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The relationship of prophylactically applied cervical cerclage with systemic inflamamatory parameters; its effect on cerclage success

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ABSTRACT

Aims: This study investigates the relationship between systemic inflammatory biomarkers-Systemic Immune-Inflammation Index (SII), Systemic Inflammation Response Index (SIRI), and Pan-Immune Inflammation Value (PIV)-and pregnancy outcomes following prophylactic cervical cerclage.

Methods: A retrospective analysis was conducted on 60 pregnant women who underwent prophylactic McDonald cerclage between November 2022 and September 2024. Patients were divided into two groups based on whether they delivered at term (≥37 weeks) or preterm (<37 weeks). Demographic, clinical, and laboratory data-including SII, SIRI, and PIV were collected and analyzed using SPSS 27. ROC curve analysis was performed to evaluate the predictive value of these biomarkers.

Results: There were no significant differences in maternal age, obstetric history, cerclage week, or cervical length between the term and preterm groups. However, preterm deliveries were significantly associated with higher platelet counts and elevated levels of SII, SIRI, and PIV ($p<0.05$). ROC analysis revealed moderate predictive value for all three biomarkers, with SII and PIV demonstrating the highest sensitivity and specificity for predicting preterm labor.

Conclusion: Elevated maternal systemic inflammatory markers-particularly SII, SIRI, and PIV-are associated with increased risk of preterm birth after cervical cerclage. These non-invasive biomarkers may serve as valuable tools for monitoring inflammation and predicting cerclage outcomes, potentially enabling earlier intervention in high-risk pregnancies. Larger multicenter studies are needed to validate these findings and refine clinical application.

Keywords: Cervical cerclage, prophylactic cerclage, inflammatory biomarkers

INTRODUCTION

Cervical insufficiency is a relatively uncommon condition, affecting fewer than 0.5% of pregnancies, yet it remains an important contributor to preterm birth, with incidence rates reaching up to 2% in certain populations.[1,2] It is characterized by painless, progressive cervical shortening and dilatation during the mid–late second trimester, often without significant symptoms, making early diagnosis challenging. Monitoring cervical changes is therefore essential for the successful management of pregnancy. Transvaginal ultrasonography (TVUSG) is considered the most sensitive tool for evaluating cervical length, providing reliable measurements for early detection and timely intervention. Cervical length below 25 mm or below the 5th percentile in the second trimester is widely recognized as a major indicator of cervical insufficiency.[3]

Cervical cerclage remains the primary and most effective treatment for cervical insufficiency, aiming to reinforce the cervix and reduce the risk of preterm delivery.[4,5] Surgical techniques such as the McDonald and Shirodkar procedures can be performed transvaginally or via an abdominal route, with comparable success rates.[6] Reported fetal survival rates following cerclage range between 46% and 100%.[7,8] Despite the clinical value of cerclage, predicting pregnancy outcomes and identifying early markers of cerclage success remain significant challenges.

Previous research has shown that elevated levels of pro-inflammatory cytokines and chemokines in amniotic fluid correlate with adverse outcomes after cervical cerclage.[9,10] Amniotic fluid concentrations of interleukins such as IL-1, IL-6, and IL-8 have been suggested as potential markers for evaluating post-cerclage prognosis.[11-13] However, obtaining amniotic fluid is invasive and not practical for routine monitoring.

In recent years, novel systemic inflammatory indices-such as the SII, and pan-immune-inflammation value (PIV)-have gained attention for their ability to reflect the body's systemic immune status through simple, non-invasive blood tests.[14-16] These markers combine circulating neutrophil, lymphocyte, monocyte, and platelet levels to provide a broader representation of immune activation. Their practicality

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and accessibility make them promising tools for evaluating inflammatory responses in pregnancy-related conditions.

Although SII, SIRI, and PIV have been studied in various obstetric and gynecologic settings, there is a noticeable gap in the literature regarding their predictive value specifically after cervical cerclage. Only a limited number of studies have examined the association between these systemic inflammatory indices and cerclage outcomes, and none have evaluated their potential as dynamic, non-invasive biomarkers for monitoring post-cerclage prognosis.

The objective of our research was therefore to investigate whether maternal blood-based dynamic inflammatory markers-SII, SIRI, and PIV-could serve as reliable, non-invasive biomarkers for forecasting pregnancy outcomes following cervical cerclage.

By focusing on systemic inflammatory indices instead of invasive amniotic fluid markers, this study aims to contribute a practical, objective, and clinically applicable approach to predicting cerclage success.

