

Application of Platelet Rich Plasma in High-Risk Population Undergoing Cesarean Section; Could it Benefit Pain Perception and Wound Healing?

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Received: 01 Sep 2026; Accepted: 03 Oct 2026 Published: 12 Oct 2026

Citation: Asmaa A Azab, Magdy R Ahmed, Ahmed M Gadallah, et al. Application of Platelet Rich Plasma in High-Risk Population Undergoing Cesarean Section; Could it Benefit Pain Perception and Wound Healing?. Gynecol Reprod Health. 2026; 10(10): 1-6.

ABSTRACT

Aim: To assess efficacy of PRP on wound healing and pain perception after elective cesarean section (CS) in high-risk population.

Material and Methods: 112 patients were admitted for elective CS. Participants were randomly equally assigned into two groups. In study group, prior to skin closure 5 ml PRP was applied to subcutaneous tissue by micro-injections. In control group, subcutaneous tissue was cleaned with normal saline only. Primary endpoint used Visual Analogue Scale (VAS) for pain intensity and REEDA scale (redness, edema, ecchymosis, discharge, approximation) for wound healing. Secondary outcome were Vancouver scar scale (VSS) for Scar quality and overall satisfaction using numeric scale. All participants were evaluated at day 1, day 7 and at sixth weeks after CS.

Results: Although pain was not statistically significantly different between both groups; surprisingly, study patients required fewer analgesics doses per day than the control group: 39.3% in the PRP group and 58.9% in the control group ($P=0.03$). PRP group showed a greater reduction in REEDA score compared to the control group ($P=0.001$). Significant differences between both groups in the scar quality assessment by VSS in the favor of the PRP group ($P < 0.001$).

Conclusion: Confirmation of PRP's usefulness in improving wound healing, scare quality and reduction of analgesics after CS in the high-risk population may further lead to the implementation into ERAS protocols and everyday clinical practice.

Keywords

Platelet-rich plasma, High-risk cesarean section, Wound healing, Postoperative pain.

Introduction

Cesarean section (CS) is one of the most common surgical procedure worldwide that has witnessed an alarmingly rising trend in the last two decades. These rising trends has rendered it from a lifesaving mandatory surgical procedure into a rather trendy socially driven method of delivery. According to WHO reports, the, global CS rates tripled from 7% in 1990 to 21.1% in 2021, with projections indicating its rise to 28.5% by 2030 [1]. Egypt in particular has experienced an skyrocketing CS rates rising from

27.6% in 2008 , to 51.8% in 2014 up-till reaching to 72.2% per the 2021 [2,3] with rapid escalation is particularly pronounced in private health facilities, where rates have reached as high as 81% [4]. All these figures are well above the established desirable 15% CS rate recommended by WHO [5].

Wound healing following is a regulated process of biochemical events, involving the interaction of multiple cell types, growth factors including platelet-derived growth factor (PDGF), transforming growth factor- β (TGF- β), and vascular endothelial growth factor (VEGF), cytokines, including TNF α , IL 1 and IL6 and chemokines. Many of these factor's release has been directly related to platelets release [6]. Disruption of this coordinated

mechanism leads to either, chronic, non-healing wounds or excessive granulation tissue with arrest at the chronic inflammatory phase. Surgical site repair passes through 4 stages viz, hemostasis, inflammation, proliferation, and remodeling, a disruption at any of these 4 stages may lead to non-healing CS wound [7].

Pain is a very common postoperative problem following CS. It is an inevitable occurrence after CS that involves several factors including tissue breakdown, nerve disruption and hyperalgesia [8]. Pain control either by adequate prevention or proper treatment is an essential part of cesarean section to allow adequate wound healing and prevent post-operative complications including delayed recovery, psychological changes that impair quality of life and chronic post-operative pain [9].

Platelet-rich plasma (PRP) is an autologous blood product containing a platelet concentration higher than its baseline concentration within whole blood. Over the past two decades. It has been promoted to treat several conditions in the field of obstetrics and gynecology and outside it with mixed results. Based on platelets role in aggregation during early wound stages, their release of various growth factors and cytokines during wound repair and defense role that platelets exert via producing signaling proteins that attract macrophages, PRP has been suggested to assist in skin rejuvenation and wound healing in different surgeries including cesarean section [10]. PRP formation from whole blood involves several preparation protocols, with a common principle of achieving platelets concentration 3-5 times the physiological concentration in a small volume of plasma [7,10].

