EFFECT OF PROPHYLACTIC ONDANSETRON ON SPINAL ANAESTHESIA - INDUCED HYPOTENSION DURING CAESAREAN SECTION AT MOI TEACHING AND REFERRAL HOSPITAL, ELDORET, KENYA.

BY

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A THESIS SUBMITTED IN PARTIAL FULFILLMENT FOR THE AWARD OF MASTER OF MEDICINE DEGREE IN ANAESTHESIA AND CRITICAL CARE OF MOI UNIVERSITY, ELDORET, KENYA.

DECLARATION

Declaration by the Candidate

I declare that this thesis is my original work and has not been presented for the award of a degree in any other University.

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DEDICATION

This work is dedicated to my family for their never-ending support and prayers.

To all healthcare workers who show tireless efforts in ensuring the delivery of quality services to patients.

ACKNOWLEDGEMENT

I would like to acknowledge the Almighty God for His unwavering love and for giving me the strength, wisdom, knowledge and understanding in order for me to complete this study.

I would also like to acknowledge my supervisors Dr. Rose Shitsinzi, Dr. Elisha K. Kirwa and Dr. Peter M. Itsura for their immense support and guidance in completing this study.

I would also like to thank my biostatisticians, Prof. Anne Mwangi and Mr. Henry Mwangi for their unending support.

Much gratitude goes to my study participants, my research assistants, and the Data Safety and Monitoring Board for making this study a success.

I would like to acknowledge the Department of Surgery and Anaesthesiology and the Department of Reproductive Health for their immense support.

Finally, I wish to express my gratitude to the leadership and staff of Moi Teaching and Referral Hospital (MTRH) for granting me the opportunity to conduct this study, and to Uasin Gishu County for supporting me in furthering my education.

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LIST OF ABBREVIATIONS AND ACRONYMS

5-HT3	5- Hydroxytryptamine or Serotonin
APGAR	Appearance, Pulse, Grimace, Activity, and Respiration
ASA	American Society of Anaesthesiologists
BJR	Bezold- Jarisch Reflex
BP	Blood Pressure
CS	Caesarean Section
ETT	Endotracheal Tube
IREC	Institutional Research and Ethics Committee
IU/L	International Units Per Liter
IV	Intravenous
L3, L4, L5	Third, Fourth and Fifth Lumbar vertebrae in the human spine
Mcg	Microgram
Mg	Milligram
Mls	Milliliters
mmHg	Millimeters of mercury
MTRH	Moi Teaching and Referral Hospital
NACOSTI	National Commission for Science, Technology and Innovation
NCPAP	Nasal Continuous Positive Airway Pressure
PPV	Positive Pressure Ventilation
RCT	Randomized Controlled Trial
SA	Spinal Anaesthesia
SAIH	Spinal Anaesthesia-Induced Hypotension
SBP	Systolic Blood Pressure
STATA	Statistics and data

OPERATIONAL DEFINITION OF TERMS

APGAR Score: it is a test which assesses a newborn's health by evaluating five criteria: heart rate, muscle tone, skin color, reflex responses, and breathing.

Aortocaval compression: compression of the maternal abdominal aorta and inferior vena cava by the gravid uterus.

Bezold- Jarisch Reflex: a cardiovascular response consisting of a decrease in heart rate and arterial blood pressure automatically evoked as a direct consequence of chemical or pharmacological stimulation of receptors in the heart or lungs.

Blood pressure: The force of circulating blood on the walls of the arteries, measured in millimeters of mercury (mmHg).

Bradycardia: heart rate of less than 50 beats per minute.

Chemoreceptor: a cell that is specialized to detect chemical substances and relays that information centrally in the nervous system.

Co-loading: the administration of intravenous fluids to optimize the blood volume during spinal anaesthesia.

Hypotension: defined as systolic blood pressure of less than 100mmHg.

Mild hypotension: systolic blood pressure less than 100mmHg to 90mmHg.

Moderate Hypotension: systolic blood pressure less than 90mmHg to 70mmHg.

Mechanoreceptor: a sense organ or cell which responds to mechanical stimuli such as touch or sound.

Neuraxial Anaesthesia: using local anaesthetics close to the spinal cord to prevent or reduce pain that is conveyed from various parts of the body. It involves inserting a needle between the vertebrae to administer medicine into the subarachnoid space (for spinal anaesthesia) or the epidural space (for epidural anaesthesia).

Parturient: a woman who is about to give birth or is in labor.

Preloading: administration of intravenous fluids before implementation of spinal anaesthesia.

Prophylaxis: treatment given or action taken to prevent a physiological event e.g. hypotension.

Preganglionic Sympathetic block: injection of medications (e.g. local anaesthetics) around sympathetic nerve roots along the spine to provide temporary relief from pain.

Severe hypotension: systolic blood pressure below 70mmHg.

Systolic blood pressure: the highest pressure in the cardiac cycle, measured during heart contractions when blood is pumped out and noted as the top number in a blood pressure reading.

Spinal Anaesthesia: injecting a local anaesthetic into the subarachnoid space, blocking spinal nerves and causing loss of sensation and motor function in the lower body.

5-HT3 antagonists: (serotonin receptor antagonists or serotonin blockers) are a class of medicines that are used for the prevention and treatment of nausea and vomiting, particularly caused by chemotherapy, radiation therapy, or postoperatively.

ABSTRACT

Background: Spinal anaesthesia (SA) technique is widely preferred for caesarean sections due to its safety and effectiveness. However, spinal anaesthesia-induced hypotension (SAIH) remains a common and serious complication, with global incidence rates between 50–80% and local rates around 64%. SAIH can lead to adverse maternal effects like cardiovascular collapse, and fetal risks such as hypoxia and acidosis. Existing prevention methods, such as fluid loading and prophylactic vasopressors, are inadequate when used individually. Ondansetron, a 5-HT3 receptor antagonist, may mitigate SAIH by inhibiting serotonin-mediated activation of the Bezold-Jarisch reflex via vagal cardiac receptors. While international data on its efficacy is controversial, its role at Moi Teaching and Referral Hospital (MTRH) also remains unexplored. This study investigates ondansetron's potential to reduce SAIH and enhance maternal outcomes within the MTRH setting.

Objectives: This study aimed to determine the effect of prophylactic ondansetron on the incidence of spinal anaesthesia-induced hypotension and bradycardia, and vasopressor requirements in pregnant women undergoing elective caesarean sections at MTRH.

Methods: A randomized, double-blind, control trial was conducted at Moi Teaching and Referral Hospital (MTRH) involving 194 pregnant women undergoing elective caesarean sections under spinal anaesthesia. Block randomization and consecutive sampling were employed. Participants were assigned to two groups (97 each): one received 4 mg intravenous ondansetron (Group O), and the other received saline (Group S), both administered 15 minutes prior to anaesthesia. To minimize bias, blinding was applied to both the anaesthetists administering the intervention and the study participants. Data on demographics, clinical and surgical outcomes, vasopressor usage, and neonatal results were collected and analyzed using STATA version 16. Statistical tests included the two proportions z-test and Mann-Whitney U test, with significance set at $P < 0.05$.

Results: SAIH incidence proportion was 85.6%. Group O had lower SAIH occurrence (77.3%, n=75) compared to group S (93.8%, n=91), **P=0.001**. Bradycardia was observed in 14.4% (n=14) of Group S and 8.2% (n=8) of Group O participants, with no significant difference (P=0.17). Ephedrine was administered more frequently in Group S (92.8%, n=90) than in Group O (75.3%, n=73), (**P<0.001**). However, the median total dose was comparable between the groups; 18.0 mg (IQR: 12.0–24.0) in Group S and 18.0 mg (IQR: 12.0–30.0; P >0.99). Phenylephrine was administered at almost similar frequencies in Group S (10.3%, n=10) and Group O (7.2%, n=7; P=0.446), though the total dose was significantly higher in Group S (200 mcg) than Group O (100 mcg; **P=0.023**). In addition, occurrence of nausea, vomiting, and shivering was significantly less in Group O (**P<0.05**).

Conclusion: Prophylactic 4mg IV ondansetron is effective in reducing the occurrence of SAIH, the vasopressor requirement, and the total dose of vasopressors. Prophylactic ondansetron has no effect on the occurrence of bradycardia.

Recommendations: Prophylactic administration of 4 mg IV ondansetron 15 minutes before spinal anaesthesia should be considered for elective caesarean sections at MTRH to reduce the incidence of SAIH and vasopressor requirement. The Anaesthesia Department should consider adding ondansetron in the prevention and management protocol of SAIH.

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background Information

Caesarean section (CS) is currently one of the most frequently performed operations on women globally (Atousa et al., 2018). According to the World Health Organization, approximately 21% of births worldwide are currently delivered by Caesarean section. In contrast to general anaesthesia, which carries risks like aspiration, difficult intubation, and unfavorable fetal effects due to the general anaesthetics, spinal anaesthesia (SA) is currently the preferred anaesthesia technique for caesarean sections in hospitals worldwide. At Moi Teaching and Referral Hospital (MTRH), SA is used in over 70% of CS cases (MTRH database, 2020). The total global rate of maternal mortality from anaesthesia appears to have decreased between 2006 and 2010, accounting for 0.9% of pregnancy-related deaths. From 2014 to 2017, the estimated proportion decreased even further, to 0.4%, potentially as a result of increased usage of regional anaesthetic during labor and delivery caesarean sections (Butterworth et al., 2022). When neuraxial anaesthesia is used during a cesarean delivery, the newborn is exposed to less maternal anaesthetic medications, airway manipulation is avoided, postoperative pain is reduced, and the birthing parent can see the child nearly immediately after delivery (Gropper et al., 2025).

Despite being well tolerated, spinal anaesthesia is also associated with some complications. Incidence rates for common spinal anaesthesia-related complications are estimated at 33% for hypotension, 18% for nausea, 13% for bradycardia, 7% for vomiting, 2% for dysrhythmias, and below 1% for post-dural puncture headache (Gwinnutt & Gwinnutt, 2012). Maternal hypotension is the most common posing harm to both the mother and the child (Atousa et al., 2018). Severe hypotension, epidural

hemorrhage, or spinal cord sepsis are the leading causes of death or severe maternal morbidity in regional anaesthesia (Agasti, 2011).

A drop in systolic blood pressure brought about by the spinal anaesthesia can impair uterine blood flow as well as fetal circulation, potentially causing fetal hypoxia and acidosis (Šklebar et al., 2019).

Globally, the occurrence of maternal hypotension post spinal anaesthesia during cesarean section ranges from 50% to 80% (Q. Wang et al., 2014). The definition that is used as well as the amount of intrathecal local anaesthetic that is given determine the incidence of hypotension (Lee et al., 2017).

A cross- sectional study conducted in 2016 at Gandhi Memorial Hospital, Ethiopia with 60 parturients scheduled for elective caesarean section found an incidence of 80% in the first five to fifteen minutes post spinal anaesthesia and 83.7% in fifteen to twenty-five minutes. They described hypotension as systolic blood pressures under 85–90 mm Hg or a reduction of more than 20%–30% from the baseline level (Nigussie Yirgu et al., 2020). Another institution- based cross- sectional study carried out at the same hospital in Ethiopia with 410 patients found the incidence of spinal anaesthesia-induced hypotension during caesarean section to be 64% (Shitemaw et al., 2020). In Kenya, Kahoro, (2009) conducted a cross- sectional study at the Kenyatta National Hospital with 112 full term pregnant women scheduled for both elective and emergency caesarean sections and found that the incidence of spinal anaesthesia- induced hypotension was also 64%.

Spinal anaesthesia induces a preganglionic sympathetic block, resulting in vasodilatation and subsequent maternal hypotension, which may jeopardize

uteroplacental perfusion plus the fetal circulation, potentially causing hypoxia, bradycardia and acidosis (Šklebar et al., 2019).

Spinal anaesthesia blocks the sympathetic nervous system resulting in arterial and venous vasodilation and in return, decreased systemic vascular resistance accompanied by decreased preload and afterload. High spinal distribution levels may lead to bradycardia and a reduction in stroke volume through blockage of accelerating sympathetic cardiac fibers. The occurrence of bradycardia has also been linked to mechanisms such as parasympathetic predominance, enhanced baroreceptor activity, and the triggering of the Bezold–Jarisch reflex (Massoth et al., 2020).

The Bezold–Jarisch reflex (BJR), mediated by serotonin (5-HT3) receptors in intracardiac vagal nerve endings, represents another mechanism implicated in SAIH and bradycardia. The Bezold-Jarisch reflex, often referred to as a cardioinhibitory reflex, involves bradycardia, vasodilation, and hypotension triggered by the stimulation of cardiac receptors. Spinal anaesthesia administration triggers release of serotonin released from activated thrombocytes. Serotonin then activates 5-HT3 chemoreceptors in the vagal nerve endings on the cardiac wall to produce the BJR (Owczuk et al., 2008). Various techniques, including intravenous fluid preloading and co-loading, mechanical methods like lower-leg compression, and pharmacological interventions with vasopressors, have been reported to mitigate SAIH during caesarean delivery. However, no individual technique has demonstrated complete effectiveness when used in isolation (Gao et al., 2015).

Current research indicates that ondansetron, a 5-HT3 receptor antagonist, mostly administered as an antiemetic drug also attenuates spinal anaesthesia–induced hypotension (Gao et al., 2015). Thus, administering ondansetron prophylactically may

lessen the occurrence of SAIH and bradycardia by occluding the interaction of serotonin with 5-HT3 receptors in the left ventricle (Gao et al., 2015).

(Nnacheta et al., 2020) also added that ondansetron's capacity to inhibit serotonin activity on serotonergic receptors in the Bezold-Jarisch reflex pathway accounts for its capacity to mitigate the bradycardic and hypotensive reactions to spinal anaesthesia. However, its use in this context remains under-explored, particularly in the local setting. International data on its efficacy is also controversial and warrants more studies to be conducted.

The purpose of this study was to investigate the impact of prophylactic ondansetron on the occurrence of spinal anaesthesia- induced hypotension during Caesarean Sections at MTRH.

1.2 Problem Statement

Spinal anaesthesia-induced hypotension (SAIH) has a very high global incidence of 50 to 80% (M. Wang et al., 2014). Locally, the incidence of SAIH is 64% (Kahoro, 2009). SAIH during Caesarean section is associated with a high maternal and fetal morbidity and mortality (Bishop, 2014).

If not prevented or managed SAIH can lead to adverse effects for both the mother and the baby. Effects to the mother include syncope, nausea, vomiting, whereas the baby is at risk of acidosis, hypoxia and eventually poor Apgar Scores (O'Sullivan & Cockerham, 2016).

In the absence of prophylactic treatment spinal hypotension leads to fetal effects such as a decrease in uteroplacental blood flow that results in fetal acidosis. More than 2 minutes of maternal hypotension is linked to fetal umbilical acidosis, and more than

4 minutes is linked to neuro-behavioral abnormalities between days 4 and 7 of life (Elriedy & Cockerham, 2019).

In severe cases of spinal hypotension the resulting effect would be total maternal cardiovascular collapse (Fichter & Nelson, 2019).

With a maternal mortality rate of 269 per 100,000 live births, South Africa reported that SAIH contributed 2% of the total maternal deaths (Bishop, 2014). This poses a great concern as to how this condition can be prevented in order to save more lives in the near future.

Many strategies to prevent spinal- induced hypotension have been reported with no single method guaranteed to be effective when used alone (Gao et al., 2015). The strategies include; Fluid preloading prior to initiation of the SA using colloids like hydroxyethyl starch, co-loading during the administration of SA with crystalloids or colloids, and use of vasopressors like Ephedrine, Phenylephrine, or Norepinephrine.

Anecdotal findings at MTRH showed that preloading and co-loading with crystalloids are the common practiced strategies to prevent SAIH but studies show that both preloading and co-loading alone are ineffective in preventing the hypotension associated with spinal block (O'Sullivan & Cockerham, 2016). In the event that hypotension due to spinal anaesthesia occurs during caesarean section, vasopressor drugs such as ephedrine, phenylephrine or norepinephrine are usually used to manage the hypotension. In MTRH, ephedrine is the primary vasopressor, with occasional use of phenylephrine. High doses of ephedrine have been linked to an increased likelihood of fetal acidosis (Butterworth et al., 2022).

In MTRH, however, there is no protocol on when and how to intervene in case a patient develops hypotension as a result of the spinal block during caesarean sections. For this

reason, so many patients tend to have low blood pressures for a longer period than is required and thus increasing the patient's risk of having a cardiovascular collapse. The absence of a standardized, evidence-based protocol for preventing SAIH at MTRH highlights a vital gap in clinical practice and calls for research into safe and effective preventive strategies.

1.3 Study Justification

Moi Teaching and Referral Hospital (MTRH) being a busy facility, approximately 3,200 patients underwent caesarean sections in the year 2020. Approximately 2,200 (68%) of the cases including 215 elective ones, were done under spinal anaesthesia (MTRH database, 2020). Based on the 64% incidence reported by Kenyatta National Hospital (Kahoro, 2009), more than half of caesarean section patients in MTRH are likely to experience hypotension during spinal anaesthesia. This is attributed to the growing preference for spinal anaesthesia in caesarean deliveries. Despite the rising incidence of hypotension during spinal anaesthesia and its detrimental effects on both mother and infant, there is a notable lack of regional studies in East Africa aimed at its prevention or reduction. In contrast, substantial research has been conducted in Asian countries and other parts of Africa, particularly in the Northern region. This underscores the need for more localized research initiatives rather than relying predominantly on findings from Asian contexts. Additionally, there remains a significant gap in studies involving individuals of Black African descent compared to the volume of research focused on populations in Asia and Europe. On the other hand, no study has been done locally in Kenya, particularly at MTRH, assessing the effect of prophylactic ondansetron on the occurrence of spinal anaesthesia- induced hypotension. This study will determine the incidence proportion of SAIH at MTRH and evaluate whether

ondansetron influences its occurrence, providing valuable insights for improving anaesthesia practices and reducing poor maternal and neonatal outcomes.

In MTRH, IV ondansetron is readily available and is usually given at the end of surgeries to effectively prevent post-operative nausea and vomiting. In comparative trials, ondansetron has been shown to be more superior in terms of efficacy in addition to having less or no side effects as well as drug interactions, as compared to metoclopramide and phenothiazines (Tripathi, 2013). Thus, ondansetron is a safe drug to use without anticipating any serious adverse events. It has few non-life-threatening side effects like headache, fatigue, and malaise.

Recent studies across the globe have shown that ondansetron reduces the incidence of SAIH which will lead to fewer mothers developing the hypotension. In return, there will be better neonatal outcomes because few neonates would be exposed to apnea or fetal acidosis that is brought about by reduced fetal circulation resulting from maternal hypotension.

Other scholars have shown that ondansetron has no significant effect on the incidence of spinal anaesthesia- induced hypotension and thus recommend more studies to be done especially with a larger sample size than they had. Nivatpumin et al. (2017) reported that ondansetron was a safe drug considering the fact that they had been administering it at their institution especially during caesarean delivery for many years to prevent and treat nausea and vomiting. However, its effect on reducing the incidence of SAIH was still unclear thus the need for further studies (Nivatpumin et al., 2017). It is therefore justifiable to study the effect of this drug in reducing the incidence of spinal anaesthesia- induced hypotension in order to contribute to the body of knowledge.

Ondansetron is cheap and readily available in MTRH plus it is commonly given to pregnant women with hyperemesis gravidarum but has no known negative impact on the fetus in-utero. It readily crosses the placenta barrier but has no negative effects on the fetus (Elkomy et al., 2015). This implies that the drug poses no harm to both the mother and the fetus and that it is a safe drug to use.

This study seeks to uncover a new, cost-effective preventive measure for complications arising from spinal anaesthesia. This is likely to lead to lower maternal and fetal morbidity and mortality rates and ultimately reduce healthcare expenses. Additionally, it supports Sustainable Development Goal 3, which promotes good health and well-being.

Since there is no protocol on administration of SA during caesarean sections at MTRH, this study will also influence the policy makers on the formulation of proper guidelines and protocols to be used while administering spinal anaesthesia for Caesarean sections at MTRH.

1.4 Research Question

- What is the impact of using prophylactic ondansetron on the incidence of spinal anaesthesia induced hypotension, bradycardia and vasopressor requirement in parturients undergoing elective caesarean section over a 12 - month period?

1.5 Hypothesis

H_0 Hypothesis: Intravenous ondansetron injection 15 minutes prior to administration of spinal anaesthesia does not significantly reduce the incidence of maternal spinal anaesthesia induced hypotension.

1.6 Objectives

1.6.1 Primary Objective

1 To determine the effect of 4mg intravenous prophylactic ondansetron on the incidence of spinal anaesthesia- induced hypotension during cesarean section at MTRH.

1.6.2 Secondary Objectives

1. To determine the effect of 4mg intravenous prophylactic ondansetron on the occurrence of bradycardia in pregnant women under spinal anaesthesia during caesarean section at MTRH.

2. To compare the vasopressor requirement and total dose of vasopressor administered for the treatment of SAIH between the intervention and the control group during caesarean section at MTRH.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Introduction

Caesarean section (CS) refers to the operative delivery of a fetus via abdominal (laparotomy) and uterine (hysterotomy) incisions. Fetal malpresentation, non-reassuring fetal condition, labor dystocia (difficult or obstructed labor), multiple gestation, suspected fetal macrosomia, and previous caesarean birth are common indications for cesarean delivery (Gropper et al., 2025).

Regional anaesthesia (spinal anaesthesia, epidural anaesthesia, and combined spinal-epidural anaesthesia) and general anaesthesia are the two types of anaesthesia used for caesarean section. Many factors influence the selection of anaesthesia for a caesarean section, such as the indication for the procedure, the urgency of the delivery, the preferences of the patient and the obstetrician, and the anesthetist's skill level (Butterworth et al., 2022). General anaesthesia is linked to increased maternal morbidity and mortality, increased hemodynamic fluctuation during anaesthetic induction, and the demand for additional analgesia during anaesthetic recovery. This has resulted in a growing preference toward regional anaesthesia technique. Aspiration pneumonitis, inability to ventilate, and inability to intubate are among the most common airway complications linked to deaths with general anaesthesia.

The primary causes of deaths linked to regional anaesthesia are either local anaesthetic toxicity or excessive dermatomal spread of blockade (Butterworth et al., 2022). There are, however, several advantages associated with regional anaesthesia during CS. When neuraxial anaesthesia is used during a caesarean delivery, the newborn is exposed to less maternal anaesthetic medications, airway manipulation is avoided, postoperative

pain is reduced, and the birthing parent can see the child nearly immediately after delivery (Gropper et al., 2025).

2.2 Spinal Anaesthesia

For caesarean birth, spinal anaesthesia is the most often utilized regional anaesthetic technique. Technically, the block is simpler than an epidural anaesthetic; it also takes effect faster, has a lower risk of systemic drug toxicity because of its smaller dosage; and is more reliable when it comes to administering surgical anaesthesia from the midthoracic level (T4) to the sacrum (Pardo & Miller, 2018).

