Predicting Factors on Cervical Ripening and Response to Induction in Over 37 Weeks Pregnant Women

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Abstract: Induction of labor is conducted in special fetal or maternal conditions. Labor is induced in about 20 percent of women. The aim of this study was realizing the relationship between some factors and cervical ripening and also response to induction so we could predict Induction outcome much better. The present prospective study was based on 101 pregnancy cases admitted at labor ward in Urumieh from March 2010 until December 2010. Maternal age ranges from 17 to 41 years and the gestational age between 37 to 42 weeks according to an ultrasound or reliable last menstrual period, as criteria of study inclusion. After admission, patients had vaginal speculum for R/O of PPROM, Abdominal Ultrasonography for biometry and Amniotic fluid Index, transperineal Ultrasonography for measuring fetal head distance to maternal perineum, and vaginal Ultrasonography for measuring cervical length and posterior angle of fetal head with cervix. Bishop score was assigned with another person. Labor was induced by administering either intravaginal misoprostol (25 microgram every six hours for bishop score lower than 7) or intravenous oxytocin (low dose regimen for bishop score equal to or more than 7). Misoprostol was used for 75 patients and 26 patients had induction of labor with low dose oxytocin. Eighty one patients had NVD while 20 were delivered via Cesarean Section. For cervical ripening, Bishop Score ($P<0.001$), cervical length ($P= 0.04$) and parity ($P= 0.06$) were predicting factors. The cervical posterior angle $P=0.02$ had predicting role in natural delivery. The cervical posterior angle was a predicting factor for natural delivery. Altough cervical length, BMI, and parity were not predicting factors for natural delivery, these factors were good predictors for cervical ripening.
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Introduction:

Induction means stimulating uterine contractions before spontaneous onset of labor (with or without premature rupture of membranes). Labor induction is indicated whenever its advantages for mother or embryo be more than continuing pregnancy. For such indications it is possible to mention to urgent disorders such as rupture of membranes alongside with chorioamnionitis or sever pre-eclampsia (1). Totally about 20% of pregnancies need induction to be terminated (2). Pregnancy termination by induction increases caesarean section comparing with spontaneous delivery (3, 4)by 25% in nulliparous and 5% in multiparous cases (5). It seems useful to determine caesarean risk before starting induction. The standard method of predicting response to induction is based on "Bishop score" for determining cervical ripening (6). Bishop score is defined based on scoring cervical position, cervical consistency, fatal station, cervical effacement, and cervical dilation which are subjective (1, 7). Although other studies have shown that prediction of Bishop score is weak in consequence of induction labor (8, 9). In recent years, great deal of attention has been paid to measure cervical length using transvaginal ultrasound for predicting induction result. This is an objective method (object dependent without personal bias) and lots of studies have been conducted to compare this method with Bishop score in predicting induction results and their results don't correspond (2, 10). In a lot of studies it has been found that probably high BMI(body mass index) decreases contraction due to its need to high dosage of oxytocin (2, 11-13).

There are lots of studies about lack of correspondence among results of prediction methods; Based on the results of a study by Park et al there was not a significant difference in predicting induction success between cervical length and Bishop score (14) but in study of Uyar et al it was found that in spite of direct relation between cervical length and induction

to delivery interval, there was no relationship between induction to delivery interval and bishop score (15). In study of Gomez et al it was found that cervical length was more successful than Bishop score was, in predicting induction result (16) but Eggebo et al resulted that the fetal head to perineum distance could predict induction result as cervical length and Bishop score could, but researcher claimed that none of findings above are successful to predict induction results singly (17, 18). The aim of present study was to detect the parameter which can predict cervical ripening and successful induction in term pregnancies.

Material & Methods:

In this prospective study we selected 101 samples to investigate due to sample volume determination based on previous studies (3, 9, 19, 20) and response rate of 60% and 95% confidence and 10% accuracy which needs 92 samples. Sampling was conducted in simple non-probabilistic form and the first people who referred and had inclusion criteria were selected in random. Inclusion criteria were: singleton pregnancy, pregnancy age of 37-42 weeks (pregnancy age with under 20 weeks' ultrasound or Last Menopause Period (LMP) which considered reliable), fetal membranes intact (negative Fern and Nitrazin tests) and cephalic presentation was approved. Exclusion criteria were: non cephalic presentation, vaginal bleeding, history of surgery on uterus, placenta previa, placental abruptiont, onset of labor pains, multiple gestations, macrosomia, and patient's disapproval.

