A RESEARCH THESIS TO BE SUBMITTED TO DEPARTMENT OF ANESTHESIA COLLEGE OF PUBLIC HEALTH AND MEDICAL SCIENCES, ADDIS ABABA UNIVERSITY IN PARTIAL FULFILLMENT FOR THE REQUIREMENT OF THE DEGREE, MASTER OF SCIENCES IN CLINICAL ANESTHESIA

JUNE, 2017

ADDIS ABABA, ETHIOPIA
PROSPECTIVE COHORT STUDY ON EFFECT OF TIMING ON FLUID ADMINISTRATION FOR PREVENTION OF SPINAL ANESTHESIA INDUCED HYPOTENSION IN OBSTETRIC MOTHERS AT GHANDI MEMORIAL HOSPITAL, DECEMBER 2016 TO FEBRUARY 2017

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ABSTRACT

Introduction: Neuraxial anesthesia remains the preferred choice for Cesarean deliveries across the world. Hypotension is the physiologic consequence of spinal anesthesia and can have a potentially deleterious maternal and fetal impact. Measures to decrease the incidence and severity of maternal hypotension include left uterine displacement, fluid preload, fluid co-load, prophylactic vasoconstrictors, trendelenburg position and leg elevation. Acute hydration has become the cornerstone of prophylaxis of hypotension in obstetrics previously but recently studies showed that co-loading also may be better option in prevention of spinal induced hypotension.

Objective: To compare crystalloid preload and coload for the prevention of maternal hypotension in pregnant mothers undergoing elective cesarean section under spinal anesthesia. Secondary outcomes studied included requirement of vasssopressor for treatment of hypotension, maternal nausea and vomiting and neonatal APGAR scores.

Materials and Methods: Prospective cohort study design; 96 parturients, American Society of Anesthesiologist (ASA) physical status 1 or 2, with uncomplicated pregnancies scheduled for cesarean section under spinal anesthesia were involved into two groups. The preload group takes fluid over 20 min before the placement of spinal block; while the coload group received fluid rapidly starting as soon as CSF was tapped. Independent sample t test, Chi-square test or fisher exact test were used and p value <0.05 considered as statistically significant.

Results: The number of mothers who develop hypotension in preload group and Coload group was 39 and 17 respectively and which was statistically significant. Incidence of nausea vomiting was higher in preload group than coload group 25/48 (52%) VS 13/48 (27 %) respectively (x² =6.27,RR=1.65 ,95%C11.24-6.86). Neonatal wt and APGAR score at 1 and 5 minute are comparable and there is no statistically significant difference between the groups.

Conclusions: Even if both techniques were in effective in the prevention of spinal-induced maternal hypotension, coloading was better than preloading in the prevention of hypotension after spinal anesthesia. Therefore it is unnecessary to delay surgery in order to deliver a preload of fluid before spinal anesthesia.
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ACRONYMS
APGAR-Appearance, Pulse, Grimace, Activity, Respiration
ASA-American society of Anesthesiology
BMI- body mass index
BP - blood pressure
C/S - cesarean section
FHB- fetal heart beat
GA- gestational age
HR - heart rate
HGB-hemoglobin
KG-Kilo gram
ML-Mille litter
SA - spinal anesthesia
Vs-versus
VS- Vital sign
WT-Weight
CHAPTER ONE- INTRODUCTION

1.1 Background

Caesarean section is a common procedure done in hospitals. A study done in Pakistan showed that it accounts for 21.4% cases in hospital deliveries (1). In Ethiopia also there is a higher percentage of caesarean section delivery with 31.1% in governmental and 48.3% in private hospitals (2). Neuraxial anesthesia remains the preferred choice for Cesarean deliveries across the world with low failure rate. From hospital delivery 28% by general anesthesia and 78% performed by spinal anesthesia (3). However, hypotension is the physiologic consequence of spinal anesthesia and can have a potentially deleterious impact on both the mother as well as the fetus.

Measures to decrease the incidence and severity of maternal hypotension after spinal Anesthesia are left uterine displacement, fluid loading, prophylactic vasoconstrictors, tredelenburg position and leg elevation (4). Fluid loading has become the cornerstone of prophylaxis of hypotension; despite this measure the incidence of maternal hypotension is very high 30% to 70% (5).

Several studies have been done to evaluate the efficiency of fluid administration technique by comparing crystalloid with colloid fluids but none of them effectively prevent spinal induced hypotension in obstetrics (6). Studies also done on timing of fluid administration; preloading and co-loading, but still they did not conclude that which technique is superior in prevention of spinal induced hypotension (7).
1.2 Statements of the problem

Currently UNFPA estimates that 22000 Ethiopian women and girls die annually, Ethiopian 2016 DHS shows that also 412 Mather’s die from 100000 live births. From obstetric care caesarean section is a common procedure under spinal anesthesia.

Spinal anesthesia have its own complication like hypotension, nausea, vomiting, shivering, post Dural puncture head ache and high spinal. Spinal anesthesia induced hypotension Is the commonest complication and the incidence ranges from 53.3 % to 83% (8).

