

---

**"TO ASSESS THE ROLE OF TRANEXAMIC ACID IN  
REDUCING THE BLOOD LOSS IN WOMEN AT HIGH  
RISK FOR POSTPARTUM HEMORRHAGE  
UNDERGOING CESAREAN SECTION – A  
RANDOMIZED CONTROLLED TRIAL"**

---

**By**

**Registration No. BJ0120002**

**Dissertation**

**Submitted to**

**KAHER, Belagavi, Karnataka**

**In partial fulfilment**

**of the requirements for the degree of**

**MASTER OF SURGERY (M.S.)**

**In**

**OBSTETRICS AND GYNAECOLOGY**

**J.N. MEDICAL COLLEGE, NEHRU NAGAR,**

**BELAGAVI-590010**

---

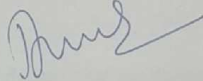
**JUNE/JULY-2023**

---

KLE ACADEMY OF HIGHER EDUCATION AND RESEARCH,  
BELAGAVI, KARNATAKA

**Endorsement by the HOD, Principal/Head of the  
Institution**

This is to certify that the dissertation entitled “TO ASSESS  
THE ROLE OF TRANEXAMIC ACID IN REDUCING THE  
BLOOD LOSS IN WOMEN AT HIGH RISK FOR POSTPARTUM  
HEMORRHAGE UNDERGOING CESAREAN SECTION – A  
RANDOMIZED CONTROLLED TRIAL” is a bonafide research work  
done by **Reg No: BJ0120002**.



**Dr. ANITA DALAL MD**  
Professor & Head  
Department of Obstetrics,  
& Gynaecology  
J.N. Medical College  
Nehru Nagar, Belagavi-590010

Date: 13/1/2023  
Place: Belagavi



**Dr. (Mrs.) N. S. MAHANTSHETTI MD**  
Principal  
J.N. Medical College  
Nehru Nagar, Belagavi-590010

Date: 13/1/2023  
Place: Belagavi

## UNDERTAKING

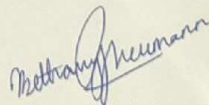
"I, Reg No. BJ0120002, hereby declare that the information and the data mentioned in my dissertation entitled "TO ASSESS THE ROLE OF TRANEXAMIC ACID IN REDUCING THE BLOOD LOSS IN WOMEN AT HIGH RISK FOR POSTPARTUM HEMORRHAGE UNDERGOING CESAREAN SECTION – A RANDOMIZED CONTROLLED TRIAL" belongs to me and is original. I am aware of the definition of plagiarism as detailed below:

- An act or instance of using or closely imitating the language and thoughts of another author without authorization and the representation of that author's work as one's own, as by not crediting the original author.
- A piece of writing or other work reflecting such unauthorized use or imitation.
- The deliberate or reckless representation of another's words, thoughts or ideas as one's own without attribution in connection with submission of academic work, whether graded or otherwise.

I hereby declare that the dissertation prepared by me is original and does not involve plagiarism anywhere. In case at a later stage, it is found that I have indulged in plagiarism, then I am solely responsible for the same and the institution is at liberty to take any disciplinary action against me including cancellation of dissertation or any other penalties imposed by the University."

Date: 13/1/2023

Place: Belagavi



REGN NO BJ0120002

# ANTI-PLAGIARISM CHECK – ACCEPTANCE LETTER



## JAWAHARLAL NEHRU MEDICAL COLLEGE

(Recognized by Medical Council of India, New Delhi)

Accredited 'A+' Grade by NAAC (3<sup>rd</sup> Cycle)

Placed in Category 'A' by MHRD (GoI)



Nehru Nagar, Belagavi- 590 010, Karnataka, INDIA

0831 - 2471350



0831 - 2470759



www.jnmc.edu



principal@jnmc.edu

Ref No: MDC/PG/

Date: 14-12-2022.

### ACCEPTANCE LETTER

The softcopy of thesis entitled: "TO ASSESS THE ROLE OF TRANEXAMIC ACID IN REDUCING THE BLOOD LOSS IN WOMEN AT HIGH RISK FOR POSTPARTUM HEMORRHAGE UNDERGOING CESAREAN SECTION - A RANDOMIZED CONTROLLED TRIAL" has been submitted for Anti-Plagiarism check through Turnitin software. The scan has been carried out and the scanned output reveals a match percentage of 05% which is within the acceptable limits of 10% as per the guidelines given by UGC.

Guide.



Dr. (Mrs.) N.S. Mahantashetti.  
Chairperson-Antiplagiarism Committee &  
Principal,  
J. N. Medical College, Belagavi.

To,  
Reg. No. BJ0120002,  
Postgraduate Student,  
2020-21 Batch,  
Department of Obst. & Gynaecology,  
J. N. Medical College, Belagavi.

# ETHICAL CLEARANCE CERTIFICATE



K.L.E. ACADEMY OF HIGHER EDUCATION AND RESEARCH  
(Deemed - to-be- University)

Accredited 'A' Grade by NAAC (2<sup>nd</sup> Cycle)

Placed in Category 'A' by MHRD (GoI)

**JAWAHARLAL NEHRU MEDICAL COLLEGE,**  
**NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)**

Website: <http://www.jnmc.edu>  
E-Mail : [dome@jnmc.edu](mailto:dome@jnmc.edu)

Phone: (+ 91-(0)831 Office : 2472550  
Principal: 2471701

Fax No. +91 (0)831 – 2470759

**Ref: MDC/DOME/ 147**

**Date: 25/01/2021**

To.

Registration No. BJ0120002

PG student in Obstetrics and Gynecology,  
J.N.Medical College,  
BELAGAVI.

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled  
**"TO ASSESS THE ROLE OF TRANEXAMIC ACID IN REDUCING THE BLOOD LOSS  
IN WOMEN AT HIGH RISK FOR POSTPARTUM HEMORRHAGE UNDERGOING  
CESAREAN SECTION – A RANDOMIZED CONTROLLED TRIAL"**, is ethical and  
justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics  
Committee on Human Subjects Research.

**(Dr. Smita Sonoli)**  
Member Secretary  
JNMC Institutional Ethics Committee  
on Human Subjects Research,  
J.N.Medical College, Belagavi.

**(Dr. Harsha Hegde)**  
Chairman,  
JNMC Institutional Ethics Committee  
on Human Subjects Research,  
J.N.Medical College, Belagavi.

## ABSTRACT

**Background:** Postpartum hemorrhage (PPH) is a leading cause of maternal morbidity and mortality. Efforts to reduce blood loss during and after delivery are imperative. Tranexamic acid is an anti-fibrinolytic agent that reduces blood loss. This study is conducted to shed light on its role in women with high-risk factors for PPH undergoing cesarean sections.

**Objective:** To assess the role of tranexamic acid in reducing blood loss during elective and emergency cesarean deliveries in women at high risk for postpartum hemorrhage.

**Materials & Methods:** This prospective, placebo-controlled, randomized controlled trial was conducted from March 2021 to February 2022 at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi. A total of 212 women who met the inclusion criteria were randomized into two groups. Group A received 1g of tranexamic acid slow iv at least 10 minutes before skin incision. Group B received the placebo. Estimated blood loss was calculated by a formula using pre and post op hematocrit levels. Gravimetrically measured blood loss was also recorded. Data was analyzed using SPSS software version 21 and  $p < 0.05$  was considered significant.

**Results:** Estimated mean blood loss was 400.87 ml in Group A compared to 597.93 ml in Group B. Mean gravimetrically measured blood loss was 379.2 ml in Group A versus 431.1 ml in Group B. There was also a significant difference in the fall in Hb (1.04 g/dL versus 1.61 g/dL) and change in PCV (3.2% versus 4.95%) from the pre to post operative period between the two groups.

**Conclusion:** There is a significant decrease in the blood loss in the group that received tranexamic acid as compared to the placebo among women at high risk for postpartum hemorrhage undergoing cesarean sections.

**Key words** – Postpartum hemorrhage, Tranexamic acid, Cesarean section, Randomized controlled trial.

## **ABBREVIATIONS**

ACOG	-	American College of Obstetricians and Gynecologists
BMI	-	Body mass Index
CDC	-	Center for Disease Control
CDMR	-	Cesarean Done at Maternal Request
CTRI	-	Clinical Trials Registry – India
DBP	-	Diastolic Blood Pressure
DVT	-	Deep Venous Thrombosis
EDD	-	Expected Date of Delivery
FDA	-	Federal Drug Association
FFP	-	Fresh Frozen Plasma
GABA	-	Gamma-amino butyric acid
GIT	-	Gastrointestinal Tract
Hb	-	Hemoglobin
ICU	-	Intensive Care Unit
IM	-	Intramuscular
IMP	-	Investigational Medicinal Product
IV	-	Intravenous
JNMC	-	Jawaharlal Nehru Medical College
KAHER	-	KLE Academy of Higher Education and Research centre
KLES	-	Karnataka Lingayat Educational Society
LMP	-	Last Menstrual Period
LSCS	-	Lower Segment Cesarean Section
MC	-	Chi square test with Monte Carlo simulation
mL	-	Millilitre

MMR	-	Maternal Mortality Ratio
MTP	-	Medical Termination of Pregnancy
MW	-	Mann Whitney U test
NICU	-	Neonatal Intensive Care Unit
PCV	-	Packed Cell Volume
PPH	-	Postpartum Hemorrhage
PRBC	-	Packed Red Blood Cells
PT	-	Paired t Test
RCT	-	Randomized Controlled Trial
RDP	-	Random Donor Platelets
SD	-	Standard Deviation
SBP	-	Systolic Blood Pressure
SDP	-	Single donor platelets
t test	-	Two sample t test
TXA	-	Tranexamic Acid
UNICEF	-	United Nations International Children's Education Fund
USG	-	Ultrasound
VBAC	-	Vaginal birth after cesarean section
WHO	-	World Health Organization

## TABLE OF CONTENTS

<b>S. No.</b>	<b>Particulars</b>	<b>Page No.</b>
<b>1.</b>	<b>Introduction</b>	<b>1-2</b>
<b>2.</b>	<b>Objectives</b>	<b>3</b>
<b>3.</b>	<b>Review of literature</b>	<b>4-16</b>
<b>4.</b>	<b>Materials and Methods</b>	<b>17-24</b>
<b>5.</b>	<b>Results</b>	<b>25-38</b>
<b>6.</b>	<b>Discussion</b>	<b>39-44</b>
<b>7.</b>	<b>Conclusion</b>	<b>45</b>
<b>8.</b>	<b>Summary</b>	<b>46-48</b>
<b>9.</b>	<b>References</b>	<b>49-56</b>
<b>10.</b>	<b>Annexures</b>	
	<b>I: Consent form</b>	<b>57-61</b>
	<b>II: Screening Form &amp; Proforma</b>	<b>62-70</b>
	<b>III: Master Chart</b>	<b>71-73</b>

## LIST OF FIGURES

<b>Figure No.</b>	<b>Title</b>	<b>Page no.</b>
1	Consort Diagram	26
2	Distribution of participants by gestational age	29
3	Distribution of participants according to obstetric score	29
4	Mode of delivery	30
5	Distribution of participants over risk factors for PPH	31
6	Mean plot of hemoglobin at different time points	34
7	Mean plot of hematocrit at different time points	35

## LIST OF TABLES

<b>Graph No.</b>	<b>Title</b>	<b>Page no.</b>
1	Demographic characteristics of study participants	27
2	Comparison of clinical details	28
3	Distribution of risk factors for postpartum haemorrhage	32
4	Estimated blood volume	33
5	Comparison of change in hemoglobin and hematocrit	33
6	Comparison of blood loss	36
7	Medical Interventions	37
8	Surgical Interventions	38

## **INTRODUCTION**

Hemorrhage is the leading cause for maternal mortality and morbidity, accounting for 27.1 % of all maternal deaths worldwide. 72.6% of these deaths are due to postpartum hemorrhage.<sup>1,2</sup> It leads to challenges like severe anaemia, need for blood transfusion and increased risk of infection, as well as extending hospital stay and costs.<sup>3</sup> While maternal mortality rates due to postpartum hemorrhage have decreased in the last four decades, it still accounts for many pregnancy-related deaths.<sup>4</sup> It is therefore necessary to concentrate efforts towards reducing the amount of blood loss during and after delivery.

Postpartum hemorrhage (PPH) is one of the life-threatening emergencies in the postpartum period. It is quantitatively defined as blood loss in excess of 500 ml following the birth of the baby (WHO). Clinically, it can be defined as any amount of bleeding from or into the genital tract following birth of the baby up to the puerperium which adversely affects the general condition of the patient, evidenced by rise in pulse rate and falling blood pressure.<sup>5</sup>

Studies have compared Active Management of Third Stage of Labour with expectant management and found a substantial reduction in the occurrence of postpartum hemorrhage by approximately 60-70%. This includes uterotonic administration, early cord clamping and cutting, and controlled cord traction.<sup>6</sup> Uterotonics are agents used to contract the uterus. These are the first-line treatment for postpartum hemorrhage caused by uterine atony. The choice of which specific agent is to be used is the clinician's decision. Other medical and surgical approaches include intrauterine balloon tamponades and tranexamic acid. Tranexamic acid is useful in controlling bleeding after delivery. According to the latest recommendations by WHO

and ACOG, “Tranexamic acid can be administered when initial therapies fail and has been shown to reduce mortality when given within three hours of birth.<sup>4</sup>”

Tranexamic acid is a synthetic drug which is an analogue of lysine. It is an anti-fibrinolytic agent. It competitively blocks the lysine binding sites on plasminogen molecules. Tranexamic acid is FDA category B, which is safe in pregnancy. However, risk of potential thromboembolic events and other adverse effects must be kept in mind.<sup>7</sup>

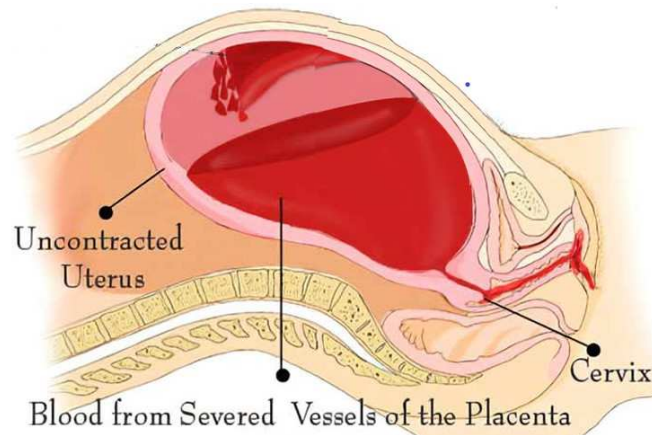
Several studies have been conducted regarding the use of tranexamic acid to prevent postpartum hemorrhage and to reduce bleeding among women undergoing elective cesarean sections with standard risk for postpartum hemorrhage.<sup>8,9</sup> However very little research has been conducted among women with high-risk pregnancies, with greater risk of postpartum hemorrhage. This study aims to shed light on this particular area.

## **OBJECTIVE**

- To assess the role of tranexamic acid in reducing blood loss during elective and emergency cesarean deliveries in women at high risk for postpartum hemorrhage.

