ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

DEPARTMENT OF ANESTHESIA

EFFECTIVENESS OF PROPHYLACTIC BOLUS PHENYLEPHRINE ON THE PREVENTION OF POSTSPINAL HYPOTENSION DURING ELECTIVE CESAREAN SECTION AT GANDHI MEMORIAL HOSPITAL, ETHIOPIA 2024, OBSERVATIONAL COHORT STUDY

PRINCIPAL INVESTIGATOR: GEDIWON G/HIWOT (B.SC)

ADVISOR: BETELIHEM GIRMA (B.SC, M.SC)

BIRUK TESFAYE (B.SC, M.SC)

A THESIS SUBMITTED TO, ADDIS ABABA UNIVERSITY COLLEGE OF HEALTH SCIENCES, DEPARTMENT OF ANESTHESIA, FOR PARTIAL FULFILMENT OF THE REQUIREMENT FOR MASTERS OF SCIENCE (MSC) IN ANESTHESIA.

MAY 2024 GC

ADDIS ABABA ETHIOPIA

Name of Investigator	❖ **GEDIWON G/HIWOT**
Name of advisor(s)	• Betelihem Girma (B.Sc. M.Sc.) • Biruk Tesfaye (B.Sc. M.Sc.)
Full title of the research project	EFFECTIVENESS OF PROPHYLACTIC BOLUS PHENYLEPHRINE ON THE PREVENTION OF POSTSPINAL HYPOTENSION DURING ELECTIVE CESAREAN SECTION AT GANDI MEMORIAL HOSPITAL, ETHIOPIA,2024:OBSERVATIONAL COHORT STUDY
Duration of the research	FEBRUARY 01/2024 – MAY 15 / 2024
Study area	ADDIS ABABA, ETHIOPIA
Total cost of the project	28,000.00Eth.birr
Address of investigator	**Tel: +251-937275782** **E-mail: gebrehiwotgediwon@gmail.com**

Declaration

The undersigned people certify that the research entitled Observational cohort study on Effectiveness of prophylactic bolus phenylephrine on the prevention of post-spinal hypotension during elective caesarean section at Ghandi Memorial Hospital, from February 01/2024 to May 15/2024 G.C

This is my original thesis work and any literature or data cited in this article were listed in the reference section.

Author Name _____signature _____ date _____

Approval of the Board of Examiners

Advisors:

1. _____signature_____ date_____
2. _____signature _____date_____

Internal Examiner

Name _____signature _____ date _____

External Examiner

Name _____ signature _____ date _____

Table of Contents

Abbreviations/Acronyms

APGAR: Appearance, Pulse, Grimace, Activity and Respiration

ASA: American Society of Anaesthesiology

CI: Confidence interval

CS: Caesarean section

DBP: Diastolic blood pressure

HR: Heart rate

Hgb: Hemoglobin

IQR: Interquartile range

NIBP: Non-invasive blood pressure

N&V: Nausea and Vomiting

PSH: post-spinal hypotension

PUD: Peptic ulcer disease

SA: Spinal anaesthesia

SD: Standard deviation

SBP: Systolic blood pressure

SPSS: Statistical package for social science

WHO: World health organization

Acknowledgment

First and foremost, I want to thank my advisors, Ms Betelihem Girma (MSc in anesthesia and critical care) and Mr Biruk Tesfaye (MSc in anaesthesia and critical care) for their valuable comments and friendly help in the preparation of this thesis. In addition I would like to express my deepest gratitude to Addis Ababa University College of health science for providing me the chance and funding me to carry out this research.

In addition I would like to express my sincere thanks and admiration to my data collectors as well as Ghandi memorial hospital anaesthetists.

I want to express my gratitude in particular to Dr Eyayalem Melese, Mr Ashenafi Seifu, Mr Wosenyeleh Admasu and Mr Hirbo Samuel for their professional advices and suggestions in my work.

Lastly I want to express my gratitude to my friends and family: Endashaw Chombe, Tsion Teferi, Elias G/Hiwot, Yegle Asra and Yisehak Wolde for their golden comments and support during this thesis work.

Abstract

Introduction: Spinal anaesthesia owing to the perceived advantages is commonly used for caesarean section. However parturients under spinal anaesthesia frequently experience hypotension and if it is severe it can result in morbidity for both the mother and the fetus. The incidence of hypotension during spinal anaesthesia for caesarean section is reduced by administering intravenous fluids, drugs such as vasopressors, or by leg elevation. But in the practice of anaesthesia preventing and treating hypotension associated with spinal anaesthesia continue to be a challenging issue and there is controversy about the best way to handle it.

Objective: The objective of this study is to determine the effectiveness of prophylactic bolus phenylephrine on the prevention of post-spinal hypotension during elective caesarean section under spinal anaesthesia.

Method: Observational cohort study design was conducted at Gandhi Memorial Hospital located in Addis Ababa,Ethiopia from February 01, 2024 to May 15, 2024. The sample size was determined by using the double population proportion method using manual calculator. Statistical package for social sciences (SPSS) software version 27.0 was used for data analyses. Comparison of numerical data between study groups was done by using independent sample t- test for symmetrical data and Mann whitney U test was used to compare non parametrical data. Chi square test was used to compare categorical data of the group. Values are presented as mean SD for symmetric data and median (IQR) for asymmetric data. For categorical data values are presented by number percent. Significance was determined at P value <0.05.

Result: The incidence of hypotension in standard care group was 63.3% but in phenylephrine prophylactic group the incidence of hypotension was 28.6% [N: 105), P: 0.004]. Starting from the induction until 25th minute, phenylephrine group had higher mean value of systolic and diastolic blood pressure than standard care group (P<0.05). Incidence of nausea, incidence of vomiting, numbers of mothers that require rescue vasopressor and total dose of rescue vasopressor were significantly different between the groups. Heart rate differences between phenylephrine and standard care group were not statistically significant

Conclusion and recommendation: In conclusion, parturient undergoing elective caesarean section experienced less episode of hypotension after spinal anaesthesia when a prophylactic bolus phenylephrine was used. Administering 100 microgram of bolus phenylephrine immediately after spinal anaesthesia is recommended for better hemodynamic stability of the mothers

1. Introduction

1.1 Background

Caesarean section refers to the operation of delivering baby through incisions made in the mother's abdominal wall and uterus. Caesarean section may be indispensable when vaginal delivery might pose a danger to the mother or baby. Caesarean section is one of the most significant lifesaving procedures that played a key role to decline maternal and perinatal morbidity rate.(1)

In caesarean section, spinal anaesthesia is the anaesthesia of choice for elective surgery. And it is one of the neuraxial blocks with a massive and temporary interruption of nerve transmission within the subarachnoid space produced by injection of a local anaesthetic medication into the cerebrospinal fluid. Sensory, autonomic and motor impulses are blocked by the local anaesthetic agents administered in the subarachnoid space as the anterior and posterior nerve roots pass through the CSF. Spinal anaesthesia has been widely used and continues to be popular for so many surgeries. It is major regional anaesthetic techniques for many obstetrics and gynaecological procedures.(2)

When we compared it with general anaesthesia, spinal anaesthesia has many advantages including; low risk of aspiration, difficult intubation, low risk of airway obstruction, less cognitive impairment, decreased blood loss, low cost, good operating condition, faster return in gastrointestinal function, decreased incidence of pulmonary embolism and deep venous thrombosis.(3)

Spinal anaesthesia is associated with many complications among which the most common side effects are hypotension and bradycardia. The resulting hypotension can cause nausea and vomiting, cardiovascular collapse, and loss of consciousness in the mother, as well as acidosis in the fetus. Both spinal anesthesia and maternal physiological changes contribute to the hypotension. A reduction in systemic vascular resistance as a consequence of sympathetic blockade, more extensive neuroblockade because of a contracted subarachnoid space has been implicated as mechanisms of the hypotension.(8)

Post spinal hypotension results from temporary sympathectomy leading to reduced preload and reduced afterload, causing lower maternal mean arterial pressure (MAP) and reduced uteroplacental perfusion. Several studies have shown that the rate of hypotension is higher for spinal anaesthesia compared with general anaesthesia and epidural route.(4)Without prophylactic vasopressors post spinal hypotension affects nearly 60% of women during caesarean delivery, thus using vasopressors has been highly recommended for routine prevention of post spinal hypotension during caesarean delivery.(9)

Hypotension can be defined as reduction of blood pressure by 20% from base line or systolic blood pressure less than 90mmhg. A reduction in systemic vascular resistance as a consequence of sympathetic blockade, extensive neural blockade because of a contracted subarachnoid space, higher level of sympathetic block and aorthocaval compression by gravid uterus, as well as to the already low decreased systemic vascular resistance associated with pregnancy.(5)

There are so many factors identified as having association with a higher incidence of hypotension after spinal anaesthesia are BMI >30 and <18, age greater than forty, ASA physical status II and above, female in gender, history of hypertension, history of anti-hypertensive medications, blood pressure < 90/60 mmHg, diabetes mellitus and high level of sensory blockade.(6)

Prophylactic vasopressors infusions are increasingly considered to be standard of care during obstetric spinal anaesthesia. However few developing countries incorporate prophylactic vasopressor infusion into their management guideline. Yet, it is in precisely these context, faced by the majority of the world's population, where spinal hypotension has its greatest adverse impact.(7)

Phenylephrine is an alpha-1 adrenergic receptor agonist indicated for the treatment of clinically important hypotension resulting primary from vasodilation in the setting of anaesthesia. Unlike pseudoephedrine, which is a mixed acting sympathomimetic and therefore has more side effects than phenylephrine does. Furthermore, because of its specificity of action, phenylephrine does not exert significant stimulating effects on the Central Nervous System. There are minimal cardiovascular effects at recommended doses, and rare side effects include tachycardia, nausea, vomiting and restlessness.(8),(9)

Currently aggressive fluid management is part of prophylaxis of spinal anaesthesia-induced hypotension. But non pharmacologic measures to combat hypotension are frequently not effective. Vasopressors are frequently required in order to control post-spinal hypotension.(10)

1.2. Statement of the problem

Globally, CS usage has sharply increased. According to the most recent data from 150 countries shows, caesarean section nowadays accounts about 18.6% of all births, with regional variation of 6% to 27.2% .(11)

The pooled estimated prevalence of caesarean section in Ethiopia was 29.55%. Regarding the study area, the prevalence of caesarean section was highest in Addis Ababa, accounted for 40.39%. In the study and meta-analysis; obstructed labor, cephalopelvic disproportion, multiple pregnancies, non-reassuring fetal heart rate pattern, failed induction and augmentation, mal-presentation and malposition and antepartum haemorrhage are the most common indications of CS in Ethiopia.(12)

