

# The Effect of Magnesium as an Adjuvant to Ultrasound-Guided Transversus Abdominis Plane Block on Interleukin-6, Neutrophil-to-Lymphocyte Ratio, Platelet-to-Lymphocyte Ratio, and Postoperative Pain after Cesarean Section: A Double-Blind Randomized Controlled Trial

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## ABSTRACT

### Background:

Postoperative pain after cesarean section may delay mobilization, impair maternal recovery, and increase the need for opioid rescue analgesia. Transversus abdominis plane (TAP) block is widely used as part of multimodal analgesia for abdominal wall pain, but its effect may be limited by duration and by incomplete visceral analgesia. Magnesium sulfate has N-methyl-D-aspartate receptor antagonistic properties and may enhance regional analgesia while potentially modulating postoperative inflammation.

### Objective:

This study evaluated whether magnesium sulfate as an adjuvant to ropivacaine in ultrasound-guided TAP block reduces serum interleukin-6 (IL-6), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and postoperative pain after elective cesarean section.

### Methods:

This prospective, double-blind, randomized controlled trial included 30 patients undergoing elective cesarean section under subarachnoid block at Universitas Airlangga Academic Hospital, Surabaya. Participants were randomized to receive bilateral ultrasound-guided TAP block with 0.375% ropivacaine plus magnesium sulfate (Group A, n=15) or 0.375% ropivacaine without magnesium (Group B, n=15). IL-6, NLR, and PLR were assessed preoperatively and at 12 and 24 hours postoperatively. Pain intensity was evaluated using the visual analog scale (VAS) at rest and during movement.

### Results:

Baseline clinical characteristics were comparable between groups. At 12 hours postoperatively, resting VAS was significantly lower in Group A than Group B (median 1 [0-2] vs. 2 [1-3], p=0.030), and movement VAS was also lower (2 [1-3] vs. 3 [2-4], p=0.001). No significant differences were observed at 24 hours for resting or movement VAS. IL-6, NLR, and PLR did not differ significantly between groups at baseline, 12 hours, or 24 hours postoperatively.

### Conclusion:

Magnesium sulfate as an adjuvant to ropivacaine in TAP block improved early postoperative analgesia during the first 12 hours after cesarean section, but did not significantly alter IL-6, NLR, or PLR within 24 hours. Magnesium may be considered as part of opioid-sparing multimodal analgesia, although its systemic anti-inflammatory benefit in this setting remains unproven.

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**Keywords:** cesarean section; magnesium sulfate; postoperative analgesia; transversus abdominis plane block; interleukin-6; neutrophil-to-lymphocyte ratio; platelet-to-lymphocyte ratio

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## Introduction

Cesarean section is one of the most frequently performed obstetric surgical procedures and is associated with moderate to severe postoperative pain during the early recovery period. Inadequate analgesia after cesarean section may impair maternal mobilization, breastfeeding, bonding with the newborn, and overall satisfaction with care. It may also increase systemic stress, prolong hospitalization, and increase the need for opioid analgesics. Consequently, contemporary postoperative pain management emphasizes multimodal analgesia, combining neuraxial anesthesia, non-opioid analgesics, and regional blocks to improve analgesia while minimizing opioid-related adverse effects.<sup>1-3</sup>

The transversus abdominis plane (TAP) block is a fascial plane block targeting the thoracolumbar nerves that travel between the internal oblique and transversus abdominis muscles. Because cesarean section pain includes a major somatic component from the abdominal wall incision, TAP block is clinically relevant as part of postoperative analgesia, particularly when intrathecal morphine is not used or when additional opioid-sparing analgesia is desired. Nevertheless, TAP block has limited effects on visceral pain and the duration of analgesia depends on the local anesthetic used. These limitations have stimulated interest in adjuvants that can prolong or improve regional analgesia.<sup>1,3,4</sup>

Magnesium sulfate is an attractive adjuvant because magnesium blocks N-methyl-D-aspartate receptors and modulates calcium influx. These mechanisms may reduce central sensitization, decrease nociceptive transmission, and prolong the effect of local anesthetics. Clinical studies have reported that magnesium administered intravenously or as a regional anesthetic adjuvant can reduce pain scores, opioid requirements, or inflammatory responses in different surgical settings. However, the specific effect of perineural or fascial-plane magnesium in TAP block after cesarean section remains less clearly defined.<sup>5-8</sup>

Postoperative pain is closely linked to the surgical stress response and systemic inflammation. Interleukin-6