The risk factors for development of severe hypotension includes; Age ≥ 35 years, Obesity (body mass index ≥29-35 kg/m$^2$) ,Pre-operative hypertension, Associated co-morbidities, Level of block(block above Thoracic 6 causes more) , Baricity of the local Anesthetic agent ,speed of the local anesthesia (faster than 0.2ml/second cause more hypotension) and Higher fetal weight(9).

Maternal intravascular volume deficit with sympathetic block from spinal anesthesia causes the most sever hypotension (10). Prophylaxis use of ephedrine has been used before spinal blockage but hypotension was still occurring in 12 % of cases (11). Large volume of fluid administration before the block is also does not prevent the incidence of hypotension rather has fluid over load complication on mothers and the fetus (12). 13 ml/kg fluids were recommended in addition to maintenance fluid to decrease incidence of hypotension by 50% (13). Administration of colloid or crystalloid fluid was used for prevention method of spinal induced hypotension but there is no statistically significant difference in between fluids (14).

There are two thought in timing of fluid administration for prevention of spinal induced hypotension. Preloading and co loading, preloading means administration of fluid 10 to 20 minutes before spinal anesthesia administered whereas co loading means fluid administration at the time of spinal blockage. Traditionally pre load was considered as the best option for prevention of spinal induced hypotension, however such fluid administration, especially with crystalloids, results in rapid redistribution of the fluid into the extra vascular compartment and may induce the secretion of atrialnatriuretic peptide (ANP) which causes peripheral vasodilatation and excretion of the pre-load fluid (15).

Hypotension occur following spinal injection and at that period rapid administration of fluid is also another technique used but still the incidence of hypotension up to 46%(16). This result is not the same for all scholars and some shows that both technique fail to prevent effectively rather use both techniques with vasoconstrictor prophylaxis for a better option in prevention of spinal induced hypotension (17).
The various observational and prospective studies provide literary evidence from which it can be concluded that pre-loading may still be beneficial (18). The aim of this study is to compare the preventive effect of crystalloid pre loading and crystalloid co loading for spinal induced hypotension in obstetric mothers undergoing caesarean section and expect to get the best choice for prevention of spinal hypotension.
1.3 Significance of the study

Spinal anesthesia is the most widely practiced in obstetric surgical intervention and its complication management is widely varied. From the complication spinal anesthesia hypotension is the most common and their complication endangers both the mother and the fetus. Some studies showed that incidence of spinal hypotension can be reduced by fluid but there are controversies in the timing of fluid administration. Studies done in Europe and Asia had showed that significant difference in incidence of hypotension which could have same effect on our study area .Even the management style also varies due to economic and technological difference to our study area.

The same research was not conducted in our country Ethiopia to show the effect of timing on prevention of spinal induced hypotension .The data in this study will help as base line information for other researchers. Therefore, this study was designed to assess the preventive effect of preload and coload on spinal anesthesia induced hypotension in elective caesarean section.
CHAPTER TWO - LITERATURE REVIEW

2.1 Literature review

Spinal anesthesia is frequently used for caesarean delivery because of its rapid onset, a dense neural block, little risk of local anesthetic toxicity and minimal transfer of drug to the fetus, as well as little risk of failure of block 2%-5% (19). However, spinal anesthesia have its own complication like hypotension, nausea, vomiting, post Dural puncture head ache, high block and total spinal are the commonest complication(20).53.3% to 83% mothers develop hypotension after spinal anesthesia(8).

Age, BMI,ASA status of the mother, Wight of the neonate at birth, level of the sensory block, duration of surgery, multiple birth, prophylaxis use of vasssopressor and atropine are identified the factors for the development of maternal hypotension after spinal anesthesia(21).

Fluid loading, left uterine displacement of the mother, prophylaxis ephedrine or phenylephrine with appropriate hemodynamic monitoring are the prevention strategy of spinal induced hypotension (22).

A comparative study between fluid and ephedrine prophylaxis showed that 12%from ephedrine and 24% from fluid groups develop hypotension (10).

A united state of America study showed that left uterine displacement can effectively reduce the incidence of supine hypotension syndrome in late pregnancy by reducing the complication of ortho caval compression (23).

Another study with a total of 87 mothers grouped in to preload 20 ml/kg fluid and preload (10 ml/kg fluid) with coload (10ml/kg fluid) groups. incidence of hypotension was not statistically significant in between groups but high vasssopressor required in preload groups(39%vs72%) even the frequency of bolus administration was high in preload groups(7times vs 4 times) (24).

A Meta-analysis done in America and Europe from Jan 1989 to May 2009 with A total of 8 studies and includes 518 obstetric caesarean deliveries. The incidence of hypotension in the co load group was 159/268 (59.3%) compared with 156/250 (62.4%) in the preload group (25).

A Britain study conclude that Volume of preload fluid have no significance in prevention of spinal induced hypotension. A total of 60 health mothers for elective cesarean section, Randomly grouped in to two groups and preload with 1000 ml and 200 ml fluid 10 minute before spinal Anesthesia. There was no significance difference in fluid and ephedrine requirement in both groups. The incidence of nausea and vomiting was 53%in both groups. Fetal outcomes have no significant difference in Apgar score and umbilical arterial blood gas analysis (11).
Another study concludes that titrated phenylephrine infusion with co hydration with fluid was the best prevention strategy for spinal induced hypotension (26).

