

Efficacy Of Combined Preoperative Sublingual Misoprostol And Intravenous Tranexamic Acid In Prevention Of Postpartum Haemorrhage During Elective Caesarean Section At A Tertiary Care Hospital In Central India: A Comparative Cross-Sectional Study

Dr. Mansi Shrigiriwar¹, Dr. Srishti Shubham², Dr. Kirti P Rachwani³

¹Associate Professor, Government Medical College and Hospital (GMCH), Nagpur, Maharashtra, India.

²Post Graduation, Student, Government Medical College and Hospital (GMCH), Nagpur, Maharashtra, India.

³Assistant Professor, Government Medical College and Hospital (GMCH), Nagpur, Maharashtra, India

Abstract

Introduction: Post Partum Haemorrhage (PPH) remains the leading cause of maternal mortality in India. Oxytocin alone may be inadequate in up to 40% of caesarean sections for prevention of PPH. This study evaluates a novel dual-mechanism approach using combined preoperative sublingual misoprostol and intravenous Tranexamic Acid in prevention of PPH during elective lower segment caesarean section (LSCS).

Materials and Methods: A comparative study was conducted among 110 term women undergoing elective LSCS. The intervention group (n=55) received 600 micrograms sublingual misoprostol plus 1 g intravenous Tranexamic Acid, while controls (n=55) received standard care. Blood loss was measured by suction and gravimetric methods, and outcomes were analysed using t-tests and chi-square tests.

Results: Both the groups were demographically comparable. Mean blood loss was significantly lower in the intervention group (681.8 ± 111.9 mL vs. 842.7 ± 118.0 mL, $p < 0.001$). PPH incidence reduced from 12.7% to 1.8% ($p = 0.028$). Fewer additional uterotonics (9.1% vs. 40%, $p < 0.001$), blood transfusions (1.8% vs. 12.7%, $p = 0.028$), and surgical interventions (7.3% vs. 23.6%, $p = 0.040$) were required. Postoperative haemoglobin was better preserved ($p = 0.004$). No primigravidae in the intervention group developed PPH. No major adverse events occurred.

Conclusion: Combined preoperative sublingual misoprostol and intravenous Tranexamic Acid provides superior PPH prevention compared to standard care, with significant reductions across all measured outcomes. This cost-effective, thermostable, and easily administered dual-mechanism approach addresses both uterine atony and enhanced fibrinolysis, making it particularly suitable for resource-limited settings where maternal mortality from PPH remains high.

Keywords: Post Partum Haemorrhage, caesarean section, misoprostol, Tranexamic Acid, blood loss prevention, dual prophylaxis.

INTRODUCTION

Post Partum Haemorrhage (PPH) continues to be a leading cause of maternal mortality and morbidity worldwide, with its incidence ranging between 5% to 10% of deliveries globally, responsible for approximately 27% of maternal deaths¹. India bears a substantial share of this burden, with PPH being the most common direct cause of maternal deaths, accounting for about 38% of maternal fatalities and an estimated 70,000 maternal deaths attributed to PPH annually^{2,3}. The incidence of Post Partum Haemorrhage in India is reported at 2-4% after vaginal delivery and approximately 6% following caesarean section, escalating to 15% in subsequent deliveries among rural and high-parity pregnancies.⁴

Caesarean section, while often lifesaving, carries an increased risk of Post Partum Haemorrhage, roughly double that of vaginal delivery and with uterine atony accounting for 70-90% of cases.

⁵According to the World Health Organization (WHO, 2017; reaffirm 2023), severe PPH is defined as blood loss of 1000 mL or more within 24 hours after birth, and in caesarean section context, many studies and guidelines prefer the ≥ 1000 mL threshold for defining clinically significant PPH, given the higher baseline blood loss during operative delivery.⁶

The cornerstone of Post Partum Haemorrhage prophylaxis during caesarean section is oxytocin, used to stimulate uterine contractions. However, oxytocin requires cold chain storage (4-8°C), which poses significant logistical challenges in low-resource settings⁷. These limitations underscore the need for alternative or adjunctive agents

that are stable, cost-effective, and feasible in resource-limited contexts. Nevertheless, oxytocin alone may be insufficient for a significant proportion of women, with 10-40% requiring additional uterotonic agents such as methylergometrine or prostaglandin analogues.⁸

Misoprostol is a synthetic prostaglandin E1 analogue that binds to EP2(prostaglandin E2 receptor 2), EP3(prostaglandin E2 receptor 3), and EP4(prostaglandin E2 receptor 4) receptors on uterine smooth muscle, causing strong sustained uterine contractions and myometrial tone⁹. EP 1/ EP 3 receptor activation increases intracellular calcium via phospholipase C activation, causing strong sustained uterine contractions and myometrial tone. EP 2/ EP 4 receptor activity stimulates Camp (Cyclic Adenosine Monophosphate) pathways, aiding cervical ripening and uterine involution. Its thermostability and multiple routes of administration (sublingual, oral, rectal) make it especially useful in low-resource settings where cold-chain storage for oxytocin is not feasible¹⁰. Pharmacokinetically, sublingual misoprostol provides rapid onset (8-16 minutes), high bioavailability (72%), and peak plasma concentration within 30 minutes¹¹.

Tranexamic Acid (TXA) is a synthetic lysine analogue that competitively inhibits the binding of plasminogen and plasmin to fibrin, thereby preventing the breakdown of fibrin clots (anti fibrinolytic effect)¹². By stabilizing the clot at the placental site, TXA reduces ongoing blood loss. After intravenous administration, TXA has near complete bioavailability, rapid onset of action within minutes, and a half-life of approximately two hours¹³. The latest WHO guidance (2023) strongly recommends administering 1 g of I.V. TXA within three hours of birth, in addition to standard PPH care¹⁴. The landmark WOMAN trial (2017) demonstrated that Tranexamic Acid significantly reduced death due to bleeding when given within 3 hours of childbirth¹⁵.

While both misoprostol and TXA are individually recognized for their effectiveness in managing PPH, there is scant evidence regarding their combined prophylactic use during elective lower segment caesarean sections. Combining a potent uterotonic (misoprostol) with an antifibrinolytic (Tranexamic Acid) may offer synergistic protection against intraoperative haemorrhage, particularly in settings where cold-chain storage for oxytocin is unreliable or where access to skilled care may be limited. This dual approach ensures mechanical and biochemical hemostasis, addressing both primary (uterine atony) and secondary (enhanced fibrinolysis) causes of Post Partum Haemorrhage.