Table 1. Mean and standard deviation (SD) of clinical and demographic factors among study population

Variant	Mean ± SD	Variant	Mean ± SD
Age (year)	26.7±6.35	posterior cervical angle	109.7±16.45
BMI (kg/m^2)	29.8±2.74	estimating fetal weight (gr)	3470±333.3
pregnancy age (Days)	278.42±6.35	fetal head to perineum distance (cm^2)	6.54±0.99
Parity	1.1±0.78	time from including to study till cervical ripening (min)	452.2±505.8
Bishop score	4.4±2.5	time from entrance to active phase delivery (min)	608.56±7.37
Cervix Length (cm)	2.93±0.82	time from entrance to delivery (min)	639.27±9.33
liquid index	8.98±3.51	estimating fetal weight (gr)	3470±333.3
BMI: Body Mass Index			

Study were explained to samples one by one. After inclusion to study, first Body Mass Index (BMI) was calculated for patients, and then by ultrasound (Accuvix –V ten and Hoonda HS-2100) fetal biometric was measured and AFI and diameter of the largest pocket were measured using abdominal probe. Fetal weight was estimated by Hadlock method (20). Then the distance between fetal head to mother's perineum was measured by abdominal probe using transperineal method (probe was hold transverse) (20). Then transvaginal ultrasound was performed with empty bladder and cervical length (interval of internal and external cervical canal) was measured and posterior cervical angle with fetal head was calculated by a same gynecologist (20). Posterior angle was being calculated during cervical length measurement using printed photo – according to figure. During measurement cervical length it was tried to impose the minimum load over cervix in order to prevent cervical deformation. Each time it was measured for three times and mean of measurements was considered. Then vaginal examination was conducted by another person and Bishop score was exactly determined based on its five parameters. This person had no information about result of cervical length. Cervical ripening with misoprostol (25 microgram every 6 hours in posterior fornix of vagina) was considered for patients with Bishop score of 6 and lower and induction of labor with low dose oxytocin (2 m Unit per minute) for Bishop score of 7 and more was considered.

Number of needed suppositories until cervical ripening, required time from the first suppository until cervical ripening, induction response time and entrance to active phase (cervical dilation more than or equal to 4 centimeter) were registered. Time interval between beginning cervical ripening or induction and natural delivery or caesarean was also registered as well as sex and weight and Apgar score of infant. It should be mentioned that limitation of using suppository was maximum up to2 for cervical ripening

and up to 4 suppositories (25 microgram every 6 hours) for entrance to active phase, and of induction of labor with oxytocin for 2 times, or not entrance to active phase in more than 48 hours after inclusion to study.

All information was collected by checklist and finally using SPSS 16.0 software, qualitative variables were analyzed by chi-square statistical test and quantitative variables were analyzed by t-test and significance level was set at P value ≤ 0.05 significant to determine relationship between factors and cervical ripening and response induction.

Patients were free to leave study and privacy policy was considered for patients. All stages of study were verified by Ethical Committee of Urmia University of Medical Sciences which was in accordance with Declaration of Helsinki.

Results:

In this study 101 women were included in study based on inclusion criteria and need for delivery, and descriptive information of patients was studied and their results were submitted. (Table 1)

The reason for caesarean was fetal distress in 9 cases (45%), Ceohalopelvic Disproportion (CPD) in 6 cases (30%), placental abruption in 3 cases (15%), and meconium staining of amniotic fluid in 2 cases (10%).

Patients was categorized based on their parity as: 59 persons (58.4%) were nullliparous, 20 persons (19.8%) had one, 12 persons (11.9%) had two, 6 persons (5.9%) had three, 3 persons had four (3%), and 1 person (1%) had five vaginal delivery experiences and as results show (58.4%) of patients had no vaginal delivery experience at all.

The reasons for hospitalization of patients under study have been shown in Table 2. Beside the reasons shown in Table 2 some other patients were hospitalized because of IUGR (intra-uterine growth retardation), Diabetes, Oligohydramnios, reduce fetal movement, cholestasis and Postdate.

Table 2. Hospitalization reasons and their frequency

Reason of Hospitalization	Frequency: N (%)
Low movement	37 (36.6)
Postdate	16 (15.8)
Oligohydramnios	15 (14.9)
Hypertension	14 (13.9)
Biophysical profile Low	5 (5)
Thrombocytopenia	3 (3)
Proteinuria	3 (3)

Among 101 patients, due to the definition those who had Bishop score 6 and less were 75 persons (74.3%) for whom E1 (misoprostol intravaginal) was used at the beginning of intervention for their cervical ripening, and for remaining 26 persons (25.7%) who had Bishop score ≥ 7 induction was started by 2 m Unit per minute. Patients who reached Bishop score ≥ 7 during 12 hours and examinations by required intervals were considered as successful in cervical ripening and those who had still cervical Bishop score less than 7 after 12 hours of intervention were considered as failed group in cervical ripening.