The standard procedure involves positioning the patient in a lateral decubitus or sitting posture and injecting a hyperbaric solution of intrathecal bupivacaine (10–15 mg) or lidocaine (50–60 mg). It's often simpler to identify the anatomical midline when a patient is sitting rather than in the lateral decubitus position, especially for obese patients. In the sitting position, patients can rest their elbows on their thighs or a bedside table, or hug a pillow, which helps with stability and comfort during the procedure (Butterworth et al., 2022). In the event that the obstetrician cannot likely finish the procedure in 45 minutes or less, bupivacaine should be selected. The occurrence of post dural puncture headache is reduced by using a pencil-point spinal needle (Whitacre, Sprotte, or Gertie Marx) with a gauge of 22 or smaller (Butterworth et al., 2022).

The most widely used local anaesthetic is hyperbaric 0.5% bupivacaine (10 to 15 mg [2 to 3 mL]). It consistently delivers surgical anaesthesia for 90 to 120 minutes. Adding fentanyl (10 to 25 μg), sufentanil (5 to 10 μg), or morphine (0.05 to 0.3 mg) as an adjunct to the local anaesthetic solution can augment perioperative anaesthesia and analgesia. Whilst fentanyl acts quickly, it has a limited duration of action and offers minimal further analgesic effects after surgery. As opposed to fentanyl, morphine has

a longer latency and can offer pain relief lasting up to 24 hours postpartum, although patients must be monitored for respiratory depression that occurs post administration (Barash et al., 2017; Butterworth et al., 2022).

Pregnancy induces several physiological changes that significantly influence the administration and effects of spinal anaesthesia. These changes differentiate pregnant patients from non-pregnant individuals and other patient groups, requiring tailored approaches to ensure safety and efficacy. In pregnant women, the spread of neuraxial block is accelerated. Increased epidural blood volume during pregnancy, as confirmed by magnetic resonance imaging, results in diminished epidural space capacity and reduced lumbar cerebrospinal fluid volume. During pregnancy, the volume of adipose tissue within the epidural space and the caliber of the epidural venous plexus increases, leading to a reduction in spinal cerebrospinal fluid volume. These factors explain why there is increased spread of local anaesthetic in pregnant women. Furthermore, multiple studies have shown that pregnancy increases sensitivity to local anaesthetic agents. Exogenous progesterone was found to increase the sensitivity of rabbit vagus nerves to bupivacaine, suggesting that progesterone may be the reason for the increased sensitivity (Chestnut et al., 2020).

Because sympathectomy proceeds more quickly with spinal anaesthesia than with epidural anaesthesia, maternal hypotension is more likely to occur and to be more severe. Spinal anaesthesia- induced hypotension is the most prevalent complication of spinal anaesthesia in parturients undergoing caesarean delivery (Lee et al., 2017). Reported incidence rates for spinal anaesthesia-related complications are as follows: hypotension (33%), nausea (18%), bradycardia (13%), vomiting (7%), dysrhythmias (2%), and post dural puncture headache (<1%) (Gwinnutt & Gwinnutt, 2012).

2.2.1 Indications for Spinal Anaesthesia

Spinal anaesthesia is ideally suited for procedures below the umbilical region. This includes surgeries such as hernia repairs, gynaecological, obstetrics and urological operations, as well as interventions on the perineum or genitalia. Using spinal anaesthesia for these types of surgeries helps ensure effective pain management and patient comfort.

While spinal anaesthesia can facilitate all types of leg surgeries, it's important to consider the patient's comfort, particularly in cases like amputation. Although the procedure will be painless, the experience may be distressing for an awake patient. In such situations, it may be more compassionate to enhance the spinal anaesthesia with substantial sedation or even a light general anaesthetic to ensure the patient's mental and emotional well-being. Spinal anaesthesia is a suitable option for managing trauma patients, provided they have been properly resuscitated and are not experiencing hypovolemia. In obstetrics, it proves ideal for the manual removal of a retained placenta, as long as there is no presence of hypovolemia. This approach ensures effective pain relief while maintaining patient safety (Ankcorn & Casey, 2015).

2.2.3 Contra-indications to Spinal Anaesthesia

Most contraindications for spinal anaesthesia are similarly applicable to other regional anaesthesia methods. One key contraindication is the lack of adequate resuscitative drugs and equipment. The administration of neuraxial analgesia or anaesthesia necessitates the availability of specific resuscitation equipment and emergency drugs, including:

Recommended Drugs

- **Hypnotic–amnestic agents**: Propofol, Ketamine, Midazolam
- **Neuromuscular blocker**: Succinylcholine
- **Vasopressors**: Ephedrine, Epinephrine, Phenylephrine
- **Anticholinergic**: Atropine
- **Electrolyte and buffer agents**: Calcium chloride, Sodium bicarbonate
- **Opioid antagonist**: Naloxone

Essential Equipment

- Oxygen delivery system
- Suction apparatus with appropriate tubing and catheters
- Self-inflating bag (Ambu-bag) and mask for positive-pressure ventilation
- Assorted face masks
- Oropharyngeal airways
- Laryngoscope with a range of blades
- Endotracheal tubes with stylet
- Eschmann stylet / bougie
- Qualitative carbon dioxide detector

It is crucial that no regional anaesthetic technique be attempted without having these essential tools and medications immediately available (Chestnut et al., 2020).

Clotting disorders are a major concern. If an epidural vein is punctured by the spinal needle, bleeding into the epidural space can occur, leading to a hematoma that might compress the spinal cord. This is particularly risky for patients with low platelet counts or those on anticoagulants like heparin or warfarin. Additionally, patients with liver

disease often have abnormal clotting profiles, and both low platelet counts and abnormal clotting can be present in pre-eclampsia (Ankcorn & Casey, 2015).

Hypovolemia, regardless of its origin such as bleeding, dehydration from vomiting, diarrhea, or bowel obstruction poses significant risks. Patients need to be properly rehydrated or resuscitated before undergoing spinal anaesthesia. If they are not, they may experience severe hypotension during the procedure.

Presence of sepsis or infection on the back near the lumbar puncture site is a significant contraindication for spinal anaesthesia. This is due to the risk of spreading the infection into the central nervous system, which could lead to severe complications. Ensuring the area is free from infection is crucial for patient safety during the procedure.

Patient refusal is an important consideration. Patients may initially feel apprehensive and express a preference for general anaesthesia. However, after being informed about the benefits of spinal anaesthesia, many may change their minds and be pleasantly surprised by the outcome. If, despite a thorough explanation, the patient still declines spinal anaesthesia, their decision should be respected. It is crucial to honor the patient's autonomy and ensure they are comfortable with their choice of anaesthesia

Uncooperative patients present a unique challenge. While spinal anaesthesia can be appropriate for children, their cooperation is essential and should be thoroughly evaluated during the pre-operative visit. Similarly, patients with mental disabilities or psychiatric issues require careful pre-operative assessment to determine their suitability for spinal anaesthesia and ensure their comfort and safety throughout the procedure.

Septicaemia poses significant risks for patients undergoing spinal anaesthesia. Due to the presence of infection in the bloodstream, there is a possibility that these patients

could develop meningitis if a hematoma forms at the lumbar puncture site and becomes infected. This serious complication underscores the importance of careful patient selection and monitoring when considering spinal anaesthesia for individuals with septicaemia.

Anatomical deformities of the patient's back present a relative contraindication for spinal anaesthesia, primarily because they can complicate the process of performing a dural puncture.

In cases involving neurological disease, a thorough assessment is required to weigh the benefits and potential risks. Any postoperative exacerbation of the neurological condition might be mistakenly attributed to the spinal anaesthetic. Conversely, raised intracranial pressure is an absolute contraindication, as a dural puncture in such situations can trigger brainstem herniation (Ankcorn & Casey, 2015).

Reluctant surgeons can pose a significant challenge. If a surgeon feels uncomfortable operating on a conscious patient or lacks sufficient experience, it might be prudent to avoid using spinal anaesthesia in such cases. Ensuring the surgeon's confidence and skill level is crucial for the safety and well-being of the patient (Ankcorn & Casey, 2015).

2.2.3 Spinal Anaesthesia- induced Hypotension

Neuraxial anaesthesia is frequently associated with hypotension. This type of anaesthesia, often used in the course of labor and delivery, can lead to a drop in blood pressure. Interestingly, the risk of experiencing hypotension differs between women who are in labor and those who are not. Among term pregnant women, those in active labor exhibit a lower incidence of hypotension compared to their non-laboring counterparts. This variation may be attributed to physiological changes that occur

during labor, which may help stabilize blood pressure. However, it's crucial for healthcare providers to closely monitor and manage blood pressure in all patients receiving neuraxial anaesthesia to ensure their safety and well-being (Barash et al., 2017).

In current textbooks and literature, hypotension is typically defined as a decrease greater than 20% of the patient's baseline systolic blood pressure or an absolute systolic blood pressure (SBP) value below 100 mmHg (Butterworth et al., 2022).

Different scholars came up with several definitions of spinal anaesthesia- induced hypotension. Agasti, (2011) defined it as SBP below 100 mmHg or a mean arterial pressure (MAP) of < 20% of previous one after the spinal injection of a local anaesthetic drug. A survey done in the United Kingdom of the specialist obstetric anaesthetists discovered that most of them preferred absolute SBP cutoffs of below 90 mmHg or below 100 mmHg to be the definition of spinal anaesthesia induced hypotension (Zwane et al., 2019). It can also be described as a reduction in blood pressure by >25% of the resting value following administration of spinal anaesthesia (Gwinnutt & Gwinnutt, 2012). Though several studies have come up with different definitions of spinal anaesthesia-induced hypotension (SAIH); the most common definition is a SBP of below 100 mmHg or blood pressure (BP) below 80% of the baseline (O'Sullivan & Cockerham, 2016).

2.2.4 Mechanisms of Spinal Anaesthesia Induced Hypotension

Hypotension and bradycardia are basically the most frequent side effects observed post spinal anaesthesia (Neesa & Sharma, 2020).

The principal mechanism underlying post-spinal anaesthesia hypotension is thought to be a reduction in systemic vascular resistance due to sympathetic nerve blockade. SA also causes preganglionic sympathetic block which decreases vascular resistance

leading to hypotension. Contributing mechanisms to bradycardia include parasympathetic system predominance, elevated baroreceptor activity, and the Bezold–Jarisch reflex, which is brought about by serotonin receptors (Mojtaba et al., 2014). Bezold- Jarisch reflex (BJR) comprises a triad of responses that include bradycardia, hypotension and peripheral vasodilation that occur during regional anaesthetic techniques such as spinal anaesthesia leading to sympathetic block (Warltier et al., 2003). Receptors that trigger the BJR are the mechanoreceptors and chemoreceptors found in the heart walls, which take part in systemic responses to high and low blood volume levels. These receptors, especially the chemoreceptors, are responsive to serotonin (5-HT3 receptors). Spinal anaesthesia administration triggers release of serotonin released from activated thrombocytes. Serotonin then activates chemoreceptors, the 5-HT3 receptors, situated in the vagal nerve endings on the cardiac wall to produce the BJR (Owczuk et al., 2008). Serotonin acts as a potent vasoconstrictor of arterioles and veins, except in the heart and skeletal muscle. In the heart, its vasodilatory effect is dependent on the presence of intact endothelium. However, when the myocardial endothelium is damaged due to injury, serotonin induces vasoconstriction. Vasodilation in skeletal muscle may contribute to a reduction in blood pressure, resulting in hypotension (Butterworth et al., 2022).

A decrease in the right ventricular filling as a result of sympathetic block activates mechanoreceptors and chemoreceptors present in the cardiac wall, causing vasovagal Bezold- Jarisch reflex, which is associated with a sudden extreme bradycardia, vasodilation, and probably may lead to cardiovascular collapse (Massoth et al., 2020). Gao et al., (2015) found that the decline in venous return resulting from the sympathetic blockade caused by spinal anaesthesia plus direct aortocaval compression, activate mechanoreceptors in the heart's left ventricle thus triggering the Bezold-Jarisch reflex

that includes bradycardia, vasodilation, and hypotension. Chemical substances like venoms, nicotine, serotonin (5-HT3), potassium chloride, and histamine, also trigger the Bezold-Jarisch reflex (Morris, 1996).

2.2.5 Effects of Spinal Anaesthesia – Induced Hypotension

Vasodilatation caused by the sympathetic block as a result of spinal anaesthesia leads to lowering of the peripheral vascular resistance as well as the venous return to the heart thus bringing about a fall in cardiac output. This results in serious complications like cardiac arrest if not prevented or managed early enough.

Maternal hypotension may precipitate nausea and vomiting, and also adverse neonatal effects, like apnea (Q. Wang et al., 2014). Nausea and vomiting are mostly the first indications of hypotension and cerebral hypoxia. It can also be due to vagal stimulation during upper abdominal surgery. Other symptoms of SAIH include dizziness and dyspnea (Pardo & Miller, 2018).

It has also been reported that episodes of hypotension persisting for two minutes or longer are associated with adverse neonatal outcomes (Hasanin et al., 2021). Maternal hypotension leads to oxygen deprivation to the neonate leading to acidosis which is a process by which the neonate's blood becomes abnormally acidic, and could result in lifelong disabilities. Knigin et al. (2020) did a retrospective analysis of women between 37- 41weeks of gestation with singleton pregnancy who underwent spinal anaesthesia for planned caesarean delivery, and reported that SAIH resulted in neonatal acidosis.

In the absence of prophylactic treatment spinal hypotension leads to fetal effects such as a decrease in uteroplacental blood flow and fetal acidosis, plus maternal symptoms like nausea, vomiting and reduced level of consciousness. In severe cases of spinal

hypotension the resulting effect would be total maternal cardiovascular collapse thus the urgent need to prevent this from occurring (Fichter & Nelson, 2019).

2.2.6 Factors Associated with Maternal Hypotension

There are several factors associated with the occurrence of maternal hypotension. Hypotension due to aortocaval compression occurs more frequently in patients with multiple gestations, especially following regional anaesthesia. Since the weight of the gravid uterus exerts pressure on the inferior vena cava, patients in the third trimester of pregnancy should never be permitted to lie in the supine position for any reason unless they have a left lateral tilt that displaces the uterus. Fainting may occur as a consequence of markedly reduced venous return to the heart, often secondary to uterine compression of the inferior vena cava (Lin et al., 2016).

A prospective study with 511 full-term pregnant women (gestational age: 37–42 weeks) carried out in Iran found that the key determinants of hypotension in the maternal multivariate model were: age more than 35 years, Body Mass Index (BMI) ≥ 30 kg/m^2, gravidity ≥ 4, weight gain during pregnancy of 11-20 Kg, baseline Systolic Blood Pressure of less than 120 mmHg, baseline Heart Rate (HR) > 100 beats/min, and history of hypotension ($P < 0.05$) (Atousa et al., 2018). Three of the parameters in the multivariate model related to anaesthesia were also shown to be statistically correlated with hypotension. There was a lower risk of hypotension with fluid preloading ≥1000 ml (Relative Risk Reduction (RRR) = 0.25 [P = 0.003] for mild hypotension, and RRR = 0.34 [P = 0.04] for moderate hypotension). Compared with pure bupivacaine, the addition of 1 μg sufentanil to the intrathecally administered local anaesthetic was associated with a reduced risk of hypotension (RRR = 0.19; P = 0.02 for moderate, and RRR = 0.15; P = 0.008 for severe cases). However, a higher prevalence of hypotension

was linked to sensory block height greater than T4 (RRR = 5.07; P = 0.04 for mild hypotension and RRR = 7.33; P = 0.01 for severe hypotension) (Atousa et al., 2018).

A prospective, Cross-sectional study with 251 done at Wad Medani Maternity Teaching Hospital, Sudan, found that; advanced age > 30 years, emergency cesarean section, ASA class II group (Pregnancy + Controlled Hypertension), increased gravidity, gestational age > 38 weeks, and puncture site at the level of L2-L3 were all risk factors for the increase in incidence of SAIH (Sahidin, 2018). Age above 30 years increased the incidence of SAIH, accounting for 63.6% of all the total occurrences. It appears that alterations in the baroreceptor and sympathetic nervous system responses, as well as a decrease in cardiac reserve, may play a role in increasing the risk of hypotension in older individuals.

Higher gravidity (number of pregnancies) was also linked to a greater risk of spinal anaesthesia- induced hypotension. During a normal, healthy pregnancy, textbooks indicate a natural reduction in peripheral vascular tone. This decrease in systemic vascular resistance due to pregnancy is more pronounced in women with multiple pregnancies than in those experiencing their first pregnancy.

Emergency cesarean section was also linked as a risk factor for SAIH due to less time for preoperative assessment and preparation. Additionally, the majority of these patients endure prolonged periods of dehydration and labor pain while in labor wards (Sahidin, 2018). However, this contrasts with Elriedy & Cockerham, (2019) who stated that the absence of labor was a risk factor for hypotension in the obstetric population after spinal anaesthesia.

A gestational age of over 38 weeks was also recognized, by Sahidin, (2018), as a risk factor for spinal anaesthesia- induced hypotension. This could be explained by the

increased weight of the pregnant uterus, which puts more pressure on the aorta and vena cava (aorto-caval compression).

The study also demonstrated that patients who received larger volumes, ≥1000 ml, of crystalloid fluid as preload experienced significantly less hypotension. Meanwhile, those given less than 1000 ml had a higher incidence, accounting for 86% of total cases (123 patients). Nigussie Yirgu et al., (2020) found a strong link between the amount of fluid preloading (less than 500ml) and the duration of crystalloid loading before spinal anaesthesia with post-spinal hypotension occurring within five to fifteen minutes. Mothers who received a fluid preloading of 500ml or less were found to have twice the likelihood of developing post-spinal hypotension compared to those who received more than 500ml of fluid. This means that a lower volume of fluid preloading significantly increased the risk of hypotension after the spinal anaesthesia procedure in these mothers.

On the newborn factors, Shitemaw et al., (2020) found that mothers with newborns weighing 4kg or more were five times more likely to develop hypotension compared to those with newborns weighing 2.4kg or less (Adjusted Odds Ratio (AOR): 5.3, 95% Confidence Interval (CI): 1.6–17.7). The increased risk may be due to the larger baby compressing the inferior vena cava and major arteries, leading to reduced venous return, decreased preload, and ultimately hypotension.

Other factors that can influence blood pressure after delivery include the administration of oxytocin, which may cause vasodilation or vasoconstriction depending on the dose, and blood loss, which can lead to hypovolemia and subsequent hypotension (Terkawi et al., 2015).

Oxytocin is widely recognized as the primary medication for preventing and treating postpartum haemorrhage. However, guidelines for its administration during cesarean delivery vary significantly across clinical practices worldwide. The World Health Organization suggests a 20 IU/L infusion of oxytocin. In contrast, the American Academy of Obstetricians and Gynecologists advise infusions within a range of 10–40 IU/L. Meanwhile, the Royal College of Obstetricians and Gynecologists recommend discontinuing the use of a 10 IU oxytocin bolus due to hemodynamic side effects. Instead, it advocates for a reduced bolus dose of 5 IU, administered gradually to minimize risks (Heesen et al., 2019). Vascular endothelial cells contain oxytocin receptors, and the interaction between oxytocin and these receptors triggers vasodilation through the release of nitric oxide. Vasodilation is the initial cardiovascular response following oxytocin administration and often leads to hypotension. While oxytocin induces vasodilation in peripheral blood vessels, it causes vasoconstriction in coronary vessels (Aslanlar, 2024).

2.3 Incidence of spinal Anaesthesia- Induced Hypotension

Globally, it has been reported that the incidence of SAIH during elective caesarean delivery is 70 - 80% in the absence of pharmacological prophylaxis (Mercier et al., 2013). The different definitions of spinal anaesthesia- induced hypotension make it difficult to approximate the incidence of hypotension in a given specific population and thus the resulting different incidence proportions (Zwane et al., 2019). A study in Croatia stated that the incidence of SAIH in parturients undergoing caesarean section was 75% (Šklebar et al., 2019). A study done in Germany at Christian Albrechts University on detection of spinal anaesthesia induced hypotension during caesarian sections using noninvasive blood pressure monitoring found an incidence of 91% via

the continuous non- invasive arterial pressure measurement as compared to 55% via the intermittent non- invasive arterial pressure measurement (Ilies et al., 2012).

At Gandhi Memorial Hospital in Addis Ababa, Ethiopia, the incidence of hypotension following spinal anaesthesia in parturients undergoing caesarean section was reported as 64% (Shitemaw et al., 2020). Another cross- sectional study carried out in 2016 at Gandhi Memorial Hospital, Ethiopia with 60 parturients scheduled for elective caesarean delivery found an incidence of 80% in the first five to fifteen minutes after spinal anaesthesia and a higher incidence of 83.7% in fifteen to twenty-five minutes after spinal anaesthesia (Nigussie Yirgu et al., 2020). In Sudan, at the Wad Medani Maternity Teaching Hospital, Gezira State, incidence of hypotension following spinal anaesthesia for caesarean section was documented at 57% (Sahidin, 2018).

Locally, Kahoro, (2009) found that the incidence of spinal anaesthesia- induced hypotension during caesarean section at Kenyatta National Hospital was 64%. This is a very high incidence considering the fact that maternal hypotension is linked to higher rates of morbidity and mortality of parturients intraoperatively.

Increased sensitivity to local anaesthetics, coupled with aortocaval compression by the gravid uterus, are the principal factors underlying the greater frequency and severity of hypotension observed in obstetric women compared with non-obstetric patients (Šklebar et al., 2019).

2.4 Prevention and Treatment of Spinal Anaesthesia- induced Hypotension

Different techniques have been employed to prevent spinal anaesthesia- induced hypotension and these include: left lateral tilt of 15˚- 30˚ of the pregnant mother to avoid aortocaval compression, uterine displacement to the left, lower leg compression, fluid preloading prior to initiation of the SA using colloids like hydroxyethyl starch, co-

loading during the administration of SA with crystalloids or colloids, and use of vasopressors such as ephedrine, phenylephrine, or norepinephrine (Ferré et al., 2020). Some of these methods however have been shown to be ineffective whereas some methods, though they are effective, have resulted in serious complications to the neonate. The degree of hypotension following spinal anaesthesia for cesarean delivery can be lessened by intravenous infusion of crystalloids or colloids. After evaluating 27 studies with 2009 women, comparing colloid vs crystalloid, a Cochrane review concluded that significantly fewer women experienced hypotension following colloids (RR 0.69; 95% CI, 0.58–0.81) (Gropper et al., 2025).

Nevertheless, concerns persist regarding the safety profile of synthetic colloids in both intraoperative and critical care resuscitation settings. Notably, fluid co-loading is usually used in conjunction with a vasopressor and is believed to have limited effectiveness in reliably preventing post spinal hypotension.

A meta-analysis done by the Cochrane collaboration found that, while various pharmacological and non-pharmacological strategies can reduce its incidence, no single technique fully prevents spinal anaesthesia-induced hypotension in women undergoing caesarean delivery (Am et al., 2020). For this reason, there is a requirement for large, several high-quality studies using those clinically relevant methods, either alone or in combination.

