ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Cervico Vaginal Fluid Fibronectin Level in Assessing Risk of Preterm Labour.

Vidya A Gaikwad[1], Unnati G Rajput[2], and Mangal S Puri*.

Department of Obstetrics and Gynaecology, Padmashree Dr.D.Y. Patil Medical College, Hospital and Research centre, Pad. Dr. D.Y. Patil University-Pimpri, Pune, Maharashtra, India

ABSTRACT

In the era of modern obstretics where there has been rapid advancement in all specialities preterm labor still remains enigma for an obstretician today. The clinicians are in need of a test which could diagnose preterm labour with fair degree of accuracy.Detection of fetal fibronectin from cervico vaginal secretions has a very high positive predictive value and a low negative predictive value thus providing a useful tool in hands of clinician to avoid perinatal mortality, fetal wastage and post delivery expenses of NICU. 30 cases were screened in gestational age of 22-34 weeks who attended tertiary care hospital. High cervico vaginal swab was taken in patients presented with pain in abdomen, heaviness in pelvis or backache. Patients presenting with threatened preterm labor, who are fetal fibronectin test positive would be ideal candidates for admission and interventional therapy like bed rest, tocolysis and antibiotics to possibly delay preterm labor where facilities for conducting delivery are not available or skilled person are absent, this simple bedside test can be used as a guideline to refer these patients to higher centre.Thus by including this test in the protocol management of threatened preterm labor, fetal wastage can be avoided. However it is too premature to recommended this test as a routine because the study group is small.

Keywords: Preterm labour, fetal fibronectin, perinatal mortality.

Corresponding author

ISSN: 0975-8585

INTRODUCTION

Preterm labor is a challenging issue for the obstetricians even today and a largest contributor to the perinatal morbidity and mortality throughout the World. With improvement of neonatal care, there has been a dramatic improvement in neonatal survival rates of preterm infants. But neonatal intensive care unit (NICU) care is expensive and a preterm baby is at an increased risk of many complications like respiratory distress syndrome (RDS), hyperbilirubinemia, sepsis, learning and behavioral difficulties, hearing loss, retinopathy of prematurity, etc [1,2], leading to not only a medical and social problem, but also an economic burden.

Complications of preterm birth are the single largest direct cause of neonatal deaths, responsible for 35% of the world's 3.1 million deaths a year, and the second most common cause of under-5 deaths after pneumonia [3].Therefore all efforts to be directed towards early diagnosis and prevention of preterm labor and preterm birth.

At the other hand overzealous diagnosis of threatened preterm leads to unnecessary admission in hospital, over use of steroids and tocolysis and thus increases the financial burden on patient. Hence, the clinicians are in need of a test which could diagnose preterm labor with fair degree of accuracy.

Fetal fibronectin (fFN) has been very widely studied over the last 14 years as a potential marker for the selection of patients who require intervention for true preterm labour [4]. Fibronectin is an extracellular protein in association with basement membranes at chorio-decidual layer. It can be detected in the cervicovaginal secretions of women in early pregnancy [5]. In a normal pregnancy it becomes no longer detectable after 24 weeks of gestation because the fetal membranes are isolated from the upper vagina and lower cervix by the thick secretions within the cervical canal. However, as labour approaches, it reappears in cervicovaginal secretions because of separation of the membranes from the decidua in the lower uterine segment, cervix and vagina, giving rise to biochemical marker indicating delivery. It has been proposed that the presence of fFN in the cervicovaginal fluid after 24 weeks is a marker for preterm labour [6].

MATERIALS AND METHODS

The study was started at a Tertiary care centre and teaching hospital from April 2011 to November 2013.

30 antenatal patients in the gestational age of 22-34 week with symptoms of threatened preterm labour who were admitted in hospital for treatment were included in the study.

Quik Check fFN test kit, made in UK was used to detect the presence of fFN in cervicovaginal secretions. It is a bedside test where cervicovaginal swab was taken from posterior fornix in patients between 22-34 weeks of gestation with diagnosis of preterm labour.

Ethical committee permission was taken for the study. Each woman was counselled and informed consent was taken before the vaginal swab was taken.

Patients complaining of heaviness in pelvis and pain in abdomen due to uterine contractions with singleton pregnancy were included in this study.

Patients giving history of coitus within 24hr, use of betadine or lubricant gelly, PVexamination, TVS (trans vaginal ultrasound) were excluded from the study to eliminate false positive tests. Patients with abruption placenta, placenta previa, moderate to gross PV bleeding, cervical encerclage, PROM, active labor(more than 3 cm dialatation) and multi fetal gestation were excluded from the study.

Test is performed as discussed below: Polyester tipped swab stick is provided in the specimen collection kit. During speculum examination, swab is lightly rotated across posterior fornix of vagina for 10-15 seconds to absorb cervicovaginal secretions. Now remove swab and insert the tip into test tube with buffer. Mix vigorously in the buffer for 10-15 seconds. Discard swab. Insert test strip (dip area indicated by arrow) into the buffer for exactly 10 minutes. Remove test strip and read results.

