International Journal of Medical Science and Clinical Research Studies

ISSN(print): 2767-8326, ISSN(online): 2767-8342

Volume 04 Issue 09 September 2024

Page No: 1675-1685

DOI: https://doi.org/10.47191/ijmscrs/v4-i09-15, Impact Factor: 7.949

Efficacy of Tranexamic Acid in Reducing Blood Loss Following Vaginal Delivery: A Double-Blind Randomized Controlled Trial

Dr. Kusum Saini[1]*, Dr. Pushpa Nagar[2], Dr. Neha[3]

[1,2,3] Department of Obstetrics and Gynaecology, SMS Medical College, Jaipur, India

ABSTRACT

Background: Postpartum haemorrhage (PPH) is a major cause of maternal mortality worldwide. This study aimed to evaluate the efficacy of tranexamic acid (TXA) in reducing blood loss following vaginal delivery in an Indian setting.

Method: A double-blind, randomized controlled trial was conducted at SMS Medical College, Jaipur, from April 2023 to October 2023. A total of 130 women undergoing vaginal delivery were randomly assigned to receive either 1g of TXA (Group A) or placebo (Group B) intravenously within 2 minutes of delivery. Blood loss was measured using graduated drapes and weighed swabs. Secondary outcomes included estimation of change in hemoglobin and hematocrit levels, need for additional uterotonics, and blood transfusions. Statistical analysis was performed using IBM SPSS version 23.0.0.

Results: The TXA group demonstrated a significant reduction in mean blood loss (347.23 ± 96.92 ml) compared to the placebo group (399.07 ± 98.08 ml, $p = 0.003$). Hemoglobin and hematocrit levels were significantly higher in the TXA group post-delivery (hemoglobin: 9.97 ± 0.80 gm%, $p < 0.001$; hematocrit: 37.47 ± 1.55%, $p = 0.001$). Additionally, fewer patients in the TXA group required additional uterotonics (7.6% vs. 21.53%, $p = 0.025$) and blood transfusions (3.07% vs. 12.30%, $p = 0.048$). Hospital stay was shorter for the TXA group ($p = 0.048$).

Conclusion: Prophylactic administration of TXA significantly reduces blood loss following vaginal delivery, decreases the need for additional uterotonics, and shortens hospital stay. These findings suggest that TXA can be a valuable tool in the prevention of PPH, particularly in resource-limited settings.

KEYWORDS: Postpartum haemorrhage, Tranexamic acid, Vaginal delivery, Blood loss, Maternal mortality.

ARTICLE DETAILS

Published On:
24 September 2024

Available on:
https://ijmscr.org/

INTRODUCTION

Postpartum haemorrhage (PPH) is a critical obstetric complication and remains one of the leading causes of maternal mortality and morbidity worldwide [1]. According to the World Health Organization (WHO), PPH accounts for approximately 27% of maternal deaths globally, with a disproportionately higher incidence in low- and middle-income countries [2]. Every year, about 14 million women experience PPH resulting in about 70,000 maternal deaths globally [3]. Its distribution varies across regions with the highest prevalence of 5.1%25.7% in Africa, 4.3%-13% in North America and 1.9%-8% in Asia [4]. With the advent of prevention strategies, better treatment options and improved quality of health care, the incidence of PPH has reduced, progressively reducing maternal mortality and morbidity. The MMR in India has decreased gradually from 130 in 2014-2016 to 97 in 2018-20, with fluctuations of 122 in 2015-17, 113 in 2016-18, and 103 in 2017-19 [5].

WHO defined PPH as a condition in which the patient becomes haemodynamically unstable, as evidenced by tachycardia and hypotension, as a result of blood loss of more than 500ml or any quantity of bleeding from or into the genital tract following the birth of the baby to the end of the puerperium (6 weeks) [6]. Historically, it has been challenging to define PPH. In situations of sudden haemorrhage or in resource-poor settings, the delay of

appropriate intervention may result from waiting for a patient to satisfy PPH criteria. If left untreated, any haemorrhage that has the potential to lead to haemodynamic instability should be classified as PPH and managed accordingly. Average blood loss after vaginal delivery, caesarean section, and caesarean hysterectomy is 500 ml, 1000 ml, and 1500 ml, respectively [7]. Depending upon the amount of blood loss, PPH can be classified as minor (500ml-1L), moderate (1-2L) and severe PPH (>2L) [8].

In the literature, (PPH) is classified into two types. The first type is primary PPH, which is defined as the loss of 500 mL or more of blood from the genital tract within the first 24 hours following the birth of the baby [9]. Primary PPH accounts for more than 99% of all PPH cases. The second type is secondary PPH, which refers to haemorrhage occurring beyond the initial 24 hours and within six weeks postpartum [10].

Despite the identification of several risk factors, many instances of PPH occur unexpectedly. The predisposing factors contributing to PPH include a range of personal, antepartum, intrapartum, and miscellaneous causes. Personal factors such as advanced maternal age, multiparity, anemia, malnutrition, and a history of previous PPH, placenta previa, or accreta, as well as bleeding or coagulation disorders and the presence of fibroid uterus, play a critical role [11]. Antepartum factors such as an overdistended uterus—seen in cases of multiple pregnancies, large-sized fetuses, or polyhydramnios—antepartum haemorrhage, and chorioamnionitis also contribute significantly [11]. During labor, factors such as induction, prolonged labor, precipitate labor, instrumental delivery, operative manipulation, uterine rupture, genital tract trauma, and the non-judicious use of oxytocics and sedatives can exacerbate the risk [11]. Miscellaneous causes, including sepsis, further complicate the risk landscape [11].