Vasopressor drugs are administered to treat maternal hypotension following spinal anaesthesia. Ephedrine, for several years, has been commonly used as the best vasopressor agent for the management of SAIH. It is also used to prevent spinal anaesthesia- induced hypotension during caesarean sections. However, its use has been correlated with a 5-fold heightened risk of fetal acidosis than using phenylephrine. Nevertheless, compared to ephedrine, prophylactic or therapeutic phenylephrine in

boluses or as an infusion causes less fetal acidosis and has a lower transfer to the fetus in addition to being beneficial in lowering hypotension. Phenylephrine, an α-adrenergic receptor agonist, is however often associated with reduced heart rate and reduced cardiac output state due to the absence of β-mimetic activity (Biricik & Unlugenc, 2021). Norepinephrine is linked to increased heart rate as well as cardiac output, and is equally effective in sustaining arterial blood pressure under spinal anaesthesia for cesarean delivery as phenylephrine. To evaluate norepinephrine's safety and effectiveness as the preferred vasopressor for treating and preventing post spinal hypotension, more research is required (Gropper et al., 2025).

For these reasons, there has been a gap in identifying a drug that is both effective in preventing hypotension and at the same time safe to the neonate. Several studies have thus come up using ondansetron as an alternative drug to reduce the incidence of hypotension due to its high safety profile to both the mother and the neonate.

In a randomized controlled trial conducted in Cairo, Egypt, both prophylactic ondansetron alone and the combination of vasoconstrictors with fluid preload were found to significantly lower the incidence of SAIH, with no statistically significant difference between the two approaches (S. A. Mohamed et al., 2018). These findings indicate that ondansetron represents an effective alternative for reducing the incidence of SAIH in parturients undergoing caesarean delivery. Ondansetron (serotonin receptor antagonist) has been recently used since it not only prevents nausea and vomiting, but also reduces the incidence of spinal anaesthesia- induced hypotension and bradycardia by blocking the Bezold-jarisch Reflex (Ferré et al., 2020).

2.5 Ondansetron

Ondansetron is the leading drug in a unique class of antiemetics known as selective 5-hydroxytryptamine3 (5-HT3 or serotonin) receptor antagonists. It was developed to manage vomiting induced by cancer chemotherapy or radiotherapy. 5-HT3 receptors are located within the central nervous system, especially in the chemoreceptive area and vomiting center, as well as in peripheral, sensory, and enteric nerves. These receptors facilitate excitation via a serotonin -gated cation channel.

Ondansetron is also very effective in managing postoperative nausea and vomiting, in addition to nausea and vomiting arising from diverse medical conditions and pharmacological agents. It exerts its effect by inhibiting 5-HT_3 receptor activity, a critical pathway in the onset of these symptoms. This makes ondansetron a valuable medication for a range of conditions beyond just chemotherapy or radiotherapy-induced vomiting (Tripathi, 2013). Ondansetron can be utilized both preventatively and therapeutically. As a prophylactic, it is administered to prevent the onset of nausea and vomiting, particularly before procedures like chemotherapy, radiotherapy, or surgery. In its therapeutic use, ondansetron is given to treat existing symptoms of nausea and vomiting, regardless of their cause, whether from surgery, medical conditions, or medications (Ye et al., 2001).

2.5.1 Mechanism of Action

Ondansetron selectively binds to 5- HT3 receptors, inhibiting serotonin activity both peripherally at vagal nerve terminals and centrally within the chemoreceptor trigger zone. Its primary effects are most evident in the gastrointestinal tract.

Unlike many other drugs, ondansetron does not interact with dopamine receptors, effectively eliminating the potential for extrapyramidal side effects.

2.5.2 Pharmacokinetics

Ondansetron can be given orally in the form of tablets, oral solution, or oral soluble films, or administered parenterally via intravenous or intramuscular injection using a 2 mg/ml injectable solution. When ondansetron is orally administered, it is well absorbed, with a bioavailability of 56-71%, which increases by 17% when taken with food. Time to initial therapeutic effect for ondansetron is 30 minutes.

Peak plasma concentrations are achieved following an intravenous infusion within 10 minutes, 30 minutes after an intramuscular injection, 2 hours after administering oral tablets, and 1 hour after taking oral soluble films.

Ondansetron's plasma protein binding capacity is estimated at 70–76% and demonstrates a substantial volume of distribution, ranging from 1.7 to 3.7 L/kg in children and 2.2 to 2.5 L/kg in adults, approximately equivalent to 160 liters. It undergoes extensive liver metabolism, involving hydroxylation followed by glucuronide or sulfate conjugation of the indole ring. The elimination half-life is 2-7 hours in children under 15 years and 3-7 hours in adults. Ondansetron is eliminated from the body primarily through urine, with 44–60% excreted as metabolites and approximately 5% as the unchanged drug. Additionally, around 25% is excreted via feces.

2.5.3 Indications and Dosing

During pregnancy, ondansetron is commonly used to manage hyperemesis gravidarum. It is administered intravenously at a dosage of 4–8 mg every 8 hours, depending on the patient's needs. Preoperatively, it is administered to prevent postoperative nausea and vomiting, particularly in obstetric patients undergoing caesarean delivery. The

recommended dosage is 4 mg, delivered either intravenously or intramuscularly, immediately before anaesthetic induction.

Ondansetron is widely administered for the prophylaxis and treatment of nausea and vomiting among patients undergoing cancer chemotherapy. The standard dosage is 0.15 mg/kg, infused over 15 minutes intravenously, commencing roughly 30 minutes before chemotherapy initiation. For radiotherapy patients, an oral dose of 8 mg is administered 1–2 hours prior to radiation therapy. Postoperatively, a 4 mg intravenous dose is given following the procedure to manage nausea and vomiting effectively.

2.5.4 Adverse effects of Ondansetron

5-HT3 receptor antagonists exhibit an excellent safety profile, remaining free from significant side effects even when administered at doses multiple times higher than the recommended amount (Butterworth et al., 2022). They seem unlikely to induce sedation, extrapyramidal symptoms, or respiratory depression. Headache is the predominant adverse event reported. Additional side effects may include fatigue and gastrointestinal disturbances, such as constipation or diarrhea.

2.6 Effect of Prophylactic Ondansetron on the Incidence of Spinal Anaesthesia-Induced Hypotension and Vasopressor Use

Several studies involving human subjects have investigated the effect of ondansetron in reducing the incidence of spinal anaesthesia-induced hypotension (SAIH) during cesarean sections. Some of these studies indicate that preventive use of ondansetron preceding spinal anaesthesia can attenuate SAIH. However, other studies have concluded that there was no significant variation in SAIH incidence between patients administered ondansetron and those without the prophylaxis. Due to these conflicting results, further research has been recommended to provide clearer insights.

Recent prospective comparative studies have demonstrated the superiority of ondansetron in mitigating spinal anaesthesia-induced hypotension compared to other pharmacological agents. For instance, a prospective randomized comparative study was conducted at Dhaka Medical College Hospital in Bangladesh involving 120 parturients scheduled to undergo elective caesarean delivery. The parturients were divided into two groups: one group received ondansetron (0.1mg/kg) and the other group received ephedrine (0.5mg/kg) before spinal anaesthesia. Following the administration of spinal anaesthesia, the ondansetron group exhibited a significantly lower decline in mean arterial pressure (MAP) within 45 minutes compared to the ephedrine group ($P < 0.05$). This led to the conclusion that ondansetron had a statistically significant advantage over ephedrine in reducing spinal anaesthesia-induced hypotension (Islam et al., 2022).

A comparative randomized double-blind trial was carried out in Egypt at Bab El Shearia University Hospital, involving 153 patients who were divided into three groups. The study aimed to compare the therapeutic effectiveness of ondansetron (IV 4mg), ephedrine (Intramuscular (IM) 25mg), and dexamethasone (IV 4mg) in preventing spinal anaesthesia- induced hypotension in pregnant women undergoing cesarean sections. The incidence of spinal anaesthesia- induced hypotension was 38.5% in the ephedrine group, 27.5% in the dexamethasone group, and significantly lower at 16% in the ondansetron group ($P < 0.05$). The study concluded that ondansetron demonstrated superior efficacy in mitigating spinal anaesthesia- induced hypotension compared to dexamethasone, with ephedrine being the least effective (Fodiel et al., 2022).

In a comprehensive meta-analysis, Gao et al. (2015) found that spinal anaesthesia-induced hypotension occurred at significantly lower rate with the prophylactic administration of ondansetron. The study comprising of obstetric and non-obstetric patients, demonstrated a statistically significant decline in hypotension ($P = 0.0005$)

when ondansetron was injected before spinal anaesthesia (Gao et al., 2015). Another meta-analysis found that ondansetron administered intravenously 5 minutes before a subarachnoid block significantly mitigated the occurrence of SAIH and bradycardia. This further supports the potential benefits of using ondansetron as a prophylactic measure in such medical procedures (Kane & Pugh, 2017).

A randomized controlled trial was conducted at Sri Jagannath Medical College and Hospital, India, to assess the efficacy of a 4.5 mg prophylactic intravenous dose of ondansetron in reducing the occurrence of SAIH in women undergoing surgical delivery via caesarean section. The results demonstrated that prophylactic ondansetron not only decreased the incidence of SAIH and bradycardia but also significantly lowered the need for vasopressors in parturients who had elective caesarean section (CS) (Mohanty, 2023).

A study conducted in Tunisia found that ondansetron not only helps in reducing spinal anaesthesia-induced hypotension but also improves metabolic and vital parameters of newborns. The study reported that babies born to mothers who received ondansetron had higher Apgar scores, umbilical artery pH values closer to normal ranges, and lower lactate levels as opposed to the group without ondansetron prophylaxis. This suggests that ondansetron may have beneficial effects on the overall health and well-being of newborns (Trabelsi et al., 2015). Ondansetron not only effectively reduces the incidence of maternal hypotension caused by spinal anaesthesia but also poses minimal or no harm to neonates. The improved metabolic and vital parameters of newborns, such as higher Apgar scores and normal umbilical artery pH values, highlight its safety and efficacy in obstetric care.

A study by Yamano et al. demonstrated that inhibiting 5- HT3 receptors abolished the serotonin-mediated Bezold-Jarisch reflex (Owczuk et al., 2008). Furthermore, a meta-

analysis conducted in 2016 determined that 5-HT3 receptor blockers effectively inhibited the Bezold-Jarisch reflex in both human and animal studies. The analysis revealed that 5-HT3 antagonists, particularly 4 mg of ondansetron, were effective in preventing both hypotension and bradycardia. This was observed not only in obstetric trials but also in studies involving a combination of obstetric and non-obstetric surgeries (Heesen et al., 2016).

In a dose-dependent study carried out at Wuxi Maternity and Child Health Hospital in Shanghai, China, 150 pregnant women randomized into five groups of 30 participants each to evaluate the efficacy of varying ondansetron doses (2 mg, 4 mg, 6 mg, and 8 mg) in reducing the incidence of spinal anaesthesia-induced hypotension. Participants who received 4 mg or 6 mg of ondansetron experienced a significantly lower rate of SAIH (30.0% and 31.0%, respectively) than those given normal saline (60%) ($P < 0.05$). Based on these findings, the researchers established 4 mg of ondansetron as the optimal dose for prophylactic use during caesarean delivery (M. Wang et al., 2014).

At Wuxi Maternity and Child Health Hospital in China, another study was conducted to determine whether preloading with ondansetron in combination with crystalloid infusion could contribute to a reduced occurrence of SAIH. Women who received 4 mg of ondansetron intravenously (IV) had a 25% incidence of SAIH compared with 56.3% in the saline group, with the reduction reaching statistical significance ($P = 0.011$). Additionally, the consumption of phenylephrine was significantly reduced among patients receiving ondansetron compared with those receiving normal saline ($P = 0.029$) (Q. Wang et al., 2014).

In India, a double-blind, randomized, placebo-controlled study involving fifty-two parturients concluded that those who were administered a 4 mg IV dose of ondansetron 5 minutes preceding the spinal block experienced a significant reduction in SAIH than

the saline (control) group (P = 0.038) (Sahoo et al., 2012). Additionally, another study conducted at Airforce Hospital in Kalaikunda, India, supported ondansetron's pharmacological efficacy in reducing the occurrence of SAIH. A statistically significant difference was observed in the incidence of spinal hypotension, with rates of 39.3% in the ondansetron group and 60.7% in the normal saline group (P = 0.0359) (Raghu et al., 2018). A similar study conducted at Holy Family Hospital in Rawalpindi, Pakistan, demonstrated a reduction in the incidence of spinal anaesthesia - induced hypotension by 20.8%. In this study, the incidence of SAIH was 7.5% among participants in the ondansetron group, versus 28.3% in the normal saline group (P = 0.005). This statistically significant result further supports the effectiveness of ondansetron in reducing the occurrence of hypotension during spinal anaesthesia (Baig et al., 2017).

A prospective, randomized, double-blind, controlled trial in Turkey enrolled 108 parturients and examined the effect of administering 8 mg of prophylactic IV ondansetron on the incidence of SAIH, norepinephrine usage, and associated adverse effects. The findings showed no statistically significant variation in SAIH rates between the ondansetron and saline groups (P = 0.767). The study concluded that administering 8 mg of intravenous ondansetron 5 minutes prior to spinal block reduced the incidence of SAIH but did not prevent SAIH (Karacaer et al., 2018).

A randomized controlled trial carried out at Al-Shohada Central Hospital in Al-Shohada, Egypt, involved one hundred parturients. The study found a significant decline in the systolic blood pressure measurements in group II, who got normal saline as a placebo, more than group I, where participants got ondansetron (P<0.05). Prophylactic administration of 4 mg intravenous ondansetron significantly lowered vasopressor needs in parturients, suggesting improved hemodynamic stability (P = 0.005) (Shabana et al., 2018).

Some studies have demonstrated that using ondansetron prophylactically before a spinal block can significantly decrease the need for vasopressor drugs, thanks to its effectiveness in reducing the occurrence of hypotension. However, a recent systematic review conducted in Turkey recommends the routine and prophylactic use of vasopressors. This recommendation stems from the frequent occurrence of maternal hypotension during caesarean deliveries performed under spinal anaesthesia (Biricik & Unlugenc, 2021). Vasopressor drugs like ephedrine, especially when administered in high doses, have been significantly associated with fetal acidosis (Kinsella et al., 2017). This is due to ephedrine's ability to cross the placenta, potentially increasing the fetal metabolic rate and leading to anaerobic metabolism and lactic acidosis. Consequently, this can result in lower umbilical artery pH levels and increased fetal acidosis.

According to a study by Karacaer et al., (2018) in Turkey, there was no statistically significant variation in the incidence of SAIH between the ondansetron group (88.9%) and the saline group (87%) ($P = 0.767$). However, the study found that the total occurrences of SAIH, along with norepinephrine use during caesarean delivery, were significantly higher in parturients in the saline group in comparison with those in the ondansetron group ($P = 0.009$ and $P = 0.009$, respectively).

In Tunisia, Trabelsi et al., (2015) evaluated the impact of intravenous ondansetron on maternal hemodynamic and neonatal parameters in parturients receiving spinal anaesthesia for caesarean delivery. Their findings indicated that participants who received ondansetron not only had a lower incidence of SAIH but also had a significantly reduced ephedrine requirement in comparison with the saline (placebo) group. Neonates whose mothers received prophylactic intravenous ondansetron had increased Apgar scores, decreased lactate concentrations, and umbilical artery blood

pH levels that were closer to normal physiological ranges compared to those in the placebo group (Trabelsi et al., 2015).

In a study carried out in Saudi Arabia by Mowafi et al. (2008), the researchers examined the impact of a different 5-HT3 receptor blocker, Granisetron (1 mg IV), on the characteristics of sensory and motor blockade induced by intrathecal bupivacaine. The aim was to determine if Granisetron could affect the requirement for ephedrine to manage hypotension in parturients. The findings revealed that there was absent statistically significant variation in ephedrine requirement for treating hypotension between the group that was treated with Granisetron and the group that was treated with saline as a placebo. This indicates that Granisetron did not significantly alter the need for vasopressor intervention in this context.

An Egyptian randomized controlled trial investigated the effects of administering 4 mg of prophylactic intravenous ondansetron to parturients undergoing cesarean delivery under spinal anaesthesia. The study discovered that women in the ondansetron group experienced a significant decrease in hypotension ($P = 0.007$), a substantial reduction in the need for vasopressors ($P = 0.005$), and required lower doses of vasopressors ($P = 0.01$) in comparison with the control group (Shabana et al., 2018).

A double-blind randomized controlled study conducted at Cairo University, Egypt, explored the effectiveness of ondansetron in preventing post-spinal shivering (PSS) in parturients scheduled for caesarean delivery. The study found that administering 8 mg of ondansetron not only reduced the incidence of PSS but also decreased the occurrence of SAIH in parturients undergoing elective cesarean sections (Badawy & Mokhtar, 2017). Their study also discovered that the incidence of SAIH in the control group, which received saline, was 60%. In comparison, the incidences of SAIH in the

ondansetron groups were 48.3% for the 2 mg dose, 30% for the 4 mg dose, 31% for the 6 mg dose, and 40% for the 8 mg dose.

Another study in Egypt evaluated the effects of 4 mg intravenous ondansetron and 1 mg granisetron on the hemodynamic changes, as well as motor and sensory blockade, caused by spinal anaesthesia among sixty parturients undergoing elective caesarean sections. The study concluded that administering 4 mg of ondansetron before the subarachnoid blockade significantly reduced both the incidence of SAIH and the doses of vasopressors required ($P < 0.05$), than the granisetron and saline (control) groups (Rashad & Farmawy, 2013).

In Nigeria, Nnacheta et al. (2020) conducted a prospective, double-blind, placebo-controlled, randomized study with 109 patients to compare the impact of tramadol and ondansetron as prophylaxis against post-anaesthetic shivering under spinal anaesthesia. The study concluded that ondansetron was significantly more effective than tramadol in preventing shivering in parturients who underwent caesarean sections with spinal anaesthesia. The results also indicated that the ondansetron group had a superior hemodynamic profile than the saline and tramadol groups. This was evident because the cumulative consumption of ephedrine was lowest in the ondansetron group. Additionally, ondansetron was shown to lessen the incidence of spinal anaesthesia-induced hypotension compared to the placebo group. The incidence of SAIH was reported as 39.4% in the tramadol group, 54.5% in the placebo group, and 50.0% in the ondansetron group. Tramadol was found to have the highest incidence of vomiting at 18.2%, while no instances of nausea or vomiting were reported in patients who received ondansetron (Nnacheta et al., 2020).

2.7 Effect of prophylactic Ondansetron and the Occurrence of Bradycardia

Occurrence of bradycardia in obstetric patients during caesarean section (CS) under spinal anaesthesia is usually associated with a high sympathetic block which is also known as high spinal block. High spinal blockade is a condition where the level of anaesthesia reaches higher spinal segments than necessary for surgery. A decrease in heart rate in the context of high neuraxial blockade may occur due to the inhibition of thoracic sympathetic fibers, specifically the preganglionic accelerator fibers of the heart arising from T1 to T4 (Gropper et al., 2025). When the sensory level reaches T3 or higher, it can cause significant cardiovascular and respiratory issues, which is why it is considered a high spinal block (Gwinnutt & Gwinnutt, 2012). Another mechanism contributing to bradycardia involves the incidence of hypotension following spinal anaesthesia. This occurs due to reduced vascular resistance, leading to blood pooling and resulting in hypovolemia. The hypovolemia activates cardiac receptors at the vagal nerve endings. Serotonin links to these receptors, initiating the Bezold-Jarisch reflex arc, which responds to the hypovolemia by reducing the heart rate (Mohanty, 2023). Reflexive heart rate slowing can result from vasodilation, which reduces systemic venous blood flow into the right atrium (Gropper et al., 2025).

Extreme bradycardia, characterized by a resting heart rate of under 50 beats per minute, requires prompt treatment with atropine to prevent the risk of cardiac arrest (Butterworth et al., 2022). Factors that could contribute to exaggerated bradycardia (40 – 50 beats per minute) include the following: a baseline heart rate below 60 beats/minute, being younger than 37 years, male sex, non- emergency cases, the use of β- adrenergic blockers, and extended case duration. Severe bradycardia (<40 beats per minute) is particularly linked to a baseline heart rate under 60 beats per min, and the male sex. Additionally, heart rate may decline due to extensive excision or ablation of

sympathetic ganglia and connecting fibers from the fifth thoracic (T5) through the second lumbar (L2) levels to disrupt sympathetic outflow, which leads to venous pooling in the lower extremities as well as in the abdominal and pelvic viscera (Gropper et al., 2025).

Hypotension activates a compensatory sympathetic reflex via baroreceptor activation, leading to vasoconstriction and elevates heart rate above the level of the neural blockade. However, the accompanying decline in venous return and atrial filling lowers the signals generated by stretch receptors within the right atrium and major veins. This triggers a significant rise in parasympathetic activity, or vagal tone. These opposing mechanisms generally balance out, causing either a slight reduction or minimal change in heart rate (Gropper et al., 2025). Unopposed vagal tone may be responsible for the occurrence of sudden bradycardia, complete heart block, or cardiac arrest that can occasionally arise during spinal anaesthesia (Butterworth et al., 2022).

The occurrence of bradycardia following spinal anaesthesia is around 13% (Gwinnutt & Gwinnutt, 2012). However, a considerable number of studies investigating the prophylactic administration of ondansetron before the onset of spinal anaesthesia have demonstrated a reduction in the rates of bradycardia. Additionally, these studies have shown a decrease in the incidence of hypotension among patients. This suggests that ondansetron is not only effective in managing nausea and vomiting but also plays a role in stabilizing cardiovascular parameters during spinal anaesthesia. Some studies, however, have indicated that ondansetron does not influence heart rate, highlighting the necessity for additional research to better understand its cardiovascular effects.

In a meta-analysis executed by Gao et al., (2015), multiple studies on the effects of prophylactic ondansetron on spinal anaesthesia-induced hypotension were examined.

The combined data from various randomized controlled trials (RCTs) revealed that ondansetron not only significantly lowered the incidence of SAIH but also decreased the occurrence of bradycardia subsequent to spinal anaesthesia. The analysis reported a risk ratio (RR) of 0.27 (95% CI 0.16 to 0.47), indicating a substantial reduction in these adverse events.

Kane & Pugh, (2017) performed a meta-analysis to investigate the effects of ondansetron on mitigating SAIH and bradycardia in both obstetric as well as non-obstetric subjects. The combined analysis of the studies revealed that the preventive administration of ondansetron significantly lowered the occurrence of bradycardia in participants who received the treatment before undergoing spinal anaesthesia. The results indicated a 69% relative reduction in the risk of bradycardia, with a risk ratio (RR) of 0.31 and a confidence interval (CI) ranging from 0.19 to 0.50.

In 2018, Shabana et al. carried out a trial at Al-Shohada Central Hospital in Egypt, administering a prophylactic dose of 4 mg IV ondansetron 5 minutes prior to spinal anaesthesia. Their results revealed a statistically significant variation in heart rate between the control and ondansetron groups. This was observed immediately post-spinal anaesthesia ($P = 0.02$), 20 minutes after spinal anaesthesia ($P = 0.01$), and 50 minutes after spinal anaesthesia ($P = 0.02$). Consequently, they concluded that administration of 4 mg IV ondansetron significantly decreases heart rate fluctuations, in addition to reducing both hypotension and the dose of vasopressor used (Shabana et al., 2018).

