Research Square

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Diagnostic Performance of the Naples Prognostic Score in Missed Abortion During Early Pregnancy

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Abstract

Background

Missed abortion is a common obstetric complication affecting 10–20% of pregnancies. The Naples Prognostic Score (NPS), which combines inflammatory markers (neutrophil-to-lymphocyte ratio [NLR], lymphocyte-to-monocyte ratio [LMR]) and nutritional parameters (albumin, total cholesterol), has not been previously evaluated in the context of early pregnancy loss. This study aimed to evaluate the predictive value of NPS for missed abortion.

Methods

This retrospective comparative study included 228 pregnant women (119 with missed abortion, 109 healthy controls) between 6 and 12 gestational weeks at Karamanoğlu Mehmetbey University Training and Research Hospital (June 2023–June 2025). Demographic and laboratory data were collected from medical records. ROC curve analysis and multivariate logistic regression were performed to assess the predictive performance of NPS.

Results

Patients with missed abortion had significantly lower LMR, albumin, and total cholesterol, and a higher NPS (median 2 vs 1, $p < 0.001$). NPS showed nigh-excellent discriminatory power to identify patients with missed abortion (AUC = 0.883, 95% CI: 0.839–0.927, $p < 0.001$). At an optimal cut-off value of > 1.5, the sensitivity was 95.80% and the specificity was 71.56%.

Conclusion

NPS is a novel, easily calculable, and non-invasive marker with high sensitivity for identifying missed abortion. These findings suggest that NPS may serve as a useful complementary marker in the early evaluation of pregnancies at risk, although further prospective validation is needed.

Introduction

Missed abortion (MA), which is clinically defined as the retention of a nonviable intrauterine pregnancy after fetal death, is a type of spontaneous pregnancy loss. It can occur in up to 15% of pregnancies and poses a substantial risk to maternal health [1]. Similar to recurrent pregnancy loss, the exact cause and factors contributing to MA remain unknown [1, 2].

MA has been associated with defective placental implantation and oxidative stress. An imbalance between metabolic demands and antioxidant defenses during early development may result in

trophoblastic apoptosis and necrosis, ultimately causing pregnancy loss [3, 4]. Recent meta-analyses have indicated that elevated neutrophil-to-lymphocyte ratio (NLR) and altered lymphocyte counts serve as accessible indicators of this systemic inflammatory response in early pregnancy loss [2, 5]. Furthermore, maternal nutritional and metabolic status is critical for sustaining pregnancy. Serum albumin functions as a vital antioxidant and anti-inflammatory agent, while cholesterol is essential for steroid hormone synthesis and can undergo disruptive oxidative changes due to inflammation [6, 7]. Alterations in metabolic parameters, including hypoalbuminemia and dyslipidemia, have already been linked to unfavorable obstetric outcomes such as preeclampsia [8–10]. However, the majority of available literature assesses these inflammatory and nutritional parameters independently or presents inconsistent findings attributable to individual variability [1, 11].

Composite scoring systems can allow more comprehensive assessment of properties that are associated with multiple factors. The Naples Prognostic Score (NPS), a composite scoring system introduced by Galizia and colleagues, was designed to assess systemic inflammatory and nutritional status using NLR, lymphocyte-to-monocyte ratio (LMR), serum albumin, and total cholesterol [12]. Initially created for colorectal cancer, the NPS has shown utility as a reliable predictor of adverse outcomes in other malignancies, cardiovascular diseases, and pulmonary disorders [12–15]. The integrated nature of the NPS allows for a more refined assessment of immune-nutritional balance, often providing more accurate predictions than its individual parts [15, 16]. Although the NPS has been successful in other medical areas, its use in obstetrics is still limited [10].

Owing to the impact of inflammation and nutrition on MA, NPS may hold promise as a practical tool for early risk stratification. Therefore, we aimed to assess the predictive value of NPS in distinguishing patients with MA from women with healthy early-term pregnancies and to evaluate the relationship between NPS and early pregnancy loss.

