

PROPHYLACTIC TRANEXAMIC ACID IN CAESAREAN DELIVERY: EFFICACY, SAFETY, AND BLOOD TRANSFUSION REQUIREMENTS — A SYSTEMATIC REVIEW OF RANDOMIZED CONTROLLED TRIALS

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Received : 05/08/2026
Received in revised form : 04/09/2026
Accepted : 17/09/2026

Keywords:
Cesarean Section; Postpartum Hemorrhage; Pregnancy; Tranexamic Acid; Blood Transfusion.

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DOI: 10.47009/jamp.2026.8.5.98

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2026; 8 (5); 618-632



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ABSTRACT

Background: Prophylactic tranexamic acid (TXA) is increasingly used during cesarean delivery to reduce perioperative blood loss and postpartum hemorrhage (PPH), but its effect on transfusion requirements and maternal safety remains uncertain. This systematic review evaluated the efficacy and safety of prophylactic intravenous TXA during cesarean delivery. **Materials and Methods:** Randomized controlled trials evaluating prophylactic intravenous TXA versus placebo or control during cesarean delivery were reviewed. The outcomes included maternal blood transfusion, PPH, intraoperative and postoperative blood loss, thromboembolic events, maternal adverse effects, and neonatal outcomes. **Results:** Forty-two randomized controlled trials were included. Transfusion requirements were reported in 29 trials; 10 trials reported statistically significant reductions with TXA, while several others showed numerical but non-significant reductions. In the largest trial (N=11,000), transfusion occurred in 3.6% vs. 4.2% with TXA and placebo, respectively (RR 0.86, 95% CI 0.71–1.03; $P=0.19$). PPH and major blood loss were reduced in several trials, including PPH rates of 11.9% vs. 50.0% in Ifunanya et al. ($P<0.0001$) and 1% vs. 19% in Ortuanya et al. ($P=0.001$). Sentilhes et al. reported calculated blood loss >1000 mL in 26.4% vs. 31.5% ($P=0.003$). No significant increase in thromboembolic events was reported. **Conclusion:** TXA generally reduced measured blood loss and PPH, whereas its effect on transfusion was less consistent, particularly in low-risk populations.

INTRODUCTION

Postpartum hemorrhage (PPH) remains one of most common and serious complications of childbirth and is still a major cause of maternal death worldwide, accounting for approximately 27% of maternal deaths globally.^[1,2] Cesarean delivery is associated with greater blood loss than vaginal birth and therefore contributes to hemorrhage-related maternal complications and the need for blood transfusion.^[3-5] As cesarean delivery rates continue to increase worldwide, preventing excessive blood loss during surgery has become an important clinical priority.^[3-5] Tranexamic acid (TXA) is an antifibrinolytic drug that prevents the breakdown of blood clots and is well established in the treatment of PPH.^[1,6] In recent years, its use before or during cesarean delivery has

received increasing attention as a way to reduce blood loss.^[3-6] However, the evidence for its clinical benefit remains inconsistent. The large TRAAP2 trial found that prophylactic TXA significantly reduced a composite outcome of calculated blood loss greater than 1000 mL or red-cell transfusion by day 2, although it did not significantly reduce postpartum transfusion or several other secondary bleeding outcomes.^[7,8] The large TXA-CS trial found no significant reduction in its primary composite outcome of maternal death or blood transfusion, even with modest reductions in blood loss-related outcomes and hemoglobin decline.^[9] These findings are important because a reduction in blood loss does not necessarily lead to a clinically meaningful reduction in blood transfusion, which is an important outcome for maternal care and

healthcare-resource use.^[3,7] Smaller randomized trials have reported substantial reductions in blood loss and, in some cases, transfusion requirements.^[6,10] whereas larger contemporary trials have shown less consistent effects.^[7,9] This variation raises the possibility that the effect of prophylactic TXA may differ according to the timing or dose of administration, baseline risk of hemorrhage, cesarean characteristics, or methodological features of the trials.^[4,6]

Despite the growing number of randomized controlled trials (RCTs), uncertainty remains about the effect of prophylactic intravenous TXA on maternal blood transfusion requirements.^[6,7] Its safety also needs further assessment, particularly regarding thromboembolic events and other adverse effects across different populations.^[1,7]

This systematic review therefore brings together evidence exclusively from RCTs to evaluate the effect of prophylactic intravenous TXA on maternal blood transfusion requirements, blood loss, and maternal safety, and to explore population, treatment-related, and methodological factors that may explain differences in its reported effects.

Aim

To systematically evaluate the efficacy, safety, and effect of prophylactic intravenous TXA on blood transfusion requirements in women undergoing cesarean delivery.

Objectives

1. To determine the effect of prophylactic intravenous TXA on maternal blood transfusion requirements following cesarean delivery.
2. To evaluate the efficacy of prophylactic intravenous TXA in reducing PPH and intraoperative, postoperative, and total blood loss following cesarean delivery.
3. To assess the safety of prophylactic intravenous TXA and explore clinical and methodological factors, including timing, dose, and baseline risk, that may explain differences in treatment effects.

MATERIALS AND METHODS

Study Design and Reporting Guidelines

This systematic review evaluated the efficacy and safety of prophylactic intravenous TXA for reducing blood transfusion, blood loss, and PPH in women undergoing cesarean delivery. The review was conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement (Figure 1).¹¹ Only RCTs were included.

Research Question and PICOS Framework

The review question was structured according to the PICOS framework. Population: women undergoing cesarean delivery, irrespective of baseline PPH risk. Intervention: prophylactic intravenous TXA administered before or during cesarean delivery, irrespective of dose or timing. Comparator: placebo, no TXA, or standard care without TXA. Outcomes:

the primary outcome was maternal blood transfusion requirement; secondary outcomes included PPH, intraoperative, postoperative and total blood loss, hemoglobin/hematocrit changes, additional uterotonic use, thromboembolic events, and other adverse events. Study design: RCTs only.

Eligibility Criteria

RCTs involving women undergoing cesarean delivery were eligible if they evaluated prophylactic intravenous TXA and compared it with placebo, no TXA, or standard care without TXA. Studies were required to report maternal transfusion or at least one prespecified secondary outcome. In multi-arm trials, only eligible intravenous TXA and corresponding control groups were included.

Observational and non-randomised studies, reviews, editorials, letters, case reports, case series, animal and in-vitro studies were excluded. Studies evaluating TXA for treatment of established PPH, non-intravenous TXA without an eligible IV-TXA arm, vaginal delivery without separately reported cesarean data, duplicate publications, and studies with insufficient outcome data were also excluded.

Information Sources and Search Strategy

PubMed/MEDLINE, PubMed Central (PMC), Google Scholar, and the Directory of Open Access Journals (DOAJ) were searched from inception to 24 July 2026. Reference lists of eligible studies and relevant systematic reviews were also screened manually.

The search combined controlled vocabulary and free-text terms related to cesarean delivery, TXA, PPH, and blood loss using Boolean operators. A representative strategy was:

("cesarean section" OR "caesarean section" OR "cesarean delivery" OR "caesarean delivery") AND ("tranexamic acid" OR TXA) AND ("postpartum hemorrhage" OR "postpartum haemorrhage" OR blood loss OR hemorrhage OR haemorrhage)

No publication-year restriction was applied.

Study Selection

Retrieved records were screened after removal of duplicates. Titles and abstracts were assessed initially, followed by full-text evaluation of potentially eligible studies. Reasons for full-text exclusion were documented, and the selection process was presented using a PRISMA 2020 flow diagram (Figure 1). A total of 42 RCTs met the eligibility criteria and were included.