In a recent randomized controlled trial conducted in Ethiopia, researchers investigated the efficacy of prophylactic ondansetron in preventing SAIH and bradycardia in pregnant women undergoing elective CS. The study utilized a higher dose of 10 mg

intravenous ondansetron. However, the results indicated no statistically significant variance in the incidence of SAIH and bradycardia between the two groups. Consequently, the researchers concluded that the prophylactic administration of intravenous ondansetron at a 10 mg dose prior to spinal anaesthesia was not effective in reducing the occurrence of SAIH and bradycardia in pregnant women having caesarean sections (S. Mohamed et al., 2021). In contrast to these observations, a 2014 study by M. Wang et al. (2014), conducted in China at Wuxi Maternal and Child Health Hospital, explored the dose-dependent effectiveness of prophylactic IV ondansetron in preventing hypotension during cesarean delivery. Their research established that the optimal dose for preloading with intravenous ondansetron to effectively prevent SAIH and bradycardia was 4 mg (M. Wang et al., 2014).

Karacaer et al. (2018) conducted their study at Cukurova University Hospital in Turkey, administering 8 mg of IV ondansetron 5 minutes preceding spinal anaesthesia. The results showed no significant variance between the ondansetron group and the saline group regarding the incidence of SAIH, bradycardia, nausea, or vomiting.

A comparable study carried out in Nepal at Tribhuvan University Teaching Hospital reported no statistically significant variations in heart rates between the two groups of parturients, with neither group experiencing episodes of bradycardia (Balla et al., 2019).

A study conducted at Dilla University Referral Hospital in Ethiopia also used the standard recommended dose of 4 mg IV ondansetron but still observed no statistically significant variation in the occurrence of bradycardia between the two groups. Participants in the ondansetron group had a bradycardia incidence of 5.3%, compared to 2.9% in the saline group ($P > 0.05$) (S. Mohamed et al., 2021).

2.8 Conceptual Framework

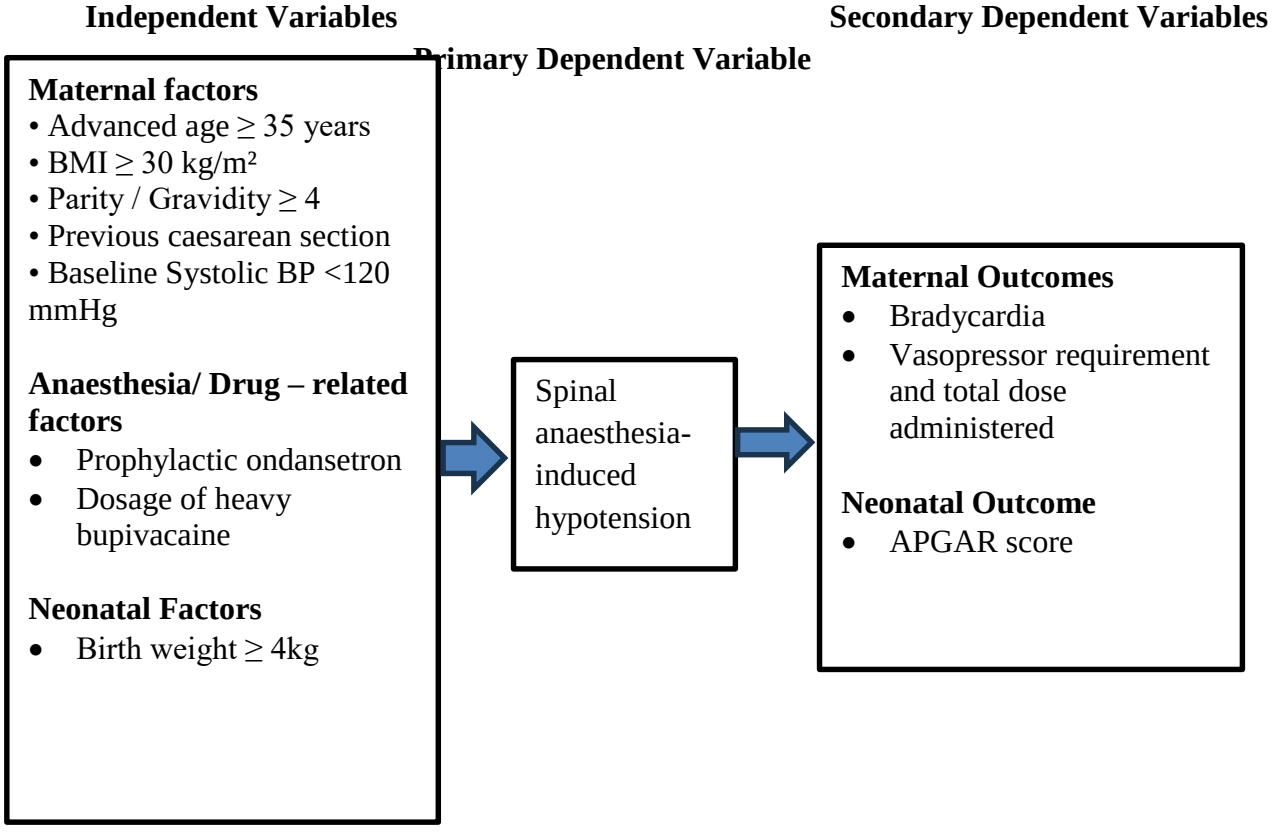

Figure 1: Conceptual Framework

CHAPTER THREE

3.0 METHODOLOGY

3.1 Study Site

This study was conducted at Moi Teaching and Referral Hospital (MTRH) within the Riley Mother and Baby Hospital theatres, where both elective and emergency caesarean sections are performed. MTRH operates 12 distinct surgical theatres, each serving various specialties on a daily basis. The Riley Mother and Baby Hospital theatres perform approximately 3,200 caesarean sections annually. In 2020, about 3,000 of these were emergency cases, while 215 were elective procedures. According to the MTRH database, spinal anaesthesia was administered in 2,200 of these caesarean sections. To manage the high patient volume, the hospital has designated two operating rooms specifically for this purpose. Elective caesarean sections are scheduled twice a week, whereas emergency caesarean sections are conducted daily.

MTRH is Kenya's second-largest National Referral Hospital, following Kenyatta National Hospital. It serves as a National and International Teaching and Referral Hospital, providing ambulatory care, inpatient, and specialist medical services. Located along Nandi Road in Eldoret town, Uasin Gishu County, it lies 310 kilometers northwest of Nairobi, the capital city of Kenya. The hospital caters to a population of over 24 million people, serving residents from 23 counties in Kenya, as well as parts of Tanzania, Eastern Uganda, the Democratic Republic of Congo, and South Sudan.

Founded in 1917 with an initial bed capacity of 60 to address the healthcare needs of Africans, MTRH later transitioned into a District Hospital before being officially designated as a referral hospital through Legal Notice No. 78 issued on June 12, 1998, under the State Corporations Act (Cap 446).

The hospital has a capacity of 1,020 specialized beds, with an average of 1,300 inpatients at any given time and 1,500 outpatients per day. MTRH also serves as the teaching hospital for Moi University College of Health Sciences, which offers training to undergraduate medical students, nurses, and several master's programs in medical specialties. Over 240 postgraduate students (Registrars) are enrolled across various programs. Additionally, several other medical training institutions, including Kenya Medical Training College and the University of Eastern Africa (Baraton), utilize MTRH for their training programs.

The hospital offers a broad range of specialized services, including oncology treatments such as radiotherapy, brachytherapy, and chemotherapy, as well as Intensive Care Unit services. Additional specialties include renal and urology care, alcohol and drug rehabilitation services, spine and neurosurgical procedures, cardiology and cardiothoracic treatments, ophthalmology, orthopedic surgeries, and pediatric services. Other available services encompass plastic surgeries, general surgeries, obstetrics and gynecological procedures, as well as Ear, Nose, and Throat care and dental services. Over the years, the hospital has experienced significant growth in various areas, including infrastructure development, the number of patients treated, the complexity of diagnoses managed, and the expansion of its Human Resources for Health.

Moi Teaching and Referral Hospital has established strategic partnerships and alliances with the Ministry of Health and various esteemed development partners, including Indiana University and Duke University from the United States, Suez Canal University from Egypt, University of Toronto from Canada, Shoe4Africa Foundation in New York, University of Linköping in Sweden, Doctor to Doctor Foundation in Amsterdam,

Stellenbosch University and University of Cape Town in South Africa, as well as Stryker Corporation and North Carolina University in the United States, among others. These collaborations have contributed to the creation of several centers of excellence, such as the Chandaria Cancer and Chronic Diseases Centre, Shoe4Africa Children's Hospital, Cardiac Care Unit, Riley Mother and Baby Hospital with a Neonatal Intensive Care Unit, and the Academic Model Providing Access to Healthcare (AMPATH). Other accomplishments include a 30-bed Intensive Care Unit, a modern 80-bed Mental Health Unit, a 25-bed Hemodialysis Unit, and improved capacity-building initiatives for staff across various specialties.

The Shoe4Africa Children's Hospital, the only public children's hospital in Eastern Africa, is a comprehensive facility that addresses all childhood diseases. It is equipped with its own operating theatres, an ICU, and an oncology unit, among other services. AMPATH stands as the largest HIV/AIDS treatment center in Africa, with over 180,000 patients enrolled for HIV care. These exceptional services are delivered by a well-trained, dedicated, and skilled workforce.

3.2 Study Design

This was a double- blind randomized controlled trial.

This study divided participants into two equal groups: the intervention group, referred to as the ondansetron group (Group O), and the placebo group, referred to as the saline group (Group S). The intervention group received 4 mg of intravenous ondansetron 15 minutes before spinal anaesthesia, while the placebo group was given an equivalent volume of normal saline to ensure blinding for both the provider and the participant.

In this research, double-blinding involved the on-duty pharmacist and the principal investigator preparing the drug. The anaesthetist on duty then administered the drug

without knowing its type, and the participant also remained unaware of the drug they received. This process ensured that neither the participant nor the anaesthetist had knowledge of the specific drug administered, maintaining the integrity of the study.

3.3 Target Population

All women scheduled for elective caesarean section under spinal anaesthesia at MTRH from the month of August 2022 - September 2023.

3.4 Study Population

The target population was subjected to study eligibility criteria to determine the study population.

3.5 Eligibility Criteria

3.5.1 Inclusion criteria

All pregnant women who were 37 weeks gestation or more, classified as ASA class I or II, aged 18 years and above, and scheduled for an elective cesarean section under spinal anaesthesia at the MTRH theatres.

3.5.2 Exclusion Criteria

a) Pregnant women with pre- anaesthetic hypotension (systolic BP < 100 mmHg).
b) Patients with hypersensitivity (allergy) to ondansetron.
c) All hypertensive patients (with controlled BP or with BP >130/80mmHg).
d) Patients who did not consent to the study.
e) Parturients with any cardiac disease.

3.6 Sample size estimation

Sample size formula for comparing two proportions as described by Fleiss in 1981 was employed in this case (Fleiss, 1981). In a study done in Kenyatta the incidence of spinal anaesthesia- induced hypotension was 64% (Kahoro, 2009). Research conducted in

low- and middle-income countries has shown that using ondansetron to prevent hypotension caused by spinal anaesthesia can reduce the incidence by 18% to 21% (Baig et al., 2017; Raghu et al., 2018; Rakshith et al., 2023). For this study, based on above literature, we hypothesized that the intervention would reduce the incidence by 20%. Thus, to achieve a power of 80% at a 5% level of significance we needed to recruit:

$$n = 2\frac{(Z_\alpha + Z_\beta)^2 * [p_0(1-p_0) + p_1(1-p_1)]}{(p_1 - p_0)^2}$$

Where n = desired sample size

Z_α = the standard normal deviate of 1.96 (95% confidence level).

Z_β = the standard normal deviate of 0.84 for (Power=80%).

p_0 = estimated incidence value of 64% in the control arm.

p_1 = estimated national incidence value of 44% in the intervention arm

Therefore n=194

Thus, we recruited 97 participants per arm.

3.6.1 Sampling Technique and Randomization Procedure

A consecutive sampling technique was employed.

Participants for the study were recruited at least 12 hours prior to surgery from the antenatal wards at Riley Mother and Baby Hospital, MTRH. All women who met the study inclusion criteria were provided with an explanation of the study and asked to complete an informed consent form if they agreed to participate.

Randomization for the study was performed using block randomization with computer-generated numbers. The participants were first put into 49 blocks each block containing 4 participants. The biostatistician produced random numbers that matched the study

arms in a 1:1 ratio and placed them in Sequentially Numbered Opaque Sealed Envelopes (SNOSE). This clinical trial was testing the efficacy of ondansetron (drug O) and placebo/ normal saline (drug S) on spinal anaesthesia- induced hypotension. To randomize patients and ensure that neither the patients nor the anaesthesia team knew which treatment each patient received, we used SNOSE. This process involved:

- **Generating Random Numbers:** The biostatistician used a computer to generate random numbers assigning either 1 or 2 to the two study arms, ensuring a 1:1 ratio; where 1 represented the saline (control) group and 2 represented the ondansetron (intervention) group.
- **Preparing the Envelopes:** Each random number coinciding with the different study arms was written on a piece of paper, and the papers were placed inside small opaque envelopes. The small opaque envelopes were numbered sequentially on the outside (e.g., 001, 002, 003 up to 194). Those envelopes were then given to the pharmacist who with the help of the principal investigator, prepared the different medications in identical syringes and numbered them according to the serial number provided in the envelopes in the absence of the research assistants or the anaesthetists to ensure blinding. The principal investigator maintained the records of the random numbers and the serial numbers of the envelopes.
- **Enrollment:** When a new patient enrolled in the study, the anaesthetist on duty was given the next envelope in sequence (e.g., 001 for the first patient, 002 for the second) by the principal investigator or the research assistant on arrival of the patient at the Riley Mother and Baby operating room. The serial number of the participant filled on the questionnaire corresponded to the serial number on the sealed envelopes.

- **Blinding:** The anaesthetist on duty opened the opaque envelope that had a syringe labeled with the participant's serial number and not the real identity of the study drug used. The treatment assignment (Ondansetron or Saline) was also not revealed to the patient or the rest of the medical team. This was done to ensure double blinding.

This process ensured that treatment assignments were random and concealed, reducing bias and maintaining the integrity of the study.

3.7 Study Procedure

Upon receiving approval from both the Institutional Research and Ethics Committee (IREC) and the National Commission for Science, Technology and Innovation (NACOSTI), the principal investigator, assisted by five research assistants who were higher diploma clinical officer anesthetist trainees, commenced data collection process. Prior to beginning the study, these research assistants received comprehensive training and evaluation from the principal investigator to ensure their readiness for the research activities. The principal investigator also took the time to explain to all the anaesthetists on duty. These lead anaesthetists then disseminated the information to the rest of the anaesthesia team, including trainees, ensuring that everyone was aware of the study's objectives and requirements. This process was essential for fostering cooperation and coordination with the research assistants and the principal investigator throughout the study.

Elective caesarean sections were scheduled every Tuesday and Friday, with the theater list being prepared the day before surgery by the obstetric team. The qualified anaesthesia provider on duty was responsible for deciding on the anaesthesia technique to be used. All eligible women were identified in the antenatal wards of Riley Mother and Baby Hospital, with the theatre list aiding the process, 12 hours before their

scheduled surgeries. Once they met the specified criteria, they were approached for participation in the study. After providing a comprehensive briefing on the study, all participants signed a written informed consent form. The responsibility for obtaining the consent form fell to either the primary investigator or one of the research assistants. This ensured that participants were fully informed and had formally agreed to be part of the study before any research activities commenced. Through this process, the study maintained a high standard of ethical conduct and respect for participant autonomy. The patient's demographic data and obstetric history was then recorded on the data collection sheet.

Upon arriving at the operating room, participants were assigned to one of the study arms according to their serial numbers, using pre-determined randomization methods to maintain the study's integrity and ensure objectivity. The research assistants would then get the already prepared study drugs in sequentially numbered, opaque, sealed envelopes (SNOSE) from the pharmacist or the primary investigator and hand it over to the anaesthesia team on duty.

Prior to initiating any surgical preparations, participants were connected to a cardiac monitor to record their baseline vital signs. These included non-invasive blood pressure (BP), mean arterial pressure (MAP), heart rate (HR), and peripheral oxygen saturation (SPO2). Two peripheral 18-gauge intravenous (IV) cannulas were then inserted in all patients by the anaesthetist before administration of any drug.

As soon as the baseline vital signs were recorded, 15 minutes prior to the spinal block, group O participants received intravenous 4mg (2 mls) ondansetron, whereas group S participants received 2mls of intravenous normal saline. The anaesthetist on duty, who was unaware of the study drugs, administered these injections. The identity of the study

drugs was concealed by labeling identical syringes with coded numbers. Both drugs were clear fluids, making it difficult to distinguish which drug was in each syringe. This ensured the blinding process was maintained. All participants were then pre-loaded with 500mls of normal saline prior to the spinal block.

All participants were positioned in the sitting position on the operating table to ensure proper alignment of the spine. Thorough hand hygiene was performed using an antiseptic solution, followed by the anaesthetist donning sterile gloves. The skin over the intended puncture site was cleaned with an antiseptic solution (iodine) applied in a circular motion from the center outward. This technique ensured thorough disinfection of the area and reduced the risk of infection during the procedure. Sterile drapes were placed around the puncture site to ensure a sterile environment. Before the spinal injection, the anaesthesia provider identified the necessary landmarks on the patient's back using the Tuffier's line, which is an imaginary line drawn across the highest points of the iliac crests and intersects the spine at the L4 level.

The subarachnoid puncture was subsequently performed with a fine, 25-gauge, cutting-bevel (Quincke), sterile spinal needle at the L3-L4 or L4-L5 interspace while the participant remained in the sitting position. Proper needle placement was verified by the presence of free-flowing cerebrospinal fluid (CSF) from the needle hub, and by aspirating the CSF before injecting the spinal drugs. Two ml (10mg) of hyperbaric bupivacaine 0.5% combined with 25mcg of fentanyl was injected intrathecally, and the needle was immediately removed afterward. During the administration of spinal anaesthesia, fluid co-loading was implemented using 500 ml of normal saline. After the injection, participants were returned to the supine position. To prevent aortocaval compression, a wedge was placed under the right hip to achieve left uterine displacement.

The anaesthetist monitored the participant's vital signs, including heart rate, blood pressure, and peripheral oxygen saturation, at three-minute intervals. However, these measurements were documented in the data collection tool at five-minute intervals for the first thirty minutes and subsequently every fifteen minutes until the surgery concluded and the participant reached the recovery room. Intravenous fluids were administered as needed to maintain hydration and blood pressure. The type of fluid administered and the total volume given were recorded in the questionnaire at the end of the surgery.

The level of sensory and motor block was assessed by having the participant report their sensations and perform simple movements. Sensory assessment was performed through cold sensation using an alcohol cotton swab whereas the motor assessment was done by asking the patient to do straight leg raises. The obstetrician was allowed to proceed with skin incision once the sensory level achieved was at a dermatomal level of T6 and above i.e. the xiphoid process.

In the event a participant developed hypotension (systolic blood pressure < 100 mmHg), a 6 mg bolus of intravenous ephedrine or 50 mcg – 200mcg bolus of phenylephrine was given at 3-minute intervals until the hypotension was resolved. In cases where the participant developed bradycardia (heart rate below 50 beats per minute), 0.5 mg of intravenous atropine was administered at 5-minute intervals. The total doses of vasopressors and atropine administered were recorded in the data collection sheet. Any other intraoperative complications, such as postpartum hemorrhage, were managed by the anaesthesia provider in accordance with the hospital's management protocols for each specific complication. Maternal hemorrhage was defined as an estimated blood loss of greater than 1000 ml. In the event of this occurrence, blood and blood products were readily available for transfusion if necessary. Additionally, other complications of

spinal anaesthesia, such as shivering, nausea, and vomiting, were documented in the data collection tool and managed as they occurred. 8mg IV dexamethasone or 10mg IV metoclopramide were administered to participants who developed nausea and vomiting as per the anaesthetists' preference.

Right after the newborn was delivered, participants were administered 10 units of oxytocin intravenously. This was then followed by a slow intravenous infusion of 20 units of oxytocin diluted in 500 ml of normal saline. Alternatively, some anaesthesia providers opted to administer a slow intravenous push of 100 mcg carbetocin in place of the initial dose of 10 units of oxytocin. This administration helped promote uterine contractions and reduce the risk of postpartum hemorrhage. After delivery, the newborns were handed over to perioperative nurses who are highly trained in newborn assessment and resuscitation. The nurses conducted newborn assessments utilizing the APGAR scoring system, ensuring a comprehensive evaluation of each baby's health status immediately after delivery. The newborn's birth weight and APGAR scores at 1 minute, 5 minutes, and 10 minutes after birth were carefully recorded. Other parameters recorded at the end of the surgery included the estimated amount of maternal blood loss, and the total duration of the surgery, measured from the incision to the completion of wound dressing. The estimated maternal blood loss was determined by the anaesthesia team in consensus with the obstetric team.

After surgery, the participants were transferred to the Post-Anaesthesia Care Unit (PACU) for close monitoring. Vital signs, including systolic blood pressure, peripheral oxygen saturation, and heart rate, were recorded at 15-minute intervals for at least one hour. In the absence of any postoperative complications, they were then transferred to the postnatal wards.

