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Predictive value of the quantitative fetal fibronectin levels for the management of women presenting with threatened preterm labour – A revised cut off level: A retrospective cohort study

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ABSTRACT

Objective: To evaluate a new a cut off level of fetal fibronectin as a predictor of birth in women with threatened preterm labour.
Design: A retrospective cohort study performed at Ipswich hospital, Ipswich, Queensland, Australia, in women with threatened preterm labour with intact membranes between 23 weeks to 34+6 week gestation.
Study design: A quantitative fetal fibronectin (fFN) was performed. Maternal demographics and birth outcome data were extracted from the routinely collected perinatal data held by the hospital. The odds of preterm birth were estimated for each cut off value of fFN (10, 50 and 200 ng ml^{-1}) using logistic regression and accounting for multiple presentations by the same woman.
Results: Among the 447 presentations and 376 pregnancies, rates of preterm birth <34 weeks were 2.9%, 9.2%, 3.3%, 19.6%, 4.2% and 35.3% for each category of values respectively (fFN <10, ≥10, <50, ≥50, <200 and ≥200 ng ml^{-1}). Birth rates within 7 d of testing were 1.1%, 7.5%, 1.8%, 16.1%, 2.1% and 41.2% respectively. Comparing fFN level of <10 to a level of 10-199 ng ml^{-1} there was no significant increase in odds of preterm birth < 34 weeks or birth within the next 7 d (OR 2.28, 95% CI 0.84-6.17 and OR 3.61, 95% CI 0.89-14.7 respectively.
Conclusion: In women presenting with TPL, those with levels of <200 ng ml^{-1} have a low risk of birthing within 7 d or before 34 weeks gestation. This allows a personalised decision making and probable discharge home without need for steroid loading.

Introduction

Preterm birth is a leading cause of perinatal mortality and morbidity which include respiratory distress syndrome (RDS), necrotizing enterocolitis, intraventricular haemorrhage and sepsis [1], Spontaneous preterm birth (< 37 weeks) is reported to occur in 8.6% of all mothers in Australia [2].

Many women who present with regular uterine contractions with intact membranes are not in true preterm labour and > 70% will ultimately deliver at term [3]. Fetal fibronectin (fFN) testing and transvaginal ultrasound scan of cervical length are being used by clinicians to assist in the management of women presenting with threatened preterm labour (TPTL), particularly in relation to need for transfer to a tertiary hospital. Ultrasound cervical length (CL) assessment requires trained personnel with standardised measurements and reporting [4,5] and is less readily available in many settings than is fFN testing. Fetal fibronectin test has thus become widely accepted as a tool for the rapid assessment of these women. The positive predictive value (PPV) at threshold levels of 10, 50, 200 and 500 ng ml^{-1} have been reported to be 19, 32, 61 and 75% respectively for birth <34 weeks [6]. Two recent papers [7,8] reported that in symptomatic and asymptomatic women at risk of preterm labour, none birthed within 7 d if fFN levels were < 50 ng ml^{-1}; however, they also reported that none birthed within 7 d even with levels of 50 – 199 ng ml^{-1}. Regional metropolitan hospitals do not have neonatal intensive care units and thus have a policy of transfer of women at risk of birth < 32 weeks to a higher-level facility. When used appropriately, fFN testing could therefore, minimise unnecessary health care utilisation and interventions [9,10].

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The aim of this study was to evaluate the predictive value of preterm birth (defined as birth <37 and <34 weeks gestation as well as birth within 7 and within 14 d of the fFN testing) for fFN levels of <10, 10-49.9, 50-199, 10-199 and >200 ng ml^{-1}. Our hypothesis was that use of fFN levels of <200 ng ml^{-1} would have a good negative predictive value for birth within 7 d of testing or at <34 weeks gestation. We classified fetal fibronectin value <10 ng ml^{-1} as a negative test result, but we also used cut off levels of <50 ng ml^{-1} as this level has to date been used in many units here and some countries still only use the qualitative fFN.

