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ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA*

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# A Prediction Model for Severe COVID-19 Infection and Intensive Care Unit Admission in Pregnant Women

## Gebe Kadınlarda Ağır COVİD-19 Enfeksiyonu ve Yoğun Bakım Ünitesine Kabul için Bir Tahmin Modeli

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**ABSTRACT** *Objective:* This study developed a prediction model that can predict the intensive care admission of coronavirus disease-2019 (COVID-19) pregnant and postpartum women.
*Materials and Methods:* The study was retrospective and single-center and was conducted with pregnant and postpartum patients 18 years of age and older who had been diagnosed with COVID-19 and were admitted to the obstetrics clinic between April 2020 and December 2021. The clinical and radiological featuresand laboratory values of the patients were recorded to develop a prediction model. Two different multivariate logistic regression models and the Naive Bayes classification algorithm were used for estimation. The results of the developed prediction models were summarized with the nomogram, and the prediction successes were evaluated with the receiver operating characteristic (ROC) curve.
*Results:* The study included 436 pregnant and postpartum patients. Twelve of 51 patients admitted to the intensive care unit died. The specificities of the three different classification models that we developed to determine the risk factors for intensive care admission were found to be over 95% and their sensitivities were 70.6%, 86.3%, and 87%, respectively. Additionally, the area under the ROC values were found to be 0.94, 0.941 and 0.978 for the models, respectively. High procalcitonin level, fever, dyspnea, and moderate-to-severe radiological involvement were determined as risk factors for admission to intensive care in pregnant and postpartum women patients.
*Conclusion:* It is thought that the risk models we have developed will be easy to implement and will help identify pregnant women who are at risk of severe COVID-19 disease in the early period and to take measures.
**Keywords:** COVID-19, mortality, pregnant women, intensive care units, SARS-CoV-2

**ÖZ** *Amaç:* Bu çalışmada koronavirüs hastalığı-2019 (COVİD-19) tanılı gebe ve postpartum kadınların yoğun bakım ihtiyacını öngörebilecek tahmin modeli oluşturulması amaçlanmıştır.
*Gereç ve Yöntem:* Tek merkezli ve retrospektif olarak planlanan çalışma Nisan 2020 ve Aralık 2021 tarihlerinde COVİD-19 tanılı ve kadın doğum kliniğine kabul edilen 18 yaş üzeri gebe ve postpartum hastalar ile yapıldı. Tahmin modeli oluşturulması için hastaların klinik özellikleri, laboratuvar değerleri ve radyolojik özellikleri kaydedildi. Tahmin için iki farklı çok değişkenli lojistik regresyon modeli ve Naive Bayes sınıflandırma algoritması kullanıldı. Geliştirilen tahmin modellerinin sonuçları nomogram ile özetlendi ve tahmin başarıları alıcı işletim karakteristik (ROC) eğrisi ile değerlendirildi.
*Bulgular:* Çalışmaya 436 gebe ve postpartum hasta dahil edildi. Yoğun bakıma yatırılan 51 hastadan 12'si eksitus oldu. Yoğun bakıma yatış risk faktörlerini belirlemek için oluşturduğumuz üç faklı sınıflama modelinin spesifitelerinin %95'in üzerinde ve sensitivitelerinin sırasıyla %70,6, %86,3 ve %87 olduğu belirlendi. Ayrıca ROC'un altındaki alan değerlerinin modeller için sırasıyla 0,94, 0,941 ve 0,978 olduğu bulundu. Yüksek prokalsitonin seviyesi, ateş, dispne ve orta-ağır radyolojik tutulum varlığının gebe ve postpartum kadınlarda yoğun bakım yatışı ile ilişkili risk faktörleri olarak belirlendi.
*Sonuç:* Geliştirdiğimiz risk modelinin uygulanması kolay ve erken dönemde ağır COVİD-19 hastalık riski taşıyan gebeleri belirlemeye ve önlem alınmasına yardımcı olacağı düşünülmektedir.
**Anahtar Kelimeler:** COVİD-19, mortalite, gebe kadınlar, yoğun bakım üniteleri, SARS-CoV-2

## Introduction

The immunological, physiological, and anatomical changes that occur during pregnancy may cause more severe viral respiratory tract infections in pregnant women (1,2). Previous studies have reported pregnancy itself to be a risk factor for severe disease when other factors associated with severe disease were considered in age-matched symptomatic pregnant and non-pregnant patients (3,4). Some 7-15% of pregnant women develop moderate and severe diseases requiring hospitalization, so the need for intensive care, mechanical ventilation and extracorporeal membrane oxygenation are high in this patient group (5).

When compared with other diseases, the early symptoms of coronavirus disease-2019 (COVID-19) is insidious and the disease can progress very quickly. One of the greatest challenges to disease management during the pandemic has been the wide spectrum of COVID-19 manifestations, and the resulting need to determine risk factors that can predict the severe course of the disease. Studies of adult patients other than pregnant women have put forward various models for the determination of intensive care unit (ICU) admission and mortality (6-8), while there have been limited studies to date exploring the prediction of severe disease, the need for intensive care and mortality in pregnancy (9-11).

We aimed to develop a model for the determination of the risk factors that could serve as predictors of the need for intensive care based on a retrospective assessment of the pregnant women admitted to our hospital with COVID-19.

## Materials and Methods

This single-center retrospective observational study was conducted with pregnant and postpartum women patients over 18 years of age with COVID-19 confirmed by reverse transcriptase-polymerase chain reaction (RT-PCR) for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) between 01.04 2020 and 31.12 2021 in the Gynecologic Infectious Diseases Ward of University of Health Sciences Turkey, Bursa City Hospital. The study protocol was approved by University of Health Sciences Turkey, Bursa City Hospital Clinical Research Ethics Committee (decision no: 2022-1/13, date: 09.02.2022) and the study was conducted following the principles of the Declaration of Helsinki. Since our study was retrospective, informed consent was not obtained from the patients.

Patient data were obtained from the electronic archives of the hospital. Included in the study were pregnant and postpartum women (within 6 weeks postpartum) who tested positive for SARS-CoV-2 with a RT-PCR test. Pregnant and postpartum women with a critical illness at the time of diagnosis, those younger than 18 years of age, those with a negative SARS-CoV-2 test result and those with previous COVID-19 infections were excluded from the study. All patients were managed in line with the Ministry of Health Diagnosis and Treatment Guidelines.

