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Comparison between Fetal Fibronectin Versus Ultrasonographic Assessment of The Cervical Length in Patients with Unfavourable Cervix in Prediction of Successful Induction of Labor

Waleed M. Khalaf, Ayman A Abulnour*, Mohamed E. Mohamed, Hytham M Elhamy , Abdelrhman Mohamed Saleh
Obstetrics and Gynaecology Department, Faculty of Medicine, Ain Shams University
Corresponding Author: Waleed **M. Khalaf, Email:** waleed.khalaf1980@yahoo.com,
Mobile: +201226274935/ +966552165630

ABSTRACT

Background: When the advantages of delivery for the mother or the foetus outweigh the hazards of continuing the pregnancy, labour should be induced.

Objective: The purpose of the study was to examine the effectiveness of foetal fibronectin (fFN) and transvaginal cervix ultrasonography in predicting successful labour induction for unfavourable cervixes (Bishop score 5 or below).

Subjects and Methods: In the Maternity Centre, Faculty of Medicine, Ain Shams University, a prospective study was carried out. Patients in this study were selected from those attending in Obstetrics Outpatient Department who were nullipara pregnant women. 40 women were assessed for study eligibility and fulfilled all inclusion criteria.

Results: Mode of delivery had a significant correlation with Bishop score, while there was no discernible correlation between delivery method and transvaginal ultrasound. The bishop score was significantly correlated with fFN, all the cases with bishop 3 were negative fFN. The OSS showed insignificant relation with fFN. Also, there was no significant difference between negative and positive fFN regarding cervix (CX) length. The sensitivity of CX in prediction of successful labor induction occurring within 24 hours at cut off value of 3.11 was 50.0% and the specificity was 53.2%, and the accuracy was 51.1%. The Bishop score at cut off value of 4.0, the sensitivity was 60%, specificity was 64.5% and the accuracy was 62%. The sensitivity of fetal fibronectin in prediction of successful labor induction occurring within 24 hours at cutoff value 1.56 was 85%, the specificity was 80% and the accuracy was 82.6%.

Conclusion: Although transvaginal cervical length measurement provides an objective way to evaluate the cervix when the Bishop score is equivocal, it may not be able to predict failed inductions with enough accuracy but it can help identify women who are at risk for caesarean delivery. fFN showed a highly significant sensitivity, specificity and accuracy to predict the successful induction of labor .

Keywords: Fetal fibronectin, Ultrasonography, Unfavourable cervix, Induction, Labor, Cervical length, Nulliparous.

INTRODUCTION

When the advantages of delivery for the mother and foetus outweigh the hazards of continuing the pregnancy, we induce labour. Many recognised obstetric and medical conditions, such as chorioamnionitis and oligohydramnios, as well as maternal medical conditions, such as hypertensive disorders, preeclampsia/eclampsia, gestational hypertension, diabetes mellitus, renal disease, chronic pulmonary disease, etc., all are indications for labour induction [(1)] .

When labour is induced yet the cervix is unfavourable, there are between 22% and 24% more caesarean sections performed [(2, 3)]**.** Preinduction Bishop score is the only technique now used to anticipate if a successful vaginal birth will result from an induced labour [(4)]**.**

Within seven days, sonographically measured cervical length and fetal fibronectin (fFN) in cervicovaginal secretions show potential in predicting premature birth according to growing data [(5)].

Numerous researches assessed the accuracy of using sonographic cervical length evaluation to gauge how well a labour induction will go. It is still unknown how ultrasound examination would be used to choose women who will have effective inductions [(6)].

The possibility that nulliparous women undergoing labour induction will make progress is independently predicted by transvaginal sonographic assessments of cervical length. These findings firmly establish that preinduction cervical length in nulliparous women undergoing labour induction significantly influences labour progression only during the latent period of labour, not the active phase [(7)].

It is not recommended to use the Bishop score to determine whether to induce labour because it is a poor predictor of the results of doing so at term [(8)].

