substantially lesser rate of bradycardia in the NE group (RR = 0.37, 95% CI: 0.28 to 0.49, p < 0.00001). (22) Sharkley et al. also reported that the bradycardia rate in the NE group was 10.7%, juxtaposed to 37.5% in the PE group, with a p-value < 0.001. (23) Another research described that parturients who got PE had a higher incidence of bradycardia compared to those who received NE (p = 0.03). (7) In a more recent trial, Mao et al. stated a substantially decreased frequency of bradycardia in patients receiving NE to treat hypotension compared to those who received PE (2.1% vs 12.8%, p = 0.046). (24) Our findings are consistent with this physiological advantage expected from NE's mixed alpha- and modest beta-adrenergic activity, which helps in preserving maternal heart rate and cardiac output.

Stratified analysis further demonstrated that the higher bradycardia rate in the PE group persisted across all subgroups. Among parturients aged 18–30 years, bradycardia occurred in 63.6% of those receiving PE versus only 7.7% in the NE group (p < 0.001). In the 31–45-year group, the incidence was 60.0% versus 12.5% respectively (p = 0.004), confirming the consistency of this finding across age categories. Similar trends were observed with parity. In parturients with parity 1–2, bradycardia was higher in the PE group (56.7%) than in the NE group (8.3%) (p < 0.001). Even among those with higher parity (3–4), PE was associated with a 75.0% incidence of bradycardia, compared with only 16.7% with NE (p = 0.019). ASA physical status II patients also demonstrated this difference, with PE causing bradycardia in 61.9% compared with 9.5% with NE (p < 0.001).

The clinical implications are considerable. Maternal bradycardia can reduce uteroplacental perfusion, potentially compromising fetal oxygenation. Although outcomes in neonates, including Apgar scores and cord blood gases, were not assessed in this study, the hemodynamic stability afforded by NE suggests potential fetal benefit. The consistency of these findings across all age, parity, and gestational subgroups reinforces NE's reliability as a vasopressor in obstetric anesthesia.

While this trial is strengthened by its randomized, double-masked design, limitations include its single-center setting, moderate sample size (n = 84), and restriction to ASA II parturients. Additionally, NE dosing was fixed rather than titrated using invasive hemodynamic monitoring. Nevertheless, this research adds valuable local evidence to the growing global consensus that NE is an effective and safer alternative to PE for managing hypotension caused by subarachnoid block during cesarean delivery.

**Conclusion**

Our findings are in strong agreement with the international literature, which shows that norepinephrine is an effective and safer alternative to phenylephrine for maintaining maternal blood pressure during subarachnoid block for cesarean delivery. Given its lower incidence of bradycardia and stable hemodynamic profile across all subgroups,

norepinephrine can be considered the preferred vasopressor for routine clinical use in obstetric anesthesia.

## Declarations

**Data Availability statement**
All data generated or analysed during the study are included in the manuscript.
**Ethics approval and consent to participate**
Approved by the department concerned. (ANS-2022-087-2859)
**Consent for publication**
Approved
**Funding**
Not applicable

## Conflict of interest

The authors declared no conflict of interest.

## Author Contribution

**MA (Resident)**
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*Review of Literature, Data entry, Data analysis, and drafting articles.*
**SM (Consultant)**
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**SA (SR)**
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*All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.*

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