Data Extraction

Data were extracted using a standardized form and included author, year, country, study design, sample size, population characteristics, baseline PPH risk, TXA dose and regimen, route and timing of administration, and comparator.

Outcome data included transfusion requirements, number of transfused units, PPH, intraoperative and postoperative blood loss, total blood loss, hemoglobin/hematocrit changes, additional uterotonic use, thromboembolic events, and other adverse events. Outcomes not reported were recorded as "NR" (not reported), and zero events were

distinguished from missing data. No values were estimated when not explicitly reported.

Outcomes of Interest

The primary outcome was maternal blood transfusion requirement, including any transfusion, red blood cell transfusion, number of units transfused, and other blood products where reported.

Secondary outcomes included PPH incidence and severity, intraoperative, postoperative and total blood loss, hemoglobin/hematocrit changes, additional uterotonic requirements, thromboembolic events, and other maternal adverse events. Where definitions or measurement periods differed between studies, the original definitions were retained.

Risk of Bias Assessment

Risk of bias was assessed using the Cochrane Risk of Bias 2 (RoB 2) tool.¹² Results were presented using traffic-light and summary plots generated with the ROBVIS visualization tool.¹³

Data Synthesis

Study characteristics and findings were synthesized descriptively. The primary focus was maternal blood transfusion, with secondary consideration of PPH, blood loss, hematological outcomes, additional uterotonic use, and maternal safety.

Clinical and methodological heterogeneity related to population characteristics, baseline hemorrhage risk, TXA dose and timing, cesarean characteristics, outcome definitions, blood-loss measurement methods, and follow-up periods was considered when interpreting the findings. Reported effect measures, including risk ratios, proportions, mean differences, P values, and confidence intervals, were retained. Continuous outcomes were presented according to the original study as mean $\pm$ standard deviation or median with range/interquartile range.

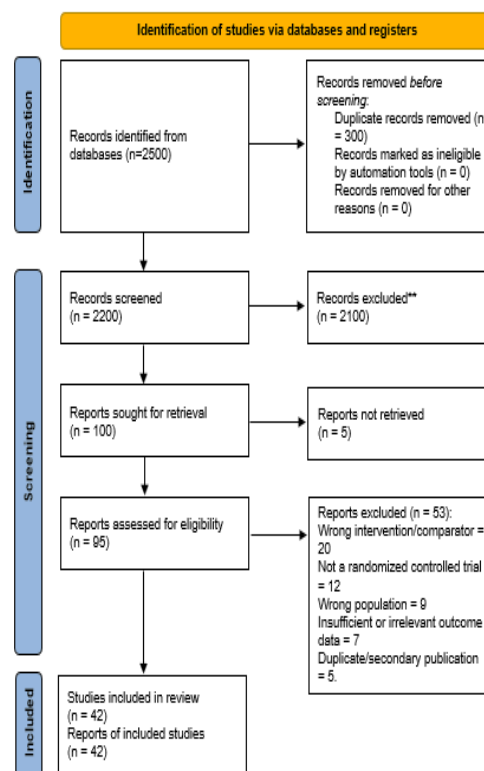


Figure 1: PRISMA 2020 flow diagram showing the identification, screening, eligibility assessment, and inclusion of studies in systematic review

RESULTS

3.1 Study Selection

A total of 2,500 records were identified through database searches. After removal of 300 duplicate records, 2,200 records were screened by title and abstract, of which 2,100 were excluded. The remaining 100 reports were sought for retrieval, with 5 reports not retrieved. Thus, 95 full-text reports were assessed for eligibility.

Of these, 53 reports were excluded for reasons including wrong intervention or comparator (n = 20), non-randomized study design (n = 12), wrong population (n = 9), insufficient or irrelevant outcome data (n = 7), and duplicate or secondary publication (n = 5). Finally, 42 RCTs met the eligibility criteria and were included in the systematic review. The study selection process is presented in Figure 1.

Table 1: Characteristics of All Included Studies

Study ID	Study Design	Country	N	Population / Baseline Risk	CS Type	TXA Dose / Regimen	Timing	Comparator / Control
Abdel-Aleem et al., 2013 ¹⁴	Open-label RCT	Egypt	740 (373 TXA/367 control)	Low risk; singleton, ≥ 37 wk	Elective	1 g IV	10 min pre-incision	No TXA
Ali et al., 2019 ¹⁵	RCT	Egypt	200	Unselected/NR	Elective	NR	20 min pre-anesthesia	Oxytocin only
Bharati et al., 2022 ¹⁶	DB RCT (3-arm)	India	150	High risk – placenta previa	NR	IV: 1 g + oxytocin; Topical:	IV: pre-incision; Topical:	Oxytocin only (control)

						2 g + oxytocin	post- delivery	
Chaiyakarn et al., 2023 ¹⁷	DB, PC RCT	Thailand	60	High risk – placenta previa	All	1 g IV	10 min pre-incision	Placebo (saline)
Dhivya Lakshmi & Abraham, 2016 ¹⁸	Open-label RCT	India	120	Low risk; term	Elective	1 g IV	≥20 min pre-incision	Routine care (oxytocin)
El-Gaber et al., 2019 ¹⁹	DB RCT	Egypt	500	Low risk; full-term	Elective	1 g IV	≥10 min pre-incision	Placebo (saline)
Gai et al., 2004 ²⁰	RCT	China	180 (91/89)	Primiparous	NR	TXA (NR)	Immediately pre-op	No TXA
Garg et al., 2026 ²¹	RCT	India	240	High risk (multiple factors)	NR	1 g IV	Pre-incision	Placebo (saline)
Gobbur et al., 2014 ²²	RCT (case-control)	India	100	Low risk	NR	1 g IV	20 min pre-incision	Oxytocin + ergometrine
Goswami et al., 2013 ²³	DB RCT	India	90	High risk – anemia	NR	10 mg/kg IV (T1); 15 mg/kg IV (T2)	20 min pre-incision	Placebo
Gungorduk et al., 2011 ²⁴	DB, PC RCT	Turkey	660 (330/330)	Low risk; elective	Elective	1 g IV	Pre-op	Placebo (glucose)
Hemapriya et al., 2020 ²⁵	RCT	India	200 (100/100)	Low risk	All	10 mg/kg IV	10 min pre-incision	Routine care (oxytocin)
Ibrahim et al., 2019 ²⁶	DB RCT	Saudi Arabia	46	High risk – placenta accreta	Elective	NR	NR	NR
Ifunanya et al., 2019 ²⁷	DB RCT	Nigeria	168 (84/84)	High risk – PPH	All	1 g IV	10 min pre-incision	Placebo
Jafarbegloo et al., 2021 ²⁸	PC RCT	NR	50	NR	NR	NR	10 min pre-CS	Placebo (distilled water)
Lee et al., 2023 ²⁹	DB, PC RCT	Singapore	200 (194 analyzed)	Mixed risk	Elective	IV TXA (NR)	10 min pre-incision	Placebo (saline)
Maged et al., 2015 ³⁰	SB RCT	Egypt	200 (100/100)	NR	Elective	1 g IV	15 min pre-op	Placebo (glucose)
Martadiansyah et al., 2025 ³¹	DB, PC RCT	Indonesia	88	Unselected	NR	1 g IV	At incision	Placebo (saline)
Movafegh et al., 2011 ³²	DB RCT	Iran	100 (50/50)	NR	NR	10 mg/kg IV	20 min pre-incision	Placebo
Nambiath Sujata et al., 2016 ³³	RCT (blinded)	India	60 (30/30)	High risk – PPH	All	10 mg/kg IV	10 min pre-incision	Placebo (saline)
Nargis & Dewan, 2020 ³⁴	DB, PC RCT	Bangladesh	120	Low risk; term	NR	1 g IV bolus	Post-delivery	Placebo (distilled water)
Neumann et al., 2024 ³⁵	PC RCT	India	212	High risk – PPH	All	1 g IV	≥10 min pre-incision	Placebo (saline)
Obi et al., 2019 ³⁶	DB, PC RCT	Nigeria	120 (115 analyzed)	Low risk; term	Elective	1 g IV	Preoperative	Placebo
Ogunkua et al., 2022 ³⁷	DB, PC RCT	NR	110 (55/55)	Elective repeat CS	Elective (repeat)	1 g IV × 2 (pre- & post-placenta)	Pre-incision + post-placenta	Placebo
Omawumi et al., 2023 ³⁸	SB, PC RCT	Nigeria	148 (143 analyzed)	Low risk; term	Elective	1 g IV	10 min pre-incision	Placebo
Ortuanya et al., 2024 ³⁹	DB, PC RCT	Nigeria	200	High risk – PPH	NR	1 g IV	≥10 min pre-op	Placebo (saline)
Oseni et al., 2021 ⁴⁰	DB, PC RCT	Nigeria	244	Low risk; emergency CS	Emergency	1 g IV	≥5 min pre-op	Placebo (saline)
Pacheco et al., 2023 ⁹	Multicenter, DB RCT	United States	11,000 (10,995 analyzed)	Unselected/gener al	All	TXA (NR)	≤3 min post-cord-clamp	Placebo
Ray et al., 2016 ⁴¹	PC, open-label RCT	India	100 (50/50)	NR	Elective	1 g IV	NR	Placebo
Sekhavat et al., 2009 ⁴²	PC RCT	Iran	90 (45/45)	Primiparous	NR	TXA (NR)	Immediately pre-op	Placebo

