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The diagnostic value of fetal thymus and spleen size as lymphoid organs in predicting delivery time; a cross-sectional study

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Abstract

Introduction: Preterm delivery is a leading cause of neonatal morbidity and mortality, and early prediction remains a clinical priority. Fetal lymphoid organs such as the thymus and spleen may reflect intrauterine stress and immune development, offering potential as noninvasive markers.
Objectives: This study evaluated their diagnostic value in predicting delivery time.
Patients and Method: This cross-sectional study was conducted at Imam Khomeini Hospital, Tehran, Iran, between August 2025 and February 2026. Using a simple randomized sampling method, 108 pregnant women with singleton gestations were enrolled at the time of delivery. Demographic and clinical data were collected through maternal interviews and review of medical records, while fetal thymus and spleen dimensions (length, width, and circumference) were measured immediately after birth by sonography performed by a gynecologist. Statistical analyses were conducted using SPSS version 27 to assess the association and diagnostic performance of fetal thymus and spleen size in predicting preterm delivery.
Results: Out of 108 pregnant women, 56 had term and 52 preterm deliveries. Fetal thymus size showed a significant inverse association with preterm delivery, with each 1-mm increase in thymus length (adjusted odds ratio [OR] = 0.75, 95% CI: 0.62–0.91), width (adjusted OR = 0.77, 95% CI: 0.63–0.93), and circumference (adjusted OR = 0.87, 95% CI: 0.77–0.97) reducing the odds of preterm birth. In contrast, larger spleen dimensions were directly associated with higher risk, as reflected by adjusted ORs of 1.16 (95% CI: 1.04–1.28) for length, 1.19 (95% CI: 1.02–1.39) for width, and 1.17 (95% CI: 1.06–1.26) for circumference.
Conclusion: The findings suggest that a smaller thymus and a larger spleen appear to be associated with an increased likelihood of preterm birth occurring. Therefore, we concluded that fetal thymus and spleen measurements may serve as useful predictors of preterm delivery.

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Introduction

The fetal immune system undergoes rapid and dynamic development throughout gestation (1,2), with the thymus and spleen serving as central lymphoid organs essential for T-cell maturation and hematopoietic regulation (3-5). The fetal thymus, in particular, is highly sensitive to intrauterine stress, and its size has been increasingly recognized as a potential biomarker of adverse pregnancy outcomes (6). Several studies have demonstrated that thymic dimensions are associated with preterm birth, maternal inflammation, and fetal growth disturbances (7,8). Story et al showed that fetuses who delivered before 32 weeks had significantly smaller thymus volumes on antenatal magnetic resonance imaging (MRI), suggesting early thymic involution as a marker of impending preterm delivery (8). Ultrasound-based assessments have similarly linked diminished thymus size with spontaneous preterm birth and maternal complications such as morbidity and neonatal sepsis (7). These findings underscore the potential diagnostic value of thymic measurements in predicting delivery timing.

The fetal spleen, although less extensively studied, also reflects systemic fetal conditions and may serve as an indicator of immune activation and infection (9). Advances in prenatal imaging have enabled

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Key point

The study demonstrated that fetal thymus and spleen size are significantly associated with delivery time. Thymus dimensions (length, width, and circumference) were inversely correlated with preterm delivery, indicating that reduced thymus size increases the risk of early birth. In contrast, larger spleen measurements showed a direct association with preterm delivery, suggesting that spleen enlargement may serve as a marker of intrauterine stress leading to earlier labor. Overall, the findings suggest that a combination of smaller thymus and larger spleen dimensions may serve as potential predictors of preterm delivery.

more accurate evaluation of splenic size and volume, with studies demonstrating associations between splenic enlargement or reduction and fetal hematologic or inflammatory states (10-12). Annan et al reported that assessment of fetal spleen volume correlates with fetal hematologic parameters, highlighting its potential utility as a complementary biomarker (12).

Despite growing interest in assessing fetal lymphoid organs, few studies have simultaneously examined thymus and spleen size in relation to delivery outcomes. Existing research often focuses on isolated organ metrics or specific high-risk populations, limiting broader clinical applicability. Moreover, normative reference ranges for these organs vary across studies, emphasizing the need for population-specific data and standardized measurement protocols. The present cross-sectional study aims to evaluate the diagnostic value of fetal thymus and spleen size in predicting delivery time, contributing to a more comprehensive understanding of fetal immune-organ biomarkers and their potential role in obstetric risk stratification.