(IL-6) is a key cytokine involved in the acute phase response after tissue injury and may reflect the magnitude of postoperative inflammation. In addition, hematological indices such as the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are inexpensive markers of systemic inflammatory and immune stress responses. NLR reflects the balance between innate neutrophil activation and adaptive lymphocyte response, whereas PLR reflects platelet-related inflammatory activation relative to lymphocyte-mediated regulation.<sup>2,9-15</sup>

Previous studies have examined TAP block or other fascial plane blocks in relation to postoperative pain and inflammatory biomarkers, and magnesium has been evaluated as an adjuvant in different regional techniques. However, evidence remains limited regarding whether adding magnesium sulfate to ropivacaine in TAP block can modulate IL-6, NLR, and PLR after cesarean section. Therefore, this study aimed to evaluate the effect of magnesium sulfate as an adjuvant to ultrasound-guided TAP block on IL-6, NLR, PLR, and early postoperative pain in patients undergoing elective cesarean section.<sup>7,16-22</sup>

## Methods

### Study design and setting

This study was designed as a prospective, double-blind, randomized controlled trial with a pretest-posttest control group design. The study was conducted in the operating room and postoperative ward of Universitas Airlangga Academic Hospital, Surabaya, Indonesia, during November-December 2025. The manuscript is prepared in accordance with the general structure used in international clinical research journals and may be further adapted to the author guidelines of the selected target journal.

Eligible participants were adult obstetric patients undergoing elective cesarean section under subarachnoid block. After preoperative screening and informed consent, participants were allocated into two groups: Group A received ultrasound-guided bilateral TAP block using ropivacaine with magnesium sulfate, and Group B

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received ultrasound-guided bilateral TAP block using ropivacaine without magnesium.

## Participants

The study population consisted of patients scheduled for elective cesarean section under subarachnoid block. Inclusion criteria were age 18-45 years, American Society of Anesthesiologists physical status I-II, and willingness to participate with written informed consent. Exclusion criteria included contraindications to spinal anesthesia or peripheral nerve block, allergy to magnesium or the anesthetic agents used, body mass index greater than 35 kg/m<sup>2</sup>, cerebrovascular disease, cardiovascular disease, valvular heart disease, hypertension, diabetes mellitus, hepatic or renal dysfunction, autoimmune disease, or active systemic infection.

Patients were excluded or dropped out if they experienced failed spinal anesthesia or nerve block requiring conversion of anesthetic technique, high or total spinal block, bleeding exceeding 20% of estimated blood volume, prolonged operation requiring anesthetic technique change, or postoperative pain with VAS greater than 3 requiring fentanyl rescue analgesia according to the study protocol.

## Randomization and blinding

Participants who met eligibility criteria were randomized into Group A or Group B after preoperative assessment. The study was conducted using a double-blind design. The patients and outcome assessors were blinded to group allocation, and the study solutions were prepared so that both groups received comparable total injection volumes during TAP block.

## Anesthetic and TAP block protocol

Before surgery, patient identity, diagnosis, consent status, and anesthetic plan were rechecked in the premedication area. Standard monitoring was applied in the operating room, including electrocardiography, non-invasive blood pressure, heart rate, respiratory rate, and oxygen saturation. Oxygen supplementation was provided via nasal cannula. Preemptive analgesia consisted of intravenous paracetamol 1 g. Subarachnoid block was then performed using the institutional protocol with a target sensory level of T6.

After completion of surgery, postoperative analgesia included metamizole 1 g every 8 hours. Bilateral ultrasound-guided TAP block was performed in

the supine position. The ultrasound probe was positioned transversely between the costal margin and iliac crest at the midaxillary line. The needle was introduced using an in-plane approach from anteromedial to posterolateral, with the tip targeted between the internal oblique aponeurosis and the transversus abdominis muscle. Correct spread was confirmed by visualization of hypoechoic separation of fascial layers.<sup>1,4</sup>

In Group A, each side received 18 mL ropivacaine 0.375% plus 2 mL magnesium sulfate 20%, for a total volume of 20 mL per side. In Group B, each side received 18 mL ropivacaine 0.375% plus 2 mL normal saline 0.9%, for a total volume of 20 mL per side. Postoperative pain was evaluated using VAS at rest and during movement. Blood samples for inflammatory biomarkers were collected preoperatively and at 12 and 24 hours postoperatively.

