

Comparative effectiveness of ephedrine and norepinephrine for hypotension in cesarean section under spinal anesthesia: A systematic literature review

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Abstract

Background: High-risk deliveries are generally managed via cesarean section. Spinal anesthesia is frequently chosen due to its rapid onset and sufficient duration of action. However, hypotension remains a major complication that may compromise maternal hemodynamics stability and fetal perfusion. Vasopressors such as ephedrine and norepinephrine are used to address this condition. Ephedrine is associated with increased tachycardia and higher rates of placental abruption, whereas norepinephrine is considered more stable in maintaining maternal hemodynamics without an increase in heart rate and with minimal placental abruption, although evidence of its effectiveness remains limited. Therefore, the researchers conducted a systematic review comparing the effectiveness of ephedrine and norepinephrine in managing hypotension in patients undergoing cesarean section under spinal anesthesia.

Method: This study utilized a PICO-based literature review and the PRISMA protocol, with inclusion criteria for quantitative studies (RCTs, cohort studies, and retrospective comparative studies) examining the use of ephedrine and norepinephrine in patients undergoing cesarean section with spinal anesthesia, published between 2015 and 2025 and written in English. Databases: Google Scholar, PubMed, and ScienceDirect. Article quality was assessed using the JBI Critical Appraisal Tools with narrative data synthesis.

Results: Based on 9 studies (8 RCTs and 1 comparative clinical study) involving a total of 1,006 patients (ages 18–46 years, ASA I and II). 5 of 9 studies (55.6%) reported better outcomes with norepinephrine in maintaining maternal hemodynamic stability, with a lower incidence of tachycardia and lower placental transfer. A total of 22.2% reported no significant difference between the two groups, while another 22.2% stated that ephedrine was more effective despite a higher risk of tachycardia. Maternal effects (nausea, vomiting, chills, dizziness, palpitations) as well as umbilical artery pH and APGAR scores were generally similar across groups.

Conclusion: Norepinephrine effectively maintains maternal hemodynamic stability while being associated with a reduced occurrence of tachycardia, along with a favorable neonatal profile and minimal maternal adverse effects. Therefore, it may be considered as an alternative vasopressor in patients undergoing cesarean section with spinal anesthesia.

Keywords: Ephedrine, Hypotension, Norepinephrine, Sectio Caesarea, Spinal Anesthesia

INTRODUCTION

Cesarean section is a surgical intervention performed when vaginal delivery is not feasible due to potential risks to both maternal and fetal safety (1). According to a report by the World Health Organization (2023), the rate of cesarean section procedures has continued to rise annually. Globally, the incidence increased to 21% in

2013 and is projected to reach 29% by 2030 (2). This procedure involves an incision through the abdominal wall, thereby requiring anesthesia to manage pain. Spinal anesthesia is considered a preferred option because of its rapid onset, minimal drug exposure to the fetus, and relatively prolonged duration of action (3,4).

Approximately 78 out of 149 patients undergoing cesarean section were reported to develop hypotension following spinal anesthesia, corresponding to an incidence of 52.5%(5). Several factors contribute to this condition, including higher fetal weight—particularly above 2,500 grams—and an elevated sensory block level exceeding T6. These conditions may induce vasodilation, leading to sympathetic nerve blockade. In addition, a higher body mass index (BMI) has been associated with a prolonged interval between anesthetic injection and surgical incision. Hypotension not only affects maternal blood pressure but also compromises fetal perfusion. If not promptly managed, it may disrupt maternal hemodynamic stability and impair uteroplacental blood flow (6,7).

To reduce complications associated with spinal anesthesia, several preventive strategies have been proposed. One approach involves maintaining the patient in a seated position for approximately two minutes after spinal anesthesia, which may slow the cephalad spread of the anesthetic to the upper thoracic region. In addition, fluid preloading with either colloid or crystalloid solutions is commonly administered to increase intravascular volume (8). Vasopressors such as ephedrine, phenylephrine, and norepinephrine are also widely used in the management of hypotension, each with distinct advantages and limitations. Ephedrine has historically been used due to its ability to increase blood pressure; however, it is associated with a higher incidence of tachycardia and greater placental transfer. Phenylephrine is effective in maintaining maternal blood pressure but may lead to bradycardia. In contrast, norepinephrine, as a newer vasopressor agent, is considered capable of maintaining maternal hemodynamic stability with a lower risk of tachycardia and reduced placental transfer (9).

Previous research by J. Liu et al. (2026) indicates that studies directly comparing ephedrine and norepinephrine in obstetric settings remain limited. This is largely due to the predominance of research focusing on

comparisons between norepinephrine and phenylephrine (10). In addition, the long-term effects of vasopressor use on both maternal and neonatal outcomes have not been extensively evaluated. Most available studies emphasize short-term outcomes, often involving small sample sizes and limited reporting of neonatal parameters (11,12). Therefore, further investigation is warranted to assess the comparative effectiveness of ephedrine and norepinephrine in the management of hypotension among patients undergoing cesarean section under spinal anesthesia, through a systematic review of relevant literature.

METHODS

In this study, a systematic approach to reviewing the literature was applied based on the PICO framework and PRISMA protocol. The literature search was performed across several databases, including PubMed, ScienceDirect, and Google Scholar. To identify relevant studies aligned with the research objective, a combination of Medical Subject Headings (MeSH) terms and free-text keywords was applied, including “(Ephedrine) AND (Norepinephrine) AND (Cesarean Section) AND (Hypotension) AND (Spinal Anesthesia)” with the use of Boolean operators (AND, OR).

