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**ADMINISTRATIVE INFORMATION****Support** - None.**Review Stage at time of this submission** - Completed but not published.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202640041**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 12 April 2026 and was last updated on 12 April 2026.**INTRODUCTION**

**Review question / Objective** Does intraoperative application of platelet-rich plasma (PRP) improve skin scar quality, reduce early wound inflammation, reduce uterine scar defect (isthmocele/niche) formation, reduce postoperative pain intensity, and decrease analgesic consumption compared to standard care in women undergoing cesarean section?

**Population:** Women aged  $\geq 18$  years undergoing cesarean section for any indication.

**Intervention:** Intraoperative PRP application (autologous maternal or cord blood PRP).

**Comparator:** Standard wound closure without PRP or placebo.

**Outcomes:** Scar quality (POSAS, VSS), wound inflammation (REEDA), uterine niche formation, postoperative pain (VAS/NRS), analgesic consumption.

**Study design:** Randomized controlled trials.

**Rationale** Cesarean section accounts for approximately 21% of all births worldwide, with wound complications affecting 3–15% of patients. Platelet-rich plasma (PRP) is an autologous concentrate enriched with growth factors including platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF- $\beta$ ), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), fibroblast growth factor (FGF), and insulin-like growth factors (IGF-1/2), all of which play established roles in tissue regeneration, angiogenesis, and extracellular matrix remodeling. Despite several individual randomized controlled trials examining PRP in cesarean wound healing, no quantitative synthesis existed prior to this review. Furthermore, the uterine scar – specifically isthmocele (niche) formation – has been largely overlooked in prior PRP literature, despite its clinical significance for future pregnancy complications. This systematic review and meta-analysis was conducted to pool RCT evidence using validated outcome measures, quantify heterogeneity, and provide the first synthesis addressing both skin scar quality and uterine scar

integrity following PRP application at cesarean section.

**Condition being studied** Wound healing and scar formation following cesarean section, encompassing: (1) skin incision scar quality assessed by validated scales; (2) early wound inflammatory response measured by the REEDA scale; and (3) uterine scar integrity, specifically the formation of isthmocele (niche defect) and residual myometrial thickness at the hysterotomy site.

## METHODS

**Search strategy** The following search string was applied across PubMed/MEDLINE, Embase, CENTRAL (Cochrane), Scopus, and Web of Science from inception through March 2026: ("platelet-rich plasma" OR "PRP" OR "platelet rich plasma" OR "cord blood platelet" OR "platelet concentrate") AND ("cesarean" OR "caesarean" OR "C-section") AND ("wound healing" OR "scar" OR "uterine niche" OR "isthmocele" OR "surgical site infection"). ClinicalTrials.gov and WHO ICTRP were searched for unpublished and ongoing trials. Reference lists of all included studies were manually searched.

**Participant or population** Women aged 18 years and older undergoing cesarean section for any obstetric indication.

**Intervention** Intraoperative application of platelet-rich plasma (PRP) — either autologous maternal PRP or cord blood-derived PRP (CB-PRP) — applied locally at the time of cesarean section to the uterine incision, fascia, subcutaneous tissue, or skin closure site.

**Comparator** Standard wound closure without PRP application, or placebo (saline or no additional treatment).

**Study designs to be included** Randomized controlled trials (RCTs) only.

**Eligibility criteria** Inclusion criteria: (1) Randomized controlled trial design; (2) Women aged  $\geq 18$  years undergoing cesarean section; (3) Intraoperative PRP (autologous or cord blood) as the intervention; (4) Standard care or placebo as comparator; (5) Any language; (6) Any date of publication.

Exclusion criteria: (1) Non-RCT study designs (cohort, case-control, observational); (2) Conference abstracts without extractable full data; (3) Studies evaluating PRP in non-cesarean

surgical wounds; (4) Duplicate publications from the same cohort (concurrent observational studies excluded, only the RCT data used).

**Information sources** PubMed/MEDLINE, Embase, CENTRAL (Cochrane Central Register of Controlled Trials), Scopus, Web of Science (from inception to March 2026); ClinicalTrials.gov; WHO International Clinical Trials Registry Platform (ICTRP); manual searching of reference lists of all included studies and relevant review articles.