This has inspired us to evaluate the role of PRP application into the wound during cesarean delivery in improving wound healing and reducing postoperative pain in high-risk population.

Materials and Methods

This randomized controlled trial was carried out on one hundred and twelve pregnant full-term females scheduled for elective CS at the obstetrics and gynecology department at Suez Canal University Hospitals during the period from April 2024 till August 2025. Sample size was estimated based on a clinically significant difference in reduction of Visual Analogue Scale (VAS) score of 26.2% between the two groups using a two-tailed Z-test of proportions between the two groups with 80% power and a 95% level of significance, considering a 10% dropout rate [11].

Inclusion criteria were pregnancies in terms of previous CS, obesity (BMI ≥ 25 Kg/m²), diabetes mellitus either gestational or pre gestational, twin pregnancy and *corticosteroids therapy*. Exclusion criteria were women with chronic pain disorders, blood coagulation disorders, platelet count less than 150×10^3 , HB level < 10 mg/dl, patients requiring either subcutaneous or peritoneal drains, emergency CS or an allergy to analgesics. Study outcomes were assessed as primary outcomes including pain perception and wound healing. Whereas, secondary outcomes included scar formation and patient satisfaction.

Simple randomization was performed by using a shuffled, sealed envelope technique in which two opaque envelopes, each containing a single group letter (A or B) were shuffled in the recovery room. A single envelope was then chosen and opened with the letter inside corresponding to the allocation group of the patient who is going to be operated upon. Shuffling and choice of envelopes were performed at the recovery room. Group A (study group) 56 patients who subjected to application of PRP subcutaneously before wound closure and group B (control group) 56 patients who were subjected to application of 0.9% NaCl solutions subcutaneously before standard wound closure. In the operating room before the start of each procedure, approximately 30 ml of whole blood was drawn from the uninvolved arm of each patient in group A into a sterile syringe containing citrate for anticoagulation. The sample was centrifuged at 1,200 rpm for 12 minutes. This produced three layers: a platelet- and leukocyte-rich upper layer, a leukocyte-dense buffy coat, and a lower red blood cell layer. The upper and intermediate buffy layers were transferred to a sterile tube and centrifuged again at 3,300 rpm for 7 minutes, forming soft platelet pellets. The upper two-thirds of the resulting platelet-poor plasma was discarded. The pellet was re-suspended in the remaining one-third about 5 mL of plasma to obtain PRP.

In the study group (group A), after closure of the rectus sheath and prior to skin closure, 5 ml PRP was directly applied to the subcutaneous tissue of the wound site by a series of micro-injections into the subcutaneous tissue using a sterile syringe. In the control group (group B), the patients received no topical treatment and the subcutaneous tissue was cleaned with normal saline before skin closure. For all participants, no drains were used and the skin was closed with Monocryl 2-0. After skin closure, a wound dressing with a compressed bandage was applied. All participants received the routine postoperative care including I.V fluids in form of 1 Liter of normal saline and lactated ringer were used on the 1st day to prevent post spinal hypotension. Analgesia if needed were in form of non-steroidal analgesics (Diclofenac sodium 75mg IM), I.V antibiotic was continued as protocol (cefotaxime 1gm /12 hours) all over hospital stay and shifted to oral form (Amoxicillin and clavulanic acid 1gm /12 hours) for a week. The patients were examined by an obstetricians who were blind to group allocation of the patients on day 1, and then day 7 and at sixth weeks after the procedure.

Pain intensity was assessed using the Visual Analogue Scale (VAS; 0 = no pain, 10 = worst pain imaginable) by measuring the distance from the zero point to the patient's mark [12]. Wound healing was assessed using the REEDA scale, which scores redness, edema, ecchymosis, discharge, scoring from 0–3 each. Total scores range from 0–15; with lower scores reflecting better healing [13]. Scar quality was evaluated using the Vancouver Scar Scale (VSS) assessing vascularity, height, pliability, and pigmentation (total score 0–13), where higher scores indicate more scarring [14]. Overall satisfaction was measured using a 0–10 numeric scale (0 = not satisfied, 10 = fully satisfied). Scores were grouped into 3 groups: < 3 unsatisfied, 3–7 partially satisfied, and > 8 satisfied [15].