2015 turkey study done for a total of 90 mothers by three groups’ preload, crystalloid co-load and colloid co-load groups the incidence of hypotension and ephedrine requirement were high in preload groups. The incidence of hypotension 66% from preload, 43% from crystalloid co-load and 20 % colloid co-load groups. The fetal out comes is the same across the groups (27).

A study done in Sweden to assess the kinetics of ringer lactate solution and got maximum effect of ringer lactate solution to restore cardiac output and maintaining blood volume while the infusion was fast (28).

A Study conducted in china to determine the effective volume to prevent spinal induced hypotension in 67 parturient .The crystalloid was infused at a rate of 100-150 mL.min-1 prior to the spinal anesthetic injection. The initial volume of crystalloid was 5 mL/kg Volume-effect data were fitted to a sigmoidal maximum efficacy model and the median effective volume (EV50) (41.8%) patients developed hypotension with their base line. With Firth’s correction, the pooled probability of an effective preventive volume of crystalloid at 13 mL/kg was 50.2% (95% CI, 30% to 83.1%) (12).

A 2015 Indian study, which includes 60 healthy pregnant women , revealed that the incidence of hypotension was lesser in co-load group (40%) as compared to the preload group (60%) and vassopressor requirement also more in the preload group than in the co-load group(29).

Another study done in India with a total of 120 mothers grouped in to preload and co-load groups, even if they did not get statistically significant result incidence and episode of hypotension were high in preload groups. First episode 31.7% vs 25%, second episode 10% vs 5% but third episode of hypotension was 3.33% vs 0%.Mothers need vassopressor support before the baby out was also high in preload mothers (30 % vs 3.33%). The fetal out comes were the same in both groups (30).

Another study with a total of 100 healthy parturient grouped in to pre load and coload 20 ml/kg crystalloid fluid was given for both with timing variation .the incidence of hypotension after spinal anesthesia was high from preload groups (23% vs 72%).maternal HR and neonatal Apgar score doesn’t show significant variation between groups (31).

Another study done in India, 2015 compare the hemodynamic change between colloid fluid preloading and co-loading in elective caesarean delivery. A total of 75 parturient grouped in to three. Group A preload with 500ml and Group C were co-loaded with colloid fluids. Group B had ringer lactate on flow.
The incidence of Hypotension in the preload group was 28% and in the co-load group was 8% but 64% from ringer lactate group. The heart rate also rise significantly in the ringer lactate group. Neonatal outcome was the same in the groups (32).

Another prospective randomized controlled study done in India with a total of 100 mothers grouped in to preload and coload. Hypotension was high from preload groups (70% vs 44%) and Heart rate increased in the first 10 minute on preload groups but not on co load groups (33).

Another study done with a total of 40 mothers in two groups preload and co load. Incidence of Hypotension was high in preload (40% vs 15%) but episode of hypotension higher in co load groups. Heart rate increase in co load but decrease in pre load groups for the first 5 minute but increase in both groups after five minute. Incidence of nausea vomiting is comparable in both groups and fetal outcome also have no statistically significance difference (14).

A study conducted in Iran with a total of 72 healthy mothers for caesarean section grouped in to two as crystalloid and colloid preload (500ml each). The incidence of hypotension was high from preload (47.2 vs 25%), nausea vomiting also high from preload groups (41.6% vs 22.2%) (34).

A Pakistan 2010 control trial study which includes 60 adult parturient and randomly divided into two groups of 30 each, and given 10 ml/kg as pre load or coload. Incidence of hypotension high in preload group (70% vs 50%) and also vassopressor requirement high in preload group (mean 15.2mg vs 7mg with P=0.017) (35).

Another 2009, Pakistan study a total of 60 mothers used 0.5% and 0.75% hyperbaric bupivacaine and assessed level of block and hemodynamic changes. Mothers that received 0.5% develop high block up to T2 and maximum bradycardia but maximum block in 0.75% was T4. Sever hypotension recorded and more ephedrine used in mothers who received 0.75% hyperbaric bupivacaine (36).

Another 2013 Random control trial study done in Pakistan with a total of 74 mothers grouped in to preload and co-load group but they did not get statistically significant result (48.6% from co-load and 62.2% from preload develop hypotension with P=0.242) and conclude neither of the two technique effectively prevent spinal induced hypotension (37).

A prospective randomized double blinded experimental study done in Nigeria for elective C/S grouped in to two, group 1 mothers given 750 ml crystalloid with 250 ml colloid fluid and group 2 mothers given only 500 ml colloid fluid before spinal anesthesia administered. The crystalloid /colloid combination
show better efficacy as prophylaxis for the first 10 minute rather have no significant difference in prevention of spinal induced hypotension (38).