The demographic characteristics at the time of admission to hospital, age, body mass index (BMI), comorbidities [pregestational diabetes mellitus (DM), chronic hypertension, cardiac diseases, bronchial asthma], smoking, history of medication, gestational age at admission, egravidity/parity, symptomatic (cough, nasal congestion, body temperature etc.) or asymptomatic infections at the time of admission, variant of SARS-CoV-2, laboratory values [white blood cells, hemoglobin, platelets, lymphocytes, neutrophil/lymphocyte (N/L) ratio, ferritin, fibrinogen, D-dimer, C-reactive protein (CRP), procalcitonin, lactate dehydrogenase (LDH), alanine aminotransferase (ALT), aspartate aminotransferase (AST), international normalized ratio, activated partial thromboplastin time (aPTT), prothrombin time], peripheral oxygen saturation ($SpO_2$), heart rate and respiratory rate, medical treatments (remdesivir, steroids, favipiravir, low molecular weight heparin), COVID-19 vaccination status, radiological findings [mild, moderate, severe according to the World Health Organization (WHO) classification], length of stay in the ward, time from diagnosis to the ICU admission for patients requiring intensive care, length of stay in the ICU and hospital (days) of those involved in the study were recorded.

Thoracic computed tomography (CT) scans and chest radiographs were evaluated using the Picture Archiving and Communication System. Thoracic CT scans and chest radiographs were reviewed by a radiologist with more than 10 years of experience in thoracic radiology. Pneumonia was classified as mild, moderate and severe based on radiological imaging. The classification of chest radiographs was made using the RALE Scoring System (12). Thoracic CT scans were classified based on the Chest Computed Tomography score (13), for which both lungs were divided into five lobes, and each lobe was assessed individually.

Patients were also classified as mild, moderate and severe based on their clinical presentation COVID-19 Treatment Guidelines Panel (14).

**Mild illness:** Patients with any of the various signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but without shortness of breath or abnormal chest imaging.

**Moderate illness:** Patients with evidence of lower respiratory disease during clinical assessment or imaging, and with ≥94% $SpO_2$.

**Severe illness:** Patients with $SpO_2$<94%, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen ($PaO_2/FiO_2$) <300 mmHg, a respiratory rate >30 breaths/min (tachypnea) or lung involvement >50%.

Patients vaccinated with two doses of mRNA (Pfizer-BNT-162b2, Germany) or two doses of inactivated (SINOVAC, China) COVID-19 vaccine were included in the vaccinated group, while those who had one dose of vaccine or who were not vaccinated at all were included in the unvaccinated group.

Patients were divided into two groups; those who were admitted to the ICU and those who were treated in the Gynecologic Infectious Diseases Ward. Based on the above-mentioned recorded data, the risk factors for admission to the ICU were established and prediction models for intensive care were created.

## Statistical Analysis

The categorical variables are summarized as numbers and percentages. The continuous variables are presented as mean, standard deviation, median and interquartile range according to the distribution characteristics. The unadjusted effects of the measured features, whose effects on admission to the ICU will be examined, were evaluated with univariate analyses, for which a Pearson chi-square test and a Mann-Whitney U test were applied.

Candidate risk factors with a p-value of less than 0.10 according to the univariate test results were included in the multivariate models, and the adjusted effects of each variable were examined because this value generally used for variable selection step in the model (15). A total of 24 predictors were included in the multivariate models, and three different classification models were used (Figure 1). Before proceeding to the classification stage, missing data was resolved using a model-based imputer, which constructs a model for the prediction of the missing value based on values of other attributes; a separate model is constructed for each attribute. The model is the 1-nearest neighbour learner, which takes its value from the most similar example for the log-likelihood ratio test.

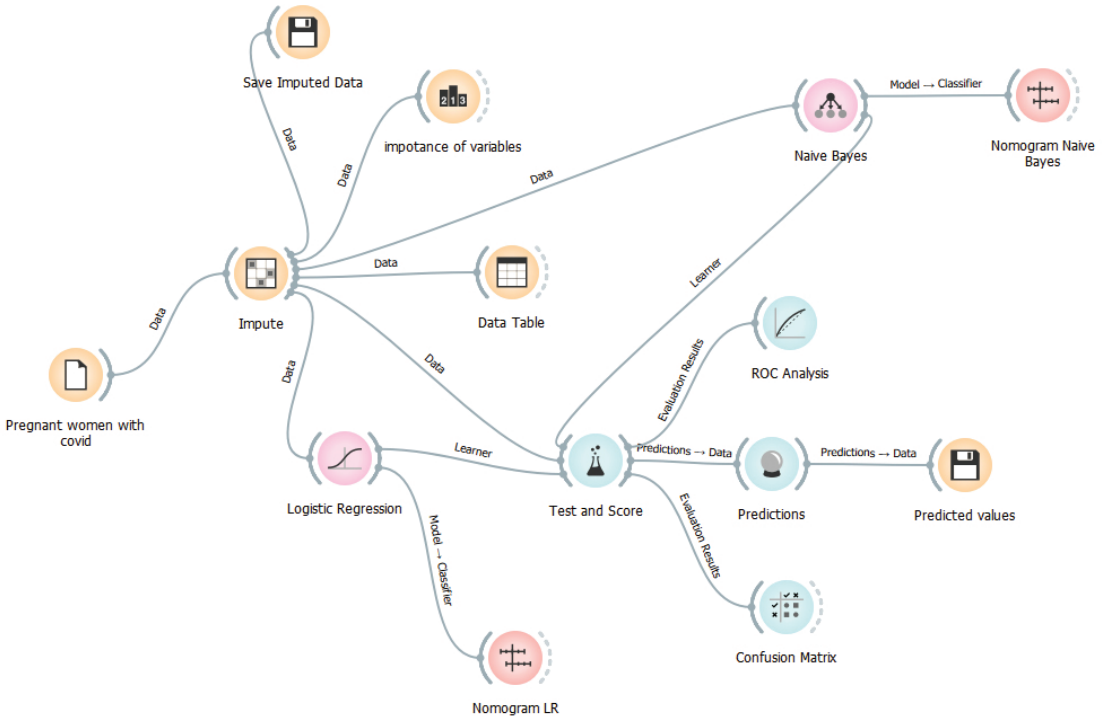


**Figure 1.** The multivariate model construction process
LR: Logistic regression

The first model used to predict ICU admission is the Lasso (L1) logistic regression (LR) model. L1 regularized LR is often used for feature selection and has demonstrated good generalization performance in the presence of many irrelevant features (16). The second model is the LR model, which is applied together with the backward variable elimination method. In the model development process, backward procedures were used for the selection of the predictors with a p-value <0.10. The Naive Bayes classification algorithm was used as the third model (Figure 2). The 10-fold cross-validation method was used for the interval validation of the models.