Data analysis was performed using SPSS software (Version 20, IBM) for Windows. Continuous variables were presented as mean $\pm$ standard deviation (SD), and comparisons between groups were made using the Student's t-test. Categorical variables were summarized as frequencies and percentages, and group differences were assessed using the Chi-square test or Fisher's exact test when appropriate. To evaluate changes in quantitative measures over time within the same group, paired one-way analysis of variance (ANOVA) followed by post hoc testing was applied. A p-value of less than 0.05 was considered statistically significant.

Results

Baseline maternal characteristics at cesarean delivery of both study and control groups were presented in Table 1. No statistical difference was noted regarding the mean duration of CS (37.1 ± 3.8 min in study group versus 37 ± 3.2 min in control group). The most common indication for CS was previous CS delivery (43% and 37% in the study and control groups, respectively). DM was the commonest medical disorder in both groups (30% and 23% in the study and control groups, respectively). Both groups were matched regarding age, Parity, body mass index (BMI), hemoglobin levels,

operative blood loss and duration of hospital stay (Table 1).

Pain was statistically decreased significantly over time within each group only ($p = 0.001$). On postoperative day 1, mean VAS scores were 7.4 in the study group and 7.5 in the control group without a statistical significant difference. By one week, scores declined to 1.6 and 1.5 respectively, with insignificant statistical difference. At six weeks, VAS scores further decreased to 0.8 in the study group and 0.6 in the control group, again without a significant statistical difference. Surprisingly, study patients required fewer analgesics doses per day than the control group: 22 (39.3%) patients in the PRP group and 33 (58.9%) patients in the control group required analgesics two doses of per day with a significant statistical difference ($p = 0.038$) (Table 2).

The results showed that REEDA scores, which reflect wound healing, were lower in the study group, indicating better healing. Both groups demonstrated significant reductions in REEDA scores over time ($p = 0.001$). On postoperative day 1, mean scores were 2.67 in the study group and 2.75 in the control group. At one week, scores decreased to 1.3 and 2.3, respectively, showing a statistically

Table 1: The demographic and clinical characteristics of the study participants.

		Study group (n=56)	Control group (n=56)	p-value
Age	Mean $\pm$ SD	33.2 ± 4.8	34.5 ± 5.1	0.166(NS)
	Range	25 – 41	25 – 42	
BMI (Kg/m ²)	Mean $\pm$ SD	29.5 ± 2.5	30.1 ± 2.8	0.258(NS)
	Range	26 – 34	26 – 34	
Parity	Median	2	2	0.8 (NS)
	Mean $\pm$ SD	1.8 ± 0.6	1.7 ± 0.7	
Gravidity	Median	3	3	0.8 (NS)
	Mean $\pm$ SD	2.8 ± 0.6	2.8 ± 0.7	
Medical disorders	Diabetes mellitus	17 (30.36%)	13 (23.21%)	0.4 (NS)
	Hypertension	8 (14.29%)	4 (7.14%)	0.2 (NS)
	Steroid therapy	2 (3.57%)	3 (5.36%)	0.6 (NS)
	Immunosuppressive therapy	1 (1.79%)	1 (1.79%)	0.9 (NS)
CS indications	Maternal indications	39 (69.6%)	35 (62.5%)	0.5 (NS)
	• Preeclampsia	6 (10.7%)	4 (7.1%)	
	• cephalopelvic disproportion	9 (16.1%)	10 (17.9%)	
	• Previous CS	24 (42.9%)	21 (37.5%)	
	Fetal indications	17 (30.4%)	21 (37.5%)	
	• Breech presentation	5 (8.9%)	5 (8.9%)	
	• Transverse lie	2 (3.6%)	4 (7.1%)	
	• Fetal macrosomia	6 (10.7%)	6 (10.7%)	
Preoperative Hemoglobin	Mean $\pm$ SD	11.5 ± 0.8	11.6 ± 0.9	0.4 (NS)
	Range	10 – 13.5	10.1 – 13.5	
Postoperative hemoglobin	Mean $\pm$ SD	11.03 ± 0.86	11.2 ± 0.88	0.3 (NS)
	Range	9.5 – 12.8	9.5 – 12.9	
Operative time (minutes)	Mean $\pm$ SD	37.1 ± 3.8	37 ± 3.2	0.9 (NS)
	Range	30 – 45	30 – 45	
Intraoperative blood loss (ml)	Mean $\pm$ SD	740.3 ± 121.6	710.7 ± 134.4	0.2 (NS)
	Range	500 – 1000	500 – 1000	
Hospital stay (days)	Mean $\pm$ SD	2.5 ± 0.5	2.4 ± 0.4	0.133(NS)
	Range	2 – 3	2 – 3	

