

Evaluation of the Relationship between Shoulder Tip Pain Following Cesarean Section and Inflammatory Response Measured by High-sensitivity C- Reactive Protein

Nahid Zirak¹, Leila Mashhadi¹, Elaheh Jajarmi¹, Negar Morovatdar², Parisa Mohebbi², Nahid Javdani Haji³, Shahrzad Maraghehmoghadam³, Leili Hafizi^{4*} 

1. Lung Disease Research Center, School of Medicine Mashhad University of Medical Sciences, Mashhad, Iran
2. Clinical Research Development Unit, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
3. Mashhad University of Medical Sciences, Mashhad, Iran
4. Department of Obstetrics and Gynecology, Neonates and Women's Health Research Center, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran



Article Info

 [10.30699/jogcr.7.3.171](https://doi.org/10.30699/jogcr.7.3.171)

Received: 2021/06/26;

Accepted: 2021/09/15;

Published Online: 12 Jan 2022;

Use your device to scan and read the article online



Corresponding Information:

Leili Hafizi,

Department of Obstetrics and Gynecology,
Neonates and Women's Health Research
Center, School of Medicine, Mashhad
University of Medical Sciences, Mashhad,
Iran

Email: LTRC@mums.ac.ir

ABSTRACT

Background & Objective: This study aimed to investigate the relationship between the level of high-sensitivity C-reactive protein (hs-CRP; as an indicator of inflammatory response) and shoulder tip pain (STP) following cesarean section (C-section).

Materials & Methods: In this cohort study, a total of 120 pregnant women who were candidates for elective C-section at Imam Reza Hospital were included. The level of hs-CRP was measured perioperatively. STP was measured after the operation.

Results: Mean hs-CRP was significantly higher in females with STP compared to counterparts (19 ± 13.1 vs. 7.2 ± 4.5 ; $P < 0.001$). There was a positive and strong correlation between STP and postoperative hs-CRP ($P < 0.001$).

Conclusion: The release of acute-phase proteins (such as hs-CRP) plays a significant role in STP after C-section; the intensity of STP is associated with the level of hs-CRP.

Keywords: Cesarean section, High-sensitivity C-reactive protein, Shoulder tip pain



Copyright © 2022. This is an original open-access article distributed under the terms of the Creative Commons Attribution-noncommercial 4.0 International License which permits copy and redistribution of the material just in noncommercial usages with proper citation.

Introduction

Shoulder tip pain (STP) is a common complaint among women after cesarean section (C-section). In certain cases, it can be severe and debilitating and last for several days. It can cause severe movement restrictions in the upper limb region. STP also seems to be associated with increased hospitalization time and costs; it negatively affects the patient's physical and mental health (1). Pain makes breastfeeding and caring for newborns even more difficult. Due to the distress faced by mothers, many mothers seek help from orthopedic services aiming to alleviate the pain (2, 3). In a study carried out in 2010 in Mashhad, 131 (39.45%) of 332 women who had undergone C-section complained of STP, mostly on the right side (4). This was the first study that brought this issue to the attention of researchers.

Furthermore, another study suggested that postoperative STP was less likely to occur after spinal anesthesia compared to general anesthesia (5). The mechanism behind this pain has been proposed to be a referred pain caused by the phrenic nerve. Arising from C3-C5 nerve roots, the phrenic nerve innervates both iliopsoas and diaphragm muscles. It also carries sensory fibers from parietal peritoneum layers located on the inferior surface. Hence, the phrenic nerve can be stimulated by any tension on the diaphragm or parietal peritoneum. This leads to the stimulation of the C5 nerve, referring pain signals in the musculocutaneous, radial, median, and axillary nerve dermatomes (6).

The main causes of tension on the diaphragm are the accumulation of subdiaphragmatic free air or blood clots and/or postoperative inflammation of the

peritoneum (7, 8). Accordingly, this study aimed to evaluate the relationship between the intensity of the inflammatory process and the level of STP after C-section. C-reactive protein (CRP), as a common inflammatory marker, has been employed by many researchers to measure the intensity of inflammation (9-12).

The lower levels of CRP could be accurately detected using high-sensitivity CRP (hs-CRP). This can eliminate the risk of false-negative results caused by low CRP levels (9, 13). False-positive results can be caused by storing the samples in a refrigerator and medications such as non-steroidal anti-inflammatory drugs (NSAIDs), steroids, contraceptives, and anti-convulsants. If there is a significant link between STP after C-section and inflammatory response measured by hs-CRP, pain can be alleviated using anti-inflammatory measures perioperatively. This study was conducted in 2014 after gaining approval from the Ethics Committee of Mashhad University of Medical Sciences.

Patient Selection

The sample size was calculated regarding the prevalence of STP after C-section as 40% (type I error was 0.05, and power was 80%). Accordingly, a total of 120 pregnant women who were candidates for an elective C-section at Imam Reza Hospital were included. The method of sampling was convenience sampling. Inclusion criteria were patients >18 years old and with an indication for elective C-section at ≥ 37 weeks of gestation. Exclusion criteria included a history of any shoulder problems, chronic neuromuscular disease or diseases such as heart diseases, asthma, malignancies, autoimmune diseases, liver diseases, inflammatory skin, and mucosal diseases, taking any medications in the week prior to the operation, history of smoking, duration of surgery more than an hour, and any intraoperative surgical complications including possible hysterectomy, severe bleeding, and rupture of the bladder, abdominal, and pelvic organs. Patients with previous C-sections and fetal macrosomia were also included.

Laboratory Sample Processing

To measure hs-CRP levels, 4 mL of blood was taken from the brachial vein before the operation, and this was repeated again 6 h after the operation to measure hs-CRP levels. The blood samples were stored at 2°C-8°C. Enzyme-linked immunosorbent assay (ELISA) was used 48 h after sampling.

Surgical Technique

All C-section operations were performed by a gynecology consultant at Imam Reza Hospital. All patients received spinal anesthesia using 15 mL of 0.5% bupivacaine (Aspen, France) using a G25 spinal

needle (Dr. J, Japan). A horizontal incision (Pfannenstiel incision) was performed to begin the surgery. Single-layer uterine repair was performed after delivery. No repair was made to visceral and membranous peritonea. A routine suturing technique was used for the closure of the rectus sheath and skin. Full intraoperative monitoring was performed for patients. No steroids or NSAIDs were administered during the operation. For every patient, duration of surgery, surgeon's name, possible use of cautery, and any surgical complications were recorded. Postoperatively, a checklist was used to evaluate patients' STP and its intensity at 6, 12, and 24 h. Pethidin (Caspian, Iran) (25 mg) was administered intramuscularly to control the postoperative pain.

Pain Assessment

Using the visual analog scale (VAS) rated from 0 to 10, postoperative STP was subjectively measured. This tool is widely used and its validity and reliability is approved (14).

Statistical Analysis

Data were analyzed using SPSS 16 (SPSS Inc., Chicago, Ill., USA). Frequency tables and diagrams were employed to describe the data. The normal distribution of data was assessed by the Kolmogorov-Smirnov test. Continuous variables based on the normal distribution were tested using the independent sample *t* test or the Mann-Whitney U test. The chi-square test was used to determine differences in the frequency of variables between the two study groups. Spearman's correlation coefficient was used to assess the correlation between quantitative variables. A regression model was used to estimate the independent effect of hs-CRP on STP. A P-value ≤ 0.05 (two-sided) was considered to be statistically significant.

Results

Mothers' mean age was 28.8 ± 5.3 years, mean gestational age was 38.6 ± 1.1 weeks, and mean body mass index (BMI) was 29.6 ± 2.1 kg/m². The mean duration of C-section was 55.1 ± 6.4 min. Subdiaphragmatic free air was reported in 59 patients (49.2%). Previous cesarean delivery was regarded as the most common reason for performing C-section (65.8%). Other indications for C-section included faulty presentation (14.2%), narrow pelvis (12.5%), fetal macrosomia, (4.2%), and genital herpes (3.3%).

Mean hs-CRP was 5.6 ± 3.1 mg/dL preoperatively. Six hours after the surgery, it raised to 11.6 ± 10.4 mg/dL. Within the first 24 h after the surgery, 45 patients (37.5%) reported STP during the first 6 h, 35 patients (29.2%) during the first 12 h, and 21 patients (17.5%) during the first 24 h (Figure 1).

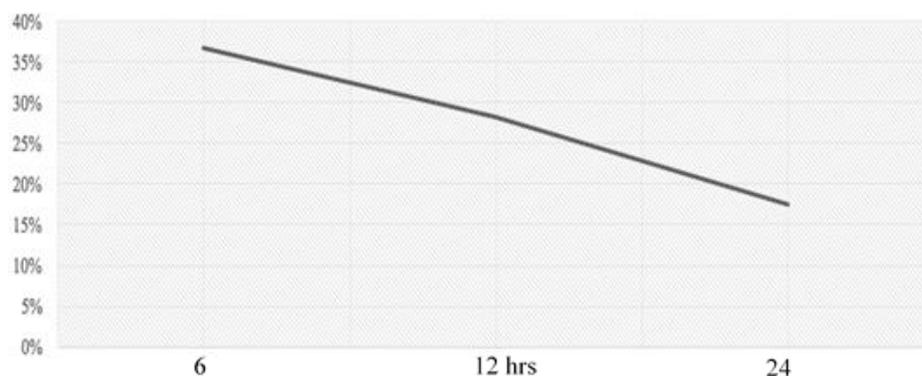


Figure 1. Pain alleviation process after the surgery

There was no significant difference between women with and without 24-h STP in age (28.8 ± 5 vs. 28.7 ± 5.5 years; $P=0.91$), gestational age (38.3 ± 1.1 vs. 38.7 ± 1.2 weeks; $P=0.65$), and time of surgery (55.5 ± 6.3 vs. 54.8 ± 4.5 min; $P=0.57$). Interestingly, BMI (31.2 ± 1.9 vs. 28.7 ± 1.6 kg/m²; $P<0.001$) and hs-CRP (6.6 ± 4.1 vs.

5.08 ± 2.3 mg/dL; $P=0.03$) before C-section were significantly greater in women with STP than in counterparts. After 6 h, hs-CRP was significantly higher in women with STP compared to counterparts (19 ± 13.1 vs. 7.2 ± 4.5 mg/dL; $P<0.001$; [Table 1](#)).

Table 1. Comparison of the effect of different factors on shoulder pain

P-value	Shoulder pain		
	Positive	negative	
0.910	28.8 ± 5.0	28.7 ± 5.5	Age (years)
0.658	38.3 ± 1.1	38.7 ± 1.2	Gestation age (weeks)
<0.001	31.2 ± 1.9	28.7 ± 1.6	BMI (Kilogram per meter square)
0.576	55.5 ± 6.3	54.8 ± 4.5	Duration of C-section (minutes)
0.031	6.6 ± 4.1	5.08 ± 2.3	hs-CRP pre-op (mg/Decilitre)
<0.001	19.0 ± 13.1	7.2 ± 4.5	hs-CRP 6 hours post-op (mg/Decilitre)

We found a positive and strong correlation between the postoperative hs-CRP level and STP score ($r=0.71$; $P<0.001$; [Figure 2](#)).

Using a regression model, hs-CRP (at 6 h after C-section) and BMI were independently associated with

the STP score ($B=0.05$; $P<0.001$ and $B=0.06$; $P<0.001$).

We used a multivariable regression model to adjust confounders. Also, we included a presurgical hs-CRP variable in the model to confront for this difference between the groups.

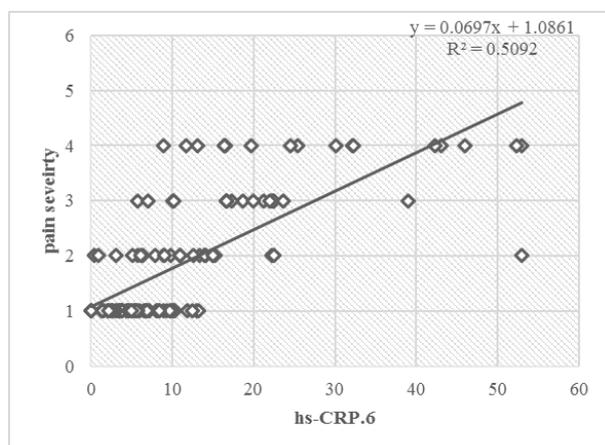


Figure 2. Relation between level of hs-CRP at 6 hours post C-section and the pain severity

Discussion

This study showed a high incidence of post-C-section STP. The intensity of this pain is sometimes reported to be higher than the intensity of incision pain; therefore, there is a high chance that it can interfere with breastfeeding and caring for newborns (15). Several studies have hypothesized that the stimulation of the supraclavicular and phrenic nerves could be the root of postoperative STP (16, 17). According to some studies, carbon dioxide used in laparoscopic surgeries is very likely to exert pressure on supraclavicular and phrenic nerves. It can chemically and physically stimulate these nerves, leading to postoperative STP (18).

Peritoneal irritation caused by amniotic fluid and blood is also associated with this common C-section morbidity (19). Studies have shown that although repositioning of the patient and the use of spinal anesthesia may lead to a reduction in the intensity of STP, these factors could not completely control the pain (5, 20). Based on the current literature, even though numerous studies have been conducted on hs-CRP as an inflammatory marker, its relationship with the incidence and intensity of postoperative STP is yet to be assessed in human models. The prevalence of STP was reported to be 37.5% in the immediate postoperative period, which declined to 17.5% within 24 h. In a study carried out in Turkey, the prevalence of STP in women undergoing C-sections under spinal anesthesia and general anesthesia was reported to be 26.6% and 43.9%, respectively. The reason behind this inconsistency was probably the different sample sizes and the duration of STP assessment and measurement. Furthermore, another study in 2012 (4) showed an incidence rate of 39.4%, which is similar to our findings.