3.7.1 Study Flow Chart

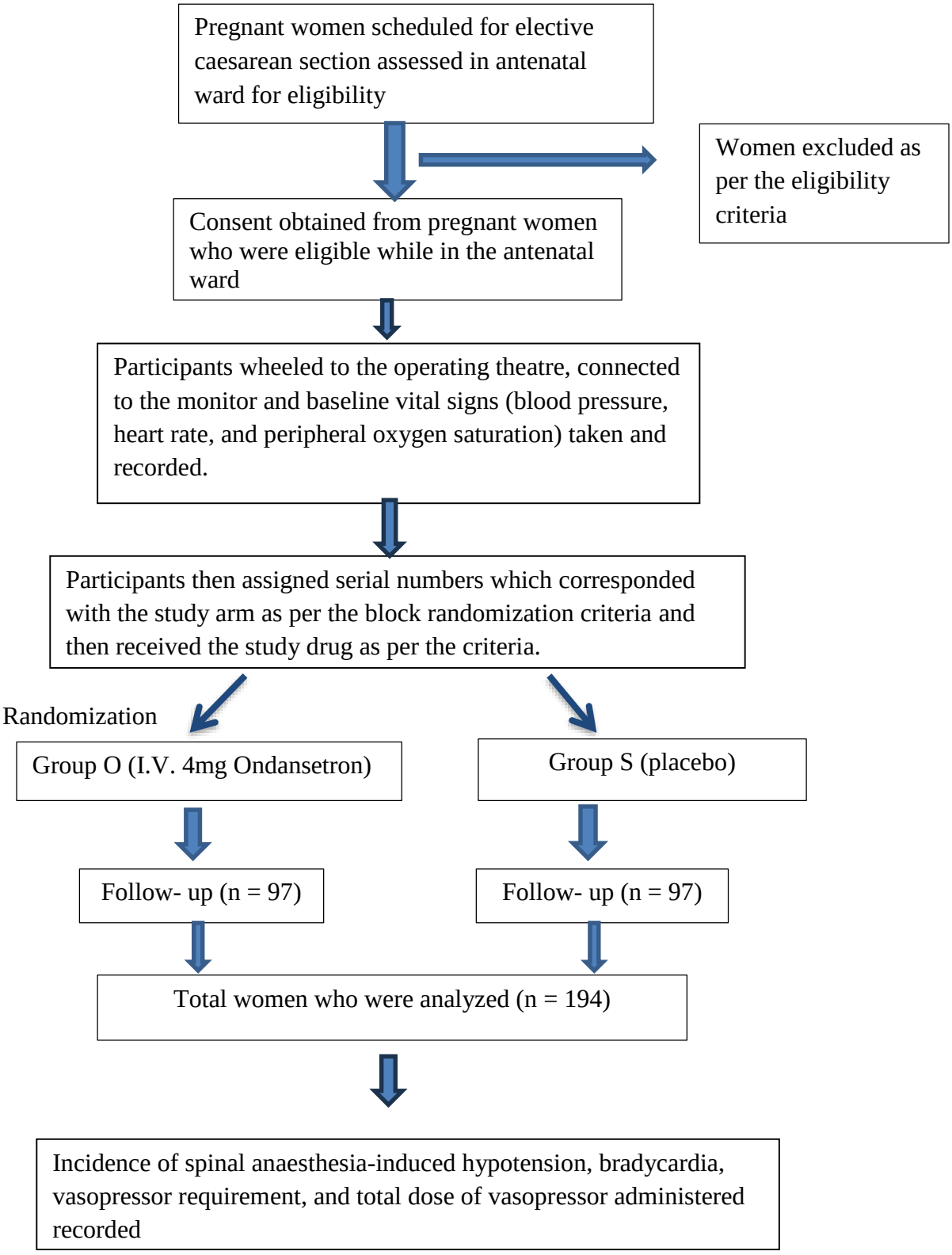

Figure 2: Study Flow Chart

3.8 Measures: Variables of interest

Independent variables

Prophylactic ondansetron

Age, parity, weight, height, BMI, gestational age, baseline vital signs

Indication for surgery (maternal or fetal cause)

Birthweight

Dependent (Outcome) Variables

Incidence of spinal anaesthesia –induced hypotension

Total dose of vasopressor agent used

Occurrence of Bradycardia

APGAR score

3.9 Data collection method

A structured questionnaire was utilized to collect data from all consenting women who met the study's eligibility criteria. The questionnaire was designed with three sections (Appendix 8).

Section A included the patient's demographics, such as age, weight, height, and BMI.

Section B of the questionnaire covered the medical and obstetric history of the patients. This included gestational age, parity, any existing comorbidities, and any current medications the patient was taking. The indication for the cesarean section, whether due to maternal or fetal reasons was also included.

Section C included the anaesthesia records from the time the patient entered the operating room, as well as the neonatal outcomes. This covered the administration times of ondansetron or the placebo, the time spinal anaesthesia was given, and the incision time. It also recorded baseline vital signs (such as non-invasive blood pressure, heart rate, peripheral oxygen saturation (SPO_2), and mean arterial pressure (MAP) which are

standard monitoring parameters for patients under anaesthesia) and subsequent vital signs throughout the surgery. Additionally, adverse effects of spinal anaesthesia such as Hypotension, bradycardia, nausea, vomiting, shivering among others, the vasopressor agent used along with its total dosage, the type and total amount of fluids administered, other medications given, the duration of the surgery, and the estimated blood loss were documented. The neonatal outcomes recorded included the APGAR score and birthweight.

3.10 Data and Safety Monitoring Board

The Data and Safety Monitoring Board (DSMB) was constituted. The committee comprised of a chairperson from the anaesthesia department, and other three members included one anaesthesiologist, one reproductive health consultant and a biostatistician. This was an independent group of experts whose roles and responsibilities were to:

- Advice IREC and the investigator and give independent recommendations on the study.
- Periodically review and evaluate accumulated study data for participant safety, study conduct and progress.
- Make recommendations to IREC concerning continuation, modification or termination of the trial.

3.11 Data Analysis

Data collected using questionnaires were checked for completeness and consistency by the primary investigator on a daily basis during the entire study period. All data collected was sorted, coded and entered in an electronic database. On completion of data collection, the electronic data was imported into a statistical analysis tool, STATA version 16, where data management and analysis were done.

Preliminary analysis involved a summary of study participants' demographic and clinical characteristics stratified by treatment arm and comparison was done to assess

balance in the covariate distribution between the two groups. Categorical variables such as comorbidities present, indication for caesarean section, hypotension, and bradycardia were summarized as frequencies and their corresponding percentages. Numerical variables such as age, weight, height, SPO2, duration of surgery, estimated blood loss and total fluids administered were summarized as means and their corresponding standard deviation if they assumed normal distribution else as medians and their corresponding interquartile ranges. Baseline vital signs, BMI, parity, and baseline systolic blood pressure collected in numerical form were categorized in clinically meaningful groups and summarized as categorical variables.

Further analysis was done as per each objective as summarized in the table below.

Objective	Outcome	Independent	Statistical Test
One: To determine the effect of prophylactic ondansetron on the incidence of spinal anaesthesia-induced hypotension during cesarean section at MTRH	Hypotension (Yes/ No) – binary categorical variable	Arm (intervention/ control) – binary categorical variable	A two proportions z-test
Two: To determine the effect of prophylactic ondansetron on the occurrence of bradycardia in pregnant women under spinal anaesthesia during caesarean section at MTRH	Dependent variable: Bradycardia (Yes/No) – binary categorical variable	Arm (intervention/ control) – binary categorical variable	A two proportions z-test
Three: To compare the vasopressor requirement and total dose administered for the treatment of SAIH between the intervention and the control group during caesarean section at MTRH	Dose of vasopressor agent – Numerical	Arm (intervention/ control) – binary categorical variable	Mann Whitney U test

All the test results were considered statistically significant if P - value was less than 0.05.

3.12 Data Presentation

The study findings were presented using figures, tables, and graphs.

3.13 Ethical considerations

Approval to conduct the study was sought from the institution's research and ethics committee (IREC), approval number 0004102, and from the Chief Executive Officer of MTRH, under reference number ELD/MTRH/R&P/10/2/V.2/210. After receiving approval from IREC and MTRH, the study was registered with the National Commission for Science, Technology, and Innovation (NACOSTI), and a research license was issued with license number NACOSTI/P/22/18648, authorizing the commencement of the study and data collection.

Written informed consent was obtained from all willing participants by either appending a signature or a thumbprint on the provided consent form.

Participation in this study was entirely voluntary, and participants had the freedom to opt out at any stage.

All information collected was coded and secured on computers with passwords and firewalls to ensure confidentiality and to be used solely for the purposes of this study.

Participants were not subjected to any additional costs or provided with any incentives for their participation in the study.

The study posed no risk to the participants and did not expose them to any harmful or unapproved procedures.

3.14 Dissemination of findings

The study findings will be presented to Moi University as part of the requirements for the award of a Master of Medicine degree in Anaesthesia and Critical Care. A copy of this thesis will be made available in the Moi University library and online repository for public access and reference. Additionally, the study manuscript has been approved by the East African medical journal for publication. The findings will also be disseminated to anaesthesia providers at MTRH, and presented in scientific conferences.

CHAPTER FOUR: RESULTS

4.1 Introduction

Between September 2022 and August 2023, a total of 252 pregnant women scheduled for elective cesarean sections under spinal anaesthesia at the MTRH Riley Mother and Baby Theatres were approached in the antenatal wards to enroll in this study. Out of the 252, 58 pregnant women were excluded from the study for various reasons: 33 women declined to consent, 20 women had preeclampsia, and 5 women had cardiac diseases. A total of 194 women were subsequently enrolled in the study.

An intention-to-treat analysis method was applied. The data analysis was conducted based on these 194 study participants, who were classified as ASA class I or II, aged 18 years or older, with term pregnancies, and scheduled for elective caesarean sections under spinal anaesthesia. The participants were randomized into two groups: the intervention group (Group O), who received 4mg (2ml) of IV Ondansetron 15 minutes before the spinal anaesthesia, and the control group (Group S), who received an equivalent volume of normal saline 15 minutes before spinal anaesthesia. Each group consisted of 97 participants, as shown in the recruitment flow chart (Figure 3).

4.1.1 Recruitment flow chart

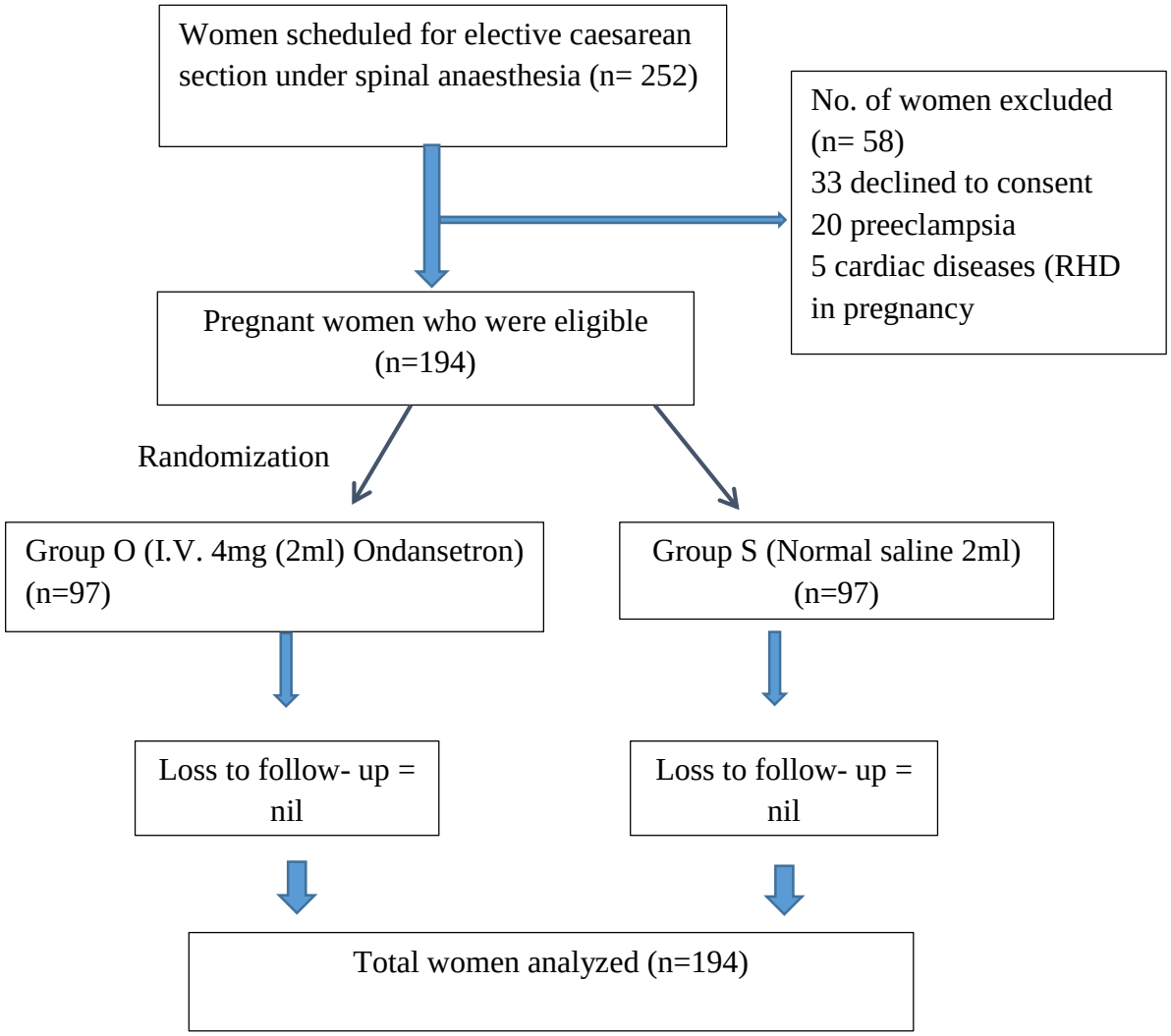

Figure 3: Recruitment flow chart

4.2 Comparison of the Demographics and Clinical Characteristics between Group S (Saline) and Group O (Ondansetron)

The demographics and clinical characteristics of the participants are detailed in Table 1a. The ages of the study participants ranged between 19 and 42 years. There was no significant difference in the mean maternal age between the two groups; the mean age in the Group S was 29.9 ± 4.8 years, while in Group O, it was 30.3 ± 4.7 years (P = 0.56). Most of the participants were under 35 years of age in both groups, with 80.4% (n=78) in Group S and 77.3% (n=75) in Group O, showing no significant difference (P = 0.598). Women of advanced maternal age, defined as 35 years or older, comprised 19.6% (n=19) of Group S and 22.7% (n=22) of Group O, also with no significant difference (P = 0.598).

The mean weight of the participants in group S was 72.3±15.1 kg, while group O was 74.4±14.8 kg (P = 0.34).

The mean height of the participants in the saline group was 161.3±7.4 cm, which was nearly identical to the ondansetron group, at 162.3±7.9 cm (P = 0.36).

The mean body mass index (BMI) in the saline group and the ondansetron group showed no significant difference, with 28.0±5.8 in Group S and 28.1±5.8 in Group O (P = 0.88). Most of the pregnant women in both groups were in the overweight category, with 36.1% (n=35) in Group S and 37.1% (n=36) in Group O. This was followed by women in the obese category, comprising 33.0% (n=32) in Group S and 35.1% (n=34) in Group O. The normal weight category included 29.9% (n=29) in Group S and 26.8% (n=26) in Group O. The smallest proportion was in the underweight category, with 1.0% (n=1) in each group (P = 0.951).

The indications for cesarean section were categorized into maternal causes and fetal causes. Maternal causes included previous scars, postdates with previous scars, a history of adverse obstetric outcomes, complete placenta previa, pelvic fracture, placenta previa, postdates, previous myomectomy scars, and uterine fibroids in pregnant women. Fetal causes consisted of malpresentation, macrosomia, hydrocephalus, and twin pregnancies where the first twin was in breech presentation, as detailed in Table 1b. The most common maternal indication for cesarean section was a previous uterine scar, while the most common fetal indication was multiple gestation in breech presentation.

In both groups, maternal causes were the primary reason for elective cesarean sections, constituting the majority of cases—91.8% (n=89) in Group S and 86.6% (n=84) in Group O—with a P-value of 0.25. Fetal causes accounted for 12.4% (n=12) in Group S and 17.5% (n=17) in Group O, with a P-value of 0.31.

There was no significant difference in maternal parity between the placebo and intervention groups ($P > 0.99$). Most of the pregnant women were multiparous, having had between one and four previous births at 28 weeks or later, accounting for 92.8% (n=90) in Group S and 91.8% (n=89) in Group O. Nulliparous women, who had never given birth to a viable baby, represented 5.2% (n=5) in each group. Grand multiparous women, with five or more births at 28 weeks or later, made up 2.1% (n=2) of Group S and 3.1% (n=3) of Group O.

Most of the participants were free of underlying illnesses, with 93.8% (n=91) in Group S and 95.9% (n=93) in Group O. A few had comorbidities such as Human Immunodeficiency Virus (HIV), Diabetes Mellitus (DM), and hepatitis, with 6.2%

(n=6) in Group S and 4.1% (n=4) in Group O. The specific comorbidities are detailed in Table 1b. This difference was not statistically significant (P = 0.52).

Table 1a: Patient Demographics and Clinical Characteristics

	Group S N=97	**Group O** N=97	**P-value**
Patient age (years)			
< 35 years	78 (80.4%)	75 (77.3%)	0.598[1]
≥ 35 years	19 (19.6%)	22 (22.7%)	
Weight (Kg)			
Mean (SD)	72.3 (15.1)	74.4 (14.8)	0.339[2]
Range	41 – 118	48.5 – 131	
Height (cm)			
Mean (SD)	161.3 (7.4)	162.3 (7.9)	0.361[2]
Range	143 – 184	150 – 190	
BMI (Kg/m^2)			
Underweight (< 18.5)	1 (1.0%)	1 (1.0%)	0.951[4]
Normal (18.5 – 24.9)	29 (29.9%)	26 (26.8%)	
Over weight (25.0 – 29.9)	35 (36.1%)	36 (37.1%)	
Obese (≥ 30)	32 (33.0%)	34 (35.1%)	
Indication for caesarean section			
Maternal cause			0.248[1]
No	8 (8.2%)	13 (13.4%)	
Yes	89 (91.8%)	84 (86.6%)	
Fetal cause			0.314[1]
No	85 (87.6%)	80 (82.5%)	
Yes	12 (12.4%)	17 (17.5%)	
Parity			>0.99[4]
Nulliparous (0)	5 (5.2%)	5 (5.2%)	
Multiparous (1 – 4)	90 (92.8%)	89 (91.8%)	
Grand Multiparous (≥ 5)	2 (2.1%)	3 (3.1%)	
Comorbidities			0.516[1]
Absent	91 (93.8%)	93 (95.9%)	
Present	6 (6.2%)	4 (4.1%)	

[2] *t*test

[1] Chi Square test

[4] Fisher's exact test

Table 1b: Specified Indications for Caesarean Section and Comorbidities Present

	Group S N=97	**Group O N=97**	**p-value**
Maternal Indications			0.398
1 previous scar	42 (47.7%)	42 (51.2%)	
2 previous scars	32 (36.4%)	27 (32.9%)	
3 previous scars	10 (11.4%)	7 (8.5%)	
4 previous scars	0 (0.0%)	2 (2.4%)	
Bad Obstetric History	0 (0.0%)	1 (1.2%)	
complete placenta previa	0 (0.0%)	1 (1.2%)	
pelvic fracture	0 (0.0%)	1 (1.2%)	
placenta previa	2 (2.3%)	0 (0.0%)	
post dates	1 (1.1%)	0 (0.0%)	
previous myomectomy scar	0 (0.0%)	1 (1.2%)	
Fetal Indications			0.738
Macrosomia (≥ 4 Kg)	1 (8.3%)	1 (5.6%)	
Breech presentation	3 (25.0%)	8 (44.4%)	
Hydrocephalus	1 (8.3%)	0 (0.0%)	
Transverse lie	2 (8.3%)	1 (5.6%)	
Multiple gestations	6 (50.0%)	8 (44.4%)	
Comorbidities			0.26
None	91 (93.8%)	93 (95.9%)	
HIV	3 (3.1%)	3 (3.1%)	
Diabetes Mellitus	3 (3.1%)	0 (0.0%)	
Hepatitis	0 (0.0%)	1 (1.0%)	

Fisher's exact test

4.3 Anaesthesia and Surgery-related Characteristics

The anaesthesia and surgery-related characteristics of the participants are outlined in Table 2. These include the time elapsed from saline/ondansetron administration to the start of surgery, the duration from spinal anaesthesia administration to skin incision, baseline systolic blood pressure along with subsequent measurements, surgery duration, estimated blood loss, and the type and total volume of fluids administered.

The median duration of time from the administration of the placebo or ondansetron to the surgical incision in both study arms did not show a significant difference: 26.0 minutes in the placebo group with an interquartile range (IQR) of 24.0 to 30.0 minutes, and 29.0 minutes in the intervention (ondansetron) group with an IQR of 24.0 to 33.0 minutes (P = 0.073).

The median duration of time from spinal anaesthesia administration to skin incision was 10 minutes in Group S, with an interquartile range (IQR) of 7 to 12 minutes, and 10 minutes in Group O, with an IQR of 8 to 15 minutes. This difference was not statistically significant (P = 0.080).

Figure 4 outlines the comparison of mean systolic blood pressure between Group S and Group O. The baseline systolic blood pressure (BP) for participants in Group S ranged from 101 to 139 mmHg, with a mean of 120.0 mmHg and a standard deviation (SD) of 10.2. For participants in Group O, it ranged from 100 to 138 mmHg, with a mean of 120.3 mmHg and an SD of 9.0. This difference was not statistically significant (P = 0.909). The systolic blood pressure dropped within the first 5 minutes after spinal anaesthesia administration, showing almost identical mean values in both groups. In Group S, the mean was 109.2 mmHg with an SD of 18.1, and in Group O, the mean was 109.1 mmHg with an SD of 18.6 (p = 0.966). Ten minutes after the administration

of spinal anaesthesia, the mean systolic blood pressure decreased slightly further in both groups, with no significant difference observed. In Group S, the mean was 106.4 mmHg with a standard deviation (SD) of 17.8, while in Group O, the mean was 107.7 mmHg with an SD of 19.8 (P = 0.636). The subsequent systolic blood pressure readings up to 30 minutes after the administration of spinal anaesthesia showed no statistically significant difference between the two groups.

The median surgery duration was significantly longer in the placebo group (group S), with a median time of 59.0 minutes, compared to 50.0 minutes in the ondansetron group (group O) (P = 0.030).

There was no statistically significant difference in the median estimated blood loss at the end of the surgery between group S (600.0 mL) and group O (550.0 mL) (P = 0.072).

Crystalloids were the most commonly administered fluids to the participants, with no significant difference between the two groups (P = 0.72). The mean volume was 2175.3 mL in group S and 2149.5 mL in group O. Blood and colloids were administered only to Group S participants as needed. The total amount of intravenous fluids administered to the participants in both groups by the end of the surgery showed no significant difference (P = 0.197). The mean volume was 2257.2 mL in Group S and 2149.5 mL in Group O.