The most common etiologies of primary PPH are categorized as Tone, Trauma, Tissue, and Thrombin. Tone refers to uterine atony, which accounts for approximately 70% of PPH cases and is characterized by ineffective contraction and retraction of uterine muscle fibers after placental separation [12]. Trauma includes genital tract injuries such as lacerations in the cervix, vagina, perineum, paraurethral regions, and uterine rupture, contributing to about 20% of PPH cases. Tissue-related causes involve retained products of conception and blood clots, which can delay uterine involution [13]. Thrombin pertains to coagulopathy, where conditions such as Immune Thrombocytopenic Purpura (ITP), Thrombotic Thrombocytopenic Purpura (TTP), von Willebrand's disease, and haemophilia affect blood coagulation and may lead to PPH [13]. Additional rare causes include uterine inversion, rupture, and abnormal placentation [14-16].

Current management strategies for postpartum haemorrhage (PPH) focus on a combination of preventive measures and active interventions to reduce incidence and severity. Prevention of PPH includes antenatal care, such as routine screening for anaemia, planning deliveries with skilled attendants, and identifying high-risk pregnancies for delivery in well-equipped hospitals [17]. During labor, supportive care, limiting induction and augmentation, and avoiding unnecessary interventions help mitigate risk [18]. The third stage of labor, the critical period immediately following childbirth, is managed actively to prevent PPH through the Active Management of the Third Stage of Labor (AMTSL). This involves administering uterotonics, controlled cord traction, and delayed cord clamping to facilitate the delivery of the placenta and reduce bleeding [19-21]. Oxytocin is the primary uterotonic used due to its effectiveness in inducing uterine contractions and minimizing blood loss [21]. Methylergometrine, another key drug, promotes uterine contraction but is contraindicated in patients with hypertension [22]. Carboprost, a synthetic prostaglandin F2α analogue, enhances uterine contractility and is useful in cases where oxytocin is ineffective, though it can have side effects such as nausea and diarrhoea [22]. Misoprostol, a prostaglandin E1 analog, is an alternative when other uterotonics are unavailable and are particularly valued for its stability and ease of administration [22].

Despite their efficacy, oxytocin and other uterotonics may not always be sufficient, especially in cases of severe or refractory PPH, necessitating the exploration of adjunctive therapies [23]. In this context, tranexamic acid (TXA), a synthetic antifibrinolytic agent, has garnered attention for its potential to reduce blood loss by inhibiting fibrinolysis and stabilizing formed clots [24].

TXA has been extensively studied in various surgical settings, including orthopedic and cardiac surgeries, where it has been shown to significantly reduce perioperative blood loss and the need for transfusions [25]. In obstetrics, the landmark WOMAN trial demonstrated that TXA reduces mortality due to bleeding in women with PPH when administered within three hours of childbirth [26]. Previously, studies on the European and African populations have shown TXA to be effective in preventing PPH [27-29]. Given the high rates of PPH and its impact on maternal health, exploring TXA's preventive role in the Indian context could enhance current practices and improve outcomes in settings with limited resources.

Therefore, the study aims to evaluate the efficacy of TXA in reducing blood loss following vaginal delivery in an Indian setting through a double-blind, randomized, controlled trial. By determining whether early administration of TXA can serve as an effective prophylactic intervention against PPH, this research seeks to contribute valuable insights into the optimization of obstetric care and the reduction of maternal mortality rates in India.

METHODS

Study Design and Setting

This study was a double-blind, randomized controlled trial conducted at the Department of Obstetrics and Gynecology, SMS Medical College, Jaipur, in the time period from April 2023 to October 2023. Ethical approval was obtained from the institutional review board (Reg. No. 502/MC/EC/2023 on 12th March 2023) of SMS Medical College, Jaipur, India and informed consent was obtained from all participants after meeting inclusion criteria.

Participants

A total of 130 women were recruited for this study, with 65 participants allocated to each of the two groups. The sample size was determined based on a statistical formula for comparing two groups [30],

Sample size = $2SD^2 (Z_{\alpha/2} + Z_{\beta})^2/d^2$ which accounted for the standard deviation of blood loss in the treatment group (SD = 119.8 ml) [29], a type I error rate (Zα/2Z_{\alpha/2}Zα/2) of 1.96 at a 5% significance level, a power (ZβZ_{\beta}Zβ) of 0.84 corresponding to 80% power, and a minimum detectable mean difference (d) of 60 ml. This calculation recommended a minimum of 63 participants per group, which was rounded up to 65 participants per group to ensure adequate power for the study (Figure 1).

