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Evaluation of the efficacy of maternal hemogram parameters in predicting meconium presence at birth in healthy pregnancies

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Abstract

The presence of meconium-stained amniotic fluid (MSAF) is a critical indicator of fetal distress, associated with increased neonatal morbidity and mortality. The aim of this study was to evaluate the potential of maternal blood parameters to predict the presence of meconium-stained amniotic fluid (MSAF) in term pregnancies. Data were retrospectively analyzed from healthy pregnant women who presented to Samsun Education and Research Hospital between 2014 and 2023 and delivered either by normal spontaneous delivery or cesarean section. The study included healthy pregnant women aged 18 and over who gave birth between 37 and 42 weeks of gestation. The non-invasive laboratory parameters investigated were neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), systemic immune-inflammation index (SIRI), aggregate index of systemic inflammation (AISI), and procalcitonin levels. Results showed that NLR, MLR, SIRI, AISI, and procalcitonin levels were significantly higher in the MSAF group. The ROC curve analysis demonstrated that SIRI (cutoff: 3.55) had an AUC of 0.826 (sensitivity: 89.2%, specificity: 71.8%). AISI (cutoff: 1340.39) had an AUC of 0.749 (sensitivity: 75.8%, specificity: 70.9%). NLR (cutoff: 3.58) showed an AUC of 0.757 (sensitivity: 87.5%, specificity: 56.3%). MLR (cutoff: 0.55) presented an AUC of 0.822 (sensitivity: 87.5%, specificity: 74.8%). However, SII demonstrated negligible and statistically non-significant diagnostic value. PLR and procalcitonin exhibited lower diagnostic efficacy. This study demonstrates that NLR, MLR, SIRI, AISI, and procalcitonin are effective non-invasive biomarkers for predicting the presence of MSAF in term pregnancies. These parameters can assist clinicians in anticipating fetal distress and the risk of meconium aspiration syndrome (MAS), thereby improving perinatal outcomes through timely intervention.

Keywords: meconium, amniotic fluid, inflammation mediators, biomarkers

1. Introduction

Amniotic fluid surrounds the fetus within the uterus, providing a protective and low-resistance environment. Meconium is a dark green substance typically found in newborns, composed of bile, mucus, and epithelial cells. Under acute or chronic hypoxic conditions, the fetus may pass meconium into the amniotic fluid. The presence of meconium in the amniotic fluid is a serious indicator of fetal distress and is associated with increased neonatal morbidity and mortality (1). Even in women with a low risk of obstetric complications, meconium-stained amniotic fluid (MSAF) is common and is associated with a fivefold increase in perinatal mortality compared to low-risk patients with clear amniotic fluid (2).

MSAF is observed in approximately 13% to 16% of births (3). Several maternal and fetal factors contribute to the occurrence of MSAF, including hypertension, gestational diabetes mellitus (GDM), chronic respiratory or cardiovascular diseases, post-term pregnancy, preeclampsia, eclampsia, oligohydramnios, intrauterine growth restriction, and a poor biophysical profile (4, 5). MSAF is associated with higher rates of intervention during delivery, cesarean sections, low birth weight, fetal distress, the need for admission to the neonatal intensive care unit (NICU), and neonatal death (6). The presence of MSAF may indicate normal gastrointestinal maturation, but it can also be a sign of fetal distress due to acute or chronic hypoxic events (7, 8). Meconium aspiration syndrome (MAS) occurs when the baby aspirates meconium, affecting approximately 2% to 10% of all MSAF cases (7). Around 12% of infants with MAS result in neonatal death (9). The passage of meconium increases after the 37th week of pregnancy, and MSAF is associated with higher rates of cesarean delivery (1). Meconium aspiration can occur in the uterus, during delivery, or after birth. Causes of meconium passage in the uterus include increased motilin levels, a post-term fetus with normal gastrointestinal function, vagal stimulation caused by cord compression, and fetal stress in utero (10).

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Recent studies have highlighted the importance of various maternal hemogram and serum biochemistry parameters in predicting adverse pregnancy outcomes. The complete blood cell count, which is routinely performed and relatively inexpensive, can provide valuable insights into maternal and fetal health. Combined hematological indexes of inflammation, such as the neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte Ratio (MLR), platelet-to-lymphocyte ratio (PLR), systemic inflammation index (SII), systemic inflammation response index (SIRI), and aggregate inflammation systemic index (AISI), are already studied as biomarkers in several disorders (11-17).

