Original Article

HEALTH SCIENCES
MEDICINE

DOI: 10.32322/jhsm.1562989
J Health Sci Med. 2025;8(1):40-46

Perinatal outcomes of patients who underwent cervical cerclage and their relationship to systemic inflammatory indices

Gülşan Karabay, Zeynep Şeyhanlı, Ahmet Arif Filiz, Betül Tokgöz Çakır, Serap Topkara Sucu, Nazan Vanlı Tonyalı, Mevlüt Bucak, Hatice Ayhan, Şevki Çelen, Ali Turhan Çağlar

Department of Obstetrics and Gynecology, Ankara Etlik City Hospital, Ankara, Turkiye

Cite this article as: Karabay G, Şeyhanlı Z, Filiz AA, et al. Perinatal outcomes of patients who underwent cervical cerclage and their relationship to systemic inflammatory indices. *J Health Sci Med.* 2025;8(1):40-46.

Received: 07.10.2024 ◆ **Accepted**: 26.11.2024 ◆ **Published**: 12.01.2025

ABSTRACT

Aims: This study aimed to evaluate the perinatal outcomes of patients who underwent cervical cerclage and to investigate the relationship between these outcomes and systemic inflammatory indices.

Methods: A retrospective study was conducted at Ankara Etlik City Hospital between November 2022 and November 2023. Patients were divided into three groups based on the indication for cerclage: history-indicated cerclage (H-IC), ultrasound-indicated cerclage (U-IC) and physical examination-indicated cerclage (PE-IC). The systemic inflammatory markers neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), Systemic Immune-Inflammation Index (SII), Systemic Inflammatory Response Index (SIRI), pan-immune inflammation value (PIV) and multi-inflammation indices (MII), were measured. The perinatal outcomes, including gestational age at delivery, birth weight and APGAR Scores, were compared among the groups.

Results: Seventy patients were included in the study. The rate of preterm birth was highest in the PE-IC group (61.1%), followed by the U-IC group (40.9%) and the H-IC group (36.7%). Birth weight, 1- and 5-minute APGAR Scores were significantly lower in the PE-IC group, and neonatal intensive care unit admission rates were significantly higher in the PE-IC group. Inflammatory markers NLR, SII and PIV were significantly higher in the U-IC group compared to the H-IC group. However, no significant differences were observed between the U-IC and PE-IC groups in terms of these markers.

Conclusion: Patients who underwent PE-IC had poorer perinatal outcomes compared to those who underwent H-IC or U-IC. The systemic inflammatory indices NLR, SII and PIV may serve as useful markers for predicting pregnancy outcomes and guiding early interventions in patients at risk of preterm birth. Further large-scale prospective studies are needed to validate these findings.

Keywords: Cervical cerclage, cervical insufficiency, perinatal outcomes

INTRODUCTION

Preterm births, which include 5 to 15% of all pregnancies, are defined as births that occur before the 37th week of pregnancy.[1,2] Increased newborn mortality and morbidity are linked to this disease.[3] Cervical insufficiency affects about 1% of pregnant women and is a major risk factor for preterm birth.[4-6] The incapacity of the cervix to sustain a pregnancy prior to the commencement of labour is known as cervical insufficiency and the therapy as well as the management of this condition are complicated by our incomplete understanding of its pathogenesis.[4] Mechanical injuries to the cervix (e.g. conization, dilatation of the cervix during curettage), congenital anomalies of Muller's system, collagen disorders of the cervix and infections, are among the causes that are held responsible for the ethology of cervical insufficiency.[4,6,7]

The cervix has a mechanical function as well as serving as a barrier to keep ascending pathogens out of the uterus and the best way to treat cervical insufficiency is with a cervical cerclage, which strengthens the cervix by offering mechanical support.[5] Studies to determine how the systemic inflammatory response affects the outcome of pregnancy have been bolstered by the observation that 80% of patients with cervical insufficiency, also have an intrauterine infection.[8,9] Research has demonstrated a negative correlation between a patient's prognosis and elevated proinflammatory cytokines and chemokines in the amniotic fluid, during cerclage surgery.[10,11] Neutrophils, lymphopenia, thrombocytosis and elevated C-reactive protein (CRP) are laboratory indicators that are readily tested in mother blood and

Corresponding Author: Gülşan Karabay, drgulsankarabay@gmail.com

are related with systemic inflammation.[12] These novel and comprehensive inflammatory markers, which can appropriately influence local immune status and systemic inflammation throughout the human body, include the neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), systemic immune inflammation index (SII), systemic inflammatory response index (SIRI), pan-immune inflammation value (PIV) and multi-inflammation index (MII)1-2-3.[11,13-16]

Considering the relationship between inflammation and cervical insufficiency, evaluation of systemic inflammation markers in patients undergoing cervical cerclage is of great importance. For the purpose of managing preterm labour, birth planning and postpartum care, it is critical to evaluate the prognosis of both the mother and the fetus in patients receiving cervical cerclage. The purpose of this research is to examine the perinatal outcomes of cervical cerclage patients and how they relate to systemic inflammatory indices.