**Main outcome(s)** (1) Skin scar quality assessed by validated scales: Patient and Observer Scar Assessment Scale (POSAS — patient subscale and observer subscale) and Vancouver Scar Scale (VSS); measured at  $\geq 30$  days postoperatively. (2) Early wound inflammatory response assessed by the REEDA scale (redness, edema, ecchymosis, discharge, approximation) at 7–14 days postoperatively. (3) Uterine scar integrity: rate of isthmocele (niche) formation and residual myometrial thickness (RMT) assessed by transvaginal ultrasound at  $\geq 3$  months postoperatively.

**Additional outcome(s)** (4) Postoperative pain intensity measured by Visual Analogue Scale (VAS) or Numerical Rating Scale (NRS) at 24–72 hours. (5) Total analgesic consumption in the postoperative period. (6) Surgical site infection rate. (7) Wound dehiscence rate.

**Data management** Two independent reviewers (S.Ş. and F.G.Ş.) screened titles and abstracts, then full texts, using a standardized eligibility form. Data were extracted independently using a pre-specified extraction form covering study characteristics, participant demographics, intervention details, outcome measures, and follow-up duration. Discrepancies were resolved by consensus; unresolved discrepancies were referred to a third reviewer. Statistical analyses were performed using RevMan 5.4 and Stata 17.

**Quality assessment / Risk of bias analysis** Risk of bias was assessed independently by both reviewers (S.Ş. and F.G.Ş.) using the Cochrane Risk of Bias 2 (RoB 2) tool across five domains: (1) randomization process; (2) deviations from intended interventions; (3) missing outcome data; (4) measurement of the outcome; (5) selection of the reported result. Each study received a domain-level judgment (low risk, some concerns, high risk) and an overall risk of bias rating. Disagreements were resolved by consensus.

**Strategy of data synthesis** Continuous outcomes were synthesized as standardized mean difference (SMD; Hedges'  $g$ ) with 95% confidence intervals using the DerSimonian-Laird random-effects model. A negative SMD indicates benefit in favor of PRP. Dichotomous outcomes were analyzed as risk ratio (RR) with 95% CI. Heterogeneity was assessed using the  $I^2$  statistic, Cochran's Q test, and  $\tau^2$ . Pooling was considered inappropriate when  $I^2 > 75\%$ . For one included study (Thanachaivivat 2024), dispersion measures were verified by back-calculation from reported p-values to distinguish SEM from SD; corrected values were used in the primary analysis with the naive assumption as a sensitivity analysis.

**Subgroup analysis** Pre-specified subgroup analyses: (1) PRP type: autologous maternal PRP versus cord blood PRP (CB-PRP); (2) population risk: standard obstetric risk versus high-risk population; (3) outcome measurement timing: early ( $\leq 7$  days) versus late ( $\geq 30$  days).

**Sensitivity analysis** (1) Exclusion of studies rated as high or unclear overall risk of bias by RoB 2. (2) Alternative dispersion measure assumptions for Thanachaivivat 2024 (SEM-corrected values versus naive SD values). (3) Comparison of fixed-effects model versus random-effects model results.

**Language restriction** No language restriction was applied.

**Country(ies) involved** Turkey (review conducted). Included studies from: Iran, Poland, Romania, Thailand, China.

**Other relevant information** This review was registered retrospectively. Data extraction and analysis were completed between January and March 2026 prior to registration; retrospective registration is submitted to ensure transparency and to comply with journal submission requirements. One included study (Brezeanu 2025, NCT06978010) has a concurrent single-arm observational publication from the same group; only the registered RCT data were used and the observational study was cited for transparency. A statistical anomaly was identified in Chaichian 2022: the study-reported  $p=0.002$  for niche formation could not be reproduced from the published  $2 \times 2$  table (Fisher's exact  $p=0.109$ ); this discrepancy is discussed in the review.

**Keywords** platelet-rich plasma; cesarean section; wound healing; scar; uterine niche; isthmocele; POSAS; REEDA; meta-analysis; systematic review.

**Dissemination plans** Results will be submitted for publication in a peer-reviewed international obstetrics and gynecology journal. No additional dissemination activities are planned at this time.

#### **Contributions of each author**

Author 1 - Serhat Şen - Conceived and designed the review; conducted literature search; performed data extraction and risk of bias assessment; conducted statistical analysis; drafted and revised the manuscript.

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Author 2 - Feyza Gulgel Sen - Independent data extraction; independent risk of bias assessment; critical revision of the manuscript for important intellectual content.

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