For instance, studies have shown that NLR and PLR can predict fetal distress during labor and are associated with low APGAR scores (10, 18). Elevated levels of MLR and SIRI have also been observed in septic infants (19). NLR and MLR have been implicated in predicting preeclampsia and other pregnancy-related complications (5). Additionally, SIRI and AISI have been associated with gestational diabetes and intrahepatic cholestasis of pregnancy (18, 20). Research has demonstrated that MSAF is linked with increased maternal and fetal inflammation, highlighting the inflammatory nature of this condition (21).

Meconium births are generally associated with fetal distress or hypoxia, yet the relationship between this condition and maternal blood values is not clearly understood. Identifying conditions that can lead to fetal distress is crucial for reducing neonatal mortality and morbidity rates. Meconium is a cause of fetal distress that can complicate many births.

Early detection of meconium is crucial for preventing fetal distress. The ability of maternal hemogram parameters, including derived indices like PLR, NLR, MLR, SII, SIRI, and AISI, to predict meconium presence is critical for understanding the potential risks and management strategies for meconium-stained births. In our study, we aimed to identify a parameter from maternal blood values before birth that could predict meconium-stained births and enable early preventive measures to reduce meconium-associated complications such as neonatal asphyxia.

2. Materials and Methods

In our study, data from healthy pregnant women who attended the Samsun Training and Research Hospital Gynecology and Obstetrics Clinic between January 1, 2014, and December 31, 2023, and who had normal spontaneous deliveries or cesarean sections, were retrospectively analyzed. The data were obtained from the hospital's information system or by requesting files from the archive. The study included healthy pregnant women aged 18 and over who gave birth between 37 and 42 weeks of gestation. Pregnant women with conditions that could alter blood parameters, such as preeclampsia, intrauterine growth restriction, diabetes, chronic hypertension, and rheumatologic diseases, were excluded from the study.

The participants were divided into two groups: those who had meconium-stained deliveries and those who did not. The collected data were compared between these two groups. The evaluated parameters included age, body mass index, gravida, parity, mode of delivery, hemoglobin (Hb), hematocrit, white blood cell count (WBC), platelet count, lymphocyte-monocyte-neutrophil percentages, SII, SIRI, AISI, NLR, MLR, PLR, baby birth weight, APGAR scores at 1 and 5 minutes, presence or absence of meconium aspiration, need for neonatal unit admission, neonatal intubation status, gestational age, and procalcitonin levels. Maternal blood values were calculated based on the last blood samples taken for birth preparation before delivery and were compared accordingly.

The statistical analysis of the data obtained from the study was performed using the SPSS (v21.0, Illinois, US) program. The data were presented as mean ± standard deviation (SD) and median (min-max). The Kolmogorov-Smirnov test was used to analyze the assumption of normal distribution of quantitative results. Multiple group comparisons were performed using the Kruskal-Wallis H test. Bonferroni correction was applied for post-hoc pairwise comparisons following multiple group comparisons. Mann-Whitney U and Student's t-tests were used for pairwise comparisons. The relationship between variables was evaluated using Spearman's Rank correlation analysis. The ROC curve was used to determine the diagnostic value of the study data. The area under the ROC curve (AUC) was considered as a measure of the diagnostic test's discriminative power. Confidence intervals for AUC were calculated, and sensitivity and specificity values were determined. For all tests, a p-value of <0.05 was considered statistically significant.

3. Results

In this study, 120 pregnant women with MSAF and 103 healthy pregnant controls evaluated. Demographic, clinical, and biochemical data regarding the study groups has been presented in the table 1. No significant differences were observed in maternal age, gravidity, and parity. In the MSAF group median Body Mass Index (BMI) was significantly lower compared to healthy pregnant group ($p=0.013$). Vaginal deliveries were less common in the MSAF group (42.5%) compared to the control group (74.8%), with cesarean sections accounting for 57.5% in the MSAF group and only 25.2% in the control group ($p<0.001$).

