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**EFFECT OF PROPHYLACTIC EPHEDRINE ON BLOOD PRESSURE
CHANGES DURING CESAREAN SECTION UNDER SPINAL
ANESTHESIA AT TIKUR ANBESA SPECIALIZED HOSPITAL,
ETHIOPIA, 2018: PROSPECTIVE COHORT STUDY**

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**A THESIS SUBMITTED TO DEPARTMENT OF ANESTHESIA, COLLEGE OF
MEDICINE & HEALTH SCIENCES, ADDIS ABABA UNIVERSITY, IN PARTIAL
FULFILLMENT OF THE REQUIREMENTS FOR M.Sc. IN CLINICAL ANESTHESIA.**

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COLLEGE OF MEDICINE AND HEALTH SCIENCE

DEPARTMENT OF ANESTHESIA

MASTER OF SCIENCE IN CLINICAL ANESTHESIA

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Table of Contents

Acknowledgement.....	I
Abbreviations/Acronyms.....	VI
Abstract	VII
1. Introduction	1
1.1. Background.....	1
1.2. Statement of the problem.....	2
1.3. Justification.....	4
2. Literature review	5
2.1. Prevention of spinal induced hypotension.....	5
2.2. Ephedrine dose as a prophylaxis and other alternative vasopressor	6
3. Objective	8
3.1. General Objective.....	8
3.2. Specific Objective	8
4. Methods and Materials	9
4.1. Study Area.....	9
4.2. Study design and Study period	9
4.3. Source Population.....	9
4.4. Study Population	9
4.5. Inclusion and Exclusion criteria	10
4.5.1. Inclusion criteria.....	10
4.5.2. Exclusion criteria.....	10
4.6. Sample size and sampling procedure.....	10
4.6.1. Sample size calculation	10
4.7. Sampling procedure.....	12
4.8. Data collection.....	13
4.8.1. Data source, Data collection tools, procedure and personnel	13
4.9. Study variables	14
4.9.1. Dependent Variables	14
4.8.2. Independent variable	14
4.9. Operational Definition.....	15
4.10. Data processing and analysis.....	16

4.11.	Data quality assurance	16
4.12.	Ethical consideration	17
5.	Result	18
5.1.	Demographic and baseline vital signs Characteristics of patients	18
5.2.	Surgical and anesthesia factors.....	19
5.3.	Intraoperative characteristics	20
5.4.	Blood pressure Incidence between prophylactic and non-prophylactic groups.....	21
5.5.	Total dose required for treatment of hypotension	22
5.6.	Mean of the blood pressure trends between prophylactic and non-prophylactic group	23
5.7.	Trends of heart rate between prophylactic and non-prophylactic group.....	24
5.8.	The time of hypotension occurrence between prophylactic and non-prophylactic group .	25
6.	Discussion	27
7.	Strengths and Limitations of the study	30
7.1	Strengths of the study	30
7.2	Limitation of the study	30
8.	Conclusion and Recommendations	31
8.1	Conclusion.....	31
8.2	Recommendations	31
9.	Reference	32
Annexes		35
Annex 1:	Declaration.....	35
Annex 2:	INFORMATION SHEET.....	37
Annex 3:	Consent form	39
Annex 4:	Consent form (Amharic version)	40
Annex 5:	Data collection Questioner.....	41

List of Table

Table 1: Demographic and baseline vital signs of patients who underwent Elective cesarean section TASH, Addis Ababa, 2018.....	24
Table 2: Comparison of factor associated with surgery and anesthesia of patients who underwent Elective cesarean section at TASH , Addis Ababa, 2018.....	25
Table 3: Intraoperative Characteristics of patients who underwent Elective cesarean section at TASH, Addis Ababa, 2018.....	26

List of Figures

Figure 1: Sampling procedure for elective cesarean section at TASH	12
Figure 2: Incidence of hypotension between non-prophylactic and prophylactic groups under spinal anesthesia for elective cesarean section at TASH, 2018.	21
Figure 3: Median, range, and 25 percentile and 75 percentile of the Total rescue dose of nor-epinephrine between non-prophylactic and prophylactic group under spinal anesthesia for elective cesarean section from January 01, 2018 to April 27, 2018 at TASH.	22
Figure 4: Change in Systolic and diastolic arterial pressure of the prophylactic and non-prophylactic group under spinal anesthesia for elective cesarean section at TASH, 2018.....	23
Figure 5: Changes in mean heart rate in prophylactic and non-prophylactic group under spinal anesthesia for elective cesarean section at TASH, 2018.	24
Figure 6: Kaplan–Meier survival curves showing systolic blood pressure from the initiation of spinal anesthesia to end of surgery.	26

Abbreviations/Acronyms

APGAR	Appearance, Pulse, Grimace, Activity, Respiration
ASA	American Society of Anesthesiologists
BP	Blood Pressure
BMI	Body Mass Index
CEmONC	Comprehensive Emergency Obstetric and Newborn Care
CI	Confidence Interval
CS	Cesarean Section
CSE	Combined Spinal Epidural
DBP	Diastolic Blood Pressure
EC	Ethiopian Calendar
ECS	Elective Cesarean Section
EDHS	Ethiopia Demographic and Health Survey
Hgb	Hemoglobin
HR	Heart Rate
IV	Intra Venous
IU	International Unit
KG	Kilo Gram
L	Lumbar Vertebrae
MAP	Mean Arterial Pressure
NIBP	Non-Invasive Blood Pressure
PSH	Post Spinal Hypotension
SA	Spinal Anesthesia
SBP	Systolic Blood Pressure
SPSS	Statistical Packages for Social Science
T	Thoracic Vertebrae
TASH	Tikur Anbessa Specialized Hospital
WHO	World Health Organization

Abstract

Introduction: Spinal anesthesia is commonly used for caesarean section; however hypotension is a common clinical problem after spinal anesthesia. Prophylaxis Ephedrine can be used as an alternative to decrease this problem. Ephedrine can safely be administered by bolus IV route which is simple and cheap, because of its longer duration of action than other vasopressors.

Objective: The objective of this study is to determine the effect of prophylactic ephedrine on blood pressure changes after spinal anesthesia during elective cesarean section at Tikur Anbessa Specialized Hospital (TASH), 2018.

Materials and Methods: This institutional based Prospective observational cohort study used systematic random sampling to randomly select a total of 88 parturients scheduled for elective cesarean section under spinal anesthesia with 1:1 ratio. Patients in prophylactic group received prophylactic intravenous ephedrine (10mg) while the non-prophylactic group patients received fluid coload only. Comparisons of numerical variables between study groups were done using unpaired student t- test for symmetric data and Manny Whitney U test for asymmetric data. For categorical variable statistical difference between groups were tested using Chi square. The first hypotension incidence time between groups were analyzed by Kaplan-Meier survival analysis using the log-rank test. Significance was determined at P value <0.05. The results are presented by using text, table's, charts and graphs.

Results: Hypotension occurred in 50% of patients in non-prophylactic group and in 22.7% of patients in prophylactic group [$\chi^2(1, N=88) = 7.07, P= 0.008$]. Prophylactic group had higher mean values of systolic and diastolic blood pressure starting from 5th minute until the 20th minute after induction than the non-prophylactic group ($P < 0.05$). The first hypotension incidence time, number of patient that required rescue vasopressor, total dose of rescue vasopressor and incidence of Nausea were significantly different between the groups. Differences in heart rate between groups were not statistically significant.

Conclusion: Combination of coload of fluid with prophylactic 10 mg bolus ephedrine reduced the occurrence of hypotension and greater hemodynamic stability was achieved following spinal anesthesia in parturient undergoing cesarean delivery.

1. Introduction

1.1. Background

Cesarean section is the most common major surgical procedure done with increasing frequency in obstetrics. Optimal outcome require an effective teamwork among obstetrician, anaesthetist and nurse. Goals of anesthesia for cesarean section (CS) must include the comfort and safety of the parturient, and the well-being of the fetus and neonate(1, 2).

In the past, general anesthesia was considered to be the technique of choice. However, the proportion of caesarean sections performed under general anesthesia has dropped significantly(3).

The type of anesthesia chosen for caesarean section is dependent on numerous factors such as the urgency and indication of the operation, maternal preference as well as coexisting medical problems(3).

Spinal anesthesia owing to the perceived advantages of a clear end point in locating the subarachnoid space, fast onset of local anesthetic effect, and reduced risk of local anesthetic toxicity is commonly used for caesarean section. Advantages for the mother include remaining awake for the birth, avoiding risks of general anesthesia and facilitating effective postoperative pain relief(4, 5).

Spinal blocks also have the advantage of being more cost-effective when compared with epidural anesthesia(3). To successfully administer spinal anesthesia for cesarean delivery, however, requires consistent attention to details to minimize side effects such as nausea, vomiting, failed or total block and the predominant one and most common being maternal hypotension(4, 5).