Materials and methods

This was a retrospective cohort study at Ipswich Hospital, a metropolitan hospital in Queensland, Australia, over a 3-year period (January 2015 to December 2017). This is a level 2 facility without a neonatal intensive care unit performing about 2800 births annually. Women who are likely to birth before 32 completed weeks are transferred by road to the tertiary hospital 37 km away. The study population included all women presenting with symptoms of preterm labour (PTL) with intact membranes between 23 weeks to 34

week of gestation; and had a fFN test (as confirmed by a recorded fFN test in the fFN test register). Women with multiple pregnancy and asymptomatic women with short cervix were excludedfrom the study. Women with TPTL with evidence of spontaneous rupture of membranes, vaginal bleeding or a history of sexual intercourse within 24 hours of presentation, cervicaldilation ≥ 3 cm and cervical cerclage in-situ would not normally have a fFN test and were therefore, not part of the study. All women who presented with TPTL were seen by the birthsuite Registrar and all clinicians are competent in performing fFN test.

Study data were extracted from medical records and from routinely collected perinatal data held by the hospital. Extraction was carried out by a member of the research team who was not involved with the data analysis. The following variables of interest were recorded from the medical records: age, parity, body mass index (BMI), history of previous preterm birth, history of large loop excision of transformation zone (LLETZ) or cone biopsy of cervix, gestational age at presentation and on the presenting symptoms. Our primary study outcome was preterm birth defined as birth within 7 and within 14 d as well as birth <34 and <37 weeks' gestation.

As this study fulfils the criteria for an audit, no ethics review was sought, in line with National Health and Medical Research Council (NHMRC) standards [11].

Statistical analysis

Characteristics of the study population were summarised using frequencies and percentages for categorical data; and means and standard deviation for normally-distributed continuous data. Maternal characteristics were described in relation to the first presentation within each pregnancy during the study period. Preterm birth rates were calculated within fetal fibronectin categories: <10 vs ≥10 ng ml^{-1}, <50 vs ≥50 ng ml^{-1} and <200 vs ≥200 ng ml^{-1}. This reflected the three cut off levels being evaluated: 10, 50 and 200 ng ml^{-1}. Fetal fibronectin values of <10, <50 and <200 ng ml^{-1} were classified as negative test results, respectively. The odds of preterm birth occurring for each cut off level were estimated using logistic regression with robust standard errors to account for multiple presentations by the same woman. Multivariate logistic regression was used to estimate the adjusted odds of preterm birth accounting for previous preterm birth. Sensitivity, specificity, negative and positive predictive values were calculated for combinations of preterm birth and fetal fibronectin cut off level. All analyses were carried out using Stata/SE 13.1 for Windows (StataCorp LP, College Station, TX, USA).

Results

During January 2015 to December 2017, there were 449 presentations representing 366 women and 376 pregnancies. Two presentations for one woman were missing data on gestational age at birth and were excluded from analyses. This left 447 presentations by 365 women during 375 pregnancies – 10 women had two pregnancies during the study period. Among the 447 presentations by 365 women, 299 women had one presentation, 57 women had two presentations, 7 women had 3 presentations and one woman each had six and seven presentations. During 447 presentations contractions were palpable in 239 (53.5%) women whilst the rest complained of varying degrees of abdominal pain and or backache.

Table 1 shows the characteristics of the 365 women at the time of the first presentation in each of the 375 pregnancies. Nearly a quarter of the pregnancies, 92 (24.5%) were in first time mothers, 84 (29.7%) had a previous preterm birth and 118 (33.2%) had a BMI of ≥ 30 kg m^{-1}2.

Among the 447 presentations, 112 (25.1%) resulted in hospital admission for TPTL. There were 20 recorded transfers, all of which occurred in presentations resulting in admission for threatened preterm labour.