METHODS

Between November 2022 and November 2023, a retrospective study was carried out in the Perinatology Clinic of Ankara Etlik City Hospital. Three groups of patients were assigned to the study group: those who received physical examination-indicated cerclage (PE-IC), ultrasound-indicated cerclage (U-IC) and history-indicated cerclage (H-IC). The Ankara Etlik City Hospital No. 1 Clinical Researches Ethics Committee gave its permission to the study protocol (Date: 16.08.2023, Decision No: AEŞH-EK1-2023-473). The Declaration of Helsinki's guidelines were followed in the conduct of this study.

Regardless of the status of the current pregnancy, patients with a history of two or more preterm deliveries or mid-trimester pregnancy losses were included in the H-IC group. In the mid-trimester, U-IC is recommended for asymptomatic patients with a small cervical length (<25 mm), particularly for those who have a history of preterm births.[17] Patients with an asymptomatic cervical dilatation of at least 2 cm, a cervical effacement of at least 60% or an amniotic membrane prolapse in the middle trimester, were included in the PE-IC group.[5,7,18] The decision on cerclage was made after the first trimester screening test in the group in which the medical history was decisive, as well as at the time of diagnosis in the group in which the ultrasound scan and physical examination were decisive. Patients were checked for uterine contractions, fever, membrane rupture, hemorrhage, chorioamnionitis, placental abruption and fetal distress prior to cerclage. Vaginal and urine cultures were requested from all patients for whom a cerclage was planned and patients with positive culture results received appropriate antibiotic therapy. Cerclage procedures were not performed on pregnant women beyond twenty-four weeks of pregnancy and all cerclage procedures in patients were performed by experienced physicians in our perinatology department using the McDonald technique, under anesthesia. In the lithotomy posture, a 5 mm long braided polyester fiber (Mersilene®-40 cm) was positioned in a circular motion around the cervix. All patients received 1 g of cefazolin intravenously prophylactically during the operation. After discharge, all pregnant women received intravaginal progesterone treatment. Cerclage is removed in individuals who are at or beyond the 37th week of pregnancy.

The first day of the last menstrual cycle and/or the fetal crown-rump length, which was assessed in the first trimester and verified by ultrasound examinations, were used to compute the gestational age of the study participants. Exclusion criteria included chronic maternal conditions such as heart disease and thyroid dysfunction, smoking, alcohol consumption, the presence of congenital anomalies, multiple pregnancies and patients for whom no information could be obtained. Our hospital's data network was investigated for the patients past medical records and demographic information was noted. Hemoglobin, leukocytes, monocytes, lymphocytes, platelets, thyroid-stimulating hormone, alanine aminotransferase, aspartate aminotransferase, albumin, CRP and fibrinogen were all analyzed from maternal venous blood drawn before cerclage. Neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), platelet count×neutrophil count/lymphocyte count (SII), monocyte count×neutrophil count/lymphocyte count (SIRI), NLR×CRP (MII-1) and PLR×CRP (MII-2) and SII×CRP (MII-3) and neutrophil count×platelet count×monocyte count/lymphocyte count (PIV).[9,14]

The patients' birth information, birth weight, gender, APGAR 1/APGAR 5 Scores and any neonatal morbidities, if any, were recorded.

Statistical Analysis

The G-Power 3.1.9.7 application was used to calculate the sample size for the investigation. The sample size was calculated using the Student's Paired Test with a power of 80%, a probability of error of α=0.05 and a Cohen effect size of 'medium'. Accordingly, it was considered appropriate to complete the study with at least forty-six patients. The IBM Corporation SPSS version 22.0 (IBM Corporation, Armonk, NY, USA) was used to conduct the statistical analysis. The normal distribution conformance was examined using the Kolmogorov-Smirnov test. Descriptive statistics of continuous variables are shown as "mean±standard deviation" for those with normal distribution and as "median (min-max value)" for those that did not. The Analysis of variance (ANOVA) test was used to compare more than two groups. The statistical significance of the ANOVA test was determined according to the number of groups. The Fisher's exact test or the chi-squared test were used to compare categorical variables. The independent sample t-test and the Mann-Whitney U test were used to compare continuous variables that were and were not regularly distributed. All tests were considered statistically significant if the P-value was less than 0.05.

RESULTS

This study includes seventy patients who had cervical cerclage. Three groups of patients were created: H-IC, U-IC, and PE-IC. Thirty H-IC patients (42.9%), twenty U-IC patients (31.4%) and eighteen PE-IC patients (25.7%) were identified. The demographic details and test results of the individuals who had cerclage are displayed in Table 1. Age, body-mass index (BMI), weight gain during pregnancy, and