Sentilhes et al., 2021 ⁷	Multicenter, DB RCT	France	4,551 (4,153 analyzed)	Mixed risk	All	1 g IV	≤3 min post-birth	Placebo
Shady et al., 2017 ⁴³	DB RCT (3-arm)	Egypt	120	High risk – placenta previa	NR	IV: 1 g + oxytocin; Topical: 2 g + oxytocin	IV: pre-incision; Topical: post-delivery	Oxytocin only
Shahid & Khan, 2013 ⁴⁴	DB, PC RCT	Pakistan	74 (38/36)	NR	NR	IV TXA (NR)	Immediately pre-op	Placebo (distilled water)
Shalaby et al., 2022 ⁴⁵	DB, PC RCT	Egypt	160	High risk – PPH	Elective	1 g IV	15 min pre-op	Placebo (glucose)
Shree et al., 2026 ⁴⁶	DB RCT	India	300	Unselected; low-resource	All	1 g IV	10 min pre-incision	Placebo (saline)
Sinha et al., 2024 ⁴⁷	DB, PC RCT	India	72 analyzed	Low risk	Elective	1 g IV	≥20 min pre-incision	Placebo (saline)
Soliman et al., 2021 ⁴⁸	RCT	Egypt	100	Low risk	Elective	1 g IV	20 min pre-incision	No TXA
Tarabrin et al., 2012 ⁴⁹	DB, PC RCT	NR	37 (19/18)	Hypercoagulable; risk NR	NR	10 mg/kg IV	30 min pre-op	Placebo
Wongjiariyakul et al., 2025 ⁵⁰	DB, PC RCT	Thailand	50	High risk – PPH	All	1 g IV	Pre-incision	Placebo (saline)
Xu et al., 2013 ⁵¹	DB RCT	China	174 (88/86)	Primiparous	NR	10 mg/kg IV	Immediately pre-op	No TXA
Yehia et al., 2014 ⁵²	DB RCT	Egypt	223 (212 analyzed)	Low risk; term	Elective	1 g IV	At induction	Oxytocin only
Zhang et al., 2026 ⁵³	Multicenter, DB, PC, Phase 3 RCT	China	1,732 (1,694 analyzed)	High risk – placenta previa	NR	1 g IV	≤5 min post-cord-clamp	Placebo + oxytocin

3.2 Characteristics of Included Studies

A total of 42 RCTs were included, published between 2004 and 2026. Studies were conducted across multiple countries, with the largest numbers from India, Egypt, and Nigeria, followed by China, Thailand, Iran, Turkey, Saudi Arabia, Singapore, Indonesia, Bangladesh, the United States, France, and Pakistan. Country was not reported for Ogunkua et al.^[37] Tarabrin et al.^[49] and Jafarbegloo et al.^[28]

Most trials were double-blind, randomized, placebo-controlled studies, while others were single-blind, open-label, or non-blinded. Pacheco et al.^[9] Sentilhes et al.^[7] and Zhang et al.^[53] were large multicenter trials; most others were single-center studies.

Sample sizes ranged from 37 participants (Tarabrin et al.^[49]) to 11,000 (Pacheco et al.^[9]). The three largest trials were Pacheco et al.^[9] (n = 11,000), Sentilhes et al.^[7] (n = 4,551), and Zhang et al.⁵³ (n = 1,732); most remaining studies enrolled fewer than 250 women.

Study populations ranged from low-risk or unselected women to high-risk groups, including placenta previa, placenta accreta, maternal anemia, and other PPH risk factors. Both elective and emergency cesarean deliveries were represented.

TXA was most commonly administered as 1 g intravenously, although some studies used 10–15 mg/kg. Timing varied from 20–30 minutes before skin incision to after delivery or cord clamping. Bharati et al.^[16] and Shady et al.^[43] also evaluated topical TXA; only eligible intravenous TXA and control groups were included.

Most trials used placebo with standard uterotonic prophylaxis, usually oxytocin, while others used no-TXA or routine-care controls. Overall, substantial variation existed in population risk, cesarean characteristics, TXA dose, timing, and study design.

3.3 Effect of Prophylactic TXA on Maternal Blood Transfusion Requirements

Blood transfusion requirements were reported in 29 of the 42 included trials (Table 2), including four trials with no transfusion events in either arm. Overall, most trials reporting comparative data showed a numerical reduction in transfusion requirements with TXA, though the magnitude and statistical significance varied.

Ten trials reported statistically significant reductions in transfusion requirements or volume with TXA, with the largest effects seen in high-risk populations undergoing surgery for placenta previa or placenta accrete,^[16,17,26,43] and other high-risk indications.^[23,27,39]

In contrast, the three largest multicentre trials found no significant between-group difference in transfusion rates,^[7,9,53] and a further seven trials in mixed or lower-risk populations similarly reported non-significant reductions. 15,21,29,45,46,47,50

Five additional trials reported numerically fewer transfusions with TXA without formal statistical comparison.^[24,34,37,44,51] and three trials recorded no transfusion events in either arm.^[18,35,48] Yehia et al. reported significantly lower postoperative oral iron replacement requirements with TXA.^[52] Transfusion data were not reported in the remaining 13 trials.

Overall, findings generally favoured prophylactic TXA numerically for reducing transfusion requirements, but significant reductions were not consistently demonstrated, particularly in the largest trials.

3.4 Effect of Prophylactic TXA on PPH and Blood Loss

Incidence and Severity of PPH

Several trials reported significant reductions in PPH or clinically important blood loss with prophylactic TXA (Table 2). In high-risk populations, particularly those with placenta previa, TXA was associated with substantially lower rates of PPH >1000 mL,^[16,17,27,39] and a repeat-caesarean population showed significantly fewer cases of blood loss >2000 mL with TXA (Ogunkua et al.^[37]).