Large glycoprotein known as fibronectin, with a molecular weight of roughly 420 kDa, is often found in virtually all tissues and bodily fluids. Its main functions are in phagocytosis and cell adhesion [(9)].

Foetal fibronectin (fFN) is a glycoprotein that is infrequently present in cervicovaginal secretions in the late second and early third trimesters and serves as an adherent at the maternal-fetal interface. Despite the fact that foetal fibronectin has only been studied as a qualitative test, with a result of 50 ng/dL or higher being considered positive, the risk for preterm birth grows as the level of foetal fibronectin rises . A positive test typically indicates that the maternal-fetal decidual bond has been broken. A positive foetal fibronectin test was observed to increase the chance of preterm birth before

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35 weeks in asymptomatic women, particularly in the first two weeks after the finding. Although, the fibronectin test at 22 to 24 weeks was only 25% sensitive for all spontaneous deliveries occurring before 35 weeks, one study found that sensitivity for births occurring before 28 weeks was 65% [(10)].

Qualitative and quantitative fast-reactive fFN assays have been developed for the common clinical practise of anticipating preterm delivery and premature rupture of membranes (PROM) [(11)]. For cervical assessment prior to labour induction, fFN has been suggested as a novel tool. A substantial chance of labour induction success is produced when fFN is present in cervicovaginal secretion of term births. Induction of labour should not be tried in women who have cervicovaginal discharge that is fibronectin negative and a poor cervix score [(12)].

AIM OF THE WORK

This study aimed to forecast whether an unfavourable cervix (Bishop score of 5 or less) would be successfully induced into labour and to evaluate the effectiveness of fFN versus transvaginal ultrasonography of the cervix.

MATERIAL AND METHODS

At the Maternity Hospital of Ain Shams University, this prospective study was carried out through the period from January 2019 to January 2020. It included 40 pregnant women who were recruited for induction of labor from those women attending Outpatient Clinic and ER of ASUMH after fulfilling inclusion criteria.

Inclusion criteria: The study comprised women who were primigravidae and carrying a singleton, with gestational ages ranging from 37 to 42 weeks, cephalic presentations, Bishop scores of 5 or less, and no clinical signs of regular contractions, as well as those who had signs that labour should be induced.

Exclusion criteria: Patients who have a ruptured membrane and vaginal haemorrhage, or any other condition that makes vaginal delivery impossible like malpresentation, contracted pelvis and soft tissue obstruction.

Sampling:

Foetal fibronectin is associated with vaginal birth within 24 hours (OR=6.1) according to a prior study (Uygur et al., 2016), hence the needed sample is 40 cases. Sample size was estimated to be 40 women by utilising the PASS programme, setting alpha error at 5% and power at 80%.

Methods:

Counselling on all study steps was given to all participating ladies with full explanation of procedure. History taking, which comprised personal, obstetric, medical, and surgical histories as well as the past menstrual cycle. Examination: General examination that included blood pressure, heart rate and temperature. Bilateral lower limb examination. Abdominal examination including inspection fundal level and any previous scar. Palpation of Fundal level to detect gestational age using ulnar border of left hand. Fundal grip to detect presentation using palm of both hands. Umbilical grip to detect position using both hands placing on both sides of uterus at level of umbilicus. Pelvic grip to confirm position. Auscultation of fetal heart sound. U/S for confirmation of gestational age, presentation and viability. Non-stress test was performed prior to the induction process to exclude fetal distress. The posterior vaginal fornix was sampled using a Dacron swab, and samples were then tested for fFN using a qualitative fast responding immunoassay with a +ve cutoff value set at 50 ng/ml or greater and reviewed at the bedside. The passage of specimens via a membrane containing an anti-fFN monoclonal antibody. Results are positive when a coloured spot becomes apparent after five minutes. After that we performed digital examination to evaluate Bishop score. Bishop score 5 or less were considered unfavorable cervix and included in our study and we did transvaginal ultrasonography for evaluation of cervix. A 6.5-MHz transvaginal probe was employed with a logic C5 ultrasound machine.