Table 2: Anaesthesia and Surgery-related Characteristics

	Group S	Group O	P-value
	N=97	N=97	
Time taken from saline/ondansetron administration to start of surgery (minutes)			
Median (IQR)	26 (24-30)	29 (24-33)	0.101[3]
Range	22 – 50	20 – 65	
Time taken from spinal anaesthesia to skin incision (minutes)			
Median (IQR)	10 (7 – 12)	10 (8 – 15)	0.080[3]
Range	5 – 28	5 – 35	
Baseline Systolic Blood Pressure (BP) (mmHg)			0.909[2]
Mean (SD)	120.0 (10.2)	120.3 (9.0)	
Range	101 – 139	100 – 138	
Systolic BP 5 minutes after spinal anaesthesia			0.966[2]
Mean (SD)	109.2 (18.1)	109.1 (18.6)	
Range	66 – 172	47 – 148	
Systolic BP 10 minutes after spinal anaesthesia			0.636[2]
Mean (SD)	106.4 (17.8)	107.7 (19.8)	
Range	52 – 158	64 – 158	
Systolic BP 15 minutes after spinal anaesthesia			0.191[2]
Mean (SD)	109.2 (18.2)	112.8 (20.5)	
Range	64 – 164	70 – 205	
Systolic BP 20 minutes after spinal anaesthesia			0.849[2]
Mean (SD)	108.2 (15.2)	107.8 (19.2)	
Range	76 – 148	70 – 166	
Systolic BP 25 minutes after spinal anaesthesia			0.371[2]
Mean (SD)	111.4 (14.8)	113.4 (15.4)	
Range	79 – 154	78 – 153	
Systolic Bp 30 minutes after spinal anaesthesia			0.649[2]
Mean (SD)	110.8 (13.7)	111.7 (13.4)	
Range	79 – 146	79 – 142	
Surgery duration (minutes)			
Median (IQR)	59.0(45.0-73.0)	50.0(41.0-65.0)	**0.030[3]**
Range	28 – 200	21 – 157	
Estimated Blood loss (milliliters)			
Median (IQR)	600.0 (500.0-650.0)	550.0 (500.0-600.0)	0.072[3]
Range	350 – 3600	400 –1100	
Type of Fluids Administered			
Crystalloids (milliliters)			
Mean (SD)	2175.3 (500.2)	2149.5 (485.0)	0.72[2]
Range	1500 – 3500	1500 – 4000	
Blood (milliliters)			
Mean (SD)	681.3 (634.1)	0	
Range	450 – 2250		
Colloids (milliliters)			
Mean (SD)	625.0 (250.0)	0	
Range	500 – 1000		
Total fluids administered (milliliters)			
Mean (SD)	2257.2 (659.5)	2149.5 (485.0)	0.197[2]
Range	1500 – 6250	1500 – 4000	

[3] Mann Whitney U test

[2] *t*test

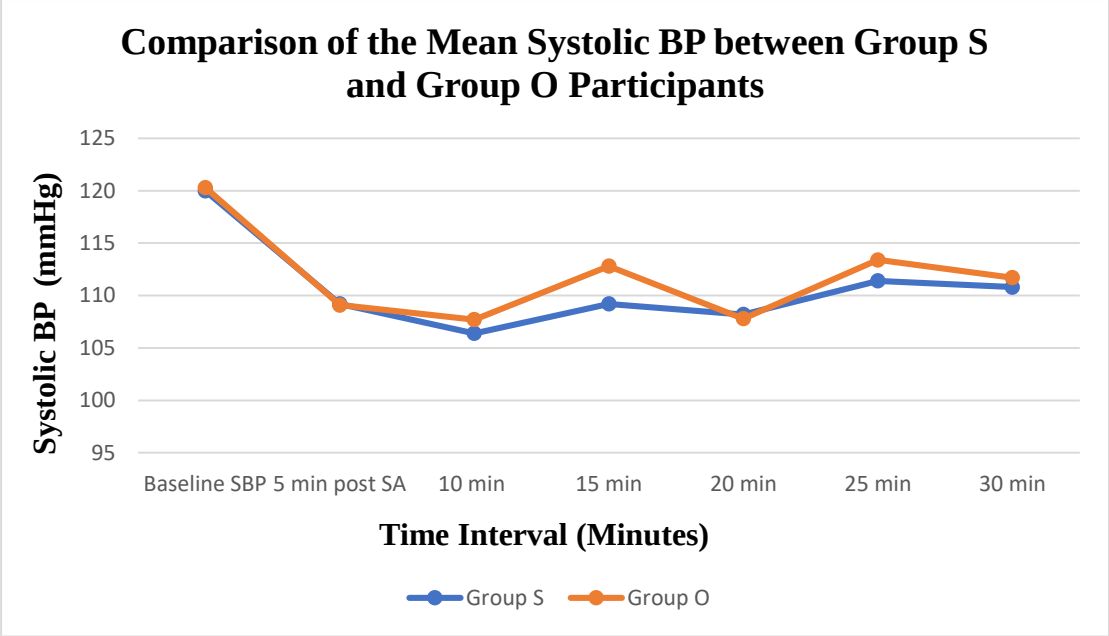

Figure 4: Comparison of Mean Systolic Blood Pressure Between Group S and Group O

4.4 Neonatal Outcome

Neonatal outcomes for both groups are comprehensively shown in Table 3.

Neonatal outcomes in both groups were assessed using the APGAR score after delivery at 1 minute, 5 minutes, and 10 minutes. At each of these time points, there was no significant difference in APGAR scores between the two study groups (P > 0.05).

Table 3: Neonatal Outcome

	Group S N=97	**Group O N=97**	**p-value**
Neonatal Outcome			
Apgar score at 1 minute			
Median (IQR)	9.0 (8.0-9.0)	9.0 (8.0-9.0)	0.737[2]
Range	5 – 10	5 – 10	
Apgar score at 5 minutes			
Median (IQR)	10.0 (9.0-10.0)	10.0 (9.0-10.0)	0.638[2]
Range	6 – 10	6 – 10	
Apgar score at 10 minutes			
Median (IQR)	10.0 (10.0-10.0)	10.0 (10.0-10.0)	0.588[2]
Range	8 – 10	8 – 10	

[2] **Mann Whitney U test**

4.5 Effect of Prophylactic Ondansetron on the Incidence Proportion of Spinal Anaesthesia-Induced Hypotension

The overall incidence proportion of spinal anaesthesia induced hypotension was **85.6% (n= 166).**

Table 4: Effect of Prophylactic Ondansetron on Spinal anaesthesia Induced Hypotension

	Group S	**Group O**	**P-value**
	N=97	**N=97**	
Hypotension			**0.001**
No	6 (6.2%)	22 (22.7%)	
Yes	91 (93.8%)	75 (77.3%)	

The incidence proportion of spinal anaesthesia-induced hypotension, as illustrated in Table 4 and Figure 5 was significantly lower in group O compared to group S (77.3%, n=75 vs 93.8%, n=91), respectively, with a P-value of **0.001**).

The null hypothesis in this study states that intravenous ondansetron injection 15 minutes prior to administration of spinal anaesthesia does not significantly reduce the incidence of maternal spinal anaesthesia induced hypotension.

The incidence proportion of maternal spinal anaesthesia induced hypotension reduced by 16.5% (95% CI 6.9 – 26.1) in the ondansetron group which was not statistically different from the hypothesized reduction (P = 0.223).

Hence, we reject the null hypothesis.

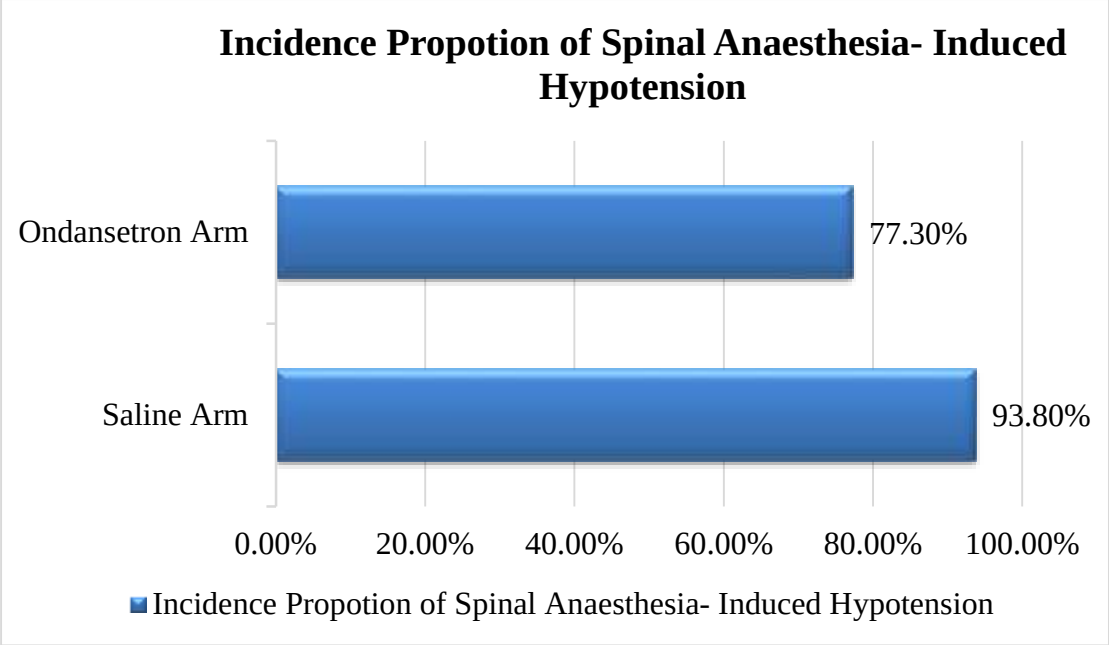

Figure 5: Comparison of the Incidence Proportion of Spinal Anaesthesia- Induced Hypotension in the Placebo and Ondansetron Arms

4.5.1 Comparison of the Hypotension Severity Between Group S and Group O

Table 5 shows the comparison of the hypotension severity between participants in group S and group O. Among the participants who developed SAIH, there was no statistically significant variation in the distribution of hypotension severity between group S and group O (P=0.672). While some numerical differences are observable—with a higher proportion of mild hypotension in group S (47.3%, n=43) compared to group O (41.3%, n=31), and a higher proportion of moderate hypotension in group O (52.0%, n=39) compared to group S (45.0%, n=41)—these differences were not large enough to be considered statistically significant. The rates of severe hypotension were nearly identical between the two groups.

Table 5: Comparison of the Hypotension Severity between Participants in Group S and Group O

Hypotension	Study Arm		p-value
	Group S	**Group O**	
Mild hypotension	43 (47.3%)	31 (41.3%)	0.672
Moderate hypotension	41 (45.0%)	39 (52.0%)	
Severe hypotension	7 (7.7%)	5 (6.7%)	

Chi Square test

4.6 Factors associated with Spinal Anaesthesia-induced Hypotension

4.6.1 Bivariate Analysis of Factors associated with Hypotension

The bivariate analysis revealed that participants who did not receive ondansetron, those with a baseline systolic blood pressure of less than 120 mmHg, and those who received a 10 IU intravenous bolus of oxytocin were significantly associated with spinal anaesthesia-induced hypotension. These findings are summarized in Table 6 below.

Table 6: Bivariate Analysis of Factors associated with Maternal Hypotension

	Hypotension		
	Absent	**Present**	**p-value**
Variables	**N=28**	**N=166**	
Arm			**0.001**[1]
Control (Placebo)	6 (6.2%)	91 (93.8%)	
Case (Ondansetron)	22 (22.7%)	75 (77.3%)	
Patient age			0.588[1]
<35yrs	21 (13.7%)	132 (86.3%)	
≥35yrs	7 (17.1%)	34 (82.9%)	
Parity			0.568[2]
Nulliparous	2 (20.0%)	8 (80.0%)	
Multiparous	25 (14.0%)	154 (86.0%)	
Grand Multiparous	1 (20.0%)	4 (80.0%)	
BMI (Kg/m²)			0.447[2]
Underweight	1 (50.0%)	1 (50.0%)	
Normal	8 (14.5%)	47 (85.5%)	
Over weight	11 (15.5%)	60 (84.5%)	
Obese	8 (12.1%)	58 (87.9%)	
Birth weight			>0.99[2]
<4000g	27 (14.5%)	159 (85.5%)	
≥4000g	1 (12.5%)	7 (87.5%)	
Baseline systolic blood pressure (mmHg)			**0.013**[1]
≥120	20 (20.8%)	76 (79.2%)	
<120	8 (8.2%)	89 (91.8%)	
Anaesthesia to cutting time (minutes)			0.589[3]
Mean (SD)	11.3 (3.9)	10.8 (5.1)	
Range	5 – 20	5 – 35	
Ondansetron to cutting time (minutes)			
Mean (SD)	29.9 (8.0)	28.0 (7.3)	0.222[3]
Range	22 – 58	20 – 65	
Oxytocin (10 IU intravenous bolus)			**0.046**[2]
No	5 (33.3%)	10 (66.7%)	
Yes	23 (12.8%)	156 (87.2%)	
Tranexamic acid (1g intravenous)			0.918[1]
No	9 (14.1%)	55 (85.9%)	
Yes	19 (14.6%)	111 (85.4%)	
Carbetocin (100mcg intravenous)			0.261[1]
No	15 (17.6%)	70 (82.4%)	
Yes	13 (11.9%)	96 (88.1%)	
Estimated Blood Loss (mL)			0.172[4]
Median (IQR)	550 (500-600)	550 (500-650)	
Range	400 – 700	350 – 3600	
Total fluids (mL)			0.192[4]
Median (IQR)	2000.0 (2000.0-2250.0)	2000.0 (2000.0-2500.0)	
Range	1500 – 3500	1500 – 6250	
Comorbidities			>0.99[2]
Absent	27 (14.7%)	157 (85.3%)	
Present	1 (10.0%)	9 (90.0%)	

[1] Chi Square test
[2] Fisher's exact test
[3] *t*test
[4] Mann Whitney U test

4.6.2 Multivariate Analysis of Factors Associated with Maternal Hypotension

In the multivariate analysis, detailed in Table 7, logistic regression was utilized to evaluate all variables that demonstrated statistical significance in the bivariate analysis, as shown in Table 6. After adjusting for maternal, anaesthesia-related, surgery-related, and neonatal characteristics, the analysis revealed that patients who did not receive prophylactic ondansetron before spinal anaesthesia were 4.841 times more likely to develop spinal anaesthesia-induced hypotension. Additionally, patients with a baseline systolic blood pressure below 120 mmHg were 3.562 times more likely to develop spinal anaesthesia-induced hypotension. The administration of oxytocin was not associated with spinal anaesthesia-induced hypotension.

Table 7: Multivariate Analysis of Factors Associated with Maternal Hypotension

Hypotension	**AOR**	**P - value**	**95% CI**
Arm			
Case (Ondansetron)	Ref		
Control (Saline)	4.841	**0.002**	1.782 – 13.149
Baseline systolic Blood Pressure			
≥120	Ref		
<120	3.562	**0.008**	1.389 – 9.137
Oxytocin			
No	Ref		
Yes	2.546	0.154	0.704 – 9.205
Blood loss	1.003	0.193	0.998 – 1.008
Total fluids	1.000	0.272	0.999 – 1.001

AOR: Adjusted Odds Ratio

4.7 Effect of Prophylactic Ondansetron on the Incidence of Bradycardia

The overall incidence proportion of bradycardia among pregnant women in both groups was 11.3% (n=22).

The incidence proportion of women who developed bradycardia due to spinal anaesthesia was slightly lower in the ondansetron group compared to the placebo group (8.2%, n=8 vs 14.4%, n=14, respectively). However, this difference was not statistically significant (P = 0.17). This information is illustrated in Table 8.

Table 8: Effect of Prophylactic Ondansetron on the Incidence of Bradycardia

	Group S N=97	**Group O N=97**	**P-value**
Bradycardia			0.17
No	83 (85.6%)	89 (91.8%)	
Yes	14 (14.4%)	8 (8.2%)	

4.7.1 Bivariate Analysis of Factors associated with maternal bradycardia

The bivariable analysis revealed that maternal bradycardia was significantly associated with both patient age and the use of phenylephrine. Among patients aged 35 years and above, 22% experienced bradycardia—a proportion significantly higher (P = 0.025) than that observed in patients aged 35 years or younger. Additionally, 35.3% of phenylephrine users exhibited bradycardia, a rate that was notably higher (P = 0.006) compared to non-users of phenylephrine. These findings are clearly presented in Table 9.

Table 9: Bivariate Analysis of Factors associated with maternal bradycardia

	Bradycardia		
	No	**Yes**	**p-value**
	N=172	**N=22**	
Arm			0.174[c]
Control	83 (85.6%)	14 (14.4%)	
Case	89 (91.8%)	8 (8.2%)	
Patient age			**0.025**[f]
<35yrs	140 (91.5%)	13 (8.5%)	
=>35yrs	32 (78.0%)	9 (22.0%)	
BMI			0.208[f]
Underweight	2 (100.0%)	0 (0.0%)	
Normal	51 (92.7%)	4 (7.3%)	
Over weight	65 (91.5%)	6 (8.5%)	
Obese	54 (81.8%)	12 (18.2%)	
Phenylephrine			**0.006**[f]
No	161 (91.0%)	16 (9.0%)	
Yes	11 (64.7%)	6 (35.3%)	

[c] Chi Square test

[f] Fisher's exact test

4.7.2 Multivariate Analysis of Factors Associated with Maternal Bradycardia

A multivariable binary logistic regression was used to fit variables that had a p-value of less than 0.2, as presented in Table 10. The analysis showed that both age and phenylephrine use were independently associated with bradycardia. Holding phenylephrine use and study arms constant, participants aged 35 years and above were 2.9 times more likely to developed bradycardia compared to those aged below 35 years. Similarly, phenylephrine users were 4.7 times more likely to experience bradycardia than non-users while holding age and study arm constant.

Table 10: Multivariate Analysis of Factors Associated with Maternal Bradycardia

Variables	aOR	p-value	95% CI
Arm			
Control			
Case	0.519	0.181	0.199-1.358
Patient age			
<35yrs			
=>35yrs	2.869	**0.034**	1.081-7.612
Phenylephrine			
No			
Yes	4.722	**0.009**	1.486-15.004

aOR: Adjusted Odds Ratio

4.8 Comparison of the total dose of vasopressors administered for the treatment of spinal anaesthesia-induced hypotension between Group S and Group O

The comparison of the type and total dose of vasopressors administered for the treatment of spinal anaesthesia-induced hypotension between the ondansetron group (Group O) and the saline group (Group S) is well illustrated in Table 11.

Ephedrine and Phenylephrine were used by anaesthetists to manage spinal anaesthesia-induced hypotension, with their selection based on severity of the condition, drug availability, and provider preference. Ephedrine was the most commonly used vasopressor compared to phenylephrine. However, its requirement was significantly lower in the ondansetron group compared to the saline group (75.3%, n=73 vs 92.8%, n=90, respectively, with a P-value of **<0.001**).

Table 11: Vasopressors and Total dose administered by treatment arm

	Group S N=97	**Group O N=97**	**P-value**
Vasopressors used			
Ephedrine			**<0.001[1]**
No	7 (7.2%)	24 (24.7%)	
Yes	90 (92.8%)	73 (75.3%)	
Phenylephrine			0.446[1]
No	87 (89.7%)	90 (92.8%)	
Yes	10 (10.3%)	7 (7.2%)	
Total dose administered			
Ephedrine (in mg)			
Median (IQR)	18.0 (12.0-24.0)	18.0 (12.0-30.0)	>0.99[2]
Range	6 – 60	6 – 48	
Phenylephrine (in mcg)			
Median (IQR)	200.0 (100.0-200.0)	100.0 (100.0-150.0)	**0.023[2]**
Range	100 – 800	50 – 200	

[2] Mann Whitney U test

[1] Chi Square test

The total dose of ephedrine administered to each parturient who developed spinal anaesthesia-induced hypotension ranged from 6 to 60 mg in the placebo group and 6 to 48 mg in the ondansetron group, with no significant statistical difference (P > 0.99), both with a median dose of 18.0 mg.

On the other hand, the median total dose of phenylephrine administered was significantly higher in the placebo group (Group S), with a median dose of 200.0 mcg (IQR 100.0-200.0), compared to the ondansetron group (Group O), which had a median dose of 100.0 mcg (IQR 100.0-150.0) (**P = 0.023**).

4.9 Other Complications of Spinal Anaesthesia

The incidence proportions of additional complications associated with spinal anaesthesia, as observed in patients during cesarean sections, are presented in Table 12 and Figure 6.

The incidence proportion of nausea was significantly higher in Group S (35.1%, n=34) compared to Group O (13.4%, n=13), **P < 0.001**.

Similarly, the incidence proportion of vomiting was significantly higher in Group S (11.3%, n=11) than in Group O (1.0%, n=1), **P = 0.005**.

Moreover, the incidence proportion of shivering was significantly higher in Group S (17.5%, n=17) compared to Group O (7.2%, n=7), **P = 0.029**.

On the other hand, incidence proportion of headache in both groups had no statistically significant difference, P = 0.721.

Table 12: Incidence Proportions of Nausea, vomiting, shivering and headache

	Group S N=97	**Group O N=97**	**P-value**
Nausea			**<0.001[1]**
No	63 (64.9%)	84 (86.6%)	
Yes	34 (35.1%)	13 (13.4%)	
Vomiting			**0.003[1]**
No	86 (88.7%)	96 (99.0%)	
Yes	11 (11.3%)	1 (1.0%)	
Shivering			**0.029[1]**
No	80 (82.5%)	90 (92.8%)	
Yes	17 (17.5%)	7 (7.2%)	
Headache			0.721[2]
No	92 (94.8%)	94 (96.9%)	
Yes	5 (5.2%)	3 (3.1%)	

[2] Fisher's exact test
[1] Chi Square test

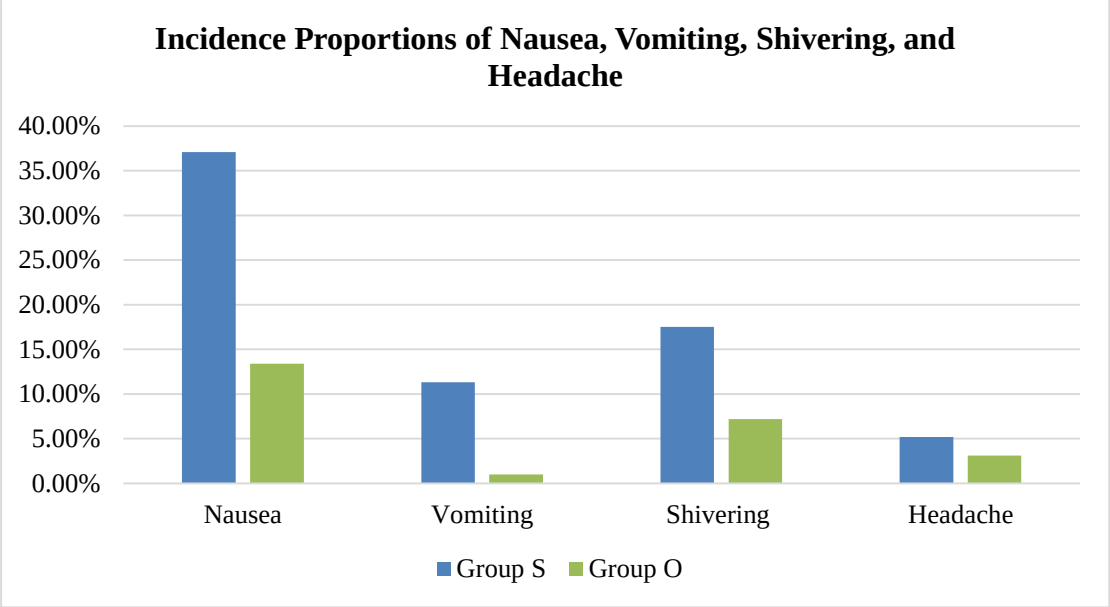

Figure 6: Incidence Proportions of Nausea, Vomiting, Shivering, and Headache

CHAPTER FIVE

5.0 DISCUSSION

5.1 Demographic and clinical characteristics

In this clinical trial, there were no statistically significant variations observed in the parturients of both groups regarding age, weight, height, BMI, indications for cesarean section, parity, or the presence of comorbidities. This indicates that the randomization process was effective, with no potential for selection bias. A similar study conducted in Palestine, West Bank, at Rafidia governmental hospital included ASA 1 and 2 pregnant women within the age bracket of 18 – 50 years and they also found no significant difference in the patient demographic characteristics (Salahat et al., 2021). A comparable study conducted in Nepal also found that both study arms were similar with respect to patient demographic characteristics (Balla et al., 2019).