In hemogram parameters, white blood cell counts and hematocrit ratio was comparable between the groups. Hemoglobin levels were lower in the MSAF group than in the control group ($p<0.001$). Lymphocyte and monocyte count also differed significantly, with the MSAF group presenting lower lymphocyte and higher monocyte and neutrophil counts ($p<0.001$). Analysis of the percentage distribution of white blood cell subtypes revealed statistically significant elevations in the rates of lymphocytes and monocytes in the MSAF group ($p<0.001$, $p=0.046$ respectively), despite higher absolute lymphocyte counts in the control group. Conversely, the

percentages of neutrophils did not show a significant difference between the groups. Besides, platelet counts were significantly lower in the MSAF group compared to control group (p<0.001). Detailed data has been presented in the table 1.

Table 1. Demographic, clinical and biochemical data of patients[a]

		MSAF (n=120)	Control (n=103)	*p*
Maternal characteristics				
Age (years)		26.5 (23.3-29.8)	27.1 (24.3-30.5)	0.164[b]
BMI (kg/m^2)		25 (23-28)	27 (24-30)	**0.013**[b, *]
Gravidity		2 (1-2)	2 (1-3)	0.787[b]
Parity		1 (0-2)	1 (0-2)	0.281[b]
Mode of delivery	**Vaginal**	51 (42.5%)	77 (74.8%)	**<0.001**[c, *]
	Cesarian section	69 (57.5%)	26 (25.2%)	
Hb (g/dl)		9.5 (9-10.2)	10.8 (9.3-11.9)	**<0.001**[b, *]
Hct (%)		29.9 (27.7-33.6)	30.3 (26.6-33.1)	0.465[b]
WBC (10^3/µl)		12.2 (10.7-14.1)	12.5 (9.7-15.3)	0.964[b]
Lymphocytes (10^3/µl)		1.3 (1.1-1.6)	1.9 (1.4-2.3)	**<0.001**[b, *]
Lymphocytes (%)		14.3 (11.8-18.2)	12.1 (9.3-15.2)	**<0.001**[b, *]
Monocytes (10^3/µl)		2.1 (1.3-3.0)	0.7 (0.5-1.1)	**<0.001**[b, *]
Monocytes (%)		6.2 (5.0-7.7)	5.8 (4.6-6.7)	**0.046**[b, *]
Neutrophils (10^3/µl)		7.1 (6.3-10.9)	5.9 (5.1-7.2)	**<0.001**[b, *]
Neutrophils (%)		80.7 (77.3-84.8)	78.8 (76.8-83.5)	0.052[b, *]
Platelets (10^3/µl)		238.5 (181.3-270.1)	381.5 (344.6-420.3)	**<0.001**[b, *]
SII		1415.3 (937.9-1904.3)	1303.6 (975.5-2012.6)	0.939[b]
SIRI		12.2 (5.6-21.3)	2.2 (1.6-2.1)	**<0.001**[b, *]
AISI		2930.7 (1359.3-4637.5)	822.8 (560.9-1805.5)	**<0.001**[b, *]
NLR		5.8 (4.2-8.4)	3.5 (2.6-5.4)	**<0.001**[b, *]
PLR		176.9 (136.5-235.9)	222.8 (169.2-266.7)	**0.001**[b, *]
MLR		1.7 (0.7-2.6)	0.4 (0.3-0.6)	**<0.001**[b, *]
PCT (ng/ml)		0.20 (0.17-0.26)	0.18 (0.16-0.22)	**0.018**[b, *]
Fetal characteristics				
Gestational age at birth (weeks)		39 (38-39)	38 (37-38)	**<0.001**[b, *]
Birth weight (g)		3370 (3152-3650)	3800 (3700-4060)	**<0.001**[b, *]
Apgar score (1st min.)		9 (7-9)	9 (9-9)	**0.037**[b, *]
Apgar score (5th min.)		10 (8-10)	10 (10-10)	**<0.001**[b, *]
NICU		43 (35.8%)	17 (16.5%)	**0.001**[c, *]
Intubation		20 (16.7%)	8 (7.8%)	**0.046**[c, *]