Internal to external os were used to measure the cervical length. We avoided compression of cervix with the probe as it lengthens the cervical measurement. The internal and external cervical os were simultaneously visualised as the cervical length was measured using ultrasound in the sagittal plane along the length of the endocervical canal. The cervical length was determined to be the shortest of three measurements.

Using 25 g of vaginal misoprostol (PGE1), repeated every 4 hours up to a maximum of 3 doses, preinduction cervical ripening was carried out. We evaluated cervical dilation and doing amniotomy and if there is no efficient contraction we will give oxytocin. Starting at 2 mU/min, oxytocin was raised by 2 mU/min every 30 minutes until labour had begun. Then labor was followed up according to the protocol of the hospital.

Ethical and legal aspect:

Detailed informed written consent was given to participants including their rights, nature, objectives, benefits and hazards of the study in a form understandable for her in Arabic language containing all locally required data and specifications. The original form was signed by personally dated signature, then retained by the investigator. If any woman was unable to read, oral presentation and explanation of the written consent in the presence of impartial witness would be available. Alternatively, the participant could use the thumbprint or a mark in presence of witness who

would also sign and personally date it. Nothing done till a valid consent was obtained. The protocol and any corresponding element according to the local regulations was approved before the beginning of the study by the Obstetrics & Gynaecology Department Council, Faculty of Medicine, Ain Shams University Ethical Committee.

This study was registered on clinical trial.gov, no. NCT03925922. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

Data were loaded into the computer using the IBM SPSS software programme, version 20.0, for the statistical analysis of the data. Number and percentage were used to describe qualitative data.

The Chi-square test was used to compare differences in categorical variables between several groups. Mean and standard deviation were used to explain quantitative data for regularly distributed data. Median, minimum, and maximum were used to communicate data with an aberrant distribution. For normally distributed data, the independent t-test was used to compare two independent populations, and the F-test (ANOVA) was used to analyse more than two populations. Results of significance tests are expressed as two-tailed probability. At the 5% level, significance of the results was determined. At $p \leq 0.05$, correlation was deemed significant.

RESULTS

The age of our patients ranged from 20-38 with a mean value of 28.93 □□5.42 years. The gestational age ranged from 39-42 with a mean value of 40.45 □□0.68 weeks. The estimated fetal weight ranged from 2900 - 3600 with a mean value of 3162.50 □□186.31 gm. The Bishop score ranged from 3-5 with a mean value of 4.3 □□ 0.71.

The radiological findings show that closed OS was 27 (67.5%) followed by funneling 10 (25%) and closed internal was 3 (7.5%). CX length ranged from 2-4.5 cm with a mean value of 3.64 □□0.70 cm. The Positive fFN was positive with 26 (65%) and negative fFN was 14 (35%). The mode of delivery. LSCS delivery was 21 (52.5%) and vaginal delivery was 19 (47.5%).

The results of relation between mode of delivery and different studied variables found that there was statistical significant relation between Bishop and mode of delivery ($P < 0.05$). There was no statistical significant relation between OS and mode of delivery ($P > 0.05$) .

According to table (1), there was no statistically significant relationship between the length of the CX and the mode of delivery ($P > 0.05$).

Table (1): Relation between Bishop Oss, fFN and CX length in relation to mode of delivery

		Delivery				**TestP**
		NVD		**CS**		
		No.	**%**	**No.**	**%**	
Bishop	**3**	0	0.0	5	22.7	X^2= 5.4880.023*
	4	3	16.7	5	22.	
	5	15	83.3	12	54.5	
Oss	**Closed**	12	66.7	15	68.2	X^2=0.2690.872
	Closed internal	1	5.6	2	9.1	
	Funneling	5	27.7	5	22.7	
fFN	**Positive**	15	83.3	11	50.0	X^2=4.835
	Negative	3	16.7	11	50.0	0.029*
CX length (cm)	Range	2.00-4.00		2.00-4.50		**T=** 0.445
	Mean	3.5556		3.7045		0.509
	SD	0.70479		0.70134		

The relation between fetal FN and other variables showed that there was statistical significant relation between Bishop and FFN (P < 0.05). There was no statistical significant relation between OS and FFN (P > 0.05). Also, there was no statistical significant relation between FFN and CX length (P> 0.05) as shown in table (2).

