THE EFFECTS OF ISOBARIC AND HYPERBARIC BUPIVACAINE ON MATERNAL HEMODYNAMIC CHANGES AFTER SPINAL ANESTHESIA FOR ELECTIVE CESAREAN SECTION AT GANDHI MEMORIAL HOSPITAL, ADDIS ABABA, ETHIOPIA: PROSPECTIVE COHORT STUDY

MASTER THESIS TO BE SUBMITTED TO ADDIS ABABA UNIVERSITY COLLEGE OF HEALTH SCIENCES, DEPARTMENT OF ANESTHESIA IN PARTIAL FULFILLMENT OF THE REQUIRMENT FOR DEGREE OF MASTERS OF SCIENCE IN ADVANCED CLINICAL ANESTHESIA

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ADDIS ABEBA UNIVERSITY

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ADDIS ABABA UNIVERSITY
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ABSTRACT

Background: The most common local anesthetic used for spinal anesthesia in obstetric and non-obstetric surgery is bupivacaine that can be used as isobaric or hyperbaric solutions. Cesarean section is usually performed under spinal anesthesia using hyperbaric bupivacaine which is associated with an increased incidence of severe hypotension. Isobar bupivacaine is not commonly used but it could be a good alternative due to having lower maternal hemodynamic changes than hyperbaric bupivacaine.

Objective: To compare the effects of isobaric and hyperbaric bupivacaine on maternal hemodynamic changes after spinal anesthesia for elective cesarean section at Gandhi memorial hospital, Addis Ababa, Ethiopia from December 1 2017 to January 30, 2018.

Methods: Hospital based prospective cohort study design was employed on a total of 100 parturients with a group exposed to isobaric received 12.5 mg of isobaric bupivacaine and unexposed to hyperbaric group received 12.5 mg of hyperbaric bupivacaine to see the effect on maternal hemodynamic changes after spinal anesthesia. Study participants were selected by using systematic random sampling. Symmetric data was analyzed by using independent t-test and asymmetric data by Mann-Whitney U-test and homogenous categorical data by using chi-square test. The level of statistical significance for all tests was $P < 0.05$.

Results: The incidence of hypotension was higher in isobaric than hyperbaric groups (82% vs. 60% respectively; $p = 0.015$). There was no statistical significant differences in mean arterial pressure value at baseline, but after spinal anesthesia statistically significant changes were observed among the groups ($p < 0.05$) at all study timing, but at 30^{th} min. There was no statistical significant differences in the mean heart rate variability after spinal anesthesia at all periods, except at 15^{th} minute ($p = 0.033$). Higher rate of vasopressor was used in isobaric than hyperbaric groups (36% vs. 14% respectively; $p = 0.011$).

Conclusion: Baricity is a significant factor for the maternal hemodynamic changes in parturiants for elective cesarean section. Isobaric bupivacaine produces higher change in blood pressure and incidence of hypotension, increase vasopressor requirement than hyperbaric bupivacaine after spinal anesthesia for elective cesarean section.

Key words: isobaric bupivacaine, hyperbaric bupivacaine, maternal hemodynamic changes, elective cesarean section.

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LIST OF ACRONYMS AND ABBREVIATIONS

ASA	American Society of Anesthesiologist
BMI	Body Mass Index
BSc	Bachelor of Science
CPD	CephaloPelvic Disproportion
CS	Cesarean Section
CSF	Cerebrospinal Fluid
CVP	Central Venous Pressure
DBP	Diastolic Blood Pressure
DC	Data Collector
HF	High Frequency
HR	Heart Rate
LA	Local Anesthetics
LF	Low Frequency
MAP	Mean Arterial Blood Pressure
MSc	Masters of Science
PI	Principal Investigator
SA	Spinal Anesthesia
SBP	Systolic Blood Pressure
SpO_2	Peripheral Capillary oxygen Saturation
SPSS	Statistical Package for the Social Sciences
$T_{(4, 6, 8, 10)}$	Thoracic vertebrae at 4^{th}, 6th, 8^{th} and 10^{th} dermatome

CHAPTER ONE: INTRODUCTION

1.1 Background

Spinal anesthesia (SA) is a form of regional anesthesia used frequently in various lower abdominal, orthopedic, and gynecologic operations. It is also widely used for cesarean section (1-4). Its rapid onset and short duration of action, straightforward application, lower costs, fewer side effects, and complications constitute significant advantages for obstetric procedures (2).

The most common local anesthetic used for spinal anesthesia in obstetric and non-obstetric surgery is bupivacaine that can be used as isobaric or hyperbaric solutions (5-7). Cesarean section is usually performed under spinal anesthesia using hyperbaric bupivacaine. This has been reported to be associated with an increased incidence of severe hypotension (8). Isobar bupivacaine is not commonly used for spinal anesthesia, but could be a good alternative for obstetrics due to having lower maternal hemodynamic changes than hyperbaric solution (9). Besides to the volume, concentration and dose of local anesthetics (LA), as well as the baricity of the solutions can affect spinal block profile (10-13).

Baricity of anesthetics represents the ratio of the specific density of anesthesia and cerebrospinal fluid. Addition of dextrose to bupivacaine produces hyperbaric bupivacaine, whereas dextrose free (plain) solution of bupivacaine is called isobaric. The mean CSF density in term parturient is 1.00030±0.00004). Baricity differences between spinal anesthetic solutions are thought to produce differences in hemodynamic parameters and distribution of anesthetics within subarachnoid space which may affect onset, extent, and duration of sensory block as well as side effects (14). It is commonly believed that hyperbaric solutions are more suitable to reach the higher thoracic dermatomes as opposed to their plain equivalents (15).

Induction of SA has a significant effects on many organ systems, including cardiovascular, respiratory, gastrointestinal, renal, endocrine and coagulation system. The effects of SA on cardio-circulatory system is primarily indirect and occurs through blockade of the sympathetic

nervous system with inhibiting a reflex response to the primary cardiovascular effects. Most significant easily measurable effects of SA have changed blood pressure and heart rate.

The aim of all anesthesia professionals is to perform SA with lowest deviation in blood pressure and heart rate, assuming that the clients having normal hemodynamics preoperatively. In doing so we are using local anesthetics of various baricity (16).

The recommended spinal block height to ensure client comfort for cesarean section is at T_{4-6} dermatome levels. The spread of local anesthetic in subarachnoid space should not be higher than the T_4 dermatome level in order to avoid expanded sympathetic block and a subsequent hypotension (17).

1.2 Statement of the Problem

Hypotension is the most common effect of neuraxial anesthesia, particularly in obstetric surgery. The prevalence of hypotension in obstetrics under spinal anesthesia particularly in cesarean section (CS) is 80-90% (8). Hypotension causes unpleasant symptoms such as nausea and vomiting (32%), bradycardia (13%), unconsciousness (0.05%), respiratory depression (0.2%), and cardiac arrest (0.003%) in mothers who undergo cesarean section. In severe and prolonged conditions, it leads to impairment of uterine perfusion and ultimately fetal acidosis and neonatal depression (9, 18).

Factors that increase the risk of hypotension include patient factors (advanced age, female sex, pregnancy, obesity, diabetes mellitus, hypertension, and anemia) and technical factors such as a block level at or above T5, baricity of drugs, use of opioids as premedication, and high local anesthetic dosages (19, 20).

The baricity of local anesthetics used for spinal anesthesia can influence the block level, as a result, the severity and the frequency of changes in blood pressure. Hyperbaric bupivacaine has a greater tendency for cephalic spread than isobaric bupivacaine; therefore, it has a greater peak sensory block height, so as a greater incidence of low blood pressure and heart rate (25).

Spinal anesthesia has the definitive advantage on nerve block in a large part of the body by the relatively simple injection of a small amount of local anesthetic. However, the greatest challenge of the technique is to control the spread of that local anesthetic through the cerebrospinal fluid

(CSF), to provide block that is adequate (in both extent and degree) for the proposed surgery but without producing unnecessarily extensive spread and its consecutive increase risk in maternal hemodynamic changes. The greater interpatient variability between isobaric and hyperbaric bupivacaine was observed (21).

The specific influence of the baricity of local anesthetics on the efficacy of the spinal block is controversial related to the onset of time, degree and level of sensory blockage, hemodynamic effects, intrathecal distribution and complications (24, 25, 29, 30).

Published data shows that different measures was taken to reduce spinal induced hypotension in parturient undergoing elective cesarean section like left lateral tilt, Iv fluid preloading or co loading, leg elevation and prophylactic use of vasopressors but the incidence of hypotension is till high (22, 23).