## REVIEW OF LITERATURE

### POSTPARTUM HEMORRHAGE



Postpartum hemorrhage (PPH) has proved to be the most dangerous complication of childbirth. Even after years of innovation and expertise, it continues to be the most common cause of maternal mortality worldwide.<sup>10</sup> The incidence of PPH in India is approximately 2% to 4% following vaginal deliveries and 6% following cesarean sections.<sup>11</sup> Uterine atonicity, is the most common cause, accounting for around 70% to 80% of all hemorrhage.<sup>12</sup> Most deaths due to postpartum hemorrhage (79.1%) occur on the first postpartum day.<sup>13</sup>

Postpartum hemorrhage was traditionally defined as greater than 500 mL blood loss in the case of vaginal deliveries or greater than 1000 mL blood loss in cesarean deliveries.<sup>14</sup> In 2017, the American College of Obstetrics and Gynecology redefined postpartum hemorrhage as “cumulative blood loss greater than 1000 mL with signs and symptoms of hypovolemia within 24 hours of the birth process, regardless of the route of delivery.” This definition was changed because blood loss at the time of delivery is generally underestimated. Despite this, more than 500 mL of blood loss at delivery is abnormal, and may require intervention.<sup>4</sup>

Bleeding that occurs in the first 24 hours after delivery is known as primary postpartum hemorrhage, while bleeding that occurs 24 hours to 12 weeks after delivery is known as secondary postpartum hemorrhage. The causes of primary postpartum hemorrhage are - uterine atonicity, lacerations of the genital tract, retained products of conception, uterine inversion, abnormal placentation and disorders of coagulation. Secondary causes of postpartum hemorrhage are - retained placenta, infection, subinvolution of the uterus and inherited coagulation disorders.<sup>14</sup>

Uterine atonicity is the lack of effective uterine contraction after delivery. It is the most common cause of postpartum hemorrhage, and therefore maximum efforts should be made to combat atonicity post-delivery.<sup>15</sup>

Many factors increase the risk for postpartum hemorrhage. These include a history of severe PPH, anticoagulant medication, anemia, severe pre-eclampsia or HELLP syndrome, uterine fibromas, multiple pregnancy, assisted reproductive technologies, induction of labour, use of oxytocin for augmentation of labour, and other factors.<sup>17</sup>

### **MATERNAL MORBIDITY AND MORTALITY IN INDIA**

India has been successful in implementing good standards of maternal health care, thus reducing the rates of maternal morbidity and mortality substantially over the past few decades. Fewer maternal deaths in India have contributed to about 40% of the decline in Maternal Mortality Ratio worldwide from 342 in the year 2000 to 211 in 2017.<sup>17</sup> The MMR in India declined by about 70% from 398 per 100 000 live births in 1997–98 to 99 in 2020. About 1.30 million maternal deaths occurred between 1997 and 2020, with most occurring in poorer states (63%) and among women aged 20–29 years (58%). The MMRs for Assam (215), Uttar Pradesh/Uttarakhand (192) and Madhya

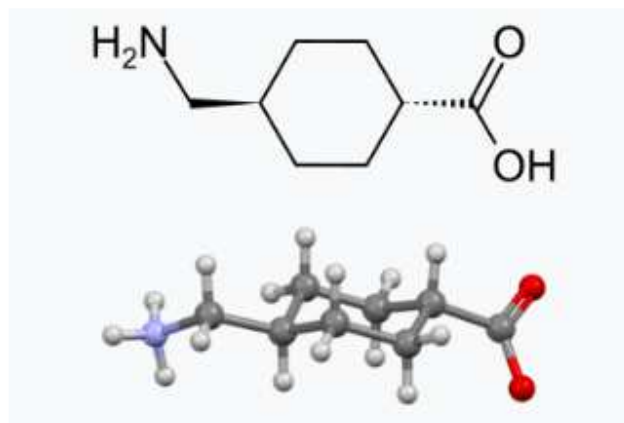
Pradesh/Chhattisgarh (170) were highest. The MMR in Karnataka is 83 (2020), which is the highest among the South Indian states.<sup>18</sup>

Data from cross sectional surveys conducted in India from 1997 to 2020 was published by C. Meh et al in an article in the British Journal of Obstetrics and Gynaecology in March 2022, titled “Trends in maternal mortality in India over two decades in nationally representative surveys”. This research looked into trends, giving cause-specific delineation of India’s death rates in different regions. Obstetric hemorrhage was found to be the universal leading cause of maternal morbidity and mortality across all states of India, with 47% deaths attributable to hemorrhage. In 2020 alone, around 11200 maternal deaths were caused by maternal hemorrhage. Deaths due to hemorrhage in Bihar, Uttar Pradesh and Uttarakhand are more in recent years when compared to the 2001–2003 data. This implies that underlying conditions like severe anemia, which are more common in these areas, contribute to postpartum hemorrhage. Delayed management also exacerbates morbidity. The other major factors resulting in maternal mortality are pregnancy-related infection (12%) and hypertensive disorders of pregnancy (7%).<sup>18</sup>

The United Nations Sustainable Development Goals (SDGs), state a target maternal mortality ratio (MMR) of less than 70 deaths per 100 000 live births by 2030.<sup>19</sup> The Government of India is a signatory to this target. This goal is achievable if India continues to maintain the average rates of reduction in maternal mortality.<sup>18</sup> However, to achieve this, intervention must be targeted at every major risk factor for maternal death, including postpartum hemorrhage. Hence it is imperative to develop strategies and techniques to this effect.

A major portion of research is targeted at combating these major causes of maternal deaths. In the past, most drugs used for the treatment of postpartum hemorrhage were uterotonics. They promote contraction of the uterus, since atonicity is thought to be the main causal factor for bleeding. But coagulopathy is also a part of the pathophysiology of hemorrhage. Recent guidelines suggest using tranexamic acid along with uterotonics, to manage postpartum hemorrhage.<sup>15</sup> Therefore, tranexamic acid is now being used to treat PPH.

### **TRANEXAMIC ACID**



Tranexamic acid (TXA) is an antifibrinolytic agent with the empirical formula: C<sub>8</sub>H<sub>15</sub>NO<sub>2</sub>. Its chemical name is trans-4-(aminomethyl) cyclohexane carboxylic acid. It is also known as Cyklokapron and Lysteda.<sup>7</sup>

Tranexamic acid is used to treat or prevent excessive blood loss due to various causes like trauma, surgery, postpartum bleeding, tooth extraction, epistaxis, and heavy menstruation.<sup>7</sup> The FDA-approved uses of tranexamic acid are for menorrhagia and for short-term prevention of bleeding, including heavy menstrual bleeding, in hemophilia patients. Off-label uses of the drug are to reduce loss of blood in surgeries, as a part of massive transfusion protocols (MTP) and in hyper-fibrinolysis. It is also useful to

reduce bleeding in trauma patients requiring at least one unit of blood within 24 hours of presentation.<sup>20</sup>

### **Pharmacology**

**Route of administration:** Tranexamic acid injection is available for oral, topical, and intravenous use.<sup>7</sup>

**Dosage:** Tranexamic acid for intravenous injection, is a clear and colourless solution. It is available in doses of 1 gram as 10 mL single-dose vials or as 500 milligrams in a 5 mL ampoule. Each mL of the sterile solution for intravenous injection contains 100 milligrams of the drug.<sup>7</sup> The recommended dose of tranexamic acid for adults is one gram bolus given over 10 minutes by slow intravenous injection. Rapid infusion may cause hypotension. A second dose of 1 gram of the drug may be repeated after 8 hours. Dosage should not exceed more than 2 grams per day.<sup>20</sup>

**Storage Conditions:** 20° to 25°C (68° to 77°F)<sup>7</sup>

**Monitoring:** Monitor hemodynamics and watch for thromboembolic events when using tranexamic acid.<sup>7</sup>

### **Pharmacokinetics**

- **Absorption:** The bioavailability of tranexamic acid after oral administration in humans is approximately 30 to 50% of the ingested dose and is not affected by food intake.<sup>24</sup>
- **Distribution:** The initial volume of distribution is 9 to 12 litres. Tranexamic acid binds to plasminogen, but not to serum albumin. The plasma protein binding is about 3% at therapeutic plasma levels.<sup>7</sup>

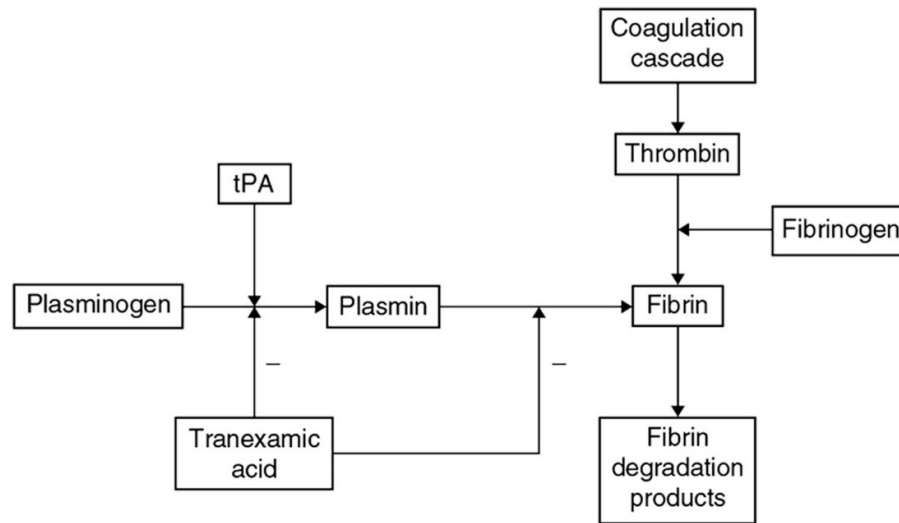
- Metabolism: According to prescribing information, approximately 1% and 0.5% of an orally administered dose are excreted as a dicarboxylic acid and acetylated metabolite, respectively.<sup>22</sup>
- Excretion: Mainly excreted via glomerular filtration through the kidneys. Only 5% of the dose is metabolised and more than 95% is excreted unchanged in the urine. Excretion of tranexamic acid is about 90% at 24 hours after intravenous injection.<sup>7</sup>
- Half-life: The half-life of tranexamic acid is 2 to 11 hours. The peak action is 3 hours after the initial dose. An antifibrinolytic concentration of tranexamic acid remains for about 17 hours in the tissues, and for up to 7 or 8 hours in the serum.<sup>7</sup>

### **Pharmacodynamics**

Tranexamic acid is an antifibrinolytic agent that competitively inhibits the activation of plasminogen to plasmin.<sup>22</sup> At much higher concentrations it behaves as a non-competitive inhibitor of plasmin. Off-target antagonism of GABA(A) receptors may be associated with the development of convulsions and hyperexcitability following tranexamic acid administration.<sup>24</sup> The risk appears higher with improper administration or administration during cardiovascular surgery.<sup>21</sup>

Tranexamic acid is found to prolong the thrombin time, but has no influence on the platelet count, coagulation time or various coagulation factors.<sup>7</sup>

**Mechanism of Action**



Tranexamic acid is a synthetic lysine amino acid derivative. It is a reversible competitive inhibitor to the lysine receptor found on plasminogen. It decreases the dissolution of hemostatic fibrin by plasmin. Tranexamic acid occupies the lysine receptor binding sites for fibrin on plasmin. The binding of this receptor prevents plasmin (activated form of plasminogen) from binding to fibrin monomers, thus preserving and ultimately stabilizing the fibrin's matrix structure. This aids in the prevention of bleeding by preventing the breakdown of fibrin.

The antifibrinolytic effects of tranexamic acid are mediated by reversible interactions at multiple binding sites within plasminogen. Native human plasminogen contains 4 to 5 lysine binding sites with a low affinity for tranexamic acid ( $K_d = 750 \mu\text{mol/L}$ ) and one binding site with high affinity ( $K_d = 1.1 \mu\text{mol/L}$ ). The high affinity lysine site of plasminogen is involved in its binding to fibrin. Saturation of the high affinity binding site with tranexamic acid displaces plasminogen from the surface of fibrin. Although plasmin may be formed by conformational changes in plasminogen, binding to and dissolution of the fibrin matrix is inhibited.<sup>7</sup>

## **Indications**

### Intravenous Uses

- Hemorrhagic shock, including postpartum hemorrhage and in trauma patients.
- Elective cesarean sections - Intravenous tranexamic acid 1 g over 5 minutes at least 10 minutes before skin incision.

### Oral uses

- Menorrhagia
- Post minor surgical procedures

### Topical uses

- Epistaxis
- Nebulization of tranexamic acid in hemoptysis<sup>7,20</sup>

## **Tranexamic acid in pregnancy and lactation**

Tranexamic acid is classified as a pregnancy category B drug. This means that some risk has been noted in studies in animals, however not many studies have been done in human population to determine the effects of the drug. It has been administered to “a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed.<sup>27</sup>” Studies, case reports and series regarding second and third trimester use of tranexamic acid and administration at the time of delivery have not confirmed if there is a risk of miscarriage or adverse maternal or fetal outcomes. Some studies enumerate outcomes like low Apgar score, neonatal sepsis and

cephalohematoma. Others discuss results like low birth weight and prematurity in fetuses exposed to tranexamic acid antenatally. Therefore, it should be used in pregnancy only when benefit is deemed to outweigh the risks as per the clinician's decision.

Tranexamic acid crosses the placenta. After an intravenous injection of 10mg/kg of tranexamic acid, cord blood concentration has been found to be around 30 mg/L, which is similar to maternal serum concentrations of the drug.<sup>7</sup>

**Lactation:** Tranexamic acid is excreted in breastmilk. There is little known of the effects on lactation or the side effects on the breastfeeding child. Studies have shown that the baby is likely to be exposed to very minimal concentrations of the drug, so there is no reason to stop use of tranexamic acid while breastfeeding if it is beneficial for the mother. In a study done on the long-term effects of tranexamic acid used during breastfeeding, no increase in adverse outcomes was found, supporting the continuation of breastfeeding in women requiring treatment with tranexamic acid.<sup>25</sup>

### **Adverse Effects**

Adverse reactions include headaches, backache, abdominal pain, nausea, vomiting, diarrhea, and fatigue. Serious adverse effects like pulmonary embolism, deep vein thrombosis, cardiac arrhythmias, anaphylaxis, impaired color vision, and other visual disturbances can also occur following administration of tranexamic acid.<sup>7</sup>

### **Contraindications**

1. Subarachnoid hemorrhage - Cerebral edema or infarction may be caused in these patients.
2. Active intravascular clotting
3. Known hypersensitivity to tranexamic acid or any ingredients or excipients.
4. Thromboembolism – current or past. Avoid use along with other pro-thrombotic drugs like hormone contraceptives, Factor IX Complex concentrate etc.
5. Defective colour vision<sup>7,20</sup>

### **Cautions**

- Tranexamic acid should not be given more than 3 hours after trauma or injury.<sup>23</sup>
- Tranexamic acid is 95% excreted in the urine, hence it should be used judiciously in the renally impaired.
- No adjustments are required in the hepatic impaired patient.<sup>7</sup>

### **Patient Counseling Information**

Patients should be informed that this injection may amplify risk of thrombotic and embolic phenomena. It may also cause seizures, dizziness, disturbance in vision or allergic reactions.

## **OTHER STUDIES**

1. In 2010, the CRASH-2 trial was conducted. Adult patients who had trauma and severe bleeding were given tranexamic acid or placebo in this RCT. Tranexamic acid improved survival if given within 3 hours of injury. All-cause mortality was significantly reduced with 14.5% in the tranexamic acid group versus 16.0% in the placebo group. The risk of death due to bleeding was significantly reduced from 5.7% to 4.9% among those who received tranexamic acid. It concluded that tranexamic acid safely reduced the risk of death and should be considered for use in bleeding trauma patients.<sup>26</sup>
2. The MATTERS study was done in 2011. This retrospective observational study compared giving TXA with no TXA in cases where a minimum of one PRBC transfusion was needed in a setting of combat trauma. It assessed complications like thromboembolism, need for blood and blood product transfusions and death rates. Among 896 patients, it concluded that tranexamic acid decreased deaths, especially when massive transfusion was required. This is the only trial that shows higher rates of thrombosis with TXA.<sup>27</sup>
3. In the TRAAP2 study published in the New England journal of medicine in April 2021, Loïc Sentilhes et al analyzed the use of tranexamic acid for preventing blood loss after cesarean deliveries. It was a multicenter, double-blind, randomized, controlled trial among 4153 women. Women at a gestational age of 34 weeks or more were randomized to receive either 1g TXA or placebo within 3 minutes of the delivery of the baby. Primary outcome studied was incidence of postpartum hemorrhage, defined as a calculated estimated blood loss by formula of greater than 1000 ml or packed cell transfusion within 2 days of delivery. Estimated blood loss

was calculated as the estimated blood volume  $\times$  (preoperative hematocrit–postoperative hematocrit)  $\div$  preoperative hematocrit; where the estimated blood volume was calculated as body weight in kilograms  $\times$  85. The primary outcome, as defined, occurred in 26.7% of the women in the tranexamic acid group, and in 31.6% of women in the placebo group. No significant difference was seen in the mean gravimetrically measured blood loss or need for additional uterotonic agents to control blood loss. No difference was seen in the need for postpartum blood transfusion. In the 3 months after delivery, thromboembolic events (deep vein thrombosis or pulmonary thromboembolism) were noted in 0.4% of the women who received tranexamic acid and in 0.1% of those who received the placebo.<sup>28</sup>

4. A randomized controlled trial conducted in women with increased risk for PPH undergoing cesarean delivery at Max hospital in New Delhi showed that the group given tranexamic acid required additional uterotonics to control blood loss in 23% of the cases, while those who received placebo required additional uterotonics in 83% of the cases.<sup>29</sup>
5. An RCT in Coimbatore showed that tranexamic acid reduced blood loss in women with no additional risk factors undergoing elective LSCS (347.17 ml in study group versus 517.72 ml in control group) 9.3% of those in the study group and 39% of subjects in the control group had more than 10% fall in Hemoglobin perioperatively.<sup>30</sup>
6. An RCT done in Egypt among 500 women at low risk for PPH showed a mean blood loss of  $387.68 \pm 93.05$  ml in the treatment group who received tranexamic acid

and mean blood loss of  $560.79 \pm 107.46$  ml in the placebo group during elective cesarean sections, which was statistically significant.<sup>8</sup>

7. A meta-analysis of nine RCTs which evaluated the efficacy of prophylactic tranexamic acid in reducing postpartum blood loss at cesarean delivery, showed that tranexamic acid is associated with a significant decrease in incidence of PPH and severe PPH, a significantly lower hemoglobin drop, and significantly lower need for additional uterotonic agents. The RCTs used either of two controls (either placebo or no treatment) and were conducted among low-risk pregnancies. It suggested to consider adding TXA 1g (or 10 mg/kg) iv 10-20 mins before skin incision or spinal anesthesia in addition to oxytocin prophylaxis given after delivery of the neonate, as prophylaxis to reduce loss of blood at cesarean delivery.<sup>9</sup>

## MATERIALS AND METHODS

### Source of data

Women undergoing elective or emergency cesarean sections according to inclusion criteria at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi.

### Method of collection of data

- **Study design:** A Prospective, Placebo-controlled, Single blinded, Randomized Controlled Trial.
- **Study setting:** KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi.
- **Study duration:** 12 months
- **Study period:** March 2021 to February 2022
- **Study population:** Women undergoing elective or emergency cesarean sections according to inclusion criteria at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi.