Hypotension is a common clinical problem faced by anesthetists after spinal anesthesia induction and if severe it can lead to both maternal and fetal morbidity and mortality. Severe hypotension poses serious risks to mother (such as loss of consciousness, aspiration and even cardiac arrest) and to the baby (such as lack of oxygen and brain damage)(4, 5).

The incidence of hypotension during spinal anesthesia for caesarean section is reduced by different method, such as administering intravenous fluids, drugs such as ephedrine or phenylephrine, or by leg compression and elevation(4).

Ephedrine is an indirect acting non-specific adrenergic agonist which increases blood pressure mainly by increasing cardiac output (beta effect) and vasoconstriction (alpha effect). The onset of action after intravenous administration is immediate; the onset of action after intramuscular administration is 10 to 20 minutes(6).

According to the 2016 American Society of Anesthesiologists (ASA) Intra Venous (IV) ephedrine and phenylephrine both may be used for preventing hypotension during neuraxial anesthesia(7). Ephedrine has been the vasopressor of choice in obstetric anesthesia; Because of the mixed alpha and beta effects it does not reduce uterine blood flow, unlike pure alpha agonists(8).

In most areas, it is a practice to give prophylactic bolus ephedrine by intravenous (IV) or add ephedrine to IV fluid bottle after subarachnoid block for caesarean section to prevent hypotension(9). Bolus IV injection of ephedrine is more effective than infusion to prevent arterial hypotension during Caesarean section(10).

1.2. Statement of the problem

The rate of CS has increased dramatically worldwide. According to the latest data from 150 countries, currently 18.6% of all births occur by CS, ranging from 6% to 27.2% in different region of the world(11).

The 2016 Ethiopian demographic and health survey (EDHS) found that 2% of live births in the 5 years before the survey were delivered by CS. One percent of the CS was decided after the onset of labor pains, compared to the less than 1% that were decided before onset of labour pains. The caesarean section rate in urban areas is more than 10 times (11%) that of in rural areas (1%). 21.4% of new born is delivered by CS in Addis Ababa, capital city of Ethiopia(12).

A national review of cesarean delivery in Ethiopia in 2011 showed that overall institutional CS rate was 18%, which varied between 46% in the private for-profit sector and 15% in the

public sector. In the public and not-for-profit sectors, approximately 85% of cesareans were emergencies (and 15% electives), compared with 47% in the private sector(13).

With increasing CS rate, the complication also needed to be addressed. Maternal hypotension is the most common complication during CS under spinal anesthesia with a reported incidence greater than 80% if not prevented.(14) Moreover surveys on 40,000–550,000 spinal anesthetics indicate an incidence of cardiac arrest from 0.04– 1/10,000(15).

Spinal hypotension can occur precipitously and, if severe, can result in important maternal and perinatal adverse outcomes, such as maternal nausea and vomiting, fetal acidosis and can be an important contributory factor for maternal death related to regional anesthesia. As a consequence, prevention of spinal hypotension has been a key research area with in the field of obstetric anesthesia(16).

Hypotension during obstetric spinal anesthesia has traditionally been managed by such measures as fluid preloading, positioning of the patient (Lower limb compression and elevation techniques) and the use of vasoconstrictors. However, in the anesthesia practice, prevention and management of hypotension related to spinal anesthesia remains a difficult problem and there was no consensus on its optimal management(17).

In most health institution in Ethiopia, practice of prevention of hypotension after spinal anesthesia is done by administering preloading or coload of crystalloid fluid and ephedrine or other vasopressor drugs are given as Intra Venous (IV) boluses for treatment after hypotension occurred.

In unpublished study done in Addis Ababa comparing preloading versus co-loading of crystalloid, coload was better than preloading in the prevention of hypotension after spinal anesthesia even though the incidence were still high in both group(18).

1.3. Justification

The high incidence of post spinal hypotension (PSH) with most of the pharmacological and non-pharmacological methods suggests the need for multimodal protocols for prevention and management of this problem. Spinal hypotension in cesarean section is a common daily situation facing all anesthetists. This necessitate for researches focusing on simple and rapid protocols that can be easily applied by anesthetists with moderate and low experience and minimal need to complex devices.

The incidence of PSH is still high with all fluid loading protocols; thus, the use of fluid loading as a sole method for prophylaxis might not be satisfactory for many anesthetists as it won't avoid the occurrence of PSH. Best prophylaxis of maternal hypotension during caesarean section is still controversial(19). The combination of simultaneous rapid crystalloid infusion with vasopressor has been suggested without harming mother and baby.

Prophylaxis Ephedrine can safely be administered by bolus IV route which is simple and cheap, because of its longer duration of action than other vasopressors. This property is advantageous for those facilities expensive controlled infusion devices are unavailable.

Hence the aim of this study is to determine the effect of standard prophylaxis ephedrine on blood pressure change during elective caesarean section under spinal anesthesia, the result will show alternative management for anesthetists which can improves the outcome of the mother and the baby leading to better client satisfaction.

In addition to this, research lack on this specific area in our context and this study may serve as a base line for further country wide study.

2. Literature review

Despite many research in the past, hypotension during spinal anesthesia for cesarean delivery remains a common clinical problem that is associated with morbidity for both mother (nausea and vomiting) and fetus (fetal acidosis)(17). The prevention and treatment of maternal hypotension associated with spinal anesthesia for CS remains a problem. Protocols that aim to prevent hypotension during spinal anesthesia for CS may result better outcomes than protocols of treatment after the hypotension occurred(20).

2.1. Prevention of spinal induced hypotension

In A study done by Rout CC, even though volume preload in the elective cesarean section is advocated, hypotension associated with spinal anesthesia for cesarean section did not eliminated by volume preloading in the supine wedged patient(14). another study shows that Crystalloids were more effective than not giving any fluids and colloids were even more effective than crystalloids in preventing hypotension following spinal anaesthesia at caesarean section(4).

A meta-analysis done on the timing of fluid administration for prevention of spinal anesthesia concluded With the available evidence that fluid coload is preferred to preloading because it carries more success or at least the same results in prevention of PSH with the advantage of being less time consuming(21).

Based on the evidences, even though fluid coload is effective in preventing maternal hypotension after CS than pre loading fluid there is still high incidence of hypotension. Thus adding prophylactic vasopressor becomes the current practice for preventing the complication of spinal anesthesia(16).

In a research comparing prophylactic ephedrine with fluid co-loading only, the frequency of hypotension was significantly higher (56%) in the coload group as compared to the ephedrine group (16%). Additional ephedrine bolus was given to more patients (54%) in the fluid coload compared to groups with prophylactic ephedrine(8%)(5). This result is also supported

by other study with Ephedrine prophylactic group significantly more effective than control (no fluid) or crystalloid coload group in preventing hypotension(4).

In another study comparing prophylactic ephedrine with coload of crystalloid in Elective Cesarean Section (ECS) the mean of highest and lowest heart rate in the ephedrine group was higher than those of coload group. There were significant lower incidences of hypotension and nausea and vomiting in the ephedrine group compared with the coload group (4 [19%] vs. 12 [57.1%])(9). Same result was reported with prophylactic ephedrine given by infusion along with fluid contributes to less incidence of intraoperative nausea and vomiting. The first rescue ephedrine time in the ephedrine group was significantly longer (14.9 ± 7.1 min vs. 7.9 ± 5.4 min) than that of the coload group. There were significant decrease total doses of rescue ephedrine required in the ephedrine group(22).

Research done in Africa, Nigeria, 70.0% in the non-prophylactic group and 40.0% in the ephedrine group had hypotension. This occurred most frequently at 5 min in non-prophylactic group but at 10 min in the ephedrine group. Eleven hypotensive patients in non-prophylactic group (52.4%) required ephedrine boluses to maintain blood pressure compared with 4 (33.3%) in ephedrine group(8).

2.2. Ephedrine dose as a prophylaxis and other alternative vasopressor

The dose of ephedrine for prophylactic use is still controversial. While increasing the dose will decrease incidence of hypotension, the side effect of ephedrine such as tachycardia and hypertension will be the concern. The rate of maternal hypotension associated with spinal anesthesia for cesarean section was found higher in women receiving only a 10-mg prophylactic bolus of ephedrine in a random trial study done in France. Increasing the dose of the prophylactic bolus of ephedrine to 15 or 20 mg significantly reduced the incidence of hypotension without increasing the incidence of undesirable tachycardia and/or hypertension(19).

On another study, where three groups were compared at a dose of 10mg, 15mg, and 20mg prophylactic IV ephedrine and significantly higher incidence of reactive hypertension found in the groups receiving 20 mg ephedrine(20). This result was supported by a study that reported significant dose-response relationships were found for hypotension, hypertension,

and umbilical arterial pH. The dose at which the likelihood of benefit marginally outweighed the risk of harm was 12mg and the use of larger doses of ephedrine does not completely eliminate hypotension but causes reactive hypertension and a minor decrease in umbilical arterial pH(6).