progesterone use prior to application did not significantly differ across the three groups (p=0.499, p=0.578, p=0.385, and p=0.443, respectively). Regarding gravidity, there was no significant difference (p=0.940) between groups 2 and 3, whereas there was a significant difference (p<0.001, p=0.005) between groups 1 and 2. In terms of parity, there was a significant difference (p=0.001 and p=0.005, respectively) between groups 1 and 2. Between groups 2 and 3, there was no discernible change (p=0.1). Hemoglobin, white blood cell count, lymphocytes, neutrophils, monocytes, platelets, thyroid-stimulating hormone, C-reactive protein, aspartate aminotransferase, alanine aminotransferase, albumin, fibrinogen and leukocytes in urinalysis, did not significantly differ between the three groups when the laboratory values were compared (p=0.076, p=0.023, p=0.024, p=0.018, p=0.096, p=0.908, p=0.766, p=0.581, p=0.529, p=0.954, p=0.310, p=0.744, respectively). In all three groups, there was a significant difference in the length of the cervix (p<0.001). The cervical length varied across the H-IC group (35.3±4.2 mm), U-IC group (15.6±5.1 mm) and PE-IC group (8.0±6.2 mm). There were no patients with funnelling in the H-IC group and the presence of funnelling varied considerably (p<0.001) across the three groups. Group 1 and groups 2 and 3 differed statistically significantly from one another when the weeks of cerclage were assessed for each of the three groups (p<0.001). Between groups 2 and 3, there was no discernible change (p=0.996). The H-IC group had a median cervical insertion week of 14+2 (12+1-20+5) weeks, the U-IC group had a median week of 21+6 (12-24+6) weeks, and the PE-IC group had a median week of 21 (14+1-24). Following cerclage, there was a significant difference in cervical length (p<0.001) between groups 1 and 2. Between groups 2 and 3, there was no discernible change (p=0.055). Following cerclage, the cervix length was measured in the H-IC group as 38.3±8.2 mm, the U-IC group as 22.7±6.4 mm, and the PE-IC group as 16.3±9.9 mm. Regarding the duration of hospital stay following cerclage, there was a statistically significant difference (p=0.012 and p=0.016, respectively) between groups 1 and 2. Between groups 1 and 2, there was no discernible difference (p=0.885). The H-IC group had a mean hospital stay of 2 (2-5)

Table 1. Descriptive and comparative analysis of demographic and laboratory data between patients with history-indicated cerclage, ultrasound-indicated cerclage and physical examination- indicated cerclage groups

Parameter	History-indicated cerclage n=30 (42.9%)	Ultrasound-indicated cerclage n=22 (31.4%)	Physical examination-indicated cerclage n=18 (25.7%)	p-value
Age[a] (y)	28.7±5.2	28.9±5.9	30.1±5.5	0.499[c]
Body-mass index[a] (kg/m^2)	31.2±6.3	29.8±6.5	30.8±5.2	0.578[c]
Weight gain during pregnancy[b] (kg)	10 (2-25)	10 (3-20)	9 (3-20)	0.385[d]
Gravida[b]	3 (2-12)	2 (1-4)	2 (1-7)	<0.001[d]
Parity[b]	1.5 (0-3)	0 (0-2)	0 (0-2)	<0.001[d]
Progesterone usage	22 (73.3%)	15 (68.2%	10 (55.6%)	0.443[e]
Hemoglobin (g/dl)	12.3±1.1	11.5±1.0	11.8±1.3	0.076[c]
White blood cell count[a] (10^9/L)	9.5±2.1	11.3±3.4	11.6±3.2	0.023[c]
Lymphocyte count[a] (10^9/L)	2.0±0.5	1.7±0.5	2.7±2.2	0.024[c]
Neutrophil count[a] (10^9/L)	6.8±1.7	8.9±3.3	8.1±3.2	0.018[c]
Monocyte count[a] (10^9/L)	0.55±0.1	0.78±0.9	0.70±0.2	0.096[c]
Platelet count[a] (10^9/L)	263.3±65.4	252.7±63.6	260.3±83.5	0.908[c]
Thyroid stimulating hormone[a] (mU/ml)	2.04±2.3	2.42±1.9	2.64±0.9	0.766[c]
C-reactive protein[a] (mg/L)	6.32±6.96	12.2±15.1	15.8±19.3	0.084[c]
Aspartate aminotransferase[a] (IU/L)	21.5±21.5	16.6±4.7	19.4±6.4	0.581[c]
Alanine aminotransferase[a] (U/L)	17.8±22.6	12.2±4.1	14.8±6.8	0.529[c]
Albumin[a] (g/L)	37.9±3.4	37.7±2.9	38.1±2.6	0.954[c]
Fibrinogen[a] (mg/dl)	439±81	475±103	453±63	0.310[c]
Leukocytes in the urine analysis	0 (0-3)	0 (0-3)	0 (0-3)	0.744[d]
Cervical Length[a] (mm)	35.3±4.2	15.6±5.1	8.0±6.2	<0.001[c]
Funneling	0 (0%)	19 (86.4%)	17 (94.4%)	<0.001[e]
Cerclage week[b]	14+2 (12+1-20+5)	21+6 (12-24+6)	21 (14+1-24)	<0.001[d]
Cervical length after cerclage[a] (mm)	38.3±8.2	22.7±6.4	16.3±9.9	<0.001[c]
Hospitalization day after cerclag[b]	2 (2-5)	2 (1-7)	5 (1-19)	<0.001[d]
Duration of antibiotic use[b] (days)	0 (0-22)	0 (0-21)	3 (0-14)	0.265[d]
Gestational weeks at deliver[b]	37+1 (20+1-40)	37 (22+3-41)	25 (19+4-40+4)	<0.001[d]
Duration from cerclage to delivery[b] (days)	158 (45-185)	104 (13-179)	35 (4-167)	<0.001[d]
Hospitalization day after the deliver[b]	3 (1-14)	2 (2-5)	4 (1-8)	0.193[d]

