Diagnostic Accuracy of Fetal Fibronectin Test In Prediction of Preterm Labor

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ABSTRACT

Objective — *To determine the diagnostic accuracy of fetal fibronectin test in detection of preterm labor.*

Study design — *Cross sectional observational study.*

Place & Duration of study — *Department of Obstetrics and Gynaecology Unit 1, Jinnah Postgraduate Medical Centre Karachi, From June 2014 to December 2015.*

Methodology — *All patients with preterm labor, meeting inclusion criteria were included after taking detailed history and physical examination. Purpose and procedure explained to patients and an informed consent taken. Fetal fibronectin test was performed. Age, gravida, parity, gestational age, newborn weight and fetal fibrinoectin test were taken as variables. Patient were monitored and followed up for timing of delivery.*

Results — *A total of 100 patients were included. Mean age of the participants was 35.49±5.7 year. Seventy-five (75%) were gravida of <3 and 25 (25%) grandmultipara. Mean gestational age was 31.36±2.6 weeks. Sixty-one (61%) women were hospitalized, 55 (55%) received steroids and 90% received tocolysis. Fifty-seven (57%) women delivered after 14 days of steroids and/or tocolysis. A total of 60% newborns weigh <2 kg and 40% weigh >=2 kg. The accuracy of fibronectin test in prediction of preterm labor was 75%.*

Conclusion — *Fibronectin test helped in prediction of preterm labor in 75% of pregnant women.*

Key words — *Preterm labor, Fetal fibronectin, Preterm birth.*

INTRODUCTION:

Preterm labor is defined as labor before 37 week of gestation. Preterm birth is a serious obstetric issue worldwide.[1] It is the major cause of neonatal morbidity and long term disability as well as neonatal death in developed countries.[2] Preterm birth accounts for 75% to 80% of all perinatal mortality and 50% of neurological morbidity.[3]

According to WHO report the incidence of preterm birth in Pakistan is about 37 %.[4] Awareness of women about the risk for preterm delivery is challenging and important in term of neonatal outcome. Precautionary measures can be taken to delay delivery with favorable outcome which include in utero transfer, tocolysis and corticosteroid therapy.[5] On the other hand an incorrect diagnosis of preterm labor may lead to inappropriate interventions such as hospitalization and unnecessary use of corticosteroids, tocolytics, antimicrobial drugs which may have potential risk to the mother and fetus in addition to social and financial costs of hospitalization. Obstetric history and risk factors alone remain unreliable in making diagnosis and identifying women at risk.[6] Fifty percent of admitted women with suspected preterm labor keep continue their pregnancies to term (false preterm labor). Currently the most effective test for diagnosing preterm labor is fetal fibronectin test (FFN).[7]

Fetal fibronectin is a high molecular weight basement membrane protein produced by the fetal membranes. It is believed to serve as biological glue that binds the placenta and membranes to the deciduas during

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a normal pregnancy. It is commonly found in the cervix and vagina until 16-20 weeks gestation. Researchers have been studying the presence of fetal fibronectin in the cervical vaginal secretions and the levels of > 50ng/ml between 24 to 35 weeks of gestation is considered abnormal and is associated with preterm delivery in symptomatic patients.[6]

According to recent systematic review, fetal fibronectin test was found superior in diagnosing preterm birth within 7-14 days of test in patients of threatened preterm labor.[2] The sensitivity of fetal fibronectin test was found to be 76.1 % and estimate of specificity 82%.[8] Inability to identify these patients may result in the failure to implement valuable obstetric measures.[2] This study aimed to detect women having preterm labor with fetal fibronectin test.

METHODOLOGY:

This study was conducted in the Department of Obstetrics & Gynaecology Unit 1, Jinnah Postgraduate Medical Centre Karachi, from June 2014 to December 2015. Approval was taken from ethical committee. A total of 100 patients with preterm labor were enrolled in the study. Patients with signs and symptoms of preterm labor (uterine contractions occurring 4 in 30 minutes, cervical dilatation <3 cm, intact membranes), gestational age between 24-35 weeks, regardless of the age and parity, were included in this study. Women with digital vaginal examination, vaginal bleeding and sexual intercourse in the preceding 24 hours, patients known or suspected of having placenta previa, multiple gestations and cervical cerclage were excluded. The purpose and procedure were explained to the patients. An informed consent was taken from each patient.

A complete history and detailed physical examination was done. Fetal fibronectin test was performed. The test was performed by using test tube with one ml of buffer solution, applicator and test strip. It is a two-step procedure. The first step obtains the cervico-vaginal secretion by applicator during speculum examination. The applicator is immersed into buffer solution. When two red lines appear on the strip, it means the test is positive and if one line appears, it means test is negative. The patient was followed up closely to determine whether she delivered within or after 14 days.

Data was analyzed by using computer package SPSS version 11.0. Clinical characteristics were summarized in terms of frequencies and percentages for categorical variables such as gravida, parity, fetal fibronectin test, whereas continuous variables like age, gestational age and weight were presented as mean and standard deviation. Stratification with respect to age, gestational age, gravida, and parity was done to find the effect of these on outcome variables. Post stratification Chi-square test was applied. A $p<0.05$ was be taken as significant. Outcome variables that are true positive, true negative, false positive, false negative, PPV, NPV and diagnostic accuracy of fetal fibronectin test in detection of preterm labor were measured in frequencies and percentages.