Other vasopressor drugs for prophylaxis of spinal hypotension are also used in the practice of anesthesia. In Comparing ephedrine with phenylephrine with randomized, comparative clinical study there was no statistically significant difference in umbilical arterial, umbilical venous pH, incidence of fetal acidosis and Apgar scores. The number of hypotensive episodes, vasopressor doses for treatment of the first hypotensive episode and the total number of doses used during the study period were comparable. More patients receiving ephedrine (24.5%) developed tachycardia than those receiving phenylephrine (3.8%) which was significant. Bradycardia was more common with phenylephrine, with 39.6% of patients in phenylephrine Group as compared to only 1.9% of patients in ephedrine Group developing a heart rate <60 beats/min after vasopressor administration(23). the result is also supported with another study with No significant differences in hypotension were seen between ephedrine and phenylephrine(4).

Another study that compare ephedrine with 5-HT₃ receptor antagonists 'granisetron' and 'ondansetron' in preventing hypotension of spinal anesthesia during cesarean section in Egypt showed all the three prophylactic drugs reduces the severity of spinal-induced hypotension, the need for rescue vasopressor, and incidence of nausea. However, significantly faster recovery of sensation down to the level of T12 was detected between granisetron group and the other groups(24).

Summary of literature

Most of the study showed the decrease of incidence of hypotension when ephedrine is administered as a prophylaxis. The route of administration are different with bolus IV and infusion at different rate reported in the literatures. The dose administered as a prophylaxis are controversial but meta analysis showed safe dose of ephedrine is below 14mg.

3. Objective

3.1. General Objective

The objective of this study is to determine the effect of prophylactic ephedrine on blood pressure changes during elective cesarean section under spinal anesthesia at Tikur Anbessa Specialized Hospital (TASH), 2018.

3.2. Specific Objective

- To compare the incidence of hypotension after spinal anesthesia between prophylactic and non-prophylactic group.
- To compare the blood pressure variation at different time between prophylactic and non-prophylactic group.
- To compare the first hypotension incidence time between prophylactic and non-prophylactic group.

4. Methods and Materials

4.1. Study Area

The study was conducted at Tikur Anbessa Specialized Hospital (TASH) in Addis Ababa, the capital city of Ethiopia. With an area of 527 square kilometers and 10 sub cities, it is the largest city in the country. The city has 12 government hospitals. TASH is Ethiopia's largest referral hospital. It offers diagnosis and treatment for approximately 370,000- 400,000 patients a year with nearly 8000 surgeries performed annually with 14 operation rooms (OR).

The Hospital provides Gynecologic, Obstetric and many other reproductive health services. On average 25 new borns delivered each day in the hospital. The hospital has one operation theatre dedicated only for cesarean section with additional emergency OR. An average number of caesarian deliveries done at the hospital is eight to ten per day out of which one third are elective cesarean section.

4.2. Study design and Study period

An institutional based Prospective observational cohort study design was conducted from January 01, 2018 to April 27, 2018 at TASH, Addis Ababa, Ethiopia.

4.3. Source Population

All mothers who gave birth by elective caesarian section under spinal anesthesia at TASH, Addis Ababa, Ethiopia.

4.4. Study Population

All mothers who gave birth by elective caesarian section under spinal anesthesia at TASH during the study period.

4.5. Inclusion and Exclusion criteria

4.5.1. Inclusion criteria

- Pregnant mothers falling in classification of American Society of Anesthesiologists(ASA) as Class-I and II
- Gestational age between 38–42 weeks,
- BMI <35, and
- Induction using 0.5% Isobaric bupivacaine

4.5.2. Exclusion criteria

- Refusal to participate on the study by the mother,
- Incomplete data
- Rescue vasopressor drugs other than nor-epinephrine,
- Mothers with combined spinal epidural anesthesia,
- Mothers with Preoperative hypotension,
- Pregnancy-induced hypertension (PIH), eclampsia, essential hypertension (diagnosed on history, BP records and lab findings on antenatal visits),
- Any known cardiovascular disease (valvular heart disease, cardiomyopathies),
- Failed spinal block or total spinal converted to general anesthesia and
- CS indication secondary to Placenta previa will be excluded from the study.

4.6. Sample size and sampling procedure

4.6.1. Sample size calculation

Sample size was determined by using Epi info version 7 stat calc program(25) and re checked by manual calculation using double proportion formula. By considering a power of 80%, confidence interval 95% and ratio of unexposed to exposed 1:1. Incidence of hypotension which is estimated from previous study done in Nigeria(8), with 40% incidence of hypotension in ephedrine prophylactic group and 70% incidence of hypotension in non-prophylactic group reported, A sample size of 44 patients per group was determined.

$$n_1 = \frac{(Z_{\alpha/2} + Z_{1-\beta})^2 \bar{p} \bar{q} (r+1)}{r (P_1 - P_2)^2} \quad n_2 = r n_1$$

$$\bar{p} = \frac{p_1 + r p_2}{r+1} \quad \bar{q} = 1 - \bar{p}$$

n_1 = number of exposed

n_2 = number of unexposed

$Z_{\alpha/2}$ = 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%)

P_1 = proportion of exposed with disease and $q_1 = 1 - p_1$

P_2 = proportion of unexposed with disease and $q_2 = 1 - p_2$

r = ratio of unexposed to exposed

$$p_1 = 0.7 \text{ and } p_2 = 0.4 \quad r=1$$

$$\bar{p} = \frac{0.7 \times (1 \times 0.4)}{1 + 1} = 0.55$$

$$\bar{q} = 1 - 0.55 = 0.45$$

$$n_1 = \frac{(1.96 + 0.84)^2 \times 0.55 \times 0.45 \times (1+1)}{1(0.7-0.4)^2} = \frac{3.8808}{0.09}$$

$$n_1 = 43.12 \sim 44$$

$$n_2 = 44$$

4.7. Sampling procedure

Selection of participant was carried out by using systematic random sampling technique each day before elective cesarean section begun. Situational analysis was done in the study hospital and we assumed there will be 3 elective CS during working days, and a total of 180 CS in the study period. This yield a “K” value of two ($K=2$), and every k^{th} unit was selected. Starting at a random selection using lottery method between the first two elective CS, every selected participant after then was placed to either group based on the responsible anesthetist’s management plan (whether they received Ephedrine prophylaxis or not). This continues until the desired sample in each groups were achieved.

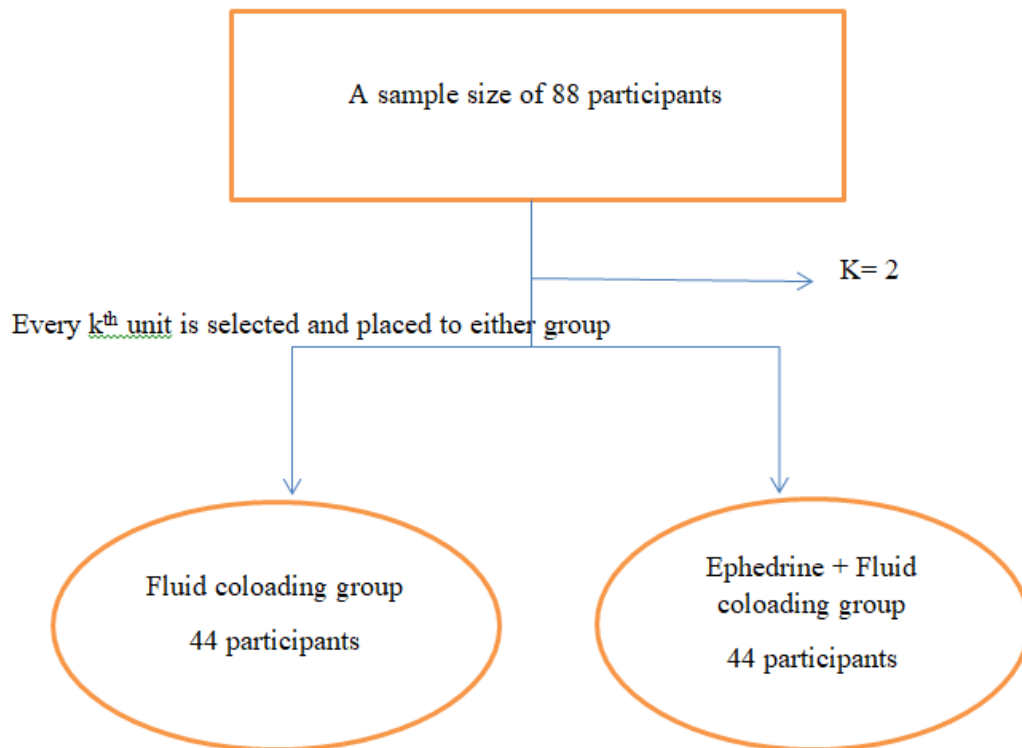


Figure 1: Sampling procedure for elective cesarean section at TASH from January 01, 2018 to April 27, 2018 at BLSH, Ethiopia.