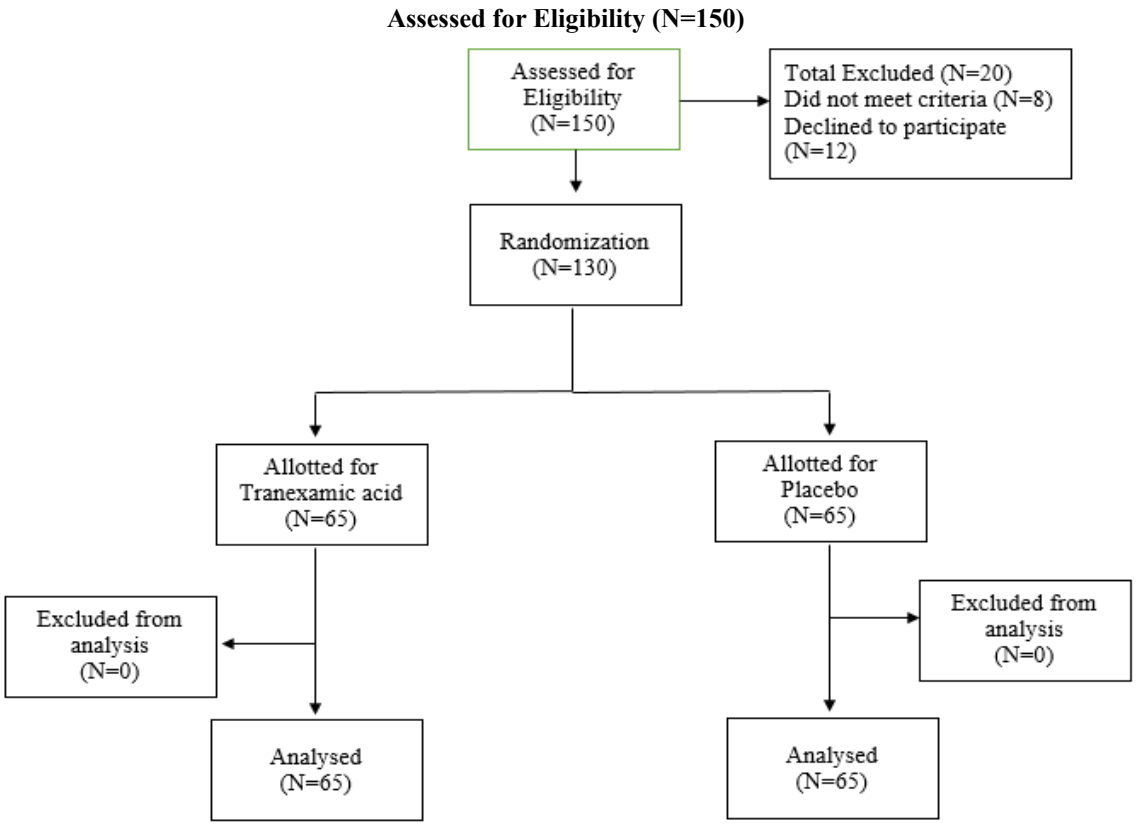

Figure 1. Flow of the study participants.

Inclusion Criteria

Participants were eligible for inclusion if they met the following criteria:

1. Primigravida or second gravida.
2. Singleton pregnancy.
3. Cephalic presentation of the fetus.
4. Gestational age of more than 38 weeks.
5. Spontaneous or induced labor.
6. Absence of contraindications to the use of tranexamic acid, and provision of informed consent.

Exclusion Criteria

Women were excluded from the study if they met any of the following criteria:

1. History of thromboembolism, autoimmune diseases, sickle cell disease, bleeding disorders, renal disease, liver pathology, known cardiovascular disease, or use of anticoagulants.
2. Intrauterine fetal death.
3. History of previous uterine surgery.
4. Presence of chronic hypertension, preeclampsia, eclampsia, HELLP syndrome, antepartum haemorrhage (including placenta previa and abruptio placentae), ruptured uterus, or varicose veins with an increased risk of deep vein thrombosis; history of epilepsy or seizures.
5. Risk factors for postpartum haemorrhage, including hemoglobin levels less than 8 g/dL, twin pregnancy,

polyhydramnios, estimated fetal weight greater than 4 kg, previous history of postpartum haemorrhage, fibroids complicating pregnancy, or parity of two or more.

This comprehensive inclusion and exclusion criteria aimed to select a homogenous group of participants and minimize confounding factors, thereby ensuring the validity and reliability of the study's outcomes.

Randomization and Blinding:

Participants were randomly allocated into Group A (tranexamic acid group) or Group B (placebo group) using a coin toss. A total of 65 patients were assigned to each group. To ensure allocation concealment, the Sequentially Numbered Opaque Sealed Envelope (SNOSE) method was employed. Each envelope, numbered 1–130, contained a slip labeled 'tranexamic acid' or 'placebo,' along with the respective drug or placebo. Randomization was carried out by a statistician and an obstetrician, while a hospital pharmacist handled the concealment process. The pharmacist remained blinded throughout the study. All envelopes were securely stored and accessible to the research team only. Upon meeting inclusion criteria and signing informed consent, participants were given a sequential study number and corresponding sealed envelope.

Intervention Dose

Group A received 1g of tranexamic acid administered intravenously over 30–60 seconds within 2 minutes of delivery, followed by prophylactic oxytocin after cord clamping.

Group B received 10 ml of normal saline for injection intravenously over 30-60 seconds, within 2 minutes after birth, and prophylactic oxytocin administration once the cord had been clamped.

Study Procedure

Participants admitted for vaginal delivery were recruited after informed consent was obtained. Their antenatal records were reviewed, and detailed medical and obstetric histories were recorded. Baseline investigations, including haematocrit, hemoglobin, and urinalysis, were conducted. Gestational age was confirmed via ultrasound, and patients were admitted to the labor ward in the active phase of labor. Labor was managed actively using a partograph, with augmentation provided as indicated.

At delivery, the assigned sealed envelope was handed to the labor ward officer by a researcher or research assistant. The officer administered the drug or placebo within 30–60 seconds, within 2 minutes of delivery. The used envelopes were resealed and stored separately for unblinding at the study's conclusion.

AMTSL was performed for all patients according to departmental protocol, involving cord clamping, administration of oxytocin, and controlled cord traction [20]. Additional uterotonics or surgical interventions were provided as necessary to control excessive bleeding. Blood transfusions were given when required, and all interventions were documented.

