

Comparison of hemodynamic effects of subarachnoid blockade in preeclamptic and normotensive healthy parturients undergoing caesarean section

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Abstract

Background: Pre-eclampsia is a multisystem disorder of unknown etiology that is exclusive to human pregnancy. Caesarean section is one of the most commonly performed surgical procedures worldwide and 80–90% of them are performed under spinal anaesthesia. Present study was planned to evaluate hemodynamic effects of regional anaesthesia in preeclamptic females. **Material and Methods:** Present study was hospital based single center longitudinal observational study, conducted parturients aged 18-45 years posted for elective /emergency caesarean section (ASA grade II and III), Parturients diagnosed with preeclampsia. **Results:** Study population comprised of 44 normotensive ASA grade II parturients planned for LSCS and 44 ASA grade III preeclamptic parturients planned for LSCS. Both groups were comparable in term of mean age, weight, gestational age and parity comparison ($p < 0.05$). All the non-preeclamptic parturients were ASA II while, All parturients in the preeclamptic group were ASA III, and this difference was statistically significant between both groups; ($p < 0.001$). We observed that heart rate, Systolic Blood Pressure, diastolic Blood Pressure, mean arterial Pressure was significantly higher in pre-eclamptic group at all point of time compare to normotensive group ($p < 0.01$). No significant difference was observed between both groups for SpO₂. The incidence of hypotension in non-preeclamptic parturients (93.2%) was significantly higher and that of preeclamptic parturients (13.7%). Bradycardia was also more commonly observed in normotensive group (29.5%) compared to pre-eclamptic group (2.3%). Need of mepehentermine was also significantly higher in normotensive women (9.27 ± 4.18 mg) compare to pre-eclamptic group (1.36 ± 3.39 mg). (p value < 0.001) No statistically significant difference was noted for neonatal weight and APGAR score between two groups ($p > 0.05$). **Conclusion:** Subarachnoid blockade is associated with better perioperative hemodynamic stability and lower risk of hypotension and vasopressor requirements in preeclamptic women compared to the rates of healthy subjects. **Keywords:** Subarachnoid blockade, preeclampsia, caesarean section, hemodynamic stability.

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INTRODUCTION

Pre-eclampsia is a multisystem disorder of unknown etiology that is exclusive to human pregnancy. It is characterized by abnormal vascular response to placentation that is associated with increased systemic vascular resistance, enhanced platelet aggregation, activation of the coagulation system, and endothelial cell dysfunction.¹ Pregnancy-induced hypertension (PIH) complicates around 6–8% of pregnancies. It is a multiorgan disease and is classified as mild PIH or severe PIH.² Worldwide preeclampsia/eclampsia is the third leading cause of maternal morbidity and mortality.³ Caesarean

section is one of the most commonly performed surgical procedures worldwide and 80–90% of them are performed under spinal anaesthesia.⁴ During the procedures, maternal hypotension is a major complication with the incidence up to 60–70%. During obstetric anaesthesia, preservation of hemodynamic stability is a big concern for anaesthetists⁴, especially for preeclamptic parturients who planned to undergo caesarean section.^{4,5} However, spinal anaesthesia-induced maternal hypotension is still the most frequent complication.^{6,7} Because of the risks related to airway oedema, difficulty with the airway or failed intubation, hypertensive response to direct laryngoscopy and aspiration pneumonitis; general anaesthesia is associated with more untoward outcomes in this particular group of patients.^{8,9} Less morbidity and mortality, less failure, dense anaesthesia, easy technique, provision of adequate operating conditions in a shorter time and several other advantages have placed neuraxial anaesthesia particularly subarachnoid block as a more preferable mode of anaesthesia for elective caesarean section to epidural block or general anaesthesia.¹⁰ There is quest for optimal regional block technique has gained traction in India and there is lack of studies evaluating effect of subarachnoid block in preeclamptic parturients in Indian population. Therefore, this prospective study was planned to evaluate hemodynamic effects of regional anaesthesia in preeclamptic females.

MATERIAL AND METHODS

Present study was hospital based single center longitudinal observational study, conducted in department of Anaesthesiology with help of Department of OBGY, Vilasrao Deshmukh Government Medical College, Latur, India. Study duration was of 18 months (January 2020 to June 2021). Study was approved by institutional ethical committee.