The results of the classification models are presented using a nomogram, which is useful for estimating the prevalence of each patient, being based on a scoring system rather than a complex formula. Nomograms provide a graphical depiction of the numerical relationships between the outcome and risk factors. Without regard to statistical significance or signs of estimated regression coefficients, each predictor is assigned a score based on the estimated regression coefficients in a nomogram (17).

Receiver operating characteristic (ROC) curves depicting the classification probabilities of the models were drawn, and the area under the ROC curve (AUC) was calculated. In addition, sensitivity, specificity, false positive, false negative, positive predictive value (PPV) and negative predictive value performance criteria were calculated to compare the examined models.

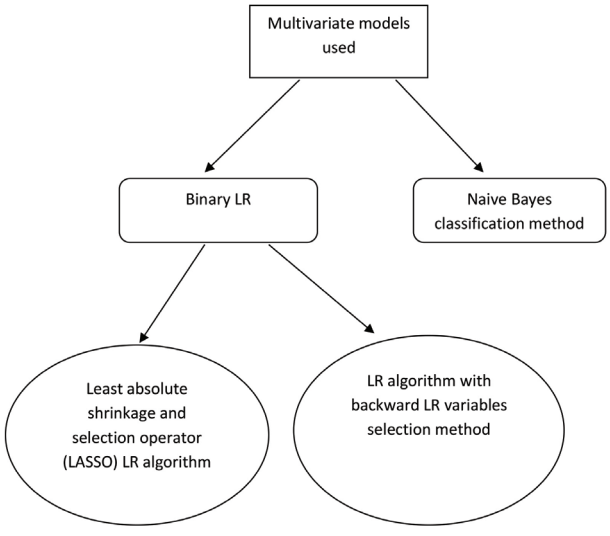


**Figure 2.** Multivariate models used in the study
LR: Logistic regression

P-value less than 0.05 considered statistically significant. The SPSS (ver. 23), Stata (ver.14.0) and Orange (ver. 3.31.1) programs were used for the statistical calculations.

## Results

A total of 436 pregnant women diagnosed with COVID-19 were included in the study. Of these, 51 were hospitalized in the ICU and 12 patients died while in the ICU. In the study sample of 436 patients, the mortality rate was 2.7% and the rate of admission to the ICU was 11.6%.

Tables 1, 2 and 3 present descriptive statistics of the characteristics of the pregnant women who were and who were not admitted to the ICU, as well as the results of a comparison of these two groups. The results show the unadjusted effects of each patient characteristic on ICU admission. Those with a p-value of less than 0.10 for these effects were included in the multivariate model as candidate predictors for the determination of ICU admission, and their unadjusted effects were examined.

A total of 24 predictors and one outcome variable (ICU) were included in the models created to analyze the adjusted effects of the candidate variables. The multivariate LR model using the L1 regularization included 19 predictors with significant effects; the Naive Bayes classification method included 24 predictors; and the multivariate LR model using the backward selection method included 11 predictors. The modelling phase was entered after estimating all the missing data in the data set in the Lasso regression and Naive Bayes methods, while there were only six missing data items in the LR model using the backward selection method. The coefficients of the LR model using the backward selection method are presented in Table 4.

An analysis of the performance measurements of the models revealed that the Naive Bayes method resulted in the highest sensitivity (in terms of the successful prediction of patients admitted to the ICU) (86.3%), although this model had the lowest PPV (52.4%), while the highest PPV was provided by the LR model using the backward selection method (87%). The specificity (successful prediction of patients admitted to the ICU) of all three models was over 95%, and all values were very close to each other. Another performance measure of the models is the AUC, for which the values were 0.941, 0.940 and 0.978, respectively (Figure 3). The performance of the three models in predicting ICU admission is summarized in Table 5. Considering the

performance measures of the model and the number of included predictors in the model together, the most successful classification model was the LR model using the backward selection method.

The nomograms of the models are presented in Figures 4-6, respectively. According to the L1 LR model, the top five predictors contributing to the risk of ICU stay are AST, ALT, CRP, respiratory rate and radiological assessment, respectively (Figure 4). The nomogram of the Naive Bayes classification algorithm reveals the top five risk factors with the greatest contribution to radiological assessment, CRP, procalcitonin, saturation and ferritin, respectively (Figure 5). The nomogram of the LR model using the backward variable elimination method is presented in Figure 6.