Table 2 shows the rates of preterm birth for the corresponding fetal fibronectin levels. For all four scenarios of preterm birth (<34 weeks, <37weeks, birth within 7 d and birth within 14 d), the rate of preterm birth increases with increasing fetal fibronectin level. Rates of preterm birth <34 weeks were 2.9% (n = 8/274), 9.2% (n = 16/173), 3.3% (n = 13/391), 19.6% (n = 11/56), 4.2% (n = 18/430) and 35.3% (n = 6/17) for fetal fibronectin values of <10, ≥10, <50, ≥50, <200 and ≥200 ng ml^{-1}, respectively. The overall rate of preterm birth <34 weeks was 5.4% (n = 24/447). Birth rates within 7 d of testing were: 1.1%, 7.5%, 1.8%, 16.1%, 2.1% and 41.2%, respectively and 3.6% overall. When we look at the odds ratios for preterm birth for each of the fFN groupings, all the estimates indicate a statistically significant increase in odds with a positive fetal fibronectin test result (ie ≥ 10, ≥50 or ≥200 ng ml^{-1}). While the magnitude of the point is estimate was higher with the higher cut off levels, the confidence intervals are wide and overlap – suggesting that the estimates are not statistically different from each other. However, the odds of preterm birth <37 weeks were higher for fetal fibronectin values of ≥ 200 (OR 14.0, 95% CI 4.50-43.4) compared to values of ≥ 10 (OR 2.34, 95% CI 1.35-4.05) (Table 3). The diagnostic test characteristics for various cut off levels of fetal fibronectin are given in Table 4. The positive and

Table 1
Characteristics per pregnancy (i.e. taking maternal characteristics at first presentation in each pregnancy- 376 pregnancies in 365 women) *denominator=-non-nulliparous women, n = 284.

Characteristics	n = 376 pregnancies
Maternal age in years, mean(SD)	26.2 (5.5%)
Parity, n (%)	
0	92 (24.5%)
≥1	284 (75.5%)
Previous preterm birth*	84 (29.6%)
Previous preterm birth <34 weeks*	30 (10.6%)
Body mass index	
Underweight (<18.5 kg m^{-1}2)	30 (8.5%)
Normal (18.5-24.9 kg m^{-1}2)	129 (36.3%)
Overweight (25-29.9 kg m^{-1}2)	78 (22.0%)
Obese (≥30 kg m^{-1}2)	118 (33.2%)
Previous LLETZ/Cone biopsy	18 (4.8%)
Maternal smoking	117 (31.1%)

Table 2
Preterm birth rates according to fetal fibronectin values (n = 447 pregnancies).

Fetal fibronectin levels (ng ml^{-1})	Preterm birth (<34 weeks)	Preterm birth (<37 weeks)	Birth within 7 days	Birth within 14 days
All (n = 447)	24 (5.4)	75 (16.8)	16 (3.6)	29 (6.5)
<10 (n = 274)	8 (2.9)	33 (12.0)	3 (1.1)	9 (3.3)
≥10 (n = 173)	16 (9.2)	42 (24.3)	13 (7.5)	20 (11.6)
<50 (n = 391)	13 (3.3)	51 (13.0)	7 (1.8)	17 (4.3)
≥50 (n = 56)	11 (19.6)	24 (42.9)	9 (16.1)	12 (21.4)
<200 (n = 430)	18 (4.2)	63 (14.7)	9 (2.1)	21 (4.9)
≥200 (n = 17)	6 (35.3)	12 (70.6)	7 (41.2)	8 (47.1)

Table 3
Unadjusted odds ratios for each preterm birth scenario by fetal fibronectin cut off level.

Fetal fibronectin levels (ng ml^{-1})	Preterm birth (<34 weeks) OR (95% CI)	Preterm birth (<37 weeks) OR (95% CI)	Birth within 7 days OR (95% CI)	Birth within 14 days OR (95% CI)
≥10 (Ref: <10)	3.39 (1.34-8.56)	2.34 (1.35-4.05)	7.34 (2.06-26.2)	3.85 (1.84-8.06)
≥50 (Ref: <50)	7.11 (3.18-15.9)	5.00 (2.66-9.40)	10.5 (3.65-30.2)	6.00 (2.82-12.8)
≥200 (Ref: <200)	12.5 (3.54-44.1)	14.0 (4.50-43.4)	32.7 (9.86-109)	17.3 (5.81-51.6)

*Robust errors used to account for multiple presentations per woman.

Table 4
Diagnostic test characteristics for various cut off levels of fetal fibronectin.