Abbreviations: MSAF, meconium-stained amniotic fluid; Hb, hemoglobin; Hct, hematocrit; WBC, white blood cell count; SII, systemic immune-inflammation index; SIRI, systemic inflammation response index; AISI, aggregate immune suppression index; NLR, neutrophil to lymphocyte ratio; PLR, platelet to lymphocyte ratio; MLR, monocyte to lymphocyte ratio; PCT, procalcitonin; NICU, neonatal intensive care unit

[a]Data are given as median (IQR) and as number (percentage)

[b]Mann-Whitney U Test

[c]Pearson $\chi 2$ test

[*]$p < 0.05$ indicates statistical significance

SII was comparable between the groups. However, SIRI and AISI were elevated in the MSAF group compared to controls [12.2 (IQR: 5.6-21.3) vs 2.2 (IQR: 1.6-2.1); 2930.7 (IQR: 359.3-4637.5) vs. 822.8 (IQR: 560.9-1805.5) respectively], both showing statistically significant differences (p<0.001). Similarly, NLR, and MLR were significantly higher in the MSAF group [5.8 (IQR: 4.2-8.4) vs 3.5 (IQR: 2.6-5.4); 1.7 (IQR: 0.7-2.6) vs. 0.4 (IQR: 0.3-0.6) respectively], indicating a heightened inflammatory state. In contrast, PLR was higher in the control group compared to MSAF group [222.8 (IQR: 169.2-266.7) vs 176.9 (IQR: 136.5-235.9)]. Additionally, procalcitonin (PCT) levels were found to be significantly higher in the MSAF group [0.20 ng/mL (0.17-0.26)] compared to the control group [0.18 ng/mL (0.16-0.22)] (p=0.018).

The median gestational age at birth was higher in the MSAF group compared to the control group [39 (IQR: 38-39) vs 38 (IQR: 37-38)] (p<0.001). Birth weights also differed, with MSAF infants having a lower median weight compared to control group [3370 (IQR: 3152-3650) vs 3800 (IQR: 3700-4060)] (p<0.001). NICU admissions and intubation rates were higher in the MSAF group, indicating more severe perinatal outcomes (NICU: 35.8% vs. 16.5%, p=0.001; Intubation: 16.7% vs. 7.8%, p=0.046).

In our study, significant correlations were observed between several inflammatory markers and key maternal and fetal outcomes (Table 2). Specifically, SIRI and AISI demonstrated positive, weak correlations with gestational age at birth (SIRI: r=0.288, p<0.001; AISI: r=0.245, p<0.001). Additionally, the MLR also showed a positive, weak correlation with gestational age (r=0.286, p<0.001). Concerning birth weight, there were notable negative, weak correlations with SIRI (r=-0.307, p<0.001), AISI (r=-0.220, p=0.001), NLR (r=-0.218, p=0.001), and MLR (r=-0.294, p<0.001). For the APGAR score at 5 minutes, a weak negative correlation was observed with PCT (r=-0.327, p<0.001).

Table 2. The correlation of inflammatory marker levels/indexes with other investigated maternal and fetal study parameters[a]

		SII	SIRI	AISI	NLR	PLR	MLR	PCT
Gestational age at birth	***r***	0.004	0.288‡	0.245‡	0.186†	0.104	0.286‡	0.072
	p	0.958	**<0.001***	**<0.001***	**0.005***	0.120	**<0.001***	0.282
Birth weight	***r***	0.070	-0.307‡	-0.220‡	-0.218‡	0.230‡	-0.294‡	-0.072
	p	0.297	**<0.001***	**0.001***	**0.001***	**0.001***	**<0.001***	0.282
Apgar score (1st min.)	***r***	0.035	0.078	0.093	0.012	0.051	0.106	-0.174
	p	0.599	0.247	0.166	0.854	0.452	0.113	**0.009***
Apgar score (5th min.)	***r***	0.169†	0.117	0.186†	0.054	0.256‡	0.162†	-0.327
	p	**0.012***	0.081	**0.005***	0.418	**<0.001***	**0.016***	**<0.001***

Abbreviations: SII,Systemic immune-inflammation index; SIRI, systemic inflammation response index; AISI, aggregate immune suppression index; NLR, neutrophil to lymphocyte ratio; PLR, platelet to lymphocyte ratio; MLR, monocyte to lymphocyte ratio; PCT, procalcitonin

