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ORIGINAL RESEARCH

Predictive Factors for the Success of Vaginal Dinoprostone for the Induction of Labour

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Objective: To evaluate factors predictive of the success of a slow-release dinoprostone vaginal insert for cervical ripening.

Methods: This retrospective study included 187 women who received dinoprostone vaginal inserts for cervical ripening. The participants were divided into two groups: the transvaginal delivery group (n = 87) and cesarean section termination group (n = 100). The correlation between the parameters present before cervical ripening with dinoprostone slow release and its success, as well as complications and adverse outcomes, was analyzed. Cesarean section predictors and area under the curve (AUC) were compared between the two Groups.

Results: There were statistical differences between the two groups in body mass index (BMI), height, cervical Bishop score, cephalic position, time of medication use, and fetal head position at the time of medication use ($P<0.05$). The optimal thresholds for identifying cesarean section in dinoprostone vaginal insert for cervical ripening were 162.5 for height (AUC = 0.61), 10.65 cm for amniotic fluid index (AUC = 0.6), S-2.5 for cephalic position (AUC = 0.61), 5.5 for bishop score of cervix (AUC = 0.65). The height, amniotic fluid index, cephalic position, and Bishop score of the cervix were included in the same model. The AUC value of the combined model was higher than the AUC value of the single factor.

Conclusion: The combined model was a better predictor of cesarean section in dinoprostone vaginal inserts for cervical ripening and labor induction. The success of cervical ripening with a dinoprostone slow-release vaginal insert can be predicted by the factors that can be recognized at admission.

Keywords: dinoprostone, cervical ripening, labor induction, predictive model

Introduction

During labor, the cervix should soften and dilate to allow the fetus to pass through the birth canal. The process by which the cervix becomes soft and partially dilated is called "cervical ripening".[1] Cervical ripening is believed to result from a combination of biochemical, endocrine, and mechanical events. When there are indications of labor induction and the cervix is in unfavorable conditions, agents for cervical maturation may be used, thus reducing induced labor time.[2,3] Induced labor refers to the process of causing uterine contractions through medical or surgical means before spontaneous delivery begins.[4] It is a widely used method for full-term delivery, accounting for 25% of pregnancies.[5] Indications for induced labor included absence of labor at 41 weeks, gestational diabetes, premature rupture of membranes, and reduced amniotic fluid. Cervical ripeness was assessed using the Bishop scoring system, with a Bishop score of ≤6 indicating an immature cervix.[6] Cervical ripening may be required if the cervix is immature before induction. The medications used for cervical ripening include prostaglandins, misoprostol, and oxytocin.[7] The use of misoprostol tablets for vaginal administration is uncertain owing to its specific characteristics, and misoprostol cannot be retrieved from the vagina in cases of maternal-fetal complications. Therefore, its clinical use is currently limited.[8] In pregnant women with an immature cervix, the failure rate of cervical ripening with oxytocin was relatively high. Oxytocin induction was prioritized when the Bishop score was > 6, oxytocin induction is prioritized.[9]

Prostaglandins act on the cervix through various mechanisms to promote cervical ripening.[10,11] Based on years of research and improvement, dinoprostone is a prostaglandin analog. Dinoprostone vaginal suppositories (trade name:

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Cervidil) are synthetic preparations, chemically and structurally identical to prostaglandin E2 (PGE2). It acts as an oxytocic.[12–14] Cervidil is designed to provide constant and sustained release of PGE2 to the cervix to promote cervical ripening, with the main advantage of being removable during labor or in case of adverse reactions, compared to other prostaglandins. It has been shown to be safe and effective for pregnant women and fetuses.[15,16] However, the probability of vaginal delivery after dinoprostone placement is still relatively low, and some cases may still require cesarean section after cervical ripening and induction to terminate the pregnancy. However, the exact reason is not provided in the text.