Diagnostic test characteristics	Preterm birth <34 weeks	Preterm birth <37 weeks	Birth within 7 days	Birth within 14 days
fFN value of ≥ 10 ng ml^{-1} classified as test positive (<10 ng ml^{-1} classified as test negative)				
Sensitivity, %	66.7 (46.7-82.0)	56.0 (44.8-66.7)	81.3 (57.0-93.4)	69.0 (50.8-82.7)
Specificity, %	62.9 (58.2-67.4)	64.8 (59.8-69.5)	62.9 (58.2-67.3)	63.4 (58.7-67.9)
Positive predictive value, %	9.25	24.3	7.5	11.6
Negative predictive value, %	97.1	88.0	98.9	96.7
fFN value of ≥50 ng ml^{-1} classified as test positive (<50 ng ml^{-1} classified as test negative)				
Sensitivity, %	45.8 (27.9-64.9)	32.0 (22.5-43.2)	56.3 (33.2-76.9)	41.4 (25.5-59.3)
Specificity, %	89.4 (86.1-92.0)	91.4 (88.1-93.8)	89.1 (85.8-91.7)	89.5 (86.2-92.1)
Positive predictive value, %	19.6	42.9	16.1	21.4
Negative predictive value, %	96.7	87.0	98.2	95.7
fFN value of ≥ 200 ng ml^{-1} classified as test positive (<200 ng ml^{-1} classified as test negative)				
Sensitivity, %	25.0 (12.0-44.9)	16.0 (9.4-25.9)	43.8 (23.1-66.8)	27.6 (14.7-45.7)
Specificity, %	97.4 (95.4-98.5)	98.7 (96.9-99.4)	97.7 (95.8-98.7)	97.9 (96.0-98.9)
Positive predictive value, %	35.3	70.6	41.2	47.1
Negative predictive value, %	95.8	85.4	97.9	95.1

negative predictive values, that may assist clinicians, are also shown in the table. Negative predictive values are consistently high. The positive predictive values for preterm birth <34 weeks or birth within 7 d for ≥10 ng ml^{-1} were 9.3% and 7.5%; these were 35% and 41% for ≥200 ng ml^{-1}, respectively. These are further evaluated accounting for previous preterm birth in Table S1.

Discussion

Main findings

In this population we have confirmed the high negative predictive value of the fetal fibronectin test for birth within 7 d of testing and for birth <34 weeks gestation. We have also confirmed the value of quantitative fFN testing reported by others [6,12–14], in its predictive value for preterm birth in symptomatic women, that the risk of preterm birth

remained low with levels of <200 ng ml^{-1} at time of presentation; rate of preterm birth within 7 d and birth <34 weeks were 1.1% and 2.9% for fFN level of < 10 and 2.1% and 4.2% for fFN level of <200 ng ml^{-1}.

Strengths and limitations

We had a large cohort of women presenting with threatened preterm labour. A weakness of this study is that this has been a retrospective and an observational study and not a randomised trial evaluating thresholds of fFN for preterm birth. It is interesting though that use of fFN in the context of randomised controlled trials [21] noted that women who were assigned randomly to the fetal fibronectin group had a similar incidence of preterm birth at <37 weeks of gestation (20.7% vs 29.2%; and at <34 weeks of gestation (8.3% vs 7.9%) compared with the control group.

Interpretations

We have focused our discussion predominantly on birth <34 weeks and birth within 7 d as these are more relevant from the management as well as from the neonatal morbidity point of view. In a previous smaller study [14] from our own unit we had evaluated the traditional cut off level of 50 ng ml^{-1}; birth <34 occurred in only 1% of women with a level of <50 ng ml^{-1} but a much larger previous study [15] that had also evaluated this cut off level had noted preterm birth within 2 weeks to be 3.9% and 5.7% respectively. In this study we noted low rates of birth within 7 d of testing and birth <34 weeks at 1.8% and 3.3% respectively with fFN level <50 ng ml^{-1}, that were not very different from the 2.1% and 4.2% respectively noted above with a fFN level of <200 ng ml^{-1}. The NPV of fFN <200 ng ml^{-1} thus clearly differentiated low risk from low risk women giving further supports for this level being used to avoid active intervention particularly in terms of geographic considerations and need or otherwise for steroid loading and or transfer to a tertiary institution. These also have cost

saving implications, which could be substantial, mostly being associated with inpatient stay *(910).