SD: Standard deviation, NA: Not applicable [a]: Mean±SD, [b]: Median (min-max), [c]: One-way anova with bonferoni, [d]: One way anova with tamhane, [e]: Pearson Chi-square, [f]: Fisher's exact test

days, the U-IC group of 2 (1-7) days, and the PE-IC group of 5 (1-19) days. Group 1 and Group 3 had significantly different weeks of birth (p=0.013). Between groups 2 and 3 (p=0.046) and 1 and 2 (p=0.831), there was no significant difference. For the H-IC group, it was 37+1 (20+1-40) weeks; for the U-IC group, it was 37 (22+3-41) weeks; and for the PE-IC group, it was 25 (19+4-40+4) weeks (Figure). There was a significant difference (p<0.001) in the duration between cerclage and delivery between groups 1 and 2. Between groups 2 and 3, there was no discernible change (p=0.052). The H-IC group experienced 158 (45-185) days, the U-IC group 104 (13-179) days, and the PE-IC group 35 (4-167) days. All three groups had comparable antibiotic use durations and hospitalization days following delivery (p=0.265, p=0.193).

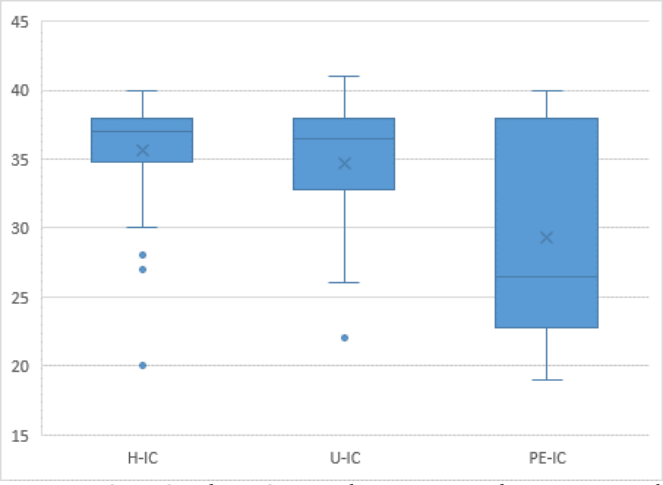

Figure. H-IC, U-IC and PE-IC groups histogram according to gestational weeks at delivery

H-IC: History-indicated cerclage, U-IC: Ultrasound-indicated cerclage, PE-IC: Physical examination-indicated cerclage

Pregnancy problems that arose during the follow-up of the study participants are displayed in Table 2. Gestational diabetes mellitus occurred in seven patients (23.3%) in the H-IC group, three patients (13.6%) in the U-IC group, and three patients (16.6%) in the PE-IC group during the pregnancy follow-up. Between the three groups, there was no discernible difference (p=0.438). Within the H-IC group, three patients (10%) had fetal growth restriction (FGR). In the other two groups, there were no patients suffering from FGR. Three patients (10%) in the H-IC group had gestational hypertension, one patient (4.5%) in the U-IC group pre-eclampsia, and one patient (5.6%) in the PE-IC group pre-eclampsia. In all three groups, there was no discernible variation in the onset of hypertensive pregnancy problems (p=0.312). One patient (3.3%) experienced postpartum hemorrhage, one patient (3.3%) experienced cholestasis of pregnancy, and one patient (3.3%) experienced chorioamnionitis in the PE-IC group.

Table 3 shows the birth-related information and the characteristics of the newborns of the patients included in the study. The study found that there were similarities in the three groups for pregnancy termination method, newborn gender, preterm delivery, and antenatal corticosteroid use (p=0.102, p=0.136, p=0.238, and p=0.443, respectively). Group 3's birth weight differed significantly from groups 1 and 2's birth weight (p=0.004 and 0.013, respectively). Between groups 1 and 2, there was no change (p=1). There was a statistically significant difference between group 3 and groups 1 and 2 in 1st minute APGAR Score (p=0.006 and p=0.007 respectively). There was no significant difference between group 1 and group 2 (p=1). There was a significant difference between group 3 and groups 1 and 2 at the 5th minute APGAR Score (p=0.007 and p=0.010, respectively). Between groups 1 and 2, there was not a significant difference (p=0.983). One patient (3.3%) in the H-IC group, four patients (18.2%) in the U-IC group, and six patients (33.3%) in the PE-IC group experienced preterm premature rupture of membranes (PPROM). Between the groups, there was a significant difference (p=0.014). There was no statistically significant difference observed between the three groups when it came to the length of hospital stay in the neonatal intensive care unit, neonatal hypoglycemia, respiratory distress syndrome, need for phototherapy, intraventricular hemorrhage, need for surfactant, and necrotizing enterocolitis (NEC) (p=0.886, p=0.215, p=0.052, p=0.403, p=0.175, p=0.035, p=0.308, p=0.144, respectively). Ten (45.5%) patients from the U-IC group, ten (55.5%) patients from the PE-IC group, and eight (27.6%) patients from the H-IC group were admitted to the neonatal critical care unit. Group 1 had a considerably lower value (p=0.043). Out of the patients in the H-IC group, five (16.6%) needed mechanical breathing and one (3.4%) needed continuous positive airway pressure (CPAP). Three patients (13.6%) and six patients (27.3%) in the U-IC group needed MV. One patient (5.5%) and seven patients (38.8%) in the PE-