In PubMed, the search was conducted on October 25, 2025, using a combination of MeSH terms and free text terms: (“Spinal Anesthesia” OR “Anesthesia Spinal” AND “Cesarean Section” AND “Hypotension” OR “Spinal Hypotension” AND “Ephedrine” AND “Norepinephrine”). The search identified 1,058 articles.

In ScienceDirect, the search was conducted on October 25, 2025, using free text keywords: (“Spinal Anesthesia” OR “Anesthesia Spinal” AND “Cesarean Section” AND “Hypotension” AND “Ephedrine” AND “Norepinephrine”). This search identified 27 articles.

In Google Scholar, the search was conducted on November 19, 2025, using free text keywords: (“Spinal Anesthesia” OR “Anesthesia Spinal” AND “Cesarean Section” OR “Cesarean Delivery” AND “Hypotension”

OR “Spinal Hypotension” AND “Ephedrine” AND “Norepinephrine”).

The inclusion criteria comprised articles published within the last ten years (2015–2025). Eligible studies involved patients undergoing cesarean section, either elective or emergency, under spinal anesthesia, and specifically examined the comparative use of ephedrine and norepinephrine for the management of post-spinal hypotension. The selected studies included quantitative designs such as randomized controlled trials (RCTs), cohort studies, retrospective studies, and comparative clinical studies. All included articles were published in English and provided full-text access with available abstracts. The interventions of interest consisted of the administration of ephedrine and/or norepinephrine, delivered either as bolus doses or continuous infusions. Maternal hemodynamic outcomes were evaluated, including blood pressure and heart rate. In addition, neonatal outcomes assessed included umbilical arterial pH and APGAR scores at one and five minutes. Maternal outcomes also encompassed adverse effects such as nausea, vomiting, shivering, dizziness, and palpitations.

The study selection process followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow. Initially, titles and abstracts were screened, followed by full-text assessment to ensure eligibility based on the predefined inclusion criteria. Duplicate articles were first identified through Mendeley reference management software and subsequently removed from the dataset.

Assessment of methodological quality and study eligibility was conducted using the Joanna Briggs Institute (JBI) Critical Appraisal Tools, which also helped in identifying

possible sources of bias before data synthesis. The evaluation was conducted using a scoring system in which “yes” was assigned a score of 1, while “no” or “unclear” was assigned a score of 0, and “not applicable (N/A)” items were excluded from the total score. The quality assessment results were categorized as follows: scores $\geq 75\%$ indicated a low risk of bias, scores between 50–75% indicated a moderate risk, and scores $< 50\%$ indicated a high risk of bias.

A cut-off score of $\geq 75\%$ was selected to ensure that the studies included in the final synthesis met a sufficient proportion of the predefined methodological quality criteria. Therefore, studies with scores below 75%, which were considered to have moderate or high risk of bias, were excluded from the final synthesis to reduce the potential influence of methodological weaknesses and bias on the findings of the synthesis. This threshold was intended to ensure that the final synthesis was based on studies with adequate methodological rigor and greater reliability. The appraisal criteria and results for each assessed study are presented in Table 1.

The extracted data included study title, authors, publication year, country, study design, sample size, and patient characteristics. In addition, information on the type of intervention and key outcomes was collected. These outcomes comprised maternal hemodynamic parameters (blood pressure and heart rate), neonatal outcomes (umbilical arterial pH and APGAR scores at one and five minutes), as well as maternal adverse effects such as nausea, vomiting, shivering, dizziness, and palpitations. The collected data were subsequently analyzed and presented using a narrative synthesis approach.

Table 1. JBI Quality Assessment

No	Authors	Title	Year	Score	Dosage	Overall Appraisal
1.	(Elnabity and Selim)	Norepinephrine versus Ephedrine to Maintain Arterial Blood Pressure during Spinal Anesthesia for Cesarean Delivery: A Prospective Double-blinded Trial	2018	100%	Norepinephrine 5 µg as an intravenous bolus and ephedrine 10 mg as an intravenous bolus for the prophylaxis of hypotension.	Include

No	Authors	Title	Year	Score	Dosage	Overall Appraisal
2.	(Elagamy et al., 2021)	Norepinephrine versus ephedrine for hypotension prophylaxis during cesarean section under spinal anesthesia.	2021	85%	Ephedrine 10 mg as a diluted intravenous bolus and norepinephrine 16 µg as an intravenous bolus for the prophylaxis of hypotension.	Include
3.	(Mohammed et al., 2022)	Norepinephrine versus Ephedrine to maintain arterial blood pressure during spinal anesthesia for cesarean section.	2022	69%	Norepinephrine 5 µg as an intravenous bolus and ephedrine 10 mg as an intravenous bolus for the prophylaxis of hypotension.	Exclude
4.	(Desalegn et al., 2022)	Effectiveness of Prophylactic Bolus Ephedrine Versus Norepinephrine for Management of Postspinal Hypotension during Elective Caesarean Section in Resource Limited Setting: A Prospective Cohort Study.	2022	73%	Norepinephrine 16 µg as an intravenous bolus and ephedrine 10 mg as an intravenous bolus for the prophylaxis of spinal hypotension.	Exclude
5.	(Xu et al., 2019)	A randomized double-blind study comparing prophylactic norepinephrine and ephedrine infusion for preventing maternal spinal hypotension during elective cesarean section under spinal anesthesia.	2019	100%	Norepinephrine 4 µg/min as an intravenous infusion and ephedrine 4 mg/min as an intravenous infusion, titrated on-off to maintain systolic blood pressure at 80–120% of baseline values..	Include
6.	(Fan et al., 2021)	Comparison of two vasopressor protocols for preventing hypotension post-spinal anesthesia during cesarean section: a randomized controlled trial.	2021	100%	Norepinephrine 0.05 µg/kg/min as an intravenous infusion and ephedrine 0.15 mg/kg as an intravenous bolus for the prophylaxis of post-spinal hypotension.	Include
7.	(Manouchehrian et al., 2022)	Comparison of the Effect of Intravenous Bolus Norepinephrine and Ephedrine on Prevention of Post Spinal Hypotension in Cesarean Section: a Randomized Double-Blind Clinical Trial.	2022	92%	Norepinephrine 5 µg as an intravenous bolus and ephedrine 10 mg as an intravenous bolus for the prophylaxis of post-spinal hypotension.	Include
8.	(Soyalp et al., 2025)	Effects of Norepinephrine-Ephedrine Combination on Maternal Hemodynamics in Cesarean Sections Performed Under Spinal Anesthesia.	2025	92%	Norepinephrine 5 µg as an intravenous bolus, ephedrine 5 mg as an intravenous bolus, and a combination of ephedrine 5 mg + norepinephrine 2.5 µg..	Include
9.	(12)	Comparison of Norepinephrine and	2021	77%	Norepinephrine 8 µg as an intravenous bolus	Include