In different literatures, additional studies are recommended to determine the relative effect of baricity of local anesthetics on spinal block characteristics, especially in obstetric parturient. As far as I searched, there is no published research found in Ethiopia that shows the effects of isobaric and hyperbaric bupivacaine on maternal hemodynamic changes. Considering the scarcity of publications and conflicting results on the topic, the present study was proposed to compare the effects of isobaric and hyperbaric bupivacaine on maternal hemodynamic changes after spinal anesthesia for elective cesarean section in our country.

CHAPTER TWO: LITERATURE REVIEW

Comparative study in Bosnia and Herzegovina reported that the baricity of local anesthetic was effective on the height of spinal block for CS and hyperbaric bupivacaine was associated with higher incidence of hypotension than the isobar solution. With systolic, mean, diastolic blood pressure and pulse frequency decreased significantly than isobaric (19, 41%) (18, 75%), (17, 54%) and (10, 26%) vs. (7, 22%, 2, 65%, 1, 62% and 9, 38%) respectively ($p<0.01$) (7).

Chinese University of Hong Kong, Prince of Wales Hospital compared the hemodynamic effects of subarachnoid block with plain bupivacaine and heavy bupivacaine and observed that the use of heavy solutions of bupivacaine (hyperbaric solution) for subarachnoid block was associated with an increased incidence of hypotension (38% vs. 20%,p=0.006) and more rapid onset of hypotension(3min vs. 6 min, p=0.005) and increase in heart rate appeared to peak earlier following hyperbaric bupivacaine than isobaric (2-3 min vs. 5-10min), a decrease in central venous pressure (CVP) [(mean (SD) = 1.8(1.5) mmHg] compared with the plain group [0.7 (1.5) mmHg, p=0.047] and a greater need for early corrective treatment of hypotension by vasopressor without statistically significant (50% vs 33% p=0.008) during the initial phase of subarachnoid block (8) .

Another comparative Study in Thailand on a randomized clinical trial in patients undergoing endoscopic urologic surgery under spinal anesthesia with hyperbaric or isobaric bupivacaine and low dose fentanyl reported that isobaric bupivacaine can provide a highest level of sensory blockage than hyperbaric bupivacaine (T4-T10 vs T6-T10 respectively, p=0.05) for surgery with minimum hemodynamic effects (9).

A randomized control trial at Royal London Hospital on the effect of baricity of bupivacaine influence intrathecal Spread in the Prolonged Sitting Position Before Elective Cesarean Delivery and revealed that the median [interquartile range] (95% confidence interval) sensory levels after spinal injection were significantly higher with decreasing baricity: hyperbaric T10 [T11-8] (T10-9), isobaric T9 [T10-7] (T9-7), and hypobaric T6 [T8-4] (T8-5) (P 0.001). The incidences of maternal hypotension and nausea and vomiting were similar among groups, although the ephedrine requirements were significantly increased in the isobaric and hypobaric groups by factors of 1.83 and 3.0, respectively, compared with the hyperbaric group ($P< 0.001$) (10).

A randomized clinical trial for the effect of plain versus hyperbaric bupivacaine in Toronto shows an earlier onset of analgesia and higher sensory block level with isobar compared to hyperbaric bupivacaine during combined spinal-epidural analgesia for vaginal delivery ($p<0.001$); without statistically significant differences in the incidence of hypotension but the incidence of both pruritus and sustained fetal bradycardia was 33% in the plain group and 10% in the hyperbaric group ($P = 0.03$) (24)

A prospective double blinded a randomized study done in United Kingdom (UK) showed that the duration of sensory and motor block was prolonged in the hyperbaric group, indicating that the duration of block is related to baricity of spinal anesthesia. The overall differences in maximal spread only differed by one dermatome, with the hyperbaric solution achieving a median maximum sensory level to T3 compared with T2 for the isobaric and hypobaric solutions. The incidence of hypotension and ephedrine use were greater in the isobaric bupivacaine (76%, $P = 0.003$ and 0.004 respectively) than the hyperbaric bupivacaine (40%, $p = 0.62$ and $P = 0.580$ respectively). There was no significant difference in the incidence of nausea and vomiting among the groups ($P = 0.709$) (25).

Prospective randomized double-blinded done in Pakistan reported that there was no difference in the onset of block, time to achieve maximum level of block and hemodynamic parameters between the two groups. However, plain bupivacaine took more time for two dermatomes sensory level regression below T4, and resulted in prolonged block duration (mean (SD) 86.23(4.677 min) vs. 69.33(3.074 min). No statistically significant difference was found for episodes of hypotension, bradycardia and use of ephedrine and atropine (26) .

A randomized control trial done in Turk compared the effects of hyperbaric and isobaric bupivacaine spinal anesthesia on hemodynamic and heart rate variability in non-obstetric surgery. They concluded that the incidence of hypotension was not different between the two groups. There were no significant differences in the LF and HF values and LF/HF ratios between groups and hyperbaric bupivacaine caused significantly greater heart rate variability ((LF/HF ratios were significantly lower and HF values were significantly higher at 20 min after spinal anesthesia (<2.5 vs. >2.5)) ($p<0.05$) (27).

A comparative study done in Agra (U.P) India did not find any difference between the two groups with respect to duration of the block despite a difference in the baricity of local anesthetic solution. They suggested that the spread of spinal solution is not dependent on the density of bupivacaine. Therefore, there was no difference in the onset time, highest level, and recovery of sensory block between the two groups of patients undergoing cesarean section under spinal anesthesia with hyperbaric or isobaric bupivacaine (28) .

Another prospective comparative study done in Canada observed that sensory and motor block developed more rapidly with the isobaric bupivacaine five minutes (5min) faster than hyperbaric bupivacaine. However, the duration of sensory block with either form of bupivacaine was similar (29). In addition, a study in Indonesia by Helmi *et.al* showed that isobaric bupivacaine produced more rapid onset and longer duration when compared to hyperbaric bupivacaine (4.8 ± 2.2 versus 7.5 ± 2.2 minutes and 4.1 ± 2.1 versus 6.4 ± 2.4 minutes, respectively, $p < 0.0010$). They did not show significant differences in the incidence of hypotension between the two groups (30).

A study done in Iran reported that the incidence of hypotension was not statistically significant between isobaric and hyperbaric bupivacaine group (42% and 70%, p=0.08) respectively. The duration of hypotension was shorter in isobaric group (1.6±7.8 min vs. 7.4±12.5 min, P=0.004). In this study, more patients of the hyperbaric group had sensory block level at T3 than the isobaric group. The dose of ephedrine was lower in the isobaric group (2.4±6.6 mg vs. 5.3±10.7 mg, P=0.006). It could easily be treated with vasopressors and did not cause adverse effects on the mother and fetus/neonate. (31).

A study on Dow University of health sciences, Pakistan comparing the effect of intrathecal isobaric and hyperbaric bupivacaine on elective cesarean section and reported that the maximum fall in blood pressure from baseline was 23% in isobaric group and 6% in hyperbaric group p=0.01). There was no significant difference in between heart rate, respiratory rate and oxygen saturation in both groups (32).

A randomized control trial by Solakvic, N., Critchley, N. and Hussain MD studied the effect of baricity and Vasopressors used, reported that vasopressors had effectively used for the treatment of hypotension after spinal anesthesia. Ephedrine (8.6%) is the most common agent (7, 9) and another study by Atashkhoei *et al*. **(**31**)** showed that greater doses of ephedrine were used in hyperbaric group (5.3±10.7 mg) than isobaric group (2.4±6.6 mg)(P=0.006) due to a higher incidence of hypotension.

2.1 Significance of the Study

The most difficulty faced by all anesthetists after administration of spinal anesthesia is controlling the spread of local anesthetics and, as a result, the severity and frequency of changes in blood pressure and heart rate. Incidence of hypotension related to baricity of local anesthetic solution accounts for 40-70% which is till high. This study compared the effects of isobaric and hyperbaric bupivacaine on maternal hemodynamic changes after spinal anesthesia for elective cesarean section.

Even though the effect of hyperbaric and isobaric bupivacaine on maternal hemodynamic changes after spinal anesthesia was studied abroad, there is a difference in research methods. Almost all of them are randomized controlled trials but my study design is prospective cohort and also a difference in management of hypotension due to low socio-economic status and difference in demographic characteristics of the study populations. Also there is a controversy on the specific influences of baricity of local anesthetics on maternal hemodynamic changes.

Therefore, the present research finding will helps to the anesthetists to choose the best type of bupivacaine related to baricity that will have an optimal hemodynamic changes which ultimately reduces maternal and neonatal morbidity and mortality.

In addition, as far as I searched there is no previous published research found on this topic in our country so that the study findings will be used as a baseline data for future researchers.

Furthermore, if it is proved having an advantage of one over the other on comparative groups it will avoid unnecessary drug importation cost in the country.