2016 study done in Egypt with a total of 50 healthy mothers for elective C/S and grouped in to two, the first group receive 15 ml/kg fluid preload, the other group receive 5mg ephedrine prophylaxis and 1 mg every minute until 15 minute after the block. Incidence of hypotension and nausea/vomiting was high in fluid groups but HR was high in ephedrine groups (39).
2.2 Conceptual framework

- Duration of the operation
- Volume of Blood loss during the operation

Biographic and medical condition of the mothers
- Age
- BMI
- Parity
- GA
- ASA
- Base line VS

Post spinal hypotension

Used local Anesthesia factors
- Type of LA
- Volume of LA
- Baricity of LA
- Level of block

Perioperative fluid factors
- Timing of fluid load
- Volume of fluid
CHAPTER THREE - OBJECTIVE

3.1 General objectives
- To assess the effect of timing of fluid administration on prevention of maternal hypotension during spinal anesthesia for cesarean delivery.

3.2 Specific objective
- To compare pre-load and co-load groups for the incidence of hypotension
- To compare pre-load and co-load groups for the severity of hypotension
- To compare pre-load and co-load groups for the use of vasssopressor
CHAPTER FOUR - METHODOLOGY

4.1 Study Area and period
The study was conducted at Gandhi Memorial Hospital which is located in capital city of Ethiopia, Addis Ababa. It is one of the thirteen government hospitals found in Addis Ababa, which is under the control of Addis Ababa Health Bureau. The Hospital primarily gives services for women and children. A study was conducted from December 2016 to February 2017.

4.2 Study design
Prospective cohort study design was employed.

4.3 Population

4.3.1 Source Population
All mothers scheduled for elective cesarean section procedures at Gandhi Memorial hospital.

4.3.2 Study Population
All elective surgical mothers scheduled for elective caesarean section in the study period under spinal anesthesia and those who fulfill inclusion criteria included in the study.

4.4 Eligibility criteria

4.4.1 Inclusion criteria
- Patients who scheduled for elective cesarean section
- ASA status I and II
- Mothers scheduled to undergo CS under spinal anesthesia plan

4.4.2 Exclusion criteria
- Failed spinal anesthesia
- Mothers used combined spinal epidural anesthesia
- Mothers refusal
- Preoperatively hypotension
- Preoperatively vasoconstrictor prophylaxis used
- Mothers who were NPO without maintenance fluid
4.5 Sampling Technique and Sample Size Determination

4.5.1 Sample size determination

Comparison of two proportions with equal sample size formula for independent cohort

\[
\frac{\alpha}{\sqrt{\frac{1}{n_1} + \frac{1}{n_2} + \frac{p_1 q_1}{n_1} + \frac{p_2 q_2}{n_2}}} + \frac{\beta}{\sqrt{\frac{1}{n_1} + \frac{1}{n_2} + \frac{p_1 q_1}{n_1} + \frac{p_2 q_2}{n_2}}}
\]

\[= \text{where } p_1 \text{ and } p_2 \text{ are the probability of hypotension from preload and co-load respectively.}
\]

\[n_1 = \text{sample for preload, } n_2 = \text{sample for co-load. } n_2 = n_1, \lambda = n_2/n_1.
\]

An Indian 2016 study showed that 40% from preload and 15% from co-load group develop hypotension (14).

\[P_1 = 0.4, q_1 = 0.6 \quad q^- (\text{change}) = 1 - p^- = 0.725
\]

\[P_2 = 0.15, q_2 = 0.85 \quad p^- (\text{change}) = p_1 + \lambda p_2/1 + \lambda = 0.275. \text{ I have plan to get 80% chance of power sample size become } n_1 = 49, n_2 = 49. \text{ A total of 98 mothers involve in the study.}
\]

4.5.2 Sampling technique

Systematic random sampling technique was used to get the required sample size during the study period.

4.6 Study variables

4.6.1 Independent Variables

- Age
- Parity
- Height
- BMI
- preoperative V/S
- ASA status
- Surgical duration
- Time of fluid administration
- Volume of fluid administered
- Baricity, type and dose of local Anesthetic agent administered
- Level of the block
- Blood loss during the operation
4.6.2. Dependent Variables

- Post spinal hypotension which could be measured by incidence, severity and episode of systolic hypotension.

- Secondary maternal outcome nausea vomiting and fetal APGAR score

4.7 Plan of Data Collection

Questioners were prepared in English which includes socio demographic data, physical characteristics of the patient, preoperative vital signs, mothers BMI, parity, gestational age, ASA classification, medical comorbidities, total estimated blood loss, type of local anesthesia and other variables. The data collection was undertaken by four Anesthetists after getting training and the principal investigator supervise the completeness of the data daily.

4.8 Data Processing and Analysis

Data will be checked manually for completeness and then coded and entered into EPI info version 7 then transferred to SPSS version 20 computer program for analysis. Descriptive statistics used to summarize data, tables and figures. Independent sample t test, Chi-square test or fisher exact test were used and p value <0.05 considered as statistically significant.

4.9 Data Quality Control and Assurance

Data collectors were trained by principal Investigators. Pretest was done for 1 week at Zewditu Memorial hospital and during data collection, regular supervision and follow up made appropriately. Principal Investigator was cross check for completeness and consistency of data every day. All materials used for data collection was arranged sequentially and data stored in safe and secure place.