Measurement of Blood Loss

Blood loss was measured using a disposable, graduated, conical drape placed under the patient immediately after delivery (Figure 2). The blood collected in the drape was transferred to a transparent plastic measuring cylinder, and the volume was documented. In addition, pre-weighed swab pads were used to estimate blood loss in the first two hours postpartum (Figure 3). The pads were re-weighed, and the difference in weight (in grams) was converted to millilitres, with 1g of weight equating to 1 ml of blood.

Total blood loss (ml) = blood in the drape (ml) + blood absorbed by the pads (swab weight post-delivery in gms – swab weight pre-delivery in gms) Blood loss exceeding 500ml was classified as PPH [20].

Figure 2. conical blood collection drape

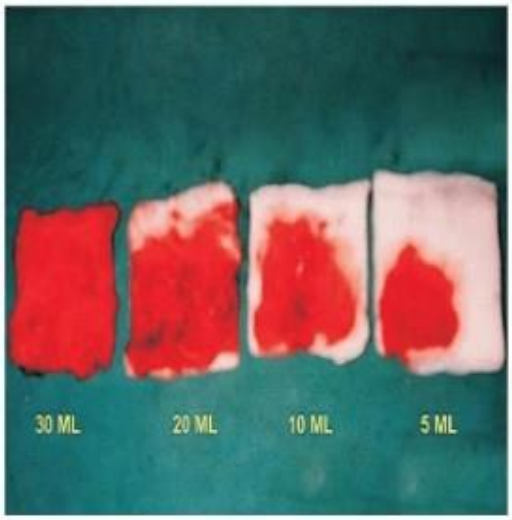

Figure 3. Swab Pads.

Monitoring and Follow-up

Patients remained under close observation in the labor ward for 1–2 hours postpartum (fourth stage of labor), during which uterine contractility and vital signs were monitored closely. Following this, they were transferred to the postnatal ward for further observation. Predelivery and post-delivery hemoglobin (Hb) and haematocrit (PCV) levels, as well as pulse rate (PR), blood pressure (BP), and respiratory rate (RR), were recorded. The need for additional uterotonic agents or blood transfusions was also noted.

Patients were expected to stay in the hospital for at least 48 hours, unless additional monitoring was required based on their clinical condition. Participants were followed up until discharge, and any unforeseen side effects were reported either in person or via phone.

Outcome Measures

The primary outcome was the amount of blood loss during vaginal delivery, quantified by measuring blood collected in the drapes and weighing blood-soaked materials. Secondary outcomes included changes in hemoglobin and haematocrit levels before delivery and 24 hours postpartum, assessed using standard laboratory methods. Additional uterotonic requirements, blood transfusions, and maternal outcomes until discharge were also evaluated [29].

Statistical Analysis

Data were collected by trained obstetric nurses who were unaware of the group assignments. The data were entered into an Excel sheet (Microsoft Corporation, Redmond, WA, USA) and analyzed using IBM SPSS version 23.0.0 (IBM, New York, USA). The normality of the data was confirmed using the Shapiro-Wilk test. Continuous variables were summarized as Mean ± SD, and categorical variables were calculated in frequency and proportions. An Independent t-test was utilized to calculate the difference in variables between both groups and to compare the categorical variables, a chi-square test was used. Furthermore, a percentage change graph was plotted for all continuous data. All statistical analyses were conducted with a predetermined significance level of 0.05.

RESULTS

The baseline characteristics of the participants were similar between the tranexamic acid and placebo groups, with no significant differences in age, socio-economic status, gestational age, parity, as well as height and weight, onset of labor, mode of delivery and changes in the duration of the third stage (Table 1).

Table 1. Demographic characteristics of the patients

Variables	TXA Group (N = 65) Freq. (%)	Placebo Group (N = 65) Freq. (%)	*p-value*
Age – years (Mean ± SD)	25.92 ± 3.63	26.12 ± 4.37	0.777
≤20 years	4 (6.15)	4 (6.15)	
21-24 years	31 (48)	34 (520	0.645
25-29 years	26 (40)	23 (36)	
>30 years	4 (6.15)	4 (6.15)	
Socio-economic status			
Upper class	1 (1.5)	2 (3)	
Upper middle class	3 (4.6)	2 (3)	
Lower middle class	30 (46)	28 (43)	0.727
Upper lower class	11 (16.9)	12 (18)	
Lower class	20 (30.7)	21 (33)	
Gravidity/Parity			
Primigravida	16 (24.61)	22 (33.84)	
2nd Gravida G2P1	35 (53.8)	31 (47.69)	0.250
G2A1	14 (21.5)	12 (18.46)	
Weight - kg (Mean ± SD)	55.2 ± 1.79	55.1 ± 1.67	0.7349
Height - cm (Mean ± SD)	154.26 ± 1.87	153.76 ± 1.70	0.1059
Onset of labor			
Spontaneous	38 (58)	35 (54)	0.596
Induced	27 (42)	30 (44)	
Mode of delivery			

Without episiotomy / perineal tear	46 (72)	39 (60)	
With Episiotomy	14 (22)	23 (36)	0.195
With perineal tear	5 (6)	3 (4)	
Changes in duration of third stage – minutes (Mean ± SD)	4.60 ± 0.62	4.45 ± 0.47	0.121

Onset of labor

All the vital signals before delivery were similar in the TXA group compared to the placebo group (Table 2). The systolic BP after 1 hour of delivery showed a significant difference between the two groups (114.06 ± 7.03 mmHg in the TXA group vs. 111.60 ± 7.09 mmHg in the placebo group, p = 0.049). Diastolic BP also differed significantly after 1 hour of delivery (74.95 ± 5.72 mmHg in the TXA group vs. 72.64 ± 5.51 mmHg in the placebo group, p = 0.021). The pulse rate was notably higher in the placebo group after 1 hour (85.44 ± 3.24 beats per minute vs. 83.61 ± 2.83 beats per minute in the TXA group, p = 0.001). However, the respiratory rate remained statistically insignificant between both groups (p = 0.542) (Table 2).