In unselected and mixed-risk populations, significant reductions were also reported for composite or calculated blood-loss outcomes. Sentilhes et al.^[7] found a lower rate of the composite outcome of cEBL >1000 mL or transfusion by day 2 with TXA (adjusted RR 0.84, 95% CI 0.75–0.94; P = 0.003), and Zhang et al. 53 reported a similarly lower cEBL ≥1000 mL rate (P = 0.01). El-Gaber et al.^[19] reported significant reductions in both overall and severe PPH.

Not all trials showed significant differences in PPH incidence. Garg et al.^[21] found no difference in atonic PPH, and in the largest trial, Pacheco et al.^[9] the rate of intraoperative blood loss >1000 mL did not differ significantly between groups (P = 0.19). Notably, while Ogunkua et al.^[37] found significantly fewer cases exceeding 2000 mL, the difference in calculated blood loss at 24 hours in the same trial was not significant illustrating that findings could vary depending on which blood-loss threshold or timepoint was assessed.

Quantification of Surgical and Postpartum Blood Loss

Several trials reported significantly lower quantified blood loss with TXA across intraoperative, postoperative, and total/calculated measures (Table 2). Significant reductions in intraoperative blood loss were reported by Ali et al.^[15] Ibrahim et al.^[26] (in placenta accreta surgeries), and Wongjariyakul et al. 50. Postoperative blood loss was similarly reduced in Movafegh et al.^[32] Sekhavat et al.^[42] and Gai et al.^[20] For total or calculated blood loss, significant reductions with TXA were reported by Abdel-Aleem et al.^[14] Sentilhes et al.^[7] and Zhang et al.^[53] while Ogunkua et al.^[37] found no significant difference in calculated blood loss at 24 hours.

Table 2: Effects of Prophylactic Intravenous TXA on Blood Transfusion and Efficacy Outcomes

Study ID	Blood Transfusion	PPH	Intraoperative Blood Loss (mL)	Postoperative / Total Blood Loss (mL)	Hb/Hct Change	Additional Uterotonic Requirement
Abdel-Aleem et al., 2013 ¹⁴	NR	NR	NR	Total: 241.6±126.0 vs 510.7±144.5 mL (P<0.05)	Hb/Hct decline smaller w/ TXA (sig.)	NS
Ali et al., 2019 ¹⁵	0/100 vs 1/100 (P=0.316)	Vaginal bleeding less severe w/ TXA (P<0.019)	386.6±105.0 vs 507.8±152.1 mL (P<0.001)	2nd period: 114.7±53.8 vs 139.7±73.4 mL (P=0.019); Total: 501.3±119.2 vs 647.4±178.8 mL (P<0.001)	Hb 11.44±1.24 vs 10.55±1.18 g/dL (P<0.001); Hct 34.5±3.7% vs 32.9±4.0% (P=0.015)	NR
Bharati et al., 2022 ¹⁶	18% (IV)/18% (Topical) vs 68% (Control) (P=0.0001)	18%/18% vs 52% (P=0.001)	533/533 vs 919 mL, medians (P=0.0001)	4h: 123.1/125.6 vs 182.2 mL; Total: 661/656 vs 1111 mL (P=0.0001)	24h Hb NS (P=0.125)	18%/18% vs 68% (P=0.0001)
Chaiyakarn et al., 2023 ¹⁷	>1 unit PRC: 16.7% vs 43.3% (P=0.047)	>1000 mL @24h: 13.3% vs 33.3% (P=0.030)	349.5 vs 619.0 mL, medians (P<0.001)	NR	24h Hct 32.8±4.3% vs 31.5±3.4% (P=0.196, NS)	Methylergometrine: 46.7% vs 86.7% (P=0.001); post-op: 3.3% vs 43.3% (P<0.001)
Dhivya Lakshmi & Abraham, 2016 ¹⁸	0 in either group	>500 mL: 3.3% vs 60% (P<0.001)	347.2±108.6 vs 517.7±150.0 mL (P<0.001)	NR	Hb decline >10%: 9.3% vs 38.9% (P<0.01)	Add'l oxytocin: 5% vs 15%
El-Gaber et al., 2019 ¹⁹	Lower w/ TXA (P<0.05)	4.4% vs 6.8% (P<0.05);	387.7±93.1 vs 560.8±107.5	159.2±51.0 vs 232.7±65.2	24h Hb 10.81±0.92 vs 10.27±0.89 g/dL (P<0.001); Hct	10% vs 17% (P<0.05)

		severe PPH: 1.2% vs 2.8% (P<0.001)	mL (P<0.001)	mL (P<0.001); Total: 546.8±106.1 vs 794.0±141.2 mL (P<0.001)	32.0±2.9% vs 30.8±2.7% (P<0.001)	
Gai et al., 2004 ²⁰	NR	NR	NR	Postop: 42.8±40.5 vs 74.0±77.1 mL (P=0.001); Total: 351.6±148.2 vs 439.4±191.5 mL (P=0.002)	NR	NR
Garg et al., 2026 ²¹	9.2% vs 10.9% (P=0.666, NS)	Atonic PPH: 11.7% vs 13.4% (P=0.696, NS)	NR	cEBL: 578±291 vs 684.6±245.3 mL (P=0.002)	% Hb drop: 10.37% vs 10.39% (P=0.990, NS)	9.2% vs 10% (P=0.826, NS)
Gobbur et al., 2014 ²²	NR	>500 mL: 12% vs 30% (P=0.02)	289.4±71.4 vs 328.4±58.9 mL (P=0.004)	71.5±53.6 vs 112.6±51.7 mL (P=0.0002)	NR	NR
Goswami et al., 2013 ²³	0% (T1/T2) vs 6.7% (C) (P=0.02)	None in any group	T1: 376.8±32.0; T2: 261.2±56.8; C: 527.2±88.7 mL (P<0.0001 vs control)	Postop negligible; total = intraop	% Hb change less w/ TXA (P=0.00); Hct T1 vs T2 sig. (P=0.00)	Methylergometrine: T2=2, T1=3, C=8 pts
Gungorduk et al., 2011 ²⁴	0.6% vs 2.1%	>1000 mL: 2.1% vs 5.8%	NR	499.9±206.4 vs 600.7±215.7 mL (P<0.001)	Decline less w/ TXA (P<0.05)	8.5% vs 14.5% (P=0.02)
Hemapriya et al., 2020 ²⁵	NR	NR	Reduced w/ TXA (sig., values NR)	NR	Post-op Hb better preserved w/ TXA (sig.)	NR
Ibrahim et al., 2019 ²⁶	Intraop units: 4.2±1.9 vs 6.1±2.2 (P=0.003); 24h: 1.2±0.8 vs 3.2±0.9 units (P<0.001)	NR	2232±1204 vs 3405±1193 mL (P=0.002)	NR	First post-op Hb NS (8.4±1.7 vs 7.9±1.6 g/dL, P=0.310)	NR
Ifunanya et al., 2019 ²⁷	6.0% vs 14.3% (P=0.03)	>1000 mL: 11.9% vs 50.0% (P<0.0001)	NR	cEBL: 450±125 vs 820±118 mL (P<0.0001)	48h Hb 11.0±1.6 vs 7.8±1.2 g/dL (P<0.0001); pre-op similar (P=0.42)	7.1% vs 33.3% (P<0.0001)
Jafarbegloo et al., 2021 ²⁸	NR	NR	NR	65.2±32.0 vs 101.1±44.9 mL (P=0.002); Total: 616.3±176.9 vs 731.5±178.8 mL (P=0.028)	Decrease lower w/ TXA (P<0.05)	NR
Lee et al., 2023 ²⁹	2.1% vs 6.1% (P=0.157)	cEBL ≥1000 mL: 16.3% vs 25.3% (P=0.148)	NR	Total cEBL: 620.6±405.7 vs 754.1±447.9	% Hb drop: -9.6±8.3 vs -12.4±7.9% (P=0.018)	NS