**Table 1. Unadjusted effects on ICU admission of categorical patient characteristics**

| | ICU no | ICU yes | | ICU no | ICU yes | | |
|---|---|---|---|---|---|---|---|
| | Absent (n/%) | Absent (n/%) | Total | Present (n/%) | Present (n/%) | Total | p |
| History of systemic diseases | 335/88.9 | 42/11.1 | 377 | 44/86.3 | 7/13.7 | 51 | 0.586 |
| Smoking | 341/89.7 | 39/10.3 | 380 | 38/95 | 2/5.0 | 40 | 0.286 |
| Cough | 181/94.3 | 11/5.7 | 192 | 204/83.6 | 40/16.4 | 244 | 0.001 |
| Fever | 330/90.2 | 36/9.8 | 366 | 55/78.6 | 15/21.4 | 70 | 0.006 |
| Dyspnea | 290/96 | 12/4.0 | 302 | 93/70.5 | 39/29.5 | 132 | 0.001 |
| Loss of taste-smell | 343/88.2 | 46/11.8 | 389 | 42/89.4 | 5/10.6 | 47 | 0.811 |
| Headache | 372/89.2 | 45/10.8 | 417 | 13/68.4 | 6/31.6 | 19 | 0.006 |
| Myalgia | 346/89.9 | 39/10.1 | 385 | 39/76.5 | 12/23.5 | 51 | 0.005 |
| GI symptoms | 341/88.1 | 46/11.9 | 387 | 44/89.8 | 5/10.2 | 49 | 0.73 |
| Sore throat | 318/88.8 | 40/11.2 | 358 | 67/85.9 | 11/14.1 | 78 | 0.466 |
| Nasal congestion | 349/88.4 | 46/11.6 | 395 | 35/87.5 | 5/12.5 | 40 | 0.873 |
| Asymtomatic | 289/85.3 | 50/14.7 | 339 | 96/99 | 1/1.0 | 97 | 0.001 |
| Gestational diabetes | 362/87.9 | 50/12.1 | 412 | 13/100 | 0/0.0 | 13 | 0.181 |
| Antibiotics | 167/96 | 7/4.0 | 174 | 210/82.7 | 44/17.3 | 254 | 0.001 |
| Delta variant | 264/91.7 | 24/8.3 | 288 | 108/80 | 27/20 | 135 | 0.001 |

ICU: Intensive care unit

**Table 2. Unadjusted effects on ICU admission of categorical patient characteristics**

| | ICU no | ICU yes | | |
|---|---|---|---|---|
| | n/% | n/% | Total (n) | p |
| **Radiological assesment** | | | | |
| Mild | 183/97.9 | 4/2.1 | 187 | **0.001** |
| Moderate | 65/91.5 | 6/8.5 | 71 | |
| Severe | 9/18.8 | 39/81.3 | 48 | |
| **Vaccination status** | | | | |
| Other | 171/77.7 | 49/22.3 | 220 | **0.007** |
| Two doses B or S | 18/94.7 | 1/5.3 | 19 | 0.08 |
| **Gestational age** | | | | |
| 1-12 weeks | 24/96 | 1/4,0 | 25 | 0.031 |
| 13-28 weeks | 114/82.6 | 24/17.4 | 138 | |
| ≥29 weeks | 246/90.4 | 26/9.6 | 272 | |

ICU: Intensive care unit, B: Biontech, S: Sinovac, n: number of patients

| Table 3. Unadjusted effects of numerical patient characteristics on ICU admission | | | | | |
|---|---|---|---|---|---|
| | ICU no | | ICU yes | | |
| | n | Mean/SD | n | Mean/SD | p |
| Age (years) | 385 | 29.11/5.43 | 51 | 31.39/5.27 | 0.006 |
| BMI | 375 | 28.72/5.31 | 49 | 28.10/4.71 | 0.484 |
| $SpO_2$ | 374 | 97.5/1.42 | 51 | 94.22/3.67 | 0.001 |
| Respiratory rate (breaths per minutes) | 351 | 19.58/1.26 | 51 | 21.82/4.32 | 0.001 |
| Pulse steroid | 372 | 89.20/12.23 | 51 | 99.04/15.53 | 0.001 |
| Fever (°C) | 377 | 36.69/0.58 | 51 | 36.79/0.70 | 0.895 |
| WBC ($10^3$ µL) | 381 | 7.92/2.72 | 51 | 7.96/3.02 | 0.851 |
| Hb (g/dL) | 380 | 11.34/1.40 | 51 | 11.14/1.37 | 0.353 |
| Plt ($10^3$ µL) | 380 | 213.87/66.29 | 51 | 222.14/97.78 | 0.958 |
| Lymphocytes ($10^3$ µL) | 383 | 1.38/0.62 | 51 | 0.99/0.53 | 0.001 |
| Neutrophils ($10^3$ µL) | 381 | 5.93/2,32 | 51 | 6.50/2,65 | 0.158 |
| N/L ratio | 381 | 5.14/3.30 | 51 | 7.69/4.62 | 0.001 |
| AST (IU/L) | 373 | 29.88/47.29 | 50 | 81.19/139.97 | 0.001 |
| ALT (IU/L) | 374 | 25.67/50.76 | 50 | 58.94/99.90 | 0.001 |
| LDH (IU/L) | 222 | 210.31/80.68 | 45 | 346.0/146.37 | 0.001 |
| CRP (mg/L) | 358 | 25.79/29.42 | 48 | 87.86/106.98 | 0.001 |
| Ferritin (µg/L) | 345 | 64.59/114.48 | 50 | 220.72/314.95 | 0.001 |
| Procalcitonin (µg/L) | 250 | 0.10/0.12 | 48 | 0.36/0.46 | 0.001 |
| D-dimer (µg/mL) | 353 | 1.42/1.26 | 50 | 1.48/1.29 | 0.539 |
| PT (sec) | 324 | 10.47/44.11 | 50 | 24.72/118.52 | 0.269 |
| aPTT (sec) | 322 | 30.56/4.82 | 50 | 33.35/6.30 | 0.001 |
| INR | 323 | 0.90/0.14 | 50 | 0.89/0.17 | 0.608 |
| Fibrinogen (mg/dL) | 82 | 49.70/98.83 | 40 | 540.30/149.53 | 0.123 |

ICU: Intensive care unit, SD: standard deviation, BMI: body mass index, $SpO_2$: peripheral oxygen saturation, WBC: white blood count, Hb: hemoglobin, Plt: platelet, N/L: neutrophils/lymphocytes ratio, AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase, CRP: C-reactive protein, PT: protrombin time, aPTT: active partial tromboplastin time, INR: international normalized ratio