The results of comparing means of factors such as mother's age, gestational age, Gravity, parity, BMI, Bishop score (cervical score), cervical length, distance between fetal head and mother's perineum, posterior cervical angle, fetal weight estimation, amniotic fluid index, and the largest pocket with success in cervical ripening have been shown in Table 3; Bishop score with PV< 0.001 has significant relationship with cervical ripening and considering the fact that the role of Bishop score was so important by its own, affecting other parameters, it was found that after excluding Bishop score, also cervical length with PV=0.04, parity with PV=0.02, and gravity with PV Borderline =0.07, have significant relations with response to the cervical ripening.

Table 3. Comparing means of factors with success in cervical ripening (12 hours)

Factors	Mean ± Standard Deviation		P
	Successful cervical ripening (N=54)	Unsuccessful cervical ripening (N=21)	
Age (year)	27.29±9.06	25.91±6.12	0.37
Pregnancy age (day)	278.80±7.76	277.86±7.62	0.63
Gravidity	2.04±1.2	1.50±0.9	0.07
Parity	0.95±1.2	0.32±0.56	0.02
BMI	29.82±2.73	30.74±2.97	0.19
Bishop score (cervix score)	3.72±1.72	1.86±1.69	0.001
Cervix length	2.96±0.79	3.37±0.84	0.04
fetal head and mother's perineum distance	6.51±1.07	6.77±0.82	0.3
posterior cervical angle	106.33±14.91	106.68±14.38	0.9
Estimated fatal weight	3443.98±356.17	3453.55±313.56	0.9
Amniotic fluid Index	8.96±3.80	9.19±3.06	0.8
Deepest Pocket of amniotic fluid	3.72±1.51	3.27±1.51	0.8

Patients from either intravaginal misoprostol receivers group or group of induction by oxytocin, who had cervical dilation of 4 cm or more since inclusion to study till 24 hours, were placed in the group of successful response to induction. The results of comparing means of factors such as mother's age, gestational age, gravity, parity, BMI, Bishop score ,cervical length, distance between fetal head and mother's perineum, posterior cervical angle, fetal weight estimation, amniotic fluid, and the deepest pocket with success in cervical ripening have been shown in Table 4; Bishop score (PV=0.004) and BMI (PV=0.04) significantly and cervical length (PV=0.06) as borderline had a successful relationship with response to induction (Table 4).

Table 4. Comparing Means of factors with success in induction

Factors	Mean ± Standard Deviation		P
	Successful induction (N=90)	Unsuccessful induction (N=11)	
Age (year)	276.9±18.20	25.91±6.12	0.61
Pregnancy age (day)	278.60±7.42	277.86±7.62	0.48
Gravidity	1.96±1.29	1.50±0.9	0.43
Parity	0.82±1.19	0.32±0.56	0.32
BMI	29.64±2.29	30.74±2.97	0.04
Bishop score (cervix score)	4.70±2.48	1.86±1.69	0.004
Cervix length	2.88±0.83	3.37±0.84	0.06
fetal head and mother's perineum distance	6.52±1.01	6.77±0.82	0.52
posterior cervical angle	110.23±17.07	106.68±14.38	0.64
Estimated fatal weight	3468.89±332.78	3453.55±313.56	0.87
Amniotic fluid Index	8.92±3.59	9.19±3.06	0.99
Deepest Pocket of amniotic fluid	3.25±1.42	3.27±1.51	0.86

The results of comparison of different variables (mother's age, gestational age, etc.) and type of delivery have been indicated in Table 5; posterior angle (PV=0.001) significantly and amniotic fluid (PV=0.06) and amniotic pocket as borderline had relationship with natural delivery.

Afterward, in order to make a more accurate relationship between measured variables and predicting response to induction in pregnant women, occurrence of delivery during 24 hours or less, and also during 36 hours or less were evaluated. Results of comparison of different variables (mother's age, pregnancy age, etc.) and natural delivery during 24 hours are available in Table 6; Variables of Bishop score (PV=0.001), cervical length (PV=0.003), and distance of fetal head to maternal perineum (PV=0.009) had significant relation with natural delivery.