No	Authors	Title	Year	Score	Dosage	Overall Appraisal
		Ephedrine Boluses in the Control of Spinal Anesthesia-Induced Hypotension during Cesarean Section			and ephedrine 3–6 mg as an intravenous bolus.	
10.	(13)	Comparison of Norepinephrine with Ephedrine Boluses for the Treatment of Maternal Hypotension during Cesarean Section Under Spinal Anesthesia: A Prospective Observational Study	2023	91%	Ephedrine 6 mg as an intravenous bolus and norepinephrine 6 µg as an intravenous bolus for the management of hypotension following spinal anesthesia in cesarean section..	Include
11.	(14).	Prevention of hypotension after spinal anesthesia in caesarean section- A prospective randomized comparative clinical study on ephedrine vs. norepinephrine	2024	54%	Norepinephrine 10 µg/mL intravenously compared with ephedrine 5 mg/mL intravenously for the prevention of spinal anesthesia-induced hypotension during cesarean section.	Exclude
12.	(15).	A Prospective Randomized Double Blind Comparative Study to Determine the Efficacy of Norepinephrine and Ephedrine to Maintain Arterial Blood Pressure During Spinal Anesthesia for Cesarean Delivery	2023	92%	Norepinephrine 6 µg as an intravenous bolus compared with ephedrine 10 mg as an intravenous bolus for the prophylaxis and treatment of spinal anesthesia-induced hypotension during cesarean section.	Include
13.	(16).	Norepinephrine versus ephedrine in hypotension during elective cesarean section and its relationship with neonatal acid-base balance	2025	69%	Norepinephrine 6 µg as an intravenous bolus compared with ephedrine 10 mg as an intravenous bolus for the management of spinal anesthesia-induced hypotension during cesarean section.	Exclude

RESULT

A total of 4,075 records were identified through database searches in PubMed, ScienceDirect, and Google Scholar. The initial search conducted on October 25, 2025 yielded 1,058 records from PubMed and 27 from ScienceDirect. A subsequent search on November 19, 2025 retrieved an additional 2,990 records from Google Scholar. Duplicate removal was performed using Mendeley, resulting in the exclusion of 27 duplicate records and leaving 4,048 articles for title and abstract screening. Of these, 4,035 studies were excluded due to alignment with the inclusion criteria, including discrepancies in

population, intervention, comparator, and study design. Consequently, 13 articles were selected for full-text assessment. Quality appraisal of the selected studies was conducted using the Joanna Briggs Institute (JBI) Critical Appraisal Tools. Four studies were excluded due to scores below 75%, indicating a moderate to high risk of bias that could affect the validity of the findings (Figure 1).

A total of 9 studies that met the inclusion criteria were subsequently extracted and analyzed. The data extraction process included information on study title, authors and publication year, country, study design,

sample size, and patient characteristics. In addition, data on the type of intervention and primary outcomes were collected. This study evaluated maternal hemodynamic status (blood pressure and heart rate), neonatal

outcomes (umbilical arterial pH and APGAR scores at one and five minutes), along with maternal adverse reactions, including nausea, vomiting, shivering, dizziness, and palpitations.