Hypotension secondary to spinal anaesthesia is believed to occur due to two possible mechanisms. The first, and most well-known, mechanism is systemic vasodilation caused by sympathetic blockade following spinal anaesthesia resulting in venous pooling of blood and reduction in systemic vascular resistance. Based on this mechanism many academics suggest that peripheral vasoconstrictors could be used to treat spinal anaesthesia-induced hypotension by raising systemic vascular resistance and facilitating venous return.(13)

If not treated, maternal hypotension during caesarean section under spinal anaesthesia has been observed to occur more than 60% of the time.(14)

Because of the sympathetic blockade secondary to spinal anaesthesia may significantly reduce venous return; mothers who have prenatal hypovolemia may be at danger of cardiovascular collapse. As a result, one of the main areas of study in the field of obstetric anaesthesia has been the avoidance of post-spinal hypotension.(15)

Traditional methods for treating post-spinal hypotension during caesarean section include fluid preloading, patient positioning and the administration of vasoconstrictors. There was no agreement on the best way to handle it, and prevention and management of post-spinal hypotension remain challenging issues in anaesthesia practice.(16)

According to recent data and a meta-analysis, crystalloid pre-hydration is ineffective at preventing post-spinal hypotension, probably because it spreads quickly. As an alternative fluid bolus was administered at the time of spinal anaesthesia administration, but it is not effective enough to prevent post-spinal hypotension.(17)

Spinal anaesthesia-induced hypotension is the most frequently observed complication during caesarean delivery and is associated with adverse foetal and maternal outcomes. Foetal acid base status has been used as a surrogate marker for neonatal well-being and has been found to correlate positively with the degree and duration of hypotension. Practice guide-lines suggest tight control of maternal blood pressure by using vasopressors as one of the strategies for management.(18)

1.3. Justifications

The prevalence of post spinal hypotension without any pharmacological prophylaxis in Ethiopia is 50%.(19) So, this situation needs important solution.

Since post-spinal hypotension is still common with all fluid loading protocols many anaesthetists may find it unsatisfactory to rely solely on fluid loading as prophylactic measure.

A study done in India recommends, a dose of 75ug of phenylephrine administration immediately after the administration of spinal anaesthesia is adequate to prevent post-spinal hypotension for caesarean section.(5). But the study done in Gondar University recommend, the use of prophylactic phenylephrine 100ug is enough for the prevention of hypotension in parturients undergoing caesarean section under spinal anaesthesia.(20). The above two differences indicated there is no standard dose of phenylephrine for the prevention of post-spinal induced hypotension in caesarean section. As the dose increases the complication associated with the medication also increases, so it is important to improve the practice with minimum dose to spare the parturients from drug related side effect.

Hypotension following spinal anaesthesia for caesarean delivery is still a common clinical issue which is linked to morbidity for both the mother and the foetus, despite a great deal of research in the past. Maternal hypotension brought on by spinal anaesthesia for caesarean section is still an issue that needs to be prevented and treated. Treatment protocols implemented after hypotension has occurred may not produce the same result as those that try to prevent it during spinal anaesthesia for caesarean delivery

Its prevention and symptomatic treatment for post-spinal hypotension during caesarean section is still unsatisfactory.

More recent clinical studies have shown that a-agonist medication are acts quickly, restoring blood pressure without causing significant change in heart rate or affecting utero-placental circulation than ephedrine.(26)

2. Literature review

The most commonly known complication after the administration of spinal anaesthesia in caesarean section is hypotension. A prospective cohort study conducted in University of Gondar Hospital in 2017 on 113 patients shows that, the incidence of hypotension was significantly lower for those participants with prophylactic phenylephrine (26% vs. 81.6%) compared to the non-treatment group. systolic and diastolic blood pressure immediately after spinal anaesthesia till delivery and after delivery of the baby were significantly lower in the non-treatment group at all times. Moreover, the number of rescue treatment and total amount of fluid given during the intraoperative period for the treatment of hypotension were more in the non-treatment group.(18)

A single-centre, prospective observational study conducted in University of KwaZulu South Africa on 523 participants which is done to show Prophylactic Phenylephrine Infusions to Reduce Severe Spinal Anaesthesia Hypotension during Caesarean Delivery in a Resource-Constrained Environment found that fixed-rate; low-dose prophylactic phenylephrine infusions reduced the incidence of severe hypotension in resource-limited conditions.(22)

Randomized double blind study conducted to show Vasopressor drugs for the prevention and treatment of hypotension during neuroaxial anesthesia for Caesarean deliver which is conducted on 4126 participants in Washington in 2019 showed the likelihood that norepinephrine, metaraminol, and mephentermine had the lowest probability of adversely affecting the fetal acidbase status as assessed by their effect on umbilical arterial base excess (probability rank order: norepinephrine > mephentermine > metaraminol > phenylephrine > ephedrine). This rank order largely held true for umbilical arterial pH and PCO2. With the exception of maternal bradycardia, ephedrine had the highest probability of being the worst agent for all assessed outcomes.(23)

A randomize double blind study conducted in united kingdom on 75 women scheduled for elective caesarean delivery in 2007 which is done to show Dose-Dependent Effects of Phenylephrine on blood pressure for Elective Caesarean Delivery Under Spinal Anaesthesia: SBP control was satisfactory in all groups; however, the group receiving phenylephrine 100 g/min required significantly higher doses to achieve arterial blood pressure control compared with the lower infusion rates. There were no significant differences in the number of times SBP decreased below 80% of baseline, or the numbers of boluses of ephedrine or phenylephrine required to maintain SBP above 80% of baseline. There were significant time and dose-dependent reductions in HR and CO with phenylephrine, such that HR and CO were seen to decrease with time in each group, and also with increasing concentrations of phenylephrine.(24)

Randomized double blind study conducted on 120 participants to show Phenylephrine for Blood Pressure Control in Elective Caesarean Section: Therapeutic versus Prophylactic Doses on 120 participants; the participants are randomly divided in three equal groups according to the regimen of phenylephrine administered, were included in this study. In Group 1, continuous infusion of phenylephrine, using an infusion pump at

0.15 µg/kg/min was administered after the spinal block. In Group 2, a single dose of prophylactic phenylephrine 50 µg was administered after the spinal block, and Group 3 received a single dose of phenylephrine 50 µg in case of hypotension, which was defined as a drop in SBP and/or DBP of up to 20% of baseline levels. The incidence of hypotension, nausea, and vomiting as well as the Apgar score were evaluated. And the incidence of hypotension was significantly greater in Group 3, affecting 85% of the gravidas. In Groups 1 and 2 hypotension was seen in 17.5% and 32.5% of the cases respectively the incidence of nausea was much higher in Group 3 affecting 40% of the patients while in Groups 1 and 2 it was 10% and 15% respectively.(25)

Prospective randomized study done in Serbia in 2018 conducted to compare the efficacy and safety of pre-emptive infusion protocols of ephedrine and phenylephrine – prevention of hypotension and effects on hemodynamic parameters during spinal anaesthesia for caesarean section. The infusion of ephedrine was administered at the rate of 5 mg/min. immediately after SA. Phenylephrine was administered at an infusion rate of 25 µg/min for two minutes prior to SA. And the result was In Group Ephedrine, mean systolic blood pressure (SBP) and heart rates (HR) were similar to baseline. CO was higher while systemic vascular resistance was lower than baseline. In Group Phenylephrine, mean SBP and diastolic blood pressure (DBP) were lower than baseline; respectively SBP, DBP, CO, SV, SVR, and HR were significantly different between the Ephedrine and Phenylephrine groups.(26)

A randomized clinical trial done on a total of 50 parturient shows, phenylephrine infusion decreased the incidence and frequency of hypotension compared with non-prophylaxis group and the dose of phenylephrine was higher in the infusion group than non-prophylaxis group. None of the parturient had any incidence of nausea or vomiting. There was no significant difference in umbilical artery blood pH and no reduction in the APGAR score. A prophylaxis infusion of phenylephrine 100ug/min in patient receiving spinal anaesthesia for elective caesarean delivery decreased the incidence of hypotension and without any deleterious neonatal outcome.(25)

A prospective randomized trial conducted in the Chinese University of Hong Kong in 2004 in 100 patients shows that, only 8 patients had developed hypotension with phenylephrine prophylaxis. No patient had umbilical arterial pH less-than 7.2 in prophylactic group and 4% of the patient had nausea and vomiting but under non-prophylaxis group the incidence of nausea and vomiting were 40%. For optimal management of post-spinal hypotension phenylephrine should be titrated to maintain maternal blood pressure at near-baseline values.(26)

A randomized double blind study conducted on 50 patients in china shows that 80% of the parturient who received phenylephrine infusion before caesarean section protected from post-spinal induced hypotension. The study confirmed that starting a prophylactic infusion of phenylephrine immediately after the induction of spinal aesthesia for caesarean delivery would be effective at reducing the incidence, frequency and severity of hypotension.(27)

A Prospective Double-blinded Clinical study conducted in India in 2017 on 120 parturient which is done to compare f Two Different Bolus Doses of Phenylephrine for Prevention of Spinal-Induced Hypotension during Cesarean Section after allocation of a participants into three groups of 40 each to receive either saline (group P0), phenylephrine 75 mcg (group P75), or phenylephrine 100 mcg (group P100) Incidence of hypotension was 70%, 25%, and 17.50% in P0 , P75, and P100 groups respectively. Maximum change in systolic blood pressure paralleled the increasing doses of prophylactic phenylephrine which was highest in P100 group as compared to P75 and P0 groups. Incidence of reflex bradycardia was higher in group P100 than groups P75 and P0 There were no other significant differences among the three groups.(29)