Although the NICE guideline [16] regarding preterm birth recommend steroids and tocolysis for fFN levels >50 ng ml^{-1}, our study and others [6] suggest that clinicians and women could be reassured to utilise fFN test in this setting to its full potential and possibly avoid unnecessary intervention when fFN level is <200 ng ml^{-1}. There is no question that timely antenatal steroids have well established benefits for the preterm infant. There have however been several publications expressing concern with the use of steroids [17–19] and thus the benefit of steroids need to be balanced against adverse maternal and possible long-term side effects in the newborn.

We had a large cohort of women presenting with threatened preterm labour. One in four women were in their first pregnancy and in those who had a previous birth, one in three had a previous preterm birth. were 38.5% and 17.1% respectively. Rates of birth within 7 d and birth <34 weeks for fFN levels ≥ 200 ng ml^{-1} were 41.2% and 35.3% overall compared to compared to 38.5% and 38.5% after accounting for a previous preterm birth (Table S2). This was contrary to study [20] that reported that preterm birth <37 weeks had a strong correlation after incorporating fFN level with history of previous preterm birth or preterm prelabour rupture of membranes (sensitivity, specificity and likelihood ratio (+) for delivery <37 weeks of 66.7, 78.9, and 3.2%, respectively).

Further research to evaluate an option of a repeat fFN test in either all women with an initial fFN level of 10-199 or only those with an initial level of 50 -199 ng ml^{-1} who have not birthed within 7 d would be interesting and could help with decision making regarding steroid loading.

What about the value of combining cervical length and fFN levels in units where this is easily available? We were not able to address this but in one such study [22] that advocated use of the combined approach, the authors concluded that “In women with threatened preterm birth,quantitative fibronectin testing alone performs equal to the combination of cervical length and qualitative fibronectin. Possibly, the combination of quantitative fibronectin testing and cervical length increases this predictive capacity. Cost-effectiveness analysis and the availability of these tests in a local setting should determine the final choice.” Again, more research into this strategy is required to further clarify use of this combined testing option.

Conclusion

Using the quantitative fFN testing in women presenting with threatened preterm labour those with levels of <200 ng ml^{-1} have a low risk of birthing within 7 d or before 34 weeks gestation and thus allowing personalised decision making and probable discharge home without steroid loading.

Disclosure of interests

None declared.

Contribution to authorship

KM conceptualised and designed the study, CB and CF collected the data and II performed the statistical analysis. KM and II drafted the manuscript All authors were consulted in the writing and have approved the final manuscript.

Details of ethical approval

The study fulfils the criteria for an audit, no ethics review was sought, in line with National Health and Medical Research Council (NHMRC) standards.

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Declaration of Competing Interest

The authors have no conflict of interest to declare.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.eurox.2019.100079.