Table 5. Comparing means of factors with delivery type			
Factors	Mean ± Standard Deviation		P
	Natural (N=80)	Cesarean (N=21)	
Age (year)	26.69±6.66	26.58±5.39	0.93
Pregnancy age (day)	278.58±7.50	278.73±7.41	0.92
Gravidity	1.96±1.31	1.69±0.97	0.33
Parity	1.18±0.81	0.98±0.62	0.43
BMI	29.75±2.68	30.24±2.72	0.42
Bishop score (cervix score)	4.55±2.60	3.61±2.66	0.11
Cervix length	2.89±0.81	3.15±0.84	0.16
fetal head and mother's perineum distance	6.55±1.01	6.65±0.87	0.64
posterior cervical angle	112.57±15.90	98.23±14.02	0.001
Estimated fatal weight	3456.89±330.83	3562.35±349.61	0.16
Amniotic fluid Index	8.55±3.24	10.02±4.01	0.06
Deepest Pocket of amniotic fluid	3.10±1.22	3.63±1.68	0.08

Natural vaginal delivery during 36 hours, comparisons above were repeated (Table 7); variables of Bishop score (PV=0.001), cervical length (PV=0.04), perineum (PV=0.02), and the largest pocket (PV=0.03) had significant relation with natural delivery.

Table 6. Comparing means of factors with occurrence of delivery procedure during 24 hours			
Factors	Mean ± Standard Deviation		P
	Successful Natural Delivery (N=69)	Unsuccessful Natural Delivery (N=12)	
Age (year)	26.88±6.72	25.56±6.14	0.53
Pregnancy age (day)	279.10±7.13	276.58±8.90	0.28
Gravidity	2.04±1.37	1.50±0.79	0.18
Parity	0.90±1.25	0.33±0.49	0.009
BMI	29.60±2.62	30.60±2.95	0.23
Bishop score (cervix score)	4.94±2.51	2.33±1.92	0.001
Cervix length	2.78±0.78	3.52±0.67	0.003
fetal head and mother's perineum distance	6.51±1.03	6.76±0.87	0.38
posterior cervical angle	112.67±16.60	112±11.60	0.89
Estimated fatal weight	3445.22±339.23	3524±380.74	0.45
Amniotic fluid Index	8.40±3.14	9.44±3.80	0.31
Deepest Pocket of amniotic fluid	3.03±1.11	3.52±1.73	0.19

Rock curve was used in order to determine cut off point related to cervical length (Diagram 1) and results show that 2.2 cut off point has sensitivity of 82% and property of 91% and could be a proper cut off pint for cervical length.

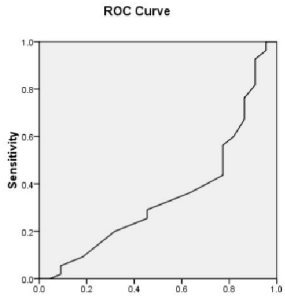

Diagram 1. ROC curve for determining cut off point related to cervical length

Table 7. Comparing means of factors with occurrence of delivery procedure during 36 hours or less

Factors	Mean ± Standard Deviation		P
	Successful Natural Delivery (N=74)	Unsuccessful Natural Delivery (N=7)	
Age (year)	26.93±6.65	24.14±6.69	0.29
Pregnancy age (day)	278.93±7.37	276.57±8.05	0.42
Gravidity	2.01±1.63	1.43±0.78	0.26
Parity	0.86±1.22	0.29±0.48	0.02
BMI	29.68±2.62	30.42±3.43	0.49
Bishop score (cervix score)	4.74±2.62	2.57±1.13	0.001
Cervix length	2.85±0.82	3.37±0.53	0.04
fetal head and mother's perineum distance	6.56±1.03	6.47±0.78	0.82
posterior cervical angle	112.64±16.45	111.86±8.76	0.90
Estimated fatal weight	3453.23±336.57	3495.57±281.37	0.74
Amniotic fluid Index	8.66±3.30	7.37±2.40	0.31
Deepest Pocket of amniotic fluid	3.15±1.25	2.54±0.58	0.03

Discussion:

In various clinical cases it is necessary to terminate pregnancy. Predicting induction success is one of the important and challenging issues, since it is always the case of question for patient and doctor. So it is important to investigate the factors affecting it. One of the most important factors is Bishop score which has been used since a long time ago. As our study showed, the role of Bishop score in predicting cervical ripening and response to induction, was more powerful than other factors.

In the study by Uyar et al, cervical length and BMI had positive relationship with interval induction to delivery time interval, while dilation and effacement had negative relationship with induction to delivery time interval. There was no relationship between induction to delivery time interval on one hand and Bishop score, parity, age, and neonatal weight in the other hand and the value of cervical length was more than other factors in predicting induction (15). But in spite of the results of this study, the role of Bishop score in predicting cervical ripening and response to induction was more powerful than other factors in our study.