Inclusion criteria: Parturients aged 18-45 years posted for elective /emergency caesarean section (ASA grade II and III), Parturients diagnosed with preeclampsia having Systolic blood pressure of 140 mm Hg or more or diastolic blood pressure of 90 mm Hg or more on two occasions at least 4 hours apart after 20 weeks of gestation in a woman with a previously normal blood pressure.¹

Exclusion criteria: Patients with severe preeclampsia and eclampsia, multiple pregnancies, Gestational diabetes mellitus, Thrombocytopenia (platelets < 100,000 mm³), requiring tocolytics. Evidence of liver dysfunction (LFTs > 2x ULN), Pre-existing renal disease. Patients with spinal deformity, contraindication to subarachnoid block, known sensitivity to the study drugs. Patient with chronic hypertension, with pre-existing cardiovascular conditions, on anticoagulant therapy. Patient with abruptio placentae/placenta previa/twin pregnancy/severe fetal

distress. Those not willing to give consent for the participation in the study

Purpose of the study was explained to the study subjects planned for LSCS during pre-operative examination in the local language and a written informed consent was taken for participation. All the preeclamptic patients were treated with a 4.0 g loading dose of intravenous magnesium sulphate (MgSO₄), followed by an -1.5 g/h infusion for 48 hours as seizure prophylaxis. Labetalol or Methyl-dopa and nifedipine or both were given for blood pressure control, but this antihypertensive protocol was not standardised and was left to the choice of the obstetrician or anesthesiologist. Mg therapy was discontinued just before the operation; antihypertensive drugs were excluded for at least 4 h before spinal puncture. The study population comprised of two groups as :

Group A: Normotensive ASA grade II parturients planned for LSCS

Group B: ASA grade III preeclamptic parturients planned for LSCS.

Patients received oral ranitidine (150 mg) and oral metoclopramide (10 mg) at the morning of the surgery. After receiving the patient in the operating room, documents were checked, a brief clinical examination was done and standard ASA monitors were attached including ECG, pulse oxymetry and temperature probe. A radial arterial line was established with a 20 G radial arterial cannula and invasive blood pressure was monitored. After establishing IV access with a 20 G IV cannula in one of the upper limbs, 20 ml/kg lactated ringer solution (RL) was administered for preloading over the course of 15 - 20 minutes. After proper aseptic precaution spinal subarachnoid block (SAB) was performed by an anesthesiologist blinded to the study in the sitting position, at L2- L3 or L3-L4 intervertebral space through a midline approach by a 26 G Quincke type spinal needle and 2 ml or 8-12 mg of 0.5% hyperbaric bupivacaine (at the discretion of anaesthetist) was administered after confirming needle location and noting free flow of clear CSF.

Surgery was allowed after adequate sensory (T4) and motor block was confirmed. The change in position if required was then allowed. HR, SBP, DBP and MAP were recorded at baseline, immediately after SAB and at 2 min, 5 min, 10 min, 15 min, 20 min, 30 min, 45 min, 60 min, 90 min intervals until the end of the surgery. The duration of surgery, dose of mephentermine consumed in each patient were noted. Separate anaesthesiologists performed the procedure and collected the data and both were unaware of the nature of the study. The data was labelled as group A for normotensives and group B for preeclamptic. Variables like age, height, BMI, ASA status, gestational age, and amount of fluid preloaded, amount of fluid consumed intraoperatively, the weight of the neonate, upper sensory

level of the spinal block at the time of skin incision, position during and after the spinal procedure were also documented. Data was collected by using a structure proforma. Data thus was entered in MS excel sheet and analysed by using SPSS 24.0 version IBM USA. Qualitative data was expressed in terms of percentages and proportions. Quantitative data was expressed in terms of Mean and Standard deviation. Comparison of mean and SD between two groups will be done by using unpaired t test to assess whether the mean difference between groups is significant or not descriptive statistics of each variable was presented in terms of Mean, standard deviation, standard error of mean. A p value of <0.05 was considered as statistically significant.