METHODS

Our research incorporated 60 patients who underwent prophylactic McDonald cerclage between November 1, 2022 and September 1, 2024 in the Obstetrics and Gynecology Clinic of Ankara Etlik City Hospital. The study was initiated after the approval of the Ethics Committee of Ankara Etlik City Hospital (Date: 16.10.2024, Decision No: AEŞH-BADEK-2024-953). and all procedures were conducted in compliance with ethical guidelines and guidelines set forth in the Declaration of Helsinki. In the study, patients who underwent cervical cerclage at 37 weeks of gestational age were considered as successful cerclage procedures. 39 of the patients reached 37th gestational week. 21 of the patients went into labor before reaching 37 weeks gestational age. Only pregnant women with spontaneous vaginal delivery were enrolled in trial; participants with cesarean section were disregarded. In this retrospective, cross-sectional analysis, patient data were collected from hospital records. Patients with a history of painless abortion, cervical opening under 5 cm and preserved membranes were included in the study. Cervical dilatation and length were measured by transvaginal ultrasonography (TVUSG). Patient demographics, pregnancy history, cervical length, cerclage placement time and gestational week were recorded. Laboratory analysis included hemoglobin, leukocytes, neutrophils, lymphocytes, monocytes, platelets, SII, SIRI and PIV. The cerclage procedure was performed under general anesthesia and patients were treated with progesterone and antibiotics after cerclage. The cerclage suture was removed immediately in cases of pain, chorioamnionitis or rupture of membranes, and at 37-38 weeks in the absence of these conditions. Pregnant women under 18 years of age, active vaginal bleeding, fetal malformation or stillbirth, regular uterine contractions, infectious status, pre-existing systemic disease, history of malignancy, active smoking, alcohol or illicit drug use, HIV, HCV or HBV infection, and any pre-existing chronic disease or history of organ transplantation were excluded. Patients who had undergone abdominal cerclage, multiple pregnancies and patients with unclear data were also excluded.

Using the calculation formulas, SII (platelet×neutrophil/lymphocyte), SIRI (monocyte×neutrophil/lymphocyte), and PIV (monocyte×platelet×neutrophil/lymphocyte) were determined based on the absolute counts of neutrophils ($\times10^9$/L), monocytes ($\times10^9$/L), lymphocytes ($\times10^9$/L), and platelets ($\times10^9$/L), respectively.

Statistical Analysis

The analysis was performed using the Statistical Package for the Social Sciences (Version 27, SPSS Inc., Chicago, IL, USA). The Chi-squared test was used for ordinal variables (gravidity, parity, abortion) and the Mann-Whitney U test for other parameters because the data did not follow a normal distribution. P values under 0.05 were regarded as statistically significant.

RESULTS

The maternal characteristics of the groups are shown in Table 1. No significant difference was observed between the age, gravida, parity and abortion values of the two groups (p values were 0.944, 0.521, 0.632, 0.137 respectively). (age, term 28.94±5.61, preterm 29.42±6.17 (p=0.944)), (gravida, term 2.84±2.21, preterm 3.23±1.92 (p=0,521)) (parity, term 0.87±0.95, preterm 1.09±1.09 (p=0.632)) (abortion, 0.97±1.59, preterm delivery 1.09±1.37 (p=0.137)). In the analyses performed for cerclage week (term 17.86±4.26, preterm 18.66±4.01) and cervical length (term 24.94±11.93, preterm 23.14±12.41), no statistically significant difference was found between term and preterm groups (cerclage week: p=0.381, cervical length: p=0.475). The gestational week of labor was 38.25±1.03 in the term group and 31.86±4.04 in the preterm group and this difference was statistically significant (p<0.001).

Table 1. Maternal characteristics of the groups

	Group	Mean±SD	p value
Age	Term (n=39)	28.94±5.61	0.944
	Preterm (n=21)	29.42±61.17	
Gravida	Term	2.84±2.21	0.521
	Preterm	3.23±1.92	
Parity	Term	0.87±0.95	0.632
	Preterm	1.09±1.09	
Abortion	Term	0.97±1.59	0.137
	Preterm	1.09±1.37	
Birth week	Term	38.25±1.03	<.001
	Preterm	31.86±4.04	
Cerclage applied week	Term	17.86±4.26	0.381
	Preterm	18.66±4.01	
Cervical length	Term	24.94±11.93	0.475
	Preterm	23.14±12.41	

SD: Standard deviation

Table 2 shows the complete blood count values and SII, SIRI, PIV values of the groups. No significant difference was observed between the hemoglobin, leukocyte, neutrophil, monocyte values of the groups (p values were 0.185, 0.486, 0.963, 0.840, 0.620 respectively). The platelet count was

228.23±55.38 x10^3 in the term group and 273.51±70.12 x10^3 in the preterm group and there was a statistically significant difference between them (p=0.017). The SII was 909.57±619.05 in the term group and 1368.61±905.09 in the preterm group and there was a significant difference between them (p=0.011). Mean SIRI was significantly different between term (66.33±42.98) and preterm (126.51±118.76) groups (p<.001). PIV showed a significant difference between term and preterm groups (506.57±484.49 and 1038.61±1019.82 respectively, p=0.003).