### Selection Criteria

- **Inclusion criteria:** Pregnant women at gestational age of 34 weeks or more, who are to undergo elective or emergency cesarean delivery, with at least one risk factor for postpartum hemorrhage, were considered for inclusion in the study. The inclusion criteria were defined as follows:-
  1. Obesity - BMI of more than 30 kg/m<sup>2</sup>.<sup>31</sup>

2. Chronic Hypertension - Known hypertension before pregnancy or hypertension diagnosed for the first time before 20 weeks of pregnancy with a SBP  $\geq$  140 mmHg or DBP  $\geq$  90 mmHg greater than 4 hours apart on at least 2 occasions or normal blood pressure in the presence of antihypertensive therapy.<sup>32</sup> (ACOG 2013)
3. Gestational hypertension - SBP greater than or equal to 140 mm Hg or DBP greater than or equal to 90 mm Hg more than 4 hours apart on at least 2 occasions, diagnosed for the first time in pregnancy after 20 weeks of gestation, without proteinuria.<sup>32</sup> (ACOG 2013)
4. Pre-eclampsia - Diagnosed by the presence of BP greater than or equal to 140 mm Hg systolic or 90 mm Hg diastolic, on two occasions, after 20 weeks of gestation, with the presence of proteinuria (defined as 300 mg or more of protein in 24 hours or a protein/creatinine ratio of at least 0.3 g/g Cr), thrombocytopenia, kidney insufficiency (defined as serum creatinine of 1.1 mg/dL or greater or a doubling of serum creatinine), impaired liver function, pulmonary edema, or cerebral or visual symptoms. Proteinuria is no longer a requirement for the diagnosis of preeclampsia, if other severe features are present.<sup>32</sup> (ACOG 2013)
5. Eclampsia - Pre-eclampsia complicated with grand mal seizures and/or coma.<sup>5</sup>
6. Anaemia - Hemoglobin less than 11.0 g/dL.<sup>33</sup>
7. Use of Oxytocin augmentation for more than 4 hours.
8. Multiparity - Parity greater than four.
9. Multiple pregnancy - More than one intrauterine fetus.
10. Abnormally implanted placenta - Morbidly adherent placenta, including placenta accreta, increta and percreta.<sup>5</sup>

11. Placenta previa - Placenta implanted partially or completely over the lower uterine segment (over and adjacent to the internal os).<sup>5</sup>
12. Abruptio - Premature separation of a normally situated placenta.<sup>5</sup>
13. Uterine Leiomyomas
14. Polyhydramnios - Diagnosis made by ultrasound with a single deepest measure fluid pocket that exceeds 8 cm or an amniotic fluid index that is 25 cm or more.<sup>34</sup>
15. Fetal macrosomia - Abdominal circumference greater than 90<sup>th</sup> centile on ultrasound.<sup>35</sup>
16. Previous LSCS – Patients who have undergone one or more caesarean sections.
17. History of postpartum hemorrhage in previous pregnancy
18. Chorioamnionitis - Maternal temperature >100.4°F, uterine fundal tenderness, maternal tachycardia (>100/min), fetal tachycardia (>160/min) and purulent or foul amniotic fluid.<sup>36</sup>
19. Cholestasis of pregnancy

**Exclusion criteria**

1. Impaired colour vision
2. Known cardiovascular, renal or liver disorders
3. Current or past history of Deep Vein Thrombosis (DVT)
4. Anticoagulant therapy
5. Coagulation defects
6. HELLP syndrome
7. Sensitivity to tranexamic acid
8. Patient diagnosed with COVID - 19

### Sample Size

According to the reference article,<sup>37</sup> the minimum sample size formula based on mean and standard deviation is

$$n = \frac{(z_{\alpha} + z_{\beta})^2 (s_1^2 + s_2^2)}{(\bar{X}_1 - \bar{X}_2)^2}$$

where  $z_{\alpha}$  is linked with the level of significance and  $z_{\beta}$  is linked with the power of the test. For 5% level of the significance,  $z_{\alpha} = 1.96$  and  $z_{\beta} = 1.28$  for 90% power of the test.

Reference:  $\bar{X}_1$  is the mean of the first group (272.05 ml) and  $\bar{X}_2$  is the mean of the second group (346.87).  $S_1$  is the standard deviation of the first group (143.23) and  $S_2$  is the standard deviation of the second group (189.49).<sup>37</sup>

With these values the sample size obtained is 106.

There will be two groups with minimum 106 cases in each group.

Hence, a total sample size of 212 subjects with 106 in each group are considered in this study.

### **Statistical Analysis**

Data is analyzed using SPSS software version 21 and Excel 2019. Categorical variables are given in the form of frequency tables. Continuous variables are given in Mean  $\pm$  SD/ Median (Min, Max) form. Chi-square test is used to check the dependency between categorical variables. Two sample t test/Welch's t test is used to compare mean of different variables over groups. Paired t test is used to compare the mean Hb and PCV over time points in both groups. Mann Whitney U test is used to compare the distributions of different variables over groups. P-values less than or equal to 0.05 indicate statistical significance.

### **Ethical Clearance**

Ethics committee approval was obtained from the JNMC Institutional Ethics Committee on Human Subjects Research on 25th Jan 2021. (Annexure 1)

The trial is registered under CTRI/2021/03/031690

### **METHODOLOGY**

- **Sampling procedure:** Patients admitted to KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi at 34 weeks of gestation and beyond, with one or more risk factors for postpartum hemorrhage who were to undergo either elective or emergency cesarean sections were included in the study.
- **Screening:** Participants were screened according to the inclusion criteria of the study. Those meeting inclusion criteria were considered for recruitment in the study, while those meeting any exclusion criteria were excluded.

- **Consent:** Written, informed consent was taken from all the participants.
- **Randomization:** Patients were classified into two groups by computer-generated randomization system. The list of randomization was concealed and expressed by sequentially numbered, sealed opaque envelopes just prior to intervention. Each number allocated the patient to either Treatment group (A) or Control group (B).
- **Intervention:** The IMP was an identical clear, colourless solution of 10ml of either the drug or the placebo loaded in a 10ml syringe and administered by intravenous injection at least 10 minutes prior to skin incision.



Group A (Treatment group) received 1g (10ml) of tranexamic acid slow iv over 10 minutes at least 10 min prior to skin incision. Group B (Placebo group) received 10 ml of Normal Saline (NaCl 0.9%) slow iv over 10 minutes at least 10 min prior to skin incision. After delivery of the baby, 10 units oxytocin im and 10 units oxytocin slow iv infusion was administered according to standard care in both the groups.

- **Data collection:** The following details were recorded in the proforma
  - Participant information: Age, Address
  - Height, Weight, BMI
  - Obstetric history: Date of last menstrual period (LMP), Expected date of delivery (EDD), Gestational age at enrollment, Obstetric score

- Mode of delivery: Elective or emergency cesarean section
- Indication for the cesarean section
- Active Management of Third Stage of Labour and use of uterotonics
- Additional interventions done to control bleeding (surgical & medical)
- Maternal and fetal outcomes
- Adverse events due to tranexamic acid

The details of the patient and obstetric history were recorded at the time of admission. Patients were followed up till the date of discharge.

Data regarding operative procedure and need for additional uterotonics was taken from the operative notes. Additional surgical and medical interventions done to control bleeding were recorded from the case sheets.

Apgar score at 1 and 5 minutes and need for NICU care was taken from the hospital records, to assess neonatal outcomes.

Maternal condition and details of maternal morbidity or mortality was also noted.

- **Investigations:** Pre and post op hemoglobin and hematocrit were recorded.
  - Preoperative hematocrit was the most recent hematocrit within one week before delivery.
  - Postoperative hematocrit was measured on Post op Day 2.

For the purpose of this study, blood loss was calculated by the following formula, and compared between the two groups:

*Estimated blood loss(ml) = Estimated blood*

$$volume(ml) \times \left\{ \frac{(Preop PCV - Postop PCV)}{Preop PCV} \right\}$$

Where *Estimated blood volume (ml) = Weight (kg) X 85*

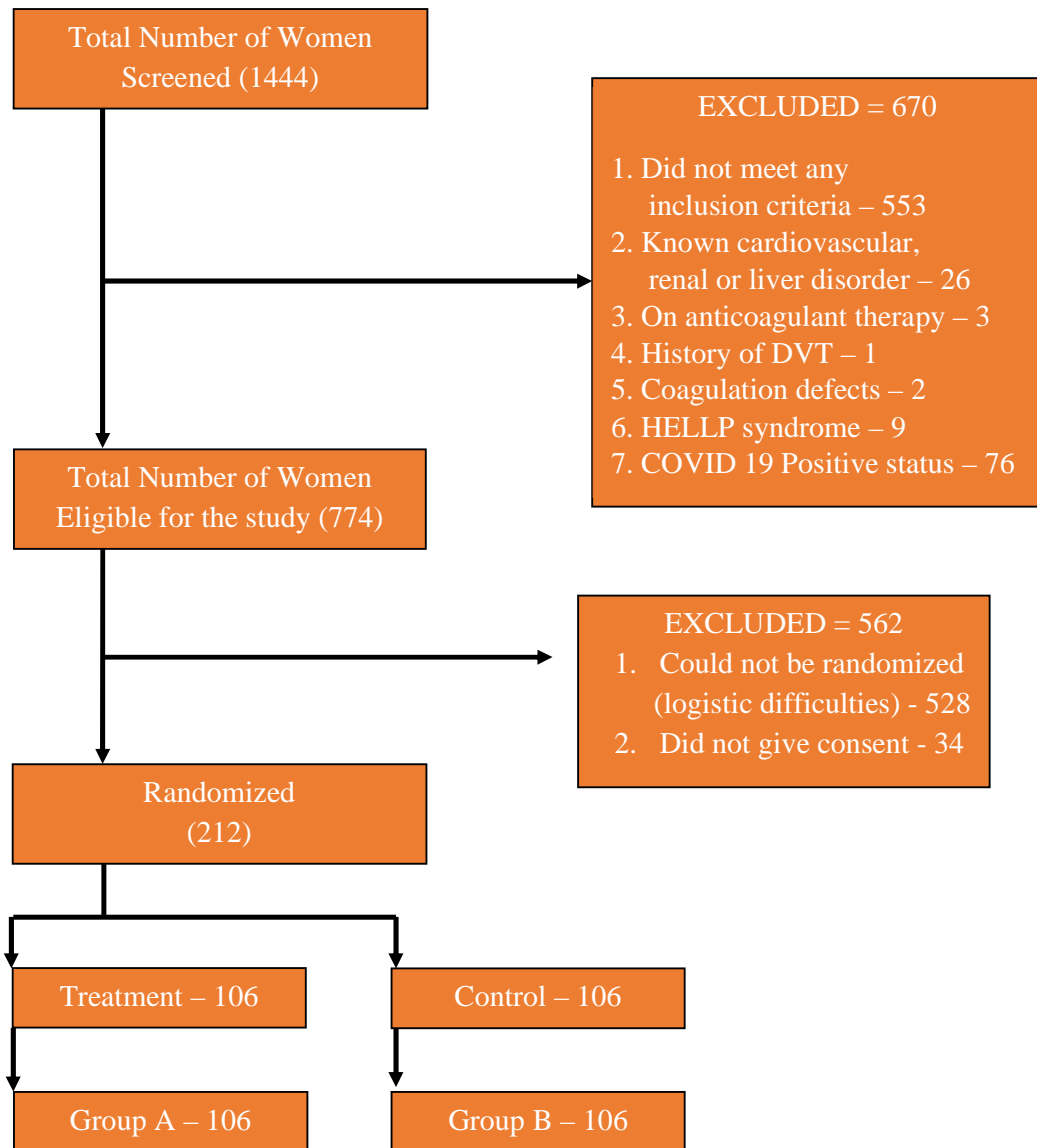
This calculation is used as a quantitative objective measure to estimate hemorrhage because blood loss is often underestimated and gravimetric methods include liquor in addition to blood, which limits accuracy.<sup>28</sup>

Incidence of PPH was defined by a calculated blood loss of >1000ml to be compared between the two groups.

## RESULTS

This study was done at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi over a period of 12 months from March 2021 to February 2022. A total of 1444 women were screened, out of which 670 were excluded as they did not meet the inclusion criteria or were ineligible as they met one of the exclusion criteria. 774 women were eligible for the study, out of which 528 patients could not be randomized and recruited in the study, due to logistic difficulties in recruitment and administration of the IMP 10 minutes before procedure as per protocol, because the patients underwent emergency cesarean sections before they could give consent or be randomized. 34 patients were excluded as they did not give consent. A total of 212 women were randomized into a treatment (106) and control group (106). A total of 106 participants in the control group and 106 participants in the interventional group were analyzed (**Figure 1**).

**FIGURE 1: CONSORT DIAGRAM**



**TABLE 1: DEMOGRAPHIC CHARACTERISTICS OF STUDY PARTICIPANTS**

<b>Variables</b>	<b>Sub Category</b>	<b>Treatment</b>	<b>Control</b>	<b>Total</b>	<b>p-value</b>
Age (years)	Mean $\pm$ SD	25.8 $\pm$ 4.1	25.9 $\pm$ 4	25.8 $\pm$ 4.1	0.419 <sup>t</sup>
	Median (Min, Max)	25 (19, 38)	25 (19, 38)	25 (19, 38)	
Height (m)	Mean $\pm$ SD	1.59 $\pm$ 0.09	1.58 $\pm$ 0.09	1.58 $\pm$ 0.09	0.419 <sup>t</sup>
	Median (Min, Max)	1.58 (1.38, 1.84)	1.56 (1.38, 1.77)	1.57 (1.38, 1.84)	
Weight (kg)	Mean $\pm$ SD	54.8 $\pm$ 8.5	54.9 $\pm$ 7.2	54.85 $\pm$ 7.84	0.475 <sup>t</sup>
	Median (Min, Max)	55.5 (40, 84)	54 (41, 74)	54 (40, 84)	
BMI (kg/m <sup>2</sup> )	Mean $\pm$ SD	21.74 $\pm$ 3.34	22.1 $\pm$ 2.16	21.92 $\pm$ 2.82	0.353 <sup>t</sup>
	Median (Min, Max)	21.07 (15.42, 36.36)	22.51 (15.78, 29.14)	22.06 (15.42, 36.36)	

*“Abbreviation: t – Two sample t test, \* indicates statistical significance.*

The two groups were similar in terms of demographic characteristics. The participants were aged between 19-38 years with a mean age of 25.8 years in the treatment group and 25.9 years in the control group. The mean height of the participants in the study was 1.58 meters. The mean weight of the participants was 54.85 kg. The treatment group had an average BMI of 21.74 kg/m<sup>2</sup>, while the control group had a mean BMI of 22.1 kg/m<sup>2</sup>. From two sample T test, we observe that, there is no significant difference in the distribution of age, height, weight and BMI over the groups. (Table 1).

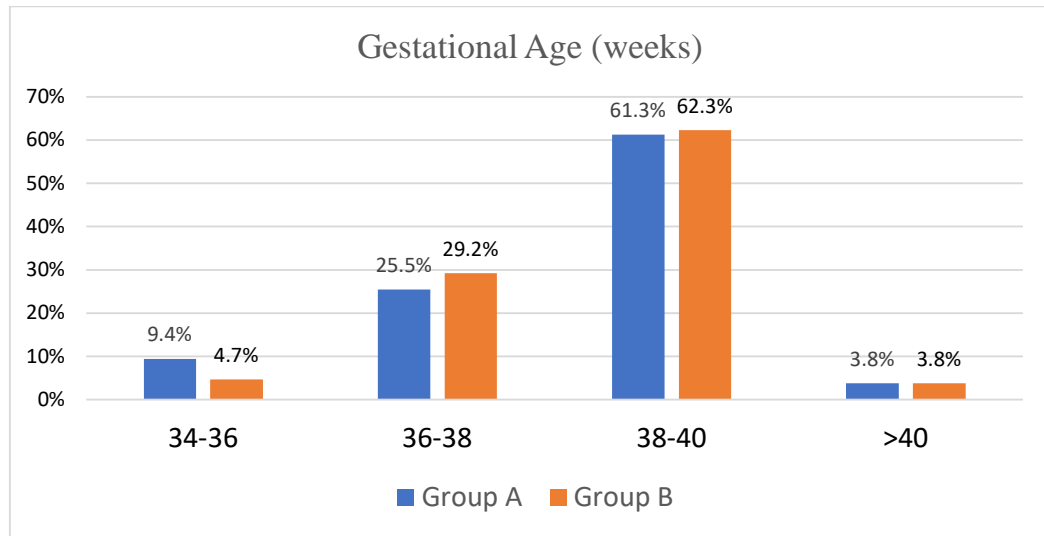
**TABLE 2: COMPARISON OF CLINICAL DETAILS**

<b>Variables</b>	<b>Sub Category</b>	<b>Group A (n=106)</b>	<b>Group B (n=106)</b>	<b>Total (n=212)</b>	<b>p-value</b>
Gestational age (weeks)	34-36	10 (9.4%)	5 (4.7%)	15 (7.1%)	0.583 <sup>C</sup>
	36-38	27 (25.5%)	31 (29.2%)	58 (27.4%)	
	38-40	65 (61.3%)	66 (62.3%)	131 (61.8%)	
	>40	4 (3.8%)	4 (3.8%)	8 (3.8%)	
Gravidity	Grand multipara	1 (0.9%)	1 (0.9%)	2 (0.9%)	0.868 <sup>C</sup>
	Multipara	87 (82.1%)	84 (79.2%)	171 (80.7%)	
	Primipara	18 (17%)	21 (19.8%)	39 (18.4%)	
Mode of delivery	Elective LSCS	31 (29.2%)	25 (23.6%)	56 (26.4%)	0.35 <sup>C</sup>
	Emergency LSCS	75 (70.8%)	81 (76.4%)	156 (73.6%)	

*“Abbreviation: C – Chi square test, \* indicates statistical significance.”*

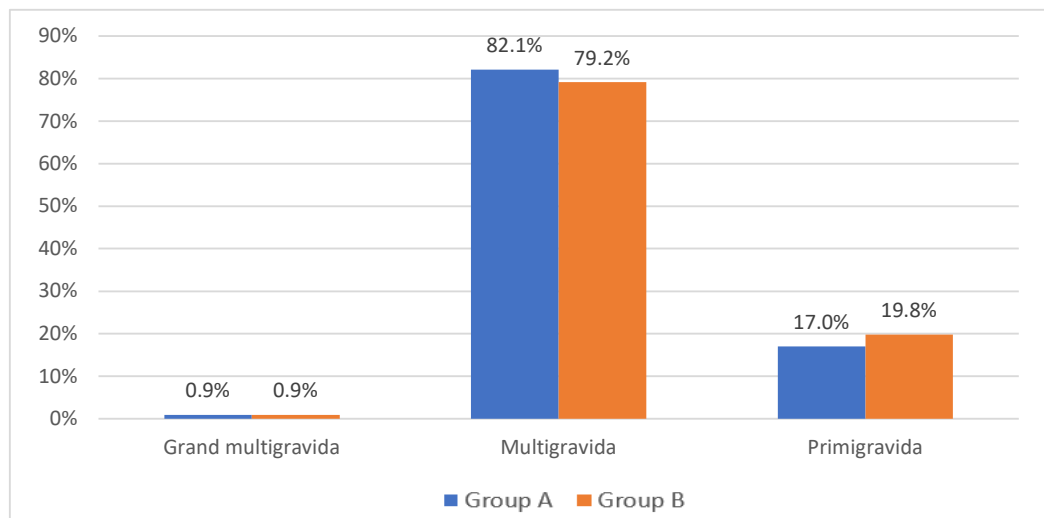
From Chi square test, we observe that, there is no significant association of gestational age, gravidity or mode of delivery within the groups. (**Table 2**).