Objectives

The objective of this study is to evaluate the diagnostic value of fetal thymus and spleen size, measured by ultrasonography, in predicting the timing of delivery. Specifically, the study aims to determine whether variations in the dimensions of these lymphoid organs are associated with earlier or later onset of labor, and to assess their potential utility as noninvasive biomarkers for identifying pregnancies at risk of preterm or delayed delivery.

Patients and Methods

Study design and participants

This cross-sectional study was conducted at Imam Khomeini Hospital, Tehran, Iran, between August 2025 and February 2026. A total of 108 pregnant women with singleton gestations were enrolled using a simple randomized sampling method to minimize selection bias and ensure representativeness of the study population. Demographic and clinical information was obtained through structured maternal interviews and review of medical records. All participants underwent a standardized sonographic assessment of fetal thymus and spleen size immediately after birth, performed by a gynecologist.

Inclusion and exclusion criteria

Pregnant women with singleton gestations who presented for delivery at the study hospital, with complete demographic and clinical data available through maternal interviews and medical records, successful sonographic assessment of fetal thymus and spleen size performed immediately after birth, and willingness to provide informed consent were included in the study. Exclusion criteria comprised incomplete clinical documentation, inability to obtain reliable sonographic measurements of the thymus or spleen, and refusal or withdrawal of maternal consent at any stage of data collection.

Data collection

Demographic and clinical information was obtained through structured maternal interviews and review of clinical records. Data collected included maternal age, body mass index (BMI), past medical history (PMH), gravidity, parity, and history of abortion, which were documented at the time of enrollment. Fetal thymus and spleen measurements were performed using standardized sonographic techniques. Immediately after fetal birth, a qualified gynecologist conducted ultrasonographic examinations to assess the dimensions of both organs. Measurements included length, width, and circumference (circle) for each organ, recorded in millimeters. All sonographic assessments were carried out using calibrated equipment under consistent conditions.

Outcome measurement

The primary outcome of this study was the occurrence of preterm delivery, defined as birth before 37 completed weeks of gestation. Outcome measurement involved assessing the correlation between fetal thymus and spleen size and delivery time. Specifically, sonographic measurements of thymus and spleen length, width, and circumference obtained immediately after birth were analyzed in relation to gestational age at delivery. Logistic regression models were used to estimate the strength and direction of associations, while receiver operating characteristic (ROC) curve analyses were performed to evaluate the diagnostic performance of these organ dimensions in predicting preterm delivery.

Statistical analysis

All statistical analyses were performed using SPSS version 27 (IBM Corp., Armonk, NY, USA). The distribution of continuous variables was assessed using the Shapiro–Wilk test to evaluate normality, and the Levene's test was applied to examine homogeneity of variances. As both parametric and corresponding nonparametric tests yielded concordant results regarding effect direction and comparable *P* values, parametric tests were selected for reporting due to their superior statistical power and

precision. Descriptive statistics were expressed as mean ± standard deviation (SD) for continuous variables and as frequencies with percentages for categorical variables. Between-group comparisons of categorical variables were conducted using the chi-square test, while continuous variables were compared using the independent samples t-test. Logistic regression analyses were performed to estimate the association between fetal thymus and spleen size and the occurrence of preterm delivery. Both univariate and multivariate models were constructed, with the latter adjusted for potential confounders including maternal age, BMI, PMH, and gravidity. Results were presented as odds ratios (ORs) with 95% confidence intervals (CIs). To evaluate the diagnostic performance of thymus and spleen measurements in predicting preterm delivery, ROC curve analyses were conducted. The area under the curve (AUC), optimal cut-off values, sensitivity, and specificity were calculated for each measurement parameter. A two-tailed *P* value < 0.05 was considered statistically significant.

Results

In this study, 108 pregnant women were enrolled, with a mean age of 29.94 ± 5.25 years and a mean BMI of 28.14 ± 4.78 kg/m². The majority had no PMH. Among them, 56 experienced term delivery and 52 had preterm delivery. The mean gravidity was 2.24 ± 1.32, while the average parity and abortion rates were each less than one (Table 1).