## Outcome measures

The primary inflammatory outcomes were serum IL-6 concentration, NLR, and PLR measured at baseline, 12 hours, and 24 hours after surgery. IL-6 was measured using enzyme-linked immunosorbent assay (ELISA). NLR and PLR were calculated from complete blood count parameters. Pain outcomes included VAS at rest and during movement at 12 and 24 hours postoperatively.<sup>11,14,15</sup>

Baseline clinical characteristics included age, body weight, height, body mass index, ASA physical status, and pain scores. The comparison of baseline variables was used to assess group homogeneity before evaluation of postoperative outcomes.

## Statistical analysis

Data were analyzed using statistical software. Continuous variables were summarized as mean +/- standard deviation for normally distributed data or median (minimum-maximum) for non-normally distributed data. Data normality was assessed using the Shapiro-Wilk test. Intergroup comparisons were performed using the independent sample t-test for normally distributed data and the Mann-Whitney U test for non-normally distributed data. Categorical data were summarized descriptively. A p value less than 0.05 was considered statistically significant.

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## Results

### Participant characteristics

A total of 30 participants were included and randomized equally into two groups, with 15 participants in Group A and 15 in Group B. Group A received TAP block with ropivacaine and magnesium sulfate, whereas Group B received TAP block with ropivacaine alone. The groups were comparable with respect to age, body weight, height, body mass index, and ASA physical status, indicating adequate baseline homogeneity for intergroup comparison.

The mean age was 30.93 +/- 6.07 years in Group A and 30.46 +/- 5.71 years in Group B (p=0.718). Mean body weight was 68.66 +/- 8.16 kg in Group A and 75.76 +/- 12.22 kg in Group B (p=0.073). Median body mass index was 29.33 (21.30-34.38) kg/m<sup>2</sup> in Group A and 33.43 (24.22-34.77) kg/m<sup>2</sup> in Group B (p=0.071). All participants were ASA physical status II.

**Table 1. Baseline characteristics.**

Variable	Group A: TAP + magnesium (n=15)	Group B: TAP only (n=15)	p value
Age (years)	30.93 +/- 6.07	30.46 +/- 5.71	0.718
Body weight (kg)	68.66 +/- 8.16	75.76 +/- 12.22	0.073
Height (m)	1.53 (1.50-1.65)	1.56 (1.47-1.65)	0.276
BMI (kg/m <sup>2</sup> )	29.33 (21.30-34.38)	33.43 (24.22-34.77)	0.071
ASA physical status	II	II	-

*Values are mean +/- SD or median (minimum-maximum). BMI: body mass index; ASA: American Society of Anesthesiologists.*

### Pain outcomes

At 12 hours postoperatively, magnesium as an adjuvant was associated with significantly lower pain scores. Resting VAS was lower in Group A than Group B (median 1 [0-2] vs. 2 [1-3], p=0.030). Movement VAS was also significantly lower in Group A (2 [1-3] vs. 3 [2-4], p=0.001). These findings indicate that magnesium improved analgesic quality during the early postoperative period.

At 24 hours postoperatively, pain scores were no longer significantly different between groups. Resting VAS was 0 (0-1) in Group A and 1 (0-1) in Group B (p=0.472), whereas movement VAS was 1 (0-2) in Group A and 1 (1-2) in Group B (p=0.199). Thus, the analgesic benefit of magnesium appeared most prominent within the first 12 hours after cesarean section.

**Table 2. Postoperative pain scores**

Variable	Group A: TAP + magnesium (n=15)	Group B: TAP only (n=15)	p value
Resting VAS, 12 h	1 (0-2)	2 (1-3)	0.030
Movement VAS, 12 h	2 (1-3)	3 (2-4)	0.001
Resting VAS, 24 h	0 (0-1)	1 (0-1)	0.472
Movement VAS, 24 h	1 (0-2)	1 (1-2)	0.199

*Values are mean +/- SD or median (minimum-maximum). VAS: visual analog scale*

### Inflammatory biomarkers

Serum IL-6 increased after surgery in both groups. Baseline IL-6 did not differ between Group A and Group B (27.46 [8.01-132.22] vs. 28.37 [4.76-198.05], p=0.852). At 12 hours, IL-6 was 121.03 +/- 38.90 pg/mL in Group A and 118.91 +/- 31.37 pg/mL in Group B (p=0.250). At 24 hours, IL-6 was 100.18 +/- 39.52 pg/mL in Group A and 127.00 +/- 42.69 pg/mL in Group B (p=0.085). Although the 24-hour value was numerically lower in the magnesium group, the difference did not reach statistical significance.