**FIGURE 2: DISTRIBUTION OF PARTICIPANTS BY GESTATIONAL AGE**



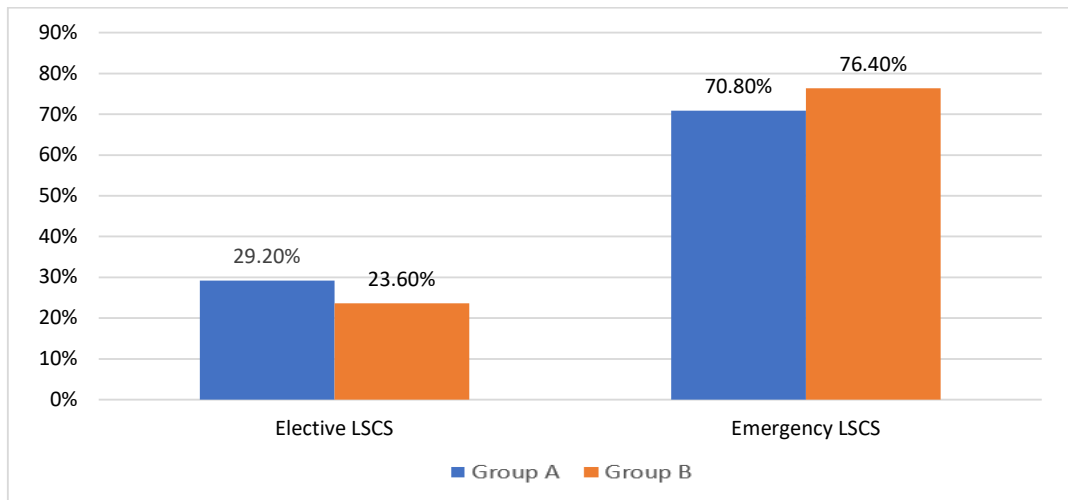
Most of the participants in both the treatment (61.3%) and the control groups (62.3%) were in the gestational age group of 38 to 40 weeks. The least number of participants were in the group of gestational age greater than 40 weeks. (Figure 2)

**FIGURE 3: DISTRIBUTION OF PARTICIPANTS ACCORDING TO OBSTETRIC SCORE**



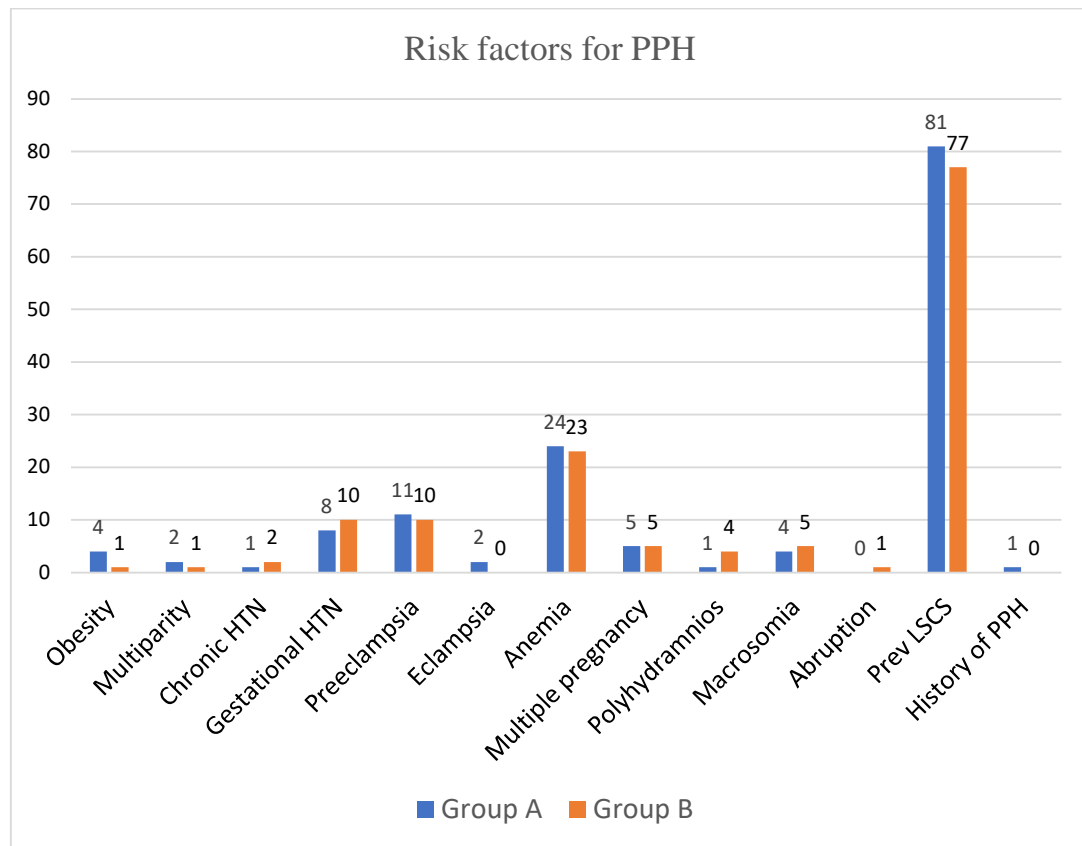
Majority of the patients in the study were multigravida with 79.20 % in control group and 82.10 % in the treatment group. (Figure 3).

**FIGURE 4: MODE OF DELIVERY**



Most of the patients in the study underwent Emergency LSCS - 76.40 % in control group and 70.80 % in the treatment group. 29.2 % of the participants in the treatment group and 23.6 % of those in the control group underwent an Elective LSCS. (Figure 4).

**FIGURE 5: DISTRIBUTION OF PARTICIPANTS OVER RISK FACTORS FOR PPH**



Participants were included in the study according to inclusion criteria satisfied, based on various risk factors for postpartum hemorrhage. The most common inclusion criteria satisfied was history of previous LSCS (81 in the treatment group and 77 in the control group). Some participants satisfied more than one inclusion criteria and had more than one high risk factor for PPH. **(Figure 5)**

**TABLE 3: DISTRIBUTION OF RISK FACTORS FOR POSTPARTUM HEMORRHAGE**

<b>Risk Factor</b>	<b>Group A (n=106)</b>	<b>Group B (n=106)</b>	<b>Total (n = 212)</b>	<b>P value</b>
Obesity	4 (3.8%)	1 (0.9%)	5 (2.4%)	0.175 <sup>C</sup>
Multiparity	2 (1.9%)	1 (0.9%)	3 (1.4%)	0.561 <sup>C</sup>
Chronic HTN	1 (0.9%)	2 (1.9%)	3 (1.4%)	0.561 <sup>C</sup>
Gestational HTN	8 (7.5%)	10 (9.4%)	18 (8.5%)	0.622 <sup>C</sup>
Preeclampsia	11 (10.4%)	10 (9.4%)	21 (9.9%)	0.818 <sup>C</sup>
Eclampsia	2 (1.9%)	0	2 (0.9%)	0.155 <sup>C</sup>
Anaemia	24 (22.6%)	23 (21.7%)	47 (22.2%)	0.869 <sup>C</sup>
Multiple pregnancy	5 (4.7%)	5 (4.7%)	10 (4.7%)	1 <sup>C</sup>
Polyhydramnios	1 (0.9%)	4 (3.8%)	5 (2.4%)	0.175 <sup>C</sup>
Macrosomia	4 (3.8%)	5 (4.7%)	9 (4.2%)	0.733 <sup>C</sup>
Abruption	0	1 (0.9%)	1 (0.5%)	0.316 <sup>C</sup>
Previous LSCS	81 (76.4%)	77 (72.6%)	158 (74.5%)	0.528 <sup>C</sup>
History of PPH	1 (0.9%)	0	1 (0.5%)	0.316 <sup>C</sup>

*“Abbreviation: C – Chi square test, \* indicates statistical significance.”*

Previous caesarean section was the most common risk factor for PPH in both the groups. In the treatment group, 76.4 % of the participants had a previous LSCS. This percentage was 72.6 % in the control group. From Chi square test it can be observed that there is no significant association between any of the variables of inclusion criteria over groups. **(Table 3)**

**TABLE 4: ESTIMATED BLOOD VOLUME**

Variable	Sub Category	Group A (n=106)	Group B (n=106)	Total (n=212)	p-value
Estimated Blood Volume (ml)	Mean ± SD	4632.8 ± 693.6	4714.4 ± 652.5	4673.64 ± 673.26	0.463 <sup>MW</sup>
	Median (Min, Max)	4675 (3400, 7140)	4760 (3485, 7140)	4717.5 (3400, 7140)	

“Abbreviation: MW – Mann Whitney U test, \* indicates statistical significance.”

Estimated blood volume is calculated by the formula *Estimated blood volume* = *Weight (kg) x 85*. From Mann Whitney U test, we observe that, there is no significant difference in the estimated blood volume between the two groups. (**Table 4**)

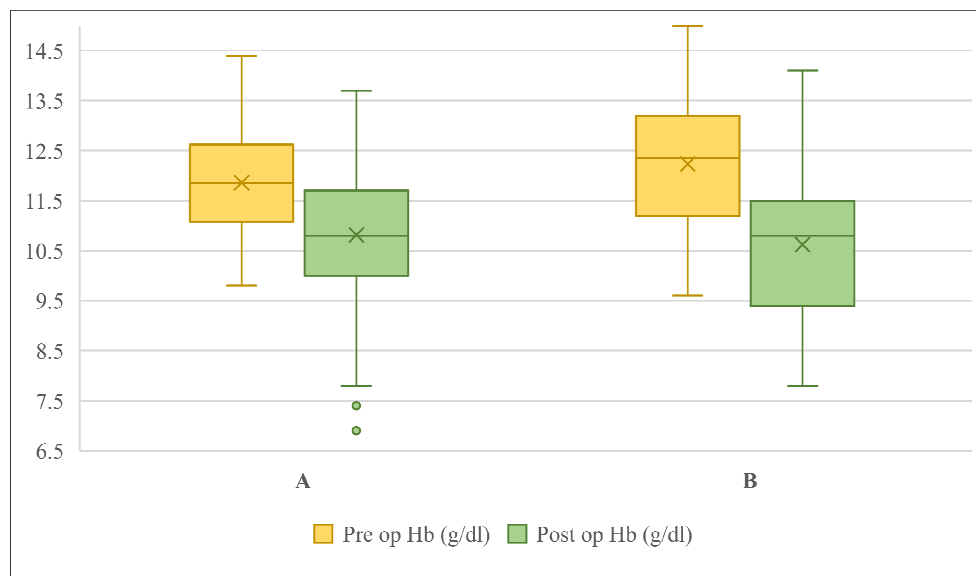
**TABLE 5: COMPARISON OF CHANGE IN HEMOGLOBIN AND HEMATOCRIT (PCV)**

Variables	Sub Category	Group A (n=106)	Group B (n=106)	Total (n=212)	p-value
Change in Hb (g/dL)	Mean ± SD	1.04 ± 0.863	1.61 ± 1.07	1.33 ± 1.01	< 0.001 <sup>MW*</sup>
	Median (Min, Max)	0.8 (0, 5)	1.4 (0.1, 4.6)	1.1 (0, 5)	
Change in PCV (%)	Mean ± SD	3.2 ± 2.33	4.95 ± 3.2	4.07 ± 2.92	< 0.001 <sup>MW*</sup>
	Median (Min, Max)	2.6 (0.68, 12.7)	4.15 (0.8, 14)	3.15 (0.68, 14)	

“Abbreviation: MW – Mann Whitney U test, \* indicates statistical significance.”

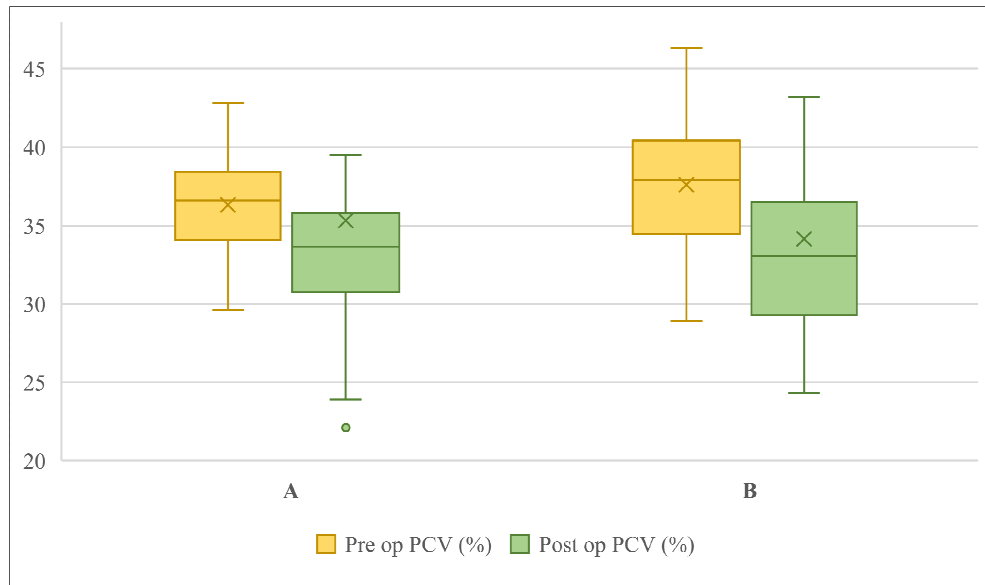
The mean fall in hemoglobin from the pre-operative to post-operative period in the treatment group was  $1.04 \pm 0.863$  mL, which was less than the mean fall in hemoglobin in the control group ( $1.61 \pm 1.07$  mL). The decrease in hematocrit from the pre-operative to post-operative period was less in the treatment group ( $3.2 \pm 2.33\%$ ) as compared to the control group ( $4.95 \pm 3.2\%$ ). From Mann Whitney U test, we observe that this fall in hemoglobin and hematocrit from the pre-operative to post-operative periods was significantly less in the treatment group as compared to the control group. ( $p < 0.001$ ). (Table 5)

**FIGURE 6: MEAN PLOT OF HEMOGLOBIN AT DIFFERENT TIME POINTS**



The mean hemoglobin noted pre-operatively was 11.9 g% and 12.2 g% in the treatment and control groups respectively. The post-operative hemoglobin was 10.8 g% and 10.6 g% in the treatment and control groups respectively. This box and whisker plot shows the change in hemoglobin over time from the pre-operative to post-operative periods in both the groups (Figure 6).

**FIGURE 7: MEAN PLOT OF HEMATOCRIT AT DIFFERENT TIME POINTS**



The mean hematocrit noted pre-operatively was 36.31% and 37.6% in the treatment and control groups respectively. The post-operative hematocrit was 33.11% and 32.65% in the treatment and control groups respectively. This box and whisker plot shows the change in hematocrit over time from the pre-operative to post-operative periods in both the groups (**Figure 7**).

TABLE 6: COMPARISON OF BLOOD LOSS

Variables	Sub Category	Group A (n=106)	Group B (n=106)	Total (n=212)	p-value
Estimated blood loss by formula (ml)	Mean $\pm$ SD	400.87 $\pm$ 280.94	597.93 $\pm$ 353.66	499.39 $\pm$ 333.57	< 0.001 <sup>MW*</sup>
	Median (Min, Max)	323.85 (102.36, 1659.37)	510.25 (110.15, 1375.42)	405.89 (102.36, 1659.37)	
Gravimetric Blood loss	Mean $\pm$ SD	379.2 $\pm$ 96.5	431.1 $\pm$ 152.2	405.14 $\pm$ 129.81	< 0.001 <sup>MW*</sup>
	Median (Min, Max)	360 (170, 680)	400 (200, 1160)	380 (170, 1160)	

Abbreviation: MW – Mann Whitney U test \* indicates statistical significance.