Therefore, this study is designed to assess whether the combined administration of sublingual misoprostol and intravenous TXA provides superior reduction in intraoperative blood loss during elective LSCS compared with standard uterotonic therapy alone. Positive findings would support an optimized, context-appropriate protocol for PPH prevention, especially crucial in resource-constrained settings in many parts of India.

MATERIALS AND METHODS

The present study is a comparative cross-sectional study. It was conducted at the Department of Obstetrics and Gynaecology, tertiary care hospital, Central India, over a 1.5-year period, from November 2022 to March 2025, after approval from the Institutional Ethics Committee (IEC), Board of Research Studies (BORS), and Maharashtra University of Health Sciences (MUHS). The institution provides clinical training to undergraduate and postgraduate medical students, making it an appropriate setting for assessing maternal outcomes during elective caesarean sections. Participation was voluntary, and written informed consent was obtained from all participants after explaining the study objectives, procedures involved, possible risks and benefits, and voluntary nature of participation. Confidentiality of participant data was strictly maintained throughout the study period. The study population included pregnant women with singleton pregnancy at 37-42 weeks gestation, aged 18-40 years, posted for elective caesarean section under spinal anaesthesia, who provided written informed consent. Participants who were available during the data collection period were included. Pregnant women with systemic illnesses (cardiac, hepatic, renal, pulmonary diseases, hemoglobinopathies), drug allergy to misoprostol/Tranexamic Acid, thromboembolic event during pregnancy, abnormal placentation (placenta previa, abruptio placentae, morbidly adherent placenta), >2 previous caesarean sections or classical caesarean scar, previous uterine rupture, preterm delivery (<37 weeks), eclampsia, concurrent therapy with anticoagulants or long-term steroids, refusal/withdrawal from participation, or incomplete data were excluded. These criteria excluded women with pre-existing risk factors for excessive blood loss, coagulopathy, or surgical complexity, which could bias the estimation of intervention effectiveness.

Using the formula for comparing two means, with α -error of 1%, power of 90%, expected mean difference of 108.33 mL, and standard deviations from literature (42.99 and 71.88), minimum sample size was calculated as 48 per group.¹⁶ After accounting for 10% dropout, final sample size was 55 per group, total 110 participants. A

convenience sampling method was used, under which consecutive eligible cases were recruited until the desired sample size was achieved.

Participants were divided into two groups: Group 1 (Study Group; n=55) received 1000 mg intravenous TXA diluted in 100 mL normal saline, infused over 10 minutes before spinal anaesthesia, plus 600 micrograms sublingual misoprostol immediately after spinal anaesthesia and before skin incision. A 5 mL venous blood sample was taken at intravenous cannulation for baseline haemoglobin and Complete Blood Count (CBC). Group 2 (Control Group; n=55) received routine care without additional prophylactic agents. All caesarean sections were performed under spinal anaesthesia using standardized surgical technique. The interval between drug administration and delivery was recorded, and additional uterotonics, if required intraoperatively, were noted for analysis. Complete Blood Count (CBC) was repeated at 24 hours post-operatively.

The primary outcome was intraoperative blood loss (in mL), while secondary outcomes included fall in haemoglobin and haematocrit at 24 hours, requirement of additional uterotonics, requirement of blood transfusion, and surgical interventions. A pre-designed semi-structured proforma was used to capture sociodemographic details, obstetric history, indication for LSCS, co-morbidities, baseline investigations (Haemoglobin, platelet count, coagulation profile), and obstetric ultrasound findings (≥ 36 weeks).

Assessment of blood loss commenced after skin incision using multiple methods: separate suction for amniotic fluid (collected separately at uterine incision) and blood collected (pre and post delivery of baby and placenta), with assistant surgeon ensuring strict separation of fluid collections; gravimetric method where swabs/mops were weighed before and after use with digital weighing balance (1 gram weight gain = 1 millilitre blood); and recovery of blood clots during surgery. Total blood loss was calculated as: Blood in suction bottle + Net mop weight gain (in grams) + Clot volume. In the present study, postpartum haemorrhage was defined as blood loss ≥ 1000 mL, in accordance with the WHO criteria for severe postpartum haemorrhage, as the threshold of ≥ 1000 mL is increasingly recommended, particularly for caesarean sections, to improve diagnostic accuracy and clinical relevance.

Drug-delivery interval was documented, additional uterotonic requirement was recorded, total blood loss (in millilitres) was calculated as the sum of blood in suction bottle + net mop weight gain (gram) + clot volume combining suction and gravimetric methods provided a more accurate estimate than either method alone. Complete blood count were measured pre-operatively and 24 hours post-operatively. Data were entered in Microsoft Excel and analysed with Epi Info software. Quantitative variables were expressed as Mean \pm SD, and categorical variables were expressed as percentages/proportions. Statistical tests included unpaired t-test, Chi-square test, or Mann-Whitney U test as appropriate. Results were tested at significance level of $p < 0.05$.

RESULTS

A total of 110 women with singleton term pregnancies undergoing elective LSCS were included in the study and divided equally into two groups of 55 each. Both groups were comparable with respect to demographic characteristics. The majority of women were in the 26-30 years age group (26 cases each, 47.3% in both groups), followed by 21-25 years and 31-35 years age groups. The age distribution between the two groups was comparable with no significant difference ($p = 0.955$), indicating both groups were well-matched for age. Regarding parity distribution, in the Misoprostol + Tranexamic Acid group, 35 (63.6%) cases were nullipara and 20 (36.4%) cases were multipara, while in the Control group, 38 (69.1%) cases were nullipara and 17 (30.9%) cases were multipara. The common indications for caesarean section included breech presentation, cephalopelvic disproportion, history of previous LSCS, transverse lie, active genital herpes, HIV patients not on Anti-Retroviral Therapy with comparable distribution between both groups. Hence both the groups were comparable and equally balanced.