RESULTS:

A total of 100 patients were enrolled in this study during study period. Mean age of the participants was 35.49±5.7 year. Fifty-two (52%) women were above 35 year of age. Seventy-five (75%) patients were gravida <3. Sixty-seven (67%) had parity of <3. Mean gestational age was 31.36±2.6. Sixty-one (61%) women were hospitalized, 55 (55%) received steroids and 90% received tocolysis. Fifty-seven (57%) women delivered after 14 days of steroids and / or tocolysis. A total of 60% newborns weigh <2 kg. The accuracy of fibronectin test in prediction of preterm labor was 75% (table I). Stratified analysis of accuracy of fibronectin test in prediction of preterm labor is shown in table II.

DISCUSSION:

Preterm delivery (PTD) is a serious issue which has great impact on maternal as well as on neonatal health. Previously obstetrical history, demographic features and signs and symptoms were considered to identify patient at risk of preterm delivery but none of them were found to be sensitive and specific.[9] Different biochemical markers were tested and different diagnostic modalities used, but it is still a

Table I: Accuracy of Fibronectin Level In Prediction of Preterm Labor

fFN Test	Preterm Labor		Total	Sn (%)	Sp (%)	PPV (%)	NPP (%)	AC (%)
	Yes	No						
Positive	35	17	52	81.4	70.2	67.3	83.3	75
Negative	8	40	48					
Total	43	57	100					

Table II: Accuracy of Fibronectin Level In Prediction of Preterm Labor

	fFN Test	Preterm Labor		P-value	Sn (%)	Sp (%)	PPV (%)	NPP (%)	AC (%)
		Yes	No						
By Age < 35 Year	**Positive**	19	5	0.018	65.5	73.7	79.2	58.3	68.7
	Negative	10	14						
By Age > 35 Year	**Positive**	21	3	<0.001	75	87.3	86.5	74	80.7
	Negative	7	21						
By Parity <3	**Positive**	23	2	<0.001	65.5	93.8	92	71.4	79
	Negative	12	30						
By Parity >3	**Positive**	17	6	<0.001	77.3	45.5	73.9	50	66.7
	Negative	5	5						
By Gravida <3	**Positive**	28	5	<0.001	68.3	85.3	84.8	69	76
	Negative	13	29						
By Gravida >3	**Positive**	12	3	0.014	75	66.7	80	60	72
	Negative	4	5						
By Gestational Age 24-30 Weeks	**Positive**	15	3	<0.001	75	81.2	83.3	72.2	77.8
	Negative	5	13						
By Gestational Age 31-35 Weeks	**Positive**	25	5	<0.001	73	78.3	82.7	71.1	73
	Negative	12	22						

Key: sn**=**sensitivity, sp=specificity, PPV=positive predictive value, NPV=negative predictive value, AC=accuracy, PTD=preterm delivery, fFn=fetal fibrinoectin

matter of debate that which of the women are at risk, and if diagnosed, its management to prolong the pregnancy is challenging.[10] Recently one of the greatest advances in prediction of preterm labor is fetal fibronectin measurement in cervicovaginal secretions.[11] this test can be performed alone or it may be combined with assessment of cervical length through transvaginal ultrasound.

Fetal fibrinoectin concentration is increased in vaginal secretions when there is disruption of choriodecidual junction and its concentration is measured.[12] A positive result suggests the possibility of imminent preterm birth and a negative test indicate great chance (>95%) of remaining undelivered.[13] This test can be repeated on weekly interval in high risk cases. This test is simple, easy and usually pain free. According to one systematic reviews, fetal fibrinoectin test is a reliable indicator of spontaneous preterm delivery before the dilatation of cervix[14]. This test can be performed below the gestation of 35 weeks.[15] Number of false positive results is increased when the test is done in presence of blood in vagina or after digital vaginal examination and intercourse.[16]

In our study we found that the sensitivity of fetal fibronectin in prediction of preterm labor was 81.4%, specificity of 70.2% and accuracy of 75%. In a study it was found that the sensitivity of fetal fibronectin test was 76.1% and specificity was 82%.[8] The negative predictive value in our study was 83.3% which is quite high and suggests that fetal fibronectin is a good test for prediction of preterm labour. Another study reported sensitivity of 93%, specificity of 82%, PPV of 29% and NPV of 99.5% while our study showed PPV of 67%.[3]

The accuracy of fibronectin can be determined by its effectiveness in detection of preterm labor and it will help in decision making for the selection of patients, who really require intervention like administration of corticosteroid in threatened preterm labor.[17,18] The maximum benefit of antenatal steroids can only be achieved when delivery occurs within 6 days of administration thus proper identification of true labor is needed.[19] By the help of this test we can filter out all those cases in whom preterm birth is imminent. In our study almost all patients received steroids who were symptomatic without knowing fibronectin test. If we had administered steroids after the results, this figure would have been remarkably low. Similar finding was also observed in a systematic

review by Honest et al.[20] Thus this test enable provider to be more confident in decision making about intervention Future research should focus on undertaking high quality primary studies that test accuracy to improve our ability to predict spontaneous preterm birth.

As fetal fibrinoectin test has high sensitivity and specificity to predict true labor. We found significantly low rates of admission. This finding is consistent with other study.[21] With this test the unnecessary admissions, undue administration of corticosteroid, tocolysis and in- utero transfer can be avoided. Fetal fibrinoectin test is not only cost effective but also reassuring for both clinician and patients.

CONCLUSION:

The accuracy of fetal fibronectin in prediction of preterm labor was high with acceptable specificity.

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