Table 2. Pregnancy complications of history-indicated cerclage, ultrasound-indicated cerclage and physical examination- indicated cerclage groups

Parameter	History-indicated cerclage n=30 (42.9%)	Ultrasound-indicated cerclage n=21 (31.4%)	Physical examination-indicated cerclage n=17 (25.7%)	p-value
Gestational diabetes mellitus	7 (23.3%)	3 (13.6%)	3 (16.6%)	0.438[a]
Fetal growth restriction	3 (10%)	0 (0%)	0 (0%)	0.179[a]
Hypertension				**0.312[a]**
Absent	26 (86.7%)	21 (95.5%)	16 (88.9%)	
Gestational hypertension	3 (10%)	0 (0%)	0 (0%)	
Preeclampsia	0 (0%)	1 (4.5%)	1 (5.6%)	
Cholestasis of pregnancy	1 (3.3%)	1 (4.5%)	0 (0%)	1[a]
Chorioamnionitis	0 (0%)	0 (0%)	1 (5.6%)	0.257[a]
Postpartum hemorrhage	1 (3.3%)	0 (0%)	0 (0%)	1[a]

[a]: Pearson Chi-square

Table 3. Comparison of findings regarding newborn characteristics and labor

Parameter	History-indicated cerclage n=30 (42.9%)	Ultrasound-indicated cerclage n=22 (31.4%)	Physical examination-indicated cerclage n=18 (25.7%)	p-value
Pregnancy termination way				0.102[b]
Cesarean section	19 (63.3%)	17 (77.3%)	8 (44.4%)	
Normal spontaneous vaginal birth	11 (36.7%)	5 (22.7%)	10 (55.6%)	
Gender				0.136[b]
Female	11 (36.7%)	14 (63.6%)	10 (55.6%)	
Male	19 (63.3%)	8 (36.4%)	8 (44.4%)	
Fetal weight (gr)	2679±794	2628±956	1683±1333	<0.003[a]
1st min APGAR Score	9 (0-9)	8 (1-9)	3 (0-9)	<0.001[c]
5th min APGAR Score	9 (0-10)	9 (3-10)	6 (0-10)	<0.001[c]
Preterm birth	11 (36.7%)	9 (40.9%)	11 (61.1%)	0.238[b]
Preterm premature rupture of membranes	1 (3.3%)	4 (18.2%)	6 (33.3%)	0.014[a]
Antenatal corticosteroid	15 (50%)	14 (63.6%)	12 (66.7%)	0.443[b]
Admission to neonatal intensive care unit	8 (27.6%)	10 (45.5%)	10 (55.5%)	0.043[b]
Hospitalization duration in neonatal intensive care unit (days)	0 (0-46)	0 (0-71)	1 (0-46)	0.886[a]
Neonatal hypoglycemia	0 (0%)	0 (0%)	1 (5.5%)	0.215[b]
TTN	1 (3.4%)	5 (22.7%)	0 (0%)	0.052[b]
Respiratory distress syndrome	5 (16.6%)	5 (22.7%)	5 (27.7%)	0.403[b]
Need for CPAP	1 (3.4%)	6 (27.3%)	1 (5.5%)	0.037[b]
Need for mechanical ventilator	5 (16.6%)	3 (13.6%)	7 (38.8%)	0.001[d]
Need for phototherapy	1 (3.4%)	1 (4.5%)	0 (0%)	0.175[b]
IVH	1 (3.4%)	1 (4.5%)	4 (22.2%)	0.035[b]
Neonatal sepsis	0 (0%)	0 (0%)	0 (0%)	NA
Need for surfactant	0 (0%)	2 (9.1%)	1 (5.5%)	0.308[d]
Neonatal Seizures	0 (0%)	0 (0%)	0 (0%)	NA
NEC	1 (3.4%)	2 (9.1%)	3 (16.6%)	0.144[d]
Blood culture of newborn	5 (16.6%)	9 (40.9%)	8 (44.4%)	0.024[b]

APGAR: Appearance, Pulse, Grimace, Activity and Respiration, TTN: Transient tachypnea of the newborn, CPAP: Continuous positive airway pressure, IVH: Intraventricular hemorrhage, NEC: Necrotizing enterocolitis, [a]: One-way anova with tamhane, [b]: Pearson chi-square, [c]: One way anova with bonferoni, [d]: Fisher's exact test

IC group needed MV. Between the three groups, there was a significant difference (p=0.037 and p=0.001, respectively). After birth, blood cultures were obtained in five (16.6%) of the newborns in the H-IC group, nine (40.9%) in the U-IC group and eight (44.4%) in the PE-IC group. In the 1st group there was one abortion (less than 500 grams) and four abortions in the 3rd group.