PRIMARY OUTCOME:

TABLE 1-MEAN TOTAL BLOOD LOSS (ML) COMPARISON BETWEEN MISOPROSTOL + TXA AND CONTROL GROUPS

	Group				t	p
	Misoprostol + TXA		Control			
	Mean	SD	Mean	SD		
Total Blood Loss (mL)	681.82	111.95	842.73	118.02	7.336	0.000

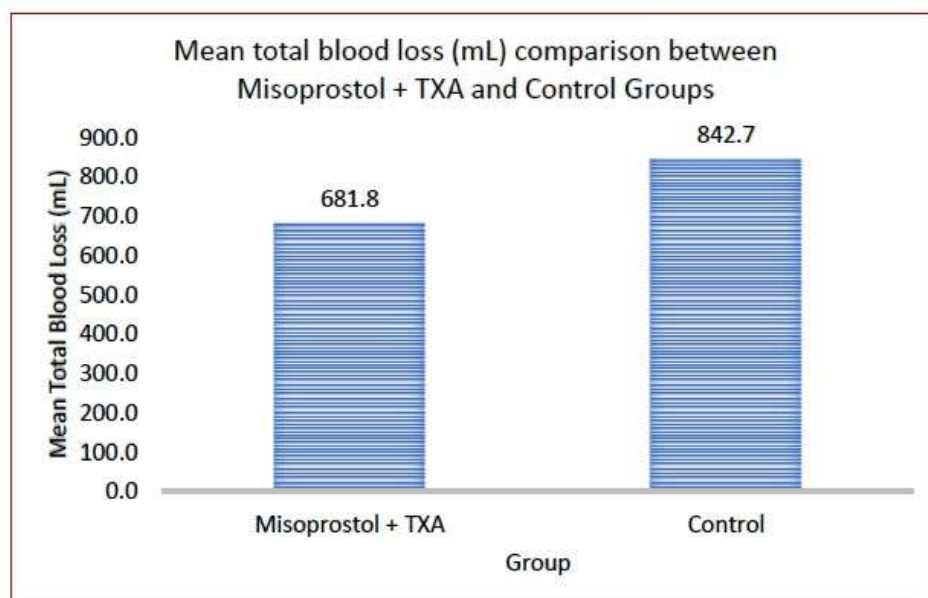


IMAGE 1

Table 1 and Image 1 highlights the primary outcome that the Intraoperative Mean total blood loss was significantly lower in the Misoprostol + Tranexamic Acid group (681.8 ± 111.9 mL) compared to the Control group (842.7 ± 118.0 mL). The difference was highly significant ($t = -7.336$, $p < 0.001$), representing a 19.1% reduction in blood loss. This reduction was consistent across all measured parameters: suction blood loss was lower in the intervention group (272.7 ± 70.6 mL vs. 330.9 ± 76.7 mL, $p < 0.001$), mean number of fully soaked mops was significantly lower (2.71 ± 0.57 vs. 3.47 ± 0.66 , $p < 0.001$), and mop blood loss was significantly lower (403.6 ± 86.0 mL vs. 520.9 ± 99.4 mL, $p < 0.001$).

SECONDARY OUTCOMES:

TABLE 2- INCIDENCE OF POSTPARTUM HAEMORRHAGE (PPH)

PPH	Group						p
	Misoprostol + TXA		Control		Total		
Yes	1	1.8%	7	12.7%	8	7.3%	0.028
No	54	98.2%	48	87.3%	102	92.7%	
Total	55	100.0%	55	100.0%	110	100.0%	

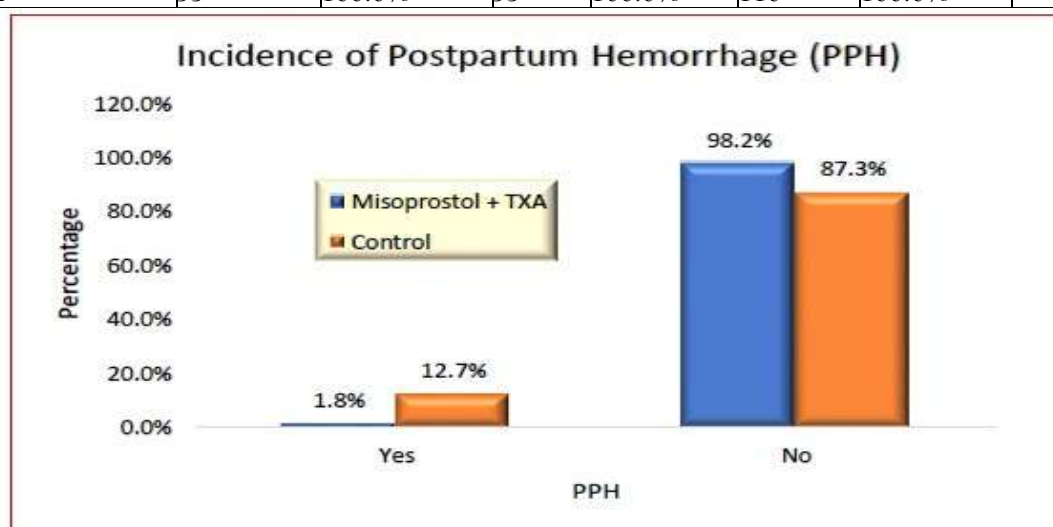


IMAGE 2

Table 2 and Image 2 highlight that the incidence of postpartum haemorrhage was dramatically reduced in the Misoprostol + TXA group, with only 1 woman (1.8%) developing PPH compared to 7 women (12.7%) in the control group. The difference between the two groups was statistically significant ($p = 0.028$), representing an 85.8% relative risk reduction, showing that the combination of sublingual misoprostol and intravenous TXA was effective in significantly reducing the incidence of PPH in elective LSCS cases.