Table 2: Visual Analogue Score (VAS) and use of analgesics for the study participants.

VAS		Study group (n=56)	Control group (n=56)	p-value
Day 1		7.4 ± 0.5	7.5 ± 0.6	0.3 (NS)
One week		1.6 ± 0.5	1.5 ± 0.5	0.086 (NS)
6 weeks		0.8 ± 0.5	0.6 ± 0.5	0.2 (NS)
p-value		0.001*	0.001*	
First request of postoperative analgesia (hours)		4.02 ± 0.56	3.9 ± 0.6	0.3 (NS)
Total dose of analgesic per ampoule/24	1 ampoule	34 (60.7%)	23(41.1%)	0.038*
	2 ampoules	22 (39.3%)	33 (58.9%)	

*Statistically significant difference.

significant difference ($p=0.001$). By six weeks, mean scores were 0.8 for the study group and 1.23 for the control group, with the difference remaining statistically significant ($p=0.001$) (Table 3).

Table 3: REEDA score changes for the study participants.

REEDA	Study group (n=56)	Control group (n=56)	p-value
Day 1	2.67 ± 0.66	2.75 ± 0.64	0.6 (NS)
One week	1.38 ± 0.6	2.3 ± 0.6	<0.001*
6 weeks	0.8 ± 0.6	1.23 ± 0.7	0.001*
p-value	<0.001*	<0.001*	

REEDA: Redness, Edema, Ecchymosis, Discharge, Approximation.

*Statistically significant difference.

Vancouver scar scale was lower among the study group. Over time, both groups showed significant reduction of VSS score ($p=0.001$). At day 1 postoperative, mean Vancouver scar scale score was 1.8 and 2.7 in the study and control groups respectively with a statistically significant difference ($p=0.001$). These values changed to 1.1 and 1.8 after one week postoperative still with a statistically significant difference between both groups ($p=0.001$). After 6 weeks mean Vancouver scar scale score was 0.7 in the study group and 1.5 in the control group with a statistically significant difference ($p=0.001$) as shown in Table 4.

Table 4: Vancouver Scar Scale (VSS) score for the study participants.

VSS	Study group (n=56)	Control group (n=56)	p-value
Day 1	1.8 ± 0.6	2.7 ± 0.5	<0.001*
One week	1.1 ± 0.5	1.8 ± 0.7	<0.001*
6 weeks	0.7 ± 0.5	1.5 ± 0.7	<0.001*
p-value	<0.001*	<0.001*	

*Statistically significant difference.

Regarding keloid scar, three patients of the control group had evidence of keloid scar formation versus none of the study group. Regarding patient satisfaction, all of the study group patients were satisfied by the results of the procedure versus 89 % of the control group with a statistically significant difference ($p=0.027$). Wound infection rates did not differ significantly; one case occurred in the study group versus five in the control group, and all were managed conservatively with antibiotics and dressing, without the need for surgical intervention (Table 5).

Table 5: Overall patient satisfaction, Keloid formation and wound infection for the study participants.

		Study group (n=56)	Control group (n=56)	p-value
Keloid scar formation	No	56 (100%)	53 (94.64%)	0.243 (NS)
	Yes	0 (0%)	3 (5.36%)	
Overall patient satisfaction	Not satisfied	0 (0%)	6 (10.71%)	0.027*
	Satisfied	56 (100%)	50 (89.29%)	
Wound infection		1 (1.8%)	5 (8.9%)	0.21 (NS)

*Statistically significant difference.