Table 4 shows the inflammation parameters examined in the three groups. Between the groups, the PLR, SIRI, MII-1, MII-2 and MII-3 values were comparable (p=0.069, p=0.037, p=0.080, p=0.152, and p=0.071, to be exact). In terms of NLR, group 1 and group 2 differed significantly (p=0.004). Between groups 1 and 3, as well as between groups 2 and 3, there was no significant difference (p=1 and p=0.025, respectively). Groups 1 and 2 differed significantly from one another in SII (p=0.006). Neither group 1 nor group 2 nor group 3 differed significantly from the other (p=1 and p=0.026, respectively). Groups 1 and 2 differed significantly from one another on PIV (p=0.013). Between groups 1 and 3, as well as between groups 2 and 3, there was no discernible difference (p=1 and p=0.185, respectively).

Table 4. Comparison of inflammatory indices between history-indicated cerclage, ultrasound-indicated cerclage and physical examination- indicated cerclage groups

Parameter	History-indicated cerclage n=30 (42.9%)	Ultrasound-indicated cerclage n=22 (31.4%)	Physical examination- indicated cerclage n=18 (25.7%)	p-value
NLR	3.7±1.5	6.19±4.07	3.8±2.35	0.004[a]
PLR	140.8±61.7	171.2±114.6	112.7±38	0.069[a]
SII	953±434	1572±1117	946±472	0.006[a]
SIRI	2.05±1.02	4.99±6.66	2.88±2.61	0.037[a]
PIV	525±254	1210±1365	713±509	0.015[a]
MII-1	25.1±35.3	75.5±115.3	52.8±77.4	0.080[a]
MII-2	890±1046	2016±2565	1897±3197	0.152[a]
MII-3	6553±8910	19723 ±26374	15067±25859	0.071[a]

NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, SII: Systemic immune-inflammation index, SIRI: Systemic inflammatory response index, PIV: Pan-immune-inflammation value, MII-1 (multiinflammatory index): NLR*C-reactive protein, MII-2: PLR*C-reactive protein, MII-3: SII* C-reactive protein, [a]: One-way anova with bonferoni

DISCUSSION

This study examined the maternal and fetal outcomes of patients who had undergone cervical cerclage for various indications and evaluated the association between these outcomes and systemic indices of inflammation. The results show that preterm birth remains a major problem in patients who have undergone cervical cerclage. The preterm birth rate was 36.7% in the H-IC group, 40.9% in the U-IC group and 61.1% in the PE-IC group. In particular, it was found that the weeks of gestation at delivery, birth weight, APGAR Score at the first minute and APGAR Score at the fifth minute were significantly lower and the need for neonatal intensive care was higher, in patients who underwent PE-IC. In PE-IC, patients typically present with significant cervical dilation, effacement or prolapsed membranes, which indicate a more severe pathological state. This advanced stage is associated with higher maternal and neonatal complication rates due to factors such as increased infection risk, preterm labour and reduced efficacy of intervention at this late stage. In addition, it was found that the systemic inflammatory markers NLR, SII and PIV were statistically significantly different between the H-IC and U-IC groups and were higher in the U-IC group.

In our study, a significantly greater cervical length and a lower rate of funnelling were observed in the H-IC group compared to the other groups. In addition, the time to delivery was longer in the H-IC group than in the other groups. The cervical length before cerclage was 38.3±8.2 mm in the H-IC group, 22.7±6.4 mm in the U-IC group and 16.3±9.9 mm in the PE-IC group. Although a significant difference in cervical length was found between all three groups, no significant difference was found between the H-IC and U-IC groups in terms of delivery weeks, preterm births and perinatal outcomes. The longer interval between the cerclage procedure and the week of delivery in the H-IC group is explained by the fact that the cerclage procedure was performed in the earlier week in this group. Although the study by Liu et al.[19] showed that cervical length before cerclage is an independent risk factor for pregnancy outcomes and that a long cervix is associated with lower adverse pregnancy outcomes, the study by Incerti et al.[20] found no improvement in preterm birth rate and pregnancy outcomes at <35 weeks in patients who underwent cerclage with cervical length measurement. This situation shows that cervical length alone is not associated with preterm birth and perinatal outcomes.