The analysis showed that the frequency distribution of demographic variables, including maternal age, BMI, PMH, gravidity, parity, and abortion, did not differ significantly between women with term and those with preterm deliveries. In contrast, all measured dimensions of the spleen and thymus (length, width, and circumference) were significantly different between the two groups (Table 2).

The analysis demonstrated a direct and statistically significant association between fetal spleen size and preterm delivery, whereas the relationship between thymus size and preterm birth was inverse. In the univariate logistic regression, each 1-mm increase in thymus measurements (circumference, length, and width) was associated with an approximately 11% to 20% reduction in the risk of preterm delivery. After adjusting for potential confounders, including maternal age, BMI, PMH, and gravidity, the strength of this inverse association increased and remained statistically significant. For the spleen, the association was direct; in the univariate model, each 1-mm increase in spleen length, circumference, and width was associated with a 14%, 15%, and 20% increase in the risk of preterm delivery, respectively. These associations also remained statistically significant after adjustment for the same confounding variables (Table 3).

The ROC curve analysis demonstrated that spleen measurements (length, width, and circumference) had only modest diagnostic ability for predicting preterm delivery. Sensitivity values were moderate across all three dimensions, whereas specificity values were the lowest, indicating limited accuracy in correctly identifying term pregnancies. Despite these limitations, the overall

Table 1. Demographic characteristics and clinical data of participants

Demographic and clinical data	Frequency (%)
PMH	
No	85 (78.7)
Yes	23 (21.3)
Time of delivery	
Term	56 (51.9)
Preterm	52 (48.1)
Quantitative variables	**Mean ± SD**
Maternal age (y)	29.94 ± 5.25
Maternal BMI (kg/m²)	28.14 ± 4.78
Gravidity (N)	2.24 ± 1.32
Para (N)	0.84 ± 0.97
Abortion (N)	0.40 ± 0.77
Thymus (mm)	
Length	26.30 ± 2.47
Width	19.21 ± 2.22
Circumference	55.50 ± 3.86
Spleen (mm)	
Length	30.37 ± 4.59
Width	22.92 ± 3.16
Circumference	62.29 ± 5.98

PMH: Past medical history, BMI: Body mass index, SD: Standard deviation.

Table 2. The frequency distribution of demographic and clinical data of the participating women according to the time of delivery

Demographic and clinical data	Time of delivery		*P* value
	Term (n = 56)	Preterm (n = 52)	
PMH			
No, N (%)	45 (80.4)	40 (76.9)	0.663*
Yes, N (%)	11 (19.6)	12 (23.1)	
Quantitative variables	**Mean ± SD**	**Mean ± SD**	***P* value**
Maternal age (y)	30.84 ± 5.75	28.96 ± 4.51	0.061**
Maternal BMI (kg/m²)	27.45 ± 4.78	28.88 ± 4.73	0.122**
Gravidity (N)	2.32 ± 1.50	2.15 ± 1.10	0.509**
Para (N)	0.88 ± 1.06	0.81 ± 0.88	0.723**
Abortion (N)	0.45 ± 0.82	0.35 ± 0.71	0.503**
Thymus (mm)			
Length	26.89 ± 2.20	25.65 ± 2.60	0.009**
Width	19.72 ± 2.30	18.67 ± 2.01	0.014**
Circumference	26.27 ± 4.02	54.68 ± 3.53	0.031**
Spleen (mm)			
Length	29.11 ± 5.31	31.72 ± 3.17	0.002**
Width	22.12 ± 2.52	23.79 ± 3.56	0.006**
Circumference	60.23 ± 5.80	64.50 ± 5.40	<0.001**

PMH: Past medical history, BMI: Body mass index, SD: Standard deviation, *Chi-square, **Independent T-test.

Table 3. The association of fetal thymus and spleen size with delivery time using logistic regression

Organ size		Occurrence of preterm delivery					
		Unadjusted			Adjusted		
		OR	95% CI	*P* value	OR	95% CI	*P* value
Thymus (mm)	Length	0.81	0.67 – 0.95	0.011	0.75	0.62 – 0.91	0.003
	Width	0.80	0.66 – 0.96	0.016	0.77	0.63 – 0.93	0.009
	Circumference	0.89	0.80 – 0.99	0.035	0.87	0.77 – 0.97	0.016
Spleen (mm)	Length	1.14	1.04 – 1.26	0.005	1.16	1.04 – 1.28	0.005
	Width	1.20	1.04 – 1.38	0.009	1.19	1.02 – 1.39	0.020
	Circumference	1.15	1.06 – 1.23	<0.001	1.17	1.06 – 1.26	<0.001

OR: Odds ratio, CI: Confidence interval.