2.2 Hypothesis testing

H_O1: There is no difference in the incidence of hypotension in isobaric group and hyperbaric group

H_A1: There is a difference in the incidence of hypotension in isobaric and hyperbaric group

H_O2: There is no difference in maternal hemodynamic changes in isobaric and hyperbaric group

H_A2: There is a difference in maternal hemodynamic changes in isobaric and hyperbaric group

H_O3: There is no difference in rate of vasopressor requirement in isobaric and hyperbaric group

H_A3: There is a difference in rate of vasopressor requirement in isobaric and hyperbaric group

Conceptual frame work

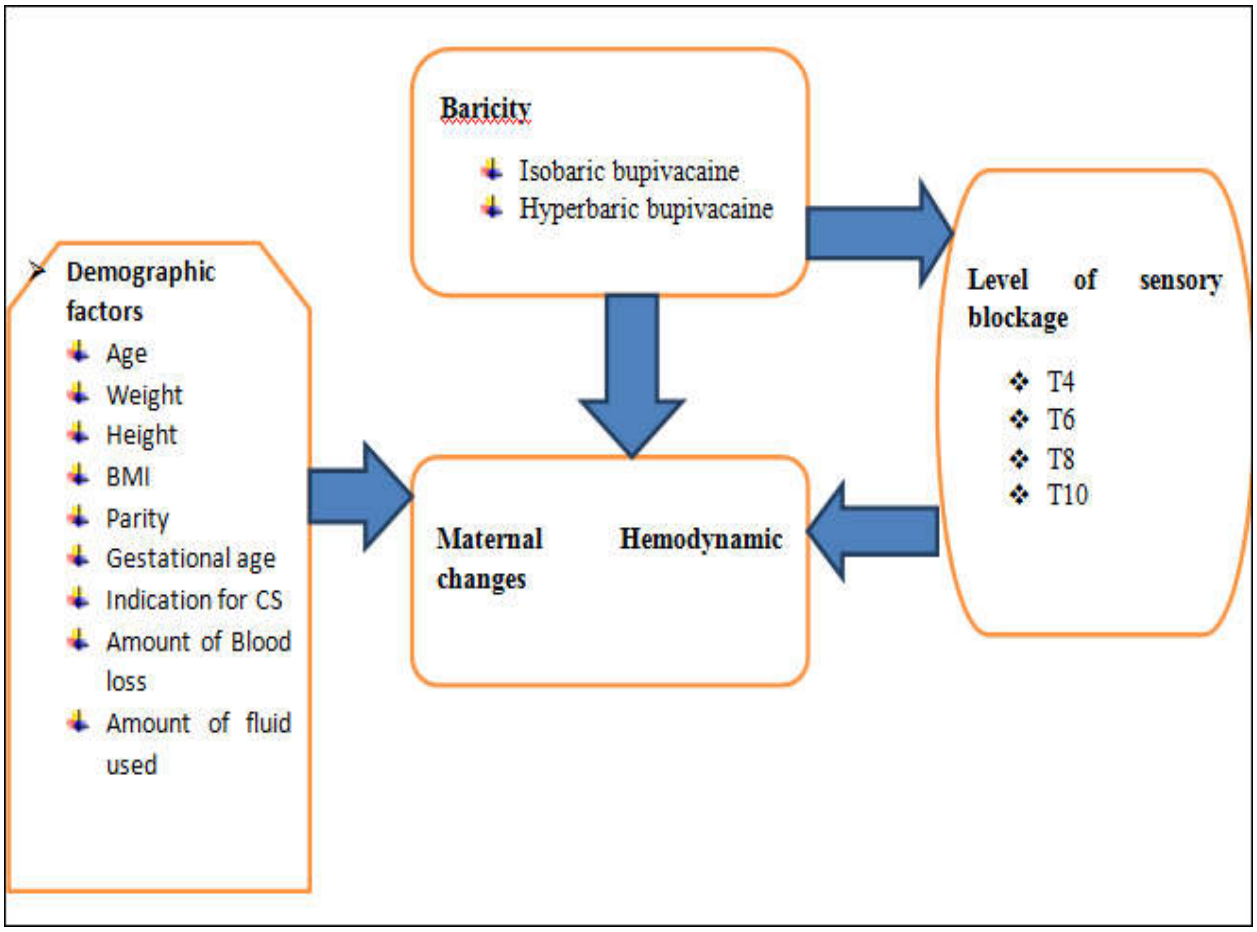


Figure 1.Conceptual frame work of the study on the effect of isobaric and hyperbaric bupivacaine on maternal hemodynamic changes after spinal anesthesia for elective cesarean section.

CHAPTER THREE: OBJECTIVES

3.1 General Objective

To compare the effects of isobaric and hyperbaric bupivacaine on maternal hemodynamic changes after spinal anesthesia for elective cesarean section from December 1, 2017 to January 30, 2018, at Gandhi memorial hospital, Addis Ababa, Ethiopia.

3.2 Specific Objectives

- To compare the incidence of hypotension between isobaric and hyperbaric bupivacaine after spinal anesthesia.
- To compare the effect of isobaric and hyperbaric bupivacaine on maternal hemodynamic changes after spinal anesthesia
- To compare the rate of vasopressor requirement between isobaric and hyperbaric bupivacaine after spinal anesthesia

CHAPTER FOUR: MATERIALS AND METHODS

4.1 Study Area and Period

This study was conducted at Gandhi memorial hospital located in Addis Ababa which is capital city of Ethiopia. It was established in 1958 G.C when it was called the only maternity hospital in Ethiopia. The hospital was named as Gandhi memorial hospital for the memory of Mahatma Gandhi. It is one of the thirteen governmental hospitals found in Addis Ababa and one of the hospitals which was administered by Addis Ababa health bureau. The hospital primarily gives services for women and children. The hospital provides gynecologic, obstetric and reproductive health services including mother and child health (MCH), infertility and sexual violence services. Currently, it is providing inpatient, outpatient services and emergency cases. In October 2016, the hospital established a neonatal unit and currently serves as inpatient unit for at least 120 neonates per month. The hospital has 110 beds and delivers 25 neonates each day. The hospital has four operation theatres and average number of elective caesarian deliveries done at the hospital is three per day. Study was conducted from December 1, 2017 to January 30, 2018.

4.2 Study Design

Hospital based prospective observational cohort study was employed.

4.3 Population

Source Population

All pregnant mothers who underwent elective cesarean section at Gandhi memorial hospital.

Study Population

Selected pregnant mothers who underwent elective cesarean section at the study period under spinal anesthesia those who fulfill inclusion criteria.

4.4 Eligibility criteria

4.4.1 Inclusion criteria

Pregnant women with

- Term singleton pregnancy
- ASA I & II
- Age range 18-40 years
- BMI <35, and
- Non-emergency cesarean section

4.4.2 Exclusion criteria

- Mothers who refuse to take part in the study
- Pregnant mothers with systemic and psychological disorders
- Complicated pregnancy (abruption placenta, placenta previa and preeclampsia)
- Emergency CS
- If intra-operative blood loss more than 1500 ml
- Weight >85 kg .....(20)
- Height <150 cm, >170cm ……(20)
- Failed spinal block
- Any contraindications for spinal anesthesia
- Allergy to local anesthetic

4.5 Sample size determination and sampling technique

4.5.1 Sample size determination.

Pregnant mothers who underwent elective cesarean section at Gandhi memorial hospital with a group exposed to isobaric and a group unexposed to hyperbaric bupivacaine was compared to see the effect on maternal hemodynamic changes among groups after spinal anesthesia.

The sample size was computed based on the used incidence of hypotension in the preliminary data from Iran (31) in exposed and unexposed groups by cohort double population proportion formula.

$$\text{Sample size, } n_1 = \frac{(Z_{\alpha/2} + Z_{1-\beta})^2 \, \bar{p} \, \bar{q} \, (r+1)}{r\,(p_1-p_2)^2}, \quad n_2 = r\,n_1, \; \bar{p} = \frac{p_1+p_2}{r+1}, \; \bar{q} = 1-\bar{p}$$

Where

n_1= the number of exposed

n_2= the number of unexposed

$Z_{\alpha/2}$ = Standard normal variance at 0.05 level of significance = 1.96

$Z_{1-\beta}$ = Standard normal variance for power or type 2 error = 0.84

r = the risk ratio of exposed to unexposed

P_1 = proportion of exposed with disease was 70% [29], $q_1 = 1-p_1$

P_2 = proportion of unexposed with disease was 42% [29], $q_2 = 1-p_2$

$P_1=0.7$, $q_2=0.3$ $\quad \bar{q}(\text{change}) = 1-\bar{p} = 0.44$

$P_2 = 0.42$, $q2 = 0.58$ $\quad \bar{p}(\text{change}) = \frac{p_1+p_2}{r+1} = 0.56$

According to the previous study the incidence of hypotension was 42% in isobaric and 70% in hyperbaric bupivacaine. By considering 95% confidence interval, 5% level of significance with 80% power and 100% of response rate, the sample size was 100 (50 per group).

$$n_1 = \frac{(1.96 + 0.84)^2 \, (0.56) \, (0.44) \, (1+1)}{1\,(0.7-0.42)^2} = 50$$

$n_1=n_2=50$, a total of 100 pregnant mothers were recruited in the study.