4.10 Dissemination plan

Copies of the research will be disseminated to college of health science, school of medicine/department of anesthesia, Addis Ababa University student research office, Ethiopian Association of Anesthetists, Different NGOs that work on maternal health, Ethiopian ministry of health. Finally it will be send to national and international journal publishers for publication.
4.11 Operational definitions

Caesarean section- Is delivery of the fetus along with placenta and Membrane under anesthesia through the incision of Abdominal and intact uterine wall after the fetus reached viability

Spinal anesthesia- It is a type of regional anesthesia in which local anesthetic Agents is administered in subarachnoid space

Co loading- giving fluid while at the same time perform spinal anesthesia

Preloading- Administration of fluid for 20 minute before anesthesia initiated

Hypotension- decrease of systolic blood pressure by 20% and above from the base line or SBP less than 90mmhg

Tredelenburg position- the body is laid flat on the back with the feet higher than the head by 15-30 degree.

4.12 Ethical Consideration

Prior to data collection, the proposal reviewed by the ethical committee of college of health science and official letter obtained. Get permission from Ghandi memorial Hospital clinical director office after submission of official letter. Moreover, the objective of the study explained to both hospital administration and the patients who included in the study. Verbal consent from the patients obtained and Confidentiality of the information assured by using code numbers than personal identification names and keeping questionnaires locked.
CHAPTER FIVE- RESULT

A total of 96 mothers who operated up on under spinal anesthesia were included and completed the study. Age, Ht, base line systolic BP and HR were comparable. From these clients 48 were given preload and 48 were coloaded. Finally variables were compared within the groups. Total blood loss during the surgery, duration of the surgery, APGAR score and neonatal wt were also comparable between the groups (table 1). All mothers used the same type of local anesthesia 40 mg (2 ml of 2%) hyperbaric Lidocaine. Only 5 mothers from preload group and 3 mothers from coload groups achieved up to T6. Used utero genic agent were Oxytocin, Ergometrine and combined form from preload groups 29,7,12 and from coload groups 28,13 and 26 mothers respectively.

Table 1. socio Demographic characteristics of study participants, mothers baseline v/s characteristics, duration of surgery and neonatal conditions in each groups Ghandi memorial hospital Addis Ababa, Ethiopia, December 2016-February 2017(n=48 preload and n=48 coload)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Preload group</th>
<th>Coload group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ( year)</td>
<td>30.3±5.2*</td>
<td>29.2±5.1</td>
<td>0.3</td>
</tr>
<tr>
<td>Ht ( cm)</td>
<td>160.8±7.7*</td>
<td>159±7.4</td>
<td>0.53</td>
</tr>
<tr>
<td>BMI(kg/m²)</td>
<td>31.1 (21.1-34.6)**</td>
<td>29.3 (17.1-34.5)</td>
<td>0.034</td>
</tr>
<tr>
<td>Gravidity</td>
<td>I(I-III)**</td>
<td>I (I-III)</td>
<td>0.4</td>
</tr>
<tr>
<td>ASA status</td>
<td>II (I-II)**</td>
<td>II (I-II)</td>
<td>0.2</td>
</tr>
<tr>
<td>Systolic BP before anesthesia</td>
<td>129.85±8.7*</td>
<td>126±10.2</td>
<td>0.52</td>
</tr>
<tr>
<td>HR before anesthesia</td>
<td>86.2±10.8*</td>
<td>87±9.9</td>
<td>0.68</td>
</tr>
<tr>
<td>Duration of surgery in min</td>
<td>≤40min (40-50min)  **</td>
<td>≤40min (40-60min)</td>
<td>0.7</td>
</tr>
<tr>
<td>Blood loss (ml)</td>
<td>605±72*</td>
<td>610±67</td>
<td>0.7</td>
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<tr>
<td>Level of sensory block</td>
<td>T10 (T10-T6)**</td>
<td>T10 (T10-T6)</td>
<td>0.3</td>
</tr>
<tr>
<td>APGARscoreat1min</td>
<td>8±0.8*</td>
<td>8.1±0.8</td>
<td>0.38</td>
</tr>
<tr>
<td>APGARscoreat5mi</td>
<td>9±0.6*</td>
<td>8.9±0.7</td>
<td>0.53</td>
</tr>
<tr>
<td>Neonatal wt (kg)</td>
<td>2.96±0.38*</td>
<td>2.96±0.23</td>
<td>0.92</td>
</tr>
</tbody>
</table>

*=mean and SD , **= median (range)
Table 2. Incidence of systolic hypotension in the first 60 minute after spinal anesthesia in the groups, Ghandi memorial hospital Addis Ababa Ethiopia, December 2016-February 2017 (n=48 preload and n=48 coload).