[a]Spearman rank correlation

*p< 0.05 indicates statistical significance

†Very weak correlation

‡Weak correlation

On ROC curve analysis, diagnostic value of SII, SIRI, AISI, NLR, PLR, MLR, and PCT evaluated to determine optimal cutoff point for identifying increased risk of MSAF (Table 3 and Fig. 1). The ROC curve analysis showed that SIRI, with a cutoff value of 3.55, demonstrated high diagnostic performance with AUC of 0.826 (95% CI: 0.767-0.886, p<0.001), achieving a sensitivity of 89.2% and a specificity of 71.8%. Similarly, AISI displayed robust diagnostic potential with a cutoff of 1340.39, yielding an AUC of 0.749 (95% CI: 0.680-0.818, p<0.001), sensitivity of 75.8%, and specificity of 70.9%. The NLR also emerged as a significant marker with a cutoff of 3.58, showing an AUC of 0.757 (95% CI: 0.691-0.823, p<0.001), sensitivity of 87.5%, and specificity of 56.3%. MLR proved particularly effective with a cutoff of 0.55, where it presented an AUC of 0.822 (95% CI: 0.763-0.881, p<0.001), along with a sensitivity of 87.5% and a specificity of 74.8%. Conversely, PLR and PCT exhibited lower diagnostic efficacy. PLR, at a cutoff of 156.47, demonstrated an AUC of 0.629 (95% CI: 0.556-0.701, p=0.001) with sensitivity and specificity of 84.5% and 40.8%, respectively. PCT, with a cutoff of 0.23 ng/ml, reported an AUC of 0.592 (95% CI: 0.518-0.666, p=0.018), sensitivity of 42.5%, and specificity of 76.7%. SII demonstrated AUC of 0.503, indicating negligible diagnostic value with a statistically non-significant result (p=0.939).

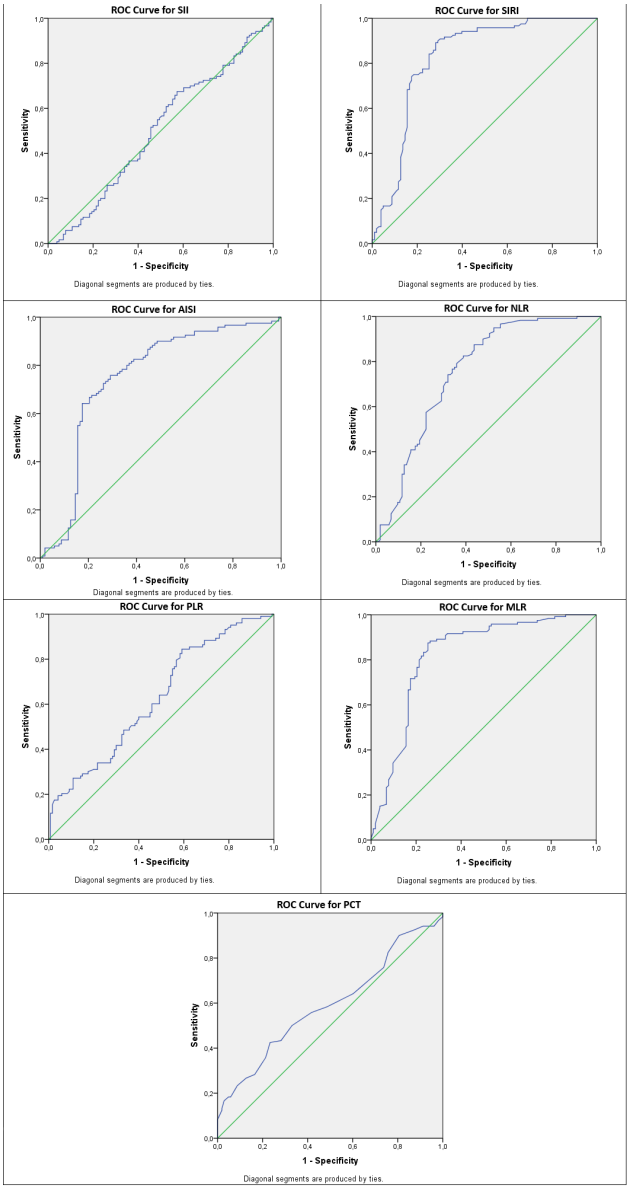

Fig. 1. Receiver operating characteristic curves for SII, SIRI, AISI, NLR, PLR, MLR, and PCT as screening tests for MSAF