4.5.2 Sampling technique

By considering an average of 3elective cesarean section was done per day and for two month duration 180, ASAI & ASAII parturient underwent elective cesarean section. Study participants were selected using systematic random sampling for each group who underwent elective cesarean section in the morning of surgery. The sample size was 100. From all scheduled parturiens who fulfilled inclusion criteria to undergo elective cesarean section on operation list, the sample were selected every 2 skip interval (K=N/n, 180/100). The random start points were selected by lottery method from the first two schedules. Based on the decision of anesthetists selected parturient were placed on either group till the required sample size filled.

Enrollment flow chart

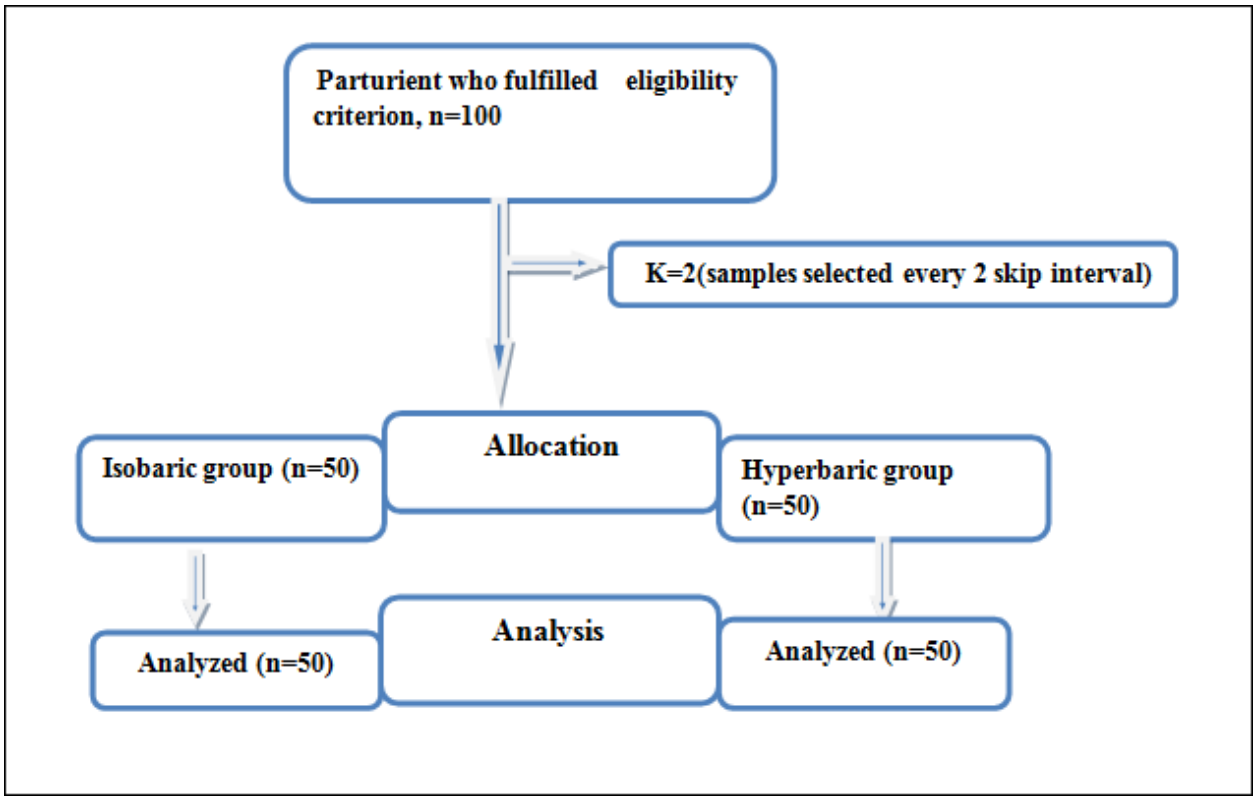


Figure 2.Flow chart of clients enrolled in the study at Gandhi memorial hospital, Addis Ababa, Ethiopia, from December1, 2017-January 30, 2018.

4.6 Study variables

4.6.1 Dependent variables

- Maternal hemodynamic changes
  - Systolic blood pressure
  - Heart rate
- Vasopressor use

4.6.2 Independent variables

- Demographic and parturient characteristics (age, weight, height, BMI, parity, gestational age, Indication for CS)
- Anesthesia related variables (level of sensory blockage, amount of fluids used, blood loss during surgery, doses of utero-tonic agents used)
- Exposure and un exposure variable: Baricity of LA (exposed: isobaric bupivacaine, un exposed: hyperbaric bupivacaine)

4.7 Operational Definitions

Elective caesarean delivery: delivery of baby incision through lower uterine segment before the onset of labor in the absence of emergent situations.

ASA I: parturient who come only for cesarean section.

ASA II: parturient having mild systemic diseases but not incapacitating.

Duration of surgery: The length of time from skin incision to skin closure during cesarean section.

Baricity: The density of bupivacaine administered for spinal anesthesia for elective cesarean section when compared to CSF (15).

Baseline value: measurements taken from pregnant mothers before administration of spinal anesthesia.

Resident: a doctor working in a hospital receives special advance training

Specialist: a doctor who has specialized in a particular area of medicine

Level of sensory blockage: assessment of a sensory level after administration of spinal anesthesia by applying cold swabs on pregnant mothers' body.

Hypotension: a decrease in Systolic blood pressure by 20% or more from the baseline value (9).

Vasopressor: a drug which produces vasoconstriction and results in rise in blood pressure (7).

Failed spinal: failure to provide adequate block after administration of local anesthetics for spinal anesthesia

Bradycardia: Heart rate below 60 beat per minute after spinal anesthesia.

4.8 Data collection tools and procedure

Data were collected by two anesthetists (BSc) and supervised by experienced senior anesthetist (MSc) using pretested structured questionnaires after taking training. Preoperative evaluation has done a day before and given orders to take informed consent, keep NPO, to fulfill necessary investigations based on finding of history and physical examination via hospital anesthetists.

The functionality of operation room equipments has checked and prepared necessary drugs early in the morning. Before the parturient enter to operation room chart review, identification of socio-demographic, maternal characteristics and indication for CS has identified by on duty anesthetists assigned per hospital program. All parturient have preloaded with 0.9% NS 10-20 ml/kg. Premeditations' ceftriaxone 1gm and metoclopramide 10 mg IV has given on arrival to waiting area of operation room.

In operation room routine standard monitoring with non-invasive blood pressure (NIBP), electrocardiogram (ECG) and pulse oxymetry monitoring has applied. Baseline blood pressure and heart rate have measured 5 minutes before administration of spinal anesthesia. The anesthetists have ordered parturient to be on sitting position after brief explanation about the type of anesthesia. Under all aseptic conditions, spinal anesthesia was instituted in sitting position using anterior superior iliac crest as a surface landmark with a 25-G pencil-point spinal needle at L3-4 inter-space level. After correct needle placement, as identified by free flow of CSF, bupivacaine 12.5mg (either isobaric or hyperbaric according to allocation) was given over 10 seconds.

Immediately after the spinal injection, the parturient were gently assisted to lie in supine position kept at 15^0 left uterine displacement. Data collectors recorded vital signs every 5 minute throughout the surgery and success of spinal anesthesia were assessed by sympathetic block, reduction in motor function. The level of sensory blockage was assessed by applying iced

gauzes on the mother's skin and documented. Based on the parturient vital sign oxytocine has given in infusion immediately after delivery of placenta.

Total duration of follow up was 30 minutes since significant hemodynynamic changes occurred within 20 minutes after spinal anesthesia. Of management of hypotension that was not enabled to correct with fluid and position, vasopressors had used for treatment of hypotension. Types and dose of vasopressor used was registered. Data accuracy and completeness was checked by principal investigator every day. Missed or inappropriate questionnaires were replaced immediately after the schedules of next days.

4.9 Data Quality Control

Questionnaires was pre-tested in 5% of the sample size at black lion specialized hospital to ensure the quality of data. Data collectors and supervisor were trained for one day on each of items included in the study tools, objectives, relevance of study, right of respondents, confidentiality of information obtained. Regular supervision was done and data completeness, accuracy and consistency were checked via supervisor and PI.