TABLE 3- DISTRIBUTION OF REQUIREMENT OF ADDITIONAL UTEROTONICS

Additional Uterotonics Given	GROUP						p
	Misoprostol + TXA		Control		Total		
Yes	5	9.1%	22	40.0%	27	24.5%	0.000
No	50	90.9%	33	60.0%	83	75.5%	
Total	55	100.0%	55	100.0%	110	100.0%	

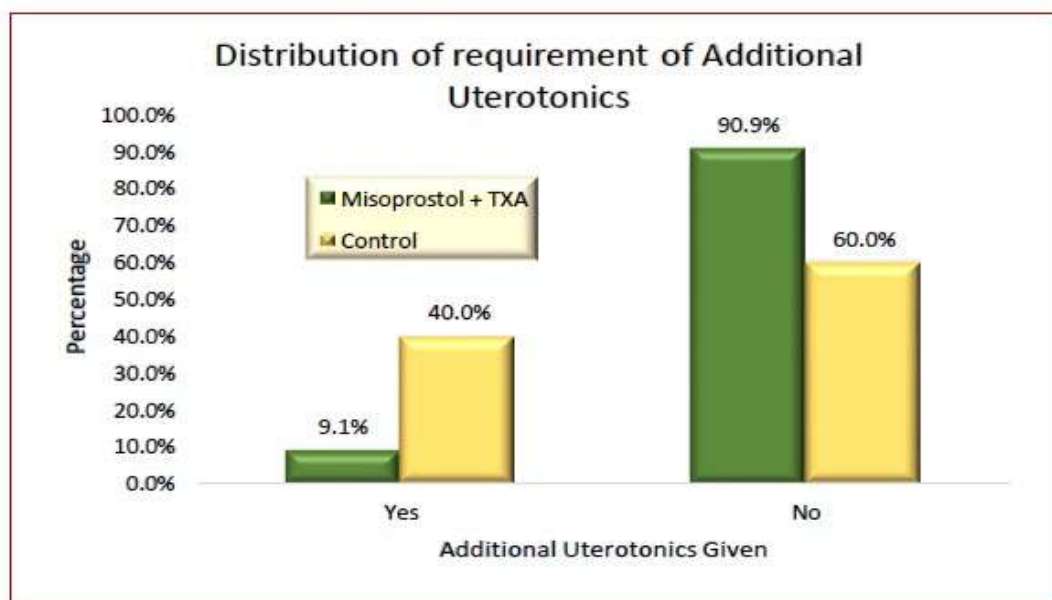


IMAGE 3

Table 3 and Image 3 highlight that the requirement for additional uterotonic agents was markedly reduced in the intervention group, with only 5 women (9.1%) requiring additional uterotonics compared to 22 women (40.0%) in the control group. The difference was highly significant ($p < 0.001$), indicating that the combined use of sublingual misoprostol and intravenous TXA markedly reduced the need for additional uterotonics during elective LSCS.

TABLE 4- NEED FOR BLOOD TRANSFUSION

Blood Transfusion Required	Group						p
	Misoprostol + TXA		Control		Total		
Yes	1	1.8%	7	12.7%	8	7.3%	0.028
No	54	98.2%	48	87.3%	102	92.7%	
Total	55	100.0%	55	100.0%	110	100.0%	

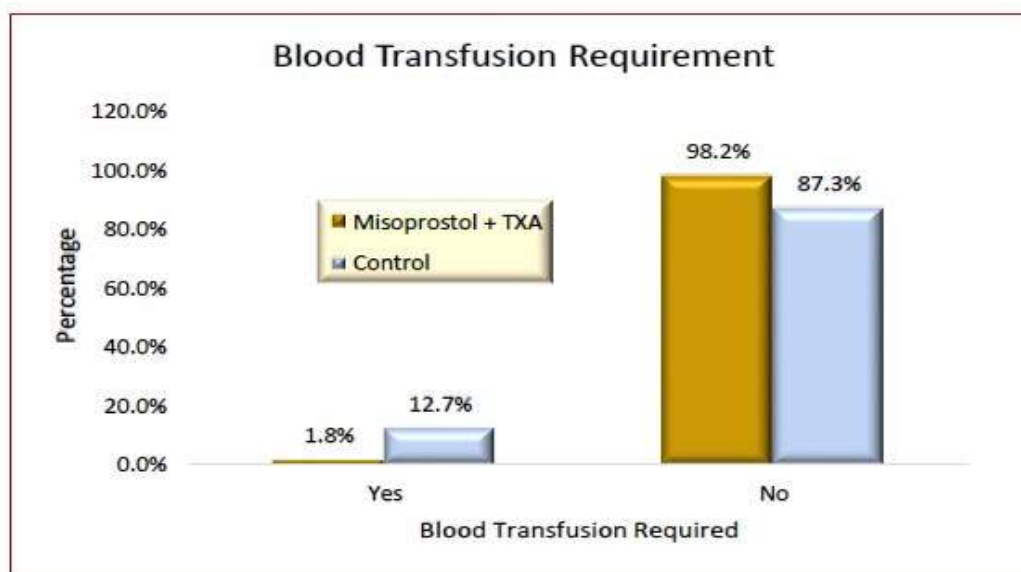


IMAGE 4

Table 4 and Image 4 highlight that blood transfusion requirements were significantly lower in the intervention group, with only 1 woman (1.8%) requiring a blood transfusion compared to 7 women (12.7%) in the control group. This difference was statistically significant ($p = 0.028$), showing that the combined use was effective in significantly reducing the need for blood transfusion during elective LSCS. In the intervention group, only 1 woman required 1 unit of blood, while in the control group, 5 women required 1 unit, 1 woman required 2 units, and 1 woman required 3 units of blood.

TABLE 5 - DISTRIBUTION OF NEED FOR SURGICAL INTERVENTIONS

Surgical Measures	Group						P
	Misoprostol + TXA		Control		Total		
Uterine artery ligation	4	7.3%	10	18.2%	14	12.7%	0.040
None	51	92.7%	42	76.4%	93	84.5%	
B-Lynch	0	0.0%	3	5.5%	3	2.7%	
Total	55	100.0%	55	100.0%	110	100.0%	