Table (2): Relation between FFN and Bishop, OSS and CX length

		FFN				
		Positive		Negative		Test P
		No.	%	No.	%	
Bishop	**3**	0	0.0	5	35.8	$X^2$11.4080.029*
	4	7	26.9	1	7.1	
	5	19	73.1	8	57.1	
Oss	**Closed**	20	76.9	7	50.0	$X^2$3.289
	Closed internal	1	3.8	2	14.3	0.201
	Funneling	5	19.2	5	35.7	
CX length (cm)						
Range		2.00-4.50		2.50-4.50		
Mean		3.7115		3.5000		**T**0.833,0.367
S.D.		0.68078		0.73380		

Table (3): Sensitivity, specificity and accuracy of CX length and Bishop and fetal fibronectin in prediction of successful labor induction occurring within 24 hs.

Variables	Area	Cutoff value	Asymptotic Sig. b	Asymptotic95%ConfidenceInterval	
				Lower Bound	Upper Bound
CX length	0.582	3.11	.395	0.389	.776
	sensitivity			50.0	
	Specificity			53.2	
	Accuracy			51.1	
Bishop	0.628	4	.187	0.429	.826
	Sensitivity			60.0	
	Specificity			64.5	
	Accuracy			62.0	
FFN	0.836	1.56	0.0001*	0.713	.958
	Sensitivity			85.0	
	Specificity			80.0	
	Accuracy			82.6	

Table 3 showed that Foetal fibronectin demonstrated significantly considerable sensitivity 85%, specificity 80% , and accuracy 82.6 % to forecast the effectiveness of labour induction.

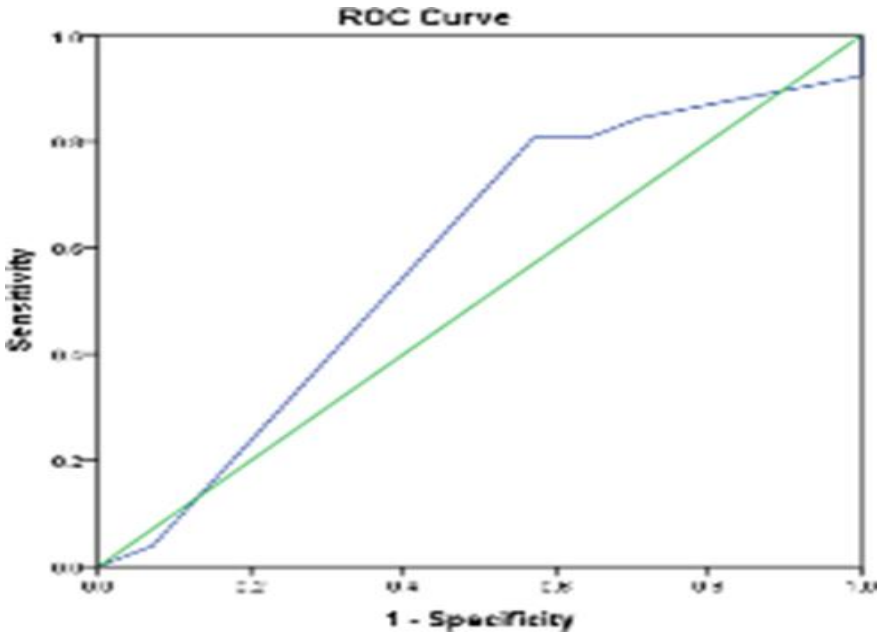

Figure (1): ROC curve to assess the CX length's sensitivity, specificity, and accuracy in determining the method of delivery. It showed reduced sensitivity and and specificity of CX length in determining the method of delivery .