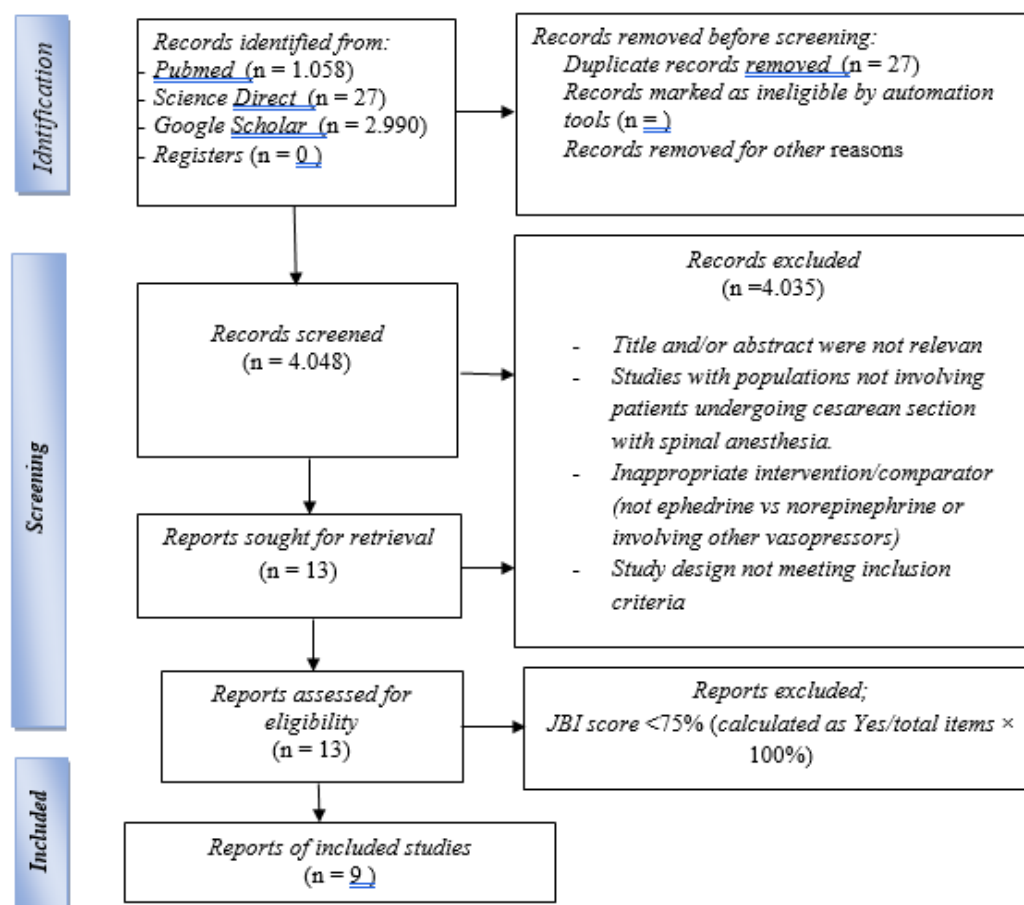


Figure 1. Skema PRISMA

Table 2. Data Extraction

Title / Authors/ Year/ Country	Study Design / Sample and Characteristics	Vasopressor Intervention Used	Main Outcomes
Norepinephrine versus Ephedrine to Maintain Arterial Blood Pressure during Spinal Anesthesia for Cesarean Delivery: A Prospective Double-blinded Trial. (17) Mesir	Study Design: Randomized Controlled Trial (RCT) Sample Size (n): 122 patients Age: Adults with term pregnancy Groups: Control group: Ephedrine (n = 61); Intervention group: Norepinephrine (n = 61) ASA Physical Status: I-II	Norepinephrine 5 µg IV bolus vs ephedrine 10 mg IV bolus.	Maternal Hemodynamics: - Lower incidence of hypotension and tachycardia was observed in the norepinephrine group. Neonatal Outcomes : - No significant differences were found in APGAR scores at one and five minutes or in umbilical arterial pH between the groups. Maternal Outcomes : - Both vasopressors were considered safe.
Norepinephrine versus ephedrine for hypotension prophylaxis during	Study Design: Randomized Controlled Trial (RCT) Sample Size (n): 120 patients Age: 21–35 years	Ephedrine 10 mg intravenous bolus versus norepinephrine	Maternal Hemodynamics : - Mean arterial pressure (MAP) was higher in the norepinephrine group.

Title / Authors/ Year/ Country	Study Design / Sample and Characteristics	Vasopressor Intervention Used	Main Outcomes
cesarean section under spinal anesthesia. (18). Mesir	Groups: Control group: Ephedrine (n = 60); Intervention group: Norepinephrine (n = 60) ASA Physical Status: I	16 µg intravenous bolus	- Tachycardia occurred more frequently in the ephedrine group. - The norepinephrine group required atropine more often due to episodes of bradycardia. Neonatal Outcomes : - No significant differences were observed in APGAR scores at one and five minutes between the groups. Maternal Outcomes: - The incidence of nausea and vomiting did not differ significantly between the groups.
A randomized double-blind study comparing prophylactic norepinephrine and ephedrine infusion for preventing maternal spinal hypotension during elective cesarean section under spinal anesthesia (Xu et al.,2019). China	Study Design: Randomized Controlled Trial (RCT) Sample Size (n): 97 patients Population: Adult pregnant women with term pregnancy Intervention group: Norepinephrine (n = 48); Control group: Ephedrine (n = 49) ASA Physical Status: I-II	Norepinephrine infusion 4 µg versus ephedrine 4 mg	Maternal Hemodynamics : - Better overall hemodynamic stability was observed in the norepinephrine group. - Lower incidence of tachycardia and more stable heart rate were noted with norepinephrine. - Systolic blood pressure (SBP) was more effectively controlled in the norepinephrine group. Neonatal Outcomes : - No significant differences were found in APGAR scores at one and five minutes between the groups. - Lower lactate levels and more favorable base excess values were observed in the norepinephrine group. Maternal Outcomes : - The incidence of nausea, vomiting, chest pain, and shivering did not differ significantly between the groups.
Comparison of the Effect of Intravenous Bolus Norepinephrine and Ephedrine on Prevention of Post Spinal Hypotension in Cesarean Section: A Randomized Double-Blind Clinical Trial (Manouchehrian et al., 2022). Iran	Study Design: Randomized Controlled Trial (RCT) Sample Size (n): 50 patients Age: 18–46 years Intervention group: Norepinephrine (n = 25); Control group: Ephedrine (n = 25) ASA Physical Status: I-II	Norepinephrine was administered as a 5 µg IV bolus, while ephedrine was given as a 10 mg IV bolus following spinal anesthesia	Maternal Hemodynamics: - No significant differences were observed in systolic blood pressure (SBP), diastolic blood pressure (DBP), or mean arterial pressure (MAP). - Heart rate was lower in the norepinephrine group. Neonatal Outcomes : - No significant differences were found in APGAR scores at one and five minutes between the groups. Maternal Outcome : - The incidence of nausea, vomiting, shivering, headache, and palpitations did not differ significantly between the groups.
Comparison of two vasopressor protocols for preventing hypotension post-spinal anesthesia during cesarean section: a randomized controlled trial (Q. Fan et al.,2021). China	Study Design: Randomized Controlled Trial (RCT) Sample Size (n): 177 patients Age: ≥ 18 years Intervention group: Norepinephrine (n = 88); Control group: Ephedrine (n = 89) ASA Physical Status: I-II	Continuous infusion of norepinephrine at 0.05 µg/kg/min versus ephedrine 0.15 mg/kg IV bolus, with a rescue dose of 5 mg administered in cases of hypotension	Maternal Hemodynamics : - The incidence of hypotension was significantly lower in the norepinephrine group compared to the ephedrine group. - The frequency of tachycardia was also significantly reduced in the norepinephrine group. Neonatal Outcomes : - No significant differences were observed in APGAR scores at one and five minutes between the norepinephrine and ephedrine groups. - Umbilical arterial blood gas analysis showed no significant differences between the groups.