4.8. Data collection

4.8.1. Data source, Data collection tools, procedure and personnel

Data was collected from selected study participants using pretested questionnaire from January 01, 2018 to April 27, 2018 at TASH, Ethiopia.

In the hospital where the present study was done, the routine anesthesia management trend before elective CS was as follows:

Pre anesthetic evaluation was done in the morning of the surgery. Vital sign, Organ-function test together with history and physical examinations are among the parameters used to decide for anesthesia plan, weather to cancel or proceed. On arrival to the operating room, patients were pre medicated with metoclopramide 10mg IV bolus before induction of anesthesia. Two 18 gauge IV cannula needle is secured on bilateral arms. While preparing the monitoring equipment, during preparation of the skin and during spinal anesthesia induction, lactated Ringer's or normal saline solution were administered for coloadng as fast as possible by both IV line secured. Sub arachnoid block was done in sitting position after strict aseptic technique. Isobaric bupivacaine with 0.5% of 2.5ml using 23 gauge needle were administered at L3-L4 level for all parturient. After intrathecal administration patients were positioned to supine position with slight head elevation using pillow.

Anesthetic management including intra-op treatment of hypotension, selection of fluid protocols and vasopressor prophylaxis given before spinal anesthesia was at the discretion of the personnel anesthetist assigned to each case. Most anesthetists use fluid coloadng while administering the spinal anesthesia while others give additional prophylaxis drug such as ephedrine 10 mg IV bolus. The prophylactic ephedrine is administered during the procedure of induction of anesthesia. During this time data collectors identify patients who were given prophylactic ephedrine and who were not and assign the study participant to the appropriate group.

The data collection was done by three anesthetists after training was given. Data collectors ask and record necessary preoperative information, review charts and document intraoperative information. Baseline blood pressure using non-invasive blood pressure (NIBP) monitor and heart rate (HR) using pulse-oximeter were recorded and continued every 5 minutes after then for 40 minutes. The level of sensory block was evaluated with cold sensation 5 min after spinal anesthesia. The principal investigator checked completeness of data every day.

4.9. Study variables

4.9.1. Dependent Variables

- Blood Pressure

4.8.2. Independent variable

Socio-demographic variables:

- Age
- Weight
- Height
- BMI

Procedure related variables:

- Duration of incision to delivery time
- Blood loss during surgery
- Type of utero genic agent used (Oxytocin or Ergometrine),
- Duration of surgery

Maternal and obstetrics characteristics

- Parity
- Previous History of CS
- Indication for CS
- Mother Hemoglobin level

Anesthesia related variables:

- Amount of fluid pre-loading
- Pre-op medication
- Level of sensory block
- Exposure variables; prophylaxis ephedrine given or not given

4.9. Operational Definition

- ❖ **American Society of Anesthesiologists (ASA) physical status classification:** developed by the ASA taskforce which classify patients according to their physical status (systemic well-being)
 - ASA class I:** normal healthy patient except the surgical complaint he/she had
 - ASA class II:** a patient with a mild systemic disease without substantive functional limitation
 - ASA class III:** a patient with severe systemic disease with substantive functional limitation
 - ASA class IV:** a patient with severe systemic disease that is a constant threat to life
 - ASA class V:** moribund patient who is not expected to survive without the operation
- ❖ **Baseline value:** measurement taken before induction or spinal anesthesia given
- ❖ **Prophylactic group:** Patients that received prophylactic intravenous bolus ephedrine (10mg) along with fluid coload.
- ❖ **Non-prophylactic group:** patients that received fluid coload only.
- ❖ **Hypotension:** defined as a decrease in SBP $\geq 30\%$ of baseline or systolic arterial blood pressure less than 80 mm Hg.(26)
- ❖ **Hypertension:** defined as an increase of SBP $> 20\%$ of baseline(8, 26)
- ❖ **Tachycardia:** an increase in heart rate of $\geq 20\%$ of the baseline value or heart rate greater than 120(8, 27)
- ❖ **Bradycardia:** a decrease in heart rate $\geq 30\%$ from baseline value or heart rate less than 60.(8, 27)
- ❖ **Failed spinal:** spinal anesthesia was attempted, but no block resulted and inadequacy relating to the extent, quality, or duration of local anesthetic action for the proposed surgery.
- ❖ **Co loading:** giving crystalloid fluid while at the same time performing spinal anesthesia
- ❖ **Post spinal hypotension:** hypotension that occurs after administration of intrathecal local anesthetics.
- ❖ **The level of sensory block:** is loss of cold sensation and will be recorded bilaterally in the anterior axillary line or mid-clavicular line.

4.10. Data processing and analysis

Data was coded, edited and then entered and cleaned using Epi Info version 7 and exported and analyzed using Statistical package for Social Sciences (SPSS) software version 20.0. Shapiro Wilk test were used to test for distributions of data while homogeneity of variance were assessed using Levene's test for equality of variance. Numeric data were described in terms of mean $\pm$ SD for symmetric and median (Interquartile range) for asymmetric data respectively. Comparisons of numerical variables between study groups were done using unpaired student t- test (independent t- test) for symmetric data (Age, Height, Weight, BMI, Maternal Hemoglobin level, Systolic BP, Diastolic BP, and Heart Rate). Manny Whitney U test were used for asymmetric data (Para, Gravida rescue dose of nor-epinephrine, APGAR, Weight of the Baby, Duration of surgery, Blood loss, Intra op IV fluid, Incision to Delivery Time). Significance was determined at P value <0.05 .

Frequency and percentage were used to describe categorical variable(Level of sensory block, Indications for caesarean section, Incidence of nausea between groups, Intra-op Bradycardia between groups, incidence of hypotension and number of patients rescue vasopressor received) and statistical difference between groups were tested using Chi square or Fisher's exact test, as appropriate. The incidence and timing of hypotension occurrence was further analyzed by using Kaplan-Meier survival analysis, with comparison between groups using the log-rank test. Significance was determined at P value <0.05 . The results are presented by using text, table's, charts and graphs.

4.11. Data quality assurance

To assure the quality of data, training on the objectives and relevance of the study and brief Orientations on the assessment tools were provided for data collectors. In case of missed measurement during intra-operative period, electronic data store of the monitoring equipment were recalled and back traced and data was filled. During data collection, each questioner was revised by the investigator for being complete and appropriate.

4.12. Ethical consideration

The study was conducted after approval by Addis Ababa University, Ethical review board to conduct the study. Before commencing the study, verbal informed consent was obtained from all parturient after full explanations of the goals and procedures of the study. After taking permission from the hospital and study participant the data collection was conducted.

5. Result

5.1. Demographic and baseline vital signs Characteristics of patients

Forty four patients were studied in each group. All the demographic data and base line vital signs were normally distributed (Shapiro Wilk test, p value > 0.05) and comparisons between groups were made using independent t- test. No significant differences were detected in maternal demographic data and vital sign between the two groups (Table1).

Table 1: Demographic and baseline vital signs of patients who underwent Elective cesarean section at black lion specialized Hospital, from January 01, 2018 to April 27, 2018 Addis Ababa.

Characteristics	Prophylactic not given	Prophylactic given	P-value
Age(yr)	27.52 ± 2.79	27.38 ± 2.68	0.816
Height (cm)	160.90 ± 6.41	159.77 ± 6.26	0.403
Weight (kg)	66.93 ± 10.10	69.43 ± 9.54	0.236
BMI (kg/m ²)	25.89 ± 3.98	27.21 ± 3.56	0.105
Maternal Hemoglobin level(gm./dl)	13.10 ± 1.07	12.82 ± 0.82	0.178
Baseline Systolic BP	125.88 ± 8.15	127.90 ± 8.80	0.267
Baseline Diastolic BP	71.27 ± 12.10	72.54 ± 12.28	0.626
Baseline HR	92.50 ± 9.45	93.84 ± 10.58	0.533

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

5.2. Surgical and anesthesia factors

Numeric variables (Gravida, Para and Time from anesthesia Induction to Skin Incision) with surgical and anesthesia factors are not normally distributed (Shapiro Wilk test, p value < 0.05) and comparisons between groups were done using Mann Whitney U test. Indications for caesarean section and Level of sensory block between groups were compared using chi-square test. Results between groups were comparable (Table 2).