4.10 Data Processing and Analysis

After finishing data collection, data was refined, coded and entered in to Epi Info version 7 computer software and was exported to and analyzed by using SPSS version 20 statistical package. The level of statistical significance for all tests was $P < 0.05$. After checking the normality of data using shapiro-wilk and kolmogrove-smirnov test, and homogeneity by levanes test of equality of variance, data was presented as mean± SD for symmetric data, median (interquartile range) for asymmetric data, and counts (number) to test independence between categorical variables of two groups. The mean was analyzed by using independent t-test and range by Mann-Whitney U-test and number by chi-square test and Fisher's exact test. The results were summarized by figures, tables and text. Finally results were interpreted, and conclusion and recommendations were drown by principal investigator.

4.11 Ethical Consideration

After obtaining ethical clearance paper and approval from Addis Ababa University, department of anesthesia research ethical committee, Gandhi memorial hospital administration gave me a permission to collect data. During data collection process each parturient was asked for his/her informed oral consent to participate in the study after brief explanation about the objectives of the study by the data collectors'. Parturient identification was coded and the questionnaire was kept in proper place by the PI. Data was used only for the study purpose.

4.12 Plan for data dissemination

The result of the study will be disseminated by hard copy to Addis Ababa University College of health Science, school of anesthesia and to Gandhi memorial hospital medical administration office to recommend the best type of bupivacaine having minimal maternal hemodynamic changes after spinal anesthesia for elective cesarean section.

The result of the study will be presented on different conference including the Ethiopian association of anesthetists to show the effect of baricity on maternal hemodynamic changes for elective cesarean section after spinal anesthesia and to forward recommendations.

The study will be released and published on different medical journals and it will serves as a baseline data for other researchers.

CHAPTER FIVE: RESULTS

5.1 Demographic, preoperative and intra-operative characteristics of parturients

A total of 100 parturients who underwent elective cesarean section were included in the study. From this, 50 took hyperbaric and 50 took isobaric bupivacaine. There were no statistically significant differences were observed among the groups with respect to age, weight, height, BMI, ASA status, parity, gestational age, indication for CS, sensory block level, amount of fluids used, amount of blood loss, baseline SBP and baseline HR (P>0.05). The majority of parturients underwent elective cesarean (56% in hyperbaric & 62% in isobaric groups) with an indication of previous CS. Types of utero-tonic drugs used between the groups was oxytocine alone 20 (0) (minimum 20 and maximum 30) (Table 1).

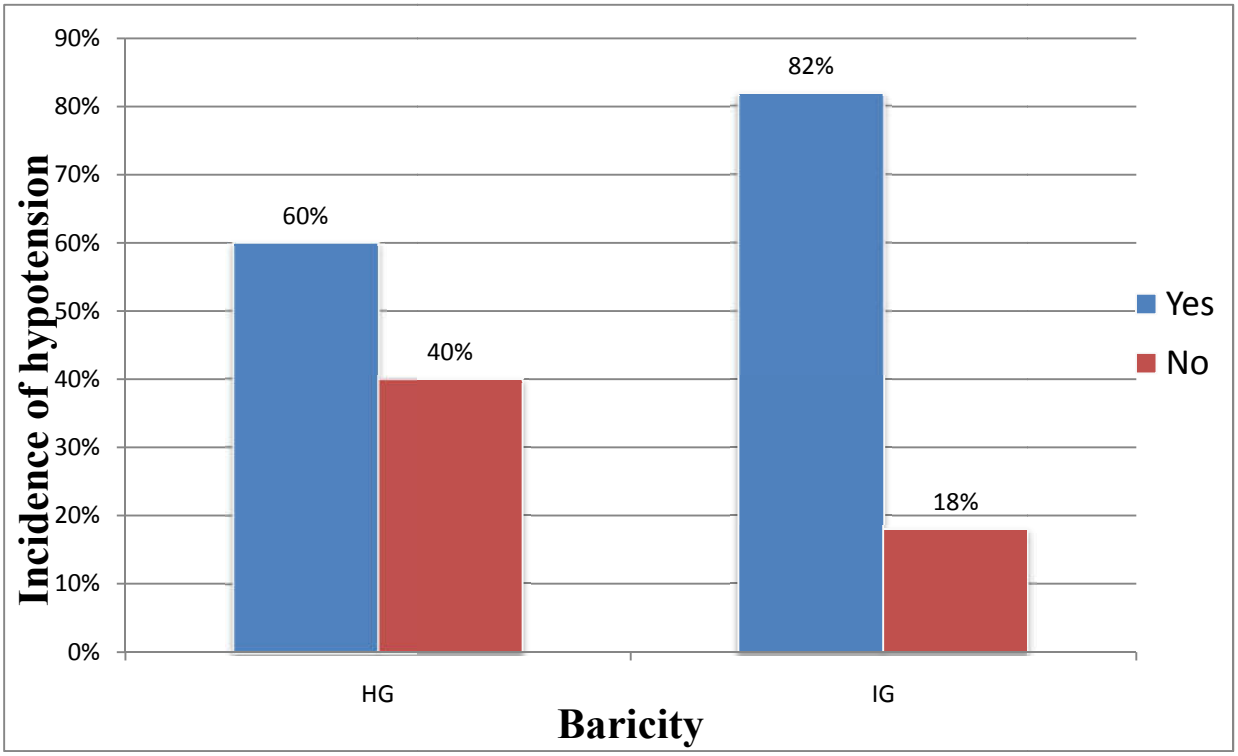
Table 4: Demographic data, preoperative and intra-operative variables among groups at Gandhi memorial hospital, Addis Ababa, Ethiopia, December 1, 2017-January 30, 2018.

Variable		**Hyperbaric group(n=50)**	**Isobaric group(n=50)**	**P value**
Age(yr)		28.60±3.39	29.72±3.67	0.11
Wight (kg)		66.32±5.76	68.74±9.62	0.13
Height (cm)		162.5 (5)	160 (5)	0.205
BMI(kg/m^2)		25.02±2.129	25.818±3.199	0.145
ASA status	I	33 (66%)	35 (70%)	0.668
	II	17 (34%)	15 (30%)	
Parity	Nullipara	5 (10%)	7 (14%)	0.780
	I	22 (44%)	18 (36)	
	II	20 (40%)	23 (46%)	
	III	3 (6%)	2 (4%)	
Gestational age(wk)		39.75±1.73	39.42±1.39	0.294
Indication for CS	Previous CS	28 (56%)	31 (62%)	0.07
	Malpresentation	12 (24%)	6 (12%)	
	CPD	8 (16%)	2 (4%)	
	Others	2 (4%)	11 (22%)	
Oxytocine dose (Iu)		20 (0)	20 (0)	0.767
Total fluid used (ml)		2750(1000)	2500 (1000)	0.458
Amount of blood loss (ml)		500 (150)	500 (163)	0.570
Baseline SBP		126.72±10.37	125.26±12.322	0.523
Baseline HR		96.04±12.665	92.12±11.783	0.112

Independent t-test for Mean and SD, Mann- Whitney U- test for median (interquartile range) and chi-square and fisher exact test for number (%), CPD: cephalopelvic disproportion

5.2 Hemodynamic characteristics of parturients

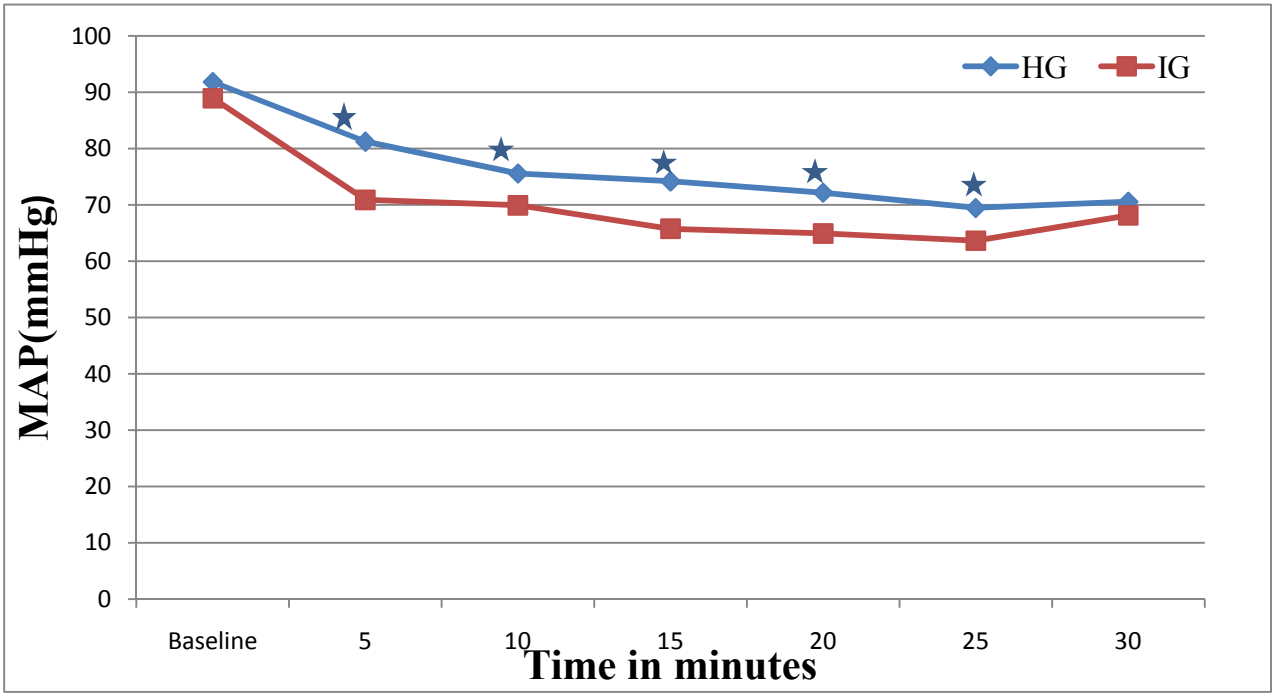
The incidence of systolic hypotension after spinal anesthesia was 60% [95% confidence interval, 46%-74%] in hyperbaric group and 82% [95% confidence interval, 71%-93%] in isobaric group with $X^2 = 5.90$, and P = 0.015. Statistically significant differences were observed between groups (p = 0.015). Higher incidence of hypotension was seen in isobaric than hyperbaric groups (figure 3).