Methods

Study Design and Setting

This case-control study was conducted at the Karamanoğlu Mehmetbey University Training and Research Hospital, Department of Obstetrics and Gynecology, between June 2023 and June 2025. Patient data were retrospectively collected from the hospital's electronic medical record system and laboratory database. The study protocol was approved by the Institutional Clinical Research Ethics Committee of Karamanoglu Mehmetbey University (Approval date: 24.12.2025, decision no: 28) and carried out in accordance with the ethical principles of the Declaration of Helsinki. As this was a retrospective study based on existing medical records, informed consent to participate was not obtained.

Participants

The study population consisted of two groups: (1) The MA group: women diagnosed with MA between the 6th and 12th gestational weeks who underwent dilatation and curettage at our clinic; and (2) The control group: women at the same gestational age (6th–12th weeks) who presented for routine antenatal care, had documented fetal cardiac activity with viable pregnancies, and had no identified complications. The control group was collected consecutively during the study period. To minimize selection bias, all eligible cases meeting the inclusion criteria during the study period were included, and the control group was collected consecutively. Information bias was reduced by using standardized laboratory measurements from the same laboratory and blinded data extraction. To address potential confounders, patients with chronic diseases, infections, or other conditions affecting inflammatory markers were excluded.

Inclusion criteria: Age between 18 and 40 years, spontaneous singleton pregnancy, and complete medical records including complete blood count (neutrophil, lymphocyte, monocyte counts) and biochemical (albumin, total cholesterol) laboratory results.

Exclusion criteria: Multiple pregnancies, known chronic systemic diseases (diabetes mellitus, hypertension, autoimmune diseases, renal/hepatic failure), active infection, known uterine anomalies, smoking or alcohol consumption, and pregnancies conceived through assisted reproductive techniques.

The diagnosis of MA was established via ultrasonography according to standard criteria: the absence of fetal cardiac activity in an embryo with a crown-rump length (CRL) of ≥ 7 mm or the absence of an embryo in a gestational sac with a mean sac diameter of ≥ 25 mm. Gestational age was determined based on ultrasonography data. A total of 228 pregnant women (119 in the MA group and 109 healthy controls) who met the study criteria were included in the analysis. During the data collection process, data extractors were blinded to the group assignments.

Variables and Measurements

Demographic data, including age, gravidity, parity, history of previous miscarriage, body mass index (BMI), and obstetric history (living children, intrauterine fetal death, ectopic pregnancy, surgical history), were recorded. Laboratory parameters, including complete blood count (neutrophil, lymphocyte, monocyte counts) and biochemical tests (serum albumin, total cholesterol), were measured from venous blood samples collected using standard venipuncture techniques after overnight fasting. Samples were analyzed in our central laboratory according to standard protocols using automated hematology and biochemistry analyzers.

The NPS was calculated for each patient based on the original definition by Galizia et al. (2017) using the following criteria: (1) NLR > 2.96: 1 point, (2) LMR < 4.44: 1 point, (3) Albumin < 4.0 g/L: 1 point, (4) Total cholesterol < 180 mg/dL: 1 point. The total score ranged from 0 to 4, with higher scores indicating poorer inflammatory and nutritional status.

Sample Size

The sample size calculation was performed using G*Power 3.1.9.7 statistical software. Based on literature data regarding NLR values in early pregnancy loss, a moderate effect size (Cohen's d = 0.5) was predicted between the MA and control groups. With an alpha (α) level of 0.05 and a power (1-β) of 0.80, the minimum required sample size for an independent samples t-test was calculated as approximately 64 participants per group. To account for potential data loss and incomplete records inherent in the retrospective design, all eligible cases from the 2-year study period were included, resulting in a final sample of 228 women (119 in the MA group, 109 in the control group), which provides sufficient statistical power.