| Table 4. The coefficients of the logistic regression model | | | | | | |
|---|---|---|---|---|---|---|
| | B | S.E. | p | OR | 95% CI for OR | |
| | | | | | Lower | Upper |
| Fever (yes/no) | 1,776 | 0.653 | 0.006 | 5,907 | 1,644 | 21,227 |
| Dyspnea (yes/no) | 2,148 | 0.682 | 0.002 | 8,564 | 2,248 | 32,622 |
| **Radiological assessment** | | | | | | |
| Moderate/mild | 0.234 | 0.848 | 0.782 | 1,264 | 0.240 | 6,660 |
| Severe/mild | 4,596 | 0.826 | 0.001 | 99,074 | 19,638 | 499,823 |
| $SpO_2$ | 0.226 | 0.140 | 0.080 | 0.797 | 0.606 | 1,050 |
| Respiratory rate (breaths per minutes) | 0.265 | 0.133 | 0.046 | 1,303 | 1,004 | 1,690 |
| Delta variant (yes/no) | 1,465 | 0.635 | 0.021 | 4,327 | 1,247 | 15,019 |
| Lymphocytes ($10^3$ µL) | -1.155 | 0.641 | 0.050 | 0.315 | 0.090 | 1,108 |
| AST (IU/L) | 0.021 | 0.009 | 0.017 | 1,021 | 1,004 | 1,038 |
| ALT (IU/L) | 0.016 | 0.010 | 0.090 | 0.984 | 0.965 | 1,004 |
| Procalcitonin (µg/L) | 3,322 | 1,091 | 0.002 | 27,721 | 3,269 | 235,106 |
| aPTT (sec) | 0.124 | 0.061 | 0.042 | 0.883 | 0.784 | 0.995 |
| Constant | 14,939 | 14,385 | 0.299 | 3076574.000 | - | - |

$SpO_2$: Peripheral oxygen saturation, AST: aspartate aminotransferase, ALT: alanine aminotransferase, aPTT: active partial tromboplastin time, CI: confidence interval, OR: odds ratio, S.E.: standard error

## Discussion

In the present study, we develop a model for the determination of the risk factors that can predict the need for intensive care among pregnant women followed up for COVID-19. The models created using three different methods recorded quite high predictive values (AUC: 0.941, 0.940 and 0.978), and the specificity of all three models was over 95% and very close to each other. The LR model using the backward selection method was identified as the most successful method based on model performance measures, with identified moderate-to-severe involvement during the radiological assessment, high procalcitonin levels, fever and dyspnea identified as the main risk factors.

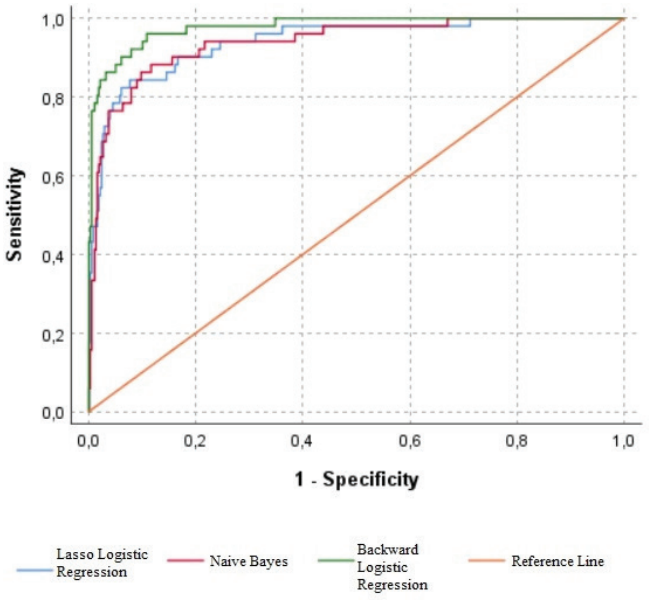


**Figure 3.** The ROC curve depicting the success of the three analyzed models in predicting ICU admission
ROC: Receiver operating characteristic, ICU: intensive care unit

In a previous study, 85-90% of pregnant patients were found to have asymptomatic COVID-19, 7-15% to have moderate or severe disease requiring hospitalization, and 2.5% to require intensive care (5). When compared to age-matched patients, however, the rates of pneumonia, ICU admission and mortality were reported to be quite high in pregnant patients (5,18). The INTERCOVID multinational cohort study reported a rate of intense ICU admission of 5-7%, although the thresholds for ICU admission are likely to be lower for pregnant women given the need for closer monitoring of such patients. When mechanical ventilation was used as an indicator of a more severe disease course, this rate was found to be in the 2-6% range (19). We found the rate of ICU admission to be 11.6% in our patient group, and an intubation rate of 4.8%, which is consistent with the literature.

Due to the more severe course of COVID-19 in pregnant patients, vaccination is very important for the prevention of maternal mortality and morbidity. Despite several studies on the efficacy and safety of vaccines during pregnancy (20,21), the rate of vaccination in the pregnant population is still low when compared to other at-risk patient groups (22). It is very important, therefore, to identify patients at most risk of a severe disease course and who will need intensive care.

Previous studies have sought to develop models for the determination of disease severity or mortality in non-

**Table 5. Classification performance of the analyzed models**

| | | Patients not in the ICU | | | Patients in the ICU | | |
|---|---|---|---|---|---|---|---|
| | | n | % in predicted model | % in actual | n | % in predicted model | % in actual |
| Lasso (L1) LR | No | 376 | 95.7 | 97.7 | 17 | 4.3 | 33.3 |
| | Yes | 9 | 20.9 | 2.3 | 34 | 79.1 | 66.7 |
| | Total | 385 | | | 51 | | |
| Naive Bayes | No | 345 | 98.0 | 89.6 | 7 | 2.0 | 13.7 |
| | Yes | 40 | 47.6 | 10.4 | 44 | 52.4 | 86.3 |
| | Total | 385 | | | 51 | | |
| LR with backward | No | 373 | 97.1 | 98.4 | 11 | 2.9 | 21.6 |
| | Yes | 6 | 13.0 | 1.6 | 40 | 87.0 | 78.4 |
| | Total | 379 | | | 51 | | |