NLR and PLR also increased postoperatively but were not significantly different between groups at any measured time point. Baseline NLR was 4.45 (2.86-6.95) in Group A and 5.36 (2.89-21.31) in Group B (p=0.254). At 12 hours, NLR was 9.56 (4.94-23.25) versus 10.25 (5.13-22.50) (p=0.395). At 24 hours, NLR was 6.69 +/- 1.90 versus 6.65 +/- 2.25 (p=0.956). Baseline PLR was 14782.61 (10320.86-25894.04) versus 16441.72 (9075.63-51428.57) (p=0.468). PLR at 12 hours was 27250 (15812.5-58500) versus 28000 (13416.67-75750) (p=0.983), and at 24 hours was 21080.32 +/- 4426.05 versus 21321.09 +/- 7946.85 (p=0.919).

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**Table 3. Interleukin-6, NLR, and PLR at baseline, 12 hours, and 24 hours postoperatively.**

Outcome	Time point	Group A: TAP + magnesium	Group B: TAP only	p value
IL-6 (pg/mL)	Baseline	27.46 (8.01-132.22)	28.37 (4.76-198.05)	0.852
IL-6 (pg/mL)	12 h	121.03 +/- 38.90	118.91 +/- 31.37	0.250
IL-6 (pg/mL)	24 h	100.18 +/- 39.52	127.00 +/- 42.69	0.085
NLR	Baseline	4.45 (2.86-6.95)	5.36 (2.89-21.31)	0.254
NLR	12 h	9.56 (4.94-23.25)	10.25 (5.13-22.50)	0.395
NLR	24 h	6.69 +/- 1.90	6.65 +/- 2.25	0.956
PLR	Baseline	14782.61 (10320.86-25894.04)	16441.72 (9075.63-51428.57)	0.468
PLR	12 h	27250 (15812.5-58500)	28000 (13416.67-75750)	0.983
PLR	24 h	21080.32 +/- 4426.05	21321.09 +/- 7946.85	0.919

Values are mean +/- SD or median (minimum-maximum). IL-6: interleukin-6; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio.

**Discussion**

This randomized double-blind study found that adding magnesium sulfate to ropivacaine for bilateral ultrasound-guided TAP block significantly reduced resting and movement pain at 12 hours after elective cesarean section. However, the intervention did not significantly reduce IL-6, NLR, or PLR at 12 or 24 hours postoperatively. The findings suggest that magnesium may provide a clinically useful early analgesic benefit when used as a TAP block adjuvant, but the dose and route used in this study were insufficient to produce measurable systemic anti-inflammatory effects using the selected biomarkers.

The analgesic finding is biologically plausible. Magnesium has antinociceptive effects mediated in part by NMDA receptor antagonism and calcium channel

modulation. NMDA receptor activation is involved in central sensitization and postoperative hyperalgesia. By attenuating excitatory neurotransmission, magnesium may reduce nociceptive amplification and prolong the effectiveness of local anesthetics. In this study, the lower VAS scores at 12 hours in the magnesium group are consistent with previous reports in which magnesium as an adjuvant in regional blocks improved postoperative pain control and reduced analgesic requirements.<sup>5-8</sup>

The result also fits the broader literature on abdominal wall blocks after cesarean section. TAP block primarily covers the somatic component of pain from the anterior abdominal wall incision. The early difference between groups at 12 hours may therefore reflect an enhancement of the somatic analgesic component. By 24 hours, however, both groups had low median pain scores and the difference was no longer significant, suggesting that the incremental benefit of magnesium was time-limited in this setting. This may relate to declining surgical pain intensity over time, concomitant multimodal analgesia, and limited visceral coverage by TAP block.<sup>1,3,4,20,22</sup>

Unlike the pain outcomes, the inflammatory biomarkers did not show significant intergroup differences. IL-6 increased postoperatively in both groups, consistent with activation of the acute inflammatory response after surgical tissue injury. NLR and PLR also increased, reflecting the expected leukocyte and platelet-related stress response. The absence of significant differences suggests that local magnesium administered in the TAP plane may not achieve sufficient systemic concentration to modulate cytokine release or hematological inflammatory indices during the first 24 hours after cesarean section. This contrasts with some studies of intravenous magnesium, in which larger systemic exposure may produce more pronounced anti-inflammatory effects.<sup>2,9-15</sup>

Several mechanisms may explain why analgesia improved while inflammatory biomarkers did not. First, the analgesic effect of magnesium within the fascial plane may be predominantly local or regional, enhancing local anesthetic action near peripheral nerves without producing systemic immunomodulation. Second, cesarean section may generate a relatively homogeneous inflammatory response that is influenced by tissue injury, uterine manipulation, surgical technique, psychological stress, neuraxial anesthesia, and perioperative medications. These factors may mask a small biomarker effect in a sample of 30 participants. Third, IL-6, NLR,