The Bishop score indicates changes in the cervical response to delivery, which can affect the success of induction. The mechanism may be related to anatomical changes in the cervix and the secretion of various cell factors and biochemical substances, which aid in the progression of labor. However, a meta-analysis conducted by Kolkman et al[17] found that, although the predictive ability of the Bishop score is limited, it is still frequently used.[18]

The relationship between body mass index (BMI) and induction success is still being studied, and research has suggested an inverse relationship between BMI and cervical ripening. However, the pathological and physiological mechanisms by which obesity negatively affects delivery are not fully understood. Zhang et al[19] reported that overweight women who underwent cesarean section had weaker and less frequent uterine contractions. Garabedian et al[20] reported an increase in oxytocin receptor expression with increasing BMI, possibly because of decreased receptor sensitivity.[18]

The analysis suggests that specific characteristics of mothers, such as BMI, height, parity, age, baseline-adjusted Bishop score, race, and newborn birth weight, can independently predict the likelihood of successful induction. Incorporating these factors into the management plan for cervical ripening induction can improve the quality of care and should be considered.[7,13]

In previous studies, the probability of cesarean delivery termination in pregnant women treated with dinoprostone was 22.5%, 24.4%, and 33.7%.[18,21–23] The failure rate of cervical ripening was 55.4%, but there were no significant differences in neonatal outcomes or maternal complications.[6]

The purpose of this study was to analyze factors predictive of the success of a slow-release dinoprostone (Trade name: Xin Pubesheng; generic name: dinoprostone (prostaglandin E2). Produced by Ferring Controlled Therapeutics Limited, specification: 10 mg/suppository, batch number: MA19P03B) vaginal insert for cervical ripening, conduct a comprehensive analysis in clinical treatment, predict the possibility of vaginal delivery in advance, make a good estimate, and reduce the pain and treatment cost of pregnant women.

Methods

General Information

Study subjects: Retrospective cohort study was conducted at the Department of Obstetrics and Gynecology at the Affiliated Hospital of Northwest University/Xi'an Third Hospital from January 2019 to January 2020. The study was also approved by the local authority. The inclusion criteria were full-term pregnancy, singleton, cephalic presentation, dinoprostone for cervical ripening, and Bishop score ≤ 6. The exclusion criteria included a history of uterine surgery, contraindications for vaginal delivery, parity equal to or greater than 4, and refusal of vaginal delivery. Ultimately, 187 pregnant women were included in the study, including those with 41-week gestation with premature rupture of membranes, oligohydramnios, gestational diabetes, and gestational hypertension. Based on the mode of delivery, the participants were divided into a vaginal delivery group (n = 87) and cesarean delivery group (n = 100). Age, height, BMI, and other basic information, as well as the cervical score before suppository placement, time of placement, and cervical score at the time of drug retrieval, were compared between the two groups. The predictive factors for cesarean delivery after the use of dinoprostone suppositories were analyzed, and the predictive ability was evaluated using ROC and AUC analyses. All participants were informed of the associated risks prior to medication administration, the purpose of the study and signed an informed consent form.

Research Methods

Procedure: Pregnant women who require cervical ripening and labor induction should undergo prenatal examinations, fetal heart monitoring, and vaginal examinations. After excluding contraindications for induction, cervical ripening and

labor induction were performed. Pregnant women underwent lithotomy and the external genitalia and vagina were strictly disinfected. A 10 mg dinoprostone suppository was placed horizontally in the posterior fornix of the vagina, with the tip remaining outside the vaginal orifice. Pregnant women were instructed to lie supine for half an hour, and fetal heart monitoring was performed every 2 h after the initiation of medication. If there are excessive uterine contractions, fetal distress, cervical score ≥ 6, regular contractions, newly ruptured membranes, inability of the pregnant woman to tolerate the medication, or if 24 h has passed without labor onset, the medication should be removed. After removing the medication, if the cervical score is ≥ 6, 2.5 units of oxytocin can be administered for labor induction. If the cervical score is < 6, the dinoprostone suppository can be inserted again, or a cervical balloon can be placed for cervical ripening.

Observational indicators: The primary outcome variable was successful induction of labor, defined as the proportion of cases that ultimately resulted in vaginal delivery after the start of treatment. The observational indicators included height, BMI, pretreatment cervical score (fetal head position), cervical score at the time of treatment (fetal head position), and logistic regression analysis of the corresponding indicators for pregnant women who underwent vaginal delivery or cesarean section. This includes basic information such as height, amniotic fluid index, cervical score, and treatment information (pre-induction cervical score, time of placement, post-induction cervical score, pre-induction the position of the fetal head from the ischial spine, post-induction The position of the fetal head from the ischial spine).