<table>
<thead>
<tr>
<th>Time in minute</th>
<th>Preload group develop hypotension</th>
<th>Coload group develop hypotension</th>
<th>X²</th>
<th>RR</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>13/48</td>
<td>6/48</td>
<td>3.2</td>
<td>1.5</td>
<td>0.07</td>
</tr>
<tr>
<td>10</td>
<td>23/48</td>
<td>9/48</td>
<td>9.8</td>
<td>1.8</td>
<td>0.002</td>
</tr>
<tr>
<td>15</td>
<td>32/48</td>
<td>16/48</td>
<td>10.6</td>
<td>2</td>
<td>0.001</td>
</tr>
<tr>
<td>20</td>
<td>33/48</td>
<td>16/48</td>
<td>12</td>
<td>2.1</td>
<td>0.001</td>
</tr>
<tr>
<td>30</td>
<td>24/48</td>
<td>12/48</td>
<td>6</td>
<td>1.6</td>
<td>0.01</td>
</tr>
<tr>
<td>40</td>
<td>19/48</td>
<td>12/48</td>
<td>2.2</td>
<td>1.3</td>
<td>0.1</td>
</tr>
<tr>
<td>50</td>
<td>9/48</td>
<td>6/48</td>
<td>0.7</td>
<td>1.2</td>
<td>0.3</td>
</tr>
<tr>
<td>60</td>
<td>8/48</td>
<td>6/48</td>
<td>0.3</td>
<td>1.1</td>
<td>0.3</td>
</tr>
</tbody>
</table>

X² = chi-square, RR = relative risk
The incidence of systolic hypotension after spinal anesthesia was 81.2% (39/48) in the preload group and 35.4% (17/48) in the coload group which is statistically significant (p < 0.05). The preload group mothers develop more hypotension with relative risk of 2.55 and \( \chi^2 = 20.7 \) (95% CI of 1.52-3.44) (Figure 1). Diastolic hypotension (79% vs 39%) and mean hypotension incidence (75% vs 37%) were also almost the same with systolic hypotension in preload and coload group respectively.

More hypotension was recorded in the first 20 minute (table 2). 5 mothers from preload and 1 mother from coload group develop sever form of hypotension (reduced more than 40% from the base line) (Figure 2). 21 mothers from preload and 11 mothers from coload group developed 4 and above episode of hypotension (Figure 3). 1 mother from preload and 2 mother from coload group use drugs in addition to fluid for hypotension management (adrenaline, atropine) but no mothers need of transfusion in both group.
Figure 1. Incidence of systolic hypotension between the groups Gandhi Memorial Hospital Addis Ababa, Ethiopia, December 2016-February 2017 (n=48 preload and n=48 coload).

Figure 2. Severity of systolic hypotension in the groups (reduction of systolic BP from the baseline) Gandhi Memorial Hospital Addis Ababa Ethiopia, December 2016-February 2017 (n=48 preload and n=48 coload).
Figure 3. Episode of systolic hypotension in the groups, Ghandi memorial hospital Addis Ababa Ethiopia, December 2016-February 2017 (n=48 preload and n=48 coload).

Figure 4. Volume of fluid administered in ml in the groups Ghandi memorial hospital Addis Ababa Ethiopia, December 2016-February 2017 (n=48 preload and n=48 coload)
Incidence of tachycardia were 11 mothers from preload and 4 mothers from coload (23% vs 4%) with \( x^2 = 3.87 \) and \( p = 0.089 \) which is not statistically significant in between groups. There is no recorded hypertension (systolic BP more than 140 mm hg or increased more than 20% from the base line) and bradycardia (HR less than 60 bpm). In both group incidence of systolic hypotension higher in mother who have high BMI 48% vs 65% in category of 25-29.9 and 30-34.9 bmi category respectively but it is not statistically significant.

Incidence of nausea and vomiting was higher in preload group than coload group 52% VS 27% respectively \( (x^2 = 6.27, \text{RR} = 1.65, 95\% \text{CI} = 1.24-6.86 \) and \( p \) value \(<0.05\)) and which was highly associated with hypotension with \( x^2 = 13.9, \text{RR} = 1.9, 95\% \text{CI} = 1.4-2.6 \) and which was statistically significant, \( P \) value \(<0.05\). Neonatal wt and Apgar score at 1 and 5 minute are comparable and there is no statistically significant difference between the groups.
CHAPTER SIX- DISCUSSION
Spinal anesthesia is considered to be safe compared with general anesthesia for cesarean section. General anesthesia is associated with higher mortality rate in comparison with regional anesthesia. However, spinal anesthesia is not without risk. Hypotension is the most common side effect after spinal anesthesia. Caesarean section under spinal block require sensory block from T4 to T6 this level of high block induces wide spread vasodilation with resultant hypotension. The sympathetic blockade after spinal anaesthesia causes arterial and venodilation resulting in hypotension; this is further aggravated by aorto caval compression.

Several preventive measures like use of mechanical or pneumatic compression of lower limbs to reduce the peripheral pooling and increase venous return, a slight head down tilt after giving spinal anaesthesia, prophylactic use of vasssopressor, infusion of crystalloid or colloid, preload or co-load have been used to reduce the incidence of hypotension following spinal anaesthesia. But fluid preloading for cesarean section under regional anesthesia has been established as routine and considered to be a safe and effective method of reducing the incidence of hypotension previously.

In this study, 81 % of mothers in the preload group and 35% in the coload group develop hypotension. The results of this study are close to the study of David bruck and et al and they gets 72% from preload and 39% from co-load groups develop hypotension (23).

Another Indian study also in line with this study and which showed that the incidence of hypotension after spinal anesthesia was high from preload groups than coload groups with 72% vs 23 % (31).