**P = 0.015* *HG = hyperbaric group* *IG = isobaric group*

Figure 3.Incidence of hypotension after spinal anesthesia among groups at Gandhi memorial hospital from December 1, 2017-January 30, 2018.

There were no statistical differences in mean MAP value at baseline, but after spinal anesthesia statistically significant changes were observed among the groups ($p < 0.05$) at all study timing, except at 30th minute. Varied intergroup decreased MAP was recorded; more reduction in isobaric than hyperbaric groups starting from 5th to 25th minutes (figure 4).



*p <0.05 HG = hyperbaric group IG = isobaric group

Figure 4.Change in mean MAP in first 30 minute after spinal anesthesia among groups at Gandhi memorial hospital from December 1, 2017-January 30, 2018.

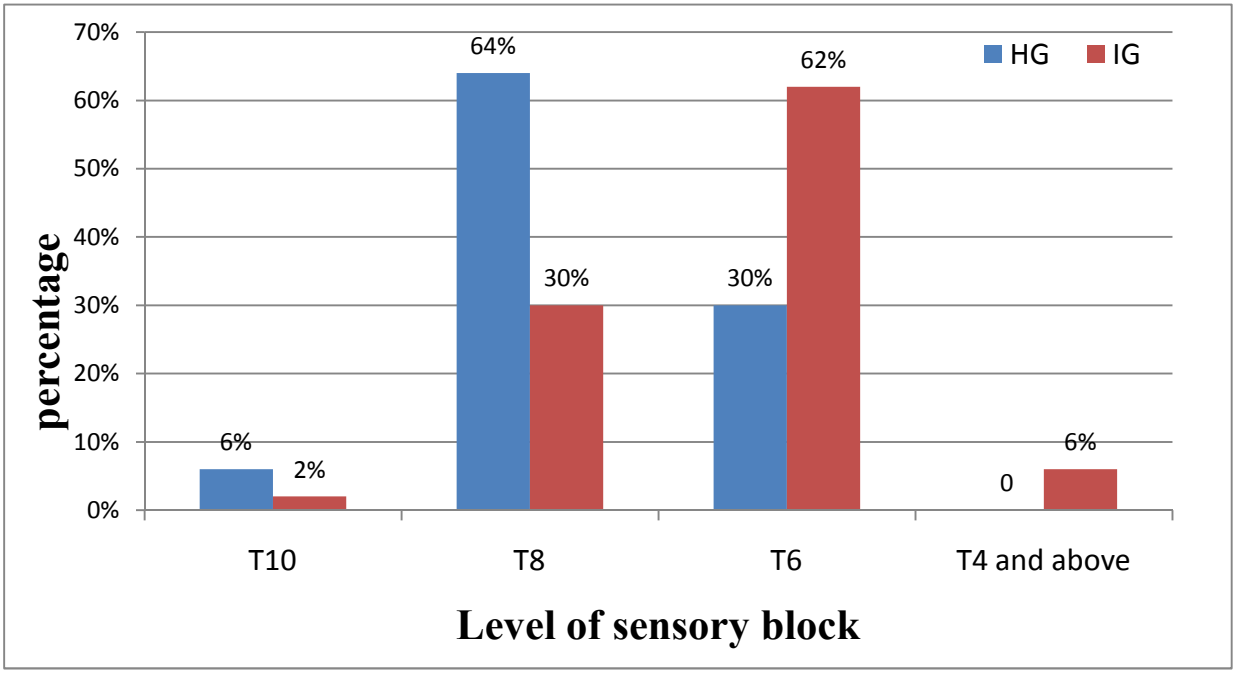
When we compared the heart rate among groups, there were no statistical significant differences in the mean HR variability after spinal anesthesia at all periods, except at 15th minute. Significantly greater heart rate variability was recorded in isobaric group at 15th minute than hyperbaric group after spinal anesthesia compared to baseline values (p =0.033). No supplementary atropine was required, since none of the clients developed bradycardia (table 2).

Table 5: Change in HR in first 30 minute after spinal anesthesia among groups at Gandhi memorial hospital, Addis Ababa, Ethiopia, December 1, 2017-January 30, 2018.

Time in minute	**Hyperbaric group (n=50)**	**Isobaric group (n=50)**	**P value**
Baseline	96.04±12.665	92.12±11.783	0.112
5	96.36±14.62	91.10±15.72	0.086
10	95.16±14.33	90.32±15.47	0.108
15	95.14±12.87	89.31±14.09	0.033*
20	94.04±13.42	88.88±15.16	0.075
25	94.08±12.87	89.82±12.79	0.1
30	92.38±12.22	89.9±11.94	0.307

Independent t-test was used for mean and SD, *$p < 0.05$*

The levels of sensory block among groups were observed and majority of clients 64% in hyperbaric group had T8 sensory block level and 62% in isobaric group had T6 sensory block level. T4 and above level of sensory block was seen in 3 (6%) in isobaric and none in hyperbaric group. T10 level of sensory blockage was observed in 6% of isobaric and in 2% of hyperbaric groups but the parturient didn't request any kind of analgesics or sedatives. There were statistically significant differences in the level of sensory blockage among groups (p =0.001) (figure 5).



*p = 0.001 HG = hyperbaric group IG = isobaric group

Figure 5.Level of sensory block after spinal anesthesia among groups at Gandhi memorial Hospital, Addis Ababa, Ethiopia, December 1, 2017-January 30, 2018.

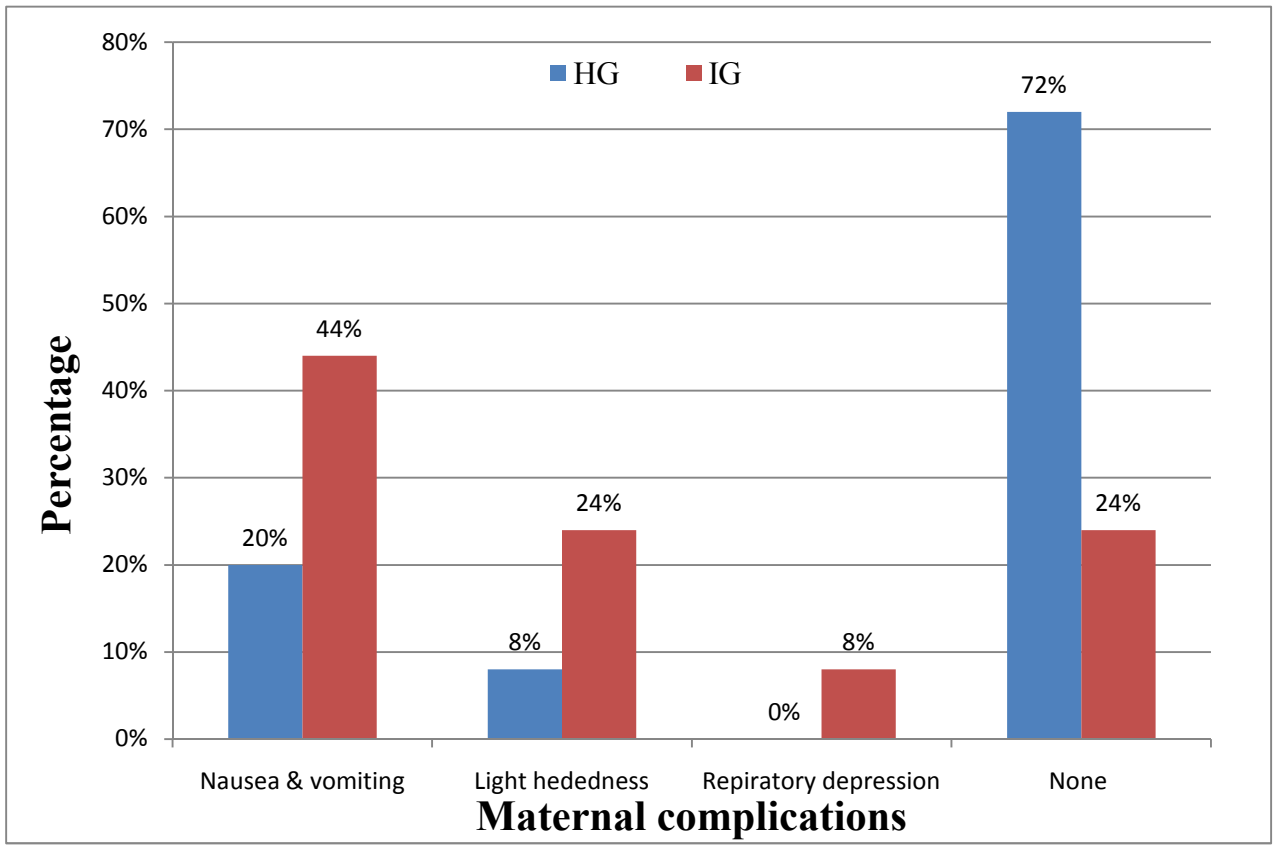
We observed that vasopressor was used for the treatment of hypotension in both groups after spinal anesthesia, but the rate of ephedrine requirement was relatively higher in isobaric 18 (36%) than hyperbaric group 7 (14%). Statistically significant differences seen between groups (p=0.011). The dose of ephedrine used in milligram was 5(0) in both hyperbaric and isobaric groups and it was insignificant (p = 0.358) (Table 3).