LR: Logistic regression, ICU: intensive care unit

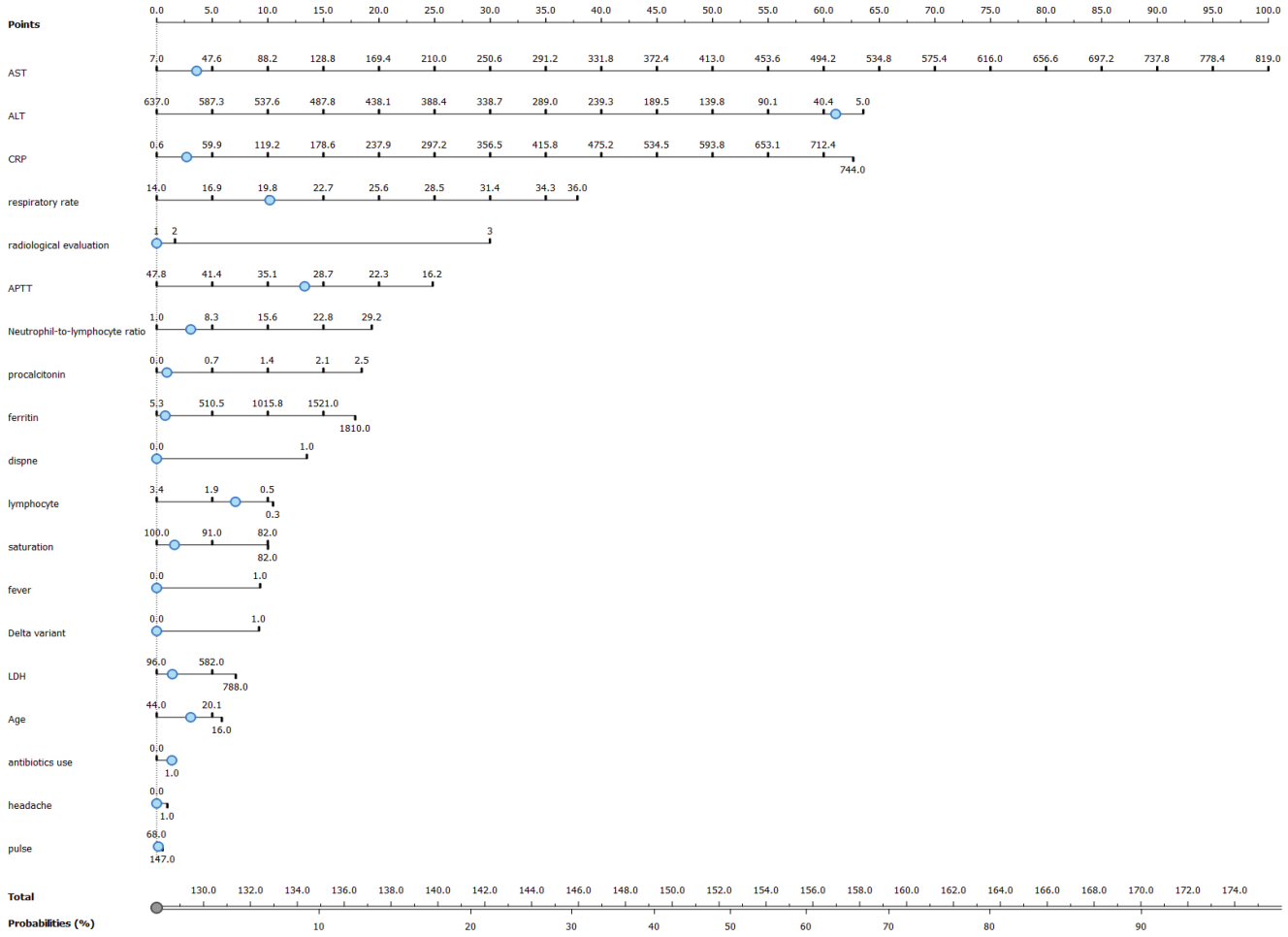


**Figure 4.** Nomogram of the Lasso (L1) logistic regression model
AST: Aspartate aminotransferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase, CRP: C-reactive protein, aPTT: active partial tromboplastin time

pregnant adult patients (23,24), while there have been few studies investigating the prediction of severe disease and the need for intensive care in the pregnant patient group. The study by Yao et al. (10) of all pregnant women who presented to the hospital for delivery and who recorded a positive PCR test result sought to identify the patient group in need of advanced respiratory support and requiring mechanical ventilation and high velocity nasal insufflation using their own Loma Linda Obstetric Warning score (OWS) model. Based on the presence of dyspnea, heart rate of >100, respiratory rate of <20 or >24, fever of >99 °F, CRP of >2.0 mg/dL and pneumonia findings on X-ray, the authors established a sensitivity of 100%, a specificity of 64%, and a PPV of 36%. They reported the model to be more effective than the previously developed COVID-19 Early Warning score (EWS) and National Early Warning score (NEWS) in the identification of clinical deterioration in a non-pregnant population (AUC: 0.97, 0.72 and 0.92 for OWS, EWS, and NEWS, respectively) (10). It should be noted, however, that the study was conducted with only 50 pregnant women. In the study by Tutiya et al. (11), involving 114 pregnant women who presented to the hospital and who recorded a positive PCR test, a model was developed for the identification of severe disease in pregnant women based on the WHO classification. The authors identified a history of asthma, non-white ethnicity, maternal age of >34 years, and gestational age of ≥35 weeks as risk factors in this model, and found the predictive value of the model to be 0.823. They found further that higher gestational age was protective against severe disease (11).

Finally, the multicenter and international study by Kalafat et al. (9) evaluated the need for intensive care and the admission interval in 789 symptomatic pregnant women through the use of two developed models. Among the developed miniCOMIT and fullCOMIT models, the authors found the fullCOMIT model to perform very well and to rule out intensive care admissions (LR; ≤0.20) (9). Both models were found to be highly effective in predicting ICU admissions of patients in a risk range of 10-24.9% (AUC: 0.73 and 0.86 for miniCOMIT and fullCOMIT, respectively). The miniCOMIT model identified age, BMI and being in the third trimester of pregnancy as risk factors, while the fullCOMIT model included the BMI, N/L ratio, CRP values, and lower respiratory tract symptoms as risk factors (9).