				mL (P=0.035)		
Maged et al., 2015 ³⁰	NR	>1000 mL: 0 vs 6 (P NR)	NR	459.4±75.4 vs 700.3±143.9 mL (P<0.001)	Decline less w/ TXA (P<0.05)	NR
Martadiansyah et al., 2025 ³¹	NR	>1000 mL: 2.3% vs 18.2% (P=0.045)	Suction/gauze loss lower w/ TXA (P=0.044/0.0 14)	Total: 459.4±174.3 vs 686.3±251.1 mL (P=0.000)	Pre-/post-op Hb NS (P=0.361/0.133)	NR
Movafegh et al., 2011 ³²	NR	NR	262.5±39.6 vs 404.7±94.4 mL (P<0.001)	67.1±6.5 vs 141.0±33.9 mL (P<0.001)	Decline less w/ TXA (P<0.05)	Oxytocin: 39±5.8 vs 43±5.4 units (P=0.001)
Nambiath Sujata et al., 2016 ³³	NR	NR	NR	NR	NR	23% vs 83% (P<0.001)
Nargis & Dewan, 2020 ³⁴	0% vs 5%	NR	358.8±28.9 vs 615.8±95.2 mL (P<0.001)	51.1±7.4 vs 77.0±5.2 mL (P<0.001)	Change: 0.98±0.23 vs 1.50±0.27 g/dL (P<0.001)	Oxytocin: 30±2.8 vs 40±2.7 units (P<0.001); add'l: 16.7% vs 40.0% (P=0.005)
Neumann et al., 2024 ³⁵	0 in either group	NR	NR	Calc.: 400.9±280.9 vs 597.9±353.7 mL (P<0.001); Gravimetric: 379.2±96.5 vs 431.1±152.2 mL (P<0.001)	Hb: 1.04 vs 1.61 g/dL (P<0.001); Hct: 3.20% vs 4.95% (P<0.001)	NS (P=0.26)
Obi et al., 2019 ³⁶	14.0% vs 44.8% (P=0.001)	≥1000 mL: 8.8% vs 27.6% (P=0.012)	NR	566.8±267.4 vs 819.1±348.4 mL (P<0.001)	Change less w/ TXA (P<0.001); post-op Hb 9.8±0.7 vs 9.2±0.9 g/dL (P=0.001)	Lower w/ TXA (P=0.001)
Ogunkua et al., 2022 ³⁷	0/55 vs 2/55	>2000 mL: 69% vs 91% (P=0.004)	NR	Calc. loss @24h: 2274±469 vs 2407±388 mL (P>0.05, NS)	Post-op Hct 32.8±3.8% vs 30.8±3.7% (P=0.009)	Standard oxytocin, all pts
Omawumi et al., 2023 ³⁸	2.8% vs 18.3% (P=0.003)	NR	503.7±170.2 vs 704.6±187.4 mL (P=0.0001)	121.4±49.4 vs 159.7±69.5 mL (P=0.001); Total: 624.9±200.8 vs 864.2±229.1 mL (P=0.001)	48h PCV 30.7±2.8% vs 28.1±3.3% (P=0.0001)	16.7% vs 50.7% (P<0.001)
Ortuanya et al., 2024 ³⁹	8% vs 26% (P=0.001)	>1000 mL: 1% vs 19% (P=0.001)	NR	Total EBL: 442.9±201.0 vs 801.3±258.7 mL (P=0.001)	48h Hb 10.39±0.96 vs 9.67±0.86 g/dL (P=0.001)	39% vs 68% (P=0.001)
Oseni et al., 2021 ⁴⁰	NR	>1000 mL: 1.6% vs 9.8% (P=0.01)	NR	Total: 414.0±143.7 vs 773.8±199.2 mL (P<0.01)	Hb 10.1±0.8 vs 9.5±0.8 g/dL (P<0.01); drop 0.7±0.4 vs 1.4±0.6 g/dL (P<0.01); PCV 31.5±2.8% vs 29.9±2.6% (P<0.01)	NR (all received oxytocin)
Pacheco et al., 2023 ⁹	3.6% vs 4.2% (RR 0.86, 95%	Intraop loss >1000 mL: 7.3%	>1 L: NS (P=0.19)	NR	-1.8±1.1 vs -1.9±1.1 g/dL (MD -0.1, 95% CI -0.2 to -0.1)	11.7% vs 13.4% (RR 0.88, 95% CI 0.80–0.97)

	CI 0.71–1.03; P=0.19)	vs 8.0% (P=0.19, NS)				
Ray et al., 2016 ⁴¹	NR	0 vs 6 cases	499.1±111.2 vs 690.9±198.4 mL (P<0.001)	59.9±12.5 vs 110.1±13.5 mL (P<0.001); Total ~30% lower w/ TXA (P<0.001)	0.26±0.22 vs 0.99±0.48 g/dL (P<0.001)	NR
Sekhavat et al., 2009 ⁴²	NR	NR	NR	28.0±5.5 vs 37.1±9.0 mL (P<0.001)	24h Hb 12.57±1.33 vs 11.74±1.14 g/dL (P=0.002)	NR
Sentilhes et al., 2021 ⁷	1.9% vs 1.8% (NS); red-cell by day 2: 1.6% vs 1.4% (NS)	cEBL>100 0 mL or transfusion by day 2 (primary): 26.7% vs 31.6% (aRR 0.84, 95% CI 0.75–0.94; P=0.003); cEBL>100 0 mL: 26.4% vs 31.5%	NR	Calc. EBL: 680±748 vs 787±750 mL (P<0.001); gravimetric: 689±887 vs 719±920 mL (NS)	Hb decrease 11±14 vs 13±15 g/L (P<0.001); PCV 3.5±5.1% vs 4.0±5.3% (P<0.001)	5.9% vs 7.2% (NS)
Shady et al., 2017 ⁴³	17.5% (IV)/17.5% (Topical) vs 67.5% (Control) (P=0.0001)	17.5%/17.5 % vs 52.5% (P=0.0001)	532/532 vs 918 mL, medians (P=0.0001)	4h: 123.1/125.5 vs 182.2 mL; Total: 660/655 vs 1110 mL (P=0.0001)	24h Hb NS (P=0.124)	17.5%/17.5% vs 67.5% (P=0.0001)
Shahid & Khan, 2013 ⁴⁴	7.9% vs 33.3%	NR	356.4±143.2 vs 710.2±216.7 mL (P<0.001)	35.7±23.3 vs 43.6±28.0 mL (P=0.188, NS)	Drop smaller w/ TXA (P<0.05)	NR
Shalaby et al., 2022 ⁴⁵	1.25% vs 6.25% (P=0.071, NS)	NR	NR	Total: 583.2±379.6 vs 896.8±519.6 mL (P<0.001)	Hb 10.1±1.2 vs 9.2±1.6 g/dL (P<0.001); % change 7.34% vs 16.36% (P<0.001); Hct 30.1±3.4% vs 27.4±4.1% (P=0.012)	13.75% vs 46.25% (P<0.001)
Shree et al., 2026 ⁴⁶	4.7% vs 9.3% (P=0.175, NS)	NR	NR	Total: 460.3±129.7 vs 511.9±164.1 mL (P<0.05)	Hb NS (P=0.907); PCV NS (P=0.913)	NS (Misoprostol/Carboprost/Carb etocin similar)
Sinha et al., 2024 ⁴⁷	0% vs 8.3% (P=0.239, NS)	NR	241.3±67.8 vs 344.9±146.7 mL (P=0.001)	Postop NS (P=0.147); Total: 284.2±76.8 vs 391.4±153.3 mL (P<0.001)	Post-op Hb NS (P=0.5887); Δ Hb: 0.48±0.62 vs 1.29±1.24 g/dL (P=0.001)	NS (P=1.000)
Soliman et al., 2021 ⁴⁸	0 in either group	None; >500 mL: 22% vs 86% (P≤0.001)	286.8±47.4 vs 406.7±60.6 mL (P<0.001)	143.5±23.6 vs 203.4±30.3 mL (P<0.001); Total: 430.3±71.0 vs 610.1±90.9 mL (P<0.001)	Hb 9.79±0.67 vs 9.22±0.76 g/dL (P<0.001); Hct 29.4±2.1% vs 27.6±2.3% (P<0.001)	None required, either group
Tarabrin et al., 2012 ⁴⁹	NR	NR	300±40.5 vs 500±60.6 mL (~40%)	NR	Haemoviscoelastogra phy; moderate hypocoagulation both groups	NR