Statistical Analysis

Statistical analyses were performed on IBM SPSS Statistics for Windows, Version 27 (IBM Corp., Armonk, NY, USA). The statistical significance threshold was accepted as $p < 0.05$. Normality assumption was evaluated using the histograms and Q-Q plots. Descriptive statistics were presented using mean ± standard deviation for normally distributed continuous variables, median (25th percentile – 75th percentile) for non-normally distributed continuous variables, while frequency (percentage) were described for categorical variables. Continuous variables were analyzed using the Student's t test or Mann Whitney U test depending on normality. Categorical variables were analyzed using chi-square tests or the Fisher's exact test. Performance of NPS to predict MA was evaluated using the receiver operating characteristic (ROC) curve analysis. The area under the curve (AUC), sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV) were calculated. Optimal cut-off points were determined using Youden's index. Missing data were checked systematically across all variables, and no missing values were detected in the final dataset.

Results

A total of 228 pregnant women were included in the study, and MA was identified in 119 (52.2%). No significant differences were observed between the two groups regarding age (28.27 ± 3.05 vs. 27.35 ± 3.90 years, $p = 0.051$), BMI (25.02 ± 1.73 vs. 25.08 ± 1.74 kg/m², $p = 0.775$), or gestational week (8.71 ± 1.28 vs. 8.78 ± 1.23, $p = 0.694$).

When obstetric characteristics were examined, gravidity [median 2 (2–3) vs. 2 (1–3), $p = 0.001$] and the number of previous miscarriages [median 0 (0–1) vs. 0 (0–0), $p < 0.001$] were significantly higher in the MA group. The groups were similar in terms of parity, number of living children, history of intrauterine fetal death, history of ectopic pregnancy, or surgical history ($p > 0.05$ for all).

Among laboratory parameters, the levels of LMR [4.80 (4.00–6.00) vs. 5.33 (4.25–7.00), $p = 0.027$], albumin (39.31 ± 3.03 vs. 42.59 ± 2.71 g/L, $p < 0.001$), and total cholesterol (168.08 ± 18.24 vs. 187.58 ± 20.68 mg/dL, $p < 0.001$) were significantly lower in the MA group, while the NPS [median 2 (2–3) vs. 1

(1–2), $p < 0.001$] was significantly higher. No significant differences were observed between the groups regarding neutrophil, lymphocyte, and monocyte counts, or the NLR ($p > 0.05$ for all) (Table 1).

Table 1
Summary of variables with regard to missed abortion

	Missed abortion			
	Total (n = 228)	**No (n = 109)**	**Yes (n = 119)**	**p**
Age	27.83 ± 3.51	27.35 ± 3.90	28.27 ± 3.05	0.051†
Body mass index, kg/m^2	25.05 ± 1.73	25.08 ± 1.74	25.02 ± 1.73	0.775†
Gestational week	8.75 ± 1.25	8.78 ± 1.23	8.71 ± 1.28	0.694†
Comorbidity	0 (0.00%)	0 (0.00%)	0 (0.00%)	N/A
Gravidity	2 (1–3)	2 (1–3)	2 (2–3)	**0.001‡**
Parity	1 (0–2)	1 (0–1)	1 (0–2)	0.120‡
Prior abortions	0 (0–0)	0 (0–0)	0 (0–1)	**< 0.001‡**
Living children	1 (0–2)	1 (0–1)	1 (0–2)	0.135‡
Intrauterine exitus history	0 (0.00%)	0 (0.00%)	0 (0.00%)	N/A
Ectopic pregnancy history	1 (0.44%)	0 (0.00%)	1 (0.84%)	1.000#
Operation history	42 (18.42%)	20 (18.35%)	22 (18.49%)	1.000§
Neutrophil, x10^3	5.79 ± 1.75	5.96 ± 1.64	5.63 ± 1.84	0.152†
Lymphocyte, x10^3	2.06 ± 0.65	2.08 ± 0.64	2.05 ± 0.67	0.710†
Monocyte, x10^3	0.41 ± 0.15	0.39 ± 0.16	0.42 ± 0.14	0.166†
NLR	2.76 (2.16–3.55)	2.88 (2.29–3.60)	2.67 (2.10–3.38)	0.128‡
LMR	5.00 (4.00–6.50)	5.33 (4.25–7.00)	4.80 (4.00–6.00)	**0.027‡**
Albumin	40.88 ± 3.31	42.59 ± 2.71	39.31 ± 3.03	**< 0.001†**
Total cholesterol	177.40 ± 21.72	187.58 ± 20.68	168.08 ± 18.24	**< 0.001†**
NPS	2 (1–2)	1 (1–2)	2 (2–3)	**< 0.001‡**