A total of 436 pregnant women were included in our study, 51 of whom were admitted to the ICU. Although the number of patients included in our study is lower than in the study by Kalafat et al. (9), it is sufficient for the calculation of a predictive model. All of our three models had predictive values (AUC: 0.941, 0.940 and 0.978) greater than those

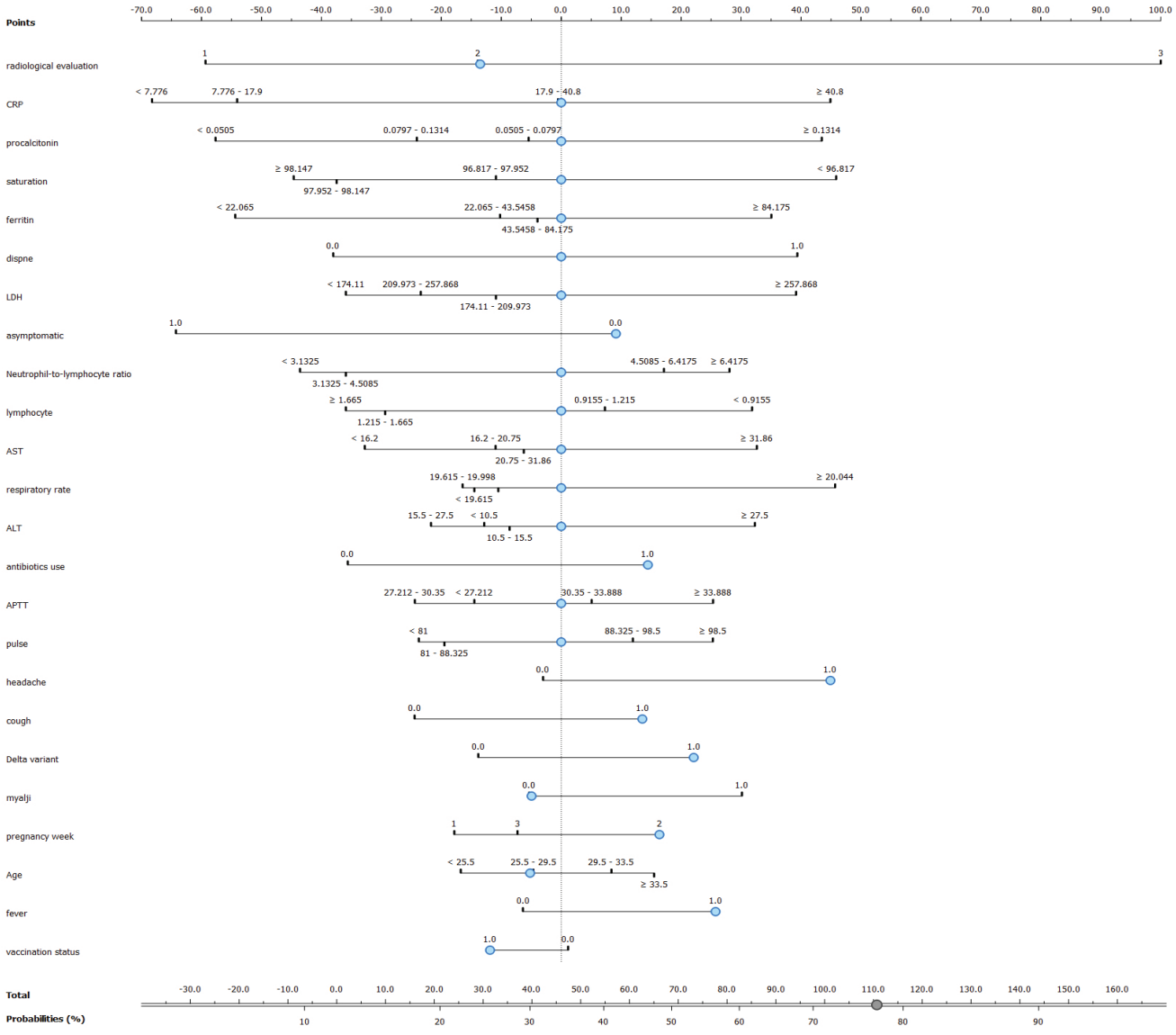


**Figure 5.** Nomogram of the Naive Bayes model
CRP: C-reactive protein, LDH: lactate dehydrogenase, AST: aspartate aminotransferase, ALT: alanine aminotransferase, aPTT: activated partial thromboplastin time

reported in the three above-mentioned studies. Unlike the studies by Tutiya et al. (11) and Kalafat et al. (9), we also included asymptomatic patients in our study. The multicenter and multinational study by Kalafat et al. (9) included patients of different ethnicities and the treatment protocols applied in different centers. In contrast, the present study group included patients from a single center and who received the same treatment protocol. Our study also assessed radiological imaging findings in the model, unlike the study by Kalafat et al. (9) who presented this as a study limitation.

Kalafat et al. (9) used the BMI of pregnant women as a risk factor in both models, while Tutiya et al. (11) and Yao et al. (10) disregarded BMI as a predictor in their models. In the present study, we recorded similar BMI values in patients with and without the need for intensive care. Kalafat et al. (9) included maternal age in their miniCOMIT model as a risk factor, and there have been other studies identifying advanced maternal age as a risk factor for both severe disease [odds ratio (OR): 1.83] and ICU admission (OR: 2.11) (25). A study of 978 pregnant patients with acute respiratory distress syndrome from Brazil examining the risk factors associated with maternal mortality, however, identified only a 2-year age difference between the non-surviving and surviving patients (26). Similarly, several studies of adult patients have also failed to identify age as a risk factor for severe disease (5,8).

No comorbidities were identified in 51.6% of the non-surviving patients in the study by Takemoto et al. (26), while the same study detected comorbidities in 20% of patients who died from COVID-19, the most common comorbidities being DM and cardiovascular disease. While our study recorded a statistical age difference between the patients admitted and not admitted to the ICU, the age difference between the groups was only 2 years. In the present study, comorbidities were detected in only 13.7% of the patients admitted to the ICU and in 86.3% of those who were