Title / Authors/ Year/ Country	Study Design / Sample and Characteristics	Vasopressor Intervention Used	Main Outcomes
Effects of Norepinephrine-Ephedrine Combination on Maternal Hemodynamics in Cesarean Sections Performed Under Spinal Anesthesia. (Soyalp et al.,2025). Turki	Study Design: Randomized Controlled Trial (RCT) Sample Size (n): 90 patients Age: 18–45 years ASA Physical Status: I–II Ephedrine (n = 33) Ephedrine + Norepinephrine (n = 29) Norepinephrine (n = 28)	Ephedrine: 5 mg IV bolus Combination (EN): Ephedrine 5 mg + norepinephrine 2.5 µg IV Norepinephrine: 5 µg IV bolus	Maternal Outcomes : - The incidence of nausea and vomiting was lower in the norepinephrine group. Maternal Hemodynamics : - Systolic blood pressure (SBP) and mean arterial pressure (MAP) were relatively more stable in the ephedrine group. - Greater reductions in SBP and MAP were observed in the norepinephrine group. - No significant differences were found in heart rate among the groups Neonatal Outcomes : - APGAR scores at one and five minutes were lowest in the ephedrine group. - Higher APGAR scores were observed in the norepinephrine group. Maternal Outcomes : - No significant differences were observed in maternal complications among the groups.
Comparison of Norepinephrine and Ephedrine Boluses in the Control of Spinal Anesthesia-Induced Hypotension during Cesarean Section (Errifaiy et al.,2021). Maroko	Study Design: Randomized Controlled Trial (RCT) Sample Size (n): 80 patients Age: 18–40 years Groups: Control group: Ephedrine (n = 30); Intervention group: Norepinephrine (n = 50) ASA Physical Status: I–II	Norepinephrine 8 µg IV bolus (n = 50) versus ephedrine 3–6 mg IV bolus (n = 30)	Maternal Hemodynamic : - Blood pressure was more stable in the norepinephrine group. - A lower incidence of tachycardia was observed in the norepinephrine group. - The norepinephrine group required fewer vasopressor boluses and demonstrated a faster onset of action. Neonatal Outcomes : - No significant differences were found in APGAR scores at one and five minutes. Maternal Outcomes : - Both vasopressors were considered safe.
Comparison of Norepinephrine with Ephedrine Boluses for the Treatment of Maternal Hypotension during Cesarean Section Under Spinal Anesthesia: A Prospective Observational Study (Phogat & Kavishvar, 2023). India	Study Design: Comparative Clinical Study Sample Size (n): 160 patients Age: 18–36 years ASA Physical Status: I–III Control group: Ephedrine (n = 80) Intervention group: Norepinephrine (n = 80)	Norepinephrine 6 µg IV bolus versus ephedrine 6 mg IV bolus	Maternal Hemodynamics: - No significant differences were observed in systolic blood pressure (SBP). The incidence of tachycardia was higher in the ephedrine group. Neonatal Outcomes : - No significant differences were found in APGAR scores at one and five minutes between the groups. Maternal Outcomes : - Adverse effects, including nausea and vomiting, did not differ significantly between the groups.
A Prospective Randomized Double Blind Comparative Study to Determine the Efficacy of Norepinephrine and Ephedrine to Maintain Arterial Blood Pressure During Spinal Anesthesia for Cesarean Delivery (Sannaboraiah & Rajegowda, 2023). India	Study Design: Randomized Controlled Trial (RCT) Sample Size (n): 110 patients Age: 18–40 years Control group: Ephedrine (n = 55); Intervention group: Norepinephrine (n = 55) ASA Physical Status: I–II	Norepinephrine 6 µg IV bolus versus ephedrine 10 mg IV bolus	Maternal Hemodynamics : - Maternal blood pressure appeared more stable in the ephedrine group. - The incidence of tachycardia was higher in the ephedrine group. Bradycardia occurred more frequently in the norepinephrine group. - The norepinephrine group required a greater number of vasopressor boluses. Neonatal Outcomes: - No significant differences were observed in APGAR scores at one and five minutes. Maternal Outcomes : - Both vasopressors were considered safe.