NLR: Neutrophil to lymphocyte ratio, LMR: Lymphocyte to monocyte ratio, NPS: Naples prognostic score.

	Missed abortion			
	Total (n = 228)	**No (n = 109)**	**Yes (n = 119)**	**p**
Descriptive statistics are presented using mean ± standard deviation for normally distributed continuous variables, median (25th percentile – 75th percentile) for non-normally distributed continuous variables and frequency (percentage) for categorical variables.				
† Student's t test, ‡ Mann Whitney U test, § Chi-square test, # Fisher's exact test, N/A Non-applicable. Statistically significant p values are shown in bold.				
NLR: Neutrophil to lymphocyte ratio, LMR: Lymphocyte to monocyte ratio, NPS: Naples prognostic score.				

The diagnostic performance of the NPS in predicting MA was evaluated using ROC curve analysis. The AUC for the NPS was calculated as 0.883 (95% CI: 0.839–0.927, p < 0.001), demonstrating nigh-excellent discriminatory power (Fig. 1). Based on the optimal cut-off value (> 1.5 points), the NPS yielded an overall diagnostic accuracy of 84.21%, with other metrics showing excellent sensitivity (95.80%) and negative predictive value (93.98%) but relatively lower specificity (71.56%) and positive predictive value (78.62%) (Table 2).

Table 2
Performance of NPS to predict missed abortion, ROC curve analysis

Cut-off	**> 1.5**
Sensitivity	95.80%
Specificity	71.56%
Accuracy	84.21%
PPV	78.62%
NPV	93.98%
AUC (95% CI)	0.883 (0.839–0.927)
p	**< 0.001**
NPS: Naples prognostic score, ROC: Receiver operating characteristic, PPV: Positive predictive value, NPV: Negative predictive value, AUC: Area under ROC curve, CI: Confidence interval	

Table 3
Significant factors independently associated with missed abortion, multivariable logistic regression analysis

Prior abortions	β coefficient	Standard error	p	Exp(β)	95% CI for Exp(β)	
	0.805	**0.374**	**0.031**	**2.237**	**1.074**	**4.658**
Albumin	-0.289	0.069	**< 0.001**	0.749	0.654	0.857
Total cholesterol	-0.039	0.012	**0.001**	0.961	0.939	0.984
NPS	3.589	0.584	**< 0.001**	36.197	11.530	113.636
Constant	16.202	3.747	< 0.001			

Nagelkerke R^2 = 0.710. CI: Confidence interval, NPS: Naples prognostic score. Statistically significant p values are shown in bold.

Discussion

This retrospective case-control study demonstrated that the NPS possesses high predictive value in the detection of MA, particularly with respect to sensitivity and negative predictive value. NPS was significantly higher in the MA group compared to the control group and NPS values showed excellent discriminatory power with a bias towards almost-perfect levels of sensitivity and negative predictive value at a cut-off value of > 1.5. It is evident that these promising results necessitate validation in different populations and through prospective designs. The fact that NPS is easily calculable from routine laboratory parameters, is non-invasive, and has excellent negative predictive value are further advantages that make it a unique score that can be utilized as a screening test for MA in clinical practice.