In this study, obstetrician-related factors were used as predictors and a combination of multiple factors was used as a predictive model to predict the use of dinoprostone oxytocin. Using this predictive model, successful cervical ripening by dinoprostone administration can be predicted using specific variables: Height, Amniotic Fluid Index, Pre-induction S-(the distance of the head from ischial spine), and Post-induction cervical scores. Risk factors included Amniotic Fluid Index and Pre-induction, whereas protective factors included Height and Post-induction cervical score. Incorporating this predictive model into hospital-induced labor protocols could help determine the indications for this procedure by using variables that best predict the success of cervical maturation. The management protocol could improve the quality of care, save costs, and reduce the time of oxytocin administration.

Statistical Analysis

All data were analyzed all the data. Student's *t*-test and Mann–Whitney *U*-test were used to compare continuous variables with and without a normal distribution. Continuous variables are expressed as mean[SD] or interquartile range (IQR). Categorical variables are presented as percentages and were tested for differences using the chi-square test. Logistic regression analysis was performed to study the relationship between predictive factors and the occurrence of cesarean section. ROC curve analysis and AUC were used to assess the predictive ability of indicators such as height, BMI, pre-medication cervical score, fetal head position, and cervical score at the time of medication for successful induction.

Results

Comparison of Basic Information Between the Two Groups of Patients

A comparison of basic patient characteristics between the two groups among 187 pregnant women who underwent cervical ripening with dinoprostone suppositories showed that the cesarean section group had a significantly higher BMI, and the amniotic fluid index was significantly higher in the cesarean section group than in the Vaginal Delivery Group. However, the Vaginal Delivery Group had a significantly greater height than the Cesarean Section Group. These results are shown in Table 1, while factors such as weight, routine blood tests, obstetric ultrasound results, oral glucose tolerance test (OGTT) results, and blood pressure showed no significant differences (Table 1).[24]

Comparison of Treatment Indicators Between the Two Groups

Comparison of treatment indicators between the two groups. A comparison of indicators during the cervical ripening process between the two groups showed that a higher pre-administration cervical score was associated with a higher probability of vaginal delivery [Vaginal Delivery Group vs cesarean section group 3 (1.4) vs 2.5 (1.3]). The fetal head position of pre-administration in the cesarean section group was significantly higher than that in the Vaginal Delivery Group. The total duration of medication administration was significantly longer in the cesarean section group than in the

Table 1 Comparison of Baseline Characteristics of Delivery Women Between the Two Groups

Group	Vaginal Delivery Group (n = 87)	Caesarean Section Group (n = 100)
Age(years) mean[SD]	28 (3.4)	28.5 (3.4)
Age(years)		
<35	83 (95.4%)	95 (95%)
35–40	3 (3.5%)	5 (5%)
>40	1 (1.1%)	0 (0%)
Prepregnancy Weight (kg)	51.5 (49.5–60.0)	53.0 (50.0–60.0)
Current Weight (kg)	69.5 (65–79)	71.5 (66–78)
BMI (kg/cm^2) median(min-max)	20.12 (18.4–22.43)	21.23 (19.49–23.44)
BMI (kg/cm^2)		
18.5–24	25 (28.7%)	27 (27%)
24–28	39 (44.9%)	41 (41%)
>28	23 (26.4%)	32 (32%)
Height (cm)	163 (160–165)	160 (158–165)
Hemoglobin (g/L)	123 (116–128)	122 (115–129)
Leukocyte (10^9/L)	7.75 (6.6–8.76)	7.82 (6.66–9.34)
AFI (cm) median(min-max)	11 (8.9–12.8)	11.6 (10.25–13.85)
AFI (cm)		
Oligohydramnios<5 (n)	3 (3.4%)	0(0%)
Low Amniotic Fluid 5–8 (n)	15 (17.2%)	11 (11.0%)
GDM (n)	17 (19.5%)	21 (21.0%)
Gestational Hypertension (n)	3(3.4%)	10 (8.0%)
Gestational Age At Delivery (wk)		
> 41	55 (63.2%)	66 (66.0%)
< 41	32 (36.8%)	34 (34.0%)
PROM (n)	5 (5.7%)	4 (4.0%)
Hypothyroidism (n)	6 (6.9%)	4 (4.0%)

Notes: AFI Amniotic fluid index. GDM Gestational diabetes mellitus. PROM Premature rupture of membranes. Hypothyroidism: 1) TSH ≥ 4 mIU/L and (or) Anti-thyroid peroxidase antibody/ thyroglobulin antibody negative; 2) TSH ≥ 2.5 mIU/L and Anti-thyroid peroxidase antibody/ thyroglobulin antibody positive. Date are presented as median (IQR), mean[SD] or n (%).