Based on the analysis of 8 randomized controlled trials (RCTs) and 1 comparative clinical study involving a total of 1,006 patients aged 18–46 years with American Society of Anesthesiologists (ASA) physical status I–II, the majority of studies (55.6%) reported that norepinephrine was more effective in maintaining maternal hemodynamic stability. This effectiveness was reflected by a lower incidence of tachycardia and reduced placental transfer. Meanwhile, 22.2% of the studies found no significant difference between the ephedrine and norepinephrine groups. In contrast, another 22.2% of studies suggested that ephedrine demonstrated greater effectiveness in maintaining maternal hemodynamic parameters.

Most neonatal outcomes (88.9%), including APGAR scores at one and five minutes, showed no significant differences between the use of ephedrine and norepinephrine. However, 11.1% of the studies reported that the norepinephrine group demonstrated lower APGAR scores and lactate levels, along with more favorable base excess values.

Regarding maternal outcomes, such as nausea, vomiting, shivering, dizziness, and palpitations, the majority of studies (88.9%) also found no significant differences between the two groups. Nevertheless, approximately 11.1% of the studies indicated a lower incidence of nausea and vomiting in the norepinephrine group.

Overall, norepinephrine was considered more effective in maintaining maternal hemodynamic stability. In addition, its use tended to be associated with more favorable neonatal and maternal outcomes compared to ephedrine.

DISCUSSION

The analysis comparing the effectiveness of ephedrine and norepinephrine in patients undergoing cesarean section under spinal anesthesia indicated that the majority of studies (55.6%) identified norepinephrine as a more effective agent for maintaining maternal hemodynamic stability. These findings are consistent with

several previous studies, including those by Elnabtity & Selim, (2018), Elagamy et al., (2021), Xu et al., (2019), Q. Fan et al., (2021), and Errifaïy et al., (2021), which reported that norepinephrine provides more stable blood pressure control with a lower incidence of tachycardia compared to ephedrine (9,12,18,19,22). In contrast, a smaller proportion of studies (22.2%), such as those conducted by Soyalp et al., (2025) and Sannaboraiah & Rajegowda, (2023) suggested that ephedrine may be more effective in maintaining maternal hemodynamic stability (15,24). Additionally, approximately 22.2% of studies reported no significant difference between the two agents, as observed in studies by Manouchehrian et al., (2022) and (Phogat & Kavishvar, (2023) (13,25).

These variations in findings may be explained by the pharmacological mechanisms of each vasopressor. Ephedrine acts on both α - and β -adrenergic receptors. Activation of α -receptors induces peripheral vasoconstriction, thereby increasing maternal blood pressure, while β -receptor stimulation enhances heart rate, contributing to a higher incidence of tachycardia in the ephedrine group (26). In contrast, norepinephrine primarily acts on α -adrenergic receptors, with relatively minimal β -adrenergic effects. This leads to peripheral vasoconstriction that increases blood pressure with only a modest increase in heart rate, which is less pronounced compared to the effects of ephedrine (27). However, the findings should be interpreted with consideration of the heterogeneity among the included studies. Differences in norepinephrine and ephedrine doses, bolus or infusion administration, dosing regimens, and study designs may have contributed to variations in the observed maternal hemodynamic outcomes. Therefore, the greater proportion of studies favoring norepinephrine should not be interpreted as evidence of universal superiority, but rather as an indication of a potential advantage under the specific conditions evaluated in the included studies.

The use of ephedrine and norepinephrine for the management of hypotension in patients undergoing cesarean

section under spinal anesthesia showed that most studies (88.9%) reported no significant differences in neonatal outcomes. These findings are consistent with previous studies, including those by Elnabtity & Selim, (2018), Elagamy et al., (2021), Xu et al., (2019), Manouchehrian et al., (2022), Errifaiy et al., (2021), Q. Fan et al., (2021), Phogat & Kavishvar, (2023), and Sannaboraiah & Rajegowda, (2023), all of which reported no significant differences in APGAR scores at one and five minutes or in umbilical arterial pH (9,12,13,15,18,19,22,25). However, a small proportion of studies (11.1%) reported different findings. A study by Soyalp et al., (2025) demonstrated that APGAR scores at one and five minutes were lower in the ephedrine group (24). In addition, Xu et al., (2019) found that, although no significant differences were observed in APGAR scores, the norepinephrine group showed lower lactate levels and more favorable base excess values (22).

These differences in neonatal outcomes may be explained by the pharmacological properties of each vasopressor. Ephedrine is lipophilic, allowing greater placental transfer, which may influence neonatal parameters such as APGAR scores and umbilical arterial pH (28). In contrast, norepinephrine is more hydrophilic and has limited placental transfer, resulting in minimal fetal exposure (29). The interpretation of neonatal outcomes should also consider the variability in vasopressor dosing and administration methods across studies. Although most studies reported comparable neonatal outcomes, these methodological differences may have influenced the magnitude of the observed effects. Thus, the absence of significant differences in most studies should be interpreted cautiously and should not be generalized to all dosing regimens or clinical settings.

Regarding maternal outcomes, the majority of studies (88.9%) indicated no significant differences between the use of ephedrine and norepinephrine. These findings are consistent with previous studies, including those by Elnabtity & Selim, (2018),

Elagamy et al., (2021), Xu et al., (2019), Manouchehrian et al., (2022), Errifaiy et al., (2021), Soyalp et al., (2025), Phogat & Kavishvar, (2023), as well as Sannaboraiah & Rajegowda, (2023) all of which reported that both vasopressors are relatively safe and do not differ significantly in the incidence of nausea, vomiting, shivering, dizziness, or palpitations (18,19,22,25), (12,13,15,24). However, a smaller proportion of studies (11.1%), such as Q. Fan et al., (2021), reported a lower incidence of nausea and vomiting in the norepinephrine group (9). This finding may be attributed to the ability of norepinephrine to maintain more stable blood pressure, thereby preserving uteroplacental perfusion and gastrointestinal function (14).