The ages of the pregnant women who participated in this clinical trial ranged from 19 to 42 years. Most of the women were under 35 years old, with the mean age being 29.9 ± 4.8 years in Group S and 30.3 ± 4.7 years in Group O. There was no statistically significant variation in age between the two groups. This finding aligns with the mean age of parturients undergoing cesarean sections in low- and middle-income countries. For instance, similar study conducted at Dhaka Medical College Hospital in Bangladesh involving 120 parturients found that the mean age was 27.4 ± 12.6 years, with the majority of patients being under 30 years old (Islam et al., 2022). Additionally, at Dilla University Referral Hospital in Ethiopia, almost identical findings were observed, with the mean age of parturients in Group O being 27.23 ± 3.50 years and in Group S being 27.5 ± 5.0 years (S. Mohamed et al., 2021). The mean maternal age of 29.9 ± 4.8 years in Group S and 30.3 ± 4.7 years in Group O were favorable for better maternal and neonatal outcomes in this study. Advanced maternal age (AMA), typically defined as

being 35 years or older at the time of delivery, is linked to a heightened risk of both maternal and fetal complications (Barash et al., 2017).

In the current clinical trial, the majority of the pregnant women were categorized as overweight, with the mean Body Mass Index being 28.0 ± 5.8 kg/m² in Group S and 28.1 ± 5.8 kg/m² in Group O. This can be attributed to the fact that the average maternal weight gain during pregnancy is about 17% of the pre-pregnancy weight, or nearly 12 kg. This increase is attributed to the enlargement of the uterus and its contents, including 1 kg for the uterus, 1 kg for amniotic fluid, and 4 kg for the fetus and placenta. Additionally, it is due to the rise in blood volume and interstitial fluid, each contributing about 1 kg, along with the accumulation of new fat and protein, which adds around 4 kg (Chestnut et al., 2020). A comparable study conducted in Dilla, Ethiopia, found that the majority of participants were also overweight, with a BMI of 25.42 ± 1.75 kg/m² in Group O and 25.94 ± 1.66 kg/m² in Group S (S. Mohamed et al., 2021).

In contrast, a similar study conducted in Egypt found that the majority of their patients were obese, with a mean BMI of 31.8 kg/m² (Shabana et al., 2018).

In this study, the primary indication for elective caesarean delivery was a previous uterine scar from a prior caesarean section. The majority of the pregnant women had one previous scar, with 47.7% in Group S and 51.2% in Group O. A study conducted in Bangladesh, which is a low-middle-income country similar to Kenya, found that most parturients underwent caesarean section having had a history of caesarean sections in their previous pregnancies (Begum et al., 2017). Women with a history of previous uterine surgeries, such as cesarean deliveries or myomectomies, face a significantly increased risk of uterine rupture if they enter labor (Chestnut et al., 2020). As a result, to reduce this risk, these women are often required to deliver via cesarean section, which contributes to the increased number of cesarean deliveries.

In this study, a large number of participants were multiparous, with 92.8% in Group S and 91.8% in Group O having previously given birth to more than one child, showing no statistically significant difference (P>0.99). This finding was comparable to a study conducted in Sudan at Wad Medani Maternity Teaching Hospital, Gezira State, which involved 251 parturients and found an average parity of 2.8, with a minimum of 1 and a maximum of 7 (Sahidin, 2018). Many African communities continue to value and uphold the tradition of having larger families, seeing it as a cultural norm or source of strength and pride.

5.2 Incidence of Spinal Anaesthesia- induced Hypotension

Hypotension, generally described as a systolic blood pressure below 100 mm Hg, is a prevalent adverse effect of neuraxial anaesthesia (Butterworth et al., 2022). The incidence of spinal anaesthesia- induced hypotension varies globally due to different definitions of hypotension, as there has previously been a lack of a consensus definition. Most specialist obstetric anaesthetists prefer absolute systolic blood pressure (SBP) thresholds set at either below 90 mmHg or below 100 mmHg (Zwane et al., 2019). There is a significant variation in the reported incidence of intraoperative SAIH, with a range of 15.8% to 91.4%, depending solely on how hypotension is defined (Zwane et al., 2019). Most common definitions from South African literature include: mean arterial pressure (MAP) below 80% of the baseline; systolic blood pressure (SBP) lower than 20% of the baseline; SBP lower than 90 mmHg; SBP lower than 90 mmHg or MAP below 80% of the baseline; and SBP lower than 100 mmHg and below 80% of the baseline (Zwane et al., 2019).

This study reported that the incidence proportion of spinal anaesthesia-induced hypotension at Moi Teaching and Referral Hospital in Eldoret was 85.6%. The incidence proportion was almost similar to a study conducted at Christian Albrechts University in Germany, which focused on detecting spinal anaesthesia-induced hypotension during cesarean sections using noninvasive blood pressure monitoring, and found an incidence of 91% (Ilies et al., 2012). The high incidence observed in this study can be explained by the fact that most of the pregnant women had a low baseline systolic blood pressure, defined as lower than 120 mmHg, which is a well-established factor linked to hypotension following spinal anaesthesia. The high incidence could also be due to the prolonged fasting hours experienced by the pregnant women in the antenatal wards as they awaited their elective surgery, leading to dehydration and consequently causing hypotension post-spinal anaesthesia. Pregnant women should be started on intravenous fluids as they await surgery. Sahidin, (2018) also found that patients who spent extended hours in their labor wards were more likely to be dehydrated, which predisposed them to SAIH during caesarean sections. Furthermore, the exclusion of hypertensive parturients and other emergency cases involving women in labor—during which blood pressure tends to increase, particularly during uterine contractions—may also explain the high occurrence rate of spinal hypotension observed in this study. Pre-eclamptic parturients are recognized for having a lower occurrence rate of hypotension, likely due to their typically higher baseline blood pressure levels, which can mitigate the drop in blood pressure associated with spinal anaesthesia (Zwane et al., 2019).

Another comparable study involving 108 parturients, who had uncomplicated pregnancies coming in for elective cesarean delivery under spinal anaesthesia, was conducted in Turkey. This study found a similar high incidence of spinal anaesthesia-

induced hypotension, with a proportion of 87.9%. They used a different definition of hypotension (<80% of the prenatal baseline) (Karacaer et al., 2018).

The high incidence proportion of SAIH in this study was similar to a cross-sectional study carried out in 2016 at Gandhi Memorial Hospital in Ethiopia. That study involved 60 pregnant women slated for elective caesarean sections, where the incidence of hypotension was 80% within the first five to fifteen minutes after spinal anaesthesia and 83.7% within fifteen to twenty-five minutes (Nigussie Yirgu et al., 2020).

However, this incidence contrasted with the results from Kenyatta National Hospital, where the incidence was lower at 64%. The lower incidence can be attributed to the principal investigator administering a prophylactic dose of 5mg ephedrine to all study participants immediately after intrathecal injection to prevent spinal hypotension. In addition, a different criterion for defining spinal anaesthesia-induced hypotension was applied, using a lower threshold of systolic blood pressure below 90 mmHg (Kahoro, 2009).

The incidence of SAIH was also lower (57%) at Wad Medani Maternity Teaching Hospital in Gezira State, Sudan, compared to this study. This difference is likely because all patients were preloaded with up to 1500 ml of crystalloid fluids and were given a prophylactic dose of 6mg ephedrine immediately after the spinal anaesthesia (Sahidin, 2018).

In a study carried out in Addis Ababa, Ethiopia, at Gandhi Memorial Hospital, the incidence of SAIH was 64%. The lower rate observed in their study can be attributed to a bigger sample size of 422 participants compared to the 194 in our study. Moreover, all participants in their study were administered ondansetron 30 minutes preceding spinal anaesthesia, which likely played a significant role in reducing the incidence of

hypotension (Shitemaw et al., 2020). In contrast, in our study, only a subset of patients received ondansetron.

5.3 Effect of Ondansetron on Spinal -Anaesthesia induced Hypotension

In this study, ondansetron has proven to be effective in reducing the incidence proportion of SAIH by 16.5%. The incidence proportion of SAIH in the normal saline group was 93.8%, compared to 77.3% in the ondansetron group. This variation was statistically significant (P = 0.001). Ondansetron blocks the Bezold-Jarisch Reflex, which is precipitated by the activation of serotonin mechanoreceptors in the heart's left ventricle when there is reduced ventricular blood volume. This reduction in volume is due to decreased systemic vascular resistance resulting from sympathetic blockade during the injection of local anaesthetics into the subarachnoid space.

A similar study conducted at Tribhuvan University Teaching Hospital in Nepal found that the group where prophylactic ondansetron 4mg was administered intravenously to pregnant women scheduled for caesarean deliveries had a statistically significant lower incidence proportion of SAIH—20.9% in comparison with 72.1% in the normal saline group (P < 0.001). This resulted in a 51.2% reduction in spinal anaesthesia-induced hypotension, proving the efficacy of ondansetron administration prior to spinal anaesthesia (Balla et al., 2019).

In most studies, prophylactic ondansetron has also proven effective in reducing the occurrence rate of SAIH. In India, a similar study conducted at K R Hospital in Mysore Medical College on 120 parturients, found an almost similar reduction rate of SAIH, which was 18.4%. In that clinical trial, the ondansetron group had 6.6% of patients experiencing spinal hypotension, whereas the normal saline group had a 25% incidence of spinal hypotension (Rakshith et al., 2023). The lower incidence of spinal hypotension

in both study arms can be attributed to them using a different definition of hypotension, where systolic blood pressure lower than 90 mmHg was considered the threshold. This cutoff was lower than the standard definition applied in this study, which classified spinal hypotension as systolic blood pressure lower than 100 mmHg.

Another study conducted at Airforce Hospital in Kalaikunda, India, also proved the efficacy of prophylactic ondansetron in reducing the occurrence of spinal hypotension. There was a statistically significant difference in the incidence proportion of spinal hypotension, with a reduction of 21.4%. The incidence proportion in the ondansetron group was 39.3%, in comparison with 60.7% in the normal saline group (P = 0.0359) (Raghu et al., 2018). A similar study conducted at Holy Family Hospital in Rawalpindi, Pakistan, also demonstrated a reduction in the incidence of SAIH by 20.8%. The incidence of SAIH in the ondansetron group was 7.5%, compared to 28.3% in the normal saline group (P = 0.005) (Baig et al., 2017).

In Tunisia, a study by Trabelsi et al. also reported a statistically significant lower incidence of spinal anaesthesia-induced hypotension in the ondansetron group by 40%. Group O had a 37.5% incidence of spinal hypotension, while Group S had a 77.5% incidence (P = 0.022) (Trabelsi et al., 2015).

In contrast to this study, some research has shown no significant difference in the incidence of spinal hypotension amongst the ondansetron group and the normal saline group. For instance, a similar study conducted at Cukurova University Hospital in Turkey found no statistically significant variation in the incidence of spinal anaesthesia-induced hypotension between patients in the ondansetron group (88.9%) and those in the normal saline group (87%) (P = 0.767) (Karacaer et al., 2018). This is likely because an 8mg dose of intravenous (IV) ondansetron was used in their study, which has been

shown to be less effective in reducing the occurrence rate of SAIH when compared to the 4mg dose, as demonstrated in a dose-dependent study (M. Wang et al., 2014).

In Ethiopia, a similar study conducted at Dilla University Referral Hospital assessing the efficacy of ondansetron on the occurrence of SAIH also showed no statistically significant difference amongst the ondansetron group (68.4%) and the normal saline group (65.8%) (P = 0.807) (S. Mohamed et al., 2021). The reason for this was probably because they used a higher dose of intravenous ondansetron, 10mg. The optimum dose for prophylactic ondansetron to attenuate the incidence of SAIH is 4mg (M. Wang et al., 2014).

5.4 Effect of Prophylactic Ondansetron on the occurrence of Bradycardia

Bradycardia, characterized by a heart rate lower than 50 beats per minute, is another significant complication that can arise during caesarean delivery under spinal anaesthesia. Spinal anaesthesia results in unopposed vagal tone and the Bezold-Jarisch reflex, leading to reduced cardiac output and subsequently a decreased supply of oxygen-rich blood to the brain as well as other vital organs. During a high neuraxial block, the heart rate may decrease due to the inhibition of thoracic sympathetic fibers, specifically the preganglionic cardiac accelerator fibers that originate at levels T1 to T4. Additionally, reflexive bradycardia can occur as vasodilation decreases venous return to the right atrium, further contributing to the slowing of the heart rate (Gropper et al., 2025). The decrease in venous return as well as right atrial filling leads to a decreased signal output originating at intrinsic chronotropic stretch receptors situated in the right atrium plus the great veins. This reduction triggers a significant increase in parasympathetic activity, also referred to as vagal tone, further contributing to the slowing of the heart rate (Gropper et al., 2025).

In this study, the incidence proportion of bradycardia was 11.3%. Group O parturients experienced an incidence of 8.2%, while Group S parturients had a slightly higher incidence of 14.4%. However, there was no statistically significant difference amongst the two groups (P = 0.17). This is because most parturients develop tachycardia as a reflex mechanism to compensate for the reduced cardiac output caused by the spinal block, rather than bradycardia. Another possibility would be that bradycardia might have gone unnoticed because sympathomimetics, such ephedrine, had been used to treat hypotension, which tends to raise heart rate and blood pressure. Another contributing factor is that only a small number of women in this study received phenylephrine to manage their spinal anaesthesia-induced hypotension. The findings also revealed that the use of phenylephrine was linked to a heightened risk of bradycardia. Phenylephrine is a selective alpha-1 adrenergic agonist that causes vasoconstriction, leading to an increase in blood pressure. This sudden rise in blood pressure can activate baroreceptor reflexes, which in turn stimulate the vagus nerve and result in reflex bradycardia, a slowing of the heart rate. Even though ondansetron is thought to reduce bradycardia by blocking serotonin-mediated reflexes like the Bezold-Jarisch reflex, it does not interfere with baroreceptor-mediated vagal responses triggered by agents like phenylephrine.

The incidence proportion in this study was almost similar to documented literature, which states that the overall global incidence of bradycardia as a complication of spinal anaesthesia is 13% (Gwinnutt & Gwinnutt, 2012).

A similar study conducted at Cukurova University Hospital in Turkey found a slightly higher overall incidence proportion of bradycardia in pregnant women during caesarean section, at 15.7%. They observed no statistically significant difference in the incidence of bradycardia between parturients who received IV ondansetron (20.4%) and those who received normal saline (11.1%) (P = 0.186) (Karacaer et al., 2018). The high

incidence of bradycardia in their study can be associated to the use of a higher cutoff in its definition, considering heart rate lesser than 60 beats per minute as bradycardia, compared to the lower threshold of below 50 beats per minute used in this study. This broader definition likely contributed to the increased reported cases.

In Ethiopia, a study conducted at Dilla University Referral Hospital also found no statistically significant variation in the incidence proportion of bradycardia among parturients in both groups. The incidence of bradycardia in the ondansetron group was 5.3%, compared to 2.9% in the saline group ($P > 0.05$) (S. Mohamed et al., 2021). The lower incidence of bradycardia in their study can be attributed to the administration of 0.5 mg IV atropine to patients whose heart rate dropped lower than 60 beats per minute (bpm), despite using the same definition of bradycardia (heart rate <50 bpm) as this study. This proactive intervention likely prevented the occurrence of bradycardia in many cases.

A similar study conducted at Tribhuvan University Teaching Hospital in Nepal also found no statistically significant difference in the heart rates among parturients in both groups, as there were no episodes of bradycardia in either group (Balla et al., 2019). This outcome might be attributed to their use of a lower cutoff for defining bradycardia—heart rate below 45 bpm—compared to the cutoff of below 50 beats per minute applied in this study.

In contrast to this study, a similar study conducted at K R Hospital, Mysore, India, reported that prophylactic ondansetron was effective in reducing the occurrence rate of bradycardia in patients undergoing elective infraumbilical surgeries under spinal anaesthesia. The IV ondansetron group had an incidence of 3.3%, while the saline group

had a significantly higher incidence of 13.3% (P = 0.047), with an overall incidence of 8.3% (Rakshith et al., 2023).

A similar study conducted at the Tunisian Military Hospital found contrasting results to this study. They discovered that prophylactic IV ondansetron was significantly effective in reducing the incidence proportion of bradycardia in parturients who had been given ondansetron during elective cesarean section. The incidence proportion of bradycardia in the ondansetron group was 15%, compared to 37.5% in the saline group (P = 0.022), with an overall incidence of 26.3% (Trabelsi et al., 2015). This high incidence might have been attributed to a different definition of bradycardia, where it was described as a 30% decrease in heart rate.

5.5 Comparing the Total Dose of vasopressor used and Vasopressor requirement between the ondansetron group and the saline group

Hypotension is often managed with vasopressor drugs, and many clinical trials regard phenylephrine as the preferred option. Direct α-adrenergic agonists like phenylephrine primarily work by inducing vasoconstriction, which raises systemic vascular resistance. However, they may also trigger reflexive bradycardia due to their mechanism of action. On the other hand, the "mixed" agent ephedrine combines direct and indirect beta (β)-adrenergic effects, enhancing heart rate and contractility, along with indirect alpha (α)-adrenergic effects that contribute to vasoconstriction. When using phenylephrine, it is important to administer it in small, carefully measured increments to avoid the risk of excessive hypertension (Butterworth et al., 2022). This study utilized phenylephrine and ephedrine as vasopressors, with ephedrine being the most frequently used due to its easy availability. In our study, the choice of vasopressor varied among anaesthesia providers, as they selected their preferred option based on availability.

In this research, the use of ephedrine was significantly higher in the saline group, with 92.8% of the parturients requiring it, compared to 75.3% in the ondansetron group ($P < 0.001$). This higher usage is attributed to the significantly higher incidence of spinal anaesthesia-induced hypotension in the saline group, necessitating a greater need for vasopressors in comparison with the ondansetron group. This finding aligns with a study carried out at Al-Shohada Central Hospital in Egypt, where it was observed that patients in the control group used phenylephrine significantly more often than those in the ondansetron group due to a higher incidence of spinal hypotension. (Shabana et al., 2018).

In Nepal, Balla et al. (2019) also found that the usage of vasopressors was considerably higher in the normal saline group. The higher incidence of spinal anaesthesia-induced hypotension in the saline group in comparison with the ondansetron group underscores ondansetron's effectiveness in reducing this complication. This reduction also led to a decreased need for vasopressors in the ondansetron group. The clinical trial in Nepal also demonstrated a significant reduction in total phenylephrine dosage among participants in the ondansetron group (37.21 mcg) compared to the saline group (146.51 mcg), with a statistically significant variation ($p < 0.05$) (Balla et al., 2019).

In this study, there was no statistically significant variation in the total dose of ephedrine among parturients who developed SAIH in both groups. However, the total dose of phenylephrine was significantly higher among parturients in the saline group as opposed to the ondansetron group. This is because phenylephrine, even in small incremental doses, is effective in treating hypotension due to its mechanism as a direct vasopressor. In contrast, ephedrine acts as an indirect vasopressor, which influences its effectiveness differently.

However, a study conducted at Menoufia University Hospital in Egypt found that both the total dose of ephedrine and its requirement were significantly raised in the saline group of parturients as opposed to the ondansetron group. (El Khouly & Meligy, 2016). This contrasts with our study, where the mean total dose of ephedrine administered to parturients in both groups showed no statistically significant variance. In contrast, the other study found a significant difference in the total dose of ephedrine administered to women in both groups. The reason for this is that most of the parturients in this study experienced severe hypotension, which was attributed to their low baseline systolic blood pressure. As a result, they required a higher dose of vasopressors.

A study at Dilla University Referral Hospital in Ethiopia involving 70 parturients reported no statistically significant difference in perioperative phenylephrine consumption between the ondansetron (36.43 ± 45.91 mcg) and saline (32.14 ± 46.79 mcg) groups (P = 0.700) (S. Mohamed et al., 2021). In contrast to our study, these findings suggest that prophylactic ondansetron did not significantly reduce both vasopressor requirements and total dose in this cohort.

5.6 Other Significant findings

Nausea, vomiting, and shivering are additional complications of spinal anaesthesia that were significantly more prevalent among parturients in the saline group compared to the ondansetron group. The significantly reduced incidence of nausea and vomiting in the ondansetron group can be associated with the well-known antiemetic properties of ondansetron. On the other hand, hypotension leads to nausea and vomiting, which explains why the incidence proportion of these symptoms was significantly raised in Group S, where participants experienced the highest incidence of hypotension.

Shivering is a reaction to spinal anaesthesia-induced hypothermia. Spinal anaesthesia may induce shivering as a result of vasodilation, which causes rapid heat loss and the redistribution of body heat coming out of the core to the peripheral tissues. Increased oxygen consumption and metabolic activity prompted by shivering may result in lactic acidosis and arterial hypoxemia. Enhanced heat loss from the patient's body surface, primarily from the lower extremities, results from a lack of vasoconstriction ability following the subarachnoid block. A thermoregulatory neurotransmitter called serotonin also causes shivering by lowering body temperature. Ondansetron is a 5- HT3 receptor inhibitor that reduces the effects of serotonin on thermoregulation (Tatikonda et al., 2019). This explains why the occurrence of shivering was lower in Group O compared to Group S.

Our findings align with a similar clinical trial conducted at Rafedia Government Hospital in Palestine, which observed a significantly reduced incidence proportion of nausea, vomiting, and shivering among parturients in the ondansetron group compared to the normal saline group (Salahat et al., 2021).

However, this contrasts somewhat with a study conducted at Al-Shohada Central Hospital in Egypt, where, despite a significantly lower incidence of nausea and vomiting in the ondansetron group, there was no significant variance in the incidence proportion of shivering amongst the two groups (Shabana et al., 2018).

5.7 Study Strengths

The strength of this study was that, due to its double-blind nature, we were able to reduce the risk of bias from both the parturients and the anaesthesia team, improving the reliability of our findings.

Another strength was that the randomization process avoided selection bias, as parturients in both groups had comparable characteristics.

5.8 Study Limitations

The lack of a consensus definition of spinal anaesthesia-induced hypotension globally made it challenging to come up with a cutoff for the definition of SAIH. This challenge was mitigated by using the definition found in current textbooks, which defines hypotension as a systolic blood pressure of less than 100 mmHg (Butterworth et al., 2022).

Another limitation was in estimating the 15˚- 30˚ table tilt to avoid aortocaval compression in the parturients. This was mitigated by using an identical wedge at an angle of 25˚ placed on the right hip of all parturients immediately after the intrathecal injection.

CHAPTER SIX

6.0 CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusions

1. A prophylactic intravenous injection of 4mg ondansetron significantly reduces the incidence of spinal anaesthesia-induced hypotension in women undergoing elective cesarean sections.
2. Prophylactic ondansetron was not effective in reducing the incidence of bradycardia among parturients undergoing elective cesarean sections under spinal anaesthesia.
3. Prophylactic ondansetron was effective in reducing the incidence of vasopressor requirement as well as the total dose of phenylephrine during elective caesarean section.