			reduction, P NR)			
Wongjariya kul et al., 2025 ⁵⁰	0/25 vs 2/25 (P=0.148, NS)	>1000 mL: 8% vs 36% (P=0.039)	495.8±294.6 vs 925.6±448.9 mL (P<0.001)	NR	Hb decline 1.1±7.0 vs 6.9±9.6 g/dL (P=0.020)	NS (P=0.065)
Xu et al., 2013 ⁵¹	9.1% vs 22.1%	PPH stopped: 92.0% vs 75.6% (P<0.01)	NS (P=0.17)	46.6±42.7 vs 84.7±80.2 mL (P<0.01); Total: 379.2±160.1 vs 441.7±189.5 mL (P=0.02)	Decline less w/ TXA (P<0.05)	NR
Yehia et al., 2014 ⁵²	0 in either group; iron replacement ↓ w/ TXA	31.1% vs 63.2% (P<0.05)	369.5±198 vs 606.8±193 mL (P<0.05)	85.0±30.7 vs 130.8±49.3 mL (P<0.05); Total: 454.5±201 vs 737.6±217 mL (P<0.05)	24h Hb 11.2±1.5 vs 9.6±1.2 g/dL (P<0.05); Hct 30.2±6.6 vs 29.2±2.8 (P=0.002)	NR
Zhang et al., 2026 ⁵³	Red cell @2d: 18.8% vs 21.6% (RR 0.88, 95% CI 0.74– 1.03, NS); by discharge: 19.4% vs 21.8% (NS)	cEBL≥100 0 mL or transfusion @2d (primary): 29.7% vs 35.1% (RR 0.85, 95.2% CI 0.75–0.96; P=0.01); cEBL≥100 0 mL: 25.7% vs 31.6%	NR	Calc. EBL: 841±1397 vs 1003±1440 mL (P=0.01); gravimetric: 790±767 vs 813±688 mL (NS); ≥1000 mL gravimetric: 15.0% vs 20.6% (P<0.05)	Hb decrease 11±14 vs 13±15 g/L (P<0.05); >20 g/L decrease: 17.9% vs 22.9% (P<0.05); Hct decrease 3.5±5.1% vs 4.0±5.3% (P<0.05)	93.0% vs 94.2% (NS)

3.5 Maternal Safety and Other Clinical Outcomes

Across the 42 included trials, prophylactic TXA was not associated with a statistically significant increase in thromboembolic events (Table 3). In the three largest trials Pacheco et al. 9 (0.2% vs. 0.3%, P = 0.81), Sentilhes et al.^[7] (0.4% vs. 0.1%, adjusted RR 4.01, 95% CI 0.85–18.92, P = 0.08), and Zhang et al. 53 (0.1% vs. 0.4%, adjusted RR 0.34, 95% CI 0.03–3.23) event rates were low and did not differ significantly between groups, though the wide confidence interval in Sentilhes et al. leaves a modest increase in risk difficult to exclude. Most remaining, smaller trials reported no thromboembolic events in either arm; given the rarity of these events and limited follow-up in these studies, the absence of reported events should be interpreted cautiously.

Nausea and vomiting were the most frequently reported minor adverse events, with significant increases in the TXA group reported by Sentilhes et al.^[7] Abdel-Aleem et al.^[14] and Omawumi et al.^[38] no significant differences were reported in the remaining trials assessing gastrointestinal effects.

Postpartum infection was significantly higher with TXA in Pacheco et al.^[9] (3.2% vs. 2.5%; RR 1.28, 95% CI 1.02–1.61) but not replicated in Sentilhes et al. 7 or Zhang et al.^[53] where differences were non-significant; Zhang et al. also reported a small, non-

significant increase in acute liver injury with TXA. 53

Where hemodynamic and laboratory parameters were assessed, TXA was not associated with adverse effects: Ali et al.^[15] reported more stable postoperative heart rate and blood pressure with TXA, while other trials found no significant hemodynamic differences and no clinically relevant abnormalities in blood counts, organ function, or coagulation parameters.

Neonatal outcomes, including Apgar scores, NICU admission, umbilical blood gases, and respiratory distress, were comparable between TXA and control groups across all trials reporting these outcomes.

3.6 Clinical and Methodological Factors Associated with Treatment Effects

Several clinical and methodological characteristics varied across the 42 randomized trials and may have contributed to differences in the observed efficacy and safety outcomes.

Timing of TXA Administration

Most trials administered TXA preoperatively, generally 10–20 minutes before skin incision.^[14,18,19,23,29,38,39,46,47,48,50,52] and these studies generally reported reductions in measured blood loss. In contrast, the three largest trials Pacheco et al.^[9] (N = 11,000), Sentilhes et al. 7 (N = 4,551), and Zhang et al.^[53] (N = 1,732) administered TXA post-delivery,

within approximately three to five minutes of birth or cord clamping. Findings among these trials were inconsistent: Sentilhes et al. and Zhang et al. reported statistically significant reductions in their respective primary/composite blood-loss outcomes, whereas Pacheco et al. found no significant difference in blood loss or transfusion requirements.^[7,53,9] Thus, post-delivery timing alone did not consistently predict treatment effect.

Dose and Route of Administration

Most trials used a fixed 1-g intravenous dose, whereas others used weight-based regimens of 10 or 15 mg/kg. Goswami et al.^[23] directly compared 10 and 15 mg/kg and reported significant reductions in blood loss with both doses. Ogunkua et al.^[37] evaluated a two-dose regimen of 1 g before incision and 1 g after placental delivery. Bharati et al.^[16] and Shady et al.^[43] additionally compared IV TXA with topical TXA (2 g applied to the placental bed) and reported significant reductions in bleeding outcomes with both routes.

Baseline Population Risk

Treatment effects appeared to vary according to baseline hemorrhagic risk. Trials involving placenta

previa, placenta accreta, maternal anemia, or high risk of atonic PPH generally demonstrated larger absolute reductions in transfusion, severe PPH, or additional uterotonic requirements. In contrast, low-risk or unselected populations often had low baseline transfusion rates, limiting the potential absolute benefit despite reductions in measured blood loss.