These findings support the potential use of norepinephrine in the development of clinical protocols, particularly in settings with adequate monitoring, as an alternative to ephedrine in obstetric anesthesia. Nevertheless, further studies are required to determine the optimal dosing strategy, evaluate safety across broader populations, and assess long-term outcomes.

This study has several limitations, including the relatively small number of included studies ($n = 9$) and the use of specific inclusion criteria, which may limit the breadth of the literature analyzed. In addition, heterogeneity across studies in terms of design, dosing regimens, and methods of vasopressor administration may have influenced the consistency of the findings.

Despite these limitations, the present review provides evidence that norepinephrine has considerable potential as an effective and safe vasopressor for the management of hypotension during cesarean section under spinal anesthesia. This is reflected in its tendency to provide better maternal hemodynamic stability without a worse adverse effect profile compared to ephedrine. These findings may serve as a foundation for the development of clinical protocols and the advancement of evidence-based obstetric anesthesia practice.

CONCLUSION

Based on the analysis of 8 randomized controlled trials (RCTs) and 1 comparative clinical study, norepinephrine showed a tendency toward better maternal hemodynamic stability and lower incidence of tachycardia than ephedrine in several included studies. It provides better maternal hemodynamic stability with a lower incidence of tachycardia and reduced placental transfer, which may contribute to more stable neonatal outcomes. Although ephedrine remains effective in increasing maternal blood pressure, its use is more frequently associated with increased heart rate and greater placental transfer. Overall, norepinephrine can be considered a suitable and effective vasopressor option for managing hypotension in this clinical setting.

REFERENCES

1. Wahabi H, Fayed A, Elmorshedy H, Esmaeil SA, Amer YS, Saeed E, et al. Prediction of Emergency Cesarean Section Using Detectable Maternal and Fetal Characteristics Among Saudi Women. *International Journal of Women's Health*. 2023;15(August):1283–93. doi:10.2147/IJWH.S414380
2. Angolile CM, Max BL, Mushemba J, Mashauri HL. Global increased cesarean section rates and public health implications: A call to action. *Health Science Reports*. 2023;6(5):1–5. doi:10.1002/hsr2.1274
3. Algarni RA, Albakri HY, Albakri LA, Alsharif RM, Alrajhi RK, Makki RM, et al. Incidence and Risk Factors of Spinal Anesthesia-Related Complications After an Elective Cesarean Section: A Retrospective Cohort Study. *Cureus*. 2023;15(1). doi:10.7759/cureus.34198
4. Sung TY, Jee YS, You HJ, Cho CK. Comparison of the effect of general and spinal anesthesia for elective cesarean section on maternal and fetal outcomes: a retrospective cohort study. *Anesthesia and Pain Medicine*. 2021;16(1):49–55. doi:10.17085/apm.20072
5. Supboon S. Incidence and Factors of Spinal Anesthesia induced Hypotension in Cesarean Section at Phra Nakhon Si Ayutthaya Hospital. 2023;99–111.
6. Liu S, Luo S, Jiang R, Su S, Zhao M. Left-lateral position versus phenylephrine prophylactic treatment for hypotension following combined spinal epidural anesthesia during elective cesarean section. *Heliyon*. 2024;10(9):e30019. doi:https://doi.org/10.1016/j.heliyon.2024.e30019
7. Thuong ND, Thi N, Mai T, Nguyen C, Minh N, Minh NT, et al. The study of maternal spinal anesthesia-induced hypotension during Cesarean section at Tu Du Maternal Hospital, Vietnam - the incidence and related risks. Vol. 6. 2025;6(1):719–31.
8. Shihab MM, Mohammed AA. The effect of preload crystalloid and colloid solutions on maternal haemodynamic state in elective cesarean section under spinal anaesthesia. *International Journal of Anesthesiology Sciences*. 2024;6(1):16–20. doi:10.33545/26649268.2024.v6.i1a.22
9. Fan Q, Wang YH, Fu JW, Dong HL, Yang MP, Liu DD, et al. Comparison of two vasopressor protocols for preventing hypotension post-spinal anesthesia during cesarean section: A randomized controlled trial. *Chinese Medical Journal*. 2021;134(7):792–9. doi:10.1097/CM9.0000000000001404 PubMed PMID: 33661141.