References

[1] Beck S, Wojdyla D, Say L, Betran AP, Merialdi M, Requejo JH, et al. The worldwide incidence of preterm birth: a systematic review of maternal mortality and morbidity. Bull World Health Organ 2010;88(1):31–8.
[2] Australian Institute of Health and Welfare. Australia's mothers and babies 2015-in brief. Canberra 2016. 2016.
[3] Hassan S, Romero R, Vidyadhari D, Fusey S, Baxter JK, Khandelwal M, et al. Vaginal progesterone reduces the rate of preterm birth in women with a sonographic short cervix: a multicenter, randomized, double blind, placebo-controlled trial. Ultrasound Obstet Gynecol 2011;38(1):18–31.
[4] Ness A, Visintine J, Ricci E, Berghella V. Does knowledge of cervical length and fetal fibronectin affect management of women with threatened preterm labor? A randomized trial. Amer J Obstet and Gynecol 2007;197(4)e1–7 426.
[5] Melamed N, Hiersch L, Domniz N, Maresky A, Bardin R, Yogev Y. Predictive value of cervical length in women with threatened preterm labor. Obstet & Gynecol 2013;122(6):1279–87.
[6] Abbott DS, Radford SK, Seed PT, Tribe RM, Shennan AH. Evaluation of a quantitative fetal fibronectin test for spontaneous preterm birth in symptomatic women. Amer J Obstet Gynecol 2013;208(2)e1–6 122.
[7] Hezelgrave NL, Shennan AH. Quantitative fetal fibronectin to predict spontaneous preterm birth: a review. Womens Health 2016;12(1):121–8.
[8] Min J, Watson HA, Hezelgrave NL, PT Seed, AH Shennan. Ability of a preterm surveillance clinic to triage risk of preterm birth: a prospective cohort study. Ultrasound Obstet Gynecol 2016;48(1):38–42.
[9] Fell DB, Sprague AE, Grimshaw JM, Yasseen 3rd AS, Coyle D, Dunn SI. Evaluation of the impact of fetal fibronectin test implementation on hospital admissions for preterm labour in Ontario: a multiple baseline time-series design. BJOG 2014;121:438–46.
[10] Parisaei M, Currie J, O'Gorman N, Morris S, David AL. Implementation of foetal fibronectin testing: Admissions, maternal interventions and costs at 1 year. J Obstet Gynaecol 2016;36(7):888–92.
[11] NHMRC. Ethical considerations in Quality Assurance and Evaluation activities. 2014.
[12] Kurtzman J, Chandiramani M, Briley A, Poston L, Das A, Shennan A. Quantitative fetal fibronectin screening in asymptomatic high-risk patients and the spectrum of risk for the current preterm delivery. Amer J Obstet Gynecol 2009;200(263):e1–6.
[13] Lu GC, Goldenberg RL, Cliver SP, Kreaden US, Andrews WW. Vaginal fetal fibronectin levels and spontaneous preterm birth in symptomatic women. Obstet Gynecol 2001;97:225–8.
[14] Mahomed K, Anwar S, Geer JE, Ballard E, Okano S. Evaluation of fetal fibronectin for threatened preterm labour in reducing inappropriate interventions. Aust N Z J Obstet Gynaecol 2018, doi:http://dx.doi.org/10.1111/ajo.12914 Nov 4.
[15] Peaceman AM, Andrews WW, Thorp JM, Cliver SP, Lukes A, Iams JD. Fetal fibronectin as a predictor of preterm birth in patients with symptoms: a multicentre trial. Amer J Obstet Gynecol 1997;177:13–8.
[16] National Institute for health and Care Excellence. NG: NICE guideline. Preterm labour and birth; 2015. p. 25 November.
[17] Myles TD. Steroids -plenty of benefits, but not without risk. Obstet Gynecol 2011;117(2,Part 2):429–30.
[18] Khalife N, Glover V, Taanila A, Ebeling H, Järvelin MR. Rodriguez A Prenatal glucocorticoid treatment and later mental health in children and adolescents. PloS one 2013;8(11)e81394.
[19] Asztalos EV, Murphy KE, Willan AR, Matthews SG, Ohlsson A, Saigal S. Multiple courses of antenatal corticosteroids for preterm birth study: outcomes in children at 5 years of age (MACS-5). JAMA Pediatrics 2013;167(12):1102–10.
[20] Kurtzman J, Chandiramani M, Briley A, Poston L, Das A, Shennan A. Quantitative fetal fibronectin screening in asymptomatic high-risk patients and the spectrum of risk of recurrent preterm delivery. Am J Obstet Gynecol 2009;200(263):e1–6.
[21] Berghella V, Saccone G. Fetal fibronectin testing for prevention of preterm birth in singleton pregnancies with threatened preterm labor: a systematic review and meta-analysis of randomized controlled trials. Amer J Obstet Gynecol 2016;215(4):431–8.
[22] Bruijn MMC, Vis JY, Wilms FF, Oudijk MA, Kwee A, Porath MM. Quantitative fetal fibronectin testing in combination with cervical length measurement in the prediction of spontaneous preterm delivery in symptomatic women. BJOG 2016;123:1965–71.