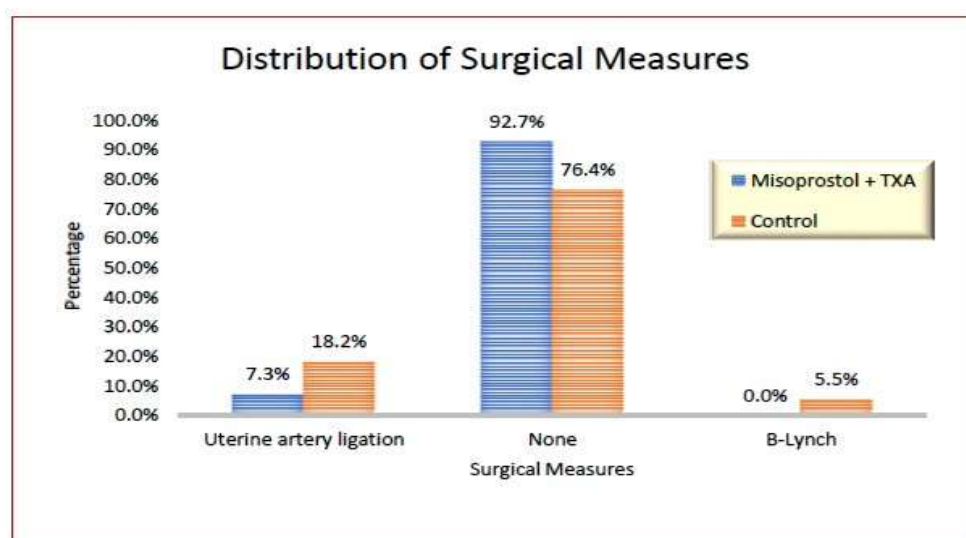


IMAGE 5

Table 5 and image 5 highlight that surgical interventions were required less frequently in the intervention group, with 4 women (7.3%) requiring uterine artery ligation compared to 10 women (18.2%) in the control group. Additionally, no women in the intervention group required a B-Lynch suture, whereas 3 women (5.5%) in the control group did. The difference between the two groups was statistically significant ($p = 0.040$), showing that combined prophylaxis reduced the need for surgical interventions to control bleeding during elective LSCS.

TABLE 6 - COMPARISON OF PRE- AND POST-OPERATIVE HAEMOGLOBIN BETWEEN MISOPROSTOL + TXA AND CONTROL GROUPS

	GROUP				T	P
	Misoprostol + TXA		Control			
	Mean	SD	Mean	SD		
Pre-op Hemoglobin (g/dL)	12.24	1.10	12.05	1.02	0.933	0.353
Post-op Hemoglobin (g/dL)	10.86	0.95	10.29	1.11	2.920	0.004

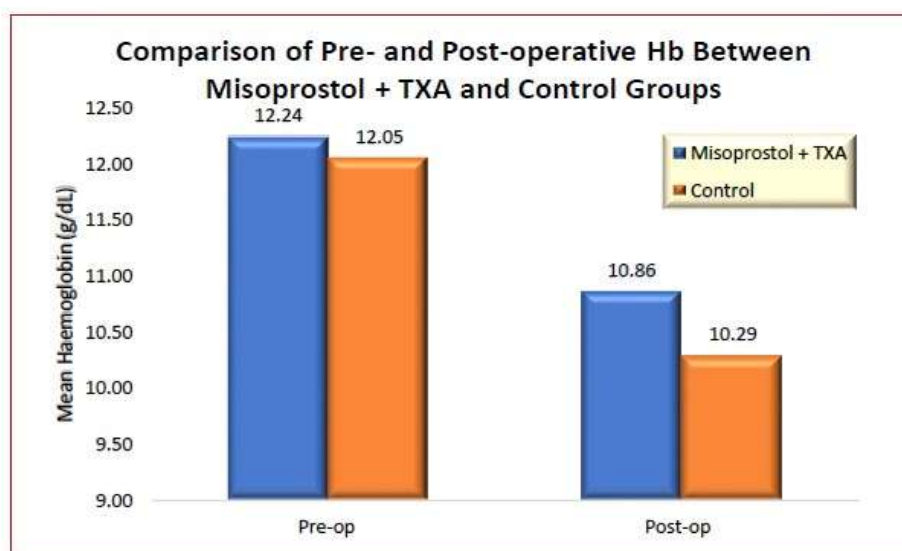


IMAGE 6

Table 6 and image 6 highlights the haemoglobin preservation in the study group. Preoperative haemoglobin levels were similar in both groups, with a mean of 12.24 ± 1.10 g/dL in the Misoprostol + TXA group and 12.05 ± 1.02 g/dL in the Control group ($p = 0.353$), indicating both groups were comparable before surgery. Post-operative haemoglobin levels were significantly better preserved in the Misoprostol + TXA group (10.86 ± 0.95 g/dL) compared to the Control group (10.29 ± 1.11 g/dL, $p = 0.004$). This result again was statistically significant emphasizing on the efficacy of dual prophylaxis.

TABLE 7- COMPARISON OF PRE AND POST OPERATIVE PACKED CELL VOLUME(PCV) BETWEEN MISOPROSTOL+TXA AND CONTROL GROUPS

	Group				t	p
	Misoprostol + TXA		Control			
	Mean	SD	Mean	SD		
PCV Pre (%)	36.01	4.65	37.03	3.71	1.265	0.209
PCV Post (%)	31.82	3.41	31.13	4.98	0.852	0.396

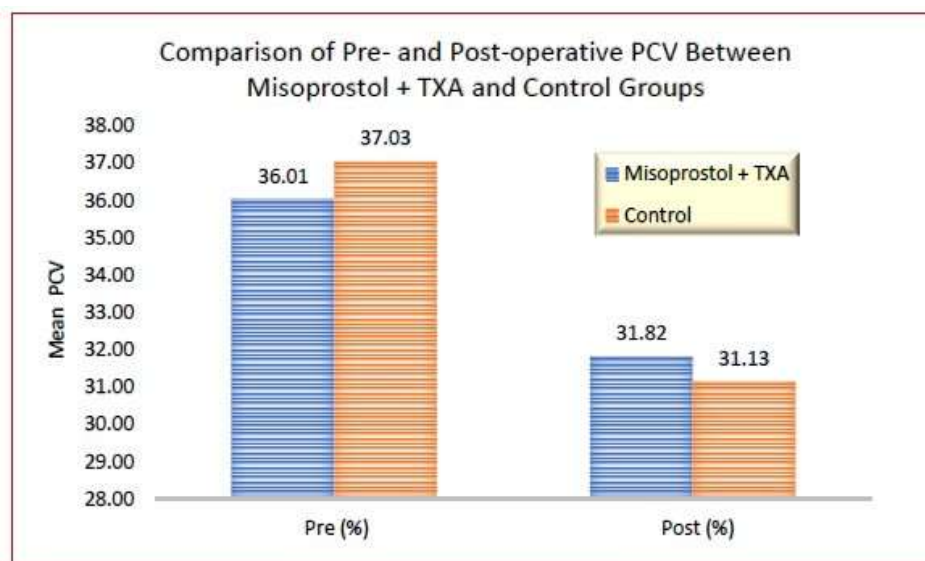


IMAGE 7

Table 7 and image 7 compares the post operative haematocrit of the patients of both groups. Pre-operative PCV: Mean values were slightly lower in the Misoprostol + TXA group ($36.01 \pm 4.65\%$) compared to the Control group ($37.03 \pm 3.71\%$), but the difference was not statistically significant ($t = -1.265$, $p = 0.209$). Post-operative PCV: Mean PCV was $31.82 \pm 3.41\%$ in the Misoprostol + TXA group is slightly higher as compared to $31.13 \pm 4.98\%$ in the Control group. The difference was however not significant ($t = 0.852$, $p = 0.396$).