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and PLR have biological variability, and the chosen sampling times of 12 and 24 hours may not fully capture peak or early changes in each marker.<sup>2,10,12</sup>

The findings should be interpreted in relation to previous research. Ahmed et al. reported that intravenous magnesium sulfate reduced postoperative NLR and pain in lower abdominal surgery, supporting the potential systemic effect of magnesium when delivered intravenously. Peng et al. showed that magnesium sulfate as an adjuvant to ropivacaine in quadratus lumborum block prolonged analgesia and reduced morphine consumption after laparoscopic gynecological surgery. Canakci et al. reported that TAP block reduced postoperative pain and proinflammatory cytokines after inguinal hernia surgery, while Domagalska et al. found lower NLR and PLR following erector spinae plane block in lumbar spine surgery. In obstetric anesthesia, Muhtadir et al. and Seger et al. demonstrated beneficial effects of abdominal wall blocks on pain-related outcomes after cesarean section, whereas Ratnawati et al. reported that local infiltration anesthesia reduced pain and IL-6 after cesarean section. Compared with these studies, the present trial contributes a more specific question: whether magnesium added directly to TAP block can reduce inflammatory biomarkers after cesarean section. The current findings suggest that the analgesic benefit is clearer than the systemic inflammatory benefit.<sup>7,16,18-22</sup>

From a clinical standpoint, magnesium as an adjuvant to ropivacaine in TAP block may be considered as part of an opioid-sparing multimodal analgesia strategy for early postoperative pain after cesarean section. This may be particularly relevant where neuraxial opioids are not used, contraindicated, or avoided. Nevertheless, the lack of significant effects on IL-6, NLR, and PLR indicates that this intervention should not be interpreted as a primary strategy for controlling systemic inflammation. Postoperative inflammatory modulation likely requires a broader perioperative approach, including minimally traumatic surgical technique, adequate analgesia, avoidance of complications, early mobilization, and optimized perioperative care.<sup>3,8</sup>

This study has several limitations. The sample size was relatively small, which may limit statistical power to detect modest but clinically meaningful differences in inflammatory biomarkers. The study assessed biomarkers at only three time points, and additional early time points such as 4, 6, or 8 hours could better characterize the temporal profile of IL-6 and hematological indices. The study did not include detailed

measurement of rescue analgesic consumption, duration of block, maternal satisfaction, time to mobilization, breastfeeding outcomes, or adverse events in the final comparative analysis. In addition, postoperative inflammation may be affected by surgical duration, operator technique, obstetric factors, baseline anxiety, and perioperative medications that were not fully controlled or stratified.

Future studies should involve larger multicenter samples and compare different doses of magnesium and ropivacaine in TAP block. Serial biomarker measurement at shorter intervals would help identify whether magnesium affects the timing or magnitude of inflammatory peaks. Future trials should also include clinically relevant recovery outcomes, such as opioid consumption, first analgesic request, time to mobilization, maternal satisfaction, breastfeeding comfort, length of stay, and adverse events. A direct comparison between TAP block, quadratus lumborum block, wound infiltration, and neuraxial opioid-based protocols may further clarify the optimal multimodal analgesic strategy after cesarean section.

### Conclusion

In patients undergoing elective cesarean section, magnesium sulfate as an adjuvant to ropivacaine in ultrasound-guided TAP block significantly reduced resting and movement pain at 12 hours postoperatively, but did not provide a significant analgesic advantage at 24 hours. The intervention did not significantly alter IL-6, NLR, or PLR within the first 24 postoperative hours. These findings support magnesium as a potential adjuvant for improving early postoperative analgesia, while its role in systemic inflammatory modulation after cesarean section remains uncertain.

### Declarations

**Ethics approval:** Ethics Committee of Universitas Airlangga Hospital, approval number 211/KEP/2025, dated 29 September 2025.

**Consent to participate:** All participants provided written informed consent before enrollment. Confidentiality of participant data was maintained throughout the study.

**Consent for publication:** Not applicable; the manuscript contains no personally identifiable patient information.

**Availability of data and materials:** The datasets generated and analyzed during the current study are available from the corresponding author on reasonable

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request, subject to institutional and ethics committee policies.

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**Authors contributions:** AAP contributed to study conception, data collection, analysis, and manuscript drafting. CSW and PK contributed to study supervision, interpretation, and critical revision. All authors approved the final manuscript.

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