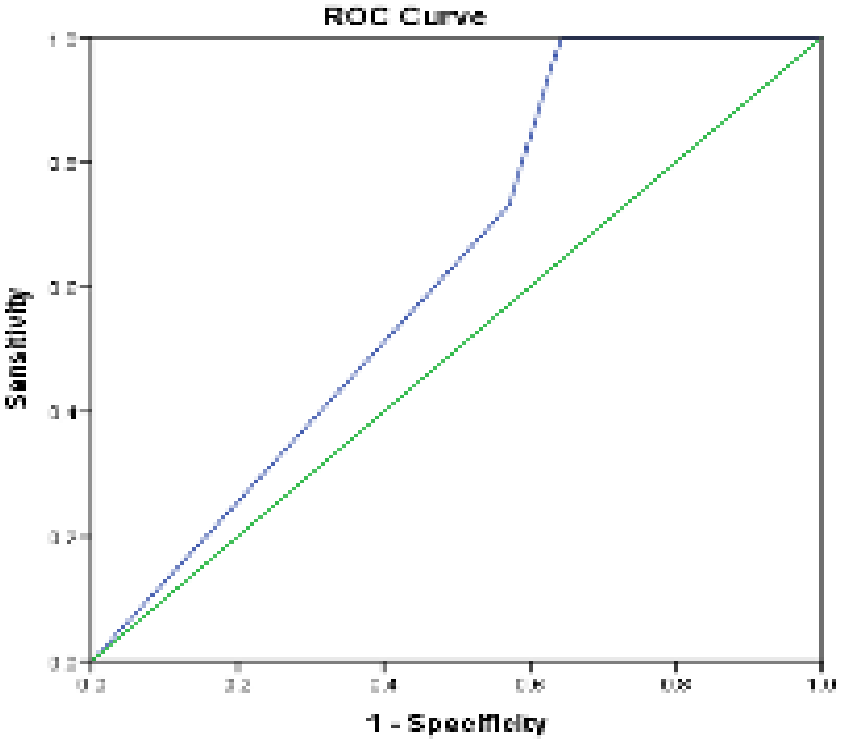

Figure (2): Bishop's ability to predict the mode of delivery is measured by the ROC curve for sensitivity, specificity, and accuracy. It showed that Bishop's score is having a better sensitivity and specificity in prediction of mode of delivery .

DISCUSSION

Based on the findings of our study, the cervical length ranged from 2.0–4.0, with a mean of 3.64 ± 0.70 cm, and the bishop score ranged from 3-5, with a mean of 4.01–0.31. In 26 cases (65.0%), the foetal fibronectin level was positive, while it was negative in 14 cases (35.0%). In our study's positive fFN 26 cases, 15 cases delivered naturally, while the 11 cases delivered by C.S., the 15 women who underwent normal delivery, 12 cases (80.0%) of whom gave birth within 24 hours, while the other 3 cases (20.0%) took longer. Ten of the negative 14 cases of fFN had CS deliveries, whereas the other four had normal deliveries.

The sensitivity, specificity, and accuracy of many examined markers to forecast a successful labour induction occurring within 24 hours were demonstrated in this study. Regarding cervical length, the accuracy was 51.1%, the specificity was 53.2%, and the sensitivity was 50.0% in predicting successful labour induction occurring within 24 hours.

The sensitivity, specificity, and accuracy of the Bishop score at the threshold value of 4.0 in predicting a successful labour induction within 24 hours. Bishop score's accuracy was 62.0%, specificity was 64.5%, and sensitivity was 60.0% in predicting labour.