The relationship between systemic inflammation and maternal nutritional status is crucial for sustaining a healthy pregnancy. Although inflammation is essential for implantation, an overactive pro-inflammatory response can compromise maternal-fetal tolerance, potentially resulting in negative consequences [1]. Prior research has examined individual markers such as the platelet-to-albumin ratio (PAR), NLR, PLR, LMR, albumin, and cholesterol [1, 2, 11, 17–19]; however, these single parameters can diverge greatly due to other patient- and disease-related factors. Our findings indicated that the NPS exhibited strong discriminatory ability (AUC = 0.883, 95% CI: 0.839–0.927, p < 0.001). This aligns with recent findings by Katırcı [10], who reported the utility of NPS in predicting preeclampsia, another placenta-related disorder. Taken together, these findings support the view that a composite score integrating inflammatory and nutritional parameters may offer clinically relevant information beyond isolated laboratory values; however, this interpretation should be confirmed in future studies specifically designed to compare composite and individual markers [12–16].

Serum albumin, a negative acute-phase reactant and a marker of nutritional status, plays a pivotal role in maintaining endothelial integrity and exerting antioxidant effects essential for placental development [6, 9]. In our study, albumin levels were significantly lower in the MA group compared to controls (39.31 vs. 42.59 g/L, $p < 0.001$). This finding is similar to recent obstetric literature linking low albumin levels to adverse outcomes driven by inflammation and endothelial dysfunction, such as preeclampsia and postpartum tissue damage [6, 10, 20, 21]. Similarly, Çakır et al. [22] demonstrated that lower albumin levels in the first trimester are significant indicators for the development of gestational diabetes mellitus, another condition associated with metabolic and inflammatory dysregulation. Serum albumin naturally decreases during pregnancy due to physiological hemodilution and plasma volume expansion [23]. However, the pronounced reduction observed in our MA group, which fell significantly below the levels of the gestational age-matched healthy controls, suggests a pathological depletion. This supports the clinical inference that maternal albumin levels are a critical parameter in the risk assessment for MA, and early detection of hypoalbuminemia may offer a window for identifying pregnancies at risk of failure due to a compromised maternal-fetal environment.

Cholesterol serves as the obligatory precursor for the biosynthesis of steroid hormones, including progesterone, which is indispensable for the secretory transformation of the endometrium, implantation, and the maintenance of early pregnancy [24–26]. During the first trimester, the corpus luteum relies heavily on the uptake of circulating low-density lipoprotein (LDL) cholesterol to sustain the high-output steroidogenesis required to prevent pregnancy loss [27, 28]. In the present study, total cholesterol levels were found to be significantly lower in the MA group compared to the control group. These findings align with evidence suggesting that hypocholesterolemia may compromise reproductive outcomes by limiting the substrate availability necessary for placental and luteal function [29, 30]. Genetic studies involving Apolipoprotein E have similarly indicated that carriers of the E2 allele, who typically exhibit lower cholesterol levels, demonstrate reduced fertility [31, 32]. Conversely, substantial literature emphasizes that pregnancy is characterized by a physiological hyperlipidemia intended to support fetal growth [33], and recent studies have reported that elevated cholesterol levels in the first trimester may actually increase the risk of early pregnancy loss due to oxidative stress and endothelial dysfunction [34, 35]. This dichotomy suggests a complex, likely U-shaped relationship between maternal lipids and pregnancy outcomes, where both insufficiency and inflammatory excess are detrimental –potentially associated with cholesterol oxidation [36, 37]. Our data support the hypothesis that blunted maternal cholesterol levels in early gestation may lead to inadequate steroidogenesis and corpus luteum insufficiency. Therefore, maternal lipid profiles warrant consideration as a component of risk assessment for MA.