Cervical insufficiency is one of the most important causes of preterm labour and the etiology is multifactorial. Inflammation is one of the most important factors emphasized. While NLR, PLR and MLR the systemic inflammatory indices assessed in patients with preterm labour were high in patients with preterm labour, SII and SIRI were similar between study groups.[9] The infection parameters are evaluated before the cerclage procedure, as the presence of an infection influences the success of the cerclage.[8,9,21,22] While amniocentesis is recommended for the detection of infection in these patients, there has recently been an increasing trend towards non-invasive methods. Lin et al.[11] investigated SII and SIRI levels, i.e. systemic inflammatory indices that can be easily measured in maternal blood, in patients undergoing cerclage. They showed that SII and SIRI levels could be important biochemical markers for predicting the outcome of cervical cerclage. They later found that SII and SIRI levels were associated with maternal and perinatal outcomes in a dynamic comparison.[13] In our study, in addition to these indices, we also had the opportunity to examine the MII values and the PIV values, which are new indices that use CRP values.[14,16] NLR, SII and PIV differed significantly between the H-IC and U-IC groups, while no difference was found between either group and PE-IC. We explained this change by the fact that the infection was not the only cause in the patients with cervical insufficiency but that the insufficiency process had already started in the PE-IC patients, as the cervix was already shortened due to the infection.

Chan et al.[23] included forty-seven patients who had undergone cerclage in their study and 59.1% of these patients gave birth after 34 weeks. In that study, patients in the H-IC and U-IC groups had a higher gestational age and better pregnancy outcomes than patients in the PE-IC group. The study conducted by Khan et al.[24] showed that 79.4% of patients who underwent cerclage in the H-IC group, 73.3% in the U-IC group and 47.1% in the PE-IC group had a cerclage by 36 weeks' gestation. While more adverse perinatal events occurred in the PE-IC group, 17.6% had a PPROM. This is one of the most common complications after cerclage.[25] In the study by Gölbaşı et al.,[7] the PPROM rate in the PE-IC group in patients undergoing cerclage, which was divided into H-IC, U-IC and PE-IC, was determined to be 40% and was significantly higher than in the other groups. In our study, adverse perinatal outcomes were also significantly higher in the PE-IC group than in the other two groups, while PPROM developed in six (33.3%) patients. The PPROM rate was higher in the U-IC and PE-IC groups. It would therefore be appropriate to inform patients who have undergone cerclage about possible complications.

Limitations

This study has several limitations. First, no multiple pregnancies were studied, as the surgical indications for multiple pregnancies are unclear. Secondly, the retrospective nature and limited sample size limit the generalizability of the results obtained. One strength of the study is that it was a single center study, which allowed homogenization of cerclage indications, surgical technique and patient follow-up.

CONCLUSION

In this study we compared the perinatal outcomes of cerclage procedures according to indication and examined their relationship to systemic indices of inflammation. Cerclage detected by physical examination was associated with increased perinatal morbidity and risk of preterm delivery, compared with cerclage detected by history and ultrasound. The high preterm birth rates and adverse perinatal outcomes observed in the PE-IC group suggest that this patient group should be monitored more closely. An elective cerclage should therefore be considered before the insufficiency process has already begun. Easily accessible inflammatory indices such as NLR, SII and PIV can help predict pregnancy outcome and