Table 2. Maternal vital signs before and after delivery

Vital Signs	**TXA Group (N = 65) (Mean ± SD)**	**Placebo Group (N = 65) (Mean ± SD)**	***p-value***
Before delivery			
Pulse rate (beats per minute)	81.24 ± 3.07	81.44 ± 2.92	0.704
Systolic BP (mmHg)	118.33 ± 6.67	118.21 ± 6.12	0.913
Diastolic BP (mmHg)	77.16 ± 4.80	77.07 ± 4.70	0.912
Respiratory rate (per minute)	16.83 ± 1.60	16.83 ± 1.60	1.000
After 1 hour of delivery			
Pulse rate (beats per minute)	83.61 ± 2.83	85.44 ± 3.24	**0.001***
Systolic BP (mmHg)	114.06 ± 7.03	111.60 ± 7.09	**0.049***
Diastolic BP (mmHg)	74.95 ± 5.72	72.64 ± 5.51	**0.021***
Respiratory rate (per minute)	18.03 ± 0.84	18.12 ± 0.87	0.542

* Significant, $p < 0.05$.

The mean blood loss was significantly lower in the TXA group (347.23 ± 96.92 ml) compared to the placebo group (399.07 ± 98.08 ml), with a mean difference of 51.84 ml (p = 0.003). Hemoglobin and Haematocrit levels before delivery were not significantly different between the two groups (p = 0.389), but after 24 hours of delivery, the fall in haemoglobin level was less in the TXA group (9.97 ± 0.80 gm %) compared to the placebo group (9.42 ± 0.90 gm %), (p < 0.001). Similarly, fall in Haematocrit levels was also significantly less in the TXA group (37.47 ± 1.55 %) after 24 hours of delivery compared to the placebo group (36.34 ± 2.16 %) (p = 0.001) (Table 3).

Table 3. Blood indices before and after delivery

Variables	**TXA Group (N = 65) (Mean ± SD)**	**Placebo Group (N = 65) (Mean ± SD)**	***p-value***
Blood loss (ml)	347.23 ± 96.92	399.07 ± 98.08	**0.003***
Before delivery			
Hemoglobin (gm %)	10.86 ± 0.81	10.99 ± 0.88	0.3.89
Haematocrit (%)	38.40 ± 2.97	38.01 ± 2.58	0.429

After 24 hours of delivery			
Hemoglobin (gm %)	9.97 ± 0.80	9.42 ± 0.90	**< 0.001***
Haematocrit (%)	37.47 ± 1.55	36.34 ± 2.16	**0.001***

* Significant, $p < 0.05$.

In terms of additional interventions, fewer patients in the TXA group (7.6%) required additional uterotonics compared to the placebo group (21.53%), and this was statistically significant (p = 0.025). Blood transfusions were also less frequent in the TXA group (3.07% vs. 12.30% in the placebo group, p = 0.048) (Table 4). Blood loss greater than 500 ml was significantly less in the TXA group (3.07%) compared to the placebo group (12.30%, p =0.04).

Table 4. Pre and post delivery variables in both groups

Variables	TXA Group (N = 65) Freq. (%)	Placebo Group (N = 65) (Freq. (%)	*p-value*
Blood loss > 500 (ml)	2 (3.07 %)	8 (12.30 %)	**0.04***
Additional interventions			
Uterotonics	5 (7.6 %)	14 (21.53 %)	**0.025***
Blood transfusion	2 (3.07 %)	8 (12.30 %)	**0.048***
Maternal complications			
Hypotension	2 (3.07 %)	6 (9.23 %)	0.144
Vomiting/Diarrhea	5 (7.69 %)	8 (12.30 %)	0.381
Duration of stay in hospital			
≤ 2 days	63 (96.92 %)	57 (87.70 %)	**0.048***
> 2 days	2 (3.07 %)	8 (12.30 %)	

* Significant, $p < 0.05$.

Maternal complications, such as hypotension and vomiting/diarrhea, were observed more in the placebo group, although the differences were not statistically significant (p = 0.144 and p = 0.381, respectively). Duration of stay in the hospital was shorter for most patients in the TXA group, with 96.92% staying ≤ 2 days compared to 87.70% in the placebo group (p = 0.048) (Table 4). Additionally, the pre to post intervention percentage change in vital signs and blood indices is presented in Figure 4.