Discussion

Topical application of PRP is used in cesarean section wounds as a novel method with a potential to prevent post - operative wound infection, enhance the wound healing because of its physiological role in wound healing [7,10,16]. PRP is being used more often for a variety of clinical applications, and it is now popular to apply it as a part of routine treatment. However, its role in topical application during cesarean section is yet to be established. We found that patients who were treated with topical autologous PRP had a significant improvements in wound healing process and scar quality after surgery in comparison with the control group in both short- and long-term assessments.

PRP is a volume fraction of blood having a high concentration of platelets above the baseline that markedly improves the adhesive properties and the process of wound healing. After application of PRP, the tissue-healing substances are released. The supra physiological concentration of platelets at the wound site accelerate the healing process and protect the wound against the infection [16,17]. PRP contains a high concentration of growth factors and cytokines, such as transforming growth factor-beta (TGF- β), fibroblast growth factor (FGF), platelet-derived growth factor (PDGF), insulin-like growth factors 1 and 2(IGF-1 and IGF-2), vascular endothelial growth factor (VEGF) and epidermal growth factor(EGF). The mechanism of PRP action in wound healing is based on stimulating the synthesis of matrix metalloproteinases (MMPs), increasing cutaneous fibroblast growth as well as the production of extracellular matrix (ECM) components including type I collagen and elastin [6,10].

To the best of our knowledge, there are only two studies [10,16]

evaluating the use of PRP application in high-risk population during CS available to date; they demonstrated that PRP application during cesarean delivery significantly improved wound healing, as assessed with the edema, ecchymosis, discharge, approximation (REEDA) scale. Additionally, patients treated with PRP experienced an improvement in pain perception as assessed by Visual Analogue Scale (VAS) score at the end of follow-up after CS.

There was no difference in the pain intensity assessment on the VAS recorded after surgery, though pain decreased significantly over time in both groups but PRP patients required fewer NSAIDs doses per day than the control group. This is particularly important for women giving birth because of the need to care for a newborn child. Childbirth, independently of other factors, is a risk condition for post-traumatic stress disorder (PTSD), and inappropriate pain treatment after delivery may increase this risk [18]. In contrast to our research, the PRP application significantly reduced postoperative pain. Noteworthy, we evaluated VAS scores only in the first 48 h after surgery, whereas other studies continued this evaluation for much longer (weeks or months after delivery).

A unique finding in our study that assessment of patient satisfaction which was higher in the PRP group, with 100% reporting satisfaction versus only 89 % in the control group which could be explained by the following reasons: (1) No keloid formation was observed in the PRP group, while three cases occurred in the control group. (2) PRP had a significant improvements in wound healing process and Scar quality after surgery in comparison with the control group in both short- and long-term assessments. (3) PRP patients required fewer NSAIDs doses per day than the control group. (4) only one case of wound infection occurred in the study group versus five in the control group.

The strength of this study is the high-risk population patients included. Adequate number of patients, use of multiple scales to evaluate pain and wound healing and patient satisfaction are other advantages added to the strength of our study. We believe that the results of our study are a good starting point for future research, particularly for evaluation of the potential use of PRP during CS in high-risk patients. Confirmation of PRP's usefulness in preventing wound complications in women undergoing CS may further lead to the implementation of PRP into enhanced recovery after surgery (ERAS) protocols and everyday clinical practice, as well as elaborating on new therapeutic and preventive strategies for certain groups of high-risk patients.

Our study had few limitation. First, it is single centre study, so further multi-centre studies should be conducted. Second, short duration of follow up, so studies with longer duration of follow up are recommended for further evaluation of the efficacy of PRP in enhancing wound healing following CS. Third, we use subjective assessment tool for patients satisfaction, we recommend evaluation of the wound by an objective method whether non pathological as scar thickness using ultrasonography or histopathology examination.

Conclusion

PRP appears to be safe, effective, and beneficial for cesarean patients significantly enhances cesarean wound healing and scar quality and may improve patient satisfaction. Although it did not influence postoperative pain intensity, it may reduce the use of analgesics after surgery.

Ethics approval

This study was approved by the Institutional Review Board of college of medicine – Suez Canal University (5656 / 2024). The patients were treated in accordance with the Declaration of Helsinki.

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