In the study of Gomez et al they investigated measurement of transvaginal cervical length with Bishop score in predicting delivery induction. In this study cervical length had priority on Bishop score in predicting the success of induction and had sensitivity and property of 66% and 76% comparing wit 77% and 56% for Bishop score (16). But in contrast to the results of this study, the role of Bishop score was more significant than other factors in cervical ripening and response to induction, in our study.

In a study by Meijer-Hoogeveen et al it was found that cervical length in standing or prone positions is a stronger factor in predicting unsuccessful induction (21), rather than Bishop score, which is against our results.

In a study for comparison between Bishop score and cervical length measurement by transvaginal ultrasound method, conducted for predicting delivery successful by induction, by Jamal et al in University of Tehran, Bishop score showed a linear relation with latent phase time and induction to delivery time. Women with cervical length < 2.6 and Bishop score >3 had shorter latent phase with higher probability for delivery and both factors predict duration and type of delivery (18). These results are in accordance with that of ours.

Of course the important point is that Bishop score had not significant relationship with vaginal delivery which is our final goal, so it is necessary to start ripening and induction even in low Bishop score cases.

In our study, cervical length finds a more important role after omitting the role of Bishop score and cut off was determined equals to 2.2 based on Rock curve with sensitivity of 82% and property of 91%, but cervical cut off has been estimated > 2.6 in the study of Jamal et al in Tehran (18).

In study of Eggebo et al predicting response to delivery induction was conducted through ultrasonographic measurement of distance between fetal head and mother's perineum and comparing it with other maternal and fetal factors. In spite of our results, distance between fetal head and perineum could predict the result similar to cervical length and Bishop score, but the researcher claimed that none of findings above singly are successful in predicting induction result and further studies should show us combination of these factors (17).

In a study by Nikbakht et al, the value of measuring cervical length was compared with that of Bishop score for predicting type of delivery. Findings showed that sensitivity levels of cervical length test and Bishop score in true predicting of natural delivery are 71.6% and 53.4% respectively and properties in diagnosing caesarean are 45% and 66.7% respectively. This study concluded that there is no difference between measuring cervical length with index of 27 millimeters and Bishop score of 4 in predicting the method of pregnancy termination (19). There was a significant relationship between parity and cervical ripening in our study, as it was so in studies of Eggebo (17) and Nikbakht et al in Iran (19).

Also similar to the study of Park et al there is a significant relationship equal to Bishop score between reaching active phase and BMI, in our study. Although in our study this relationship could not be observed in predicting cervical ripening (14).

On the other hand there was no significant relationship between variable of fetal head to perineum distance and cervical ripening or reaching active phase or vaginal delivery, but in study of Eggebo distance of fetal head to maternal perineum had significant relationship (P<0.01) with delivery in 24 hours of starting induction (17). May be ethnical and regional differences are responsible for this issue.

Similar to study of Uyar et al, there was no significant relationship between the variable of fetal weight estimation and cervical ripening amount or reaching active phase or delivery, in our study (15).

Finally there was no significant relationship between variables of amniotic fluid index, mother's age, and gestational age in one hand and cervical ripening index or reaching active phase or delivery on the other hand.

After collecting data, in order to interpret variables for a better predicting, we studied the process of natural delivery in less than 24 hours, similar to the study of Eggebo (17), less than 36 hours, and more than 48 hours, separately.

Among 81 cases of natural delivery, just one case had delivery in more than 48 hours, which shows better response of pregnant women in our region comparing with that of women in a medical center in Spain in a study by Gomez in which success in induction has been defined as natural delivery during 60 hours. In the previous study in this center patients had better response to induction (16).

In the group with natural delivery during 24 hours or less, natural delivery had significant relationship with Bishop score, cervical length, and parity which was nearly similar to the next group, that is natural delivery during 36 hours or less. Also in this level, amniotic fluid index with deepest pocket of amniotic fluid had significant relationship with natural delivery in the form of borderline. It needs more investigations in this field.

Finally the interesting finding of our study was that in spite of strong significant relationship between Bishop score in cervical ripening and also reaching active phase, there was no significant relationship between Bishop score and occurrence of natural delivery. And despite of lack of significant relationship between posterior cervical angle and cervical ripening and reaching active phase, posterior cervical angle had a significant relationship with occurrence of natural delivery which was similar to the study of Eggebo (17) in which posterior cervical angle equals to or more than 90 degrees had significant relationship (P<0.005) with delivery during 24 hours after starting induction. Our study show that predicting cervical ripening or reaching active phase could be different from predicting final vaginal delivery and on the other hand regarding to lack of routine measurement of posterior angle for predicting delivery process, may be it would be possible to propose a solution for predicting final delivery result by continuing this work and conducting supplementary researches.

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