The estimated blood loss for this study is calculated in ml by the formula:

*Estimated blood loss (ml)*

$$= \text{Estimated blood volume} \times \left\{ \frac{(\text{Preoperative hematocrit} - \text{Postoperative hematocrit})}{\text{Preoperative hematocrit}} \right\}$$

Where *Estimated blood volume (ml) = Weight (kg) X 85*

Using the above formula, the mean blood loss in the treatment group in those who received tranexamic acid was 400.87  $\pm$  280.94 ml, while for the control group it was 597.93  $\pm$  353.66 ml. This difference in blood loss was statistically significant with a p value of <0.001.

The gravimetrically measured blood loss, by measuring the volume of blood collected in the suction and the weight of the mops was also found to be statistically different between the two groups with a mean blood loss of 379.2  $\pm$  96.5 ml in the treatment group and a mean blood loss of 431.1  $\pm$  152.2 ml in the control group. (p < 0.001). (Table 6)

**TABLE 7: MEDICAL INTERVENTIONS**

<b>Variables</b>	<b>Sub Category</b>	<b>Group A (n=106)</b>	<b>Group B (n=106)</b>	<b>Total (n=212)</b>	<b>p-value</b>
Additional uterotonics used	Carboprost	4 (3.8%)	6 (5.7%)	10 (3.3%)	0.225 <sup>MC</sup>
	Methergine	1 (0.9%)	5 (4.7%)	6 (1.9%)	
	Oxytocin	1 (0.9%)	1 (0.9%)	2 (1.9%)	
	Misoprostol	2 (1.9%)	5 (4.7%)	7 (1.9%)	
	None	100 (94.3%)	93 (87.7%)	193 (91%)	
Additional tranexamic acid given	No	99 (93.4%)	99 (93.4%)	198 (93.4%)	1 <sup>MC</sup>
	Yes	7 (6.6%)	7 (6.6%)	14 (6.6%)	

*Abbreviation: MC – Chi square test with Monte Carlo simulation, \* indicates statistical significance.*

Additional uterotonics were required in some patients to control bleeding. Some participants required more than one uterotonic while others required none. The additional uterotonics used in both the treatment and the control groups are shown in **Table 7**. However, there was no statistical significance between the two groups. (p = 0.255)

Additional tranexamic acid was administered on the first postoperative day if the clinician felt that there was a risk of continued bleeding. This additional tranexamic acid was required in 7 patients in the treatment group and 7 in the control group which was not statistically significant. (**Table 7**)

Active Management of Third Stage of Labour was done in all 212 of the participants in the study.

**TABLE 8: SURGICAL INTERVENTIONS**

<b>Variables</b>	<b>Sub Category</b>	<b>Group A (n=106)</b>	<b>Group B (n=106)</b>	<b>Total (n=212)</b>	<b>p-value</b>
Additional Surgical procedure	Hayman's Sutures	0	2 (1.9%)	2 (0.9%)	0.247 <sup>MC</sup>
	Uterine Artery Ligation	4 (3.8%)	1 (0.9%)	5 (2.4%)	
	None	97 (91.5%)	96 (90.6%)	193 (91%)	

*Abbreviation: MC – Chi square test with Monte Carlo simulation, \* indicates statistical significance.*

The table above shows additional surgical interventions performed to control blood loss. 2 patients in the control group required Hayman's sutures. 4 patients in the treatment group underwent uterine artery ligation, while this was required in 1 patient in the control group. However, there was no statistically significant difference in both the groups (**Table 8**)

Nine patients (8.49%) in the treatment group and fourteen (13.2%) patients in the control group were given parenteral iron correction in view of postop anaemia. However, this was not statistically significant between the groups.

One participant in the treatment group complained of vomiting after administration of the IMP. No patients in the control group complained of any adverse reactions. No other adverse drug reactions to tranexamic acid were noted in the course of the study.

There were no adverse maternal or neonatal outcomes attributable to tranexamic acid during the study.

## DISCUSSION

This study was conducted among 212 women at high risk for postpartum hemorrhage undergoing elective or emergency cesarean sections, to compare the difference in blood loss in these women, when tranexamic acid is given prophylactically.

WHO guidelines have now recommended the use of tranexamic acid in postpartum hemorrhage when uterotonics fail to control bleeding, especially if it is thought that the blood loss may be due to trauma. According to the 2017 guidelines, “Administration of tranexamic acid should be considered as part of the standard PPH treatment package.<sup>38</sup>” This is based on clinical trials where tranexamic acid has been used in surgery and trauma. Simonazzi et al. have recommended the routine use of tranexamic acid before skin incision for all cesarean deliveries.<sup>9</sup>

There is evidence to support the early administration of tranexamic acid as beneficial in controlling blood loss as evidenced in the CRASH-2 trial. In patients treated within 3 hours of injury, tranexamic acid reduced death due to bleeding by around one third, but when given after 3 hours, it seemed to increase the risk.<sup>26</sup> Thus, treatment should be given as early as possible.

In this study, we calculated the estimated blood loss during and after the cesarean section by the formula “Estimated blood volume  $\times$  (preoperative hematocrit – postoperative hematocrit)  $\div$  preoperative hematocrit” where the estimated blood volume in millilitres was calculated as the body weight in kilograms  $\times$  85.<sup>39,40,41</sup> This formula was used to calculate blood loss because the conventional methods of measuring blood loss by visual estimation or gravimetric measurement of soakage of mops is highly subjective and usually inaccurate.

The estimated blood volume in this study is calculated by Nadler's formula:

$$\text{Average blood volume (ml)} = \text{Patient weight (kg)} \times \text{Average blood volume in mL/kg}^{42}$$

The blood volume in pregnancy gradually increases with increasing gestational age, and is maximum at about 34 to 36 weeks period of gestation, following which there is little or no further increase.<sup>43</sup> We have recruited patients at a gestational age of 34 weeks or more in this study. The average blood volume in ml/kg for a pregnant woman at 34 weeks or beyond is taken to be 85 ml/kg. This value is chosen based on other studies that used the Nadler formula to calculate blood loss, although citing literature does not have clear explanation for the use of this 85 ml multiplication factor.<sup>28,44,45</sup> The pre-pregnancy weight has been considered to calculate blood loss for the purpose of this study. Calculation of blood loss by this equation by Sentilhes et al in the TRAAP study correlated with gravimetric measurements of blood loss.<sup>26,46</sup>

The TRACES study (Tranexamic acid in haemorrhagic Cesarean section) is a pharmacobiological study with the aim to determine a therapeutic strategy for use of tranexamic acid in cesarean sections with respect to the intensity of fibrinolysis. It is a multicentre, randomized, double-blind, placebo-controlled trial. It compared the use of 0.5g or 1g of TXA with a placebo by using thrombin plasmin generation assays to quantify tranexamic acid concentrations in plasma and uterine and urine and the plasmin peak inhibition. Venous blood was sampled before injection of the drug, at the end of injection, and then at 30, 60, 120, and 360 minutes. The results of the study suggested that there was activation of fibrinolysis in PPH after Caesarean delivery. It also found that a dose of TXA 1 g was associated with lower levels of hyperfibrinolysis biomarkers as compared to placebo, and a low dose of 0.5 g of TXA was less effective

than a standard 1 g dose. Therefore, a dose of at least 1 g tranexamic acid i.v. was needed to inhibit postpartum haemorrhage-induced hyperfibrinolysis.<sup>47</sup>

A meta-analysis of nine RCTs which evaluated the efficacy of prophylactic tranexamic acid in reducing postpartum blood loss at cesarean delivery, showed that tranexamic acid is associated with a significant decrease in incidence of PPH and severe PPH, a significantly lower drop in hemoglobin, and significantly lower need for additional uterotonic agents. The RCTs used either of two controls (either placebo or no treatment). However, these studies were conducted among low-risk pregnancies. It suggested to consider adding TXA 1g (or 10 mg/kg) iv 10-20 mins before skin incision or spinal anaesthesia in addition to oxytocin prophylaxis given after delivery of the neonate, as prophylaxis to reduce loss of blood at cesarean delivery.<sup>9</sup>

Our study is a randomized controlled trial conducted among two groups of 106 participants each. One group (Group A) received 1g of tranexamic acid iv as 10 ml of a colourless solution, at least 10 minutes before skin incision. The other group (Group B) received a placebo, as 10ml of colourless solution of Normal Saline, at least 10 minutes before the skin incision for the cesarean section. All women were at high risk for PPH. All women received Active Management of Third Stage of Labour and oxytocin prophylaxis according to standard protocol, which is 10 units oxytocin im and 10 units slow iv after delivery of the baby.

An RCT done in Egypt among 500 women at low risk for PPH. This study showed a statistically significant mean blood loss of  $387.68 \pm 93.05$  ml in the treatment group and mean blood loss of  $560.79 \pm 107.46$  ml in the placebo group during elective cesarean sections.<sup>8</sup>

A study conducted in Chhattisgarh among 100 women randomized to two groups, undergoing cesarean section, showed a mean blood loss of  $436.5 \pm 118.07$  mL for the study group who received 1 g iv of TXA and  $616.5 \pm 153.34$  mL in the control group ( $P \leq 0.05$ ). Two (4%) women in the study group had a blood loss  $>500$  mL during surgery versus nine (18%) in the control group ( $P \leq 0.05$ ). None versus three (6%) had PPH. Mean change in the hemoglobin was  $0.494 \pm 0.12$  g/dL versus  $0.594 \pm 0.16$  g/dL ( $p \leq 0.05$ ) in the study and control groups, respectively. No adverse effects were reported in women or neonates.<sup>29</sup>

In our study, we found that the mean blood loss as calculated by the above formula was significantly lower in the treatment group and compared to the control group with a mean blood loss of  $400.87 \pm 280.94$  ml in those who received tranexamic acid versus  $597.93 \pm 353.66$  ml in those who received the placebo ( $p < 0.001$ ). The mean change in the hemoglobin in our study was  $1.04 \pm 0.863$  g/dL in those that received tranexamic acid versus  $1.61 \pm 1.07$  g/dL in the control group ( $p \leq 0.001$ ). This is similar to the findings in other studies.

The incidence of PPH in India is 2% - 4% after vaginal delivery and 6% after cesarean section with uterine atony being the most common cause (50%).<sup>11</sup> A recent study in Loni, Maharashtra showed the incidence of atonic PPH to be 0.88%. Incidence was 0.80% following vaginal deliveries and 1.06% following cesarean deliveries. The incidence of atonic PPH was 0.99% and 1.10% for elective and emergency cesarean sections respectively.<sup>15</sup>

The incidence of postpartum hemorrhage in our study among women at high risk for PPH undergoing caesarean sections, as determined by calculation of blood loss based on pre and post op hematocrit levels is 9.44%. Five women in the treatment group

(4.72%) and fifteen in the control group (14.15%) had a blood loss of more than 1000 ml as calculated by the formula. ( $p < 0.001$ ). This shows a higher incidence in PPH as compared to other studies.

The gravimetrically measured blood loss was also noted for the purpose of the study. This was calculated by adding the volume of blood collected in the suction to the weight of the blood-soaked mops used during the cesarean, which was recorded in the operative notes. In terms of gravimetrically measured blood loss, the incidence of PPH in our study is 0.94%, which is similar to other studies. None of the participants of the treatment group had PPH as defined, while 2 (1.89%) had greater than 1000 ml blood loss in the control group when gravimetrically measured blood loss was considered.

This difference in the blood loss as calculated by the formula and the gravimetrically measured blood loss suggests that blood loss is grossly underestimated by measuring the volume of blood in the suction and weight of mops. There is no gold standard for estimating blood loss in cesarean sections, and this topic requires further study to formulate a model for correct measurement of blood loss.

Large studies like the large WOMAN trial also found no evidence of adverse effects with tranexamic acid when used in trauma and surgery.<sup>48</sup> Our study did not find any significant adverse events attributable to tranexamic acid. There was no case of thromboembolic events or death among the women recruited in this trial. One patient complained of vomiting after administration of the drug in the tranexamic acid group. No other adverse events related to tranexamic acid were recorded in the study. However, the sample size of this study is not sufficient to comment on incidence of adverse effects of the drug.

It is imperative to reduce blood loss during and after caesarean sections to reduce the morbidity and mortality associated with postpartum hemorrhage. This study shows that prophylactic administration of tranexamic acid before caesarean sections is useful in reducing blood loss even in woman at high risk for postpartum hemorrhage. This may be a useful intervention to combat postpartum hemorrhage.

## **CONCLUSION**

In this randomized controlled trial in women undergoing elective and emergency cesarean sections at high risk for postpartum hemorrhage, we found a significant decrease in the blood loss in the women receiving tranexamic acid as compared to the women in the control group.

Tranexamic acid can be administered prophylactically before both elective and emergency cesarean sections in women at high risk for postpartum hemorrhage to reduce blood loss which may thus help to reduce the morbidity associated with excessive hemorrhage in the postpartum period.

## SUMMARY

The present study was a prospective, placebo-controlled, single blinded, randomized controlled trial conducted to assess the role of tranexamic acid in reducing blood loss during elective and emergency cesarean deliveries in women at high risk for postpartum hemorrhage at a tertiary care centre. The study was carried out at the Department of Obstetrics and Gynecology of KAHER's Dr. Prabhakar Kore Charitable Hospital and Medical Research Centre, Belagavi, Karnataka over a period of one year. Patient population included all pregnant women undergoing elective or emergency cesarean sections according to the inclusion criteria. A total of 212 patients were recruited in the study and randomized into two groups of 106 participants each. Group A (Treatment group) received 10 ml (1g) of tranexamic acid slow iv and Group B (Placebo group) received 10 ml of normal saline slow iv over 10 minutes, at least 10 minutes prior to skin incision. Data regarding demographic characteristics, investigations, treatment and outcomes was collected in the form of a structured proforma and analyzed statistically.

The key findings of this study are summarized as follows:

- The age of the participants ranged from 19 years to 38 years with mean age of  $25.8 \pm 4.1$  years. There was no correlation between age and outcomes.
- The mean height of the participants in the study was 1.58 meters. The mean weight of the participants was 54.85 kg. The treatment group had an average BMI of  $21.74 \text{ kg/m}^2$ , while the control group had a mean BMI of  $22.1 \text{ kg/m}^2$ . There was no significant difference in the distribution of height, weight and BMI over the groups.

- Most of the participants were between 38 and 40 weeks of gestation, with 61.3% of the women in the treatment group and 62.3% of the women in the control group falling under this category.
- Majority of the patients in the study were multigravida, with 79.20 % in the control group and 82.10 % in the treatment group.
- Of the patients recruited in the study, most had an Emergency LSCS with 76.40 % of the control group and 70.80 % of the treatment group. 29.2 % of the participants in the treatment group and 23.6 % of those in the control group underwent an Elective LSCS.
- All women undergoing caesarean sections were at high risk for PPH as per the inclusion criteria. The most common risk factor was a history of previous LSCS (76.4% in the treatment group and 72.6% in the control group). Some participants satisfied more than one inclusion criteria and had more than one high risk factor for PPH. High risk factors for PPH were distributed equally over both the groups.
- There was a significant difference in the decrease in Hb and decrease in PCV from the pre to post operative period between the two groups. Hemoglobin fell by an average of  $1.04 \pm 0.863$  g/dL in the treatment group as compared to a fall of  $1.61 \pm 1.07$  g/dL in the control group. The decrease in hematocrit from the pre-operative to post-operative period was less in the treatment group ( $3.2 \pm 2.33\%$ ) as compared to the control group ( $4.95 \pm 3.2\%$ )

- The mean blood loss in those who received tranexamic acid was  $400.87 \pm 280.94$  ml, while for those who received placebo it was  $597.93 \pm 353.66$  ml. This difference was significant.
- The difference in gravimetrically measured blood loss over the groups was also significant with a mean blood loss of  $379.2 \pm 96.5$  ml in the treatment group and a mean blood loss of  $431.1 \pm 152.2$  ml in the control group.
- The incidence of postpartum hemorrhage, as determined by calculation of blood loss based on the formula using pre and post op hematocrit levels was found to be 9.44% in this study. Five women in the treatment group (4.72%) and fifteen in the control group (14.15%) had a blood loss of more than 1000 ml as calculated by the formula.
- There was no difference in the need for additional uterotonics or surgical interventions performed to reduce blood loss in both the groups.
- One patient complained of vomiting after administration of the drug in the tranexamic acid group. No other adverse events related to tranexamic acid were recorded in the study.

**REFERENCES**

1. United Nations Children's Fund (UNICEF). Maternal mortality [Internet]. UNICEF Global Development Commons. [cited 2022Mar9]. Available from: <https://gdc.unicef.org/resource/maternal-mortality>
2. Filippi V, Chou D, Ronsmans C, et al. Levels and Causes of Maternal Mortality and Morbidity. In: Black RE, Laxminarayan R, Temmerman M, et al., editors. Reproductive, Maternal, New-born, and Child Health: Disease Control Priorities, Third Edition (Volume 2). Washington (DC): The International Bank for Reconstruction and Development / The World Bank; 2016 Apr 5. Chapter 3. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK361917/> doi: 10.1596/978-1-4648-0348-2\_ch3
3. Lakshmi SD, Abraham R. Role of Prophylactic Tranexamic Acid in Reducing Blood Loss during Elective Cesarean Section: A Randomized Controlled Study. J Clin Diagn Res. 2016 Dec; 10(12): QC17-QC21. doi: 10.7860/JCDR/2016/21702.9050. Epub 2016 Dec 1. PMID: 28208943; PMCID: PMC5296516.
4. ACOG expands recommendations to treat postpartum hemorrhage [Internet]. ACOG. [cited 2022Jun19]. Available from: <https://www.acog.org/news/news-releases/2017/09/acog-expands-recommendations-to-treat-postpartum-hemorrhage>
5. 2013. DC Dutta's Textbook of Obstetrics. 7th ed. New Delhi: Jaypee Brothers Medical Publishers, p.410.