Table 3. Details of the ROC curves

	Diagnostic scan					ROC curve		
Parameter	**Cutoff**	**Sensitivity (%)**	**Specificity (%)**	**PPV (%)**	**NPV (%)**	**AUC**	**CI (95%)**	***p***
SII	1156.64	65.8	43.7	53.89	56.10	0.503	0.426-0.580	0.939
SIRI	3.55	89.2	71.8	75.98	86.92	0.826	0.767-0.886	**<0.001**
AISI	1340.39	75.8	70.9	72.26	74.55	0.749	0.680-0.818	**<0.001**
NLR	3.58	87.5	56.3	66.69	81.83	0.757	0.691-0.823	**<0.001**
PLR	156.47	84.5	40.8	58.80	72.47	0.629	0.556-0.701	**0.001**
MLR	0.55	87.5	74.8	77.64	85.68	0.822	0.763-0.881	**<0.001**
PCT (ng/ml)	0.23	42.5	76.7	64.59	57.15	0.592	0.518-0.666	**0.018**

Abbreviations: PPV, positive predictive value; NPV, negative predictive value; AUC, area under the curve; CI, confidence interval; SII, systemic immune-inflammation index; SIRI, systemic inflammation response index; AISI, aggregate immune suppression index; NLR, neutrophil to lymphocyte ratio; PLR, platelet to lymphocyte ratio; MLR, monocyte to lymphocyte ratio; PCT, procalcitonin

4. Discussion

The presence of meconium in the amniotic fluid can typically be detected during labor, but it remains a concerning condition due to its potential effects in the perinatal period (1, 2). Identifying markers that can provide early prediction would be highly beneficial for clinicians. In this study, we examined maternal hemogram parameters to predict MSAF in healthy term pregnancies for the first time in the literature and found that NLR, MLR, SIRI, AISI, and procalcitonin levels were significantly higher in the MSAF group. Additionally, in the MSAF group, gestational age at delivery was higher, the cesarean rate and birth weight were lower, and the 1st and 5th minute APGAR scores were lower. Moreover, the NICU admission rate and intubation rate were significantly higher. These results indicate that the severity of inflammation is directly proportional to the likelihood of detecting MSAF.

The passage of meconium can be a natural event indicating fetal maturity, but in some cases, it can also indicate increased vagal activity due to fetal hypoxia (oxygen deficiency) or umbilical cord compression. Amniotic fluid is sterile, but the passage of meconium into the amniotic fluid is critical due to the risk of MAS. It is also associated with adverse perinatal outcomes such as birth asphyxia, sepsis, neonatal depression, neurological sequelae, and neonatal death. Therefore, detecting the presence of meconium during delivery is crucial (10). Although electronic fetal monitoring can reflect fetal problems during the intrapartum period, there is interobserver variability in interpretation. Most studies in the literature focus on morbidity and mortality that develop in the neonatal period after meconium aspiration has occurred. Our study, unlike the literature, was designed to predict the likelihood of meconium in the fetus by utilizing maternal blood parameters in term pregnancies.

There are some changes in the hematologic system during pregnancy. Blood volume increases by 30-40%, and plasma and erythrocytes increase by 30%. While the half-life of platelets shortens, RDW (Red Cell Distribution Width) and MPV (Mean Platelet Volume) increase (10). The balance between the rising neutrophils as the first line of defense and the lymphocytes representing the regulatory and protective components of inflammation represents the inflammatory process. These ratios have been shown to be important in the prediction and monitoring of many diseases during pregnancy (5, 10, 20). In a study conducted by Gomez et al., amniotic fluid samples were collected from 15 women with suspected intra-amniotic infection and/or inflammation. They found that the neutrophils in the amniotic fluid were predominantly of fetal or maternal origin, or a mixture of both. These findings suggest that both the fetus and the mother participate in host defense mechanisms against intra-amniotic infection, indicating that both fetal and maternal neutrophils can invade the amniotic cavity (22).