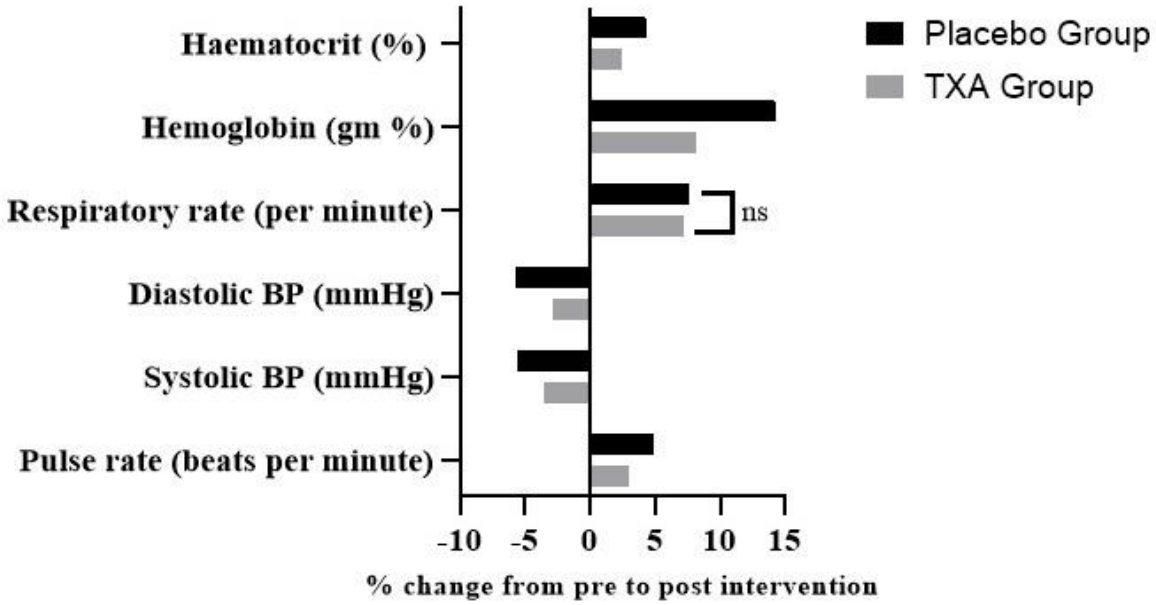

Figure 4. Percentage change (relative) in vital signs and blood indices in both groups from pre to post-intervention.

DISCUSSION

Postpartum haemorrhage (PPH) remains one of the leading causes of maternal mortality worldwide, contributing to nearly one-quarter of maternal deaths. The use of antifibrinolytic agents, such as Tranexamic Acid (TXA), has emerged as a promising preventive measure, particularly in reducing obstetric blood loss during and after vaginal delivery. This study aimed to assess the efficacy of prophylactic TXA administration following delivery to reduce blood loss and the need for additional interventions.

In our study, the age distribution and socioeconomic status of participants were similar to previous research. Most women were between 20-24 years of age, aligning with the findings of Yang et al. [31], and the majority belonged to the lower-middle and lower socioeconomic classes, as observed in studies by Shamshad Bibi et al. [32].

Moreover, the majority of women in this study were second gravidas, with 75.3% in the study group and 66.15% in the control group. Anthropometric measures such as mean height and weight were consistent across groups, and similar to the findings of Chitra Devi et al. [33], reinforcing that these variables likely did not significantly affect outcomes.

The vital signs measured before and after delivery revealed a slight but significant difference between the two groups after one hour of delivery. The TXA group showed a less increase in the pulse rate and a less fall in systolic and diastolic blood pressure compared to the placebo group, indicating that TXA may have contributed to stabilizing these parameters postdelivery by reducing the amount of blood loss. These findings are consistent with the results reported by Novikova et al. [34], who found a statistically significant change in vital signs postpartum. However, the findings diverge from those of Igboke et al. [29], who observed no significant differences in systolic or diastolic BP or pulse rates.

The primary focus of this study was the reduction in blood loss during and after vaginal delivery. The results showed a significant reduction in blood loss in the TXA group compared to the placebo group, with mean blood loss of 347.23 ml versus 399.07 ml, respectively. This finding is supported by similar studies, such as those by Novikova et al. [34] and Igboke et al. [29], both of which demonstrated that TXA effectively reduces postpartum blood loss. The reduction in the need for additional uterotonics and blood transfusions further supports the efficacy of TXA, with only 7.6% of women in the TXA group requiring uterotonics compared to 21.53% in the placebo group ($p = 0.025$), and 3.07% of women in the TXA group needing blood transfusions compared to 12.30% in the placebo group ($p = 0.048$). These results are in line with the findings of Sentilhes et al. [28] and Igboke et al. [29], who also observed the reduced need for additional interventions with TXA administration. Blood loss greater than 500 ml was significantly reduced in the TXA group compared to the placebo group a finding consistent with the study by Gungorduk et al. [37], who reported a significant reduction in blood loss >500 ml ($p < 0.01$).

Furthermore, the significant reduction in hemoglobin and hematocrit levels post-delivery in the control group compared to the TXA group ($p < 0.001$) further corroborates the effectiveness of TXA in mitigating blood loss. These results align with studies by Neumann [35] and Igboke [29], where similar reductions in hemoglobin and hematocrit levels were observed in the control groups [28,29,37], supported by Figure 4 which demonstrates notable differences ($p<0.05$) between the Placebo and TXA groups in terms of physiological changes following the intervention except the respiratory rate which remains largely unchanged in both groups ($p>0.05$).

In terms of side effects, the incidence of hypotension and gastrointestinal issues such as vomiting and diarrhea was slightly higher in the placebo group, but these differences were not statistically significant. These findings are consistent with studies by Novikova et al. [34] and Igboke et al. [29], which reported no major complications associated with TXA use. No major maternal side effects or deaths were recorded, which is consistent with the findings of similar studies [28,31, 38,39], suggesting that TXA does not adversely impact maternal outcomes.

The overall length of hospital stay was shorter in the TXA group, with only 3.07% of women needing to stay for more than two days compared to 12.30% in the control group ($p = 0.048$). This reduced hospital stay has important implications for healthcare systems, particularly in low-resource settings, as it could alleviate bed occupancy rates and reduce healthcare costs. Similar findings were reported by Roy et al. [36], who also found a significant difference in the duration of hospital stay post-delivery in women receiving TXA.