6. Begley CM, Gyte GML, Murphy DJ, Devane D, McDonald SJ, et al. (2010) Active versus expectant management for women in the third stage of labour. *Cochrane Database Syst Rev* (7): CD007412.
7. Chauncey JM, Wieters JS. Tranexamic Acid. [Updated 2020 Aug 11]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK532909/>
8. Abd El-Gaber, Abd El-Naser et al. Effect of tranexamic acid in prevention of postpartum hemorrhage in elective cesarean delivery: a randomized controlled study. *International Journal of Reproduction, Contraception, Obstetrics and Gynaecology*, [S.l.], v. 8, n. 1, p. 1-5, dec. 2018. ISSN 2320-1789. Available at: <<https://www.ijrcog.org/index.php/ijrcog/article/view/5826/4143>>. doi: <http://dx.doi.org/10.18203/2320-1770.ijrcog20185401>
9. Simonazzi G, Bisulli M, Saccone G, Moro E, Marshall A, Berghella V. Tranexamic acid for preventing postpartum blood loss after cesarean delivery: a systematic review and meta-analysis of randomized controlled trials. *Acta Obstet Gynecol Scand*. 2016;95(1):28-37. doi:10.1111/aogs.12798
10. Say L, Chou D, Gemmill A, Tuncalp O, et al. Global causes of maternal death: a WHO systematic analysis. *Lancet Glob Health*. 2014; 2: e323–33.
11. Amy JJ (1998) Severe Postpartum Hemorrhage: A Rational Approach. *Natl Med J India* 11(2): 86-88.
12. Registrar General, India and Centre for Global Health Research, *Maternal Mortality in India, 1997- 2003: Trends, Causes and Risk Factors*, New Delhi: Registrar General, India; 2006:1-40.

13. Dol J, Hughes B, Bonet M, Dorey R, Dorling J, Grant A, Langlois EV, Monaghan J, Ollivier R, Parker R, Roos N, Scott H, Shin HD, Curran J. Timing of maternal mortality and severe morbidity during the postpartum period: a systematic review. *JBIEvid Synth.* 2022 Sep 1;20(9):2119-2194. doi: 10.11124/JBIES-20-00578. PMID: 35916004; PMCID: PMC9594153.
14. Wormer KC, Jamil RT, Bryant SB. Acute Postpartum Hemorrhage. [Updated 2022 May 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK499988/>
15. Rani PR, Begum J. Recent Advances in the Management of Major Postpartum Hemorrhage - A Review. *J Clin Diagn Res.* 2017; 11(2): QE01-QE05. doi:10.7860/JCDR/2017/22659.9463
16. Nyfløt LT, Sandven I, Stray-Pedersen B, Pettersen S, Al-Zirqi I, Rosenberg M, Jacobsen AF, Vangen S. Risk factors for severe postpartum hemorrhage: a case-control study. *BMC Pregnancy Childbirth.* 2017 Jan 10;17(1):17. doi: 10.1186/s12884-016-1217-0. PMID: 28068990; PMCID: PMC5223545.
17. WHO. Trends in Maternal Mortality 2000 to 2017: Estimates by WHO, UNICEF, UNFPA, World Bank Group and the United Nations Population Division. Geneva, Switzerland: World Health Organization; 2019.
18. Meh C, Sharma A, Ram U, Fadel S, Correa N, Snelgrove JW, Shah P, Begum R, Shah M, Hana T, Fu SH, Raveendran L, Mishra B, Jha P. Trends in maternal mortality in India over two decades in nationally representative surveys. *BJOG.* 2022 Mar;129(4):550-561. doi: 10.1111/1471-0528.16888. Epub 2021 Sep 15. PMID: 34455679; PMCID: PMC9292773.

19. WHO. Strategies toward ending preventable maternal mortality (EPMM) [Internet]. Geneva, Switzerland: World Health Organization; 2015. Available from: [http://www.who.int/reproductivehealth/topics/maternal\\_perinatal/epmm/en/](http://www.who.int/reproductivehealth/topics/maternal_perinatal/epmm/en/).
20. Brenner A, Ker K, Shakur-Still H, Roberts I. Tranexamic acid for post-partum hemorrhage: What, who and when. *Best Pract Res Clin Obstet Gynaecol*. 2019 Nov; 61:66-74. doi: 10.1016/j.bpobgyn.2019.04.005. Epub 2019 Apr 30. PMID: 31128974; PMCID: PMC6891248.
21. FDA Approved Drug Products: Lysteda (tranexamic acid) tablets for oral use.
22. Tranexamic acid [Internet]. Uses, Interactions, Mechanism of Action | DrugBank Online. [cited 2022Dec17]. Available from: <https://go.drugbank.com/drugs/DB00302>
23. Furtmuller R, Schlag MG, Berger M, Hopf R, Huck S, Sieghart W, Redl H: Tranexamic acid, a widely used antifibrinolytic agent, causes convulsions by a gamma-aminobutyric acid(A) receptor antagonistic effect. *J Pharmacol Exp Ther*. 2002 Apr;301(1):168-73. doi: 10.1124/jpet.301.1.168. (PubMed ID 11907171).
24. Tranexamic acid use during pregnancy [Internet]. Drugs.com. [cited 2022Dec17]. Available from: <https://www.drugs.com/pregnancy/tranexamic-acid.html>.
25. Gilad O, Merlob P, Stahl B, Klinger G. Outcome following tranexamic acid exposure during breastfeeding. *Breastfeed Med*. 2014 Oct;9(8):407-10. doi: 10.1089/bfm.2014.0027. Epub 2014 Jul 15. PMID: 25025926.

26. CRASH-2 trial collaborators, Shakur H, Roberts I, Bautista R, Caballero J, Coats T, Dewan Y, El-Sayed H, Gogichaishvili T, Gupta S, Herrera J, Hunt B, Iribhogbe P, Izurieta M, Khamis H, Komolafe E, Marrero MA, Mejía-Mantilla J, Miranda J, Morales C, Olaomi O, Ollidashi F, Perel P, Peto R, Ramana PV, Ravi RR, Yutthakasemsunt S. Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant hemorrhage (CRASH-2): a randomized, placebo-controlled trial. *Lancet*. 2010 Jul 3;376(9734):23-32. doi: 10.1016/S0140-6736(10)60835-5. Epub 2010 Jun 14. PMID: 20554319.]
27. Morrison JJ, Dubose JJ, Rasmussen TE, Midwinter MJ. Military Application of Tranexamic Acid in Trauma Emergency Resuscitation (MATTERs) Study. *Arch Surg*. 2012 Feb;147(2):113-9. doi: 10.1001/archsurg.2011.287. Epub 2011 Oct 17. PMID: 22006852.
28. Sentilhes L, Sénat MV, Le Lous M, Winer N, Rozenberg P, Kayem G, Verspyck E, Fuchs F, Azria E, Gallot D, Korb D, Desbrière R, Le Ray C, Chauleur C, de Marcillac F, Perrotin F, Parant O, Salomon LJ, Gauchotte E, Bretelle F, Sananès N, Bohec C, Mottet N, Legendre G, Letouzey V, Haddad B, Vardon D, Madar H, Mattuizzi A, Daniel V, Regueme S, Roussillon C, Benard A, Georget A, Darsonval A, Deneux-Tharoux C; Groupe de Recherche en Obstétrique et Gynécologie. Tranexamic Acid for the Prevention of Blood Loss after Cesarean Delivery. *New England Journal of Medicine*. 2021 Apr 29;384(17):1623-1634. doi: 10.1056/NEJMoa2028788. PMID: 33913639
29. Sujata N, Tobin R, Kaur R, Aneja A, Khanna M, Hanjoora VM. Randomized controlled trial of tranexamic acid among parturients at increased risk for

- postpartum hemorrhage undergoing cesarean delivery. *Int J Gynaecol Obstet.* 2016 Jun;133(3):312-5. doi: 10.1016/j.ijgo.2015.09.032. Epub 2016 Feb 16. PMID: 26952346.
30. Lakshmi SD, Abraham R. Role of Prophylactic Tranexamic Acid in Reducing Blood Loss during Elective Cesarean Section: A Randomized Controlled Study. *J Clin Diagn Res.* 2016; 10(12): QC17-QC21. doi:10.7860/JCDR/2016/21702.9050.
31. Obesity [Internet]. World Health Organization. World Health Organization; [cited 2023Jan9]. Available from: [https://www.who.int/health-topics/obesity/#tab=tab\\_1](https://www.who.int/health-topics/obesity/#tab=tab_1).
32. ACOG Practice Bulletin No. 202: Gestational Hypertension and Preeclampsia. *Obstet Gynecol.* 2019 Jan;133(1):1. doi: 10.1097/AOG.0000000000003018. PMID: 30575675.
33. Anaemia [Internet]. World Health Organization. World Health Organization; [cited 2023Jan9]. Available from: [https://www.who.int/health-topics/anaemia#tab=tab\\_1](https://www.who.int/health-topics/anaemia#tab=tab_1).
34. Society for Maternal-Fetal Medicine (SMFM). Electronic address: [pubs@smfm.org](mailto:pubs@smfm.org). Dashe JS, Pressman EK, Hibbard JU. SMFM Consult Series #46: Evaluation and management of polyhydramnios. *Am J Obstet Gynecol.* 2018 Oct;219(4):B2-B8.
35. Rosati P, Exacoustós C, Caruso A, Mancuso S. Ultrasound diagnosis of fetal macrosomia. *Ultrasound Obstet Gynecol.* 1992 Jan 1;2(1):23-9. doi: 10.1046/j.1469-0705.1992.02010023.x. PMID: 12797002.

36. Intrapartum management of intraamniotic infection. Committee Opinion No. 712. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2017;130:e95–101.
37. Sentürk MB, Cakmak Y, Yildiz G, Yildiz P. Tranexamic acid for cesarean section: a double-blind, placebo-controlled, randomized clinical trial. *Arch Gynecol Obstet*. 2013 Apr;287(4):641-5. doi: 10.1007/s00404-012-2624-8. Epub 2012 Nov 11. PMID: 23143410.
38. WHO recommendation on tranexamic acid for the treatment of postpartum hemorrhage. Geneva: World Health Organization; 2017. Licence: CC BY-NC-SA 3.0 IGO.
39. Shook PR, Schultz JR, Reynolds JD, Spahn TE, DeBalli P. Estimating blood loss for cesarean section: how accurate are we? *Anesthesiology* 2003;98: Suppl 1:8. abstract.
40. Brecher, M., Monk, T., & Goodnough, L. (1997). *A standardized method for calculating blood loss*. *Transfusion*, 37(10), 1070–1074. doi:10.1046/j.1537-2995.1997.371098016448.x
41. ABA keywords [Internet]. OpenAnesthesia. [cited 2023Jan9]. Available from: [https://www.openanesthesia.org/maximum\\_abl\\_calculation/](https://www.openanesthesia.org/maximum_abl_calculation/)
42. Nadler SB, Hidalgo JH, Bloch T. Prediction of blood volume in normal human adults. *Surgery*. 1962; 51(2):224-32.
43. Hytten F. Blood volume changes in normal pregnancy. *Clin Haematol*. 1985 Oct;14(3):601-12. PMID: 4075604.

44. J.C. Carvalho, M. Balki, R. Windrim. Oxytocin requirements at elective cesarean delivery: a dose-finding study. *Obstet Gynecol*, 104 (2004), pp. 1005-1010,
45. S.R. Sheehan, A.A. Montgomery, M. Carey, et al. Oxytocin bolus versus oxytocin bolus and infusion for control of blood loss at elective cesarean section: double blind, placebo controlled, randomized trial. *BMJ*, 34 (2011), p. d4661
46. Maternal body weight and estimated circulating blood volume: a review and practical nonlinear approach. *British Journal of Anaesthesia*, ISSN: 0007-0912, Vol: 129, Issue: 5, Page: 716-725; 2022
47. Ducloy-Bouthors AS, Jeanpierre E, Saidi I, Baptiste AS, Simon E, Lannoy D, Duhamel A, Allorge D, Susen S, Hennart B. TRAnexamic acid in hemorrhagic Cesarean section (TRACES) randomized placebo-controlled dose-ranging pharmacobiological ancillary trial: study protocol for a randomized controlled trial. *Trials*. 2018 Mar 1;19(1):149. doi: 10.1186/s13063-017-2421-6. PMID: 29490690; PMCID: PMC5831219.
48. Shakur H, Elbourne D, Gülmezoglu M, Alfirevic Z, Ronsmans C, Allen E, Roberts I. The WOMAN Trial (World Maternal Antifibrinolytic Trial): tranexamic acid for the treatment of postpartum hemorrhage: an international randomized, double-blind placebo-controlled trial. *Trials*. 2010 Apr 16; 11:40. doi: 10.1186/1745-6215-11-40. PMID: 20398351; PMCID: PMC2864262.

**ANNEXURE I – INFORMED CONSENT FORM**

Title of Research Study: To assess the role of tranexamic acid in reducing the blood loss in women at high risk for postpartum hemorrhage undergoing cesarean section – A Randomized Controlled Trial

Principal Investigator:

Registration No. BJ0120002

Post Graduate Student

Department of Obstetrics and Gynaecology

J. N. Medical College, Belagavi

Co-Investigator:

Dr. \_\_\_\_\_

Professor

Department of Obstetrics and

Gynaecology

J. N. Medical College, Belagavi

**CONSENT FOR PARTICIPATION IN THE RESEARCH STUDY**

Mrs. \_\_\_\_\_, we are requesting you to enrol yourself in a study titled “To assess the role of tranexamic acid in reducing the blood loss in women at high risk for postpartum hemorrhage undergoing cesarean section – A Randomized Controlled Trial”, conducted by Registration No. BJ0120002, Post Graduate in M.S. Obstetrics and Gynaecology under the guidance of Dr. \_\_\_\_\_, Department of Obstetrics and Gynaecology, J.N. Medical College, Belgaum under KLE university, Belgaum.

The purpose of this study is to know the effectiveness of tranexamic acid in reducing blood loss after cesarean delivery, which will help in the effective management of postpartum hemorrhage in high-risk pregnancies. I will be the investigator for the study. The study is not being funded. I am going to give you information about this research project. Before you decide, you can talk to anyone you feel comfortable with about the research.

**Purpose of study:**

To know the effectiveness of giving 1g of tranexamic acid before surgery to reduce post-operative blood loss as compared to a placebo (Normal saline) and to study the outcomes related to blood loss following the surgery in two investigation groups with the aim to improve the management of postpartum hemorrhage in high-risk pregnancies.

**Procedure Involved:**

If you agree to enrol yourself in my study, then your detailed present and past history will be taken to know if you are eligible for this study or not. If you have even one of the exclusion criteria, you will not be enrolled in the study. If you are eligible, you will be allotted to one of two treatment groups by random selection. According to the group you are selected in, you will be given an injection of either a drug, tranexamic acid, or a placebo (Normal saline) intravenously before surgery, in addition to the normal protocol followed during the cesarean section. All necessary additional measures to control bleeding following surgery will be taken. A blood sample will be taken on the second day after surgery. In addition to detailed history, all investigations done will be taken down on the proforma sheet till the time you leave the hospital.

**Risks and Benefits:**

Tranexamic acid is safe in pregnancy. High dose of tranexamic acid may cause nausea, vomiting, diarrhoea, giddiness and headache. Rarely, allergic reaction, visual disturbance or thromboembolism (blood clots) may occur. The benefits of taking part in this research is, your participation being valuable contribution to medical research to improve treatment currently practiced.

**Voluntary Participations and withdrawal from study:**

Your participation in research is voluntary. Your decision whether to participate in the study or not will not change present or future health care services offered to you and will not affect your relationship with J.N. Medical College. If you do not choose to participate in the study, you will still be offered the treatment necessary for you. If you decide to participate you are free to withdraw at any time. There will be no penalty for withdrawal. You can be removed from the study if necessary.

**Privacy and Confidentiality:**

The only people who will know that you are the research subject will be the members of the research team. No information about you or information provided by you during the research will be disclosed to others without your written permission except:

1. In emergency to protect your rights and welfare.
2. If required by law.

**Institutional/sponsor's policy:**

In the event of any injury related to the study, treatment will be made available through KLE's Hospital & MRC, Belgaum. There is no compensation or payment for such medical treatment by law. If you are injured you may contact Registration No. BJ0120002, Post graduate student, Department of Obstetrics and Gynaecology, KLE's Hospital& MRC.

**Financial Incentives for participation:**

No financial incentives are being offered to enrolled patients. It is purely being done with the idea of research and all the cost of the study will be borne by the investigator. You will not be reimbursed for any expenses for participation in this research. In case of any complication occurring as a result of the research, you will not be given any financial compensation.

**Contact details:**

In case you have any questions related to the study, in future or in case of study related injury or illness, you can contact Registration No. BJ0120002, Post graduate student, Department of Obstetrics and Gynaecology, KLE's Hospital and MRC.