Table 4. Diagnostic value of spleen size in preterm delivery diagnosis

Spleen size	Occurrence of preterm delivery					
	AUC (0-1)	*P* value	95% CI	Cut point (mm)	Sensitivity (%)	Specificity (%)
Length	0.621	0.031	0.515 – 0.726	28.05	82	36
Width	0.629	0.021	0.523 – 0.734	19.95	88	24
Circumference	0.698	0.001	0.585 – 0.784	58.05	86	38

AUC: Area under the curve, CI: Confidence interval.

pattern suggests that spleen size provides some predictive value, although its discriminative performance remains suboptimal (Table 4 and Figure 1).

The analysis further revealed that the diagnostic performance of thymus size, across all measured dimensions, including length, width, and circumference, was poor, exhibiting the lowest sensitivity and specificity for predicting preterm delivery (Table 5 and Figure 2).

Discussion

The findings revealed a significant relationship between fetal lymphoid organ size and delivery outcomes. Reduced thymus measurements (length, width, and circumference) were strongly linked with a higher likelihood of preterm birth, underscoring the role of thymic underdevelopment as a risk indicator. In contrast, increased spleen dimensions showed a positive association with preterm delivery, suggesting that spleen enlargement may reflect intrauterine stress responses that contribute to earlier labor.

The findings of this study contribute to a growing body of evidence suggesting that fetal lymphoid organs may serve as indicators of intrauterine conditions that predispose to early delivery. The inverse association between thymus size and preterm birth observed in this study is consistent with reports that thymic shrinkage is a marker of fetal stress and may precede adverse perinatal outcomes (13). In line with our study, Story et al reported that fetuses who were delivered before 32 weeks had markedly reduced thymus volumes on antenatal MRI, indicating that early thymic shrinkage may signal an increased likelihood of very preterm birth (8). Borgelt et al examined first-trimester thymus size in relation to pregnancy outcomes and reported a positive association between early-gestation thymic measurements and the likelihood of preterm birth (14). Caissutti et al, in a systematic review and meta-analysis evaluating the clinical significance of fetal thymus size, concluded that a reduced thymic dimension

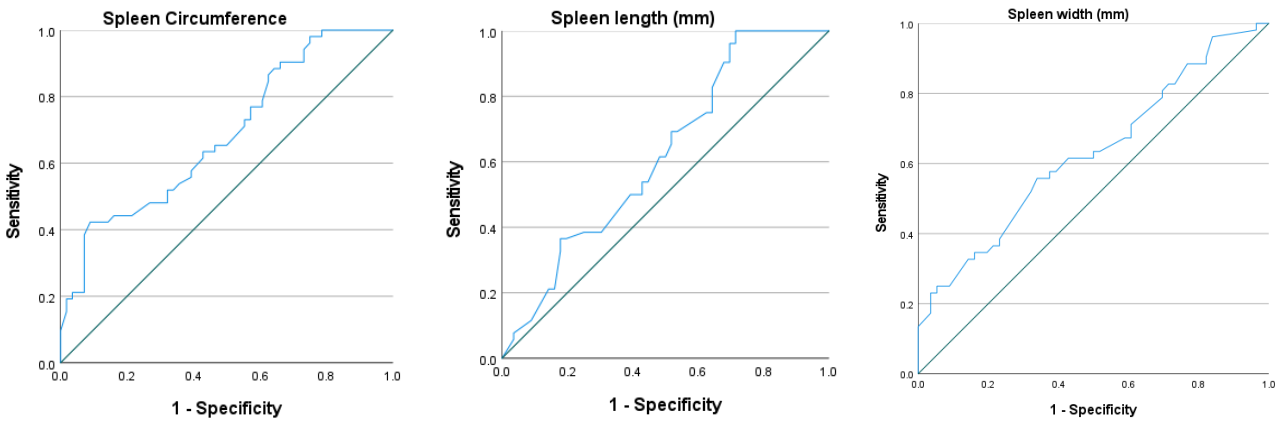

Figure 1. Spleen size as a predictor of preterm delivery using the ROC curve analysis