RESULTS

Study population comprised of 44 normotensive ASA grade II parturients planned for LSCS and 44 ASA grade

III preeclamptic parturients planned for LSCS. Mean age in normotensive group was 23.41 ± 3.35 years and in pre-eclamptic group mean age was 22.18 ± 3.03 years. The mean weight at the time of caesarean section was 70.2 ± 6.25 kgs in the preeclamptic group and 72.64 ± 7.48 kgs in preeclamptic. The mean gestational age at the time of caesarean section was 39.09 ± 0.74 weeks in preeclamptic women and 39.22 ± 0.56 weeks in normotensive. Majority of the study participants were nulliparous women in both the group (52.3% in normotensive group v/s 65.9% in pre-eclamptic group) while nearly 45.5% of the participants in the normotensive group and 29.5% in pre-eclamptic group were primipara. Both groups were comparable in term of mean age, weight, gestational age and parity comparison ($p < 0.05$). All the non-preeclamptic parturients were ASA II while, All parturients in the preeclamptic group were ASA III, and this difference was statistically significant between both groups; ($p < 0.001$).

Table 1: General characteristics of study subjects

Characteristics	Group A (Normotensive group) (n=44)	Group B (Pre-eclamptic group) n=44	P value
Mean age (in years)	23.41±3.35	22.18±3.03	0.07
Weight (kgs)	70.2±6.25	72.64±7.48	0.37
Mean gestational age (weeks)	39.22±0.56	39.09±0.74	0.33
Parity			
P0	23 (52.3 %)	29 (65.9 %)	
P1	20 (45.5 %)	13 (29.5 %)	
P2	1 (2.3 %)	2 (4.5 %)	
ASA grade			
II	44 (100.0 %)	0	
III		44 (100.0 %)	

We observed that heart rate, Systolic Blood Pressure, diastolic Blood Pressure, mean arterial Pressure was significantly higher in pre-eclamptic group at all point of time compare to normotensive group ($p < 0.01$). No significant difference was observed between both groups for SpO₂. The incidence of hypotension in non-preeclamptic parturients (93.2%) was significantly higher and that of preeclamptic parturients (13.7%). Similarly, bradycardia was also more commonly observed in normotensive group (29.5%) compared to pre-eclamptic group (2.3%).

Table 2: Incidence of hypotension and bradycardia following spinal anaesthesia

	Group A (Normotensive group) n=44	Group B (Pre-eclamptic group) n=44	P value
Incidence of hypotension	41 (93.2%)	8 (13.7%)	<0.001
Incidence of bradycardia	13 (29.5%)	1 (2.3%)	<0.001

Mean lowest SBP, DBP and MAP measured among the preeclamptic patients were consistently higher (129.68 ± 6.55 mm Hg, 83.14 ± 6.01 mm Hg and 98.65 ± 5.66 mm Hg respectively) than the corresponding values among the healthy parturients (92.68 ± 4.52 mm Hg, 54.45 ± 6.25 mm Hg and 67.19 ± 5.26 mm Hg respectively).

Table 3: Magnitude of hemodynamic changes following spinal anaesthesia

	Group A (Normotensive group) n=44	Group B (Pre-eclamptic group) n=44	P value
Lowest SBP (mm Hg)	92.68±4.52	129.68±6.55	<0.001
Lowest DBP (mm Hg)	54.45±6.25	83.14±6.01	<0.001
Lowest MAP (mm Hg)	67.19±5.26	98.65±5.66	<0.001

Need of mepehentermine was also significantly higher in normotensive women (9.27±4.18 mg) compare to pre-eclamptic group (1.36±3.39 mg). (p value <0.001) Mean duration of procedure in both normotensive group (59.66±8.24 min) and pre-eclamptic group (59.32±6.43 min) was comparable between both groups.

Table 4: Total dose of mepehentermine used (mg)

Total dose of mepehentermine used (mg)	Group A (Normotensive group) n=44	Group B (Pre-eclamptic group) n=44	P value
Dose of mepehentermine (mg)	9.27±4.18	1.36±3.39	<0.001
Duration of procedure (minutes)	59.66±8.24	59.32±6.43	0.82

Mean neonatal weight in normotensive group was 2818.18±265.25 gms and in pre-eclamptic group was 2830.68±383.10 gms. APGAR score at 1 minute was 7.98±0.45 in normotensive and 7.91±0.42 in pre-eclamptic group. APGAR score at 5 minutes was 9.05±0.37 in normotensive and 8.98±0.40 in pre-eclamptic group. No statistically significant difference was noted for neonatal weight and APGAR score between two groups (p>0.05).