Table 2: Comparison of factor associated with surgery and anesthesia of patients who underwent Elective cesarean section at TASH , from January 01, 2018 to April 27, 2018

Parameter	Prophylactic not given	Prophylactic given	P-value
Gravida	3 (4)	3 (4)	0.431
Para	2 (3)	2 (4)	0.982
Indications for caesarean section			0.854
Malpresentation	9 (20.5%)	7 (15.9%)	
Cephalopelvic disproportion	5 (11.4%)	5 (11.4%)	
previous caesarean section scar	30 (68.2%)	32 (72.7%)	
Level of sensory block			0.483
T4-T5	9 (20.5%)	11 (25%)	
T6-T7	13 (29.5%)	18 (40.9%)	
T8-T9	16 (36.4%)	12 (27.3%)	
T10	6 (13.6)	3 (6.8%)	
Time from anesthesia Induction to Skin Incision (minute)	6 (1)	6 (1)	0.779

Values are presented as: Median (IQR): Mann Whitney u test, Number (%): chi-square test and p<0.05 is statistically significant.

5.3. Intraoperative characteristics

Numeric variables (Incision to Delivery Time, Oxytocin Dose, Intra op IV fluid, Blood loss, Duration of surgery, Weight of the Baby and APGAR) of intraoperative characteristics are not normally distributed (Shapiro Wilk test, p value < 0.05) and comparisons between groups were done using Mann Whitney U test. Intra-op Bradycardia and incidents of nausea between groups were compared by chi-square test. Vomiting episodes did not occur in both groups intra-operatively. All Apgar scores at 1 and 5 minute were greater than 7 (table 3).

Table 3: Intraoperative Characteristics of patients who underwent Elective cesarean section at TASH , Addis Ababa, 2018

Parameter	Prophylactic not given	Prophylactic given	P-value
Oxytocin Dose (IU)	20.0 (10)	20.0 (10)	0.726
Incision to Delivery Time	5 (7)	5 (5)	0.529
Intra op IV fluid (ml)	2500 (2500)	2500 (1800)	0.697
Blood loss	500 (700)	500 (500)	0.656
Duration of surgery	40 (20)	40 (20)	0.515
Weight of the Baby(kg)	2.7 (0.7)	2.9 (0.7)	0.263
APGAR at 1min	8 (3)	8 (3)	0.251
APGAR at 5min	9 (2)	9 (2)	0.473
Incidence of nausea between groups			0.049*
YES	15 (34.1%)	7 (15.9%)	
NO	29 (65.9 %)	37 (84.1%)	
Intra-op Bradycardia between groups			0.241
YES	3 (6.8%)	0 (0.0%)	
NO	44 (93.2%)	44 (100%)	

Values are presented as: number (%):chi-square test, median (IQR): Mann Whitney u test and p<0.05 is statistically significant. [* = statistically significant]

5.4. Blood pressure Incidence between prophylactic and non-prophylactic groups

Blood pressure was recorded every five minute starting from induction of anesthesia. There were statistically significant decrease in the incidence of hypotension in ephedrine prophylactic group with 10 [22.7% (95% CI, 10%– 36%)] compared with non-prophylactic group 22 (50.0% [95% CI, 35%– 65%]) incidence at the end of the study period, $X^2(1, N=88) = 7.07, P= 0.008$.

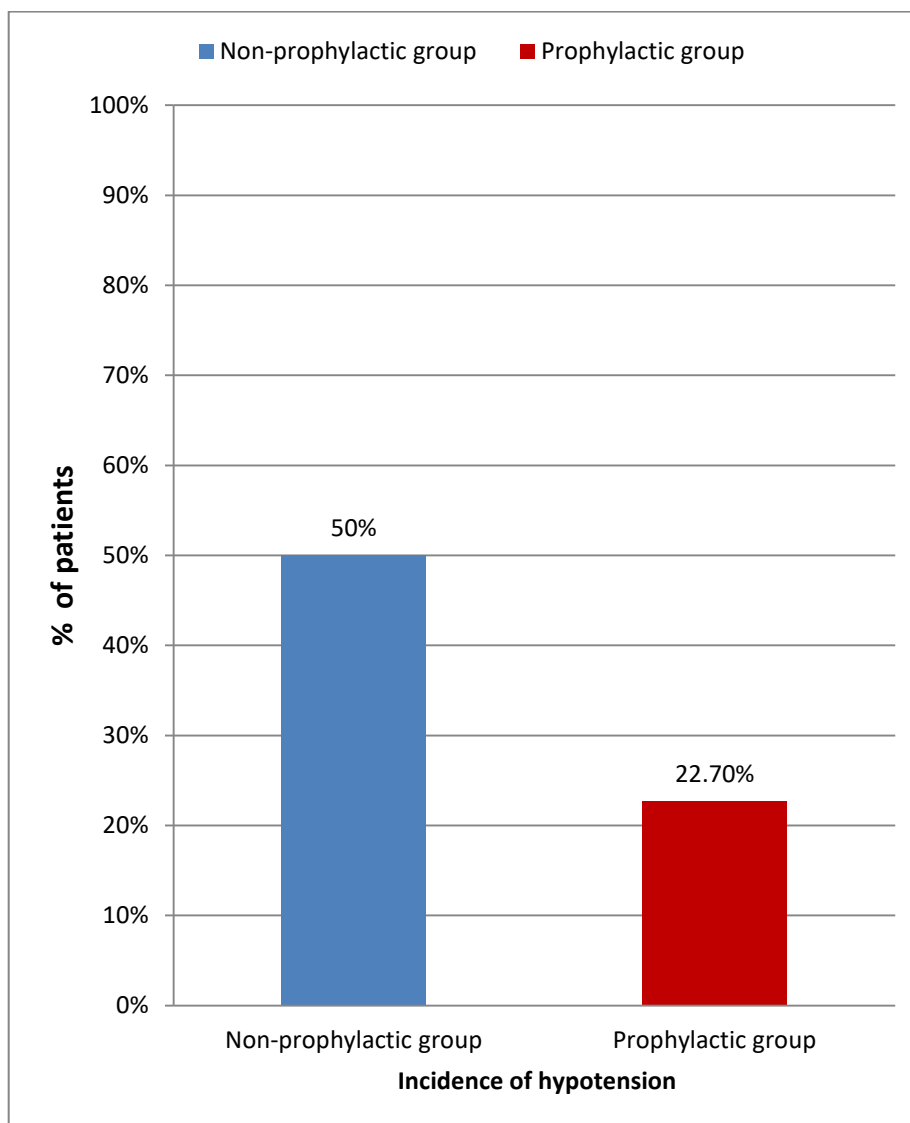


Figure 2: Incidence of hypotension between non-prophylactic and prophylactic groups under spinal anesthesia for elective cesarean section at TASH, 2018.

5.5. Total dose required for treatment of hypotension

In the non-prophylactic group for 19 [43.2% (95% CI, 27.9%– 58.4%)] patients rescue vasopressor (nor-epinephrine) was administered compared to 6 [13.6% (95% CI, 3.0%– 24.1%)] of the ephedrine prophylactic group intra operatively for the treatment of hypotension [$\chi^2(1, N=88) = 9.44, P= 0.002$].

The drug norepinephrine was used for treatment of hypotension in both groups. The total dose of rescue norepinephrine in microgram given for treatment of hypotension intra-operatively were compared using Mann Whitney U test and showed statistically significant difference between groups with median and interquartile range of [7.5(5) versus 15(15)] ($P= 0.043$).