The LMR is a surrogate marker of the balance between adaptive immunity, represented by lymphocytes, and the innate immune response, driven by monocytes. A successful pregnancy necessitates a finely tuned state of maternal-fetal tolerance, where the maternal immune system adapts to protect the semi-allogeneic fetus while maintaining defense against pathogens [26, 38, 39]. A lower LMR typically indicates a shift towards a pro-inflammatory state characterized by monocyte activation and relative lymphopenia, a profile often implicated in various pregnancy complications including recurrent pregnancy loss and preeclampsia [2, 40]. In our univariate analysis, LMR was significantly lower in the

MA group compared to the control group, consistent with the inflammatory hypothesis of miscarriage. This aligns with findings by Feng et al. [41], who reported that higher LMR levels were associated with a decreased risk of pregnancy loss, suggesting a protective benefit of immune stability. Furthermore, the interpretation of such hematological indices is complicated by the substantial physiological changes in complete blood count parameters that occur throughout gestation, such as the trimester-specific fluctuations in white blood cell and platelet counts [42]. Consequently, our findings suggest that while the immune imbalance represented by LMR is biologically relevant, it gains prognostic value when utilized in a composite index like the NPS, which accounts for the complex interaction between nutritional status and inflammatory pathways.

A history of previous miscarriage is a well-established risk factor for subsequent pregnancy loss, often pointing to persistent underlying etiologies such as chromosomal anomalies, anatomical defects, or immunological dysregulation [1]. An increased number of previous pregnancy loss is associated with a higher risk of adverse pregnancy outcomes [43]. In our study, the number of previous miscarriages was significantly higher in the missed abortion group. This finding is consistent with the concept of cumulative risk in women with prior pregnancy loss.

There are several limitations to this study. First, due to the retrospective case-control design, a causal relationship cannot be established. Second, the study was conducted at a single center, and the findings may not be generalizable to different populations; therefore, validation is required before drawing generalizable conclusions. Third, the cut-off values used for NPS components (NLR, LMR, albumin, cholesterol) were derived from original oncological studies and did not account for the physiological changes specific to pregnancy. Further studies can potentially improve diagnostic performance by determining pregnancy-specific cut-off values. Fourth, potential confounding factors (e.g., diet, lifestyle, occult infections, unmeasured genetic factors) may not have been fully controlled despite strict inclusion / exclusion criteria and well-established background characteristics.

Conclusion

This study suggests that the Naples Prognostic Score is a novel, easily calculable, and non-invasive marker associated with missed abortion in early pregnancy. NPS demonstrated good discriminatory performance and high sensitivity, supporting its potential role as a complementary tool in early clinical assessment. However, it should not be interpreted as a standalone diagnostic criterion, and abnormal results should be considered together with clinical and ultrasonographic findings. Because missed abortion has a multifactorial pathogenesis, the principal value of NPS may lie in risk stratification and closer follow-up rather than direct treatment guidance. Prospective multicenter studies are needed to validate these findings and to establish pregnancy-specific cut-off values.

Abbreviations

AUC

area under the curve
BMI
body mass index
CI
confidence interval
CRL
crown-rump length
LDL
low-density lipoprotein
LMR
lymphocyte-to-monocyte ratio
MA
missed abortion
NLR
neutrophil-to-lymphocyte ratio
NPS
Naples Prognostic Score
NPV
negative predictive value
PAR
platelet-to-albumin ratio
PLR
platelet-to-lymphocyte ratio
PPV
positive predictive value
ROC
receiver operating characteristic

Declarations

Ethics approval and consent to participate

The study protocol was approved by the Institutional Clinical Research Ethics Committee of Karamanoglu Mehmetbey University (Approval date: 24.12.2025, decision no: 28) and carried out in accordance with the ethical principles of the Declaration of Helsinki. Due to retrospective design of study, it is not neccesary and not possible to take inormed consent from recruited patients.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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Author Contribution

M.F.O. and G.S. contributed to the conception. M.O., M.F.O. and G.S. contributed to the methodology. M.F.O. and G.S. contributed to the software and formal analysis. M.O., M.F.O. and G.S. contributed to the validation and resources. M.O. and G.S. performed the investigation and data curation. G.S. wrote the original draft. M.O., M.F.O. and G.S. reviewed and edited the manuscript. M.O. contributed to the visualization. M.F.O. supervised the study. G.S. and M.O. contributed to the project administration. All authors have read and agreed to the published version of the manuscript.

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Not applicable.