Table 6: Rate and dose of ephedrine used for the treatment of hypotension after spinal anesthesia among groups in first 30 minute at Gandhi memorial hospital, Addis Ababa, Ethiopia, 2018.

Vasopressor used	Hyperbaric group(n=50)	Isobaric group(n=50)	P value
Yes	7 (14%)	18 (36%)	0.011
No	43 (86%)	32 (64%)	
Ephedrine dose (mg)	5 (0)	5 (0)	0.358

Chi-square was used for categorical data, Mann-Whitney U- test for median (interquartile range), $P^{*} = 0.011$

The most common incidence of maternal complication was nausea and vomiting which accounts 44% in isobaric and 20% in hyperbaric groups. Relatively higher incidences of maternal complications were observed in isobaric group with respect to nausea and vomiting, light headedness and respiratory depression. It was statistically significant among groups (p = 0.001) (figure 6).



*p = 0.001 HG = hyperbaric group IG = isobaric group

Figure 6.The incidence of maternal complications after spinal anesthesia among groups at Gandhi memorial Hospital, Addis Ababa, Ethiopia, December 1, 2017-January 30, 2018.

CHAPTER SIX: DISCUSSION

Hypotension is the most common effect of spinal anesthesia, accounts for 40-70% (8) from previous study**.** Even if different measures were taken to reduce spinal induced hypotension in parturient underwent elective cesarean section like left uterine tilt, IV fluid preloading or co loading, leg elevation and prophylactic use of vasopressor but the incidence of hypotension is till high (22, 23). The aim of this study was to compare baricity of bupivacaine on maternal hemodynamic changes after spinal anesthesia for elective cesarean section.

The result of this study showed that the overall incidence of hypotension was 60% in hyperbaric and 82% in isobaric groups, indicating higher incidence of hypotension in isobaric than hyperbaric groups. In this study statistically significant differences were observed between groups. This result is in line with a prospective double blinded a randomized study done in United Kingdom (UK)(25), and they got the greater incidence of hypotension in isobaric than hyperbaric groups (76% vs. 40%) respectively. Similarly another comparative study was done by S. Aftab *et al*. reported higher incidence of hypotension in isobaric (23%) than hyperbaric groups (6%) (32).

In contrast to the present study, other studies revealed that insignificant differences in the incidence of hypotension among the groups (10, 22, 26, 27, 30). L.A Critchley and J. Darrick also reported higher incidence of hypotension in hyperbaric (38%) than in isobaric (20%) groups (8).These differences might be as result of position, block height, spine curvature, sociodemographic characteristics and experiences of anesthetists. When the patients are turned supine immediately after injection in the lumbar region, a hyperbaric solution spreads under the influence of gravity down the slope created by the lumbar spinal curvature and the plain bupivacaine which is slightly hypobaric does not have gravity-dependent spread, hence results in higher incidence of hypotension. Distension of the veins of the vertebral plexus causes compression of the dura reducing CSF volume and encourages greater bulk of spread of the injected solution. The isobaric bupivacaine being less viscous mixes rather freely with CSF, thus moves easily through compressed sub arachnoid space which results in high risk of hypotension.

There were no statistical significant differences in mean MAP value at baseline, but after spinal anesthesia statistically significant changes were observed among the groups at all study timing, except at 30th minute. Varied intergroup decreased MAP was recorded; more reduction in isobaric than hyperbaric groups started from 5th to 25th minutes. The finding is nearly consistent with study conducted at Dow University of health sciences on the effect of intrathecal isobaric and hyperbaric bupivacaine on elective cesarean section that reported the maximum fall in blood pressure from baseline higher in isobaric than hyperbaric groups (32).

But our result is contradicting with findings of the other study that reports no statistical difference in hemodynamic parameters between groups (24). Similar finding was also reported by studies conducted at Cantonal and Prince of Wales hospitals that showed greater reduction in MAP in hyperbaric than isobaric groups (7, 8). These differences might be due to the position and height of parturient, volume of local anesthetics used, the possibility of dehydration, and the amount of vasoactive drugs used

When we compared the heart rate variability among groups, there were no statistical significant differences in the mean HR variability after spinal anesthesia at all periods, except at 15th minute. Significantly greater heart rate variability was recorded in isobaric group at 15th minute than hyperbaric group after spinal anesthesia compared to baseline values. No supplementary atropine was given, since none of the clients developed bradycardia. This finding is comparable with study conducted at Turk on the effects of hyperbaric and isobaric bupivacaine after spinal anesthesia on hemodynamic and heart rate variability that reported no significant differences in HR variability between groups (27).

On other hand our result is inconsistent with study done from cantonal hospital reported that the pulse frequency decreased significantly in hyperbaric than isobaric groups (7). This difference might be due to blockage of sympathetic accelerator fibers and high level of sensory blockage.

In our study there were statistically significant differences in the level of sensory blockage among the groups. The majority of clients 64% in hyperbaric group had a level at T8 and 62% in isobaric group had a level at T6 sensory blocks. T10 level of sensory blockage was observed in 6% of isobaric and in 2% of hyperbaric groups but the parturient didn't request any kind of analgesics or sedatives. Sensory blockage of T4 and above levels were seen in isobaric, 3(6%) and none in hyperbaric groups. These revealed that relatively higher level of sensory blockage on isobaric than hyperbaric groups. The result of this finding is consistent with study conducted by Rofael *et al.* showed that a higher sensory block level at all times in the first 30 minute in isobaric than hyperbaric groups (24). This finding also corresponds with study by Hallworth *et al*. revealed that the overall differences in maximal spread only differed by one dermatome, with the hyperbaric group achieved a median maximum sensory level to T3 compared with T2 for the isobaric group (25).

In contrast to our study, Atashkhoei *et al.* reported that more patients on hyperbaric group had sensory block level at T3 than isobaric (31) The observed result is also inconsistent with study by Strivastava1 Du they reported that there is no difference in level of sensory block among isobaric and hyperbaric groups (28). The observed difference might be due to adopting supine position, even with left lateral tilt, causes inferior vena cava compression, which in turn results in an engorgement of the epidural venous plexus. The consequent dural sac compression may facilitate bulk movement of drugs injected into the CSF and could explain the cephalad progression of the isobaric bupivacaine.

Our finding showed that high rate of ephedrine requirement in isobaric (36%) than in hyperbaric groups (14%) that was statistically significant. Which means ephedrine requirement in isobaric group was more than two times that of hyperbaric group. But the dose of ephedrine used for the treatment of hypotension was not significant between groups. This finding is similar to Hallworth *et al.* study found significantly high rate of ephedrine requirement in isobaric than hyperbaric groups (25).

Contrasting finding had been reported in studies at prince of Walles and Al-Zahra Hospitals on the influence of baricity on maternal hemodynamic changes after spinal anesthesia showed that ephedrine requirement was significantly higher in hyperbaric than isobaric group (8,31). The dose of ephedrine was significantly higher on hyperbaric than isobaric groups (31). The finding of this study is also incomparable with study of Gurmukh *et al.* reported that there is no significant difference in rate of ephedrine requirement between groups (26).This might be due higher level of sensory blockage, and sympathectomy.