TABLE 8- INCIDENCE OF PPH - PARITY DISTRIBUTION

Parity	Group				p
	Misoprostol + TXA		Control		
Primipara	0	0.0%	2	28.7%	1.00
Multipara	1	100%	5	71.3%	
Total	1	100%	7	100%	

Table 8 gives us the Parity-Specific Analysis of our study. The incidence of Post Partum Haemorrhage ($>1000\text{ml}$) was higher among multiparous women (6 cases, 75%) compared to primigravidae (2 cases, 25%). Notably, none of the primigravidae who received the Misoprostol + Tranexamic Acid regimen developed PPH (0 cases in intervention group), whereas 1 multiparous woman in the intervention group developed Post Partum Haemorrhage. In the control group, 2 primigravidae and 5 multiparous women developed Post Partum Haemorrhage, highlighting parity as an independent risk factor despite prophylaxis.

SAFETY PROFILE

No major maternal or neonatal adverse effects were observed in either group during the study period. Minor side effects were noted but did not require intervention, confirming the safety profile of the combined regimen.

DISCUSSION

In the present study, the effectiveness of combined preoperative sublingual misoprostol (600 micrograms) and intravenous TXA (1 g) in reducing intraoperative blood loss during elective lower segment caesarean section (LSCS) at a tertiary care hospital in Central India was assessed. A total of 110 women with singleton term pregnancies were included and divided equally into two groups. Both groups were comparable in terms of maternal age, gravida, obstetric risk factors, and indications for LSCS, thereby ensuring that the results were not biased by differences in baseline characteristics.

Effect on Intraoperative Blood Loss: The primary outcome measured was intraoperative blood loss. Mean total blood loss was significantly lower in the intervention group compared to the control group ($681.8 \pm 111.9 \text{ mL}$

vs. 842.7 ± 118.0 mL, $p < 0.001$). This 161 mL reduction represents a clinically meaningful difference that translates to improved maternal outcomes. Our findings are in agreement with Aboelnasr et al.¹⁷, who demonstrated that the combination of misoprostol and TXA nearly halved intraoperative blood loss compared to placebo (308.55 ± 42.99 mL vs. 736.41 ± 171.89 mL, $p < 0.001$). Similarly, Akpan et al.¹⁸ reported substantial reductions in both blood loss and perioperative haematocrit decline with the combined regimen. El-Gayed et al.¹⁹ also showed that adding Tranexamic Acid to misoprostol produced superior haemostatic outcomes than misoprostol alone.

Studies evaluating Tranexamic Acid as a single agent have also consistently demonstrated its efficacy. Sinha et al.²⁰ reported significantly lower intraoperative blood loss with Tranexamic Acid (241.25 ± 67.83 mL vs. 344.92 ± 146.67 mL, $P = 0.001$). Hemapriya et al.²¹ observed similar results, with mean blood loss of 265 ± 75 mL in the Tranexamic Acid group versus 410 ± 95 mL in controls ($p < 0.001$). Karya et al.²² also demonstrated the uterotonic effect of rectal misoprostol in reducing intraoperative and postoperative blood loss in caesarean delivery. Furthermore, Akpan et al.²³ showed effectiveness of pre-operative rectal misoprostol in reducing blood loss during caesarean section for high-risk cases including placenta previa. Collectively, these findings establish that Tranexamic Acid consistently reduces intraoperative bleeding, and our results suggest that concomitant use with misoprostol enhances this effect through dual mechanisms of action—uterotonic stimulation and anti-fibrinolysis.

Incidence of Post Partum Haemorrhage: In the present study, the incidence of PPH was significantly lower in the intervention group (1.8%) compared to controls (12.7%, $p = 0.028$). This finding resonates with Hemapriya et al.²¹, who reported a reduction in PPH incidence with Tranexamic Acid prophylaxis (5% vs. 15%). Yang et al.²⁴ in their systematic review and meta-analysis also confirmed the efficacy of prophylactic Tranexamic Acid during caesarean section. Importantly, the World Health Organization (WHO)¹ has formally recognized Tranexamic Acid as an essential drug in the management and prevention of postpartum haemorrhage, based on robust evidence, particularly the WOMAN Trial¹⁵, which demonstrated significant reductions in maternal mortality due to bleeding.

Requirement for Additional Uterotonics: Only 9.1% of women in the intervention group required additional uterotonics compared with 40% in the control group ($p < 0.001$). This observation mirrors the results of Sood et al.²⁵, who found that misoprostol reduced the need for additional uterotonics from 42.8% to 22.2%. Similarly, Shalaby et al.²⁶ demonstrated that Tranexamic Acid prophylaxis reduced the requirement for further ecbolics (13.75% vs. 46.25%, $p < 0.001$). The markedly lower need for supplementary uterotonics in our study highlights the superior haemostatic control achieved with combined therapy.

Blood Transfusion Requirement: The need for blood transfusion was significantly reduced in the intervention group (1.8%) compared to controls (12.7%, $p = 0.028$). These findings align with the systematic review by Franchini et al.²⁷, which concluded that prophylactic Tranexamic Acid reduces transfusion requirements without increasing thrombotic events. By reducing transfusion requirements, the combined regimen not only improves maternal safety but also decreases the burden on blood bank resources, an important consideration in resource-limited settings.

Haemoglobin and Haematocrit Preservation: The postoperative haemoglobin was significantly better preserved in the Misoprostol + Tranexamic Acid group (10.86 ± 0.95 g/dL) compared with the control group (10.29 ± 1.11 g/dL, $p = 0.004$). These findings are consistent with Lakshmi et al.²⁸, who reported significantly smaller declines in haemoglobin with Tranexamic Acid, and with Shalaby et al.²⁶, who demonstrated higher postoperative haemoglobin values in the Tranexamic Acid group.