Table 5: Comparison of neonatal parameters between both groups

	Group A (Normotensive group) n=44	Group B (Pre-eclamptic group) n=44	P value
Neonatal weight (gms)	2818.18±265.25	2830.68±383.10	0.85
APGAR score at 1 minute	7.98±0.45	7.91±0.42	0.46
APGAR score at 5 minute	9.05±0.37	8.98±0.40	0.41

DISCUSSION

Ubiquitous belief that subarachnoid block in patients with severe preeclampsia causes severe hypotension and decreased uteroplacental perfusion precluded the frequent use of this technique of regional block. However, evidence suggest that parturients with severe preeclampsia experience less frequent, less severe hypotension than normotensive parturients. Among patients with severe preeclampsia, spinal anaesthesia may cause a greater degree of hypotension than epidural anaesthesia; however, this hypotension is easily manageable and short lived and no studies have demonstrated clinically significant differences in outcomes when spinal anaesthesia is compared with epidural or general anaesthesia.^{11,12} Anaesthetists denied spinal anaesthesia for preeclamptic parturients due to the fear of profound hypotension and its management crisis (exaggerated response to vasopressor treatment and pulmonary edema following fluid challenges).⁴ Furthermore, the incidence of spinal anesthesia-induced maternal hypotension showed inconsistency across different studies, which makes it almost difficult to set standard targets and develop a local management protocol.^{6,7} A study had shown that fluid loading and vasopressor prophylaxis were effective in reducing the incidence of spinal anesthesia-induced hypotension in healthy parturients.¹³ But these pre-emptive measures could put the preeclamptic patients at increased risk of hypertension and pulmonary edema.² Due to inconsistent definition, the reported incidence of spinal anesthesia-induced maternal hypotension varies between 7 and 89.2%.^{5,14} Therefore, anaesthetic management for preeclamptic parturients who undergo caesarean section is challenging for anaesthetists.⁵ Alemayehu TY *et al.*,¹⁵ carried-out study and total of 122 parturients were enrolled

(81 non-preeclamptic and 41 preeclamptic parturients) in this study. The mean gestational age at the time of caesarean section was significantly lower in the preeclamptic group: 38.56±1.63 weeks in non-preeclamptic versus 37.44±1.25 weeks in preeclamptic (p=0.001). Nikooseresht M. *et al.*,¹⁶ in their study reported mean age in normotensive group was 28.1±5 years and in pre-eclamptic group mean age was 29.3±6.6 years (p>0.05). Though the age group was higher as compared to our findings, but there was no difference in the mean age which is again consistent with our findings. Nikooseresht M. *et al.*,¹⁶ in their study reported the mean gestational age at the time of caesarean section was 34.3± 3.8 weeks in preeclamptic women and 38.8±1.2 weeks in normotensive. The difference was statistically significant stating that both the groups are not comparable (p<0.05) which is in contrast with our findings. Alemayehu TY *et al.*,¹⁵ observed that MAP was significantly higher in pre-eclamptic group at all point of time compare to normotensive group (p<0.01) which is consistent with our study findings. Nikooseresht M. *et al.*,¹⁶ in their study reported that baseline MAP (pre-op) as 101.1±10.1 vs 119.5±15.9 mmHg in normotensive and preeclamptic respectively (P<0.05), lowest MAP was 64.9±10.1 vs 83.7±14.9 mmHg in normotensive and preeclamptic respectively (P<0.05). The findings are consistent with our study findings. Sivevski A *et al.*,¹⁴ reported that there was decreased BP after the spinal block in both groups, but the BP falls were significantly greater in the healthy parturients compared to those with preeclampsia: 31.2 ± 14.2 vs 18.2 ± 12.6% for MAP (p < 0.05). In the preeclamptic patients, SBP and DBP were consistently higher than the corresponding values among the healthy parturients, and the same trend was happening to MAP, which was at a constantly higher level in