6.2 Recommendations

1. Administration of 4mg IV ondansetron should be considered 15 minutes before spinal anaesthesia in elective caesarean sections to reduce the chances of SAIH, and the need for vasopressors.
2. It is recommended that the MTRH Anaesthesia Department incorporate prophylactic ondansetron into its protocol to reduce the incidence of SAIH during caesarean sections.
3. Further studies are needed to assess the effect of prophylactic ondansetron in reducing the incidence spinal anaesthesia-induced hypotension during non-obstetric surgeries.

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APPENDICES

APPENDIX 1: IREC APPROVAL

MTRH/MU-INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471/2/3

MOI UNIVERSITY
COLLEGE OF HEALTH SCIENCES
P.O. BOX 4606
ELDORET
Tel: 33471/2/3

Reference: IREC/2021/211
Approval Number: 0004102

31st March, 2022

Dr. Pauline Awili Omondi,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET- KENYA

Dear Dr. Omondi,

EFFECT OF PROPHYLACTIC ONDANSETRON ON SPINAL ANAESTHESIA-INDUCED HYPOTENSION DURING CAESAREAN SECTION AT MOI TEACHING AND REFERRAL HOSPITAL, ELDORET, KENYA

This is to inform you that ***MTRH/MU-IREC*** has reviewed and approved the above referenced research proposal. Your application approval number is ***FAN: 0004102.*** The approval period is **31st March, *2022- 30th March, 2023.***
This approval is subject to compliance with the following requirements;

i. Only approved documents including (informed consents, study instruments, Material Transfer Agreements (MTA) will be used.
ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by ***MTRH/MU-IREC.***
iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to ***MTRH/MU-IREC*** within 72 hours of notification.
iv. Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to ***MTRH/MU-IREC*** within 72 hours.
v. Clearance for export of biological specimens must be obtained from ***MOH at the recommendation of NACOSTI*** for each batch of shipment.
vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. Attach a comprehensive progress report to support the renewal.
vii. Submission of an executive summary report within 90 days upon completion of the study to ***MTRH/ MU-IREC.***

Prior to commencing your study; you will be required to obtain a research license from the National Commission for Science, Technology and Innovation (NACOSTI) https://oris.nacosti.go.ke and other relevant clearances from study sites including a written approval from the CEO-MTRH which is mandatory for studies to be undertaken within the jurisdiction of Moi Teaching & Referral Hospital (MTRH) and its satellites sites.

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
31 MAR 2022
APPROVED
P. O. Box 4606-30100 ELDORET

Sincerely,

PROF. E. WERE
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc CEO - MTRH Dean - SOP Dean - SOM
Principal - CHS Dean - SON Dean - SOD

APPENDIX 2: MTRH APPROVAL

An ISO 9001:2015 Certified Hospital

MOI TEACHING AND REFERRAL HOSPITAL

Telephone: (+254)-0532033471/2/3/4
Fax: 0532061749
Email: ceo@mtrh.go.ke/ceosoffice@mtrh.go.ke

NANDI ROAD
P.O. BOX 3-30100
ELDORET,KENYA

Ref: ELD/MTRH/R&P/10/2/V.2/2010

4th April, 2022

Dr. Pauline Awili Omondi,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

EFFECT OF PROPHYLACTIC ONDANSETRON ON SPINAL ANAESTHESIA-INDUCED HYPOTENSION DURING CAESAREAN SECTION AT MOI TEACHING AND REFERRAL HOSPITAL, ELDORET, KENYA

You have been authorised to conduct research within the jurisdiction of Moi Teaching and Referral Hospital (MTRH) and its satellites sites. You are required to strictly adhere to the regulations stated below in order to safeguard the safety and well-being of staff, patients and study participants seen at MTRH.

1. The study shall be under Moi Teaching and Referral Hospital regulation.
2. A copy of MTRH/MU-IREC approval shall be a prerequisite to conducting the study.
3. Studies intending to export human bio-specimens must provide a permit from MOH at the recommendation of NACOSTI for each shipment.
4. No data collection will be allowed without an approved consent form(s) to participants unless waiver of written consent has been granted by MTRH/MU-IREC.
5. Take note that **data** collected must be treated with due confidentiality and anonymity.

The continued permission to conduct research shall only be sustained subject to fulfilling all the requirements stated above.

MOI TEACHING AND REFERRAL HOSPITAL
CEO
APPROVED
04 APR 2022
SIGN.....
P. O. Box 3-30100, ELDORET

04/04/2022
DR. WILSON K. ARUASA, *MBS, EBS*
CHIEF EXECUTIVE OFFICER
MOI TEACHING AND REFERRAL HOSPITAL

c.c. - Senior Director, Clinical Services
- Director, Nursing Services
- HOD, HRISM

APPENDIX 3: NATIONAL COMMISSION FOR SCIENCE, TECHNOLOGY & INNOVATION (NACOSTI) RESEARCH PERMIT

REPUBLIC OF KENYA

NATIONAL COMMISSION FOR SCIENCE,TECHNOLOGY & INNOVATION

Ref No: **632490**

Date of Issue: **04/July/2022**

RESEARCH LICENSE

This is to Certify that Dr.. Pauline Awili Omondi of Moi University, has been licensed to conduct research in Uasin-Gishu on the topic: EFFECT OF PROPHYLACTIC ONDANSETRON ON SPINAL ANAESTHESIA - INDUCED HYPOTENSION DURING CAESAREAN SECTION AT MOI TEACHING AND REFERRAL HOSPITAL, ELDORET, KENYA. for the period ending : 04/July/2023.

License No: **NACOSTI/P/22/18648**

632490

Applicant Identification Number

Director General
NATIONAL COMMISSION FOR SCIENCE,TECHNOLOGY & INNOVATION

Verification QR Code

NOTE: This is a computer generated License. To verify the authenticity of this document, Scan the QR Code using QR scanner application.

APPENDIX 4: ASA CLASSIFICATION

American Society of Anaesthesiologists physical status classification

ASA 1	Healthy patient without organic, biochemical, or psychiatric disease
ASA 2	Mild to moderate systemic disease that is well controlled and causes no organ dysfunction or functional limitation
ASA 3	Significant or severe systemic disease that limits normal activity
ASA 4	Severe disease that is a constant threat to life or requires intensive therapy
ASA 5	Moribund patient who is equally likely to die in the next 24 hours with or without surgery
ASA 6	Brain-dead organ donor

Source: Research Gate

APPENDIX 5: EXPANDED APGAR SCORING FORM

Apgar Score

Gestational age_____weeks

Sign	0	1	2	1 minute	5 minute	10 minute	15 minute	20 minute
Color	Blue or Pale	Acrocyanotic	Completely Pink					
Heart rate	Absent	<100 minute	>100 minute					
Reflex irritability	No Response	Grimace	Cry or Active Withdrawal					
Muscle tone	Limp	Some Flexion	Active Motion					
Respiration	Absent	Weak Cry; Hypoventilation	Good, Crying					
			Total					

Comments:

Resuscitation					
Minutes	1	5	10	15	20
Oxygen					
PPV/NCPAP					
ETT					
Chest Compressions					
Epinephrine					

APPENDIX 6: BUDGET

CATEGORY	ESTIMATED QUANTITY	UNIT PRICE - Ksh.	SUB TOTAL – KSh.
STATIONERY			
Pens	15	20	300
Printing papers	10 reams	450	4,500
Photocopy		3,000	3,000
Printing		10,000	10,000
Binding		1,000	1,000
Envelopes	4 stacks (50 per stack) of envelopes (A5 size)	180	720
INTERNET AND CALLS			
Airtime		5,000	5,000
Internet bundles		15,000	15,000
PERSONNEL			
Research Assistant			40,000
Biostatistician			35,000
IREC			
IREC fee		2,000	2,000
NACOSTI Permit		1,000	1,000
DRUGS AND EQUIPMENT			
Ondansetron	100 Ampoules (4mg in 2ml)	200	20,000
Normal saline	5 bottles	75	375
Needle and syringe	200 (2ml syringes)	20	4,000
PUBLICATION			
Publication Fee			20,000
TOTAL COSTS			**161,895**

ALL BUDGET WILL BE SELF FUNDED

APPENDIX 7: TIME PLAN

Study period	**Year 2021 – 2024**
Concept Development	**December 2021- February 2022**
Proposal writing	**March 2022- May 2022**
IREC approval and NACOSTI approval	**June 2022- August 2022**
Data Collection	**September 2022 - August 2023**
Data analysis	**September 2023 - March 2024**
Thesis writing, submission and defense	**April 2024 – October 2024**

APPENDIX 8: QUESTIONNAIRE

Serial number: ……. **Date: …….**

A. <u>PATIENTS RECORDS</u>

1. **Patient's Initials: …….**
2. **Age ……. (Years)**
3. **Weight …… (Kilograms)**
4. **Height ……. (cm)**
5. **BMI (kg/m^2): ……..**
6. **Indication for Surgery (Tick where applicable)**

   Maternal Cause ☐

   Fetal Cause ☐

B. <u>MEDICAL / OBSTETRIC HISTORY</u>

7. **Gestation by dates ……. (weeks)**
8. **Parity: ……**
9. **Comorbidities (list if any)**

……

……

……

…….....

10. **Current medications and dosage (list if any)**

……

……

……

……

C. <u>ANAESTHESIA RECORDS</u>

11. Time Ondansetron or placebo was given ……..

12. Time Spinal anaesthesia was given ……..

13. Time Surgery began ……..

14. Vital Signs

Time (minutes)	Systolic BP (mmHg)	Diastolic BP (mmHg)	Mean Arterial Pressure (MAP)	Heart Rate (beats/min)	SPO2 (%)
Baseline					
5					
10					
15					
20					
25					
30					
45					
60					
75					
90					

15. Adverse effects of Spinal Anaesthesia (tick if present)

Hypotension	
Bradycardia	
Nausea	
Vomiting	
Shivering	
Headache	
Cardiac Arrest	
Others (specify)	

16. Vasopressors used

Agent	**Number of boluses given**	**Total dose given**
Ephedrine		
Others (specify)		

17. Total amount of Fluids given

Type of Fluid	**Total Amount given intraoperative (ml)**
Crystalloids	
Blood	
Colloids (other than blood)	
Total	

18. Any other medication administered and dosage:

……

19. Time surgery ended: …….

20. Duration of surgery (in minutes): ……...

21. Estimated blood loss (in mL): ……...

22. Neonatal Outcome

APGAR score: 1minute**: ……** 5minutes: **……** 10 minutes: **……...**

Birthweight (Kg): …….

APPENDIX 9: CONSENT FORM

MOI TEACHING & REFERRAL HOSPITAL / MOI UNIVERSITY COLLEGE OF HEALTH SCIENCES -INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (MTRH/MU-IREC)

INFORMED CONSENT FORM

Study Title: EFFECT OF PROPHYLACTIC ONDANSETRON ON SPINAL ANAESTHESIA - INDUCED HYPOTENSION DURING CAESAREAN SECTION AT MOI TEACHING AND REFERRAL HOSPITAL.

Name of Principal Investigator(s): DR. PAULINE AWILI OMONDI

Name of Sponsor/Funding Agency: SELF SPONSORED

Informed Consent Form for: All pregnant women (18 years and above) scheduled for elective Cesarean Section under Spinal anaesthesia and meet the criteria for this study.

This Informed Consent Form has two parts:

• Part I: Information Sheet [to share information about the study with you]

• Part II: Certificate of Consent [for signatures if you choose to participate]

PART I: INFORMATION SHEET

Introduction: You are being asked to take part in a research study. This information is provided to tell you about the study. Please read this form carefully. You will be given a chance to ask questions.

Taking part in this research study is voluntary. Saying no will not affect your rights to health care or any other services. Your treatment/payment or enrollment in any health plans or eligibility for benefits will not be affected if you decide not to take part. You are also

free to withdraw from this study at any time. If after data collection you choose to quit, you can request that information provided by you be destroyed under supervision. This would be before data is de-identified and aggregated. You will be notified if new information becomes available about the risks or benefits of this research. You will receive a copy of this form after it is signed.

Purpose of the study: The purpose of this study is to investigate the effect of prophylactic ondansetron in reducing the incidence of spinal anaesthesia-induced hypotension during Caesarean Sections.

Ondansetron is a medication commonly used to prevent nausea and vomiting during cancer chemotherapy, radiation therapy, or after surgery. The drug has been shown to reduce the incidence of spinal anaesthesia- induced hypotension when administered before the spinal anaesthesia. The drug can be given orally or by injection into a vein or a muscle. The route of administration for this study will be via injection into a vein.

Study site: This study will take place at Riley Mother and Baby Hospital in Moi Teaching and Referral Hospital.

Study population: You have been chosen to participate in this study because you perfectly meet the required criteria and are therefore a part of the group that will make it a success and add to the body of knowledge.

Study procedure: After having consented to participate in this study by filling this form, you will be allocated into either the intervention group or the control group and a drug with a low risk profile will be administered to you 15 minutes prior to the spinal anaesthesia and the response will be recorded in a questionnaire.

The expected follow up time for the participant will be a maximum of 2 hours i.e. from the time you enter the operating room to the time after leaving the post anaesthesia care unit.

Benefits: There will be no direct benefits of participating in this study. Study subjects will

be given same quality of management as the non-study subjects.

Risks/Discomforts: There are minimal or no anticipated risks to the participants attributable to this study since the medications to be used are not new, are safe and are available for daily use on patients post-operatively.

Payments and Reimbursements: Participants will not receive any payment or reimbursement for taking part in the study as the entire process of data collection will happen during their stay in hospital.

Confidentiality: All reasonable efforts will be made to keep your protected information (private and confidential). Disclosure of such information will follow National privacy guidelines. By signing the consent document for this study, you are giving permission for the use and disclosure of your study information. We may need to share your protected information with the community advisory board, MTRH//MU-IREC, NACOSTI or the healthcare team. We will retain your research records for at least six years after the study is completed. At that time, the research information is destroyed. If you decide to withdraw your permission for use of your personal data, contact the principal investigator in writing and let them know your decision. At that time, we will stop further collection of any information about you. However, the health information collected before this withdrawal may continue to be used for the purposes of reporting and research quality.

You have the right to see and copy your personal information related to the research study for as long as the study team holds this information.

PART II: CONSENT OF PARTICIPANT:

I have read or have had someone read to me the description of the research study. The investigator or his/her representative has explained the study to me and has answered all the questions I have at this time. I have been told of the potential risks, discomfort, and possible benefits (if any) of the study. I freely volunteer to take part in this study.

_____	_____	_____
Name of Participant	Signature of participant/Thumbprint	Date and Time
_____	_____	_____
Name of Witness [Optional]	Signature of Witness	Date and Time
_____	_____	_____
Name of the person obtaining consent	Signature of person Obtaining consent	Date and Time
Dr. Pauline Awili Omondi	_____	_____
Printed name of the investigator	Signature of Investigator	Date

Contacts for questions about the study

Questions about the study: You may contact Pauline Awili Omondi, 0721938909 or email pawili@yahoo.com

Questions about your rights as a participant: You may contact the Institutional Ethics and Research Committee (MTRH//MU-IREC) 0787723677 or email irec@mtrh.go.ke or irecoffice@gmail.com. The MTRH//MU-IREC is a group of people that review studies for safety and to protect the rights of participants.

APPENDIX 10: FOMU YA IDHINI
HOSPITALI YA UALIMU NA RUFAA MOI / CHUO CHA SAYANSI YA AFYA CHUO KIKUU MOI -UTAFITI WA TAASISI NA KAMATI YA MAADILI (MTRH/MU-IREC)

FOMU YA RIDHAA INAYOFAHAMISHWA

Kichwa cha Somo: **ATHARI ZA PROPHYLACTIC ONDANSETRON JUU YA ANAESTHESIA YA MGONGO - HIPOTESI ILIYOCHOCHEWA WAKATI WA KISARIA KATIKA HOSPITALI YA MAFUNDISHO NA RUFAA MOI.**

Jina la Mpelelezi Mkuu: DR. PAULINE AWILI OMONDI

Jina la Mfadhili/Wakala wa Ufadhili: SELF SPONSORED

Fomu ya Idhini Iliyoarifiwa kwa: Wanawake wote wajawazito (miaka 18 na zaidi) walioratibiwa kwa Sehemu ya Upasuaji iliyochaguliwa chini ya ganzi ya Mgongo na wanakidhi vigezo vya utafiti huu.

Fomu hii ya Idhini yenye Taarifa ina sehemu mbili:

• Sehemu ya I: Karatasi ya Taarifa [kushiriki nawe taarifa kuhusu utafiti]

• Sehemu ya II: Cheti cha Idhini [kwa saini ukichagua kushiriki]

SEHEMU YA I: KARATASI YA HABARI

Utangulizi: Unaombwa kushiriki katika utafiti wa utafiti. Taarifa hii imetolewa ili kukuambia kuhusu utafiti. Tafadhali soma fomu hii kwa makini. Utapewa nafasi ya kuuliza maswali.

Kushiriki katika utafiti huu ni kwa hiari. Kusema hapana hakutaathiri haki zako za utunzaji wa afya au huduma zingine zozote. Matibabu/malipo au uandikishaji wako katika mipango yoyote ya afya au ustahiki wa manufaa hautaathiriwa ukiamua

kutoshiriki. Pia uko huru kujiondoa kwenye utafiti huu wakati wowote. Ikiwa baada ya kukusanya data utachagua kuacha, unaweza kuomba kwamba maelezo uliyotoa yaharibiwe chini ya usimamizi. Hii itakuwa kabla ya data haijatambuliwa na kujumlishwa. Utaarifiwa iwapo taarifa mpya itapatikana kuhusu hatari au manufaa ya utafiti huu. Utapokea nakala ya fomu hii baada ya kusainiwa.

Madhumuni ya utafiti: Madhumuni ya utafiti huu ni kuchunguza athari za ondansetron ya kuzuia magonjwa katika kupunguza matukio ya hypotension ya anaesthesia-ikiwa ya uti wa mgongo wakati wa Sehemu za Kaisaria.

Ondansetron ni dawa ambayo hutumiwa kwa kawaida kuzuia kichefuchefu na kutapika wakati wa matibabu ya saratani, matibabu ya mionzi, au baada ya upasuaji. Dawa hiyo imeonyeshwa kupunguza matukio ya hypotension ya anaesthesia-ikiwa ya uti wa mgongo inapodungwa kabla ya anaesthesia ya mgongo. Dawa hiyo inaweza kupeanwa kwa mdomo au kwa sindano kwenye mshipa au kwa misuli. Njia ya usimamizi wa utafiti huu itakuwa kupitia sindano kwenye mshipa.

Tovuti ya masomo: Utafiti huu utafanyika katika Hospitali ya Mama na Mtoto ya Riley katika Hospitali ya Kufundisha na Rufaa ya Moi.

Idadi ya watu waliosoma:

Umechaguliwa kushiriki katika utafiti huu kwa sababu umekidhi kikamilifu vigezo vinavyohitajika na kwa hivyo ni sehemu ya kikundi ambacho kitaufanikisha na kuongeza maarifa mengi.

Utaratibu wa kusoma: Baada ya kukubaliwa kushiriki katika utafiti huu kwa kujaza fomu hii, utawekwa katika kikundi cha afua au kikundi cha kudhibiti na dawa iliyo na hatari ndogo itatolewa kwako dakika 30 kabla ya anaesthesia ya uti wa mgongo na majibu yatatolewa. kurekodiwa katika dodoso.

Muda unaotarajiwa wa kufuatilia kwa mshiriki utakuwa usiozidi saa 2 yaani kuanzia unapoingia kwenye chumba cha upasuaji hadi baada ya kuondoka kwenye kitengo cha utunzaji wa ganzi.

Faida:akutakuwa na manufaa ya moja kwa moja ya kushiriki katika utafiti huu. Washiriki wa masomo watapewa ubora sawa wa usimamizi kama wasioshiriki masomo.

Hatari/Masumbuko: Hakuna hatari zinazotarajiwa kwa washiriki kutokana na utafiti huu kwa kuwa dawa zitakazotumiwa si mpya, ni salama na zinapatikana kwa matumizi ya kila siku kwa wagonjwa baada ya upasuaji.

Madhara mabaya ya ondansetron ni nadra na ni pamoja na: kuvimbiwa, uchovu, maumivu ya kichwa na tachycardia.

Malipo na Marejesho: Washiriki hawatapokea malipo yoyote au fidia kwa kushiriki katika utafiti kwani mchakato mzima wa kukusanya data utafanyika wanapokuwa hospitalini.

Usiri: Juhudi zote zinazofaa zitafanywa ili kuweka maelezo yako yaliyolindwa (ya faragha na ya siri). Ufichuaji wa taarifa kama hizo utafuata miongozo ya faragha ya Kitaifa. Kwa kutia sahihi hati ya idhini ya utafiti huu, unatoa ruhusa ya matumizi na ufichuaji wa maelezo yako ya utafiti. Huenda tukahitaji kushiriki habari zako zinazolindwa na bodi ya ushauri ya jamii, MTRH//MU-IREC, NACOSTI au timu ya afya. Tutahifadhi rekodi zako za utafiti kwa angalau miaka sita baada ya utafiti kukamilika. Wakati huo, habari ya utafiti inaharibiwa. Ukiamua kuondoa ruhusa yako ya kutumia data yako ya kibinafsi, wasiliana na [PI] kwa maandishi na uwajulishe uamuzi wako. Wakati huo, tutasimamisha mkusanyiko zaidi wa taarifa yoyote

kukuhusu. Hata hivyo, maelezo ya afya yaliyokusanywa kabla ya uondoaji huu yanaweza kuendelea kutumika kwa madhumuni ya kuripoti na ubora wa utafiti.

Una haki ya kuona na kunakili maelezo yako ya kibinafsi yanayohusiana na utafiti kwa muda wote ambao timu ya utafiti inashikilia maelezo haya.

SEHEMU YA II: RIDHAA YA MSHIRIKI:

Nimesoma au kuna mtu alinisomea maelezo ya utafiti huu. Mpelelezi au mwakilishi wake amenieleza utafiti na amejibu maswali yote niliyo nayo kwa wakati huu. Nimeambiwa kuhusu hatari zinazoweza kutokea, usumbufu, na manufaa yanayoweza kutokea (ikiwa yapo) ya utafiti. Ninajitolea kwa hiari kushiriki katika utafiti huu.

_____	_____	_____
Jina la Mshiriki	Sahihi ya mshiriki/	Tarehe na Muda
_____	_____	_____
Jina la Shahidi [Sio lazima]	Sahihi ya Shahidi	Tarehe na Saa
_____	_____	
Jina la mtu anayepata idhini	Sahihi ya mtu	Tarehe na Saa

Kupata kibali

Dk. Pauline Awili Omondi	_____
Jina lililochapishwa la mpelelezi	Sahihi na Tarehe ya Mpelelezi

Anwani kwa maswali kuhusu utafiti

Maswali kuhusu utafiti: Unaweza kuwasiliana na Pauline Awili Omondi, 0721938909 au barua pepe pawili@yahoo.com

Maswali kuhusu haki zako kama mshiriki: Unaweza kuwasiliana na Kamati ya Maadili na Utafiti ya Kitaasisi (MTRH//MU-IREC) 0787723677 au barua pepe irec@mtrh.go.ke au irecoffice@gmail.com. MTRH//MU-IREC ni kundi la watu wanaopitia tafiti kwa ajili ya usalama na kulinda haki za washiriki.