Nausea and vomiting was the most common maternal complication which accounts 44% in isobaric and 20% in hyperbaric groups. Relatively higher rate of maternal complications were developed in isobaric than hyperbaric groups with respect to nausea and vomiting, light headedness and respiratory depression and it's statistically significant among groups. But any parturient didn't develop severe complications like high or total spinal, respiratory or cardiac arrests. The occurrence of nausea and vomiting might be secondary to hypotension, which was effectively reversed with fluid administration and ephedrine as a vasopressor.

Incomparable to our result, studies done at Royal London Hospital and United Kingdom (UK) found insignificant differences in the incidence of nausea and vomiting (10, 25). This might be due to difference in the incidence of hypotension, vagal hyperactivity, visceral pain, utero-tonic agents, and sympathectomy.

6.1 Limitations of the study

The following limitations were seen in this study

Inaccessibility of invasive arterial blood pressure to measure parturient beat to beat systolic blood pressure. The onset and duration of sensory and motor blockage was not evaluated. Duration of hypotension couldn't measure with every hypotensive episodes

6.2 Strength of the study

Both the exposed and unexposed groups were selected from the same source population. No lost to follow up of parturients which results in missing data.

CHAPTER SEVEN: CONCLUSION AND RECOMMENDATIONS

7.1 Conclusion

Baricity is a significant factor for the maternal hemodynamic changes in parturiants for elective cesarean section. Isobaric bupivacaine produced higher change in blood pressure and incidence of hypotension, increased vasopressor requirement, and a higher level of sensory blockage than hyperbaric bupivacaine after spinal anesthesia for elective cesarean section.

7.2 Recommendations

Based on the present research findings the following recommendations were drawn:

Anesthetists are recommended to use hyperbaric bupivacaine with close monitoring of parturient hemodynamic changes within the first 20 minute after spinal anesthesia.

Hospitals are recommended to make preferable vasopressor accessible for management of hypotension in obstetrics.

Future researchers are recommended to conduct a further study that fulfils the gaps and more strong in study design on the effect of baricity in maternal hemodynamic changes in our country.

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Annex I: Information Sheet

Title of the Research: The Effects of Isobaric and Hyperbaric Bupivacaine on Maternal Hemodynamic Changes after Spinal Anesthesia on Elective Cesarean Section at Gandhi Memorial Hospital, Addis Ababa, Ethiopia from December 1 2017 to January 30 2018: prospective cohort study

Name of Principal Investigator: Shamill Eanga (MSc Student in Advanced clinical anesthesiology)

Name of the Organization: Addis Ababa University College of health sciences, department of Anesthesiology

Introduction: Hello Dear! My name is Shamill Eanga. I am attending Masters of Science (MSc) degree in advanced clinical anesthesiology at Addis Ababa University College of health sciences. As part of this degree I am undertaking a research Project on the effect of isobaric and hyperbaric bupivacaine on maternal hemodynamic changes after spinal anesthesia for elective cesarean section at Gandhi memorial hospital from December 1, 2017 to January 30, 2018.

Purpose of the Research: The aim of this study is to determine the effect of isobaric and hyperbaric bupivacaine on maternal hemodynamic changes after spinal anesthesia for elective cesarean section at Gandhi memorial 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 by reducing complications related with drug selection.

Procedure: The data collection will be conducted at 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 caesarian 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 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 to Addis Ababa University College of health sciences, department of anesthesiology and displayed in the University Library and website. This study is also intended to be submitted for publication in scholarly journals and will serves as a baseline for future researchers.

Right to Refusal or Withdraw: Study subjects will have full right to refuse from participating in this research

Contact persons: If you have any further questions or would like to receive further information contact the principal investigator or advisor listed below

1. Shamill Eanga (BSc, MSc student) (Principal investigator):+251-922-84-83-40
2. Wossenyeleh Admasu (MSc) (Advisor):+251-911-10-49-40

Annex-II: Consent form (English version)

Hello-Dear Participant!
My name is _____. I am a researcher and am attending postgraduate program in the field of Anesthesiology at Addis Ababa University. I am going to conduct a research on comparing the effects of isobaric and hyperbaric bupivacaine on maternal hemodynamic changes after Spinal Anesthesia on elective cesarean sections from December 1, 2017 to January 30, 2018 at Gandhi memorial hospital.
The information going to be obtained will help the government and other responsible bodies to reduce the incidence of hypotension which helps to reduce maternal and neonatal morbidity and mortality. Your participation is very valuable for the success of this project. Also be mindful that whatever we will get here is for research purposes only and the information will not be used by any other person apart from this research and therefore, confidentiality can be guaranteed. However, your names will not be mentioned or be attached to anything that you say. If you have anything to ask contact data collectors and supervisors available there.

Do you want to continue yes---------- No---------- (Thank you in advance for your help!)

Name and contact address of investigator

Shamill Eanga, E-mail: eangashamill67@gmail.com Cell phone: +251 912-750-725.

Annex- III: Consent form (Amharic version)

<u>የመጠይቅ ፈቃድ</u>

<u>የተከበራችሁ የጥናቱ ተካፋዮች</u>

ጤና ይስጥልን እኔ_____እባላለሁ፡፡ በአዲስ አበባ ዩኒቨርሲቲ በአንስቴዚዮሎጂ ትምህርት ክፍል ተመራማሪ ነኝ፡፡በቀዶ ጥገና ወሊድ የአንስቴዚያ መድሀኒት በሚሰጥበት ግዜ የሚከሰቱ የደም ግፊት እና የልብ ምት ለውጦች ላይ የሚሰራ ጥናት በጋንዲ መታሰቢያ ሆስፒታል እየተመራመርኩኝ ሲሆን: 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፡፡

ጥያቄዉን ለመቀጠል ፍቃደኛ ኖት? አዎ _____ አይደለሁም_____(ስለረዱኝ በድጋሚ አመሰግናለሁ;;)

ሻሚል እንጋ (ዋና ተመራማሪ): ስልክ +251-922-84-83-40

የመረጃ ሰብሳቢ ስምና ፊርማ

ስም_____ፊርማ_____ቀን_____

Annex IV: Questionnaires

Identification card no. ----------

Part I Demographic characteristics

S.No	Question	Response	Code	Skip pattern
101	Age			
102	Weight			
103	Height			
104	Body mass index (BMI)			

Part II preoperative Assessment

S.No	Question	Response	Code	Skip pattern
201	Admission diagnosis			
202	Parity	Gravida _____		
		Para _____		
203	Gestational age in weeks			
204	Indication of C/S	Previous C/S	1	
		CPD	2	
		Others specify	3	
205	Maternal hemoglobin level			
206	Premedication	Metoclopramide	1	
		Cimetidine	2	
		Other specify	3	
207	Baseline blood pressure(MAP)	____/____mmHg (_____)		
208	Baseline heart rate	_____(bpm)		
209	Baseline RR& Spo2	_____breath/min & _____%		

Part III: Intra-operative Assessment

S.No	Question	Response	Code	Skip pattern
301	baricity of bupivacaine administred	Isobaric bupivacaine	1	
		Hyperbaric bupivacaine	2	
302	Dose of local anesthetics	_____mg		
304	Local anesthetics administered time			
305	Level of sensory blockage	T_{10}	1	
		T_8	2	
		T_6	3	
		T_4 and above	4	
306	Skin incision time			
307	Delivery time			
308	Physician status	Specialist	1	
		Resident	2	
309	Type of utero-tonic agent used	Oxytocine	1	
		Ergometrine	2	
310	Maternal complications	Nausea and vomiting	1	
		Light headedness	2	
		Respiratory depression	3	
		Other specify	4	
311	APGAR score	APGAR score at 1st min _____		
		APGAR score at 5th min _____		
312	Vasopressors used	Ephedrine _____(mg)	1	
		Adrenaline _____(mg)	2	
		Other specify _____	3	
312	Amount of fluid used	_____ ml		
313	Total blood loss	_____ ml		

Maternal vital sign from LA administeration to the first hour of operation

Vital sign	Baseline	Induction	Minutes										
			5	10	15	20	25	30	35	40	45	50	55	60
SBP														
DBP														
MAP														
HR														

Name of data collector----------signature----------date----------

Name of supervisor----------signature----------date----------

Declaration

Assurance of principal investigator

I, the undersigned, declare that I have developed and written the enclosed thesis which is my original work in partial fulfillment for the requirements of degree of Master of Science in advanced clinical Anesthesia. I understand that plagiarism will not be tolerated and all literal quotations are clearly marked.

Name of student: _____

Date: _____ Signature: _____

Approval of primary Advisor

Name of primary Advisor: _____

Date: _____ Signature: _____