Table 5. Diagnostic value of thymus size in preterm delivery diagnosis

Thymus size	Occurrence of preterm delivery					
	AUC (0-1)	*P* value	95% CI	Cut point (mm)	Sensitivity (%)	Specificity (%)
Length	0.363	0.015	0.259 - 0.468	25.8	55	27
Width	0.370	0.020	0.265 - 0.475	17.95	71	27
Circumference	0.396	0.062	0.290 – 0.502	53.7	69	29

AUC: Area under the curve, CI: Confidence interval.

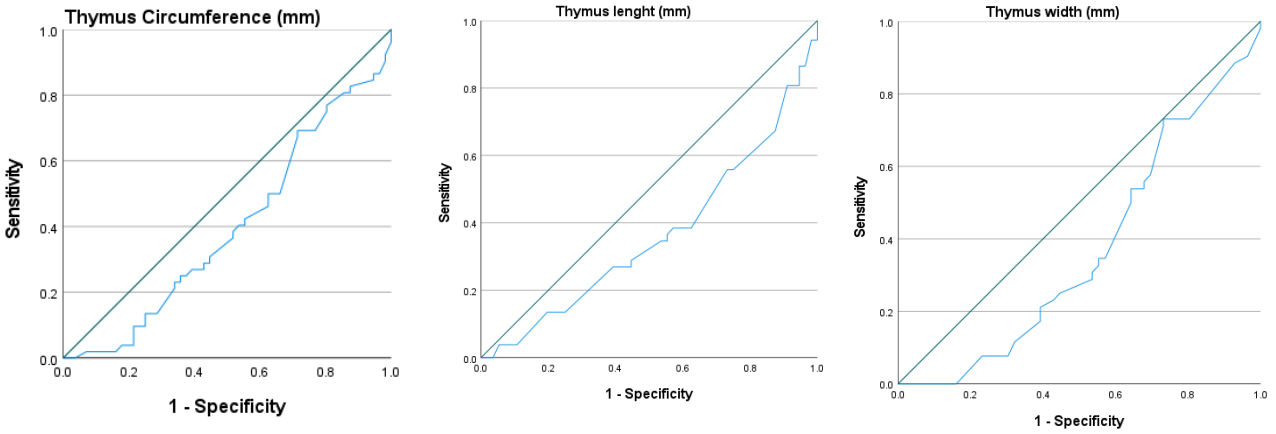

Figure 2. Thymus size as a predictor of preterm delivery using the ROC curve analysis

is associated with an increased risk of preterm birth, reinforcing the concept that thymic hypoplasia may serve as an early indicator of adverse obstetric outcomes (7). El-Haieg et al demonstrated that fetal thymic involution is closely associated with the systemic fetal inflammatory response in pregnancies complicated by preterm prelabour rupture of membranes, indicating that a reduced thymus size may serve as a reliable sonographic marker of fetal involvement in inflammatory processes (15). The study on fetal thymic involution demonstrated that a smaller thymus size is closely linked to preterm labor, and further showed that thymic shrinkage in these pregnancies is strongly associated with funisitis, the histopathologic hallmark of the fetal inflammatory response syndrome, highlighting the thymus as a sensitive marker of fetal inflammatory activation (16). On the other hand, in contrast to the associations observed in our study, Brandt et al reported that second-trimester sonographic measurements of the fetal thymus did not show any meaningful relationship with preterm birth or other adverse obstetric outcomes, concluding that routine thymus assessment during mid-pregnancy anatomy scans offers limited predictive value for such complications (6). Sciaky-Tamir et al, in a review study proposed that women presenting with preterm labor, whether with intact membranes or PPROM, should undergo detailed sonographic evaluation of the fetal thymus, as thymic assessment may serve as a useful surrogate marker of fetal involvement in intrauterine infection or inflammatory processes (17).