Foetal fibronectin had a cutoff value of 1.56 for the sensitivity, specificity, and accuracy of predicting successful labour induction within 24 hours. Foetal fibronectin was 85.0% sensitive, 80.5% specific, and 82.0% accurate in predicting labour. The significance of fFN as a marker for delivery inside 24 hours of labour induction was verified in our investigation, but funneling, transvaginal ultrasound assessments of cervical length, and Bishop score could not accurately predict effective labour induction. For cervical assessment prior to labour induction, fFN has been suggested as a novel tool. Our findings are in line with those of **Dilek *et al*. [13],** who looked at 73 nulliparous women who were having labour inductions at term and had Bishop scores below 5. Vaginal birth 24 hours after the induction period began was considered a successful labour induction. By using an immunoassay, fFN from vaginal secretion was measured. They came to the conclusion that the fFN in the vagina predicts the effectiveness of labour induction in cases with unfavourable cervixes. We also concur with **Garite *et al*. [14]** who reported the existence of fFN in the cervicovaginal secretions of term babies as a means of enhancing the likelihood of a successful induction [14]. Additionally, they came to the conclusion that labour i nduction should not be tried on women whose cervicov aginal secretions tested negative for fibronectin and wh o also had a poor cervix score.

In a study involving 160 nulliparous women wit h low Bishop scores, it
was discovered that the presence of cervicovaginal fFN independently anticipated a fruitful induction of labour [14, 15]. However, **Reis *et al.* [16]** observed that just obstetric history and digital evaluation were independently linked with labour length and could correctly anticipate vaginal birth within 24 hours. However, those authors were unable to determine the prognostic usefulness of fFN and ultrasound data. Similar to that **Sciscione *et al*. [17]** reported that fFN was unable to anticipate vaginal birth in nulliparous ladies who needed preinduction cervical softening [17].

Bishop score, parity, and patient age were the only factors that were independently related with a successful induction. According to **Droulez *et al.* [18]** in a prospective trial, which included 234 patients. The section rate and cervical fibronectin levels were not significantly correlated. Additionally, fFN is not accurate in predicting inducibility at term, according to **Ojutiku *et al.* [19]**.

The supravaginal part of the cervix typically makes up about 50% of the cervical length, thus theoretically, transvaginal ultrasonography could provide more precise information than digital inspection. Additionally, in a closed cervix, it is challenging to assess effacement. A small number of publications do, although of the presence of conflicting findings. In some of these investigations, the association between cervical length and Bishop score and the length of the latent phase was the main focus rather than the delivery method. Only the latent phase of labour is connected with ultrasonography cervical length, according to **Boozarjomehri *et al*. [20].**

According to research by **Ware and Raynor [21]**, the Bishop score and cervical length both have similar predictive values for labour length. They discovered that among women with a cervical length of under 26 mm, labour lasted less time. Contrarily, the logistic regression model of **Gonen *et al.* [22]** showed that the only factors significantly connected with vaginal delivery and labour duration were the Bishop score and parity, not cervical length. **Grimes *et al.* [23]** created a ROC curve for a newly derived Bishop score that was derived using the TV US rather than the cervical length determined by a vaginal examination. The optimal cut-off number showed less sensitivity than the conventional Bishop score (60% vs. 76%), despite the fact that the AUC of this new score was not significant. This finding emphasises the value of incorporating multiple ultrasonic parameters like cervical funneling, posterior cervical angle, and foetal head-perineum distance which can replace the parameters of Bishop score and provides indirect evidence of the importance of other individual Bishops score parameters than cervical length alone in predicting successful induction.

CONCLUSIONS

In conclusion, transvaginal cervical length measurement is an objective way to evaluate the cervix when the Bishop score is equivocal, but it may not be able to forecast failed inductions with enough accuracy. However, it can help identify women who may need a caesarean delivery. Foetal fibronectin, on the other hand, demonstrated significantly considerable

sensitivity, specificity, and accuracy to forecast the effectiveness of labour induction.

List of abbreviations

1. **OPD:** Outpatient department.
2. **fFN:** Fetal fibronectin. **3.** CX: cervix.
4. **PROM:** Premature rupture of membranes. **5. PGE1:** Prostaglandin E 1 analogue.
6. **CS:** Caesarean delivery. **7. AUC:** Area under the curve.

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