This assay can only be used for the qualitative detection of fetal fibronectin in cervicovaginal secretions.

A positive result indicating the presence of fetal fibronectin will appear as two lines. Lines may vary in appearance from very faint to very dark. If no lines appear or if the control line does not appear, the test was repeated.

All patients irrespective of positive or negative results were admitted for 7 days and given following treatment.

- Complete bed rest.
- Corticosteroids- Betamethasone 12mg, 12 hourly IM (2 dose).
- Tocolysis – NTG (Nitroglycerine) patch 5mg, 12 hourly for 72 hours.

All patients were admitted for 1week and given treatment. After 1week discharged and called for follow up every 15 days till delivery and weekly follow up was kept by telephonic communication. Patients were observed till delivery.

DISCUSSION

In our study, we included symptomatic patients of preterm labour with intact membranes. These patients were admitted to the hospital to rule out preterm labour and the presence of cervicovaginal fetal fibronectin made it possible for us to distinghuish between those with irrelevant uterine contractions and those at true risk for preterm delivery.

Simple bedside test was used to detect fFN from cervicovaginal secretions by taking a swab from posterior fornix between 22-34 weeks of gestation in 30 patients with preterm labour admitted in antenatal ward between July 2011 to September 2013.

Out of 30 patients of preterm labour, 43.3% (13 patients) presented between 30-34.6 weeks and 30% (9 patients) were between 27-30.6 weeks of gestation as shown in Table 1.

Table 1: Gestational Age(GA) wise distribution of cases in study group

GA (Wks)	No. of cases	Percentage (%)
22 – 26.6	8	26.7
27 – 30.6	9	30
31 – 34.6	13	43.3
Total	30	100

Studies conducted by Gulati A et al reported that mean gestational age at which maximum patients presented with preterm labour was 31.5 weeks, which is comparable to this study [7].

Out of 30 patients 50% (15) patients had cervical changes on digital examination and thus diagnosed as established preterm labour. Rest 50% (15 patients) patients were of threatened preterm labour, without cervical changes as shown in Table 2.

Table 2: Cervical changes wise distribution of cases in study group

Cervical change	No. of cases	Percentage (%)
Present(established PTL)	15	50
Absent(threatened PTL)	15	50
Total	30	100

We used fetal fibronectin test (fFN) as a predictor of preterm labour in our study of 30 patients. Patients with positive test results are at increased risk of preterm delivery within 7-14 days of test. Out of 30 patients fFN was negative in 83.3% (25 patients) and positive in 16.7% (5 patients) cases as shown in Table 3.

Table 3: fFN wise distribution of cases in study group

fFN	No. of cases	Percentage(%)
Positive	5	16.7
Negative	25	83.3
Total	30	100

Out of 5 patients who had fFN positive 4 patients (80%) had associated cervical changes on admission.

Out of 25 patients with negative fFN 11 patients (44%) had associated cervical changes on admission. Whereas 14 patients (56%) had no cervical changes. However presence of

cervical changes and fFN test results were not statistically significant as P value was >0.05 as shown in Table 4a.

Table 4a: Association between cervical changes and fFN +ve in study group

Cervical changes	fFN +ve	Percentage
Present(established PTL)	4	80
Absent(Threatened PTL)	1	20
Total	5	100

Z = 1.75, P>0.05

Table 4b: Association between cervical changes and fFN -ve in study group

Cervical changes	fFN -ve	Percentage
Present(established PTL)	11	44
Absent(Threatened PTL)	14	56

A total of 5 patients had a positive fFN results, leaving 25 with a negative test result. 3 patients with a positive test delivered within 7 days of testing and 1 patient tested at 30 weeks of gestation, delivered at 37.1 week of gestation. One patient who tested positive, took Discharge Against Medical Advice after 24 hours.

Among the patients with a negative test result 1 patient tested at 25 weeks of gestation and delivered preterm at 33.4 weeks of gestation i.e. after 9weeks of fFN testing and 23 patients delivered at term. 1 patient of negative test group also lost follow up after 7 days of fFN testing.

Thus, test sensitivity was 75%, specificity was 95.83% and likelihood ratio (LR) was 10.15.

The positive predictive value of fFN test for delivery within 7 days of testing was 75% and negative predictive value was 95.83% as shown in Table 5.

Table 5: Association between fFN and outcome in study group

fFN	Preterm	Term	Total
Positive	3	1	4
Negative	1	23	24
Total	4	24	28

Sensitivity = 75%, Specificity = 95.83%, PPV = 75%, NPV = 95.83, LR = 10.15, Z = 3.21, P<0.005

Present study showed sensitivity of 75%, specificity of 95.83%, PPV of 75%, NPV of 95.83% for fetal fibronectin test. These results were comparable to the studies done by Lockwood et al, Iams et al and A.Skoll et al.