allow earlier intervention in patients at risk of preterm birth. The use of these indices can add an additional dimension to the clinical decision-making process and increase the success of cervical cerclage. Future large-scale prospective studies may further define the clinical utility of these indices.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Ankara Etlik City Hospital No. 1 Clinical Researches Ethics Committee (Date: 16.08.2023, Decision No: AEŞH-EK1-2023-473).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. da Fonseca EB, Damião R, Moreira DA. Preterm birth prevention. *Best Pract Res Clin Obstet Gynaecol.* 2020;69,40-49. doi:10.1016/j.bpobgyn.2020.09.003
2. Bayraktar B, Vural T, Gölbaşı C, Gölbaşı H, Bayraktar MG. Effect of co-twin fetal sex on fetal anthropometry and birth time in twin pregnancies. *J Obstet Gynaecol Can.* 2021;43(10):1153-1158. doi:10.1016/j.jogc.2021.02.113
3. Aubin AM, McAuliffe L, Williams K, et al. Combined vaginal progesterone and cervical cerclage in the prevention of preterm birth: a systematic review and meta-analysis. *Am J Obstet Gynecol MFM.* 2023;5(8):101024. doi:10.1016/j.ajogmf.2023.101024
4. ACOG Practice Bulletin No.142: Cerclage for the management of cervical insufficiency. *Obstet Gynecol.* 2014;123(2 Pt 1):372-379. doi:10.1097/01.AOG.0000443276.68274.cc
5. Krispin E, Danieli-Gruber S, Hadar E, Gingold A, Wiznitzer A, Tenenbaum-Gavish K. Primary, secondary, and tertiary preventions of preterm birth with cervical cerclage. *Arch Gynecol Obstet.* 2019;300(2):305-312. doi:10.1007/s00404-019-05184-y
6. Brown R, Gagnon R, Delisle MF. No. 373-cervical ınsufficiency and cervical cerclage. *J Obstet Gynaecol Can.* 2019;41(2):233-247. doi:10.1016/j.jogc.2018.08.009
7. Golbasi C, Golbasi H, Bayraktar B, Sever B, Vural T, Ekin A. Effectiveness and perinatal outcomes of history-indicated, ultrasound-indicated and physical examination-indicated cerclage: a retrospective study. *BMC Pregnancy Childbirth.* 2022;22(1):217. doi:10.1186/s12884-022-04557-7
8. Lee SE, Romero R, Park CW, Jun JK, Yoon BH. The frequency and significance of intraamniotic inflammation in patients with cervical insufficiency. *Am J Obstet Gynecol.* 2008;198(6):633.e1-633.e6338. doi:10.1016/j.ajog.2007.11.047
9. Hrubaru I, Motoc A, Moise ML, et al. The predictive role of maternal biological markers and inflammatory scores NLR, PLR, MLR, SII, and SIRI for the risk of preterm delivery. *J Clin Med.* 2022;11(23):6982. doi:10.3390/jcm11236982
10. Jung EY, Park KH, Lee SY, Ryu A, Joo JK, Park JW. Predicting outcomes of emergency cerclage in women with cervical insufficiency using inflammatory markers in maternal blood and amniotic fluid. *Int J Gynaecol Obstet.* 2016;132(2):165-169. doi:10.1016/j.ijgo.2015.07.011
11. Lin Y, Fang J, Ni R, et al. Dynamic change of novel systemic ınflammation markers to predict maternal-neonatal prognosis after cervical cerclage. *J Inflamm Res.* 2023;16:1745-1756. doi:10.2147/JIR.S410211
12. Gabay C, Kushner I. Acute-phase proteins and other systemic responses to inflammation. *N Engl J Med.* 1999;340(6):448-454. doi:10.1056/NEJM199902113400607
13. Fang J, Lin Y, Chen Z, Lin Y, Pan M. The association of inflammatory markers with maternal-neonatal outcome after cervical cerclage. *J Inflamm Res.* 2023;16:245-255. doi:10.2147/JIR.S393666
14. Casadei Gardini A, Scarpi E, Valgiusti M, et al. Prognostic role of a new index (multi inflammatory index) in patients with metastatic colorectal cancer: results from the randomized ITACa trial. *Ther Adv Med Oncol.* 2020;12:1758835920958363. doi:10.1177/1758835920958363
15. Gozdas HT, Kayis SA, Damarsoy T, et al. Multi-inflammatory index as a novel mortality predictor in critically Ill COVID-19 patients. *J Intensive Care Med.* 2022;37(11):1480-1485. doi:10.1177/08850666221100411
16. Jin C, Li X, Luo Y, Zhang C, Zuo D. Associations between pan-immune-inflammation value and abdominal aortic calcification: a cross-sectional study. *Front Immunol.* 2024;15:1370516. doi:10.3389/fimmu.2024.1370516
17. Berghella V. Universal cervical length screening for prediction and prevention of preterm birth. *Obstet Gynecol Surv.* 2012;67(10):653-658. doi:10.1097/OGX.0b013e318270d5b2
18. Crane JMG, Hutchens D. Use of transvaginal ultrasonography to predict preterm birth in women with a history of preterm birth. *Ultrasound Obstet Gynecol.* 2008;32(5):640-645. doi:10.1002/uog.6143
19. Liu Y, Ke Z, Liao W, et al. Pregnancy outcomes and superiorities of prophylactic cervical cerclage and therapeutic cervical cerclage in cervical insufficiency pregnant women. *Arch Gynecol Obstet.* 2018;297(6):1503-1508. doi:10.1007/s00404-018-4766-9
20. Incerti M, Ghidini A, Locatelli A, Poggi SH, Pezzullo JC. Cervical length ≤25 mm in low-risk women: a case control study of cerclage with rest vs rest alone. *Am J Obstet Gynecol.* 2007;197(3):315.e1-315.e4. doi:10.1016/j.ajog.2007.06.029
21. Aguin E, Aguin T, Cordoba M, et al. Amniotic fluid inflammation with negative culture and outcome after cervical cerclage. *J Matern Fetal Neonatal Med.* 2012;25(10):1990-1994. doi:10.3109/14767058.2012.667177
22. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. *Lancet Lond Engl.* 2008;371(9606):75-84. doi:10.1016/S0140-6736(08)60074-4
23. Chan LLK, Leung TW, Lo TK, Lau WL, Leung WC. Indications for and pregnancy outcomes of cervical cerclage: 11-year comparison of patients undergoing history-indicated, ultrasound-indicated, or rescue cerclage. *Hong Kong Med J.* 2015;21(4):310-317. doi:10.12809/hkmj144393
24. Khan MJ, Ali G, Al Tajir G, Sulieman H. Evaluation of outcomes associated with placement of elective, urgent, and emergency cerclage. *J Obstet Gynecol India.* 2012;62(6):660-664. doi:10.1007/s13224-012-0233-x
25. Giraldo-Isaza MA, Berghella V. Cervical cerclage and preterm PROM. *Clin Obstet Gynecol.* 2011;54(2):313-320. doi:10.1097/GRF.0b013e318217d530