Need for Surgical Interventions: Only 7.3% of women in the intervention group required surgical interventions compared with 23.6% in the control group ($p = 0.040$). Notably, none of the women in the intervention group required a B-Lynch suture or uterine artery ligation, whereas three cases in the control group did. This reduced reliance on invasive measures demonstrates the preventive efficacy of pharmacological prophylaxis, particularly of importance in resource limited settings with lack of surgical expertise.

Effect of Parity on PPH Incidence: In our study, the occurrence of Post Partum Haemorrhage was disproportionately higher among multiparous women (6 cases) compared to primigravidae (2 cases). Notably, no primigravida in the intervention group experienced PPH whereas multipara continued to account for the majority of cases despite prophylaxis. Our finding therefore adds a new dimension to this evidence, highlighting that while dual therapy appears sufficient to prevent Post Partum Haemorrhage in primigravidae, vigilance remains necessary in multipara, who continue to demonstrate higher susceptibility.

Comparison with Oxytocin-Based Regimens: Oxytocin remains the first-line uterotonic for prevention of PPH. However, in elective LSCS, where the uterus has not undergone labor induced priming, oxytocin may be less effective in achieving sustained uterine tone. Our findings are in line with Lashin et al.²⁹ who compared intravenous oxytocin with intrauterine misoprostol and found misoprostol to be more effective in preventing postpartum haemorrhage, particularly in elective caesarean sections. Similarly, Samsri et al.³⁰ demonstrated that Tranexamic Acid, when compared with oxytocin and ethamsylate, significantly reduced intraoperative blood loss in high-risk women undergoing elective LSCS.

The present study thus suggests that a dual approach using misoprostol and Tranexamic Acid provides superior efficacy. This may be attributed to the complementary mechanisms: misoprostol ensuring myometrial contractility and TXA stabilizing fibrin clots, thereby addressing both uterine atony and fibrinolysis, the two major contributors to PPH.

CONCLUSION

This study demonstrated that the combined preoperative use of sublingual misoprostol and intravenous Tranexamic Acid provides a clear benefit in reducing intraoperative blood loss and the incidence of Post Partum Haemorrhage during elective caesarean section.

The intervention group consistently showed better outcomes across all parameters- they experienced lower total amount of blood loss, fewer cases of Post Partum Haemorrhage, and required fewer additional uterotonics compared to controls. The need for blood transfusion and major surgical interventions such as uterine artery ligation or compression sutures was also substantially reduced, reflecting effective haemostasis and improved uterine tone.

Haematological parameters, including postoperative haemoglobin and haematocrit, were better preserved in the intervention group, underlining the clinical relevance of blood conservation. Importantly, no safety concerns were observed, reinforcing the practicality of this regimen.

An interesting observation was that primigravidae responded particularly well, with no cases of PPH reported in this subgroup, although multiparity remained an independent risk factor. This highlights the need for targeted prophylaxis in high parity groups.

Overall, this study supports the synergistic role of combining a potent uterotonic (misoprostol) with an antifibrinolytic (Tranexamic Acid), simultaneously addressing uterine atony and fibrinolysis—the two principal causes of haemorrhage during caesarean section. The regimen is inexpensive, thermostable, easy to administer, and therefore especially valuable in resource-limited settings where timely blood transfusion or surgical expertise may be limited.

CLINICAL IMPLICATIONS

The findings have important implications for preventing postpartum haemorrhage during elective caesarean section. Since both drugs are inexpensive, stable at room temperature, and easy to administer, this regimen can be conveniently incorporated into routine clinical practice without imposing a major economic burden on healthcare facilities. The potential for reducing reliance on blood transfusion and advanced surgical procedures is particularly important in resource-constrained settings. Given its safety profile and effectiveness, adoption of this combined regimen as a prophylactic strategy in elective LSCS may significantly contribute to reducing maternal morbidity and mortality associated with Post Partum Haemorrhage.

LIMITATIONS

The study was conducted in a single tertiary care centre, which may limit the generalizability of findings. The sample size, though adequate for statistical analysis, was relatively small; larger multicentric trials would yield more robust conclusions. The study focused only on intraoperative and immediate postoperative outcomes, and blinding was not implemented, which could introduce observer bias in estimating blood loss. High-risk cases such as placenta previa and multiple gestations were excluded, hence the utility of this regimen in very high-risk pregnancies could not be assessed.

DECLARATIONS: Author Contributions have reviewed the final version to be published and agreed to be accountable for all aspects of work

Acknowledgements: The authors sincerely thank Professor and Head of Department Dr. Manjushree Waikar, the faculty and staff of the Department of Obstetrics and Gynaecology, Government Medical College and Hospital, Nagpur, India for their constant support and guidance during this study.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of Interest: The authors declare that they have no conflicts of interest related to this study.

Author Contributions

- Conceptualization and Design: Dr Mansi Shrigiriwar, Dr Srishti Shubham
- Acquisition, analysis and Interpretation of Data and Critical Review: Dr Mansi Shrigiriwar, Dr. Srishti Shubham, Dr Kirti Rachwani

Ethical Approval and Consent to Participate

The study was conducted after approval from the Institutional Ethics Committee, GMC, Nagpur. Written informed consent was obtained from all participants prior to enrolment. Confidentiality of participant data was strictly maintained.