**Authorization to Publish Results:**

When the results of the research are published or discussed, in a conference, no information will be displayed that would disclose your identity. Any information that is obtained in connection with this study and that can be identified with you will remain confidential. Results of the study will be used to improve maternal outcomes.

**CONSENT STATEMENT:**

I, \_\_\_\_\_, voluntarily agree for participating in the study. By signing this consent form, I am not giving up any of my legal rights. I may withdraw from the study anytime. I am signing the consent form after having read the above details of the study, or been read from in my own vernacular language, including the risks and benefits and having all my questions answered.

Name of participant: \_\_\_\_\_

Signature or left thumb print of participant: \_\_\_\_\_

Patient's Legally Acceptable Representative's statement  NA

I, \_\_\_\_\_, as the patient's Legally Acceptable Representative, was present during the consenting procedure and understand the preceding information describing this study. All the questions regarding the study and the patient's participation have been answered to my satisfaction and that of the patient. The patient is willing to participate in the study and I sign below on her behalf testifying to this effect.

Name of participant: \_\_\_\_\_

Name of Legally Acceptable Representative: \_\_\_\_\_

Relationship to the patient: \_\_\_\_\_

Signature of the Legally Acceptable Representative: \_\_\_\_\_

Investigators name: \_\_\_\_\_ Signature: \_\_\_\_\_

Witness Name: \_\_\_\_\_ Signature: \_\_\_\_\_

Date: \_\_\_\_\_

**ANNEXURE II – SCREENING FORM AND PROFORMA**

**PARTICIPANT INFORMATION**

First Name: \_\_\_\_\_

Middle Name: \_\_\_\_\_

Last Name: \_\_\_\_\_

Husband's Name: \_\_\_\_\_

Age (Years): \_\_\_\_\_

Address:

House Number- \_\_\_\_\_

Street- \_\_\_\_\_

Taluka- \_\_\_\_\_

District- \_\_\_\_\_

Phone Number- \_\_\_\_\_

Landline (Optional)- \_\_\_\_\_

Registered

Unregistered

---



---

**SCREENING FORM**

Screening number:

--	--	--	--

Date of Screening:

(dd/mm/yyyy)

--	--	--	--	--	--	--	--

1) **Is Gestational Age  $\geq$ 34 weeks?**

Yes

No

LMP -

EDD -

USG 1<sup>st</sup> trimester EDD -

Actual Gestational Age-

2) **Inclusion criteria –**i. Obesity (BMI  $\geq$  25 kg/m<sup>2</sup>)

Yes

No

ii. Multiparity (Parity &gt;4)

Yes

No

iii. Chronic Hypertension

Yes

No

iv. Gestational Hypertension

Yes

No

v. Pre-Eclampsia

Yes

No

vi. Eclampsia

Yes

No

vii. Anaemia (Hb &lt; 11 g/dL)

Yes

No

viii. Multiple Pregnancy

Yes

No

ix. Polyhydramnios

Yes

No

x. Fetal Macrosomia

Yes

No

xi. Abnormally Implanted Placenta

Yes

No

xii. Placenta Previa

Yes

No

- 
- |   |     |                          |    |                          |
|---|-----|--------------------------|----|--------------------------|
| xiii. Abruption                         | Yes | <input type="checkbox"/> | No | <input type="checkbox"/> |
| xiv. Uterine Leiomyomas                 | Yes | <input type="checkbox"/> | No | <input type="checkbox"/> |
| xv. Chorioamnionitis                    | Yes | <input type="checkbox"/> | No | <input type="checkbox"/> |
| xvi. Cholestasis of Pregnancy           | Yes | <input type="checkbox"/> | No | <input type="checkbox"/> |
| xvii. Previous LSCS                     | Yes | <input type="checkbox"/> | No | <input type="checkbox"/> |
| xviii. History of PPH                   | Yes | <input type="checkbox"/> | No | <input type="checkbox"/> |
| xix. Use of Oxytocin Augmentation >4hrs | Yes | <input type="checkbox"/> | No | <input type="checkbox"/> |

**3) Exclusion Criteria –**

- |  |     |                          |    |                          |
|--|-----|--------------------------|----|--------------------------|
| i. Impaired colour vision                  | Yes | <input type="checkbox"/> | No | <input type="checkbox"/> |
| ii. Known Cardiac, Renal or Liver disorder | Yes | <input type="checkbox"/> | No | <input type="checkbox"/> |
| iii. History of DVT                        | Yes | <input type="checkbox"/> | No | <input type="checkbox"/> |
| iv. On Anticoagulant Therapy               | Yes | <input type="checkbox"/> | No | <input type="checkbox"/> |
| v. Coagulation Defects                     | Yes | <input type="checkbox"/> | No | <input type="checkbox"/> |
| vi. HELLP Syndrome                         | Yes | <input type="checkbox"/> | No | <input type="checkbox"/> |
| vii. Allergy to Tranexamic Acid            | Yes | <input type="checkbox"/> | No | <input type="checkbox"/> |

- 4) Is the patient eligible for the study –** Yes  No

**RANDOMIZATION FORM**

**Eligibility:**

Is she eligible for the study?                      Yes                       No

**Consent:**

Did the woman give consent for the study?    Yes                       No

**Enrolment:**

Was the woman enrolled in the study?            Yes                       No

Was the woman randomized?                      Yes                       No

Date of Randomization                                
(dd/mm/yyyy)

Time of Randomization                               :   
(hh:mm)

Participant Number                                     
(See sealed envelope)

Investigator's name:

Signature:

**STUDY PROFORMA**

Study ID:

Date of admission:

Date of delivery:

Date of discharge:

**Maternal Data:**

Height (m):

Weight (kg):

BMI (kg/m<sup>2</sup>):

Obstetric Score: Primipara

Multipara

Grand multipara

Mode of Delivery: Elective LSCS

Emergency LSCS

Indication for Cesarean Section:

i. Uncontrolled Gestational Hypertension

ii. Pre- eclampsia

iii. Eclampsia

iv. Multiple pregnancy

v. Fetal macrosomia

- vi. Cephalopelvic Disproportion
- vii. Abnormally implanted placenta
- viii. Placenta previa
- ix. Abruptio
- x. Previous Cesarean section
- xi. Failed induction
- xii. Non progress of labour
- xiii. Deep transverse arrest
- xiv. Fetal distress
- xv. Cesarean at Maternal Request (CDMR)
- xvi. Other: \_\_\_\_\_

**Investigations -**

Pre-Op Investigations: Hb (g/dL) -

PCV (%) -

Post-Op Investigations: Hb (g/dL) -

PCV (%) -

Change in Hb (Pre op – Post op) =

Change in PCV (Pre op – Post op) =

Estimated Blood Volume (ml) = *Weight (kg) x 85* =

Estimated blood loss (ml)

$$= \text{Estimated blood volume} \times \left\{ \frac{(\text{Preop PCV} - \text{Postop PCV})}{\text{Preop PCV}} \right\} = \boxed{\phantom{000}}$$

**Intra Op -**

Active Management of Third Stage of Labour done      Yes     No

**Additional Uterotonics used: -**

i) Oxytocin      Yes     No

ii) Carboprost      Yes     No

iii) Misoprostol      Yes     No

iv) Methergin      Yes     No

**Additional Tranexamic acid given**      Yes     No

Additional dose of tranexamic acid =

**Additional Intervention/ Surgical Procedure –**

1) B-Lynch sutures      Yes     No

2) Hayman sutures      Yes     No

3) Uterine Artery ligation      Yes     No

4) Internal Iliac Artery ligation      Yes     No

5) Peripartum hysterectomy      Yes     No

6) Other (specify): \_\_\_\_\_

**Intra Op/Post Op Blood and Blood product transfusion -**

- i. PRBC Yes  No
- ii. FFP Yes  No
- iii. Platelets (RDP/SDP) Yes  No
- iv. Cryoprecipitate Yes  No
- v. Whole blood Yes  No

Parenteral Iron Transfusion - Yes  No

**Maternal Outcomes**

i) Blood loss

- Estimated blood loss by calculation (ml)
- Gravimetrically measured intra op blood loss (ml)

- ii) PPH Yes  No
- iii) Shock Yes  No
- iv) ICU Admission Yes  No
- v) Death Yes  No

If yes, cause of death: \_\_\_\_\_

**Adverse Events related to TXA-**

- i) GIT (Nausea/Vomiting/Diarrhoea) Yes  No
- ii) Seizures Yes  No



S No	Age	POG - weeks	POG - days	Obesity	Multiparity	Chronic HTN	Gestational HTN	Preeclampsia	Eclampsia	Anemia	Multiple pregnancy	Polyhydramnios	Macrosomia	Abruption	Prev LSCS	History of PPH	Group	Height (m)	Weight (kg)	BMI (kg/m2)	Obstetric score	Mode of delivery	Indication	Pre op Hb (g/dl)	Pre op PCV (%)	Post op Hb (g/dl)	Post op PCV (%)	Change in Hb	Change in PCV	Estimated Blood Volume	Estimated blood loss (ml)	Gravimetric Blood loss	AMTSL	Additional uterotonics used	Additional TXA given	Dose of additional TXA given	Additional intervention/Surgical procedure	Intraop/Post op BT - component	No. of units transfused	Adverse Maternal Outcome	Adverse Drug reaction to TXA	NICU Admission	Perinatal morbidity	Perinatal Mortality			
1	24	38	1	No	No	No	No	No	No	No	No	No	No	No	Yes	No	B	1.44	50	24.11	Multigravida	Elective LSCS	Previous LSCS	11.3	40.5	10.5	36.5	0.8	4	4250	419.75	510	Yes	None	No	NA	None	None	None	NA	None	No	Yes	Multiple Fetal Anomalies	No		
2	26	38	2	No	No	No	No	No	No	No	No	No	No	No	Yes	No	B	1.54	54	22.77	Multigravida	Elective LSCS	Previous LSCS	13.4	40.2	11.4	34.2	2	6	4590	685.07	1100	Yes	None	Yes	1g	None	PRBC	2 PRBC	None	No	No	No	No			
3	24	37	4	No	No	No	No	No	No	No	No	No	No	No	Yes	No	B	1.7	63	21.8	Multigravida	Emergency LSCS	Previous LSCS	11.7	36	11.2	33.8	0.5	2.2	5355	327.25	400	Yes	None	No	NA	Adhesiolysis	None	NA	None	No	No	No	No	No		
4	22	38	2	No	No	No	No	No	No	No	No	No	No	No	Yes	No	B	1.55	60	24.97	Multigravida	Emergency LSCS	Previous LSCS	13.4	39	11.1	34.3	2.3	4.7	5100	614.62	500	Yes	None	No	NA	None	None	NA	None	No	No	No	No	No		
5	32	39	1	No	No	No	No	No	No	No	No	No	No	No	Yes	No	A	1.58	61	24.44	Multigravida	Elective LSCS	Previous LSCS	11.6	36.5	11.2	34.2	0.4	2.3	5185	326.73	480	Yes	None	No	NA	None	None	NA	None	No	No	No	No	No		
6	24	39	5	No	No	No	No	No	No	Yes	No	No	No	No	Yes	No	B	1.6	63	24.61	Multigravida	Emergency LSCS	Previous LSCS	10.6	33.7	9.5	30.6	1.1	3.1	5355	492.6	340	Yes	None	No	NA	None	None	NA	None	No	No	No	No	No		
7	26	38	0	Yes	No	No	No	No	No	No	No	No	No	No	Yes	No	A	1.57	74	30.02	Multigravida	Elective LSCS	Previous LSCS	12.2	38.3	12.1	36.6	0.1	1.7	6290	279.19	680	Yes	Carboprost	No	NA	None	None	NA	None	No	No	No	No	No		
8	27	39	0	No	No	No	No	No	No	Yes	No	No	No	No	Yes	No	A	1.5	55	24.44	Multigravida	Elective LSCS	Previous LSCS	10.7	33.1	9.9	29.5	0.8	3.6	4675	508.46	680	Yes	None	No	NA	None	None	NA	None	No	No	No	No	No		
9	24	38	3	No	No	No	No	No	No	No	No	No	No	No	Yes	No	A	1.5	56	24.89	Multigravida	Elective LSCS	Previous LSCS	11.6	34.8	11.1	33	0.5	1.8	4760	246.21	550	Yes	None	No	NA	None	None	NA	None	No	No	No	No	No		
10	22	40	0	Yes	No	No	No	No	No	No	No	No	No	No	No	No	A	1.68	74	26.22	Multigravida	Emergency LSCS	Anamios	13.9	42.2	12.4	39.3	1.5	2.9	6290	432.25	400	Yes	None	No	NA	None	None	NA	None	No	No	No	No	No		
11	38	39	1	No	No	Yes	No	No	No	No	No	No	No	No	Yes	No	B	1.57	60	24.34	Multigravida	Emergency LSCS	Previous LSCS	11.9	37.9	11.8	37	0.1	0.9	5100	121.11	360	Yes	None	No	NA	None	None	NA	None	No	No	No	No	No		
12	23	34	1	No	No	No	No	No	No	No	No	No	No	Yes	No	A	1.38	47	24.68	Multigravida	Emergency LSCS	Previous LSCS	12.9	40.1	10.8	33.8	2.1	6.3	3995	627.64	300	Yes	None	Yes	1g	None	None	NA	None	NA	None	Yes	No	No	No		
13	20	36	3	No	No	No	No	No	No	Yes	No	No	No	No	No	No	B	1.62	60	22.86	Multigravida	Emergency LSCS	CDMR	13	38.7	10.1	30.2	2.9	8.5	5100	1120.16	440	Yes	Methergin	No	NA	None	None	NA	None	No	No	No	No	No		
14	28	37	2	No	No	No	No	No	No	No	No	No	No	No	Yes	No	B	1.45	51	24.26	Multigravida	Elective LSCS	Previous LSCS	13.2	40.1	10.4	31.7	2.8	8.4	4335	908.08	400	Yes	None	No	NA	None	None	NA	None	No	No	No	No	No		
15	24	35	6	No	No	No	No	No	No	Yes	No	No	No	No	No	No	B	1.52	46	19.91	Primigravida	Emergency LSCS	Fetal distress	13.1	39.9	11.5	34.9	1.6	5	3910	489.97	200	Yes	None	No	NA	None	None	NA	None	No	Yes	No	No	No		
16	24	35	6	No	No	No	No	Yes	No	No	No	No	No	No	No	No	A	1.46	40	18.77	Primigravida	Emergency LSCS	Fetal distress	12.4	36.2	9.9	30.5	2.5	5.7	3400	535.36	200	Yes	None	No	NA	None	None	NA	None	NA	Sepsis	No	No	No	No	
17	26	40	4	No	No	No	No	No	No	No	No	No	No	No	Yes	No	A	1.54	50	21.08	Multigravida	Emergency LSCS	Previous LSCS	12.2	38.3	11.1	34.5	1.1	3.8	4250	421.67	250	Yes	None	No	NA	None	None	NA	None	No	No	No	No	No		
18	25	38	6	No	No	No	No	No	No	No	No	No	No	No	Yes	No	A	1.45	56	26.63	Multigravida	Emergency LSCS	Previous LSCS	12.6	40.7	11.7	37.3	0.9	3.4	4760	397.64	300	Yes	None	No	NA	Uterine Artery Ligation	None	NA	None	NA	None	No	No	No	No	
19	22	37	6	No	No	No	No	No	No	No	No	No	No	No	Yes	No	A	1.47	45	20.82	Multigravida	Emergency LSCS	Previous LSCS	11.1	35.2	10.6	34.2	0.5	1	3825	108.66	250	Yes	None	No	NA	None	None	NA	None	No	No	No	No	No		
20	23	39	5	No	No	No	No	No	No	No	No	No	No	No	Yes	No	B	1.59	60	23.73	Multigravida	Emergency LSCS	Previous LSCS	11.3	35.7	10.2	32.5	1.1	3.2	5100	457.14	420	Yes	Methergin	Yes	1g	None	None	NA	None	NA	None	No	No	No	No	No
21	22	40	1	No	No	No	No	No	No	Yes	No	No	No	No	Yes	No	B	1.53	58	24.78	Multigravida	Emergency LSCS	Previous LSCS	10.6	31.5	9.1	29.1	1.5	2.4	4930	375.62	250	Yes	None	No	NA	None	None	NA	None	No	No	No	No	No		
22	37	39	4	No	No	No	No	No	No	No	No	No	No	No	Yes	No	B	1.56	56	23.01	Multigravida	Emergency LSCS	Previous LSCS	13.4	42.6	12.9	40.3	0.5	2.3	4760	257	430	Yes	None	None	NA	None	None	NA	None	NA	None	No	No	No	No	
23	25	40	1	No	No	No	No	No	No	No	No	No	No	No	Yes	No	B	1.47	50	23.14	Multigravida	Emergency LSCS	Fetal distress	14.2	42.6	11.5	33	2.7	9.6	4250	957.75	570	Yes	None	No	NA	None	None	NA	None	No	No	No	No	No		
24	23	37	4	Yes	No	No	No	No	No	No	No	No	No	No	Yes	No	B	1.55	70	29.14	Multigravida	Elective LSCS	Previous LSCS	13.4	42	11.7	35.1	1.7	6.9	5950	977.5	380	Yes	None	No	NA	None	None	NA	None	NA	None	No	No	No	No	
25	25	38	6	No	No	No	No	No	No	No	No	No	No	No	Yes	No	B	1.53	58	24.78	Multigravida	Elective LSCS	Previous LSCS	12.1	39.7	10.1	32.4	2	7.3	4930	906.52	560	Yes	None	No	NA	Uterine Artery Ligation	None	NA	None	NA	None	No	No	No	No	
26	32	37	6	No	No	No	No	No	No	No	No	No	No	No	Yes	No	B	1.73	74	24.73	Multigravida	Elective LSCS	Previous LSCS	13.3	40	12.6	36.8	0.7	3.2	6290	503.2	290	Yes	None	No	NA	None	None	NA	None	No	No	No	No	No		
27	28	38	0	No	No	No	No	No	No	No	No	No	No	No	Yes	No	A	1.58	62	24.84	Multigravida	Emergency LSCS	Previous LSCS	12.5	37.9	10.6	34.2	1.9	3.7	5270	514.49	400	Yes	None	No	NA	None	None	NA	None	No	No	No	No	No		
28	36	37	4	No	No	No	No	No	No	No	No	No	No	No	Yes	No	B	1.43	42	20.54	Multigravida	Elective LSCS	Previous LSCS	14.6	44.8	10.9	34	3.7	10.8	3570	860.63	430	Yes	Carboprost, methergin	No	NA	None	None	NA	None	NA	None	No	No	No	No	No
29	24	38	1	Yes	No	No	No	No	No	No	No	No	No	No	Yes	No	A	1.47	69	31.93	Multigravida	Emergency LSCS	Previous LSCS	12.3	38.5	10.6	35.8	1.7	2.7	5865	411.31	270	Yes	None	No	NA	None	None	NA	None	No	No	No	No	No		
30	28	39	5	No	No	No	No	No	No	No	No	No	No	No	Yes	No	A	1.53	58	24.78	Multigravida	Emergency LSCS	Previous LSCS	12.8	40.4	11.6	37.8	1.2	2.6	4930	317.28	170	Yes	None	No	NA	None	None	NA	None	No	No	No	No	No		
31	26	40	1	Yes	No	No	Yes	No	No	No	No	No	No	No	No	No	A	1.52	84	36.36	Multigravida	Emergency LSCS	Breach	13	38.5	10.5	33.6	2.5	4.9	7140	908.73	350	Yes	None	No	NA	None	None	NA	None	NA	None	No	No	No	No	
32	22	39	1	No	No	No	Yes	No	No	No	No	No	No	No	No	No	B	1.6	50	19.53	Primigravida	Emergency LSCS	Anamios	13.1	39.7	12.4	37.6	0.7	2.1	4250	224.81	310	Yes	None	No	NA	None	None	NA	None	NA	None	No	No	No	No	
33	21	41	3	No	No	No	Yes	No	No	No	No	No	No	No	No	No	A	1.43	52	25.43	Primigravida	Emergency LSCS	MSL	13.3	37.5	12.8	35.4	0.5	2.1	4420	247.52	390	Yes	None	Yes	3g	None	None	NA	None	Vomiting	No	No	No	No		
34	29	37	6	No	No	No	No	No	No	No	No	No	No	No	Yes	No	B	1.6	64	25	Multigravida	Emergency LSCS	Previous LSCS	12.8	42.7	11.2	36.7	1.6	6	5440	764.4	350	Yes	None	No	NA	None	None	NA	None	NA	None	No	No	No	No	
35	25	37	3	No	No	No	No	No	No	No	No	No	No	No	Yes	No	A	1.48	52	23.74	Multigravida	Emergency LSCS	Previous LSCS	13.2	40.7	13.1	39.5	0.1	1.2	4420	130.32	350	Yes	None	Yes	1.5g	None	None	NA	None	NA	None	No	No	No	No	
36	22	39	0	No	No	No	No	No	No	No	No	No	No	No	Yes	No	A	1.58	52	20.83	Multigravida	Emergency LSCS	Previous LSCS	13.2	39.1	12.6	36.9	0.6	2.2	4420	248.7	380	Yes	None	No	NA	None	None	NA	None	NA	None	No	No	No	No	
37	30	37	1	No	No	No	Yes	No	No	No	No	No	No	No	No	No	B	1.68	58	20.55	Multigravida	Emergency LSCS	Abruption	12.8	37	11.3	33.1	1.5	3.9	4930	519.65	520	Yes	None	No	NA	None	None	NA	None	No	No	No	No	No		
38	35	38	0	No	No	No	No	No	No	No	No	No	No	No	Yes	No	B	1.62	62	23.62	Multigravida	Elective LSCS	Previous LSCS	14.6	42.9	13.6	40	1	2.9	5270	356.25	280	Yes	None	No	NA	None	None	NA	None	NA	None	No	No	No	No	
39	28	40	1	No	No	No	No																																								