Finally, this study demonstrates that prophylactic administration of Tranexamic Acid significantly reduces blood loss during vaginal deliveries, decreases the need for additional uterotonics and blood transfusions, and results in shorter hospital stays without major complications. These findings align with global efforts to reduce maternal mortality by mitigating the risk of PPH, particularly in low-resource settings. Further research is warranted to explore the long-term benefits of widespread TXA use in obstetric care.

Limitations

This study has a few limitations. First, it was conducted at a single center, which may limit the generalizability of the findings to other settings. Second, the exclusion criteria, which included women with high-risk pregnancies and those with pre-existing medical conditions, may limit the applicability of the results to the general obstetric population. Third, while the study was adequately powered to detect differences in blood loss, it may not have been sufficiently powered to detect rare adverse events associated with TXA use. Additionally, the assessment of blood loss was limited to within 2 h of delivery.

CONCLUSION

The tranexamic acid injection is a cost effective solution in reducing blood loss following vaginal delivery and may serve as a valuable prophylactic intervention for PPH. Its use could enhance maternal outcomes, particularly in resource-limited settings where the burden of PPH is high. Further research in diverse populations and settings is recommended to confirm these findings and to explore the long-term safety of tranexamic acid in obstetric practice.

ACKNOWLEDGEMENTS

The authors wish to thank the doctors, nurses, and other healthcare staff in the Department of Obstetrics and Gynaecology of SMS Medical College and the attached hospital for their help in data collection.

AUTHORS FUNDING

No financial support was received for the conduct of this study, or for the preparation or publication of the manuscript.

CONFLICT OF INTEREST

None.

AUTHOR'S CONTRIBUTION

Kusum Saini conceived the study design. Kusum Saini and Pushpa Nagar conducted the formal analysis of the data. Kusum Saini, Pushpa Nagar and Neha drafted the manuscript. All authors read and approved the final version of the manuscript for publication.

AVAILABILITY OF DATA AND MATERIAL

All data generated during the study is included in the manuscript in the form of Table(s) or Figure(s). Any other data requirement can be directed to the corresponding author upon reasonable request.

REFERENCES

I. Khan KS, Wojdyla D, Say L, Gülmezoglu AM, Van Look PF. WHO analysis of causes of maternal death: a systematic review. Lancet. 2006 Apr 1;367(9516):106674.
II. Say L, Chou D, Gemmill A, Tunçalp Ö, Moller AB, Daniels J, et al. Global causes of maternal death: a WHO systematic analysis. Lancet Glob Health. 2014 Jun;2(6).
III. WHO Postpartum Haemorrhage Summit. Postpartum haemorrhage (PPH): a global public health concern. March 7-10, 2023.
IV. Calvert C, Thomas SL, Ronsmans C, Wagner KS, Adler AJ, Filippi V. Identifying regional variation in the prevalence of postpartum haemorrhage: a systematic review and meta-analysis. PLoS One. 2012 Jul 23;7(7).
V. Ministry of Health and Family Welfare. WHO: A roadmap to combat postpartum haemorrhage between 2023 and 2030. 2022 Nov 30.
VI. Dutta DC. Textbook of Obstetrics. 7th ed. New Delhi: Jaypee Brothers Medical Publishers; 2013. p. 410.
VII. Royal College of Obstetricians and Gynaecologists. Prevention and Management of Postpartum Haemorrhage Green-top Guideline No. 52. 2016 Dec 16.

VIII. Mousa HA, Blum J, Abou El Senoun G, Shakur H, Alfirevic Z. Treatment for primary postpartum haemorrhage. Cochrane Database Syst Rev. 2014;(2).

IX. Alexander J, Thomas P, Sanghera J. Treatments for secondary postpartum haemorrhage. Cochrane Database Syst Rev. 2002;(1).

X. Thornburg KL, Jacobson SL, Giraud GD, Morton MJ. Hemodynamic changes in pregnancy. Semin Perinatol. 2000 Feb;24(1):11-4.

XI. Escobar MF, Hidalgo AM, Fonseca C, et al. FIGO recommendations on the management of postpartum haemorrhage. Int J Gynaecol Obstet. 2022 Sep;159(Suppl 1):1-48.

XII. Anderson JM, Etches D. Prevention and management of postpartum haemorrhage. Am Fam Physician. 2007 Mar 15;75(6):875-82.

XIII. Oyelese Y, Ananth CV. Postpartum haemorrhage: epidemiology, risk factors, and causes. Clin Obstet Gynecol. 2010 Mar;53(1):147-56.

XIV. ACOG Committee on Practice Bulletins—Obstetrics. ACOG Practice Bulletin: Clinical Management Guidelines for Obstetrician-Gynecologists Number 76, October 2006: postpartum haemorrhage. Obstet Gynecol. 2006;108(4):1039-47.

XV. Westhoff G, Cotter AM, Tolosa JE. Prophylactic oxytocin for the third stage of labor to prevent postpartum haemorrhage. Cochrane Database Syst Rev. 2013 Oct 1;(10).

XVI. Andersen HF, Hopkins MP. Postpartum Haemorrhage. Glob Libr Women's Med [Internet]. 2008 [cited 2024 Jul 15]; Available from: https://www.glowm.com/sectionview/heading/Postpartum%20Haemorrhage/item/10138.