Vaginal Delivery Group [Vaginal Delivery Group vs cesarean section group = 10.3 (6.1) vs 13.5 (7.4]). The cervical scores during drug retrieval were lower in the cesarean section group than in the Vaginal Delivery Group [Vaginal Delivery Group vs cesarean section group = 5.5 (1.7) vs 4.5 (1.6]). Additionally, the position of the fetal head from the ischial spine during drug retrieval was lower in the Vaginal Delivery Group than that in the cesarean section group. (Table 2).

Analysis of Predictive Models for Termination of Pregnancy by Cesarean Section After Cervical Ripening with Dinoprostone Suppository

Receiver operating characteristic (ROC) curves were used to calculate the area under the curve (AUC) for each variable. Variables with an odds ratio (OR) of 1 (no effect on the outcome) were excluded. The optimal cut-off points for predicting cesarean delivery after cervical ripening and induction were determined to be a height of 162.5 cm, amniotic fluid index of 10.65, pre-medication fetal head position of S-2.5, and post-medication cervical score of 5.5. The corresponding sensitivities were 52.9%, 70%, 78%, and 61.6%, the specificities were 68%, 47.1%, 44.8%, and 63%, respectively.

When combining all the above indicators, the sensitivity for predicting cesarean delivery after induction was 69.8% and the specificity was 65.8%, with an AUC of 0.718. Compared with other variables, height, amniotic fluid index, pre-induction fetal head position, and post-induction cervical score had better predictive abilities. Including these four variables in the combined model aims to generate an improved predictive model. The AUC value of the combined model was higher than those of the individual variables within each group (Table 3 and Figure 1).

Table 2 Comparison of Relevant Indicators of Delivery Women Between the Two Groups

Group	Vaginal Delivery Group (n = 87)	Caesarean Section Group (n = 100)	OR (95% CI)
Pre-induction Cervical Score	3 (1.4)	2.5 (1.3)	0.9 (0.7, 1.2)
Time of Placement (h)	10.3 (6.1)	13.5 (7.4)	1.1 (1.0, 1.1)
Post-induction Cervical Score	5.5 (1.7)	4.5 (1.6)	0.7 (0.6, 0.9)
Pre-induction S-(n)			
≤ S-2	39 (44.8%)	22 (22.0%)	2.9 (1.5, 5.4)
S-3	48 (55.2%)	78 (78.0%)	
Post-induction S-(n)			
≤ S-2	65 (74.7%)	56 (56.0%)	2.3 (1.2, 4.3)
S-3	22 (25.3%)	44 (44.0%)	

Notes: Date are presented as mean[SD]or n (%), S-. The position of the fetal head from the ischial spine.
Abbreviations: OR odds ratio, CI confidence interval

Table 3 Analysis of Predictors of Cesarean Section Delivery After Dinoprostone Suppository Promoting Cervical Maturation

Variable	AUC (95% CI)	P-value	Cut-off value	Sensitivity (%)	Specificity (%)
Height (cm)	0.61 (0.53–0.69)	0.013*	162.5	52.9	68.0
Amniotic Fluid Index (cm)	0.60 (0.51–0.68)	0.029*	10.65	70	47.1
Pre-induction S-	0.61 (0.53–0.70)	0.005*	2.5	78	44.8
Post-induction cervical score	0.65 (0.57–0.72)	0.001*	5.5	61.6	63.0
Predictive Model	0.72 (0.65–0.79)	<0.001*	0.549	69.8	65.8

Notes: *$P < 0.05$. S- The position of the fetal head from the ischial spine. Predictive Model including Height, Amniotic Fluid Index, Pre-induction S- and Post-induction cervical score.

Comparison of Treatment Outcomes Between the Two Groups

According to the statistical results, the cesarean section group showed elevated infection indicators, such as postpartum procalcitonin (PCT) and neutrophils, and hemoglobin levels were significantly different after delivery. An increase in maternal infection indicators after induced labor increases the risk of infection; however, the amount of bleeding does not significantly increase. Therefore, women who have failed induced labor need to be aware of the prevention of infection (Table 4).