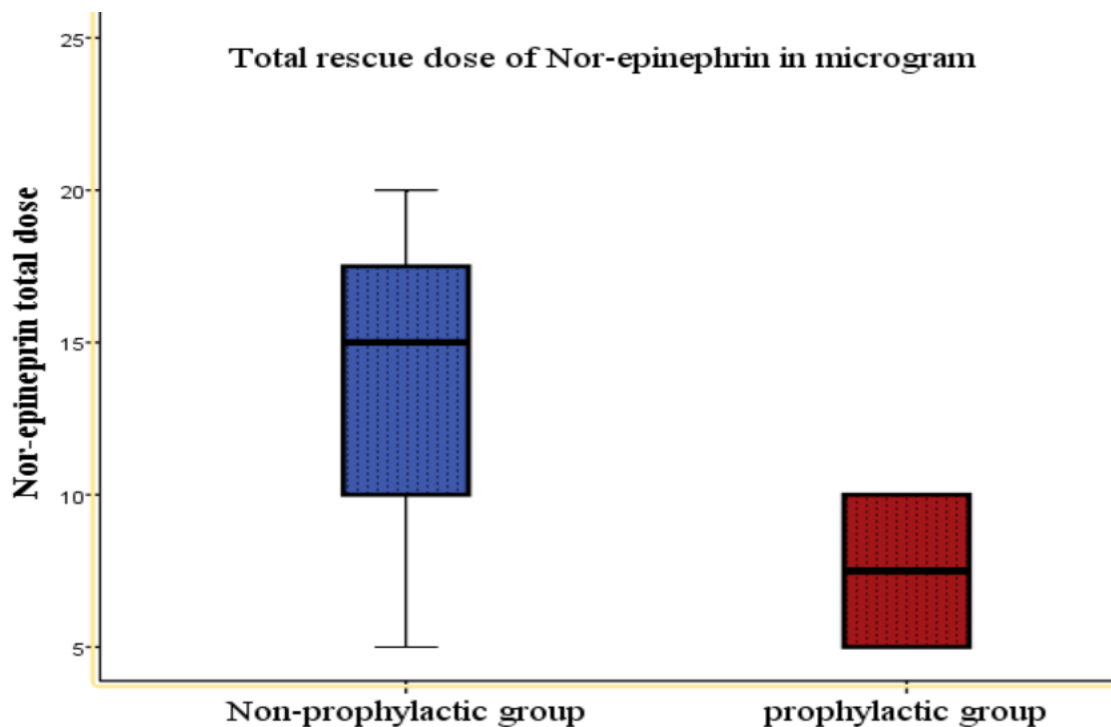


Figure 3: Median, range, IQR of the Total rescue dose of nor-epinephrine between non-prophylactic and prophylactic group under spinal anesthesia for elective cesarean section from January 01, 2018 to April 27, 2018 at TASH.

5.6. Mean of the blood pressure trends between prophylactic and non-prophylactic group

Mean of the blood pressure trends between groups are presented on Fig. 4. Starting from 5 minute into the study, patients in the ephedrine group maintained significantly higher blood pressures than those in the non-prophylactic group ($P < 0.05$) until 20 minute in both systolic and diastolic blood pressure.

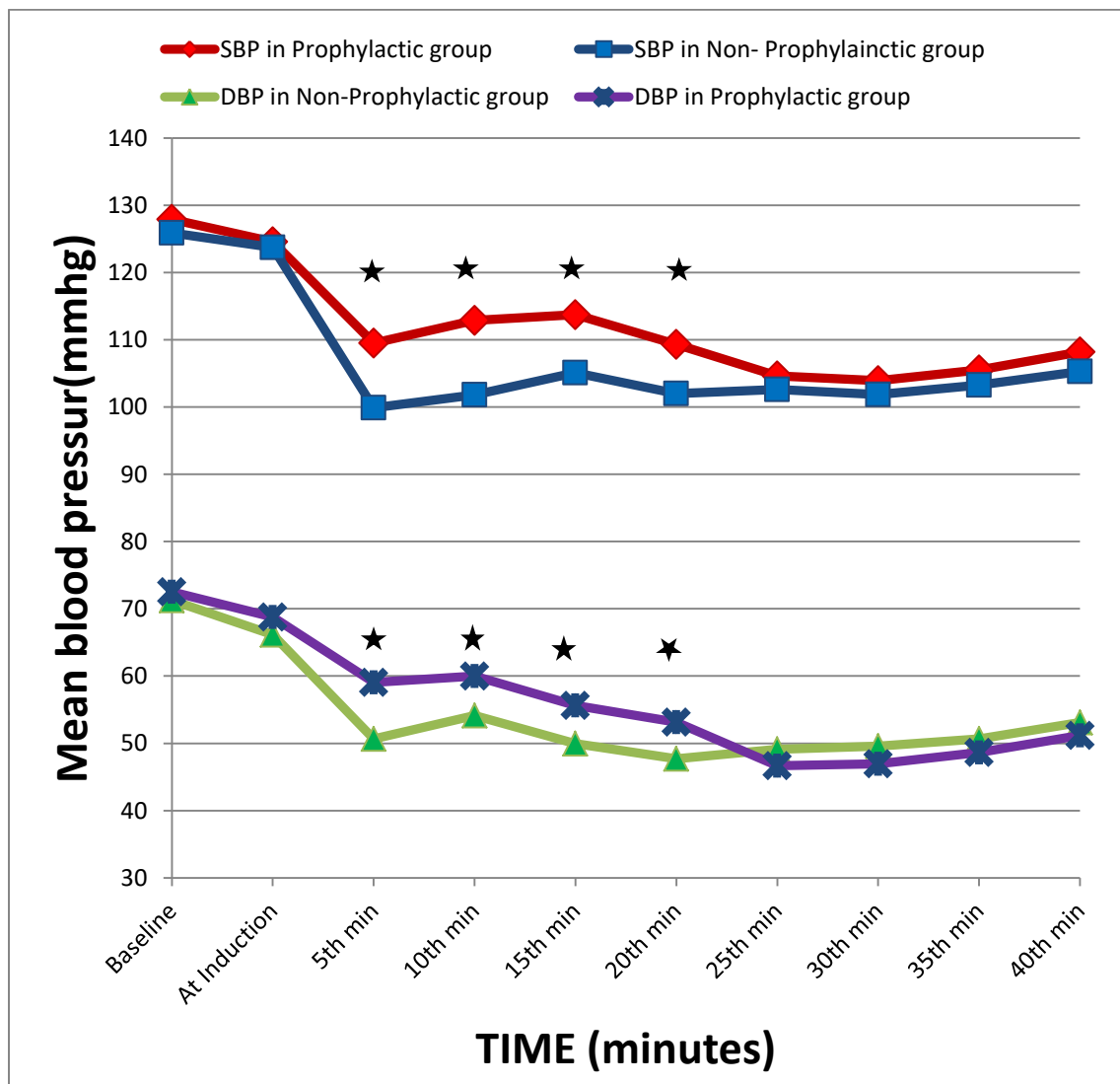


Figure 4: Change in Systolic and diastolic arterial pressure of the prophylactic and non-prophylactic group under spinal anesthesia for elective cesarean section at TASH, 2018.

★ Significant difference between groups ($P < 0.05$).

5.7. Trends of heart rate between prophylactic and non-prophylactic group

Figure 5 shows trends of heart rate across time. There was no statistical significant difference in heart rate between prophylactic group and non-prophylactic group from the start of induction of spinal anesthesia until the end of the study time, even though three patients experienced incidence of bradycardia at a certain point in the non-prophylactic group.