Table 2. Distribution of blood values of the groups

	Group	Mean±SD	p value
Hemoglobin	Term (n=39)	12.20±1.08	0.185
	Preterm(n=21)	11.53±1.06	
Leukocyte	Term	10.40±3.59	0.486
	Preterm	11.00±3.21	
Neutrophil	Term	7.96±3.64	0.963
	Preterm	7.74±2.65	
Lymphocyte	Term	2.31±2.06	0.840
	Preterm	1.93±0.65	
Monocyte	Term	0.60±0.22	0.620
	Preterm	0.7±0.7	
Platelet	Term	228.23±55.38	0.017
	Preterm	273.51±70.12	
SII	Term	909.57±619.05	0.011
	Preterm	1368.61±905.09	
SIRI	Term	66.33±42.98	<.001
	Preterm	126.51±118.76	
PIV	Term	506.57±484.49	0.003
	Preterm	1038.61±1019.82	

SII: Systemic immune-inflammation index, SIRI: Systemic inflammation response index, PIV: Pan-immune inflammation value, SD: Standard deviation

The results of the ROC curve are shown in Table 3. For SII, the AUC was 0.599, sensitivity was 0.77, specificity was 0.62, positive predictive value was 0.79, negative predictive value was 0.59 and the optimal cut-off value was 877.81. For SIRI, AUC was 0.553, sensitivity was 0.85, specificity was 0.43, positive predictive value was 0.73, negative predictive value was 0.60 and the optimal cut-off was 1.58. For PIV the AUC was 0.623, sensitivity 0.87, specificity 0.57, positive predictive value 0.79, negative predictive value 0.70 and the optimal cut-off value 447.45.

Table 3. ROC curve results

	AUC	Sensitivity	Specificity	PPV	NPV	Cut-off value
SII	0.599	0.77	0.62	0.79	0.59	877.81
SIRI	0.553	0.85	0.43	0.73	0.60	1.58
PIV	0.623	0.87	0.57	0.79	0.70	447.45

ROC: Receiver operating characteristic, SII: Systemic immune-inflammation index, SIRI: Systemic inflammation response index, PIV: Pan-immune inflammation value, AUC: Area under curve, PPV: Positive predictive value, NPV: Negative predictive value

DISCUSSION

Cervical cerclage is regarded as the most successful surgical intervention for cervical insufficiency and is commonly employed in clinical settings. However, complications such as PPROM, chorioamnionitis and cervical tears are common after cerclage and the pathophysiological mechanisms of these complications are not fully understood. This situation calls for the development of non-invasive biomarkers that can more reliably predict the pregnancy outcome of cervical cerclage.[17]

The results of our study suggest that biomarkers of systemic inflammation such as SII, SIRI and PIV may be valuable indicators in assessing the success of cervical cerclage and predicting pregnancy outcomes. Among patients who underwent cervical cerclage, pregnant women who reached 37 weeks' gestation had significantly lower levels of these parameters compared to preterm labor. Although several studies have examined SII and SIRI in relation to cerclage outcomes, our study provides additional novelty by simultaneously evaluating SII, SIRI and the relatively under-investigated PIV marker together within the same patient cohort, thereby offering a more comprehensive and integrative assessment of systemic inflammatory status after cerclage.

Several studies have highlighted that intrauterine infection and inflammation play significant roles as risk factors in determining postoperative outcomes following cervical cerclage.[11,13] Lin et al.[17] found that levels of SII and SIRI were correlated with the results of cervical cerclage and neonatal prognosis, especially SII was a strong prognostic marker.[17] In another study by Huang et al,[18] CRP level, WBC count, neutrophil count, NLR, PLR, SII and SIRI levels were found to be higher in the group of patients who delivered preterm before 34 weeks compared to the group who delivered at or after 34 weeks.