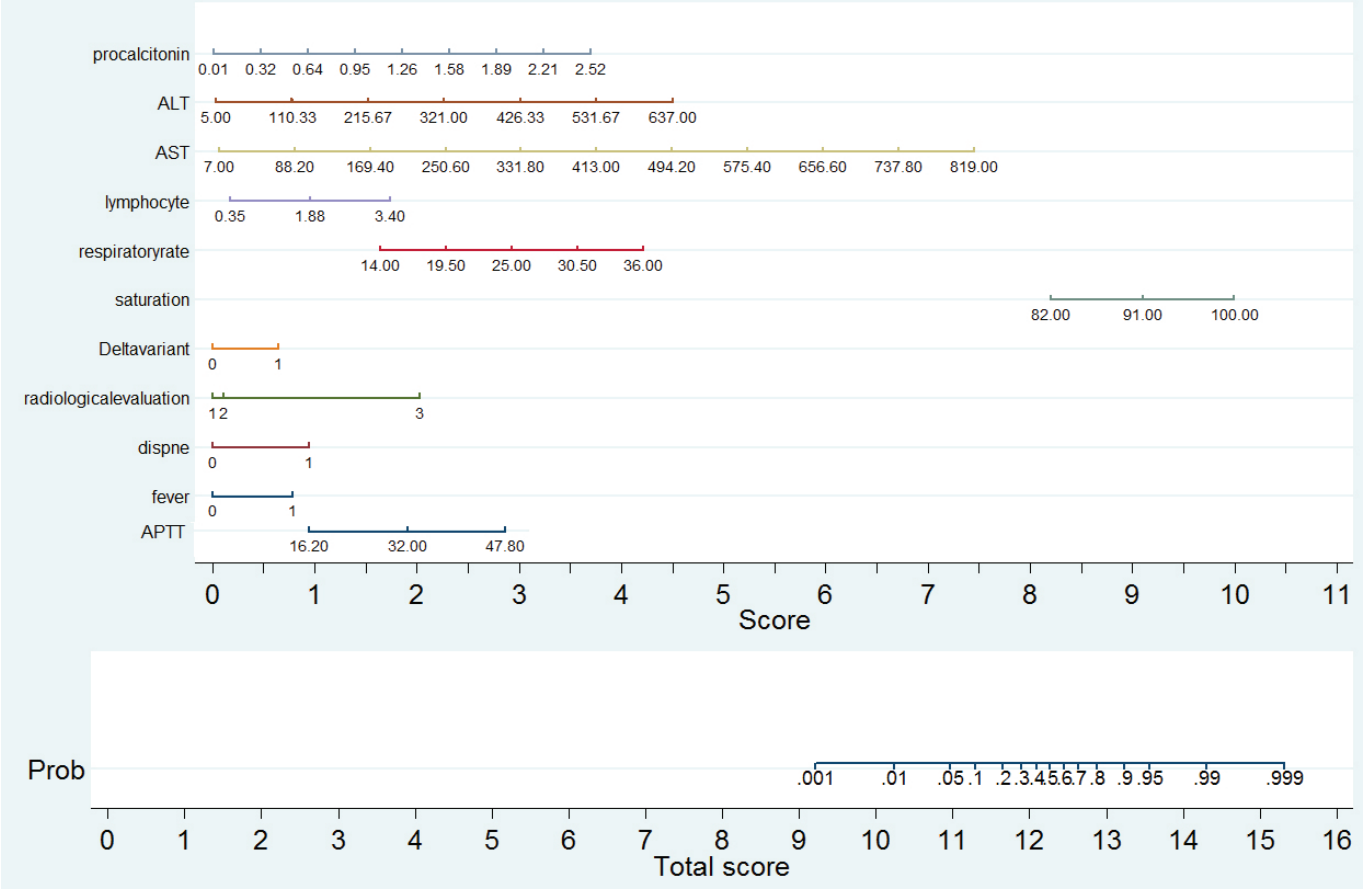


**Figure 6.** Nomogram of the multivariate binary logistic regression using the backward method
ALT: Alanine aminotransferase, AST: aspartate aminotransferase, aPTT: activated partial thromboplastin time

not, although the difference between the two groups was statistically insignificant.

In the present study, fever and dyspnea were identified as significant risk factors for ICU admission. A systematic review and meta-analysis of 11,758 pregnant women examining the effect of COVID-19 on maternal mortality in pregnant and postpartum women detected fever alone or with cough in all non-surviving patients (27). The same study reported that the most common symptoms to develop later were dyspnea and myalgia.

The current study also identified the laboratory parameters AST, ALT, procalcitonin, aPTT and lymphocyte count as risk factors in the model. Unlike other models predicting severe disease in pregnant women, we also included laboratory parameters given the importance of laboratory assessments in disease management and the determination of prognosis. A study by Zhao et al. (8) aiming to develop models for the prediction of ICU admission and mortality in adult COVID-19 patients identified LDH, procalcitonin, pulse, oxygen saturation, smoking history and lymphocyte count as the most significant predictive variables, and reported the success of their created risk score model [AUC: 0.74 (95% confidence interval, 0.63-0.85), p=0.001]. Procalcitonin is used as a parameter in the identification of severe illness in the presence of an infectious etiology (28). In viral diseases, however, interferon causes a decrease in procalcitonin levels, and so an increase in procalcitonin is considered a sign of immune system insufficiency in viral infections (10). Decreased CD4 and CD8-T cells play an important role in the spread of the virus and are a sign of poor prognosis (29).

One of the main limitations of our study is its retrospective and single-center design, although the parameters used in the model developed in the study can be applied in many different centers, and so can be considered suitable for the assessment of pregnant groups in different areas. The study is important in that it included all pregnant women who had been hospitalized since the onset of the pandemic, including those infected with the different SARS-CoV-2 variants that emerged in different periods of the pandemic. Although the total number of patients included in the study was high, our findings need to be validated, especially in groups involving more severe patients since the number of severe patients was relatively low.

## Conclusion

The risk score model developed in the present study can predict severe illness and the need for intensive care in pregnant patients with COVID-19. Our model is easy to apply, being based on objective parameters and enabling triage for clinicians in pregnant women, as a specific patient group. It is thus recommended that pregnant women who are determined to be at risk should be assessed as early as possible so that the necessary treatments can be administered and close monitoring provided.

### Ethics

**Ethics Committee Approval:** The study protocol was approved by University of Health Sciences Turkey, Bursa City Hospital Clinical Research Ethics Committee (decision no: 2022-1/13, date: 09.02.2022) and the study was conducted following the principles of the Declaration of Helsinki.

**Informed Consent:** Since our study was retrospective, informed consent was not obtained from the patients.

### Authorship Contributions

Surgical and Medical Practices: İ.K., G.A.A., S.Ü., Concept: İ.K., H.A., G.A.A., H.G.T.Ö., Design: İ.K., G.A.A., Data Collection and Process: İ.K., S.Ü., H.G.T.Ö., Analysis or Interpretation: H.A., G.A.A., Literature Search: İ.K., G.A.A., Writing: İ.K.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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