Khan M and et al also showed that 70% from preload and 44% from coload develop hypotension after spinal anesthesia(33)
However other researchers showed that timing of fluid administration had no any difference in the prevention of spinal hypotension. Zainab farid and et al got statistically insignificant difference from the group 62.2% vs 48.6% incidence of spinal induced hypotension in preload and coload group respectively (36). Another 2013 Pakistan study showed that also there are no any difference In incidence of maternal hypotension after spinal anesthesia in preload and coload groups and they conclude that neither of the two technique effectively prevent spinal induced hypotension (37). The difference was they use extensively vasssopressor when systolic BP dropped in to 90mmhg and monitor the BP every minute.

volume of fluid preload has no more role in prevention of spinal induced hypotension, from this study 13 mothers take more than 1500ml fluid but 11 mothers develop hypotension in other cases 2 mother take less than 500 ml fluid before spinal anesthesia but 1 mother develop hypotension. This result is consistent with R Jackson , et al they showed that 200ml and 1000ml crystalloid fluid preload were no significant difference in episode, incidence, severity and ephedrine requirement in both groups (11).Mothers who have high BMI develop more hypotension than who have low bmi (48% vs 65%) but it was not statistically significant. These result related with the work of Bernd Hartmann and et al they showed that higher bmi was a single factor for induction of spinal anesthesia induced hypotension in obstetrics with odd ratio of 1.08 (8).High fetal Wight and hypotension was related in this study in the preload group normal fetal wt 2.5-3.5 kg have 82% and more than 3.5 kg fetal wt develop 100% hypotension where as in coload group normal fetal wt and incidence of systolic hypotension was 38% but in both group the difference was not statistically significant with p value >0.3.Another study by Ravi Jindal et al showed that high fetal wt was a factor of spinal anesthesia induced systolic hypotension in obstetric mothers (16).

10% mothers from preload group and 2% mother from coload group develop sever form of hypotension but the difference was not statistically significant. In other studies m.m.tawfik et al showed that 15.5% from preload and 9.8 % from coload group develop sever form of hypotension (7).The difference was they use the definition of sever hypotension systolic BP less than 80mmhg but in these study defined as a sever hypotension when it reduced by 40% and above from the base line.
The episode of systolic hypotension was 43% from preload and 23% from coload group develop four and above times and which was statistically significant result (p <0.05). Other researches like A sharman et al showed that 10% from preload and 5% from coload group had 2 episode and 3.33% from preload group develop 3 episode of hypotension (29). The differences was they measure maternal BP every minute (beat to beat) and manage early with the required vasssopressor , but in this study maternal BP measured every five minute and may be double count as well as hypotension managed  by fluids .

2 mothers from coload uses adrenaline and 1 mother from preload group use adrenaline and atropine but the difference was not statistically significant. These results vary from other researches; Mueen ullah khan et al showed that ephedrine and phenylephrine requirement was high in preload group to manage spinal induced hypotension (34).The reason in ghandi memorial hospital there are no available vasssopressor like ephedrine and phenylephrine. In this study blood loss at the surgical site was a factor for maternal hypotension from preload mothers loss more than 700 ml of blood incidence was 90% ( with x²=1.7,RR=1.8 and p =0.2) and 100% in the coload group (with x²=2.23,RR=1.4 and p=0.2) but the difference was not statistically significant in both groups.

Incidence of nausea and vomiting was higher in preload group than coload group 52% VS 27 % respectively (x²=6.27 ,RR=1.65  95%C11.24-6.86 and p value < 0.05) and which was highly associated with incidence of systolic hypotension with x²=13.9,RR=1.9,95%C1=1.4-2.6 and P value <0.05.These result was highly related with the work of Ah-young oh et al they showed that 60% vs 27% incidence of nausea vomiting in preload and coload group respectively. This result also in line with Iran study and which showed that incidence of nausea and vomiting was high from preload groups with 41.6% vs 22.2% (34).

Apgar score at 1 and 5 minute are comparable and there is no statistically significant difference between the groups in this study. This work is related with the work of Kulkarni AG and other literatures which showed that there were no difference in Apgar score of the neonate in between preload and coload group (31).
The limitation of this study was;
- The used BP measurement was only non invasive blood pressure measurement and could not get beat to beat or every minute measurement of mother’s BP
- We couldn’t appreciate the duration of hypotension in between episode of hypotension.
- Clients develop hypotension even sever type of hypotension could not get the necessarily vasssopressor and could not compare effectively vasssopressor usage between the groups.
-This is observational study and have randomization problem.
CHAPTER SEVEN- CONCLUSION AND RECOMENDATION

7.1 Conclusion
This study showed that 81 % hypotension from preload and 35% from coload group. Therefore Crystalloid co-loading is more effective than preloading in prevention of spinal anaesthesia induced hypotension in elective caesarean cases.
In busy operating room schedules with rapid turnover of cases co-loading would be more efficient method in prevention of spinal induced hypotension.