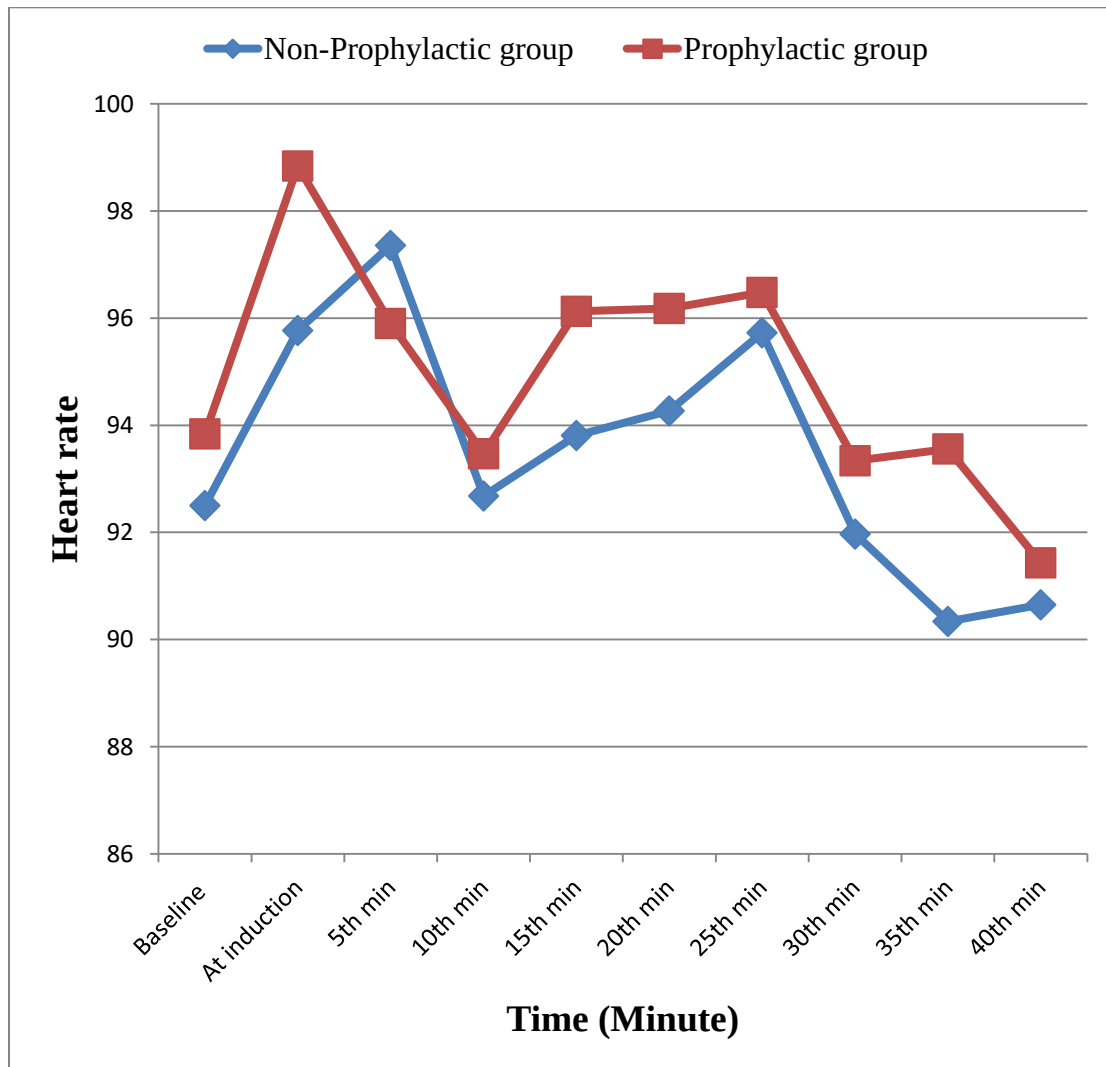


Figure 5: Changes in mean heart rate in prophylactic and non-prophylactic group under spinal anesthesia for elective cesarean section at TASH, 2018.

5.8. The time of hypotension occurrence between prophylactic and non-prophylactic group

Results of the Kaplan–Meier survival analysis are shown in Figure 6. The Kaplan–Meier survival curves shows proportion of patients with the incidence of hypotension (event) time from the initiation of spinal anesthesia to the end of the study. There was a significant difference between the groups with log rank test ($P = 0.003$).

Cumulative Proportion Surviving at the time of five minutes after induction of spinal anesthesia was 79.5% in the non-prophylactic group compared to 97.7% in the prophylactic ephedrine group.

Cumulative Proportion Surviving at the 10th minute and at 15th minute after induction of anesthesia was 65.9% and 59.1% respectively in the non-prophylactic group. All of the first events of hypotension in the non-prophylactic group were recorded within the first 30th minute after anesthesia induction.

In the non-prophylactic group from the total 22 hypotension events, 20(90.0%) of the hypotension events were recorded in the first 20 minutes. However in the prophylactic group, from the total of 10 incidence of hypotension, 6(60.0%) of hypotension events were recorded after 20 minutes.

Cumulative Proportion of patients with no occurrence of hypotension at the end of the study period for the non-prophylactic group was 50.0% and mean time to the first record of hypotension after induction of anesthesia were 25.5 (95% CI, 21.05 - 30.08) minute.

The prophylactic group Cumulative Proportion surviving (not having any occurrence of hypotension) at the end of the study period was 77.3% with mean time to the first event after induction of anesthesia being 36.2 (95% CI, 33.51 – 38.99) minute.

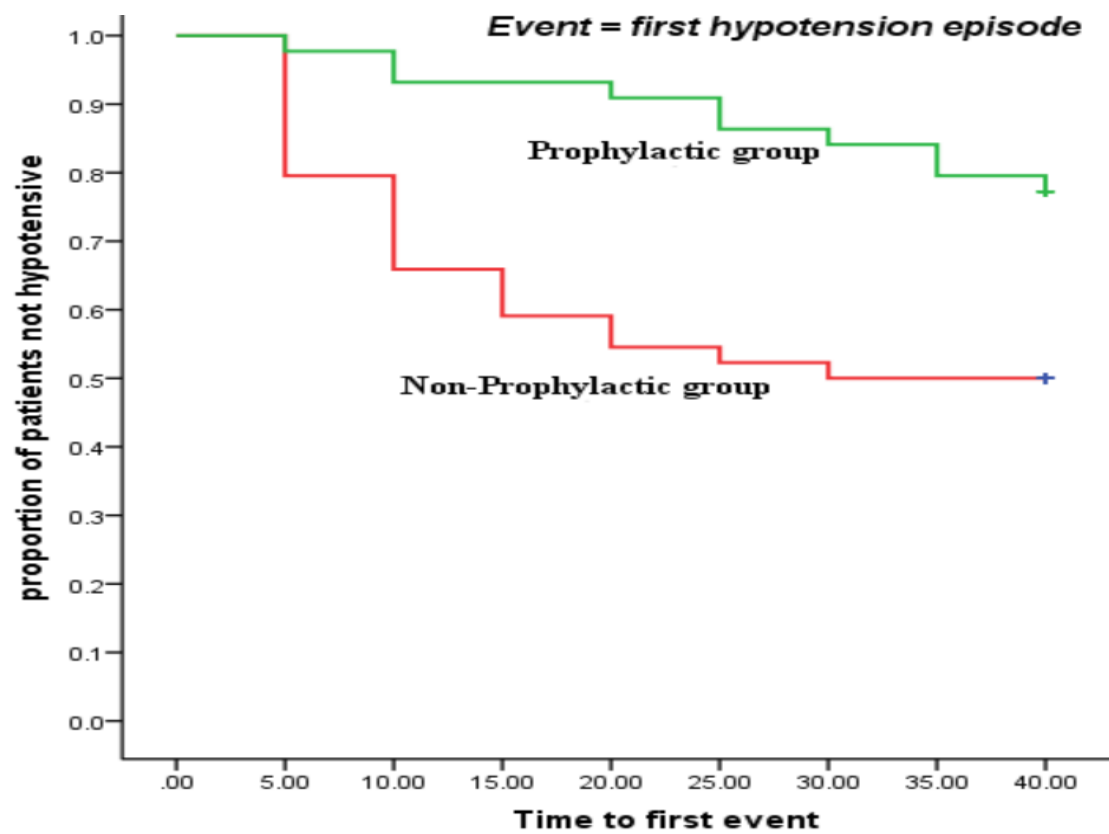


Figure 6: Kaplan–Meier survival curves showing systolic blood pressure from the initiation of spinal anesthesia to end of surgery.

Log Rank test: $P = 0.003$

6. Discussion

Spinal induced hypotension is a common problem during cesarean section associated with maternal nausea and vomiting and the risk of fetal and neonatal acidosis.(10) Hypotension remains a common and serious complications following spinal anesthesia despite different preventive measure. The aim of this study was to assess the effectiveness of administering bolus 10 mg prophylactic ephedrine on the hemodynamic (SBP, DBP, HR) response after spinal anesthesia.

Considering the results of the present study, the incidence of hypotension was high (50.0%) in those parturient who did not take prophylactic ephedrine than those who took prophylactic ephedrine (22.7%). Patients who received prophylactic ephedrine had greater hemodynamic stability compared to non-prophylactic group, as evidenced by greater values for serial measurements of SBP and DBP. The neonatal outcome was comparable between groups as it was evidenced by Apgar score of 1st and 5th min. Moreover low incidences of maternal nausea were recorded in the prophylactic ephedrine group.

The incidence of hypotension in our study is comparable with results observed by Heba Omar Ahmed et al, done in Egypt [48% vs. 24%].(21) Our finding was in accordance with a study conducted by Iram Shahzadi et al, with incidence of hypotension significantly higher (56%) in non-prophylactic group as compared to group with prophylactic group (16%).(5) Similar results to our study were reported in other studies (9,22, 28).

Our finding on incidence of hypotension was low when compared with a study conducted by I. Desalu et al(8), with incidence of hypotension in ephedrine prophylaxis group 40%. The observed difference can be due to infusion of ephedrine were used while we give a bolus ephedrine as a prophylaxis.

The intraoperative blood pressure (systolic and diastolic) stayed lower in the non-prophylactic group significantly starting from 5 minute after induction of spinal anesthesia until the 20th minute. The same result was showed in another study with statistical difference in SBP between the groups from 6 minute to 20th minute(5, 22).

Even though the sensory and motor onset of SA starts around after 5 min, its autonomic effect is expected to start immediately after SA which is evidenced by significant hypotension in those without ephedrine prophylaxis at earlier times after spinal anesthetic injection(29). The present study showed that in non-prophylactic group around 90% of the hypotension occurred within 20 minutes after spinal anesthesia induced. The same result were also observed by another study, that patients in non-prophylactic group who experienced hypotension did so earlier than those in the ephedrine prophylactic group(8).

On the present study, 60% of the hypotension incidences in the prophylactic group were recorded after 20 minutes of anesthesia induction. Ephedrine is not metabolized by catechol-O-methyltransferase enzymes because it lacks hydroxyl groups, and monamine oxidase enzyme deamination does not occur because of its α -methyl group. Thus, explains the relatively long duration of action of ephedrine compared to other vasopressors(29).