Similarly, the direct association between spleen enlargement and preterm delivery corresponds with studies showing that splenic size may increase in response to fetal inflammatory activation, a mechanism implicated in preterm labor. Hall et al reported that fetuses who subsequently delivered before 32 weeks' gestation exhibited a relatively larger spleen compared with gestational-age-matched controls, even after adjusting for overall fetal size, suggesting that splenic enlargement may reflect early biological processes associated with very preterm birth (11). Enlargement of the fetal adrenal glands has also been reported in association with preterm labor, suggesting that, similar to splenic enlargement, adrenal hypertrophy may reflect heightened intrauterine stress or activation of fetal adaptive responses that precede early delivery (18). While the diagnostic performance of spleen measurements in this study demonstrated modest sensitivity and low specificity, this pattern is comparable to other fetal biomarkers that show limited predictive accuracy when used in isolation. The relatively poor predictive performance of thymus size in ROC analysis also mirrors previous findings that single-parameter immune organ measurements may not provide strong standalone diagnostic value. Collectively, these parallels suggest that although fetal thymus and spleen size may reflect underlying biological processes associated with preterm birth, their clinical utility as independent predictors remains limited.

Overall, the results of this study indicate that smaller fetal thymus size and larger fetal spleen size are significantly associated with preterm delivery, supporting the hypothesis

that lymphoid organ morphology may reflect intrauterine stress responses contributing to early labor. These findings align with most prior research demonstrating that fetal immune organ alterations are linked to adverse pregnancy outcomes, although the modest diagnostic performance observed here underscores the need for caution in interpreting these measurements clinically. Future research should explore whether combining thymus and spleen measurements with established predictors, such as cervical length or biochemical markers, could enhance risk stratification for preterm birth. Additionally, longitudinal studies assessing organ size earlier in gestation may help clarify whether these changes precede or follow the pathophysiological processes leading to preterm labor. Despite the limitations of cross-sectional design and modest predictive accuracy, the present study adds valuable evidence to the understanding of fetal immune organ development in relation to delivery timing and highlights potential avenues for further investigation.

Conclusion

This study demonstrated that fetal thymus size is inversely associated with preterm delivery, with increases in thymus length, width, and circumference significantly reducing the odds of preterm birth, even after adjustment for maternal and obstetric confounders. In contrast, larger spleen dimensions were directly associated with higher odds of preterm delivery across all measured parameters. Although spleen and thymus size showed statistically significant associations, their diagnostic performance was modest. Overall, these findings suggest that reduced thymus size and increased spleen size may serve as complementary sonographic markers for identifying pregnancies at higher risk of preterm delivery.

Limitations of the study

This study has several limitations that should be acknowledged. First, the cross-sectional design restricts the ability to establish causal relationships between fetal thymus and spleen size and the timing of delivery, as measurements were obtained only once immediately after birth. Second, the relatively modest sample size from a single tertiary hospital may limit the generalizability of the findings to broader populations with different demographic or clinical characteristics. Third, although sonographic assessments were performed by a qualified gynecologist, potential measurement variability and operator dependence cannot be fully excluded. Fourth, the study did not account for certain maternal or fetal factors, such as subclinical infections, nutritional status, or placental pathology, which may influence lymphoid organ development and delivery outcomes.

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Authors' contribution

Conceptualization: Zahra Panahi and Negar Moradi.
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Project management: Negar Moradi.
Resources: All authors.
Supervision: All authors.
Validation: Fahimeh Ghotbizadeh.
Writing–original draft: All authors.
Writing–review and editing: All authors.

Conflicts of interest

The authors declare no conflict of interest.

Data availability statement

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

Declaration of generative artificial intelligence (AI) and AI-assisted technologies in the writing process

While preparing this work, the authors utilized AI (Grammarly and Copilot) to refine grammar points and language style. Subsequently, they thoroughly reviewed and edited the content as needed, assuming full responsibility for the publication.

Ethical issues

The research was conducted in accordance with the principles outlined in the Declaration of Helsinki. Informed written consent was taken from all participants or their legally authorized representatives. This study was conducted at Imam Khomeini Hospital and was derived from a research project (No: 90866), approved by the ethics committee of the School of Medicine, Tehran University of Medical Sciences, Tehran, Iran, under the ethical code (IR.TUMS.IKHC.REC.1404.238; https://ethics.research.ac.ir/form/h8g7ict141j2cw9b.pdf) registered on August 16, 2025. Additionally, the authors have ultimately identified ethical issues (including plagiarism, data fabrication, and duplicate publication).

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