7.2 Recommendation
   It is unnecessary to delay surgery in order to deliver a preload of fluid.
   Secure large gage double IV line and Coloaded the mother while administering spinal anesthesia .Other researchers needed for to assess the effect of colloid and crystalloid as well as other factors for better prophylactic measure in spinal induced hypotension.
REFERENCES


11. Salama AK, Goma HM, Hamid BMA. Fluid preloading versus ephedrine in the management of


Annex I. Questionnaires
A data collection formats for patients that underwent elective caesarean section at ghandi memorial hospital, Addis Ababa.

Fill the blank space provided, Encircle the alternatives when necessary finally Check the questions for completeness.

<table>
<thead>
<tr>
<th>I. Socio demographic data of the mothers</th>
<th>preload ☐ coload ☐</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. AGE………</td>
<td>2. Wt……………</td>
</tr>
<tr>
<td>3. Ht…………..</td>
<td>4. BMI………..</td>
</tr>
</tbody>
</table>

Questions on maternal general medical status

<table>
<thead>
<tr>
<th>Questions</th>
<th>1. Gravida……</th>
<th>2. GA in wks……</th>
<th>3. ASA ……</th>
</tr>
</thead>
</table>

4. Base line VS

<table>
<thead>
<tr>
<th>BP……………</th>
<th>HR……………</th>
<th>FHB ………</th>
</tr>
</thead>
</table>

5. volume of fluid

<table>
<thead>
<tr>
<th>A. Preload--------ml</th>
<th>B. Co-load…….ml</th>
</tr>
</thead>
</table>

III Intra operative VS of the mothers

<table>
<thead>
<tr>
<th>1. BP At the beginning……………reduction by %</th>
<th>2. HR At the beginning………</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. At 5 minute---------------------------%</td>
<td>A. At 5 minute---------------</td>
</tr>
<tr>
<td>B. At 10 minute------------------------%</td>
<td>B. At 10 minute--------------</td>
</tr>
<tr>
<td>C. At 15 minute----------------------%</td>
<td>C. At 15 minute-------------</td>
</tr>
<tr>
<td>D. At 20 minute---------------------%</td>
<td>D. At 20 minute-------------</td>
</tr>
<tr>
<td>E. At 30 minute-----------------%</td>
<td>E. At 30 minute-------------</td>
</tr>
<tr>
<td>F. At 40 minute----------------%-</td>
<td>F. At 40 minute-------------</td>
</tr>
<tr>
<td>J. At 50 minute----------------%-</td>
<td>J. At 50 minute-------------</td>
</tr>
<tr>
<td>H. At 60 minute----------------%</td>
<td>H. At 60 minute-------------</td>
</tr>
</tbody>
</table>

4. Episode of hypotension during intra operative and immediate post operative period

<table>
<thead>
<tr>
<th>A. one times</th>
<th>B. Two times</th>
<th>C. Three times</th>
<th>D. Four and above times</th>
</tr>
</thead>
</table>

4. How do you manage Hypotension during intra operative and immediate post operative period?

<table>
<thead>
<tr>
<th>A. By positioning</th>
<th>B. By fluid</th>
<th>C. By vassospressor (name and dose)……………</th>
<th>D. By blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>5. Severity(reduction) of hypotension from the baseline (SBP)</td>
<td>6. Type of local Anesthesia used</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------------------------------------------------------------</td>
<td>---------------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A. Only by 20 %</td>
<td>A. Lidocaine 5%,..................ml</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B.20-30%</td>
<td>B. Bupivacaine 0.5%,.............ml</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C.30-40%</td>
<td>C. Ropivacaine 0.5%,.............ml</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D. 40%-50%</td>
<td>D. Bupivacaine with additive (Opoid, neostigimine, ketamine........mg/ml)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E. 50% and above</td>
<td>8. Level of sensory block before skin incision</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>7. Baricity of used local Anesthetic agent</th>
<th>9. Surgical duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Hypobaric</td>
<td>A. Less than 40 minute</td>
</tr>
<tr>
<td>B. Isobaric</td>
<td>B. 40-50 minute</td>
</tr>
<tr>
<td>C. Hyper baric</td>
<td>C. 50-60 minute</td>
</tr>
<tr>
<td></td>
<td>D. 60 minute and more</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>10. Total blood loss ----------------------------------------</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>11. Type of uterogenic agent used</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Oxytocin--------unit</td>
</tr>
<tr>
<td>B. Ergometrine-------Mg</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>12. APGAR score of the neonate at 1 minute------</th>
<th>13. Neonatal wt..........kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>C. combined</td>
<td></td>
</tr>
<tr>
<td>D. Other (specify)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>14. Incidence of nausea vomiting</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Yes</td>
</tr>
<tr>
<td>B. No</td>
</tr>
</tbody>
</table>

Name of data collector--------------------------

Signature---------------------------

Thank you!!!
### Annex II. Declaration

#### Assurance of principal investigator

I, the undersigned, Msc in clinical anesthesia student declare that this thesis paper is my original work in partial fulfillment of the requirement for the degree of Master in clinical Anesthesia.

Name of the student: Abebe Tiruneh  
Date. 16-07-2017  
Signature __________________

#### Approval of the primary Advisor

Name of the primary advisor: Meron Abrar  
Date. 16-07-2017  
Signature __________________