Moreover, patients that were hypotensive intra-operatively were managed with additional vasopressor. Literature's show despite different maneuvers used to treat SIH, anesthetists will have to treat with vasopressor medications 40% to 60% of women undergoing cesarean delivery(29).

In our study more of the non-prophylactic group patients required rescue vasopressor (nor-epinephrine) compared to the prophylactic ephedrine group (43.2% versus 13.6%) which was significantly different. Another study reported additional rescue ephedrine bolus was given for treatment of hypotension to more patients (54%) in groups with no prophylactic ephedrine compared to group with prophylactic ephedrine (8%). Similar results were found in different studies (5,9,30).

The total dose of norepinephrine administered were also statistical significant with higher dose administered for the non-prophylactic group with a median nor-epinephrine dose of 15(15) μ g compared to 7.5(5) μ g. Our finding was in accordance with a study which reported rescue ephedrine dose (mg) of 4.3 ± 5.9 in the prophylactic group compared to 18.6 ± 12.7 in the non-prophylactic group.

On this study, the intraoperative heart rate was not significantly different between those groups with prophylactic ephedrine and without prophylaxis. Evidence has shown that

ephedrine has effects on cardiac beta receptors indirectly, which lead to sinus node stimulation and consequently preventing decrease in heart rate following spinal anesthesia. In some cases, this led to increase in heart rate though not significantly(28, 31). Other studies reported where heart rate significantly increased in the prophylactic group (5,8,32).

In our study, intra-operation nausea was recorded in 34.1% of the non-prophylactic group as compared to 15.9% of the prophylactic group which was significantly different. Nausea is thought to be secondary to brainstem ischemia or reflex response to decreased venous return. This was in agreement with the results of some previous studies(9, 22), unlike another study which found that the incidence of nausea were not significantly different between the two groups(8). In addition, this study find episodes of vomiting were not significantly different with no incidence of vomiting in both groups recorded. This might be due to the administration of prophylaxis metoclopramide before induction of anesthesia(7).

7. Strengths and Limitations of the study

7.1 Strengths of the study

- The two groups were comparable in socio demographic distribution.

7.2 Limitation of the study

- Blood pressure measurements were not beat to beat and couldn't appreciate the duration of hypotension in between episode of hypotension.

8. Conclusion and Recommendations

8.1 Conclusion

In conclusion, employing combination of coload of fluid with prophylactic bolus ephedrine reduced the occurrence of hypotension following spinal anesthesia in parturient undergoing elective cesarean section. It is associated with fewer interventions for treatment, decreased episode of nausea, as well as greater hemodynamic stability, all of which lead to increased maternal comfort.

8.2 Recommendations

Based on the findings of the present study, the following recommendations are forwarded:-

✓ For Anesthetists

- Administering prophylactic bolus dose of 10mg intravenous ephedrine in addition to fluid coload at the time of intrathecal block is recommended for better hemodynamic stability for elective Cesarean Section.
- If prophylactic ephedrine is not given, the first 20 minutes after induction of anesthesia has high incidence of hypotension and should be diagnosed and treated as soon as possible.

✓ For researchers

- Considering this study as a baseline a further long term multicenter study is recommended.

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Annexes

Annex 1: Declaration

I, the undersigned, senior clinical Anesthesia student declare that this thesis is my original work in partial fulfillment of the requirement for the degree of Masters of clinical Anesthesia.

Name: _____

Signature: _____

Place of submission: Department of Anesthesia, College of Health Sciences, School of Medicine Addis Ababa University.

Date of Submission: _____

This thesis work has been submitted for examination with my approval as university advisor.

Advisor

Name

Signature

ASSURANCE OF INVESTIGATOR

The undersigned agrees to accept responsibility for the scientific, ethical and technical conduct of the research project and for provision of required progress reports as pre terms and conditions of the research and publications office of the Addis Ababa University.

Name of the student: _____

Date: _____ Signature: _____

Approval of the advisor

Advisors

Name	Signature	Date
1. _____	_____	_____

Annex 2: INFORMATION SHEET

Title of the Research Project: EFFECT OF PROPHYLACTIC EPHEDRINE ON BLOOD PRESSURE CHANGES DURING CESAREAN SECTION UNDER SPINAL ANESTHESIA AT TIKUR ANBESA SPECIALIZED HOSPITAL, ETHIOPIA,2018: PROSPECTIVE COHORT STUDY

Name of Principal Investigator: Tewoderos Shitemaw

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

Introduction: Greetings! My name is Tewoderos Shitemaw. I am a student at Addis Ababa University Department of Anesthesia College of Medicine and Health Sciences in Masters of Science (MSc) in clinical anesthesia. As part of this degree I am undertaking a research Project “Effectiveness of prophylactic Ephedrine on blood pressure changes during cesarean section under spinal anesthesia at Tikur Anbessa Specialized Hospital, Ethiopia.”

Purpose of the Research Project: The aim of this study is to determine the Effectiveness of prophylactic Ephedrine on blood pressure changes during cesarean section under spinal anesthesia in Tikur Anbessa Specialized Hospital. The information gained from this research will be used to make clinical recommendations and increase mother’s satisfaction after cesarean section with spinal anesthesia.

Procedure: The data collection will be conducted at Tikur Anbessa Specialized 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 caesarian section delivery clients whose information is abstracted but indirectly beneficial if the result utilized by planners and clinicians at black lion specialized 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 questionnaires' 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 Anesthesia, 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. Tewoderos Shitemaw (Principal investigator):+251-911-068728

2. Adugna Aregawi (B.Sc. M.Sc.) (Advisor):

Senait (B.Sc. M.Sc.) (Advisor):

Fiseha (B.Sc. M.Sc.) (Advisor):

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

Annex 3: Consent form

Dear participant:

Hello, my name is _____ and I am a data collector for research aimed at assessing the effectiveness of prophylactic ephedrine on blood pressure changes during cesarean section under spinal anesthesia at black lion specialized 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. [Tewoderos Shitemaw](#): +251911068728
2.
 - Adugna Aregawi (B.Sc. M.Sc.) (lecturer at AAU and Advisor):
 - Senait (B.Sc. M.Sc.) (lecturer at AAU and Advisor):
 - Fiseha (B.Sc. M.Sc.) (lecturer at AAU and Advisor):

We appreciate your response to us and thank you for giving us your time.

Annex 4: Consent form (Amharic version)

የመጠይቅ ፈቃድ

የተከበራችሁ የጥናቱ ተካፋዮች

ጤና ይስጥልን እኔ _____ እባላለሁ። በቀድሞ ጥገና ወሊድ የሰመመን መድሃኒት በሚሰጥበት ጊዜ 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 የበኩሉን 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. ቴዎድሮስ ሽጦማው (ዋና ተመራማሪ): ስልክ +251911068728
2. አዲኛ አረጋዊ (አዲስ አበባ ዩኒቨርሲቲ መምህር እና የጥናቱ አማካሪ)
ሠናይት (አዲስ አበባ ዩኒቨርሲቲ መምህር እና የጥናቱ አማካሪ)
ፍስሐ (አዲስ አበባ ዩኒቨርሲቲ መምህር እና የጥናቱ አማካሪ)

የመረጃ ሰብሳቢ ስምና ፊርማ

ስም _____ ፊርማ _____ ቀን _____

Annex 5: Data collection Questioner

Questioner developed for collection of data for the study “EFFECTIVENESS of prophylactic Ephedrine on blood pressure changes during cesarean section under spinal anesthesia at Tikur Anbesa Specializes 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	Gravida		
		Para		
202	Previous History of C/S	Yes	1	
		No	2	
203	Indication for operation	Malpresentation	1	
		Previous CS	2	
		Other specify.....	3	
204	Mother Hemoglobin level			
205	Premedication			

Part Three: Data during preoperative period

S.N	Question	Response	Code	Skipping
301	Dose of local anesthetics given.	_____mg		
302	Time of intrathecal injection			
303	Level of sensory block before skin incision	T4-T5	1	
		T6-T7	2	
		T8-T9	3	
		T10	4	
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 intra op?	YES	1	
		NO	2	
310	Does the patient vomiting intra op?	YES	1	
		NO	2	

Part Four: Intra op vital sign

Vital sign	Baseline	At induction @.....am /pm	5 th Min	10 th Min	15 th Min	20 th Min	25 th Min	30 th Min	35 th Min	40 th Min
SYSTOLIC BP										
DIASTOLIC BP										
MAP										
PR										
SpO ₂										

Part Five: Question related to anesthetic interventions

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	1	
		By fluid	2	
		By Atropin	3	
		By vasopressor (name and dose).....	4	
		By blood	5	
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 boluses and total dose	Number of boluses atropine given..... Total dose.....		
506	Duration of the surgery			
507	Intravenous fluids given in intra op period	_____ml		
508	Total blood loss	_____ml		

Name of data collector..... Signature:

Name of supervisor..... Signature: