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THE EFFECT OF PLACENTA REMOVAL METHOD ON POSTPARTUM LEUKOCYTOSIS – A RANDOMIZED CONTROLLED TRIAL

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SUMMARY – The rate of cesarean section (CS) as one of the common major surgeries has been increasing every year. Standardizing of surgical technique will improve outcomes and decrease postpartum infections. The purpose of this study was to investigate whether there was an association between the placental removal method and mean postpartum white blood cell (WBC) counts. This prospective randomized controlled study included 279 singleton pregnancies having CS. Women were randomized into two groups with manual placenta removal and spontaneous delivery with controlled cord traction. There was no significant difference between the groups regarding the mean temperatures ($p>0.05$). The mean WBC and neutrophil counts (postoperative day 1 and 2) were found to be higher in manual group. However, these differences were not significant ($p>0.05$). The rate of wound infection was 2.11% in controlled cord traction group and 1.45% in manual group. The rate of endometritis was 0.35% in all cases. A negative correlation was found between the mean WBC count on postoperative day 2 and gravidity ($p=0.001$; $r=-0.195$). There also was a negative correlation between the mean WBC count on postoperative day 2 and number of CS ($p=0.001$; $r=-0.200$). In conclusion, manual removal of placenta slightly increased postpartum WBC and neutrophil counts. If the method of placenta removal increases leukocyte count, it may not be substantial enough to result in an infection.

Keywords: *Controlled cord traction; Endometritis; Leukocytosis; Placenta; Postpartum infection; Removal method*

Introduction

The rate of cesarean section (CS) as one of the common major surgeries has been increasing every year[1]. Standardizing of surgical technique will improve outcomes and decrease postpartum infections. Because there is still no consensus about optimal technique, Dahlke *et al*. proposed an evidence based standardized CS technique. The authors recommended spontaneous removal of placenta in order to decrease blood loss[2]. However, manual removal of the placenta

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is still widely used worldwide. This method provides advantage for evaluating uterine cavity and enables the surgeon quick intervention. During labor, uterine cavity is contaminated by endogenous cervicovaginal flora and manual removal of placenta can induce bacterial inoculation. Therefore, it is still controversial due to the risk of postpartum infections. An alternative method is to remove the placenta spontaneously with controlled cord traction. Manual extraction is widely preferred as it takes some time to wait for the placenta to separate spontaneously. It is assumed that controlled cord traction reduces the risk of postpartum hemorrhage and infection[3].

Complete blood count measurement after CS is part of clinical practice worldwide. Although pregnancy and labor slightly increase white blood cell (WBC) count, it is widely used to assess systemic inflammatory response. This study was conducted to investigate whether there was an association between the method of placenta removal and mean postpartum WBC count in low-risk group of term pregnancies who underwent elective CS.

Subjects and Methods

This parallel, randomized, controlled trial was conducted with an allocation ratio of 1:1 including women having CS at the Department of Obstetrics and Gynecology, Haydarpasa Numune Research and Training Hospital in Turkey. The primary aim of this study was to investigate whether there was an association between the method of placenta removal and mean postpartum WBC count, neutrophil count and temperature during hospital stay. Secondly, we aimed to investigate the effects of the placenta removal method on postpartum endometritis and wound infection.

Deliveries by CS between 37 and 41 weeks of gestation were included in the study. Women were questioned before CS regarding maternal infection. Body mass index (BMI) measurement, obstetrics and medical histories were recorded. Exclusion criteria were umbilical cord prolapse, placenta previa, meconium, preterm rupture of membranes, maternal infection, multiple gestation, antepartum hemorrhage, prolonged labor (>12 h), preeclampsia, placental abruption, placental invasion anomalies (placenta accreta spectrum), uncontrolled gestational diabetes, intrapartum fever, suspected chorioamnionitis, and significant maternal disease. The women who had blood transfusions before or after the operation and emergency CS were also excluded. All cases were examined in terms of bacterial vaginosis.

After informed consent, women were randomized into two groups as follows: manual removal of placenta (group 1) and controlled cord traction (group 2). In group 1, placenta was delivered by detaching it from the uterine wall manually. In group 2, spontaneous delivery was performed by external uterine massage and gentle traction of the umbilical cord.

Surgical procedure

Patients were scrubbed with povidone-iodine and surgeons were scrubbed with chlorhexidine. Vaginal preparation was not performed. The incisions were transverse lower segment. The operative procedures were similar in all cases. Also, all the surgeons had similar training and experience. Each case received intravenously (i.v.) 2 g cefazoline after cord clamping. After placenta removal, uterus was exteriorized. Surgeon's dominant hand was covered by sterile compress and uterine cavity was checked for placental remnants. Subcutaneous tissue was closed by three separate sutures if their thickness was more than 2 cm. Skin was closed with subcuticular absorbable suture. At the end, wound was cleaned with povidone-iodine again. Wound dressing was removed after 24 to 36 hours, and wound was cleaned with povidone-iodine daily during hospital stay. All women received empiric antibiotherapy (amoxicillin 1000 mg twice daily for five days) after CS.

Temperature was taken by forehead measurement using temporal artery thermometers (Weewell brade, WTN550R Noncontact thermometer). The highest temperature was recorded daily. Foley catheter was discontinued after 8 hours postpartum. Maternal blood sample was obtained from a peripheral vein into EDTA tube. Fever was defined as a temperature above 38 °C. Signs of wound infection (erythema, swelling, discharge, or tenderness), vaginal discharge, and uterine consistency were assessed daily. The participants were discharged on postpartum day 3 if there were no signs of complication or infection. Endometritis was defined as body temperature of 38 °C or higher after first 24 hours, with either fundal tenderness or a

foul smelling discharge, and no other obvious source of infection[4]. All women were asked to come to follow-up visit on postpartum day 10. Also, they were asked to come to follow-up examination if they had fever, abnormal vaginal bleeding, abnormal vaginal discharge, general feeling of sickness and pain in the pelvis during puerperium.

The study was approved by the Local Ethics and Clinical Investigation Committee (HNEAH/2019/KK/10, January 2019; clinical trial registration number NCT04323241, 03/25/2020). Also, study protocol conformed to the principles of the Declaration of Helsinki. Simple randomization method was used to assign participants to study groups. Informed consent was obtained from all study women. Statistical analyses were done by using Statistical Package for the Social Sciences (SPSS; Version 22.0, IBM Turkey). Descriptive statistics (mean, standard deviation, frequency) were used. Normality of data distribution was evaluated with Shapiro Wilks test. Mann Whitney U was used for data that were not normally distributed. Normally distributed parameters were compared between two groups using Student's t-test. Associations between the normally distributed data were tested with Pearson correlation analysis. Results were evaluated with a confidence interval of 95%, and $p<0.05$ was considered statistically significant.

Results

This study was conducted on 279 women who underwent CS, i.e., 142 assigned to controlled cord traction group and 137 had manual removal (Fig. 1). The mean age of women was 30.65±6.29 years and gravidity was 2.8±1.5. There was no significant difference between the groups in terms of age, BMI, gravidity, parity, and preoperative mean WBC count (p=0.913; p=0.187; p=0.160; p=0.165; p=0.432, respectively) (p>0.05). All women were questioned and examined regarding any infection before surgery. Demographic characteristics of study women are shown in Table 1.

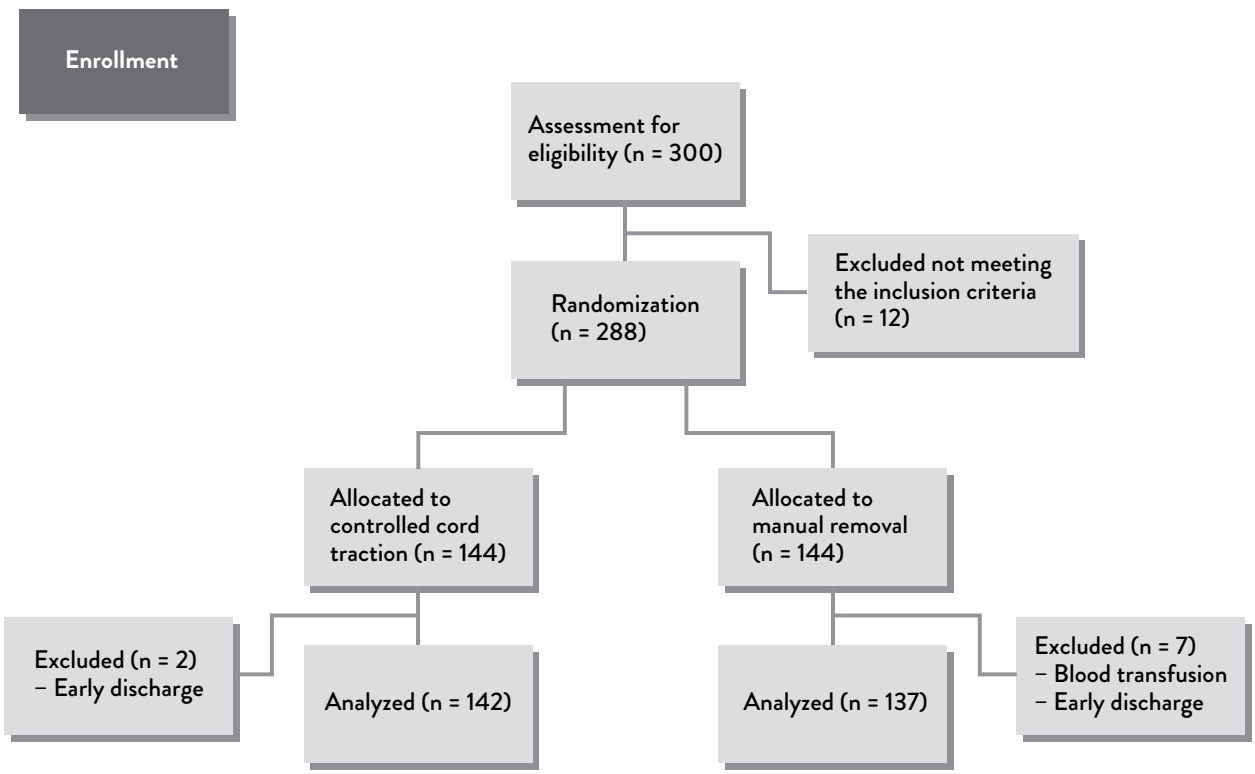

Fig. 1. Consort flow diagram.

Table 1. Demographic data on study participants

Parameter		**Min-Max**	**Mean±SD**
Age (years)		18-47	30.43±5.6
Gravidity		1-10	2.88±1.45
Body mass index (kg/m^2)		17.72-51.94	29.9±5.01
Temperature (˚C)	Postoperative day 1	36-38	36.69±0.26
	Postoperative day 2	36-37.5	36.66±0.25
White blood cell count (cells/μL)	Preoperative	4590-20720	10540±2691
	Postoperative day 1	4510-27540	13612±3752
	Postoperative day 2	4300-21070	10980±2825
Neutrophil count (cells/μL)	Preoperative	1378-18110	7826±2403
	Postoperative day 1	1270-23800	11007±3510
	Postoperative day 2	3140-17070	7996±2449
		n	**%**
Number of cesarean sections	1	78	28
	2	113	40.5
	3	65	23.3
	4 and more	23	8.2
Placenta removal	Controlled cord traction	142	50.9
	Manual removal	137	49.1

Min-Max = minimum-maximum; SD = standard deviation

Table 2. Association between placenta removal method and study variables

		Placenta removal method		**p**
		Controlled cord traction	**Manual removal**	
		Mean±SD	**Mean±SD**	
Temperature (˚C)	Postoperative day 1	36.66±0.24	36.72±0.27	0.069
	Postoperative day 2	36.65±0.23	36.67±0.26	0.490
White blood cell count (cells/μL)	Postoperative day 1	13359±3421	13874±4063	0.327
	Postoperative day 2	10869±2801	11093±2857	0.505
Neutrophil count (cells/μL)	Postoperative day 1	10689±3130	11338±3848	0.194
	Postoperative day 2	7783±2293	8215±2590	0.252

Mann Whitney U test; $p<0.05$; SD = standard deviation

There was no significant difference between the groups according to the mean temperature on postoperative day 1 (36.66±0.24 ˚C *vs.* 36.72±0.27 ˚C) (p=0.069; p>0.05). One woman had fever on postoperative day 1. This case was in the group in which the placenta was removed manually. No statistically significant difference was found between the groups regarding the mean temperature on postoperative day 2 (36.67±0.26 ˚C *vs.* 36.65±0.23 ˚C) (p=0.49; p>0.05).

The mean WBC count on postoperative day 1 was found to be higher in the manual removal group (13874±40631 *vs.* 13359±3421 cells/μL) but

this difference did not reach statistical significance (p=0.327; p>0.05). Also, the mean WBC count on postoperative day 2 was higher in the manual removal group (11093±2857 *vs*. 10869±2801 cells/μL) but this difference was not significant either (p=0.505; p>0.05). In addition, the mean neutrophil count on postoperative day 1 and 2 was higher in the manual removal group. Neither these differences were significant (p=0.194, p=0.252) (Table 2).

The rate of wound infection was 2.11% (3/142) in the controlled cord traction group and 1.45% (2/137) in the manual removal group. The rate of endometritis was 0.35% (n=1) in all cases. This endometritis case was in the group in which placenta was removed by controlled cord traction.

A significant negative correlation was found between the mean WBC count on postoperative day 2 and gravidity (p=0.001; r=-0.195). Also, there was a significant negative correlation between the mean WBC count on postoperative day 2 and number of CS (p=0.001; r=-0.200). However, there was no significant correlation between the mean temperature and WBC count on postoperative day 2 (p=0.056; r=0.369) (Table 3).

Table 3. Correlation between mean white blood cell count (postoperative day 2) and study variables

	White blood cell count (cells/μL)	
	R	**p**
Gravidity	-0.195	**0.001***
Body mass index	-0.134	**0.046***
Number of cesarean sections	-0.200	**0.001***
Temperature (°C)	0.056	0.369

*Pearson correlation, *p<0.05*

Discussion

As with all surgeries, CS is associated with infections. Approximately 2%-7% of women have wound infection after cesarean delivery[5]. The incidence of endometritis has been reported as 2% after CS[6,7]. Postpartum infections impair the quality of life of both mothers and newborns. Also, prolonged hospital stays lead to a severe economic burden. Assessment of WBC count is the first step to evaluate systemic inflammatory response. WBC count was found to be elevated during pregnancy[8]. After delivery, there may be bacterial colonization in the uterine cavity, which may also cause postpartum leukocytosis. Labor has been shown to cause slight increase in WBC count, but this does not affect infection related changes. The median WBC counts were found to be 9000 cells/μL during third trimester and 16 000 cells/μL postpartum[8]. Hartman *et al*. investigated changes in WBC count after CS among 398 women without diagnosis of antepartum infections. Of the cases, five women had infection diagnosis on the day of surgery and 12 women had diagnosis on postoperative day 1. It is suggested that WBC count on postoperative day 1 is feasible for evaluating postpartum infections[9].

During CS, placenta is commonly removed by the manual method. This method enables rapid intervention and evaluation of the uterine cavity. Many surgeons do not prefer to wait for spontaneous separation of the placenta. Uterine cavity is contaminated by endogenous cervicovaginal flora in labor. During manual removal of placenta, bacterial inoculation can occur through open venous sinuses, endometrial glands and stroma. It has been suggested that this situation may increase the risk of postpartum infection, especially endometritis[10,11]. Another placenta removal technique is controlled cord traction, which is a component of active management in the third stage of labor[3,12]. It was shown that spontaneous removal of placenta was associated with less blood loss without increasing operation time[13,14]. Besides, this method has advantages such as less endometritis and shorter length of hospital stay[1]. However, if controlled cord traction is not performed correctly, it may cause cord rupture or uterine inversion[15]. For spontaneous delivery of the placenta, it is recommended to limit the waiting time to five minutes[14]. There are many studies in the literature comparing these two main placenta removal methods. In most of these studies, primary measure outcomes were blood loss, postpartum hemorrhage, blood transfusion need, and operation time. In some studies, manual removal of placenta has been shown to have significant association with endometritis[4,11,16]. In contrast, other studies detected no significant association between placenta removal methods and endometritis[7,17,18].

Fever and uterine tenderness were common findings in endometritis. Besides, WBC count may also increase in endometritis[8]. The most important endometritis risk factors were prolonged labor, bacterial vaginosis, ruptured membranes, and preexisting lower genital tract infection[19]. Cesarean technique and placenta removal method are also risk factors for postpartum infections. We detected lower rates of endometritis (0.35%) and wound infection (1.79%) in our study. This may be related to the use of routine antibiotic therapy and exclusion of high-risk cases. Lasley *et al*. investigated the association between placenta removal method and post cesarean infections[11]. They found that the rate of postoperative infections was higher in the group where placenta was removed manually (27% *vs*. 15%, RR 0.6, p=0.01)[11]. In our study, we detected higher mean WBC and neutrophil counts (postoperative day 1 and 2) in the group where placenta was removed manually. However, this difference was not statistically significant (p>0.05). It has been reported that spontaneous removal of placenta did not help reduce wound infections in CS[11]. We found no significant difference in the rate of wound infection according to placenta removal method (2.11% *vs*. 1.45%).

In a systematic review, it was suggested that there was no significant association between placenta removal method and puerperal fever[1]. Similarly, in a randomized controlled study, no significant association was found between the placenta delivery method and post cesarean febrile morbidity[17]. In our study, we did not detect any significant difference between the groups according to the mean temperature values on postoperative day 1 and day 2. The routine antibiotic therapy after CS was one of the study limitations.

In conclusion, manual removal of placenta slightly increased postpartum WBC and neutrophil counts. The mean postpartum WBC counts were negatively correlated with gravidity and number of CS. If the placenta removal method increases leukocyte counts, it may not be substantial enough to result in an infection. Our findings showed that manual removal of placenta did not increase the wound infection rates.

References

1. Anorlu RI, Maholwana B, Hofmeyr GJ. Methods of delivering the placenta at caesarean section. Cochrane Database Syst Rev. 2008;3:CD004737. https://doi.org/10.1002/14651858.CD004737.pub2
2. Dahlke JD, Mendez-Figueroa H, Maggio L, *et al*. The case for standardizing cesarean delivery technique: seeing the forest for the trees. Obstet Gynecol. 2020;136(5):972-80. doi: 10.1097/AOG.0000000000004120.
3. Du Y, Ye M, Zheng F. Active management of the third stage of labor with and without controlled cord traction: a systematic review and meta-analysis of randomized controlled trials. Acta Obstet Gynecol Scand. 2014;93(7):626-33. doi: 10.1111/aogs.12424.
4. Magann EF, Dodson MK, Harris RL, *et al*. Does method of placental removal or site of uterine incision repair alter endometritis after cesarean delivery? Infect Dis Obstet Gynecol. 1993;1(1):65-70. doi: 10.1155/S106474499300016X
5. Kawakita T, Landy HJ. Surgical site infections after cesarean delivery: epidemiology, prevention and treatment. Matern Health Neonatol Perinatol. 2017; 3:12. doi.org/10.1186/s40748-017-0051-3
6. Axelsson D, Blomberg M. Prevalence of postpartum infections: a population-based observational study. Acta Obstet Gynecol Scand. 2014;93(10):1065-8. doi: 10.1111/aogs.12455
7. Chandra P, Schiavello HJ, Kluge JE, Holloway SL. Manual removal of the placenta and postcesarean endometritis. J Reprod Med. 2002;47(2):101-6. PMID: 11883347
8. Edelstam G, Lowbeer C, Kral G, Gustafsson SA, Venge P. New reference values for routine blood samples and human neutrophilic lipocalin during third-trimester pregnancy. Scand J Clin Lab Invest.2001;61(8):583-92.
9. Hartmann KE, Barrett KE, Reid VC, McMahon MJ, Miller WC. Clinical usefulness of white blood cell count after cesarean delivery. Obstet Gynecol. 2000;96(2):295-300. doi: 10.1016/s0029-7844(00)00911-x
10. Atkinson MW, Owen J, Wren A, Hauth JC. The effect of manual removal of the placenta on post-cesarean endometritis. Obstet Gynecol. 1996:87(1):99-102.
11. Lasley DS, Eblen A, Yancey MK, Duff P. The effect of placental removal method on the incidence of postcesarean infections. Am J Obstet Gynecol. 1997;176(6):1250-4. doi: 10.1016/S0002-9378(97)70342-9

12. Cummings K, Doherty DA, Magann EF, Wendel PJ, Morrison JC. Timing of manual placenta removal to prevent postpartum hemorrhage: is it time to act? J Matern Fetal Neonatal Med. 2016;29(24):3930-3. doi: 10.3109/14767058.2016.1154941.
13. Kamel A, El-Mazny A, Salah E, *et al*. Manual removal *versus* spontaneous delivery of the placenta at cesarean section in developing countries: a randomized controlled trial and review of literature. J Matern Fetal Neonatal Med. 2018;31(24):3308-13.
14. Morales M, Ceysens G, Jastrow N, *et al*. Spontaneous delivery or manual removal of the placenta during caesarean section: a randomised controlled trial. BJOG. 2004;111(9):908-12. doi: 10.1111/j.1471-0528.2004.00228.x.
15. Deneux-Tharaux C, Sentilhes L, Maillard F, *et al*. Effect of routine controlled cord traction as part of the active management of the third stage of labour on postpartum haemorrhage: multicentre randomised controlled trial (TRACOR). BMJ. 2013;346:f1541. doi: 10.1136/bmj.f1541.
16. McCurdy CM Jr, Magann EF, McCurdy CJ, Saltzman AK. The effect of placental management at cesarean delivery on operative blood loss. Am J Obstet Gynecol. 1992;167(5):1363-7. doi: 10.1016/s0002-9378(11)91717-7.
17. Cernadas M, Smulian JC, Giannina G, Ananth CV. Effects of placental delivery method and intraoperative glove changing on postcesarean febrile morbidity. J Matern Fetal Med. 1998;7(2):100-4. doi: 10.1002/(SICI)1520-6661(199803/04)7:2<100::AID-MFM9>3.0.CO;2-Q.
18. Gun I, Ozdamar O, Ertugrul S, Oner O, Atay V. The effect of placental removal method on perioperative hemorrhage at cesarean delivery; a randomized clinical trial. Arch Gynecol Obstet. 2013;288(3):563-7. doi: 10.1007/s00404-013-2759-2.
19. Jacobsson B, Pernevi P, Chidekel L, Jorgen Platz-Christensen J. Bacterial vaginosis in early pregnancy may predispose for preterm birth and postpartum endometritis. Acta Obstet Gynecol Scand. 2002;81(11):1006-10. doi: 10.1034/j.1600-0412.2002.811103.x.

Sažetak

UTJECAJ METODE UKLANJANJA PLACENTE NA POSLIJEPOROĐAJNU LEUKOCITOZU – RANDOMIZIRANO KONTROLIRANO ISTRAŽIVANJE

S. Arzu Arinkan i *H. Serifoglu*

Stopa carskog reza (CS) kao jedne od najčešćih velikih operacija raste svake godine. Standardizacija kirurške tehnike poboljšat će ishode i smanjiti poslijeporođajne infekcije. Svrha ove studije bila je istražiti postoji li povezanost između metode uklanjanja posteljice i srednjeg broja bijelih krvnih stanica (*white blood cell*, WBC) nakon porođaja. Ova prospektivna randomizirana kontrolirana studija obuhvatila je 279 jednoplodnih trudnoća s CS. Žene su randomizirane u dvije skupine: ručno uklanjanje posteljice i spontano rađanje uz kontroliranu vuču pupčane vrpce. Nije bilo značajne razlike između skupina u pogledu srednje temperature (p>0,05). Utvrđeno je da je srednji broj WBC i neutrofila (1. i 2. poslijeoperacijski dan) veći u ručnoj skupini. Međutim, ove razlike nisu bile značajne (p>0,05). Stopa infekcije rane bila je 2,11% u skupini s kontroliranom vučom pupčane vrpce i 1,45% in skupini s ručnim uklanjanjem posteljice. Stopa endometritisa bila je 0,35% u svim slučajevima. Utrđena je negativna korelacija između srednjeg broja WBC 2. poslijeperacijskog dana i graviditeta (p=0,001; r=-0,195). Također je utvrđena negativna korelacija između srednjeg broja WBC 2. poslijeoperacijskog dana i broja CS (p=0,001; r=-0,200). U zaključku, ručno uklanjanje posteljice neznatno je povećalo poslijeporođajni broj WBC i neutrofila. Ako metoda uklanjanja posteljice povećava broj leukocita, to ne mora biti dovoljno značajno da rezultira infekcijom.

Ključne riječi: *Kontrolirana vuča pupčane vrpce; Endometritis; Leukocitoza; Posteljica; Poslijeporođajna infekcija; Metoda uklanjanja*