Kikuchi *et al.* (19) suggested that the presence of subdiaphragmatic blood and/or amniotic fluid could be a plausible cause of STP after C-section (19). However, in our study, we were unable to obtain any clear correlation between these. Meanwhile, in a study carried out by Lahijani *et al.*, it was indicated that the use of surgical gauze and the reverse Trendelenburg position played no role in reducing STP after C-section. Other factors apart from the subdiaphragmatic collection of blood and amniotic fluid could cause diaphragm irritation and referred STP (20).

Regression analysis results in the current study revealed that although the history of previous C-sections had no direct impact on the intensity of STP, it may affect the pain if it leads to an increased level of hs-CRP. Six hours after the operation, the mean hs-CRP level was significantly higher in women with a history of previous C-sections than in women with other maternal-fetal indications of C-section (15 vs. 6.2; $P < 0.001$).

In the current study, the mean duration of C-section was 55.1 ± 6.4 min, whereas, in a study conducted by Cift *et al.* (15), it was reported to be 42.7 ± 11.4 min. This difference may be due to the sample selection, as both nulliparous and multiparous women were evaluated in the current study.

According to Cift *et al.*, intraoperative repositioning of patients was an effective factor in reducing the frequency of STP after C-section (15). However, in our study, a positive correlation was observed between BMI and the intensity of STP.

One kg/m² increase in BMI was associated with a 0.282 increase in pain intensity, that shows a significant direct correlation ($r = 0.582$; $P < 0.001$). Accordingly, due to the difficulty in appropriate positioning of obese women, they are more likely to experience STP postoperatively.

In the current study, a relationship was observed between cauterization and STP after C-section; however, using a regression model, no evidence was found that cauterization could independently affect the pain. However, cauterization, along with other factors such as high BMI, may lead to an increased risk of STP after C-section.

The most significant limitation of this study was the inability to determine when the hs-CRP level returns to normal after C-section. This may be due to the development of an unknown inflammatory process during pregnancy.

Conclusion

It seems that the release of acute-phase proteins (such as hs-CRP) plays a significant role in the process of inducing STP. Therefore, a higher level of hs-CRP is associated with a greater intensity of STP. These results could be used as an initiative to modify the anti-inflammatory regimen used perioperatively in C-section procedures. Further studies are needed to investigate the causes of high hs-CRP levels.

Acknowledgments

None.

Conflict of Interest

The authors declared no conflict of interest.