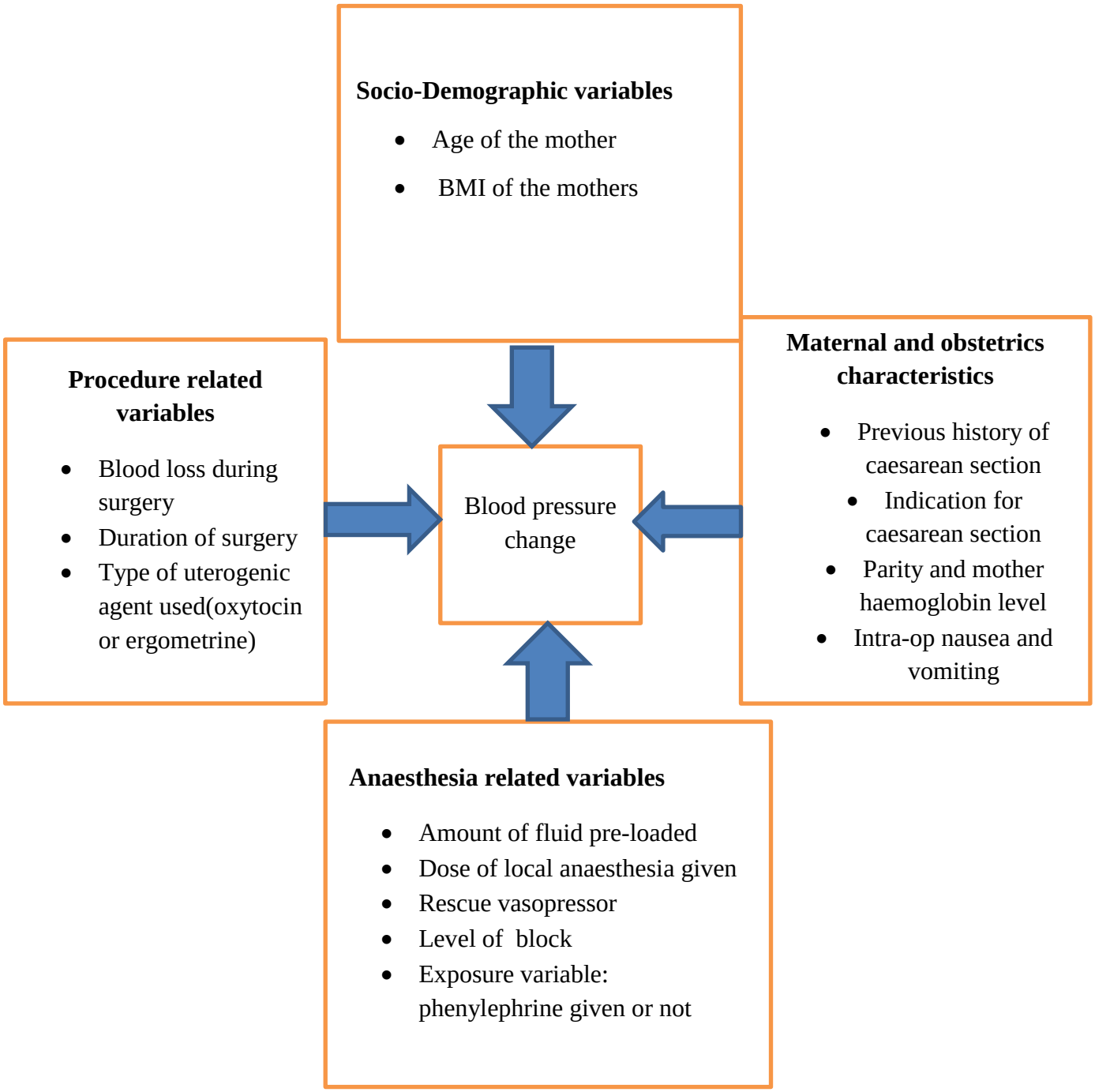
Prospective double blind study which is done in japan in 2012 on 120 participants which is conducted to compared the effects of three initial bolus doses of intravenous phenylephrine; by allocating in to three groups; 100 μg (group P100), 125 μg (group P125) and 150 μg (group P150), for the treatment of post-spinal hypotension in patients undergoing elective caesarean delivery shows 16 , 13 and 12 patients (groups P100, P125 and P150, respectively The first bolus of phenylephrine successfully treated hypotension in 34, 38 and 38 patients in groups P100, P125 and P150, respectively The Apgar scores ,umbilical arterial and venous blood gas analyses were comparable in all groups.(5)

Maternal nausea and vomiting are the common problems for caesarean section under spinal anaesthesia. A Study conducted in Bahirdar University to assess the magnitude and risk factors of post-spinal relevant hemodynamic associated with caesarean section shows that; the incidence nausea after spinal anaesthesia in caesarean section was 68% but the incidence of vomiting after spinal anaesthesia was 16%.(30)

After the administration of spinal anaesthesia sometimes intraoperative bradycardia would happen due to high level of sensory blockade. The study done in Bahirdar University in 143 mothers shows that the incidence of intraoperative bradycardia were 3%.(30)

2.1. Hypotheses

1. HO: There is no difference in mean arterial pressure after the administration of spinal anaesthesia between phenylephrine and standard care groups
   HA: There is a difference in mean arterial pressure after spinal anaesthesia between phenylephrine and standard care groups
2. HO: There is no difference in heart rate between phenylephrine and standard care groups after the administration of spinal anaesthesia
   HA: There is difference in heart rate after the administration of spinal anaesthesia between phenylephrine and standard care groups
3. HO: There is no equal consumption of rescue vasopressor between phenylephrine and standard care groups
   HA: There is equal consumption of rescue vasopressor between the two groups



Conceptual frame work

3. Objective

3.1. General objective

To assess the effectiveness of prophylactic bolus phenylephrine for the prevention of post-spinal hypotension during elective caesarean section at Ghandi Memorial Hospital.2024

3.2 Specific objective

- To compare the incidence of hypotension after spinal anaesthesia between phenylephrine and standard care groups.
- To compare vasopressor consumption between the groups
- To compare heart rate variability between the groups

4. Method and materials

4.1. Study area

The study was carried out at the Gandhi Memorial hospital in Ethiopia's capital city of Addis Ababa. Gandhi Memorial Hospital honours the memory of the leader of the indian freedom movement. It is one of the govermental Hospital in Addis Ababa run by the Addis Ababa city Health bureau administration. Obstetric, Gynacologic and numerous other reproductive health services are offered by the hospital. There are 110 beds in the Hospital and 30 babies are delivered there every day on average. The Hospital has 4 operating rooms and on average eight to ten cesarean deliveries are performed per day, from which one-third are elective.

4.2. Study design and study period

Observational cohort study design was conducted from February01, 2024 to May 15, 2024.

4.3. Source Population

All pregnant mothers who were gave birth by elective caesarean section under spinal anaesthesia at Gandhi Memorial Hospital Addis Ababa, Ethiopia during the study period.

4.4. Study Population

Selected pregnant mothers: who were grouped under phenylephrine and standard care group by assigned anaesthesia personnel to give birth by elective caesarean section under spinal anaesthesia.

4.5. Inclusion and Exclusion criteria

4.5.1. Inclusion Criteria

- ASA physical status II pregnant women
- Gestational age between 38–42 weeks
- BMI below 35 and above 17

4.5.2. Exclusion criteria

- Maternal complications(DM, Preeclampsia, cardiovascular disease)
- Placental complication(placenta previa, abruption placenta)
- Cord complication(nuchal cord, cord prolapse)
- Absolute or relative contraindication to spinal anaesthesia
- Maternal baseline systolic blood pressure less than 100 mmHg
- Baby birth weight less than 2.5kg or greater than 4.5kg
- Foetal malformation
- Incomplete data/loss to follow up

- Mothers used combined spinal epidural anaesthesia
- Failed spinal block and
- Parturient who have allergic history for phenylephrine
- Tween pregnancy
- Parturient who took anti-hypertensive medications
- Prolonged NPO time
- Polyhydraminose

4.6. Sample size and sampling procedure

4.6.1. Sample size calculation

Sample size was calculated by manual calculator. By considering 95% confidence interval, a power of 80% and ratio of phenylephrine prophylaxis (50 parturients) to standard care group (44 parturients) was 0.8:1 and the incidence of hypotension in standard care group was 50%(19) and incidence of hypotension in bolus or phenylephrine prophylaxis group was 26%, which is estimated from previous study done in Ghandi Memorial Hospital and university of Gondar in Ethiopia respectively.(18)

$n= (Z_{\alpha/2} + Z_{1-\beta})^2\ p\ (1-p)\ (r+1)/\ (d)2*r$

Where

$Z_{\alpha/2}$= 1.96 = value of the standard normal distribution corresponding to a significance level of α (1.96 for a 2-sided test at the 0.05 level)

Z_{β}= 0.84 = value of the standard normal distribution corresponding to the desired level of power (0.84 for a power of 80%)
P0= proportion of non-prophylaxis group

P_1= proportion of phenylephrine prophylaxis group

d = Margin of error

r = ratio of standard care to phenylephrine group

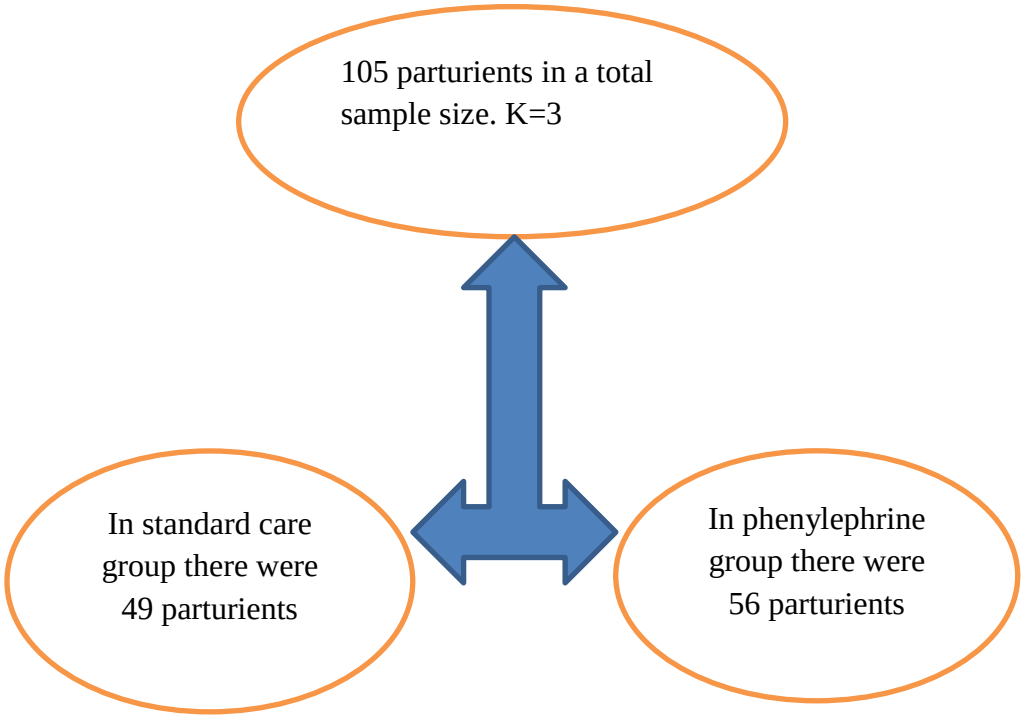
p_0 = 0.5 and p1 = 0.26 r=0.88

n=(1.94+0.84)2*0.26*(1-0.26)*(0.88+1)/(0.5-0.26)2*0.88
n prophylaxis=56
n non prophylaxis = r*n =0.88*56=49
n total=105

4.7. Sampling procedure

Selection of participants was carried out by using systematic random sampling technique each day before elective caesarean section begun. We conducted situational analysis in the study hospital and assumed that there would be 360 CS in total during the study period, with 4 elective CS occurring during working day. This yield a "K" value of three (K=3) and every Kth unit was selected initially for 56 phenylephrine prophylaxis parturients then, every Kth unit was selected for 49 non-prophylactic (standard care) parturients. Started at a random selection using lottery method between the first three elective CS based on the responsible anaesthetist's management plan.

Figure 1: Sampling frame for elective caesarean section at Gandhi Memorial Hospital from February 01-May 15/2024



4.8. Data collection

All partutients gave their informed consent prior to the study. Data was collected from selected participants by using pretested questionnaire from February 01 2024 to May 15 2024. Following thorough explanation of the objective and methods Anesthetic management including intraoperative treatment of hypotension, selection of fluid protocol and phenylephrine prophylaxis given immediately after spinal anesthesia was done with the discretion of the personnel anesthetist assigned to each case and hospital protocol. I the investigator was not involved in the perioperative management of the mothers. Parturients were classified into phenylephrine prophylaxis group (Group 1) and standard care group (Group 2) based on the responsible anesthetists independent decision. Following pre-anesthetic evaluation, all the parturients received oral Rantidine (150mg) the night before and the morning of the day of surgery with a sip of water. Then through an 18-gauge cannula, lactated Ringer's solution was infused at the rate of 10 ml/kg/hour in the pre-operative room and IV injection of Metoclopramide 10mg was administered as pre-medications for both groups.(22) By recording baseline vital sign, spinal anesthesia was done in the sitting position after aseptic technique. 2.5 ml of 0.5% isobaric Bupivacaine by using 25 gauge needles was administered at the level of L3-L4 for all parturients. 100 ug of phenylephrine IV bolus was given immediately after spinal anesthesia after positioning the parturients. The systolic blood pressure, diastolic blood pressure (DBP), means arterial pressure (MAP), and heart rate (HR) were measured at 5-minute intervals intra-operatively till the end of the operation.(20). The level of sensory block was evaluated by using cold sensation 5 minutes after spinal anesthesia. The Data's were collected by three anesthesia professionals after giving 1 day training on the objectives of the study, exclusion and inclusion criteria and data collection tool.

4.9. Variables

4.9.1. Dependent Variable

- Blood pressure change

4.9.2. Independent variables

Socio-Demographic variable

- Age of the mother
- Weight of the mother
- Height of the mother
- BMI of the mother

Procedure related variable

- Duration of incision to delivery time
- Blood loss during surgery
- Type of uterogenic medication used (oxytocin or ergometrine)
- Duration of surgery

Maternal and obstetrics characteristics

- Parity
- Previous history of cesarean section
- Indication for cesarean section
- Mother hemoglobin level
- Intraoperative nausea and vomiting

Anesthesia related variables

- Amount of fluid pre-loading
- Dose of local anesthesia given
- Preoperative medications
- Level of sensory block
- Exposure variables; prophylaxis given or not

4.10. Operational Definition

- **Spinal anaesthesia:** the administration of local anaesthetic agent into subarachnoid space
- **Baseline value:** values measured before the administration of spinal anaesthesia
- **Hypotension:** Measured by systolic blood pressure <90 mmHg or diastolic blood pressure <60 mmHg.(16)
- **Hypertension**: Measured by systolic blood pressure >20% of baseline.(31)

- **Co loading:** Administering crystalloyd fluid while performing spinal anesthesia
- **Post spinal hypotension:** Hypotension occurs immediately after the administration of spinal anesthesia.(32)
- **Bradycardia:** defined as heart rate < 60 beat per minute.(33)

- **The level of sensory block:** is loss of cold sensation and it was recorded bilaterally in the anterior axillary line or mid-clavicular line.(34)
- **Phenylephrine group:** The group of mothers who grouped under phenylephrine prophylaxis.
- **Standard care group:** The group of parturients who do not took bolus phenylephrine as prophylaxis immediately after spinal anesthesia.
- **Effectiveness of phenylephrine:** it is the ability of the drug to decrease the incidence of hypotension and it could be assessed by blood pressure change after it has given.(20)
- **Safety of phenylephrine:** it is assessed by change in heart rate (bradycardia), blood pressure (hypertension) and neonatal outcome (APGAR) score.(20)

4.11. Data analysis and interpretation

Data was coded edited and then entered and cleaned using Epi data version 4.6 and exported to Statistical package for Social Sciences (SPSS) software version 27.0 for analysis. Using SPSS Numeric data will be described in terms of mean ± SD for symmetric and median (Interquartile range) for asymmetric data. Shapiro wilk test and kolomogorov smirnov tests were used to test for normal distribution of data while homogeneity of variance was assessed by using levene's test for equality of variance. Comparison of numerical variables between study groups were done by using unpaired student t- test for symmetric data (Age, Height, Weight, BMI, Maternal Hemoglobin level and Systolic BP). Manny Whitney U test was used for asymmetric data (Diastolic blood presure, heart rate, Para, Gravida, APGAR, Duration of surgery, rescue dose of noradrenaline, Weight of the baby, Blood loss, Incision to delivery time and Intraoperative iv fluid).

Frequency and percentage were used to describe categorical variable (Indication for cesarean section, Level of sensory block, Intraoperative bradycardia between the group, Incidence of nausea and vomiting between the groups, incidence of hypotension and number of mothers rescue vasopressor received) and statistical difference between groups were tested by using Chi square test. Significance was determined at P value <0.05.

4.12. Data quality control

Data collectors received brief orientation on the assessment method and training on the goals and significance of the study in order to ensure the quality of the data. The investigator made revisions to each questioner during data collection to ensure that it was appropriate and complete. When gathering data, the data collectors were told to write a card number on the questionnaire in case a second cross-check was required.

4.13. Ethical consideration

The study was carried out with approval from the Addis Ababa University ethical review board. The Gandhi Memorial Hospital, the study's location, received a legal letter. All parturients provided verbal informed permission following thorough descriptions of the study's objectives and methods. Following approval from the Hospital and study participants, data collection was carried out.

5.0. Result Dissemination plan

The result of this study will be disseminated to the collage of health science of Addis Ababa University, Gandhi Memorial Hospital, Addis Ababa city health bureau, Ethiopian Anaesthetist Association and other responsible bodies. The outcome will be showcased at the college of Health science through various workshops, conferences seminars and meetings. Moreover, efforts will be done to publish the findings of the study.

5. Result

5.1 Comparison of demographic data and baseline vital sign between the two groups

A total of one hundred five parturients were enrolled in this study: Fifty six parturients in phenylephrine group and forty nine in the standard care group. All the demographic data and base-line systolic blood pressure were normally distributed (p-value of Kolmogorov smirnov test were >0.05). But baseline diastolic blood pressure and baseline heart rate were not normally distributed (Kolmogorov smirnov and Shapiro wilk test were <0.05). Numerical comparison between asymmetric data was done by using Mann whitney U test, and numerical comparison between normally distributed data was done by using independent student t-test. There were no significant differences in maternal baseline systolic blood pressure, baseline diastolic blood pressure, baseline pulse rate and demographic data. And the data are presented by mean and SD for symmetric data and median (IQR) for asymmetric data.

Table 1: Comparison of demographic data between phenylephrine and standard care groups Ghandi Memorial Hospital from February 01.2024 to May 15. 2024 Addis Ababa

Variables	phenylephrine group	Standard care group	p-value
Age	30.68 ± 2.84	29.88 ± 2.45	0.9
Height	1.68 ± 0.39	1.66 ± 0.37	0.237
Weight	75.82 ± 7.75	77.9 ± 8.02	0.349
BMI	26.8 ± 2.46	28.10 ± 3.2	0.549
Haemoglobin level	13.21 ± 0.4	12.9 ± 0.41	0.156
Baseline SBP	129 ± 6.825	127.67 ± 5.87	0.898
Baseline DBP	84 (3)	84(4)	0.184
Baseline HR	91 (11)	100(10)	0.209

Values are presented as: Mean ± SD, Median (IQR), Independent sample t-test, Mann whitney u test and p<0.05 is statistically significant.

5.2 Comparison between Anaesthesia, maternal and surgical factors between the two groups

Maternal and anaesthesia factors such as Gravida, Para and induction to skin incision time were not normally distributed and p value of Shapiro wilk test was <0.05. Comparison between asymmetrical data was done by using Mann whitney U test for their significance. Categorical variables such as: level of sensory block and indications for caesarean section were compared by using chi square test for their significance and numerical values for asymmetric data were presented by median and interquartile range. As well as, numerical values for categorical data were presented by percentiles.

Table 2: Comparison between: anaesthesia, maternal and surgical factors of mothers who underwent elective caesarean section at Ghandi Memorial Hospital.

Variables	**phenylephrine group**	**Standard care group**	**p-value**
Para	3(3)	4(2)	0.11
Gravida	4(3)	4(2)	0.256
Indication for c/s			
Malpresentation	8 (14.3%)	4 (8.1%)	0.296
Oligohydraminose	7 (12.5%)	13 (26%)	
Previous c/s scar	20 (35.7%)	22 (44.9%)	
Post term	12 (21.4%)	19 (38.7%)	
Level of blocks			0.7
T4-T5	3 (5.4%)	6 (12.2%)	
T6-T7	14 (25%)	16 (32.7%)	
T8-T10	39 (69.6%)	27 (55.1%)	
Induction to skin incision time	5(1)	6(1)	0.578

Values are presented by: percentiles, Median (interquartile range), chi square test, Mann whitney U test and p<0.05 is statistically significant.

5.3 Comparison of intraoperative characteristics between phenylephrine and standard care groups

Intraoperative factors such as: dose of oxytocin, intraoperative intravenous fluid, incision to delivery time, blood loss, weight of the baby, duration of surgery and APGAR score were not normally distributed. (Kolmogorov smirnov and Shapiro wilk test p value <0.05). Numerical values between the above asymmetric data were compared by using Mann whitney U test for their significance. Comparison between categorical variables such as: intraoperative bradycardia, incidence of intraoperative nausea and the incidence of intraoperative vomiting between phenylephrine and standard care groups were compared by using chi-square test for their significance. Asymmetric variables presented by median and interquartile range. And categorical variables presented by using number and percentile. From this value all APGAR score between 1 up to 5 minutes were greater than 6 and the dose of oxytocin between the groups were equal. There were 19 episode of vomiting and 38 episode of nausea recorded in both groups. Duration of the surgery, incision to delivery time, intraoperative blood loss and intraoperative fluid administration were comparable and there were no significant difference between the groups.

Table 3: Intraoperative characteristics of mothers who underwent elective CS

variables	**Phenylephrine group**	**Standard care groups**	**p-value**
Incision to delivery time (min)	5(6)	5(7)	0.465
Dose of oxytocin in IU	20.0(10)	20.0(10)	0.756
Duration of surgery (min)	38(18)	40(20)	0.262
Intra-op iv fluid (ml)	2500(1800)	2500(2500)	<0.001
Blood loss (ml)	750(200)	800(115)	0.071
APGAR at 1 min	7(1)	8(1)	0.821
APGAR at 5 min	9(0)	9(1)	0.48
Weight of the baby (kg)	3.4(0.6)	3.4(0.4)	0.298
Intraoperative bradycardia			0.496
YES	2 (3.6%)	7 (14.2%)	
NO	54 (96.4%)	42 (85.8%)	
Incidence of nausea			<0.001
YES	12 (21.4%)	26 (53%)	
NO	44 (78.6%)	23 (47%)	
Incidence of vomiting			<0.001
YES	4 (7.1%)	15 (30.6%)	
NO	52 (92.9%)	34 (69.4%)	

Values are presented as: Median (IQR), number (%), chi-square test, Mann whitney U test and p<0.05 is statistically significant

5.4. Incidence of hypotension between phenylephrine and standard care group

Blood pressure was recorded every five minute starting from the induction of anaesthesia until the end of the operation. The incidence of hypotension was lower for those parturients with phenylephrine group (28.6% vs. 63.3%) compared to standard care parturients, and it was statistically significant ($p<0.01$). After 5 minutes of inducing spinal anaesthesia until 25 minutes of the procedure systolic and diastolic blood pressure were significantly lower in the standard care group. And the values are presented by bar chart.

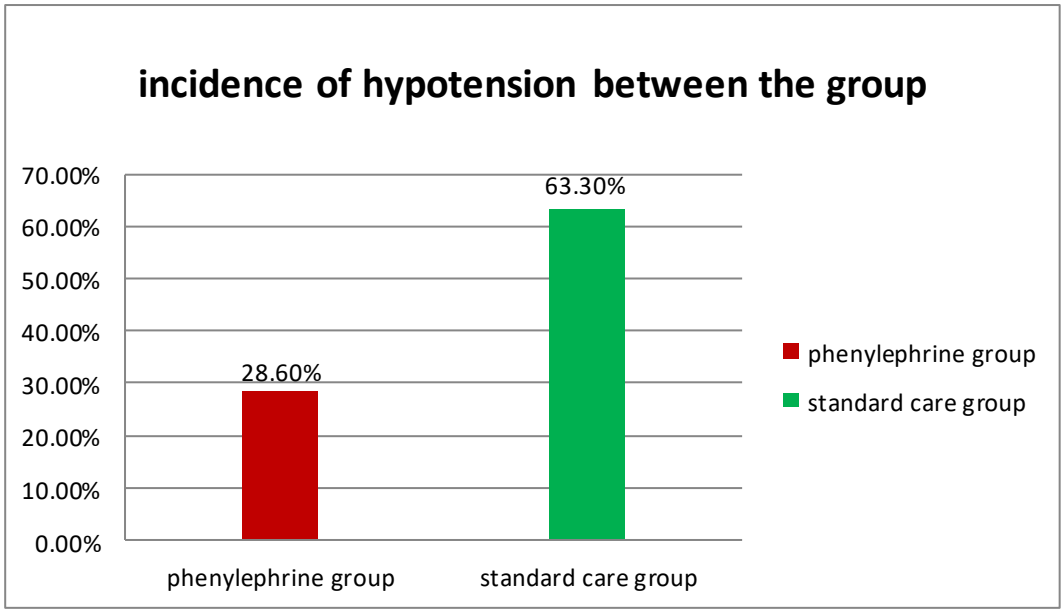


Figure 1: incidence of hypotension between phenylephrine and standard care groups for elective caesarean section under spinal anaesthesia.

5.5. The comparison of vasopressor consumption

In the case of phenylephrine prophylactic group of mothers, rescue vasopressor (nor-adrenaline) was given for 4 (7.1%) mothers. But in the case of standard care group of mothers, rescue vasopressor was administered for 24(49%) mothers for the treatment of intra-operative hypotension. In phenylephrine group of mothers the dose of nor-adrenaline was 4 microgram to manage post-spinal hypotension. But in case of mothers in standard care group the dose of nor-adrenaline was 8 microgram and the number of bolus noradrenaline given intra-operatively for standard care group was more than three times. But in case of phenylephrine group of mothers the number of bolus noradrenaline was only once.

In both group, the drug nor-adrenaline was administered for the treatment of intra-op hypotension. The total dose of rescue noradrenaline in microgram given for treatment of hypotension intra-operatively were compared by using mann whitney U test and showed statistically significant difference between groups (p=0.043)

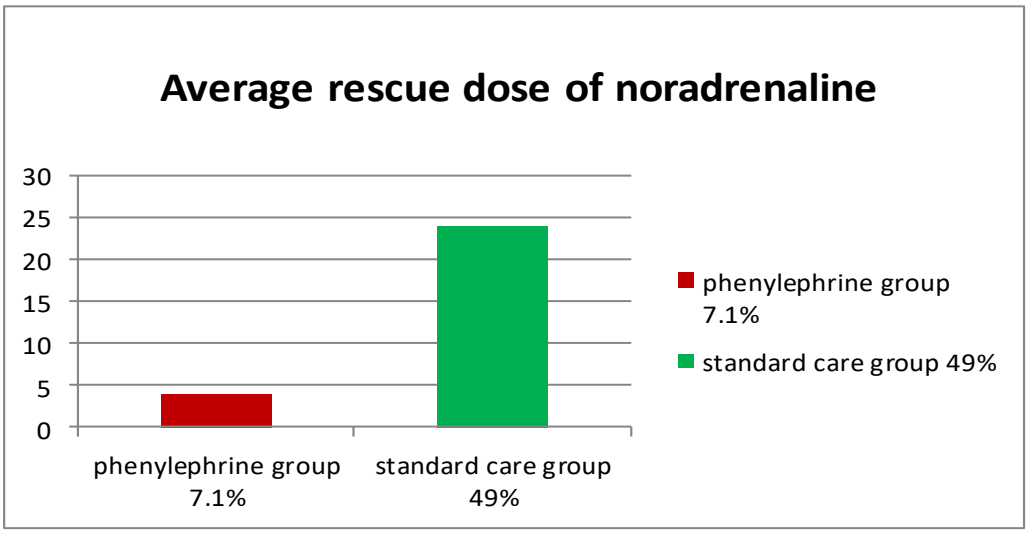


Figure 2: the average dose of rescue noradrenaline for the management of post-spinal hypotension in elective caesarean section at Ghandi Memorial Hospital 2024.

5.6. Comparison of mean arterial pressure (MAP) between phenylephrine and standard care group of mothers

Starting from the time of anaesthesia induction, the recording of the blood pressure was started and recorded every 5 minutes until the end of the operation in both groups of mothers (phenylephrine and standard care) and the mean value shows; mothers in phenylephrine group maintained their mean blood pressure higher than those mothers in standard care group until 25 minutes. Values are presented by Mean ±SD and independent student t test for comparison of the group

Table 4: comparison of mean arterial pressure between phenylephrine and standard care mothers

MAP	**Phenylephrine group (n=56) Mean ± SD**	**p-value**	**Standard care group (n=49) Mean ± SD**	**p-value**
MAP baseline	98.82 ± 5.59	0.438	99.72 ± 5.03	0.296
MAP 5	99.09 ± 4.89	0.353	87.70 ± 7.05	0.033
MAP 10	96.02 ± 6.35	0.247	80.96 ± 5.82	0.04
MAP 15	91.36 ± 7.06	0.075	74.89 ± 6.80	0.013
MAP 20	87.88 ± 8.21	0.146	74.51 ± 6.86	<0.01
MAP 25	87.47 ± 6.64	0.157	78.40 ± 6.84	0.09
MAP 30	85.69 ± 6.47	<0.01	88.35 ± 5.73	0.284
MAP 35	88.11 ± 6.10	<0.01	86.57 ± 5.89	0.419
MAP 40	91.61 ± 4.99	0.155	88.39 ± 3.86	0.226

Values are presented as: Mean ±SD independent student t test and $p<0.05$ is statistically significant.

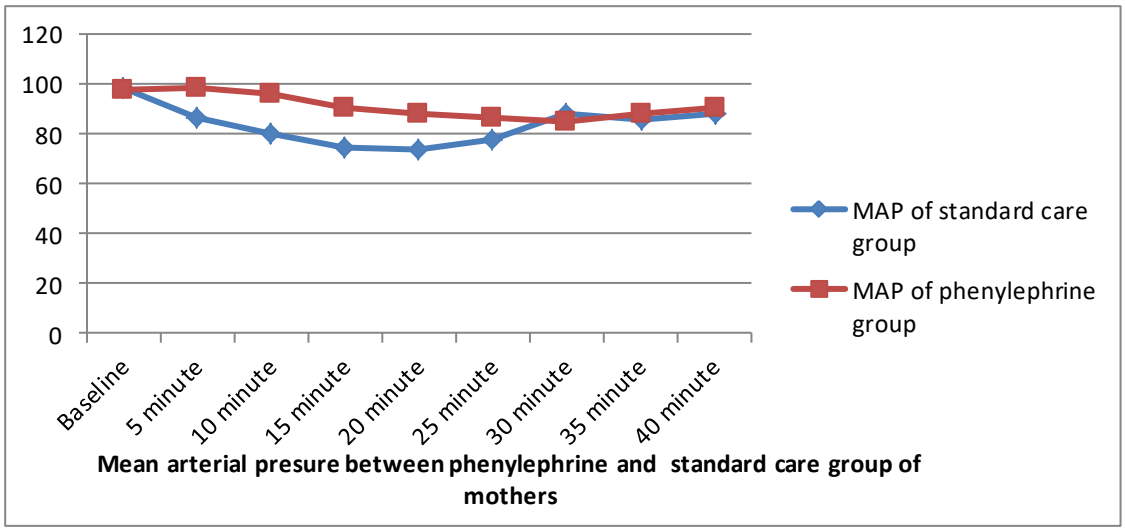


Figure 3: Mean arterial pressure between phenylephrine and standard care group of mothers under spinal anaesthesia in elective caesarean section at Ghandi Memorial Hospital. 2024

5.7. Comparison of mean heart rate between phenylephrine and standard care group of mothers

When we see the trends of heart rate across time, there was no significant difference between phenylephrine and standard care group of mothers from the baseline until the end of the study time, even though seven mothers from standard care group and two mothers from phenylephrine group experienced the incidence of bradycardia in the time of the study. Values are presented by Mean ±SD and independent student t test for numerical comparison of the group.