In another study, they concluded that maternal peripheral blood SII and SIRI were important biochemical markers for predicting maternal and neonatal outcomes after cervical cerclage.[19] Therefore, they emphasized that monitoring maternal peripheral blood levels of inflammatory markers such as CRP and SII in the perioperative period is important to predict neonatal outcomes in cervical cerclage.[19] In the study conducted by Gülücü et al.[20] between SII level and birth week, it was found that SII level decreased with increasing birth week and SII levels were higher in babies born earlier. In a multivariate analysis, Jung et al.[9] showed that inflammatory parameters such as high neutrophil/lymphocyte ratio and elevated IL-8 levels in amniotic fluid were significantly associated with preterm birth before 32 weeks. Recent research has indicated that intrauterine infection and inflammation are key risk factors influencing postoperative outcomes following cervical cerclage.[11-13]

Fang et al.[19] identified several significant indicators of poor prognosis, including higher WBC, increased neutrophil and monocyte, decreased lymphocyte, elevated platelet, as well as higher SII and SIRI levels. Additionally, earlier gestational age, lower birth weight, reduced neonatal Apgar scores at both 5 and 10 minutes, a lower rate of NICU admissions, and a decreased mortality rate were also associated with poor outcomes.

Research have investigated the role of PIV in determining the prognosis of obstetric complications, particularly preterm labor, preterm premature rupture of membranes (PPROM) and intrauterine infection. There is a limited number of

studies in the literature looking at the relationship between PIV and the success of cervical cerclage, so our study can guide future research.

Limitations

This study highlights the potential of systemic inflammation biomarkers (SII, SIRI, and PIV) in predicting pregnancy outcomes after cervical cerclage, offering a practical and non-invasive tool for clinicians. However, several limitations should be acknowledged. First, the sample size of 60 patients may be considered relatively small, which increases the risk of the study being underpowered and may limit the statistical robustness of certain associations. As cervical insufficiency is a rare clinical condition, recruiting a larger cohort within a single center is inherently challenging; nevertheless, this limited sample size should still be considered when interpreting the results. Additionally, the retrospective and single-center design, along with the absence of long-term maternal and neonatal follow-up, restricts the generalizability of the findings. Another important limitation is that several clinically relevant variables known to influence preterm birth-such as PPROM, chorioamnionitis, cervical infection findings, CRP and procalcitonin levels, vaginal culture results, the type and dosage of progesterone used, and detailed postoperative follow-up data-were not included due to incomplete or inconsistent documentation in patient records. These missing parameters may have acted as confounding factors and could partly influence the relationship observed between systemic inflammatory indices and cerclage outcomes. Furthermore, only univariate analyses were performed, as the dataset was not suitable for reliable multivariate logistic regression. The relatively small number of outcome events in the preterm birth group and the incomplete documentation of several potential confounders would have increased the risk of overfitting and produced unreliable estimates if multivariate modeling were attempted. Future studies should therefore involve larger, multicenter cohorts, include comprehensive clinical and laboratory variables, and apply robust multivariate analyses to better determine independent predictive factors and further clarify the biological mechanisms underlying the associations identified.

CONCLUSION

The results of this study suggest that maternal systemic inflammatory parameters, in particular biomarkers such as SII, SIRI, may play an important role in predicting pregnancy outcomes in patients undergoing cervical cerclage. The significantly higher levels of these parameters in patients with preterm labor provide strong evidence that inflammation may be a predictor of preterm labor risk and cerclage failure. These findings demonstrate the usefulness of non-invasive, practical biomarkers for predicting pregnancy outcomes after cervical cerclage.

Monitoring inflammatory responses after cervical cerclage may allow more accurate prognoses and personalized treatment approaches in clinical practice. Perioperative monitoring of parameters such as SII, SIRI and PIV may contribute to earlier intervention and better outcomes in patients at risk of preterm delivery. These results emphasize the critical role of inflammation in pregnancy and highlight the importance of future studies to investigate how these biomarkers can be more effectively used clinically in pregnancy management after cervical cerclage.

Considering these findings, inflammatory biomarkers such as SII, SIRI and PIV may be useful tools for prognostication and pregnancy management after cervical cerclage. However, larger and multicenter studies are needed to assess the clinical applicability of these parameters.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was initiated after the approval of the Ethics Committee of Ankara Etlik City Hospital (Date: 16.10.2024, Decision No: AEŞH-BADEK-2024-953).

Informed Consent

As this was a retrospective study, formal written informed consent was not required and was therefore not obtained.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

Financial Disclosure

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Author Contributions

Concept: S.E., M.A.S,; Design: M.P., A.K.; Control: S.E., Ş.Ç.; Data collection and/or processing: S.E., A.K., M.A.S.; Analysis and/or interpretation: S.E., M.P.; Literature review: M.A.S., Ş.Ç.; Article writing: All authors.; Critical review: All authors.

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