REFERENCE

1. World Health Organization. 2018. WHO recommendations: Uterotonics for the prevention of postpartum haemorrhage. Geneva: World Health Organization.
2. Say L, Chou D, Gemmill A, Tunçalp Ö, Moller A-B, Daniels J, et al. 2014. Global causes of maternal death: a WHO systematic analysis. *Lancet Glob Health*. 2(6):e323–33. doi:10.1016/S2214-109X(14)70227-X
3. Registrar General of India. 2022. Special bulletin on maternal mortality in India 2018–20. New Delhi: Government of India.
4. Bhadra B, Gulati BK, et al. 2016. Incidence and risk factors of postpartum haemorrhage in India: a prospective observational study. *Int J Reprod Contracept Obstet Gynecol*. 5(10):3423–7. doi:10.18203/2320-1770.ijrcog20163404
5. Sheldon WR, Blum J, Vogel JP, Souza JP, Gülmezoglu AM, Winikoff B. 2014. Postpartum haemorrhage management, risks, and maternal outcomes: findings from the WHO Multicountry Survey on Maternal and Newborn Health. *BJOG*. 121 Suppl 1:5–13. doi:10.1111/1471-0528.12636
6. World Health Organization. 2017. WHO recommendations: Prevention and treatment of postpartum haemorrhage. Geneva: World Health Organization (reaffirmed 2023).
7. Widmer M, Piaggio G, Abdel-Aleem H, et al. 2018. Heat-stable carbetocin versus oxytocin to prevent haemorrhage after vaginal birth. *N Engl J Med*. 379(8):743–52. doi:10.1056/NEJMoa1805489
8. Westhoff G, Cotter AM, Tolosa JE. 2013. Prophylactic oxytocin for the third stage of labour to prevent postpartum haemorrhage. *Cochrane Database Syst Rev*. 10:CD001808. doi:10.1002/14651858. CD001808.pub2
9. Amini M, Yari M, Vahabi S, et al. 2020. A relative bioavailability study of two misoprostol formulations administered orally and sublingually in healthy volunteers. *Front Pharmacol*. 11:50. doi:10.3389/fphar.2020.00050
10. Amini M, Jalilian N, Yari M, et al. 2022. Sublingual versus oral misoprostol solution for induction of labor: a randomized controlled trial. *Front Surg*. 9:968372. doi:10.3389/fsurg.2022.968372
11. Filgueira GCO, Oliveira CM, Costa AAS, et al. 2025. Influence of obesity on the pharmacokinetics of vaginal misoprostol in late pregnancy: a clinical pharmacology study. *J Clin Pharmacol*. doi:10. 1002/jcph.6166
12. Al-dardery NM, Abdou AM, Zidan AA, et al. 2023. Efficacy and safety of tranexamic acid in prevention of postpartum haemorrhage: a systematic review and meta-analysis. *BMC Pregnancy Childbirth*. 23:684. doi:10.1186/s12884-023-05457-4
13. Bouras M, Eshkoli T, et al. 2024. Tranexamic acid: a narrative review of its current role in hemorrhage and obstetrics. *Front Med*. 11:1416998. doi:10.3389/fmed.2024.1416998
14. World Health Organization. 2017. WHO recommendation on tranexamic acid for the treatment of postpartum haemorrhage. Geneva: World Health Organization.
15. WOMAN Trial Collaborators. 2017. Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (WOMAN): an international, randomised, double-blind, placebo-controlled trial. *Lancet*. 389(10084):2105–16. doi:10.1016/S0140-6736(17)30638-4
16. Chow S-C, Shao J, Wang H. 2017. Sample Size Calculations in Clinical Research. 3rd ed. Chapman & Hall/CRC Biostatistics Series. doi:10.1201/9781315183084

17. Aboelnasr M, Khalafallah M, Salem H, et al. 2020. Misoprostol and tranexamic acid in reduction of blood loss during elective cesarean section. *J Matern Fetal Neonatal Med.* 33(10):1720–6. doi:10.1080/14767058.2018.1529169
18. Akpan U, Essien E, Udo A, et al. 2019. Prophylactic misoprostol and tranexamic acid for blood loss reduction in cesarean deliveries. *Niger J Clin Pract.* 22(3):307–13. doi:10.4103/njcp.njcp_273_18
19. El-Gayed S, Abdelhady H, et al. 2019. Tranexamic acid combined with misoprostol for control of intraoperative blood loss during cesarean section. *Eur J Obstet Gynecol Reprod Biol.* 234:40–5. doi:10.1016/j.ejogrb.2018.12.037
20. Sinha P, Kuruba N. 2018. Use of tranexamic acid in reducing blood loss during cesarean section. *J Obstet Gynaecol Res.* 44(4):698–704. doi:10.1111/jog.13572
21. Hemapriya S, Rani PR, Subramaniam A. 2017. Role of tranexamic acid in reducing blood loss during and after cesarean section: A randomized controlled trial. *Int J Reprod Contracept Obstet Gynecol.* 6(4):1412–6. doi:10.18203/2320-1770.ijrcog20171404
22. Karya N, Patel P, Taneja P. 2017. Rectal misoprostol for prevention of postpartum haemorrhage during cesarean section. *Int J Gynecol Obstet.* 139(1):43–8. doi:10.1002/ijgo.12235
23. Akpan U, Essien E, Udo A. 2020. Rectal misoprostol for reducing blood loss in high-risk cesarean deliveries. *Niger J Med.* 29(2):226–32. doi:10.4103/NJM.NJM_33_20
24. Yang H, Han S, et al. 2021. Prophylactic tranexamic acid for cesarean delivery: a systematic review and meta-analysis. *Am J Obstet Gynecol.* 224(3):240–50. doi:10.1016/j.ajog.2020.08.017
25. Sood R, Bhatla N, et al. 2016. Misoprostol vs oxytocin in reducing need for additional uterotronics during cesarean. *Indian J Obstet Gynecol.* 66(4):289–94. doi:10.1007/s13224016-0896-3
26. Shalaby H, Mahmoud A, et al. 2019. Prophylactic tranexamic acid in cesarean section: effect on blood loss and haemoglobin. *J Obstet Gynaecol.* 39(3):322–8. doi:10.1080/01443615.2018.1493450
27. Franchini M, Mengoli C, Cruciani M, et al. 2018. Safety and efficacy of tranexamic acid for prevention of obstetric haemorrhage: an updated systematic review and meta-analysis. *Blood Transfus.* 16(4):329–37. doi:10.2450/2018.0012-18
28. Lakshmi N, Rani R, et al. 2017. Tranexamic acid in elective cesarean section: effect on blood loss and haemoglobin decline. *Int J Reprod Contracept Obstet Gynecol.* 6(7):2983–7. doi:10.18203/2320-1770.ijrcog20172962
29. Lashin M, Rashed H, et al. 2018. Comparison of intrauterine misoprostol and intravenous oxytocin for prevention of PPH in elective cesarean sections. *Middle East Fertil Soc J.* 23(2):113–7. doi:10.1016/j.mefs.2017.11.001
30. Samsri S, Karunaratne K, et al. 2019. Tranexamic acid versus oxytocin and ethamsylate in cesarean section: a randomized trial. *J Obstet Gynaecol.* 39(6):763–8. doi:10.1080/01443615.2018.1557625