Table 5: comparison of mean heart rate between phenylephrine and standard care group of mothers

Heart rate	Phenylephrine (n=56) Mean ±SD	Standard care (n=49) Mean ±SD	p-value
Baseline HR	92.0 ± 8.24	97.57 ± 6.54	0.09
HR 5 minutes	89.23 ± 14.23	99.69 ± 13.24	0.327
HR 10 minutes	92.8 ± 11.38	104.8 ± 7.65	0.775
HR 15 minutes	93.8 ± 10.22	106.41 ± 6.48	0.594
HR 20 minutes	91.71 ± 8.84	106.1 ± 7.13	0.211
HR 25 minutes	91.25 ± 9.02	104.63 ± 7.59	0.32
HR 30 minutes	90.50 ± 7.685	101.55 ± 5.93	0.866
HR 35 minutes	90.21 ± 7.89	98.82 ± 4.685	0.151
HR 40 minutes	88.96 ± 7.00	96.24 ± 4.191	0.104

HR: heart rate, SD: standard deviation, independent sample t test

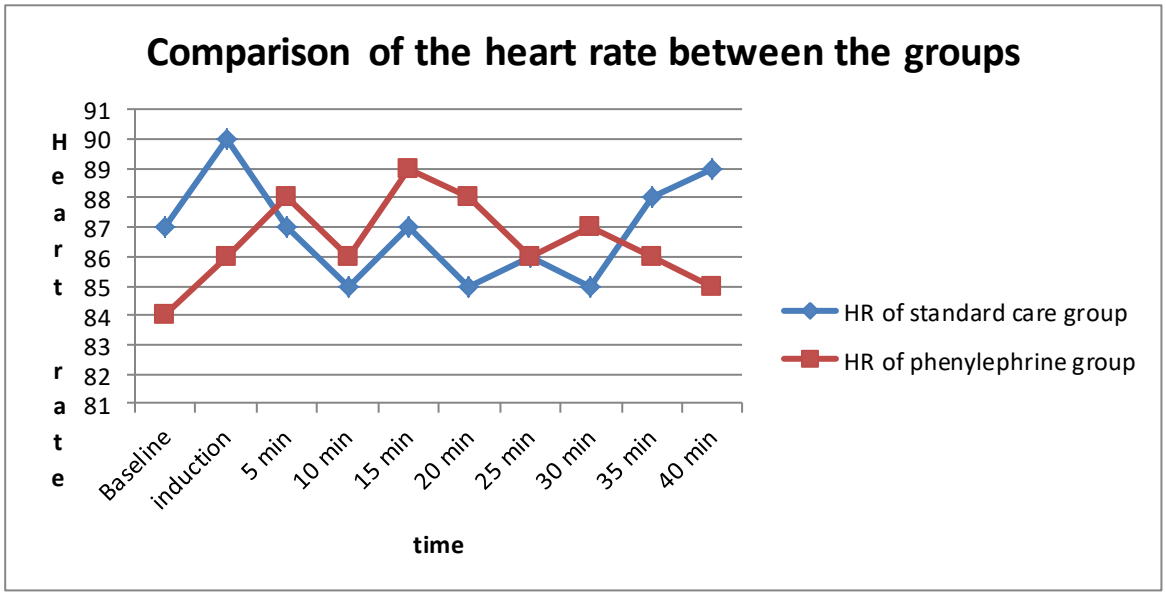


Figure 4: Mean heart rate between phenylephrine and standard care group of mothers after spinal anaesthesia in elective caesarean section at Ghandi Memorial Hospital 2024.

5.8. Intraoperative incidence of nausea and vomiting between the groups

There were a total of 56 mothers in phenylephrine prophylaxis group, from those mothers 12 (21.4%) participants developed intraoperative nausea. But, from 49 mothers who were grouped under standard care group the incidence of nausea encountered in 26 participants (53%). There were 4 incidence of vomiting from phenylephrine group (7.1%) but there were 15 (30.6%) incidence of vomiting recorded in standard care group of mothers which is statistically significant ($p<0.01$)

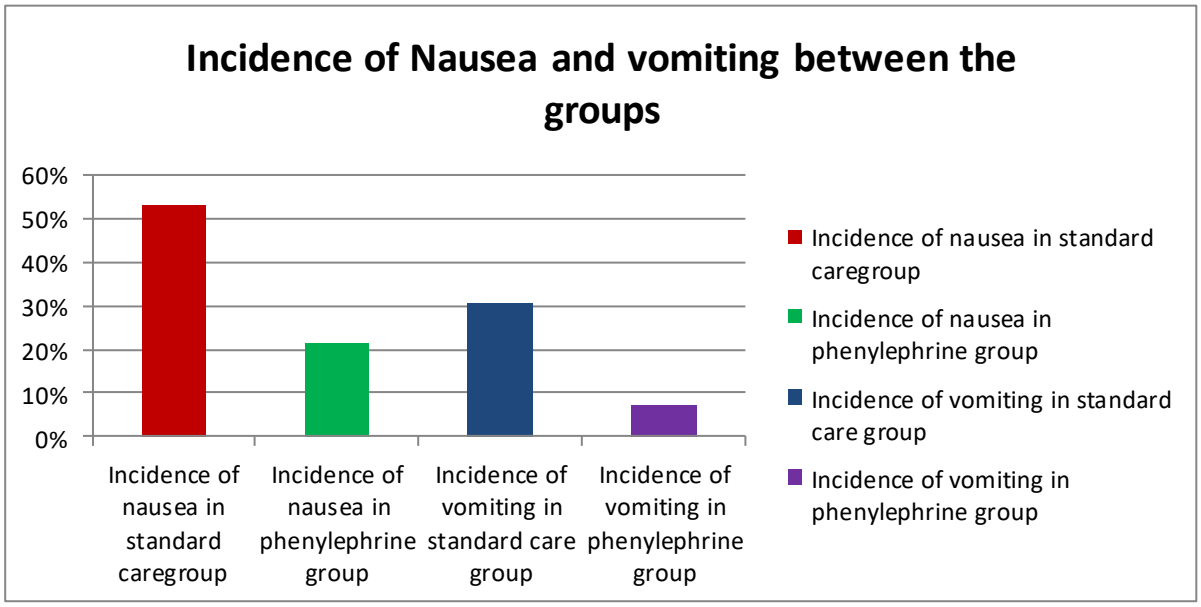


Figure 5: The incidence of nausea and vomiting between phenylephrine and standard care group of mothers who underwent elective caesarean section at Ghandi Memorial Hospital 2024

6. Discussion

Post spinal hypotension is a common condition during c caesarean section that will Couse increased fetal and new-born acidosis and to the mother it will cause nausea and vomiting.(5). The purpose of this research was to assess the effectiveness of bolus phenylephrine to prevent spinal anaesthesia induced hypotension during elective caesarean section.

In this study the incidence of hypotension in the phenylephrine group was 28.6% and the incidence of hypotension in the standard care group was 63.3% and there was no significant difference on heart rate on both groups. But nine parturients had intraoperative bradycardia. The reason for bradycardia was due to high level of block. Mothers who received prophylactic bolus phenylephrine had stable blood pressure than those who didn't receive prophylactic bolus phenylephrine and the incidence of nausea in phenylephrine group was 21.4% and 53% in the standard care group of mothers. The incidence of vomiting in phenylephrine group was 7.1% and 30.6% in the standard care group and the neonatal outcome was comparable between two groups.

In this study the incidence of hypotension was lower in phenylephrine group of mothers and the finding in this study was comparable (Specially in phenylephrine group) with a study conducted by Amare Hailekiros Gebregzi and Abatneh Feleke Agegnehu in Ethiopia Gondar, with incidence of hypotension was significantly lower (26%) in phenylephrine prophylactic group of mothers as compared to parturient in standard care group (81.6%).(20)

In this study the incidence of hypotension was higher when we compare with the study carried out by Sahr M; with incidence of hypotension in phenylephrine prophylactic group was 20%.(3)

The observed discrepancy may be the result of administering a bolus phenylephrine instead of administering phenylephrine by infusion. Because in the above study they used phenylephrine infusion for the prevention of post-spinal hypotension but in this study bolus phenylephrine was used for the prevention of post-spinal hypotension.

The incidence of hypotension in this study was lower when we compare it with the study conducted by David G. Bishop, done in South Africa: the incidence of hypotension after the administration of 100ug bolus phenylephrine was 62.1%.(22). The reason for this variation may be due to patient condition, sample size difference, study level of sensory block, study design difference and clinical setting difference.

In this study More parturient in the standard care group needed rescue vasopressor (Noradrenaline) compared to the phenylephrine group (49% vs.7.1%) which was significantly different ($p=0.043$). From 16 parturient of prophylactic group who developed intra-operative hypotension, 12 (21.4%) parturient were managed by intraoperative fluid and position but 4 (7.1%) parturient were managed by rescue vasopressor which was statistically significant ($p<0.001$) Another study reported that additional rescue phenylephrine bolus was

administered for the treatment of post-spinal hypotension for 44% of the patients in standard care group compared to group with phenylephrine prophylaxis (6%).(2) similar results were found in different studies.(21,25,28)

In the standard care group of parturient the intraoperative mean arterial pressure stayed lower in significant amount ($p<0.05$) starting from 5 minute after the induction of spinal anaesthesia until 25 minutes. The same result was showed in another study with statistical difference in systolic blood pressure and diastolic blood pressure between the groups from 6 minute to 20 minute.(19,20)

The autonomic effect of spinal anaesthesia is expected to begin immediately after the anaesthesia, despite the sensory and motor onset taking approximately five minutes to manifest. This is demonstrated by a significant drop in blood pressure in individuals who did not receive phenylephrine prophylaxis at an earlier time following the spinal anaesthesia injection.(20). According to the current study, approximately 94% of the hypotension in the standard care group happened within 20 minutes of the spinal anaesthesia administered. Another study found the same thing: parturients in the standard care group who developed hypotension did so sooner than those in the prophylactic phenylephrine group.(19)

In this study the incidence of hypotension in phenylephrine prophylactic mothers occurred 25 minutes after the induction of spinal anaesthesia. But: the incidence of hypotension in standard care group of parturients occurred after 5 minutes of the induction of anaesthesia. This might be the fact that phenylephrine has relatively long duration of action (20-25min) compared to other vasopressors.