Data Availability

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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Figures

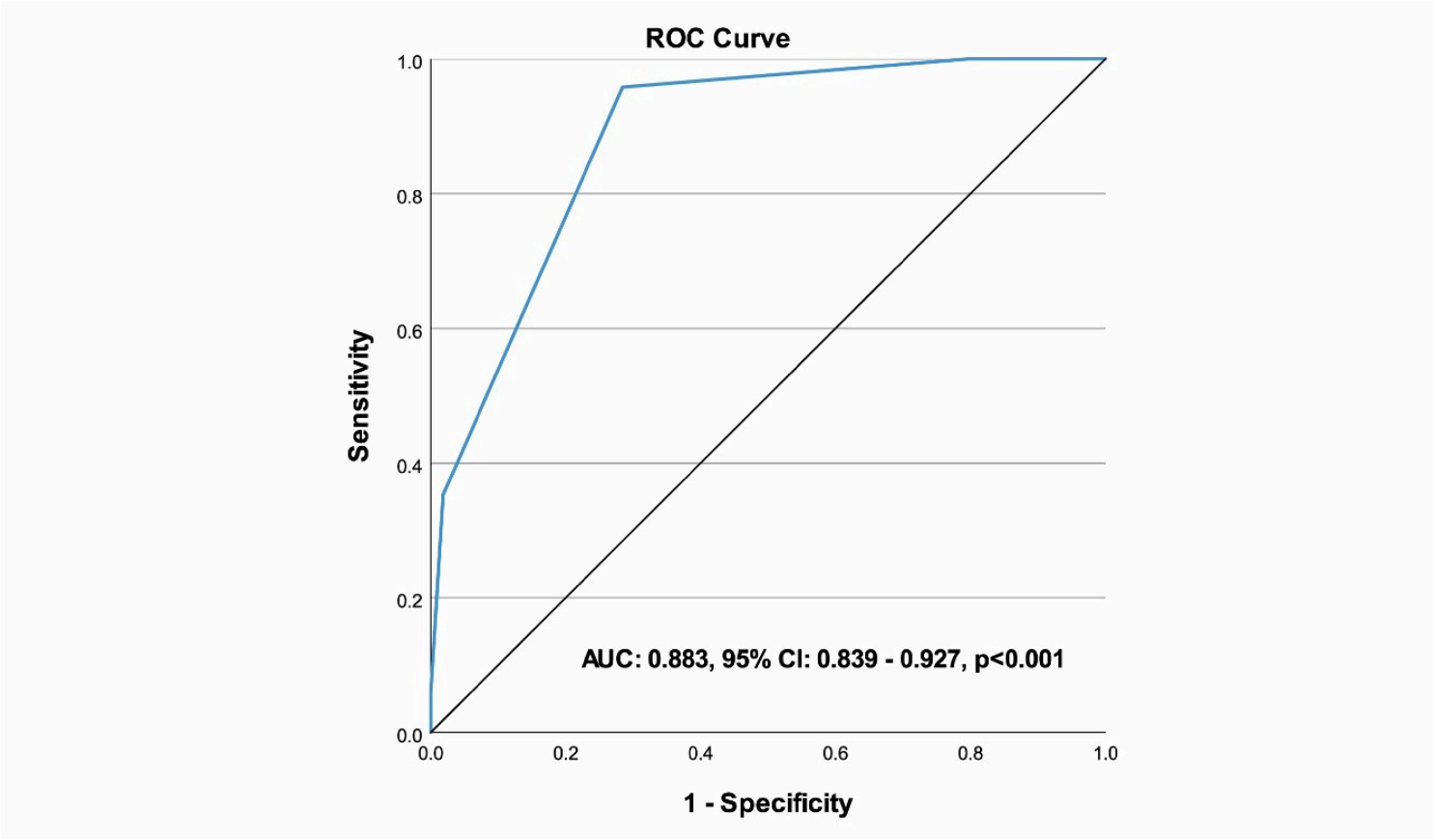


Figure 1

ROC curve of the Naples prognostic score to predict missed abortion.