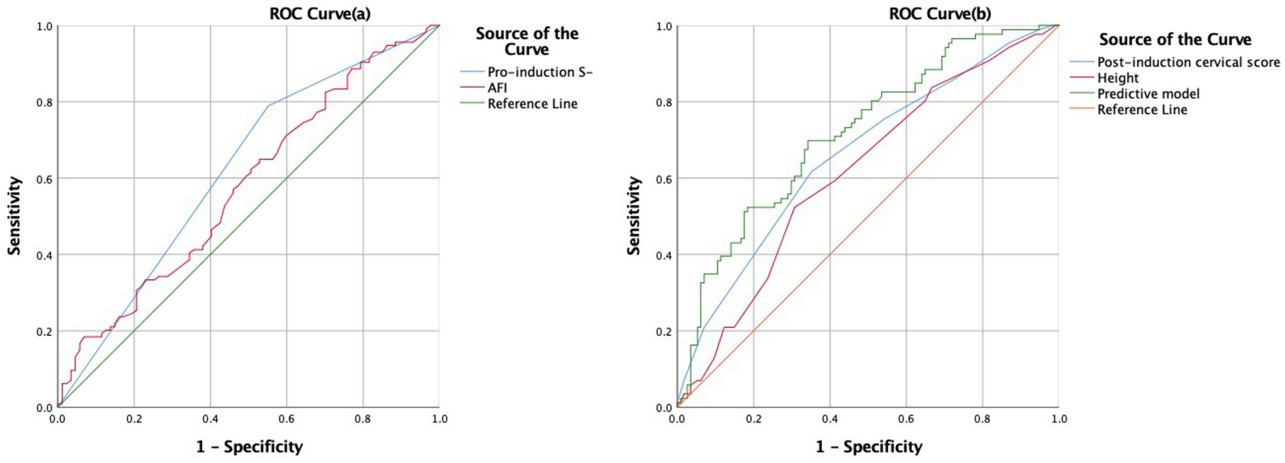

Figure 1 ROC curves for AFI, pro-induction fetal head position (S-) (**a**). ROC curves for height and post-induction cervical score and predictive model (**b**).

Table 4 Comparison of Outcomes of Treatment Between the Two Groups

Group	Vaginal Delivery Group (n = 87)	Caesarean Section Group (n = 100)	*P*-value
After Delivery Hemoglobin (g/L)	107 (17.11)	109 (12.80)	0.517
After Delivery Leukocyte (10^9/L)	11.43 (3.39)	13.70 (11.21)	0.001*
After Delivery PCT (ng/mL)	0.08 (0.21)	0.18 (0.25)	0.012*
After Delivery Neutrophil (10^9/L)	8.83 (3.19)	10.64 (3.62)	0.001*
Postpartum hemorrhage (mL)	1.26 (58.74)	246.84 (64.68)	0.704
Baby Birth Weight	3521 (338.9)	3625.6 (402.9)	0.144

Notes: *$P < 0.05$. Date are presented as mean [SD].
Abbreviations: PCT procalcitonin.

Discussion

Over the past 20 years, the number of induced laborers has gradually increased, and many methods have been tested. However, prostaglandins are still the preferred method for cervical ripening and labor induction.[25,26] Dinoprostone pessaries have been effective in promoting cervical ripening and labor induction, significantly improving the success rate of induction.[1,27] However, there are still cases where through cesarean section is necessary after vaginal placement of dinoprostone pessary.[18,28,29] The factors contributing to these failures remain unclear.[7] Therefore, this study compared and analyzed the basic information and treatment details of pregnant women who underwent cervical ripening and labor induction using a dinoprostone pessary and evaluated the factors influencing vaginal delivery.

This study found that a slow-release dinoprostone insert is effective in achieving efficient cervical ripening, and that specific factors can predict success with this method. Compared to the cesarean section group, pregnant women in the vaginal delivery group had a higher height, higher cervical score before medication (fetal head position), and higher cervical score at the time of medication (fetal head position) as protective factors. In contrast, BMI and amniotic fluid index were identified as unfavorable factors, with statistically significant differences ($P < 0.05$). According to uterine tension theory, as pregnancy progresses and the fetus continues to grow, the amount of amniotic fluid decreases, and the fetus comes into close contact with the uterine wall, especially the lower segment and cervical portion, which can induce uterine contractions through mechanical stimulation.[7,30,31] Pregnant women with a fetal head position at S-2 or below had a higher probability of successful vaginal delivery after cervical ripening and labor induction, and this difference was statistically significant ($P < 0.05$). This indicates that Xin Pubesheng (a drug or treatment) is more suitable for pregnant women with a well-engaged fetal head. This may be due to the presence of Frankenhauser nerve plexus in the cervix, which can be compressed by the low presenting part of the fetus, leading to stimulation of uterine contractions.[21,32] Women with a taller height generally have a larger pelvic size, which facilitates smooth passage of the fetus. The degree of cervical ripening is closely related to delivery success. If the cervix is not ripe, there is a higher possibility of resorting to cesarean section to terminate the pregnancy.[6,22,23,33]