Additionally, patients who were hypotensive during intraoperative time received extra vasopressor care. Literature shows despite different maneuvers used to treat spinal anaesthesia induced hypotension, anaesthetists will have to treat with vasopressor medications 40% to 60% of parturient undergoing caesarean delivery.(19)

Additionally the overall amount of noradrenaline given was statistically significant in parturient with standard care group. Parturient in standard care group received larger dose of noradrenaline. But parturients in phenylephrine group received smaller dose of noradrenaline when we compared. In this study the average dose of noradrenaline given in standard care group was 24 microgram but in phenylephrine group the average dose was 4 microgram and this study is in accordance with the study done in South Africa.(22)

A study done in china Hong Kong to assess the effect different dose of phenylephrine infusion in prevention of spinal anaesthesia induced hypotension showed that the blood pressure (systolic and diastolic) of parturient within prophylaxis group was significantly different from that of the placebo group.(21)

According to the study conducted by Lei Guo in the University of Ningxia in the republic of China: concluded that using 90-ug prophylactic bolus phenylephrine can effectively prevent post spinal hypotension in parturient during caesarean section.(35)

In this study the intraoperative heart rate was not significantly different between phenylephrine and standard care groups of mothers. But 9 (8.5%) parturients had intra-operative bradycardia due to high level of block. The incidence of bradycardia in this study was higher when we compare it with the study conducted in Bahirdar University; the incidence of bradycardia after the administration of spinal anaesthesia for caesarean section was 3%.(30)

The observed discrepancy may be due to study design, sample size difference and unknown maternal co-existing conditions (undiagnosed cardiac problems).

Studies and guidelines evidenced that phenylephrine is a selective alpha-1 adrenergic receptor agonist with virtually no beta-adrenergic activity. This important characteristic of phenylephrine is very important, because it has no direct effect on cardiac activity. But sometimes it can cause reflex bradycardia due to activation of the baroreceptor as side effect.

The incidence of nausea in this study was 53% in standard care group of mothers but the incidence of nausea in phenylephrine group of mothers was 21.4% which was significantly different. The incidence of hypotension in phenylephrine group of mothers was 16 (28.6%), from those mothers 12 (21.4%) developed intraoperative nausea. But the incidence of hypotension in standard care group of mothers were 31(63.3%) from those mothers 26 (53%) developed intraoperative nausea. This situation tells us when the incidence of intraoperative hypotension increases the incidence of intraoperative nausea also increases. Nausea is thought to be secondary to brainstem ischemia or reflex response to hypotension (decreased venous return).(2)

In this study the incidences of vomiting also significantly different in both groups of mothers. 4 (7.1%) of Parturient in phenylephrine prophylaxis group developed the incidence of vomiting but in standard care group of mothers the incidences of vomiting was 15 (30.6%) even though prophylactic metoclopramide was administered before the administration of spinal anaesthesia.(30)

In this study the incidences of nausea was lower (53%) in standard care mothers when it is compared with the study done in Bahirdar University which was 68%.(30) The observed difference may be due to pre-medication difference and pre-existing maternal conditions (motion sickness, IBS or PUD)

7. Strength and limitations

7.1. Strength of the study

- The socio demographic distribution of the study subject was homogenous
- The estimated sample size was adequate and reached within the allotted time frame

7.2. Limitation of the study

- Absence of control and randomization
- Not able to find sufficient articles with similar study design
- Blood pressure readings were not taken beat to beat, making it impossible to determine how long a hypotensive episode lasted between them

8. Conclusion and Recommendation

8.1. Conclusion

In this research the incidence of hypotension in the prophylactic group was 28.6% and the incidence of hypotension on non-prophylactic group was 63.3% and there was no significant difference on heart rate on both groups. Mothers who received prophylactic phenylephrine had stable blood pressure than those who didn't receive prophylactic bolus phenylephrine and the incidence of nausea in prophylactic group was 21.4% and 53% in the non-prophylactic group of mother and the neonatal outcome was comparable between the two groups.

8.2. Recommendations

We recommended that Administering 100 microgram bolus phenylephrine immediately after spinal anaesthesia is effective for prevention of post spinal hypotension in caesarean section and for better heart rate stability.

And we also recommend the researches to do multicentre study and if it is possible further randomized clinical trial and on-going research on neonatal outcome with various measurements is recommended.

Reference

1. Tsegaye H, Desalegne B, Wassihun B, Bante A, Fikadu K, Debalkie M, et al. Prevalence and associated factors of caesarean section in Addis Ababa hospitals, Ethiopia. Pan Afr Med J. 2019;34:1–9.

2. Maqbool MS. Efficacy of Prophylactic Phenylephrine in Prevention of Hypotension in Parturient Undergoing Spinal Caesarean Section. J Bahria Univ Med Dent Coll. 2022;12(02):93–9.

3. Siddik-Sayyid SM, Taha SK, Kanazi GE, Aouad MT. A randomized controlled trial of variable rate phenylephrine infusion with rescue phenylephrine boluses versus rescue boluses alone on physician interventions during spinal anesthesia for elective cesarean delivery. Anesth Analg. 2014;118(3):611–8.

4. Habib AS. A review of the impact of phenylephrine administration on maternal hemodynamics and maternal and neonatal outcomes in women undergoing cesarean delivery under spinal anesthesia. Anesth Analg. 2012;114(2):377–90.

5. Jaitawat S, Partani S, Sharma V, Johri K, Gupta S. Prophylactic administration of two different bolus doses of phenylephrine for prevention of spinal-induced hypotension during cesarean section: A prospective double-blinded clinical study. J Obstet Anaesth Crit Care. 2019;9(2):81.

6. Singla D, Kathuria S, Singh A, Kaul TK, Gupta S. Risk Factors for Development of Early Hypotension during Spinal Anaesthesia. 2006;22(4):387–93.

7. Heesen M, Klöhr S, Rossaint R, Straube S. Prophylactic phenylephrine for caesarean section under spinal anaesthesia: Systematic review and meta-analysis. Anaesthesia. 2014;69(2):143–65.

8. West Ward Pharmaceuticals. Phenylephrine Hydrochloride - Highlights of Prescribing Information. 2012;1–7. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/203826s000lbl.pdf

9. Following B, Committee MC, Agenda T, Medicines P, Kingdom U, Zealand N. A Justification for changing the current wording of the GSL classification of phenylephrine to include a cut-off point for solid dose products containing 10 mg or less of. Ophthalmology.

10. George RB, McKeen D, Columb MO, Habib AS. Up-down determination of the 90% effective dose of phenylephrine for the treatment of spinal anesthesia-induced hypotension in parturients undergoing cesarean delivery. Anesth Analg. 2010;110(1):154–8.

11. Fesseha N, Getachew A, Hiluf M, Gebrehiwot Y, Bailey P. International Journal of Gynecology and Obstetrics AVERTING MATERNAL DEATH AND DISABILITY A national review of cesarean delivery in Ethiopia. 2011;115:106–11.

12. Gedefaw G, Demis A, Alemnew B, Wondmieneh A, Getie A. Prevalence , indications , and outcomes of caesarean section deliveries in Ethiopia : a systematic review and meta-analysis. 2020;1–10.

13. Crystal GJ, Salem MR. The Bainbridge and the “Reverse” Bainbridge Reflexes: History, Physiology, and Clinical Relevance. 2012;114(3):520–32.

14. Doherty A, Ohashi Y, Downey K, Carvalho JCA. Phenylephrine infusion versus bolus regimens during cesarean delivery under spinal anesthesia: A double-blind randomized clinical trial to assess hemodynamic changes. Anesth Analg. 2012;115(6):1343–50.

15. Cohydration C. Prevention of Hypotension during Spinal Anesthesia for. 2005;(4):744–50.

16. Butwick AJ, Columb MO, Carvalho B. Preventing spinal hypotension during Caesarean delivery : what is the latest ? 2013;183–6.

17. Warltier DC, Ph MDD, Liu SS, Mcdonald SB. Current Issues in Spinal Anesthesia. 2001;(5):888–906.

18. Singh A, Jain K, Goel N, Arora A, Kumar P. Neonatal outcomes following prophylactic administration of phenylephrine or noradrenaline in women undergoing scheduled caesarean delivery: A randomised clinical trial. Eur J Anaesthesiol. 2022;39(3):269–76.

19. Shitemaw T, Aregawi A, Fentie F, Jemal B. Prophylactic ephedrine to prevent postspinal hypotension following spinal anesthesia in elective cesarean section: A prospective cohort study in ethiopia. J Obstet Anaesth Crit Care. 2019;9(2):75.

20. Eldemrdash AM, Gamaleldeen NM, Kamel Ahmed M, Ahmed SB. A Comparative Study between Protective Lung Ventilation versus Conventional Ventilation in Obese Patients Undergoing Abdominal Laparoscopic Surgery. J Anesth Clin Res. 2017;8(11).

21. Ngan Kee WD, Khaw KS, Ng FF. Comparison of phenylephrine infusion regimens for maintaining maternal blood pressure during spinal anaesthesia for Caesarean section. Br J Anaesth. 2004;92(4):469–74.

22. Bishop DG, Cairns C, Grobbelaar M, Rodseth RN. Prophylactic Phenylephrine Infusions to Reduce Severe Spinal Anesthesia Hypotension during Cesarean Delivery in a Resource-Constrained Environment. Anesth Analg. 2017;125(3):904–6.

23. Singh PM, Singh NP, Reschke M, Ngan Kee WD, Palanisamy A, Monks DT. Vasopressor drugs for the prevention and treatment of hypotension during neuraxial anaesthesia for Caesarean delivery: a Bayesian network meta-analysis of fetal and maternal outcomes. Br J Anaesth [Internet]. 2020;124(3):e95–107. Available from: https://doi.org/10.1016/j.bja.2019.09.045

24. Stewart A, Fernando R, McDonald S, Hignett R, Jones T, Columb M. The dose-dependent effects of phenylephrine for elective cesarean delivery under spinal anesthesia. Anesth Analg. 2010;111(5):1230–7.

25. das Neves JFNP, Monteiro GA, de Almeida JR, Sant'Anna RS, Bonin HB, Macedo CF. Phenylephrine for Blood Pressure Control in Elective Cesarean Section: Therapeutic versus Prophylactic Doses. Brazilian J Anesthesiol. 2010;60(4):391–8.

26. Vukotić AD, Green D, Jevđić JD, Vukotić MR, Petrović N, Stevanović PD. Comparison of efficacy and safety of preemptive infusion protocols of ephedrine and phenylephrine – prevention of hypotension and effects on hemodynamic parameters during spinal anesthesia for caesarean section. 2020;173–9.