Methodological Differences and Study Size

Double-blind, placebo-controlled trials generally provided more robust estimates than open-label or single-blind studies, particularly for outcomes involving estimated blood loss. The evidence base also included a marked difference in study size, from small single-center trials to large multicenter trials. Smaller studies were frequently underpowered for rare outcomes such as thromboembolism, whereas the large multicenter trials provided more precise estimates of uncommon safety events. Overall, differences in timing, dose, route, baseline hemorrhagic risk, and methodological design likely contributed to the heterogeneity of observed treatment effects.

Table 3: Safety Outcomes and Factors Associated with Treatment Effects

Study ID	Thromboembolic Events (TXA vs. Control/Placebo)	Other Adverse Events (TXA vs. Control/Placebo)
Abdel-Aleem et al., 2013 ¹⁴	0/373 vs 0/367 (none)	Nausea/vomiting: 74.3% vs 53.1% (P<0.001); other outcomes NS
Ali et al., 2019 ¹⁵	NR	Post-op HR/BP more stable w/ TXA (P<0.001); no severe reactions
Bharati et al., 2022 ¹⁶	No DVT/PE in either group	Nausea/vomiting/diarrhea NS among groups
Chaiyakarn et al., 2023 ¹⁷	0% vs 0% (none)	Nausea, vomiting, headache, myalgia, fatigue slightly ↑ w/ TXA, NS (P>0.05); no neonatal complications
Dhivya Lakshmi & Abraham, 2016 ¹⁸	NR	No maternal/neonatal adverse drug reactions or major complications
El-Gaber et al., 2019 ¹⁹	NR	Maternal AE NR; neonatal outcomes comparable
Gai et al., 2004 ²⁰	None in either group	Urinalysis, CBC, liver/renal function, coagulation — no abnormal changes
Garg et al., 2026 ²¹	0% vs 0% (none; no photopsia)	Nausea: 1.6% vs 2.08%; vomiting: 2.08% both (NS, P>0.05)
Gobbur et al., 2014 ²²	0% vs 0% (no signs of thrombosis)	Nausea: 32% vs 26%; vomiting: 18% vs 16%; diarrhea: 2% vs 0% (NS, P>0.05)
Goswami et al., 2013 ²³	NR	Hemodynamic parameters comparable among groups (P>0.05)
Gungorduk et al., 2011 ²⁴	No increase in either group	Maternal/neonatal outcomes NS
Hemapriya et al., 2020 ²⁵	NR	No significant hemodynamic changes or other AEs
Ibrahim et al., 2019 ²⁶	None in either group	Day-2 labs (Hb, platelets, INR, PT, PTT) NS; no maternal/neonatal AE
Ifunanya et al., 2019 ²⁷	Study underpowered to assess thrombosis risk	No major safety concerns; underpowered for mortality
Jafarbegloo et al., 2021 ²⁸	NR	NR
Lee et al., 2023 ²⁹	No maternal thrombotic events; 2 pts leg swelling/pain (both placebo, Doppler negative)	Neonatal outcomes similar
Maged et al., 2015 ³⁰	NR	Maternal AE NR; neonatal outcomes comparable
Martadiansyah et al., 2025 ³¹	None (DVT/PE/MI/renal failure) in either group	Nausea: 11.4% vs 0.0% (P=0.101, NS); no severe AE
Movafegh et al., 2011 ³²	NR	Maternal AE NR; neonatal outcomes comparable
Nambiath Sujata et al., 2016 ³³	NR	Maternal AE NR; neonatal outcomes comparable
Nargis & Dewan, 2020 ³⁴	None (seizures, TE, ICU, hysterectomy) in either group	Nausea/vomiting: 6.7% vs 6.7% (P=1.000)
Neumann et al., 2024 ³⁵	None attributable to TXA	1 pt (0.94%) TXA vomiting; none in control
Obi et al., 2019 ³⁶	None; no maternal deaths	Nausea/vomiting: 19.3% vs 13.8% (P=0.4286, NS)
Ogunkua et al., 2022 ³⁷	0% vs 0% (no TE or seizure)	Maternal/neonatal outcomes similar
Omawumi et al., 2023 ³⁸	None reported	Nausea: 12.5% vs 0.0% (P=0.006); vomiting: 1.4% vs 0.0% (P=1.000); other profiles similar

Ortuanya et al., 2024 ³⁹	None; no seizures/major AE/deaths	Mild AE (headache, dizziness, nausea, vomiting): 6% vs 5% (P=1.000), mostly background-condition related
Oseni et al., 2021 ⁴⁰	0% vs 0% (none)	None reported in either group
Pacheco et al., 2023 ⁹	0.2% (12/5069) vs 0.3% (13/4996) (P=0.81); new-onset seizures: 2 (<0.1%) vs 0 (P=0.50)	Postpartum infection: 3.2% vs 2.5% (RR 1.28, 95% CI 1.02–1.61); readmission: 3.9% vs 3.2% (P=0.07)
Ray et al., 2016 ⁴¹	NR	No additional AE; NICU admission NS
Sekhavat et al., 2009 ⁴²	0% vs 0% (none)	No adverse drug reactions or maternal/neonatal morbidity
Sentilhes et al., 2021 ⁷	0.4% (8/2049) vs 0.1% (2/2056) (aRR 4.01, 95% CI 0.85–18.92; P=0.08)	Nausea/vomiting: 43.0% vs 36.3% (adj. P<0.001); postpartum infection NS (1.4% vs 1.3%)
Shady et al., 2017 ⁴³	No DVT/PE in either group	Nausea: 12.5%/2.5% vs 2.5%; vomiting: 5%/2.5% vs 2.5%; diarrhea: 5%/2.5% vs 2.5% — minor, NS
Shahid & Khan, 2013 ⁴⁴	None in either group	Hb, urinalysis, liver/renal function — no abnormal changes
Shalaby et al., 2022 ⁴⁵	None; no serious maternal/neonatal AE	Neonatal outcomes similar; tolerability excellent
Shree et al., 2026 ⁴⁶	0% vs 0% (none)	Nausea/vomiting: 42.0% vs 37.3% (P=0.765, NS); comparable neonatal outcomes
Sinha et al., 2024 ⁴⁷	0% vs 0% (no PE/DVT/diarrhea)	Nausea: 11.1% vs 8.3%; vomiting: 11.1% both (P=0.9229, NS)
Soliman et al., 2021 ⁴⁸	None (no DVT)	No AE, ICU admission, or postpartum/neonatal complications; maternal survival 100%
Tarabrin et al., 2012 ⁴⁹	None in either group	NR (coagulation monitored via haemoviscoelastography)
Wongjariyakul et al., 2025 ⁵⁰	0% vs 0% (none serious)	Dizziness: 24% vs 28%; nausea/vomiting: 4% vs 16%; headache: 8% vs 0% (NS, P=0.570)
Xu et al., 2013 ⁵¹	None reported	No abnormal vital signs; mild transient AE more frequent w/ TXA (freq. NR)
Yehia et al., 2014 ⁵²	NR	Vital signs, CBC, liver/kidney function — no significant differences
Zhang et al., 2026 ⁵³	0.1% (1/837) vs 0.4% (3/845) (aRR 0.34, 95% CI 0.03–3.23; NS); no MI/stroke/seizure	OR AEs (nausea, vomiting, photopsia, dizziness, diarrhea): 2.2% vs 1.7% (RR 1.31, 95% CI 0.67–2.59; NS); acute liver injury: 0.4% vs 0.1% (RR 3.05, 95% CI 0.32–29.13; NS); postpartum infection similar (1.4% vs 1.3%)

3.7 Risk of Bias of Included Studies

Risk of bias was assessed across five domains using the RoB 2 framework (Figure 2,3). Overall, 23 of 42 studies (54.8%) were judged to have low risk of bias, 16 (38.1%) had some concerns, and 3 (7.1%) were at high risk.