Lockwood et al studied that cervicovaginal fetal fibronectin can be used to identify risk of preterm delivery in patients with preterm contraction who had ≤ 2 cm of cervical dialatation with a sensitivity of 71.4% and specificity of 83.7% [8].

Skoll et al studied the evaluation of fFN for prediction of preterm delivery in symptomatic patients. Sensitivity of test was 80%, specificity was 85.1%, PPV-37.5% and NPV-97.4% and LR was 5.3 for delivery within 7 days of testing. However the sensitivity was 63%, specificity-87.6%,PPV-53.1% and NPV-91.4% and LR was 5.07 for delivery before 34 weeks of gestation. Therefore this study provides a high negative predictive value for continuing pregnancy beyond 7 days after testing and for prolonging gestation beyond 34 weeks [4].

Iams and colleagues concluded in their study that fFN was more accurate than uterine contractions or cervical dialatation in symptomatic patients of preterm labour with sensitivity of 93%, specificity of 82%, positive predictive value (PPV) of 29%, negative predictive value (NPV) of 99.5% [9].

In this study NPV of fFN test was higher as compared to PPV. Thus patients with negative test are less likely to deliver within 7 days, as out of 25 patients only 1 patient delivered preterm (at 34 weeks of gestation) but 9 weeks after negative fFN test. All the other 24 patients with negative ffN delivered at term. Out of the 5 positive test results only 3 patients delivered preterm, 1 patient delivered at term and 1 patient took discharge against medical advice in 24 hours of test.

LR of our study was 10.15, which was more than LRs of above studies.

In this study, specificity was higher than sensitivity of the fFN test, as also noted by Iams et al, Peaceman et al, V.C.F. Heath et al, G Faron et al, Lockwood et al and A.Skoll et al [4,7,10,11,12].

CONCLUSION

A simple bed side test to detect fFN in cervicovaginal secretions in 30 patients admitted with preterm labour was done. The fFN test had a high negative predictive value (NPV). Thus negative fFN is reassuring that the patient may not deliver at or near term and need not be monitored closely. Thus decreasing the necessity of prolonged hospital stay and give assurance of continuing pregnancy.

However the fFN test had low PPV (75%) as compared to NPV (95.83%). Thus patients with positive test results may or may not undergo preterm delivery.

The sensitivity of this test was 75%, however the specificity was higher i.e. 95.83%, which was comparable to other studies.

However this study was with smaller number of patients, further trials with larger number of patients are required to support the results.

ACKNOWLEDGEMENT

We are thankful to Dr. Amarjit Singh, Dean- Pad. Dr. DY Patil Medical College, Hospital and Research Center, Pune, for his valuable inspiration.

REFERENCES

[1] Alexander GR, Kogan M, Bader D, Carlo W, Allen M, Mor J. Pediatr 2003; 111(1): e61–e66.
[2] Petrou S, Mehta Z, Hockley C, Cook-Mozaffari P, Henderson J, Goldacre M. Pediatri 2003; 112(6 Pt 1):1290-7.
[3] Born too soon: the global action report on preterm birth. May 2012. WHO and partners.
[4] Skoll A, Patrick St. Louis, Neda Amiri, et al. J Obstet Gynaecol Can 2006; 28(3):206-213.
[5] Feinberg RF, Kliman HJ, Lockwood CJ. Am J Path 1991; 138: 537–43.
[6] Berghella V, Hayes E, Visintine J, Baxter JK. Fetal fibronectin testing for reducing the risk of preterm birth (Review).The Cochrane Library 2008, Issue 4.
[7] Smith GN, Walker MC, Ohlsson A, Brien O et al. American J Obstetr Gynecol 2007; 37: 1-8.
[8] Lockwood CJ, Wein R, Lapinski R, Casal D, Berkowitz G, Alvarez M, et al. American J Obstetr Gynecol 1993; 169: 798–804.
[9] Iams JD, Goldenberg RL, Meis PJ, Mercer BM, Moawad A, Das A, Thom E, McNellis D, Copper RL, Johnson F, Roberts JM. N Engl J Med. 1996 Feb 29; 334(9): 567-72.
[10] Peaceman AM, Andrews WW, Thorp JM, Cliver SP, Lukes A, Iams JD, Coultrip L, Eriksen N, Holbrook RH, Elliott J, Ingardia C, Pietrantoni M. American J Obstetr Gynecol 1997 Jul; 177(1): 13-8.
[11] VCF Heath, G Daskalakis, A Zagaliki, M Carvalho, KH Nicolaides. 2000;107(10):1276–1281.
[12] Gilles Faron, Michel B, Alain V, Jean-Pol L. A single cervical fibronectin screening test in a population at low risk for preterm delivery: an improvement on clinical indicators?