XVII. Fissahaye B, Dheresa M, Assefa N, et al. Active management of the third stage of labor and associated factors among maternity care providers in public health facilities in Eastern Ethiopia: a multi-center study. BMC Pregnancy Childbirth. 2023 Sep 28;23(1):701.

XVIII. Marshall JE, Raynor MD. Myles Textbook for Midwives. 15th ed. Edinburgh: Churchill Livingstone Elsevier; 2014.

XIX. Elbourne D, Prendiville W, Carroli G, Wood J, McDonald S. Prophylactic use of oxytocin in the third stage of labor. Cochrane Database Syst Rev. 2001;(4).

XX. WHO. WHO recommendations for the prevention and treatment of postpartum haemorrhage. 2012 Jan 1.

XXI. Thornton P, Douglas J. Coagulation in pregnancy. Best Pract Res Clin Obstet Gynaecol. 2010 Jun;24(3):339-52.

XXII. Kongnyuy EJ, Hofman JJ, van den Broek N. Ensuring effective essential obstetric care in resource-poor settings. Trop Doct. 2009 Sep;39(3):163-6.

XXIII. Peitsidis P, Kadir RA. Tranexamic acid in pregnancy and postpartum. Expert Opin Pharmacother. 2011 Mar;12(4):503-16.

XXIV. Henry DA, Carless PA, Moxey AJ, O'Connell D, Stokes BJ, Fergusson DA, et al.Anti-fibrinolytic use for minimizing perioperative allogeneic blood transfusion. Cochrane Database Syst Rev. 2011 Jan 19;(1).

XXV. Shakur H, Elbourne D, Gülmezoglu M, Alfirevic Z, Ronsmans C, Allen E, et al. The WOMAN Trial (World Maternal Antifibrinolytic Trial): tranexamic acid for the treatment of postpartum haemorrhage: an international randomized, double-blind placebo-controlled trial. Trials. 2010 Apr 16;11:40.

XXVI. Ducloy-Bouthors AS, Jude B, Duhamel A, et al. High-dose tranexamic acid reduces blood loss in postpartum haemorrhage. Crit Care. 2011 Apr 15;15(2).

XXVII. Sentilhes L, Winer N, Azria E, Sénat MV, Le Ray C, Vardon D, et al. Tranexamic acid for the prevention of blood loss after vaginal delivery. N Engl J Med. 2018 Aug 23;379(8):731-42.

XXVIII. Igboke FN, Obi VO, Dimejesi BI, et al. Tranexamic acid for reducing blood loss following vaginal delivery: a double-blind randomized controlled trial. BMC Pregnancy Childbirth. 2022 Mar 18;22(1):178.

XXIX. Mirghafourvand M, Mohammad-Alizadeh S, Abbasali-Zadeh F, Shirdel M. The effect of prophylactic intravenous tranexamic acid on blood loss after vaginal delivery in women at low risk of postpartum haemorrhage: a double-blind randomized controlled trial. Aust N Z J Obstet Gynaecol. 2015 Feb;55(1):53-8.

XXX. Charan J, Biswas T. How to calculate sample size for different study designs in medical research. Indian J Psychol Med. 2013 Apr;35(2):121-6.

XXXI. Yang H, Zheng S, Shi C. Clinical study on the efficacy of tranexamic acid in reducing postpartum blood loss: a randomized comparative, multicenter trial. Chung-Hua Fu Chan Ko Tsa Chih. 2001 Oct;36(10):590-2.

XXXII. Bibi S, Danish N, Fawad A, Jamil M. An audit of primary postpartum haemorrhage. J Ayub Med Coll Abbottabad. 2007 Oct-Dec;19(4):102-6.

XXXIII. Devi VC, Sangeetha V, Ashwini Devi K. Role of tranexamic acid in reducing blood loss in normal labor. Int J Acad Med Pharm. 2023;5(4):306-12.

XXXIV. Novikova N, Hofmeyr GJ. Tranexamic acid for preventing postpartum haemorrhage. Cochrane Database Syst Rev. 2010 Jul 7;(7).

XXXV. Neumann BG, Metgud MC, Hoffman MK, et al. Tranexamic acid to reduce blood loss in women at high risk of postpartum haemorrhage undergoing cesarean delivery-a randomized controlled trial. AJOG Glob Rep. 2024 Jan 22;4(1):100316.

XXXVI. Roy P, Sujatha MS, Bhandiwad A, Biswas B. Role of tranexamic acid in reducing blood loss in vaginal delivery. J Obstet Gynaecol India. 2016 Oct;66(Suppl 1):246-50.

XXXVII. Gungorduk K, Asıcıoğlu O, Yıldırım G, Ark C, Tekirdağ AI, Besimoglu B. Can intravenous injection of tranexamic acid be used in routine practice with active management of the third stage of labor in vaginal delivery? A randomized controlled study. Am J Perinatol. 2013 May;30(5):407-13.

XXXVIII. Heesen M, Böhmer J, Klöhr S, Rossaint R, van de Velde M, Dudenhausen JW, et al. Prophylactic tranexamic acid in parturients at low risk for post-partum haemorrhage: systematic review and meta-analysis. Acta Anaesthesiol Scand. 2014 Sep;58(9):10758.

XXXIX. Mirghafourvand M, Mohammad-Alizadeh S, Abbasali-Zadeh F, Shirdel M. The effect of prophylactic intravenous tranexamic acid on blood loss after vaginal delivery in women at low risk of postpartum haemorrhage: a double-blind randomized controlled trial. Aust N Z J Obstet Gynaecol. 2015 Feb;55(1):53-8.