All studies were judged to have low risk of bias arising from the randomization process and bias due to missing outcome data. The risk of bias due to deviations from intended interventions was low in most studies, although some studies had concerns or high risk. Similarly, most studies had low risk for measurement of outcomes, while some had concerns, particularly where blood loss estimation could be influenced by lack of blinding. Bias in selection of the reported result was generally low, although some studies had concerns.

Overall, the included evidence was predominantly at low risk of bias, with concerns concentrated mainly in deviations from intended interventions, outcome measurement, and selection of the reported result. The three studies classified as having high overall risk of bias were Abdel-Aleem et al. (2013), Dhivya Lakshmi and Abraham (2016), and Ray et al. (2016).^[14,18,41]

3.8 Overall Synthesis of Findings

Across the 42 RCTs, prophylactic TXA generally reduced maternal blood loss and the incidence of PPH, with the most pronounced benefits observed in high-risk obstetric populations. However, reductions in blood transfusion requirements were less consistent, particularly in large multicentre trials with low baseline transfusion rates.

TXA showed a generally favorable maternal safety profile, with no clear increase in thromboembolic events, although rare-event data were limited. Mild gastrointestinal adverse effects, particularly nausea and vomiting, were reported more frequently in some trials. Neonatal outcomes were generally comparable between TXA and control groups.

Overall, the findings support prophylactic TXA as an effective strategy for reducing perioperative blood loss and PPH, while its effect on transfusion requirements appears more variable and may depend on baseline hemorrhagic risk, timing of administration, and other trial-level factors.

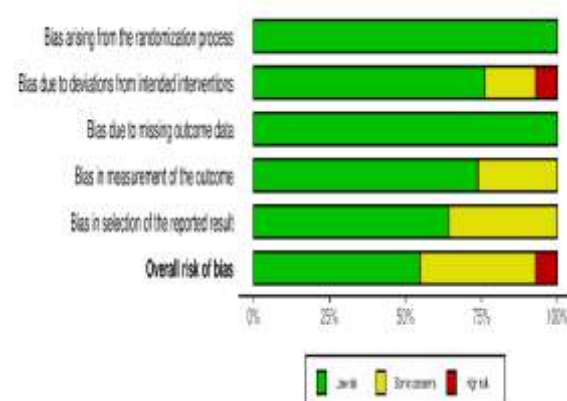


Figure 2: Summary of ROB judgments across the 42 included RCTs using the Cochrane RoB 2 tool

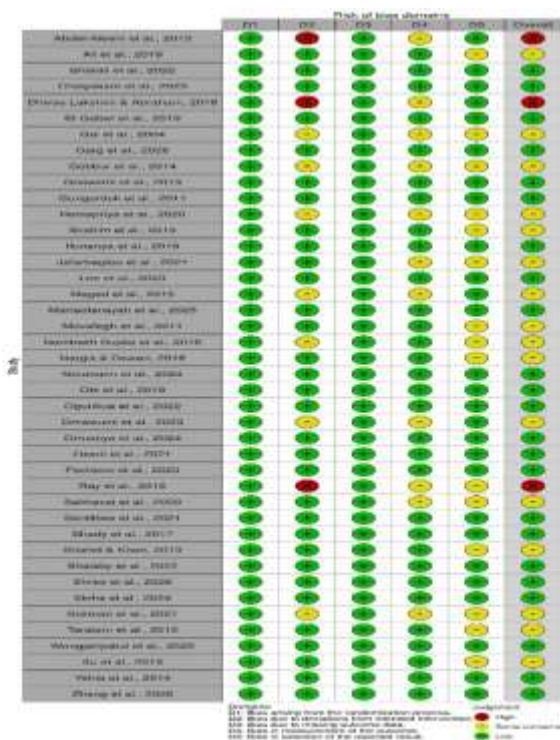


Figure 3: ROB assessment of the 42 included RCTs using the Cochrane RoB 2 tool

DISCUSSION

This systematic review included 42 RCTs evaluating whether prophylactic intravenous TXA reduces blood transfusion, blood loss, and PPH during cesarean delivery, while maintaining maternal and neonatal safety. TXA reduced measured blood loss and PPH in most trials, but the effect on blood transfusion was less uniform, particularly in the largest trials.

Previous meta-analyses and large randomized trials have reported similar patterns. The TRAAP2 trial found that TXA reduced a composite blood-loss/transfusion outcome but did not meaningfully reduce postpartum transfusion rates when considered separately.^[7,8] The TXA-CS trial also found no significant reduction in its primary composite outcome of maternal death or transfusion, although blood loss and hemoglobin decline were modestly lower with TXA.^[9] Among the 29 trials in our review that reported transfusion data, roughly one-third showed a statistically significant reduction with TXA. The clearest benefit occurred in higher-risk groups, particularly women with placenta previa and placenta accreta, where baseline transfusion rates were higher. In low-risk or unselected populations, transfusion events were uncommon, so reductions in blood loss did not always translate into fewer transfusions. Earlier reviews have also described greater TXA benefit in women with higher baseline bleeding risk.^[2,3,5,6]

The timing of TXA administration did not explain all of the differences between trials. The three largest trials administered TXA shortly after delivery rather

than before surgery. Sentilhes et al. and Zhang et al. reported significant reductions in their respective composite blood-loss outcomes, whereas Pacheco et al. did not.^[7,9,53] Pacheco et al. was the largest trial in this review, with 11,000 participants.^[9] The different results among these trials indicate that factors such as baseline maternal risk, outcome definitions, and study design also contributed to the variation in treatment effects.

Maternal safety findings were reassuring. The largest trials did not show a clear increase in thromboembolic events with TXA.^[1,7,9,53] Gastrointestinal adverse effects, mainly nausea and vomiting, occurred more frequently with TXA in several studies, including Sentilhes et al. Abdel-Aleem, and Omawumi et al.^[7,14,38] Neonatal outcomes were similar between TXA and control groups in the trials that reported these outcomes, including Apgar scores, NICU admission, umbilical artery blood gases, respiratory distress syndrome, and assisted ventilation.

Several limitations should be considered when interpreting these results. The review was not prospectively registered, and the search was restricted to freely accessible databases. The 42 trials differed in maternal risk profile, TXA dose, timing of administration, and definitions and methods used to measure blood loss and PPH, which limited quantitative pooling across studies. Nineteen of the 42 trials (45%) had some concerns or high risk of bias, with concerns particularly related to outcome measurement and blinding of blood-loss assessment. Prophylactic TXA reduced blood loss and PPH across much of the available trial evidence, while reductions in transfusion were more apparent in higher-risk obstetric populations. The large trials did not show a clear increase in thromboembolic events, although these events were rare. For low-risk women undergoing cesarean delivery, the benefit of routine TXA prophylaxis remains less certain than its benefit in women at higher risk of major bleeding.

CONCLUSION

Prophylactic intravenous TXA reduces intraoperative blood loss and PPH in women undergoing cesarean delivery, with the clearest transfusion benefit seen in high-risk populations such as placenta previa and placenta accreta. Its effect on overall transfusion requirements remains less consistent, particularly in low-risk or unselected populations. Current trial data did not demonstrate a statistically significant increase in thromboembolic events with TXA, although rare-event data limit definitive assessment of risk. A risk-based approach to prophylactic TXA may be more appropriate than routine use in all women undergoing cesarean delivery.

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