10. Liu J, Sheng Z, Guo F, Lin X, Xu L, Sun L, et al. Norepinephrine or Phenylephrine to Prevent Spinal Anesthesia-Induced Hypotension During Cesarean Section: A Double-Blinded, Randomized, Controlled Study of Fetal Cerebral Perfusion. Drug design, development and therapy. 2025;19:7571–80. doi:10.2147/DDDT.S535671
11. Ganeshnavar AS, Endigeri A, Kumar P, Chitti R. Comparison of Efficacy of Bolus Dosages of Norepinephrine , Phenylephrine , and Ephedrine in Treating Post-Spinal Hypotension During Elective Cesarean Section : A Randomized Double-Blinded Controlled Trial. Journal of Anaesthesia and Pain. 2024;(3):70–5. doi:10.21776/ub.jap.2024.005.03.04
12. Errifaiy H, Tajlejiti N, Ouzlim N, Ribahi H, Adib AG El. Comparison of Norepinephrine and Ephedrine Boluses in the Control of Spinal Anesthesia-Induced Hypotension during Cesarean Section: A Randomized Controlled Trial. SAS Journal of Medicine. 2021;7(11):627–31. doi:10.36347/sasjm.2021.v07i11.009
13. Phogat A, Kavishvar N. Comparison of Norepinephrine with Ephedrine Boluses for the Treatment of Maternal Hypotension during Cesarean Section Under Spinal Anesthesia: A Prospective Observational Study. Journal of Obstetric Anaesthesia and Critical Care. 2023;13(2):198–203. doi:10.4103/JOACC.JOACC_16_23
14. Hasan SR, Ibrahim A, Talib Razq M, Fawzi HA. Prevention of hypotension after spinal anesthesia in cesarean section – A prospective randomized comparative clinical study on ephedrine vs. norepinephrine. Ginekologia i Poloznictwo. 2024;19(1):9–13. doi:10.54615/2231-7805.105480
15. Sannaboraiah SK, Rajegowda S. A Prospective Randomized Double Blind Comparative Study to Determine the Efficacy of Norepinephrine and Ephedrine to Maintain Arterial Blood Pressure During Spinal Anesthesia for Cesarean Delivery. Archives of Anesthesiology and Critical Care. 2023;9(Autumn):522–9. doi:10.18502/aacc.v9i6.14450
16. Ayala JS, Millán-Cornejo GA, Palacios-Ríos D, López-Cabrera NG. Norepinephrine versus ephedrine in hypotension during elective cesarean section and its relationship with neonatal acid-base balance. Revista Medicina Universitaria. 2025;27(4):137–42. doi:10.24875/rmu.25000006
17. Elnabtity AA, Selim M. Norepinephrine versus ephedrine to maintain arterial blood pressure during spinal anesthesia for cesarean delivery: A prospective double-blinded trial. Anesthesia: Essays and Researches. 2018;12(1):92. doi:10.4103/aer.aer_204_17
18. Elagamy AE, Kamaly AM, Shahin MI, Saleh M. Norepinephrine versus ephedrine for hypotension prophylaxis during cesarean section under spinal anesthesia. Ain-Shams Journal of Anesthesiology. 2021;13(1). doi:10.1186/s42077-020-00124-4
19. Elnabtity AA, Selim M. Norepinephrine versus ephedrine to maintain arterial blood pressure during spinal anesthesia for cesarean delivery: A prospective double-blinded trial. Anesthesia: Essays and Researches. 2018;12(1):92. doi:10.4103/aer.aer_204_17

20. Xu S, Mao M, Zhang S, Qian R, Shen X, Shen J, et al. A randomized double-blind study comparing prophylactic norepinephrine and ephedrine infusion for preventing maternal spinal hypotension during elective cesarean section under spinal anesthesia: A CONSORT-compliant article. *Medicine*. 2019;98(51):e18311. doi:10.1097/MD.00000000000018311
21. Fan QQ, Wang YH, Fu JW, Dong HL, Yang MP, Liu DD, et al. Comparison of two vasopressor protocols for preventing hypotension post-spinal anesthesia during cesarean section: a randomized controlled trial. *Chinese medical journal*. 2021;134(7):792–9. doi:10.1097/CM9.0000000000001404
22. Xu S, Mao M, Zhang S, Qian R, Shen X, Shen J, et al. A randomized double-blind study comparing prophylactic norepinephrine and ephedrine infusion for preventing maternal spinal hypotension during elective cesarean section under spinal anesthesia: A CONSORT-compliant article. *Medicine*. 2019;98(51):e18311.
23. Soyalp C, Yuzkat N, Kurt N, Gülhaş N. Effects of Norepinephrine-Ephedrine Combination on Maternal Hemodynamics in Cesarean Sections Performed Under Spinal Anesthesia. *Trends in Surgical Sciences*. 2025;4(1):1–10. doi:10.61745/tss.1671431
24. Soyalp C, Yuzkat N, Kurt N, Gülhaş N. Effects of Norepinephrine-Ephedrine Combination on Maternal Hemodynamics in Cesarean Sections Performed Under Spinal Anesthesia. *Trends in Surgical Sciences*. 2025;4(1):1–10. doi:10.61745/tss.1671431
25. Manouchehrian N, Jeyriaee N, Hoseini S. Comparison of the Effect of Intravenous Bolus Norepinephrine and Ephedrine on Prevention of Post Spinal Hypotension in Cesarean Section: a Randomized Double-Blind Clinical Trial. *Maedica - A Journal of Clinical Medicine*. 2022;17(4):833–9. doi:10.26574/maedica.2022.17.4.833 PubMed PMID: 36818262.
26. Rebello CJ, Greenway FL, Zhang D, Johnson WD, Patterson E, Raum W. Sympathomimetic increases resting energy expenditure following bariatric surgery: A randomized controlled clinical trial. *Obesity*. 2022;30(4):874–83. doi:10.1002/oby.23384 PubMed PMID: 35244344.
27. Yu C, Garcia-Olivares J, Candler S, Schwabe S, Maletic V. New insights into the mechanism of action of viloxazine: Serotonin and norepinephrine modulating properties. *Journal of Experimental Pharmacology*. 2020;12:285–300. doi:10.2147/JEP.S256586
28. Abulifa F, Garta I, Danfour O. Impact of Intravenous Bolus Norepinephrine versus Ephedrine on Post-Spinal Hypotension during Cesarean Section in Libyan Patients. *Khalij-Libya Journal of Dental and Medical Research*. 2025;9(2):312–7. doi:10.47705/kjdmr.259226
29. Horackova H, Karahoda R, Vachalova V, Turkova H, Abad C, Staud F. Functional characterization of dopamine and norepinephrine transport across the apical and basal plasma membranes of the human placental syncytiotrophoblast. *Scientific Reports*. 2022;12(1):1–12. doi:10.1038/s41598-022-15790-7 PubMed PMID: 35804076.