In our study, NLR and MLR were found to be significantly higher in the MSAF group, while PLR was lower. We found that when we took an NLR cutoff of 3.58, it was 87.5% sensitive in predicting MSAF. It is known that the presence of MSAF can be secondary to fetal hypoxia in the intrauterine period (1, 2, 6). Similarly, Aksakal et al. demonstrated that NLR and PLR could be used to predict fetal distress during labor (10). In this study, the results of 124 pregnant women who developed fetal distress were compared with those of 126 healthy pregnant women. While APGAR scores were significantly lower in those with fetal distress, no difference was observed in terms of the need for NICU. However, the presence of intrauterine meconium in the infants was not questioned in this study (10). Karakoç et al. showed that NLR and PLR values were significantly higher in the group with APGAR <7 compared to the group with APGAR ≥7 in neonates. Studies on complete blood parameters during pregnancy in the literature have mostly been conducted on diseases such as preeclampsia and gestational diabetes (18). These studies have shown that elevated NLR and MLR provide a prediction for preeclampsia and gestational diabetes (5). Çakır et al. demonstrated the increase in MLR in septic newborns (19). However, different results exist in the literature for PLR. While an increase in PLR has been shown in preeclampsia and fetal distress, it has been observed to be unaffected in cases of premature rupture of membranes with normal amniotic volume (5, 10, 23). Taşkın et al. reported no difference in MPV, NLR, PLR, and MLR between groups with and without early sepsis in a study involving 272 babies with MSAF (24).

The use of SIRI and AISI parameters to determine inflammatory processes has been increasing in recent years. In our study, we found that SIRI and AISI parameters were significantly higher in the MSAF group. When we set the cutoff value for SIRI at 3.55, we found that it was 89.2% sensitive in identifying MSAF. Additionally, we found that birth weight was weakly negatively correlated with SIRI, AISI, NLR, and MLR. Previous studies have shown elevated SIRI in intrahepatic cholestasis of pregnancy and elevated SIRI and AISI in gestational diabetes (18, 20). Çakır et al. demonstrated that SIRI was significantly higher in the septic group in their study evaluating septic infants (19). Consonni et al. investigated MSAF and clear amniotic placentas in the African American population and evaluated the frequency, stage, and severity of the maternal inflammatory response (MIR) and fetal inflammatory response (FIR). They found that MIR and FIR were significantly higher in the MSAF group. MIR and FIR were present together in 35.8% of the MSAF group, whereas they were present together in 25.2% of the clear amniotic fluid group. In conclusion, they showed that MSAF is associated with an increase in both maternal and fetal inflammation. This histopathological study supports the increase in maternal inflammatory markers found in our study (21).

Procalcitonin, a precursor substance for calcitonin, acts as a prohormone involved in inflammatory processes. Serum levels of PCT rise faster than C-reactive protein (CRP) and can be detected in the blood within 2-4 hours, with a half-life of 24 hours. Normally, PCT levels are lower than 0.1 μg/L. During pregnancy, physiological levels of PCT increase from the first to the third trimester, reaching a cutoff value of 0.25 μg/L in the third trimester and at delivery. It has been reported that antibiotic treatment should be considered if values exceed this threshold (25, 26). New evidence in pregnancy suggests that PCT can complement clinical findings in the diagnosis of sepsis more effectively and promptly (27). In our study, the PCT serum level was found to be 0.20 (0.17-0.26) μg/L in the MSAF group and 0.18 (0.16-0.22) μg/L in the control group, with the difference being statistically significant. Although the values we detected were below the cutoff for a systemic inflammatory response, ROC analysis showed that with a PCT (ng/ml) threshold value of 0.23, sensitivity was 42.5% and specificity was 76.7% for predicting MSAF. Additionally, the 5-minute APGAR score was weakly negatively correlated with procalcitonin levels. Similarly, Taşkın et al. found high PCT levels in neonates with MSAF who were suspected of early sepsis (24). We believe that procalcitonin can be used in predicting maternal and fetal inflammation in this context.