References

- Soltani G, Khorsand M, Shamloo AS, Jarahi L, Zirak N. Comparison of Intravenous Morphine with Sublingual Buprenorphine in Management of Postoperative Pain after Closed Reduction Orthopedic Surgery. *Arch Bone Jt Surg*. 2015;3(4):280-5.
- Abedian Z, Nikpour M, Mokhber N, Ebrahimi S, Khani S. Evaluation of Relationship between Delivery Mode and Postpartum Quality of Life. *The Iranian Journal of Obstetrics, Gynecology and Infertility*. 2010;13(3):47-53.
- Shin YK. Shoulder pain in a trial of labor after cesarean delivery. *South Med J*. 1989;82(10):1320. [DOI:10.1097/00007611-198910000-00041] [PMID]
- Zirak N, Soltani G, Pakravan S, Taherzadeh M, Mashayekhi Z. Evaluation of the Prevalence of Shoulder Pain after Cesarean with General Anesthesia. *The Iranian Journal of Obstetrics, Gynecology and Infertility*. 2011;14(3):8-12.
- Zirak N, Soltani G, Hafizi L, Mashayekhi Z, Kashani I. Shoulder pain after caesarean section: comparison between general and spinal anaesthesia. *J Obstet Gynaecol*. 2012;32(4):347-9. [DOI:10.3109/01443615.2011.654289] [PMID]
- Standring S. *Gray's anatomy e-book: the anatomical basis of clinical practice*: Elsevier Health Sciences; 2020.
- Lindahl S. *Anesthesia*. 5th ed. Vol. 1 and 2. *Anesthesia & Analgesia*. 2000;90(5):1254. [DOI:10.1097/00000539-200005000-00072]
- Ardalan MR, Tubbs RS, Etemadi J, Shoja MM. Referred shoulder pain in patients undergoing peritoneal dialysis. *Biomedicine International*. 2009;1(1).
- Windgassen EB, Funtowicz L, Lunsford TN, Harris LA, Mulvagh SL. C-reactive protein and high-sensitivity C-reactive protein: an update for clinicians. *Postgrad Med*. 2011;123(1):114-9. [DOI:10.3810/pgm.2011.01.2252] [PMID]
- Carter JJ, Whelan RL. The immunologic consequences of laparoscopy in oncology. *Surg Oncol Clin N Am*. 2001;10(3):655-77. [DOI:10.1016/S1055-3207(18)30056-5]
- Lopez-Cuenca A, Manzano-Fernandez S, Lip GY, Casas T, Sanchez-Martinez M, Mateo-Martinez A, et al. Interleukin-6 and high-sensitivity C-reactive protein for the prediction of outcomes in non-ST-segment elevation acute coronary syndromes. *Rev Esp Cardiol (Engl Ed)*. 2013;66(3):185-92. [DOI:10.1016/j.rec.2012.07.019] [PMID]
- Meadows JT, Jr., Kopp BT, Shook LA, Ballard HO, Hayes D, Jr. Elevated high-sensitivity C-reactive protein in preterm infants with pulmonary colonization with *Ureaplasma*. *J Thorac Dis*. 2013;5(3):223-7.
- Wang XS, Shi Q, Shah ND, Heijnen CJ, Cohen EN, Reuben JM, et al. Inflammatory markers and development of symptom burden in patients with multiple myeloma during autologous stem cell transplantation. *Clin Cancer Res*. 2014;20(5):1366-74. [DOI:10.1158/1078-0432.CCR-13-2442] [PMID] [PMCID]
- Sans-Torres J, Domingo C, Rué M, Durán-Tauleria E, Marín A. Valoración de la calidad de vida de los pacientes con EPOC e hipoxemia crónica mediante la versión española del Chronic Respiratory Disease Questionnaire [An assessment of the quality of life of patients with COPD and chronic hypoxemia by using the Spanish version of the Chronic Respiratory Disease Questionnaire]. *Arch Bronconeumol*. 1999 Oct;35(9):428-34. Spanish. [DOI:10.1016/s0300-2896(15)30038-7] [PMID]
- Cift T, Ustunyurt E, Yilmaz C, Olmez F, Basar B. Shoulder Tip Pain After Cesarean Section. *J Clin Diagn Res*. 2015;9(8):QC04-6. [DOI:10.7860/JCDR/2015/13841.6314] [PMID] [PMCID]
- Hong JY, Lee IH. Suprascapular nerve block or a piroxicam patch for shoulder tip pain after day case laparoscopic surgery. *Eur J Anaesthesiol*. 2003;20(3):234-8. [DOI:10.1097/00003643-200303000-00009]
- Tsai HW, Chen YJ, Ho CM, Hseu SS, Chao KC, Tsai SK, et al. Maneuvers to decrease laparoscopy-induced shoulder and upper abdominal pain: a randomized controlled study. *Arch Surg*. 2011;146(12):1360-6. [DOI:10.1001/archsurg.2011.597] [PMID]
- Haghgoo A, Chaichian S, Ghahremani M, Nooriardebili S, Akbaian A, Moazzami B. The Use of Peritoneal Suction Drainage to Reduce Shoulder Pain Caused by Gynecological Laparoscopy. *Arch Iran Med*. 2016;19(3):173-8.
- Kikuchi C, Tonozaiki S, Gi E, Watanabe M, Shimizu H. [Shoulder-tip pain during cesarean section under combined spinal-epidural anesthesia]. *Masui*. 2014;63(2):149-52.
- Mortazavi Lahijani M, Manshoori A, Ghahremani M, Asadollahi Z, Shafiepour M. Comparison between Placing Surgical Sponges on both Sides of Uterus and Reverse Trendelenburg Position of 30 Degree to Reduce the Incidence of Shoulder Pain after Cesarean

Section with Spinal Anesthesia. The Iranian Journal of Obstetrics, Gynecology and Infertility. 2014;17(99):8-12.

How to Cite This Article:

Zirak N, Mashhadi L, Jajarmi E, Morovatdar N, Mohebbi P, Javdani Haji N, Maraghehmoghaddam SH, Hafizi L. Evaluation of the Relationship between Shoulder Tip Pain Following Cesarean Section and Inflammatory Response Measured by High-sensitivity C- reactive Protein. J Obstet Gynecol Cancer Res. 2022; 7(3) :171-176.

Download citation:

[BibTeX](#) | [RIS](#) | [EndNote](#) | [Medlars](#) | [ProCite](#) | [Reference Manager](#) | [RefWorks](#)