27. Kumari MR, Sathyanarayana V. A study of phenylephrine administration for the prevention and treatment of hypotension in cesarean section during spinal anaesthesia: A randomised clinical trial. J Cell Mol Anesth. 2021;6(3):240–8.

28. Kee WDN, Khaw KS, Ng FF, Lee BB. Prophylactic Phenylephrine Infusion for Preventing Hypotension during Spinal Anesthesia for Cesarean Delivery. Anesth Analg. 2004;98(3):815–21.

29. Mohta M, Harisinghani P, Sethi AK, Agarwal D. Effect of different phenylephrine bolus doses for treatment of hypotension during spinal anaesthesia in patients undergoing elective caesarean section. Anaesth Intensive Care. 2015;43(1):74–80.

30. Assessment of the Magnitude and Risk Factors of Post Spinal Relevant Hemodynamics

Associated with Caesarean Section in Bahirdar University. 2022;7(1).

31. Chattopadhyay S, Das A, Pahari S. Fetomaternal outcome in severe preeclamptic women undergoing emergency cesarean section under either general or spinal anesthesia. J Pregnancy. 2014;2014.

32. Zhang W, Wu H. ED50 of intrathecal ropivacaine for cesarean section under prophylactic infusion of phenylephrine A consort study. Med (United States). 2017;96(44):1–5.

33. Cooper DW, Gibb SC, Meek T, Owen S, Kokri MS, Malik AT, et al. Effect of intravenous vasopressor on spread of spinal anaesthesia and fetal acid-base equilibrium. Br J Anaesth. 2007;98(5):649–56.

34. Jones GW, Samuel RA, Biccard BM. Management of failed spinal anaesthesia for caesarean section. South African Med J. 2017;107(7):611–4.

35. Guo L, Xu X, Qin R, Shi Y, Xue W, He L, et al. Prophylactic Norepinephrine and Phenylephrine Boluses to Prevent Postspinal Anesthesia Hypotension During Cesarean Section : A Randomized Sequential Allocation Dose-Finding Prophylactic Norepinephrine and Phenylephrine Boluses to Prevent Postspinal Anesth. 2023;

Annex 1:

INFORMATION SHEET

Title of the Research Project: THE EFFECT OF PROPHYLACTIC BOLUS PHENYLEPHRINE FOR THE MANAGEMENT OF POSTSPINAL HYPOTENSION DURING LECTIVE CESAREAN SECTION AT GANDI MEMORIAL HOSPITAL, ETHIOPIA,2023: PROSPECTIVE COHORT STUDY

Name of Principal Investigator: Gediwon G/Hiwot

Name of the Organization: Addis Ababa University, College of Medicine and health science. Department of Anaesthesia

Introduction: Greetings! My name is Gediwon G/Hiwot. I am a student at Addis Ababa University Department of Anaesthesia College of Medicine and Health Sciences in Masters of Science (MSc) in clinical anaesthesia. As part of this degree I am undertaking a research Project "The effect of prophylactic bolus phenylephrine on post-spinal hypotension during elective caesarean section at Gandhi memorial hospital, Ethiopia."

Purpose of the Research Project: The aim of this study is to determine the effect of prophylactic bolus phenylephrine on post-spinal hypotension during elective caesarean section at Gandhi memorial hospital. The information gained from this research will be used to make clinical recommendations and increase mother's satisfaction after caesarean section with spinal anaesthesia.

Procedure: The data collection will be conducted in Gandhi memorial hospital. Standard questioner is prepared to collect necessary information from patient chart and from the monitoring device used in the operation room.

Risk and /or Discomfort: the data will be taken from medical records and vital sign monitoring device, so it will not impose any harm on patients.

Benefits: The study has no direct benefit for those caesarean section delivery clients whose information is abstracted but indirectly beneficial if the result utilized by planners and clinicians Gandhi memorial hospital will get the result of the study.

Confidentiality: During data collection the patients name will not be taken, instead they will be identified by their card number in the chart. All questionaries' collected will be kept confidential and destroyed two years after the end of the project. The information collected will be used only for research purpose. The thesis will be submitted for marking to Addis

Ababa University Department of Anaesthesia College of Medicine and Health Sciences and displayed in the University Library and website. This study is also intended to be submitted for publication in scholarly journals.

Right to Refusal or Withdraw: Approval of the manager of the hospital and participant will be required to start data collection.

Person to contact: If you have any further questions or would like to receive further information about the project, please contact:

1. Gediwon G/Hiwot (Principal investigator):+251-937275782

2. Betelihem Girma (B.Sc. M.Sc.) (Advisor):

   Biruk Tesfaye (B.Sc. M.Sc.) (Advisor):

Thank you for reading the Information Sheet, and asking any questions that you might have had.

Annex 2:

Consent form English version

Dear participant:

Hello, my name is _____ and I am a data collector for research aimed at assessing the Efficacy of prophylactic phenylephrine on hemodynamic effects during caesarean section under spinal anaesthesia in Gandhi memorial hospital, Ethiopia. Since the study is not linked with any financial aid there is no direct incentives paid as a result of you taking part in the study. However, your legitimate participation in filling the questionnaire with real information is very important and highly appreciated.

I would like to assure you, that your name will not be written on this form and all the information gathered will be kept strictly confidential.

You can decide whether you want to take part in the questionnaire or not. I would like to assure you that there are no negative impacts you face because of not taking part in the study. Please feel free to ask any questions data collector nearby.

You can also contact principal investigator with address below:

1. Gediwon G/Hiwot +251937275782
    - Betelihem Girma (B.Sc. M.Sc.) (lecturer at AAU and Advisor):
    - Biruk Tesfaye (B.Sc. M.Sc.) (lecturer at AAU and Advisor):

Annex 3:

Consent form (Amharic version)

የመጠይቅ ፈቃድ

የተከበራችሁ የጥናቱ ተካፋዮች

ጤና ይስጥልን እኔ_____እባላለሁ፡፡ በቀዶ ጥገና ወሊድ የሰመመን መድሃኒት በሚሰጥበት ግዜ ላይ የሚከሰቱ የደም ግፊት እና የልብ ምት ለውጦች ላይ የሚሰራ ጥናት መረጃ ሰብሳቢ ነኝ:: ጥናቱ ለእርሶ ምንም አይነት የገንዘብ ጥቅም አያስገኝም ነገርግን የጥናቱ ውጤት በህክምና ዘርፍ ላይ ያሉትን ችግሮች ለመቅረፍ እና የታካሚዎችን ደህንነት የሚያረጋግጡ ህጎች እንዲስተካከሉ እና ሥራ ላይ እንዲውሉ የበኩሎን አስተዋፅዖ ያበረክታሉ፡ ፡ ስምዎ በዚህ ጥናት ላይ አይፃፍም፡፡ ስለዚህም የእርሶ ምላሽ ሚስጥራዊነቱ የተጠበቀ ነው::በዚህ መጠይቅ ላይ ለመሳተፍ መስማማትም ሆነ አለመስማማት ይችላሉ፡፡ ባለመስማማቶ ምንም የሚጎዱት ነገር የለም፡፡

ምንም አይነት ጥያቄ ካለዎት ቀጥሎ በተፃፈው አድራሻ ተመራማሪውን ማግኘት ይችላሉ፡ ፡

1. ገዲዎን ገ/ህይወት (ዋና ተመራማሪ): ስልክ +251937275782

2. በተልሕም ግርማ (አዲስ አበባ ዩኒቨርሲቲ መምህር እና የጥናቱ አማካሪ)
ብሩክ ተስፋየ (አዲስ አበባ ዩኒቨርሲቲ መምህር እና የጥናቱ አማካሪ)

የመረጃ ሰብሳቢ ስምና ፊርማ

ስም_____ፊርማ_____ቀን_____

Annex 4:

QUESTIONER FOR DATA COLLECTION

ADDIS ABABA UNIVERSTY

College of Medicine and Health Science

Department of Anaesthesia

Data collector Name:

Code:

Signature:_____

Supervisor's Name:

Code:

Signature:_____

Date:_____

Annex 5:

Data collection Questioner

Questioner developed for collection of data for the study "The effect of prophylactic bolus phenylephrine on postspinal hypotension during elective cesarean section at Gandhi memorial hospital, Ethiopia."

Part one: socio-demographic

SN	Question	Possible response	code	skipping
101	Card number			
102	Date of operation			
103	Prophylactic vasopressor	Yes	1	
		No	2	
104	Age of the mother			
105	Height of the mother			
106	Weight of the mother			
107	BMI			

Part two: Clinical characteristics

201	parity	Gravid		
		Para		
102	Previous History of C/S	Yes	1	
		No	2	
203	Indication for operation	Malpresantation	1	
		Previous C/S	2	

		Other……	3	
204	Mother haemoglobin level			
205	premedication			

Part three: Data during pre and intra-operative period

S.N	Question	Response	Code	Skipping
301	Dose of local anaesthetic given	……..mg		
302	Time of intrathecal injection	……..		
303	Level of sensory block before skin incision	T4-T5	1	
		T6-T7	2	

		T8-T10	3	
304	Skin incision time			
305	Delivery time			
306	Type of utero genic agent used	oxytocin	1	
		Ergometrine	2	
307	Apgar score	APGAR score at one minute….		
		APGAR score at five minute…		
308	Weight of the baby			
309	Does the patient have nausea intraop	Yes	1	
		No	2	
310	Does the patient vomiting intraop	Yes	1	
		No	2	

Part four: Intra op vital sign

Vital sign	**Baseline**	**At induction**	**5th Min**	**10th Min**	**15th Min**	**20th Min**	**25th Min**	**30th Min**	**35th Min**	**40th Min**
Systolic BP										
Diastolic BP										

MAP										
PR										
SpO2										

Part five: question related to anaesthetic intervention

S.N	Question	Response	Code	Skipping
501	Intra-op hypotension	Yes	1	If no skip 502 and 503
		No	2	
502	Intervention done for hypotension	By positioning		
		By fluid		
		By atropine		
		By Vasopressor (name and dose)…..		
		By blood		
503	Vasopressor boluses in study groups and total dose	Number of boluses vasopressor given…..		
		Total dose		
504	Intra-op bradycardia	Yes	1	If no skip 505
		No	2	
505	Atropine bolus and total dose	Number of bolus atropine given…		
		Total dose…		
506	Duration of the surgery			
507	Intravenous fluid given in intra-op period	…….ml		
508	Total blood loss	……ml		

Name of data collector……Signature

Name of supervisor……Signature