In our study, a higher cesarean section rate was observed in patients with meconium-stained births among term pregnancies. High cesarean section rates in the presence of meconium have been reported in previous studies (1, 3, 4, 28, 29). Mundhra reported a cesarean section rate of 49.09% in a study including 165 MSAF and 190 term clear amniotic pregnancies. In these patients, the presence of a 1st minute APGAR score <7, fetal asphyxia, and the need for NICU were significantly higher (2, 30). High cesarean section rates in studies reflect not only abnormal fetal heart rates but also the concerns of the attending midwife or doctor about potential fetal morbidity and mortality. In contrast, Levin reported a cesarean section rate of 11.3%, and Wong SF reported 8.8%. Wong attributed these low rates to the inclusion of scalp pH sampling methods in their studies (29). In our study, consistent with the literature, MSAF was associated with increasing gestational age (1, 29). Mundhra and Rathoria observed that half of the meconium-stained patients were over 40 weeks and attributed this to the high frequency of unsupervised pregnancies and late hospital admissions (6, 30). However, in our region, the patients generally consisted of those who attended regular monthly check-ups, and there were no post-term patients.

In our study, 35.8% of term infants in the MSAF group required NICU, compared to 16.5% in the control group. Additionally, 16.7% of the MSAF group and 7.8% of the control group required intubation, and both rates were statistically significant. Similarly, Rathoria reported an NICU rate of 25.45%. This study showed that, when evaluating those with and without fetal distress in the MSAF group, the group with fetal distress had significantly higher rates of a low 1st minute APGAR score (≤5), emergency cesarean section, and NICU admission (4). In contrast, Levin reported a NICU need of 1.6% and a mechanical ventilation need of 0.5% in a study evaluating 11,329 births that included MSAF (31). The different results in the literature may be due to differences in sample sizes and whether the study groups included preterm and/or term patients.

MSAF is seen in one out of every seven babies, and MAS is observed in only 5% of these babies (6). Although studies have shown an increase in inflammatory markers in amniotic fluid and fetal serum following MAS exposure, to our knowledge, no studies have yet investigated maternal blood parameters in predicting MSAF. Asphyxia (antenatal and/or intranatal) has played a role in the pathogenesis of MFAS, as it has been shown that fetal breathing can lead to MSAF aspiration. In Lee's study, only 2 out of 12 neonates with MAS had an APGAR score <7 at 5 minutes after birth, and only 2 out of 12 cases had an umbilical artery pH <7.1. This suggested that the alternative mechanism of the disease might be inflammation (6). This study observed an increased risk of MAS in term infants with MSAF when funisitis was detected, whereas the MAS risk did not increase in MSAF infants without funisitis (6). Evaluating fetal systemic inflammation may target neonates born to MSAF mothers who show a suspicious clinical course for MAS. The rationale for this approach is that only 7.3% (6/82) of neonates without funisitis (one of the indicators of FIRS) developed MAS, whereas this risk increased fourfold (5/16) in neonates with funisitis. In light of these results, it can be inferred that biomarkers of fetal and maternal systemic inflammation can be used to predict MAS in

neonates exposed to MSAF.

The strength of our study is the ability to predict the presence of meconium in term pregnancies using non-invasive, simple inflammatory markers. The main limitation of our study is its retrospective design and the inclusion of a low-risk population. Different results may be obtained by evaluating the impact of the presence of meconium with additional risk factors on perinatal birth outcomes in studies including high-risk and preterm pregnancies. Furthermore, future studies that jointly evaluate samples taken from the amniotic fluid and fetal cord to examine fetal impact will provide guidance in elucidating the data we have obtained.

NLR, MLR, SIRI, AISI, and Procalcitonin have high sensitivity in predicting the presence of meconium-stained amniotic fluid in term pregnancies. The values of these parameters in maternal blood will guide clinicians in predicting the risk of fetal well-being deterioration and MAS.

Conflict of interest

The authors declared no conflict of interest.

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Authors' contributions

Concept: S.S.Ü., Y.C.Ü., Design: S.S.Ü., Y.C.Ü., Data Collection or Processing: Ö.D.Ü., Y.C.Ü., S.E., S.M.A., C.S.Ç., Z.Y., C.M.S., S.Ç., Analysis or Interpretation: S.S.Ü., S.Ç., Literature Search: Ö.D.Ü., C.S.Ç., Z.Y., C.M.S., S.Ç., Writing: Y.C.Ü., S.E., S.M.A.

Ethical Statement

Approval was obtained from Samsun University Non-invasive Clinical Research Ethics Committee, the study started. The ethics committee decision date is 22/05/2024 and the number of ethical committee decisions is 2024/10/2.

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