75	33	37	0	No	No	No	Yes	No	No	No	No	No	No	No	No	No	B	1.67	68	24.38	Multigravida	Elective LSCS	Breech	13.3	39.7	12.9	38.3	0.4	1.4	5780	203.83	390	Yes	carboprost	No	NA	None	None	NA	None	No	Yes	esophageal atresia	No		
76	26	38	3	No	No	No	No	No	No	Yes	No	No	No	No	No	No	B	1.58	62	24.84	Primigravida	Emergency LSCS	Fetal distress	9.6	31.4	8.9	29.8	0.7	1.6	5270	268.54	380	Yes	None	No	NA	None	None	NA	None	No	No	No	No		
77	30	38	1	No	No	No	Yes	No	No	No	No	No	No	No	No	No	A	1.76	70	22.6	Multigravida	Emergency LSCS	Fetal distress	12.4	35.9	11.4	34.2	1	1.7	5950	281.75	280	Yes	None	No	NA	None	None	NA	None	No	No	No	No		
78	26	38	4	No	No	No	No	No	No	No	No	No	No	No	No	No	A	1.59	56	22.15	Multigravida	Elective LSCS	Previous LSCS	12.3	36.7	11.3	33	1	3.7	4760	479.89	360	Yes	None	No	NA	None	None	NA	None	No	No	No	No		
79	22	36	0	No	No	No	No	No	No	No	No	No	No	No	No	No	B	1.67	62	22.23	Multigravida	Elective LSCS	Previous LSCS	11.1	32.4	8.2	26.6	2.9	5.8	5270	943.4	450	Yes	None	No	NA	None	None	NA	None	No	No	No	No		
80	30	38	0	No	No	No	No	No	No	No	No	No	No	No	No	No	B	1.7	58	20.07	Multigravida	Emergency LSCS	Previous LSCS	13.1	39.8	9.3	29.3	3.8	10.5	4930	1300.63	410	Yes	None	No	NA	None	None	NA	None	No	No	No	No		
81	27	39	1	No	No	No	No	No	No	No	No	No	No	No	No	No	A	1.8	79	24.38	Multigravida	Emergency LSCS	Previous LSCS	13.8	40.4	11.9	35	1.9	5.4	6715	897.55	360	Yes	None	No	NA	None	None	NA	None	No	No	No	No		
82	28	38	3	No	No	No	No	No	No	No	No	No	No	No	No	No	A	1.65	45	16.53	Multigravida	Emergency LSCS	Previous LSCS	11.3	32.9	9.4	30.1	1.9	2.8	3825	325.53	350	Yes	None	No	NA	None	None	NA	None	No	No	No	No		
83	33	38	5	No	No	No	No	No	No	No	No	No	No	No	No	No	A	1.66	49	17.78	Multigravida	Elective LSCS	Previous LSCS	13	40	12.2	36.3	0.8	3.7	4165	385.26	400	Yes	None	No	NA	None	None	NA	None	No	No	No	No		
84	29	38	4	No	No	No	No	No	No	No	No	No	No	No	No	No	B	1.68	59	20.9	Multigravida	Elective LSCS	Previous LSCS	15	43.9	14.1	41.2	0.9	2.7	5015	308.44	340	Yes	None	No	NA	None	None	NA	None	No	No	No	No		
85	22	37	0	No	No	No	No	No	No	No	Yes	No	No	No	No	No	A	1.69	62	21.71	Primigravida	Emergency LSCS	DCDA twins	12.7	38.5	11.6	33.2	1.1	5.3	5270	725.48	300	Yes	None	No	NA	None	None	NA	None	No	No	No	No		
86	26	38	2	No	No	No	No	No	No	No	No	No	No	No	No	No	A	1.77	57	18.19	Multigravida	Elective LSCS	Previous LSCS	13.4	40.1	12.2	36.6	1.2	3.5	4845	422.88	350	Yes	None	No	NA	None	None	NA	None	No	No	No	No		
87	22	39	3	No	No	No	No	No	No	No	Yes	No	No	No	No	No	B	1.72	68	22.99	Multigravida	Emergency LSCS	MCDA twins	11.7	37.4	10.8	33.6	0.9	3.8	5780	587.27	240	Yes	None	No	NA	None	None	NA	None	No	No	No	No		
88	26	38	2	No	No	No	No	No	No	No	No	No	No	No	No	No	B	1.69	56	19.61	Multigravida	Emergency LSCS	Previous LSCS	12.5	35.9	11.5	30	1	5.9	4760	782.28	410	Yes	None	No	NA	None	None	NA	None	No	No	No	No		
89	24	38	6	No	No	No	No	No	No	No	No	No	No	No	No	No	A	1.69	60	21.01	Multigravida	Elective LSCS	Previous LSCS	11.1	33.1	10.5	30.9	0.6	2.2	5100	338.97	510	Yes	None	No	NA	None	None	NA	None	No	No	No	No		
90	29	38	6	No	No	No	No	No	No	No	No	No	No	No	No	No	A	1.49	54	24.32	Multigravida	Emergency LSCS	Multiple Pregnancy	11.2	34.8	10.2	31.3	1	3.5	4590	461.64	350	Yes	None	No	NA	None	None	NA	None	No	No	No	No		
91	25	38	5	No	No	No	No	No	No	No	No	No	No	No	No	No	B	1.55	53	22.06	Multigravida	Emergency LSCS	Previous LSCS	12.7	40.5	11.4	34.7	1.3	5.8	4505	645.16	460	Yes	None	Yes	1.5g	Adhesiolysis	None	NA	None	No	No	No	No		
92	28	39	1	No	No	No	No	No	No	No	No	No	No	No	No	No	B	1.67	44	15.78	Multigravida	Emergency LSCS	Previous LSCS	13.1	40.7	12.5	39.1	0.6	1.6	3740	147.03	560	Yes	Methergin	No	NA	None	None	NA	None	No	No	No	No		
93	25	39	3	No	No	No	No	No	No	No	No	No	No	No	No	No	B	1.65	49	18	Multigravida	Emergency LSCS	Previous LSCS	13.6	41.8	13.1	39.3	0.5	2.5	4165	249.1	440	Yes	None	No	NA	None	None	NA	None	No	No	No	No		
94	29	35	0	No	No	No	No	Yes	No	No	No	No	No	No	No	No	A	1.67	43	15.42	Multigravida	Emergency LSCS	Pre-Eclampsia	12	37.3	11.7	35.5	0.3	1.8	3655	176.38	440	Yes	None	No	NA	Uterine Artery Ligation	None	NA	None	No	No	No	No		
95	30	37	6	No	No	No	No	No	No	No	No	No	No	No	Yes	No	A	1.55	43	17.9	Multigravida	Elective LSCS	Previous LSCS	12	37.1	11.2	34.2	0.8	2.9	3655	285.7	410	Yes	None	No	NA	None	None	NA	None	No	No	No	No		
96	27	36	1	No	No	No	No	No	No	No	No	No	No	No	No	No	A	1.7	56	19.38	Multigravida	Emergency LSCS	Previous LSCS	12.1	34.9	11.2	34.1	0.9	0.8	4760	109.11	320	Yes	None	No	NA	None	None	NA	None	No	No	No	No		
97	29	37	2	No	No	No	No	No	No	No	Yes	No	No	No	No	No	B	1.55	58	24.14	Multigravida	Emergency LSCS	Abrupton	11.8	35.8	10.5	31.5	1.3	4.3	4930	592.15	1160	Yes	None	No	NA	None	None	NA	None	No	Yes	No	No		
98	23	38	4	No	No	No	No	No	No	No	No	No	No	No	No	No	A	1.65	58	21.3	Multigravida	Elective LSCS	Previous LSCS	12.6	38	12.2	36.8	0.4	1.2	4930	155.68	270	Yes	None	No	NA	None	None	NA	None	No	No	No	No		
99	24	40	2	No	No	No	No	Yes	No	No	No	No	No	No	No	No	B	1.59	49	19.38	Primigravida	Emergency LSCS	CPD	12.9	40	11.4	35.8	1.5	4.2	4165	437.33	460	Yes	None	No	Yes	1.5g	None	NA	None	No	No	No	No		
100	23	38	3	No	No	No	No	Yes	No	No	No	No	No	No	No	No	A	1.66	58	21.05	Primigravida	Emergency LSCS	Imminent eclampsia	12.4	35.7	7.4	29.4	5	6.3	4930	870	680	Yes	None	No	NA	None	None	NA	None	No	No	No	No		
101	32	37	2	No	No	No	No	No	No	No	No	No	No	No	No	No	B	1.59	49	19.38	Multigravida	Emergency LSCS	Previous LSCS	11.2	32.6	8.9	24.9	2.3	7.7	4165	983.76	350	Yes	None	No	NA	None	None	NA	None	No	No	No	No		
102	25	38	6	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	B	1.77	70	22.34	Multigravida	Elective LSCS	Previous LSCS	11.5	36.5	11	35.3	0.5	1.2	5950	195.62	350	Yes	None	No	NA	None	None	NA	None	No	No	No	No	
103	27	37	1	No	No	No	No	No	No	No	No	Yes	No	No	No	No	B	1.68	48	17.01	Multigravida	Emergency LSCS	Fetal Distress	12.1	35.9	8.8	26.7	3.3	9.2	4080	1045.57	560	Yes	Carboprost, Misoprostol	No	NA	None	Parenteral Iron	500mg	None	No	No	No	No	No	No
104	26	38	1	No	No	No	No	No	No	Yes	No	No	No	No	No	No	A	1.62	56	21.34	Multigravida	Emergency LSCS	Fetal Distress	10.3	31.7	10	30.9	0.3	0.8	4760	120.13	390	Yes	None	No	NA	None	None	NA	None	No	No	No	No		
105	21	37	6	No	No	No	No	No	No	No	No	No	No	No	No	No	A	1.58	51	20.43	Multigravida	Elective LSCS	Previous LSCS	11.2	35.3	10.4	31.9	0.8	3.4	4335	417.54	320	Yes	None	No	NA	None	None	NA	None	No	No	No	No		
106	30	39	5	No	No	No	No	No	No	No	No	Yes	No	No	No	No	B	1.55	49	20.4	Multigravida	Emergency LSCS	Thick MSL	12.9	40.3	12.7	38.8	0.2	1.5	4165	155.02	540	Yes	None	No	NA	None	None	NA	None	No	No	No	No		
107	30	39	6	No	No	No	No	No	No	No	No	No	No	No	No	No	B	1.62	51	19.43	Multigravida	Emergency LSCS	Fetal Distress	11.6	35	10.8	32.4	0.8	2.6	4335	322.03	480	Yes	None	No	NA	None	None	NA	None	No	No	No	No		
108	24	37	1	No	No	No	No	No	No	No	No	No	No	No	No	No	A	1.57	47	19.07	Multigravida	Elective LSCS	Previous LSCS	12.2	37.6	12	35	0.2	2.6	3995	276.25	350	Yes	None	No	NA	None	None	NA	None	No	No	No	No		
109	38	37	0	No	No	No	No	No	No	Yes	No	No	No	No	No	Yes	No	A	1.57	43	17.44	Multigravida	Emergency LSCS	Fetal Distress	10.1	32.9	9.6	28.7	0.5	4.2	3655	466.6	410	Yes	None	No	NA	Adhesiolysis	Parenteral Iron	500mg	None	No	No	No	No	No
110	22	38	1	No	No	No	No	No	No	No	No	Yes	No	Yes	No	No	A	1.55	47	19.56	Multigravida	Emergency LSCS	Previous LSCS	11.3	35.1	10	33.8	1.3	1.3	3995	147.96	450	Yes	None	No	NA	None	None	NA	None	No	No	No	No		
111	23	38	3	No	No	No	No	No	No	Yes	No	No	No	No	No	No	A	1.65	49	18	Multigravida	Elective LSCS	Previous LSCS	10.7	39.7	10.2	31.4	0.5	8.3	4165	870.77	520	Yes	None	No	NA	None	None	NA	None	No	No	No	No		
112	19	38	3	No	No	No	Yes	No	No	No	No	No	No	No	No	No	A	1.58	45	18.03	Primigravida	Emergency LSCS	Fetal Distress	11.9	38.1	10	29.4	1.9	8.7	3825	873.43	380	Yes	None	No	NA	None	None	NA	None	No	No	No	No		
113	24	38	2	No	No	No	No	No	No	No	No	No	No	No	No	No	A	1.69	49	17.16	Multigravida	Emergency LSCS	Previous LSCS	12.3	37.9	11.6	35.1	0.7	2.8	4165	307.7	480	Yes	None	No	NA	None	None	NA	None	No	No	No	No		
114	28	37	2	No	No	No	No	No	No	No	No	No	No	No	No	No	B	1.65	52	19.1	Multigravida	Emergency LSCS	Previous LSCS	12.7	38	11	36	1.7	2	4420	232.63	400	Yes	None	No	NA	None	None	NA	None	No	No	No	No		
115	22	39	6	No	No	No	No	No	No	Yes	No	No	No	No	No	Yes	No	A	1.66	58	21.05	Multigravida	Emergency LSCS	Previous LSCS	10.3	32.18	10.3	31.5	0	0.68	4930	104.18	340													