preeclamptic. In our study, the incidence of hypotension in non-preeclamptic parturients (93.2%) was significantly higher than that of preeclamptic parturients (13.7%). Similarly, bradycardia was also more commonly observed in normotensive group (29.5%) compared to pre-eclamptic group (2.3%). Similar to our study Aya AG *et al.*,¹⁷ found that severely preeclamptic patients had a less frequent incidence of clinically significant hypotension compared to healthy parturients (16.6% versus 53.3%; $P=0.006$). The incidence of hypotension among preeclamptic parturients in our study was higher than Aya AG *et al.*,¹⁷ result. The likely reason may be the use of different criteria for defining hypotension (20% versus 30% decline to baseline MAP) and the use of the small volume of preload in our study participants compared to Aya AG *et al.* (565.38 ml \pm 318.4 vs 1653 ml \pm 331). In contradict to our result, Mendes *et al.*,¹⁸ found that there was no statistically significant difference regarding the occurrence of hypotension after spinal anesthesia between severely preeclamptic and healthy parturients. But the incidence rate of hypotension was high in both groups (84 and 70%, $p=0.45$). This difference may be due to the intraoperative administration of intravenous hydralazine in preeclamptic parturients in their study. Unlike our study, Mendes *et al.*,¹⁸ found that there was no significant difference in the lowest mean drop of SBP and DBP after spinal anesthesia between preeclamptic and healthy parturients. This difference may be due to standardized fluid management and administration of potent direct vasodilator during surgery (intravenous hydralazine) in preeclamptic parturients in their study. In this study, a decreasing dose of 0.5% bupivacaine was practiced for the caesarean section. However, the incidence of hemodynamic change had not a significant difference (10 mg versus 12.5 mg). Preeclamptic pregnancy ends with less gestational maturity carrying lower birth weight neonates (smaller uterine size) compared to a healthy pregnancy. Hence the risk of aortocaval obstruction is lower. For the same reasons, the epidural venous plexuses in preeclamptics are less exaggerated, thus leading to a lower cephalic spread of the local anaesthetic. Aya G *et al.*,¹⁷ suggested that the risk of hypotension following a subarachnoid block in preeclampsia was related to other preeclampsia-associated factors rather than to a small uterine size. The vasodilator system in preeclampsia (regulated by the endothelial pathway via endothelial-dependent relaxation of small resistant vessels) has an altered response-thus maintaining a high vascular tone on a constantly higher level, independent of spinal-induced sympathetic blockade, keeping the BP high.¹⁴ Need of vasopressor (mephentermine) was also significantly higher in normotensive women (9.27 \pm 4.18 mg) compared to preeclamptic group (1.36 \pm 3.39 mg). (p value <0.001). The

vasopressor (ephedrine) requirement for treatment of spinal-induced hypotension in preeclampsia has been reported to be lower than that required by healthy parturients.^{19,20} Preeclamptics have also been reported to require significantly less phenylephrine to treat hypotension. These results were comparable to our findings in that the total doses of IV vasopressor (mephentermine) for treating hypotension were significantly lower for the preeclamptics (6.0 \pm 2.0 mg) than for the healthy patients (16.5 \pm 8, 6 mg, $p<0.05$).²¹ Abate SM *et al.*,²² conducted the meta-analysis which revealed that the vasopressor requirement was higher in normotensive women when compared to preeclamptic counterparts who are in line with all included studies except one study by Mendes *et al.*,¹⁸ where the requirement of ephedrine dose requirement didn't show a significant difference between normotensive and preeclamptic women. Other studies in support of subarachnoid block have also shown that transient neonatal depression and birth asphyxia are more common among preeclamptic women who have received general anesthesia.²³ Abate SM *et al.*,²² conducted the meta-analysis which revealed that the first APGAR score was better in normotensive women as compared to preeclamptic women which were in line with prospective cohort studies conducted by Nikooseresht M. *et al.*,¹⁶ among eighty (37 normotensive and forty-three severe preeclamptic) women and Aya AG *et al.*,¹⁷ among sixty normotensive and preeclamptic women respectively. However, other prospective cohort studies conducted by Clark *et al.*,¹⁹ among forty and Aya AG *et al.*,¹⁶ among one hundred thirty-six normotensive and preeclamptic women showed a different result where the first APGAR score was not different between the groups. This discrepancy might be due to the inclusion of a small sample size which is observational in which confounding is unavoidable.

Limitation of study were single center study, in a small group of patients (88), effect of different size and type of needles and also different dosages of bupivacaine cannot be studied. More studies are needed to investigate the effects of vasopressors while considering the influence on fetomaternal physiology in patients with preeclampsia.

CONCLUSION

Subarachnoid blockade is associated with better perioperative hemodynamic stability and lower risk of hypotension and vasopressor requirements in preeclamptic women compared to the rates of healthy subjects. Subarachnoid block can be safely practiced in patients with preeclampsia undergoing caesarean section. The benefit of rapid, dense and reliable subarachnoid block over epidural anaesthesia should be considered for preeclamptics undergoing caesarean section.

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