Our findings suggest that BMI is inversely associated with induction success. However, the pathophysiological mechanisms underlying the adverse effects of obesity on childbirth are not fully understood. Garabedian et al[20] showed that the expression of oxytocin receptors increased with an increase in BMI, which may be caused by a decrease in receptor sensitivity.[6] According to the results of this study, logistic regression analysis showed that when evaluating the outcome of induction, the combination of the following five indicators: height less than 162.5 Â cm, amniotic fluid index greater than 10.65 cm, pre-release fetal head position > S-2.5, and post-administration cervical score less than 5.5 points, had higher specificity and sensitivity than each individual indicator alone in predicting cesarean section. The AUC was 0.721, which was higher than the area under the curve for each individual predictor. Therefore, a comprehensive evaluation of the multiple factors mentioned above for cervical ripening in pregnant women and pre-induction assessment may help avoid unnecessary interventions and save time.

In this study, 53.5% of pregnant women who underwent induction of labor with dinoprostone ended up having a cesarean section to terminate pregnancy, which is higher than the cesarean section rate reported by other researchers (22.5%, 24.4%, 33.7%).[18,33,34] The failure rate of cervical ripening was 55.4%.[6] This difference could be due to variations

in the inclusion criteria. Our study included pregnant women with gestational hypertension and diabetes. Among these participants, 5.9% had gestational hypertension and 72.7% of them had a cesarean section to terminate pregnancy. Additionally, 19.3% had gestational diabetes and 52.8% of them had a cesarean section to terminate pregnancy. Newborn weight is also an important factor that affects the results of induced labor. In the above studies, baby birth weights are 3142.13 ± 306.67, 3036±665, 3201±512.[13,18] In this study, the neonatal weights were 3521 (338.9) and 3625.6 (402.9), respectively. In addition, pregnant women in different study groups come from different races and countries, and pelvic differences and cultural differences will also lead to different pregnancy outcomes.[7,13,35] These data suggest that the probability of vaginal delivery is lower in women with complications during pregnancy. This is one of the reasons why the cesarean section rate after labor induction was higher in our study group than in other research teams.

The main limitations of this study are its retrospective design, possible bias, small sample size, and lack of standardized protocols. Cost-effectiveness and patient satisfaction need to be further evaluated. This study analyzed only obstetric characteristics that have traditionally been associated with the success of the induced labor process. Additionally, this study was insufficient to assess the risk of serious complications, neonatal outcomes, and the factors that predict these conditions. The conclusions of this study should be confirmed through subsequent large-scale cohort experiments.

In conclusion, dinoprostone significantly increased the induction success rate. Using this predictive model, the success of the vaginal prostaglandin sustained-release delivery system in achieving cervical maturation can be predicted by specific variables: Height, Amniotic Fluid Index, Pre-induction S- and Post-induction cervical score upon admission, through the use of this predictive model. For individuals shorter than 162.5 cm, with an amniotic fluid index greater than 10.65 cm, the fetal presentation position before induction higher than S-2.5, and a post-medication cervical score lower than 5.5, the possibility of eventually requiring a cesarean section is higher. Therefore, a thorough understanding of the various indicators in pregnant women and fetuses during cervical ripening and induction is helpful to avoid unnecessary interventions and time consumption. Incorporating this predictive model into hospital-induced labor protocols could help determine the indications for this procedure by using variables that best predict the success of cervical maturation. The management protocol could improve the quality of care, save costs, and reduce the time of oxytocin administration.

Data Sharing Statement

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

Ethics Approval and Informed Consent

All human studies were performed in accordance with the principles of the Declaration of Helsinki. Prior to starting the study, ethical approval was obtained for all protocols from The Affiliated Hospital of Northwest University Ethics Committee to confirm that the study met the national and international guidelines for research on humans. For all studies involving human participants, written consent to participate was obtained prior to commencement of the study.

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Disclosure

The authors declare no competing interests.

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