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ORIGINAL ARTICLE

Diagnostic accuracy of rapid *ph*IGFBP-I assay for predicting preterm labor in symptomatic patients

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Objective: To estimate sensitivity, specificity, positive and negative predictive values (PPV, NPV) of insulin-like growth factor binding protein-1 (*ph*IGFBP-1) test in predicting preterm delivery in women with symptoms of preterm labor. Secondary objectives were to compare test characteristics of the *ph*IGFBP-1 and fetal fibronectin (fFN) tests.

Study Design: Labor and delivery units in two Calgary hospitals. Subjects were 349 women with suspected labor between 24 and 35 weeks gestational age (GA). Women had cervical *ph*IGFBP-1 test +/− and fFN testing. Sensitivity, specificity, PPV and NPV were estimated. Primary outcome was birth <37 weeks GA.

Result: Sensitivity of *ph*IGFBP-1 test for delivery <37 weeks was 0.39; specificity, 0.76; PPV, 0.24; NPV, 0.86. NPV of *ph*IGFBP-1 did not differ greatly from that of fFN testing (0.88).

Conclusion: NPV did not differ between *ph*IGFBP-1 and fFN for delivery <37 weeks. Neither test improves on pretest probability of delivery <37 weeks, so clinicians must decide whether the use of either test is justified.

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Keywords: diagnostic accuracy; phosphorylated insulin-like growth factor binding protein-1; fetal fibronectin; preterm delivery

Introduction

Preterm birth is a growing entity and the single most important contributor to perinatal mortality.[1] Prematurity is also a major source of morbidity, with overwhelming long-term disability and economic consequences.[1] Although management of threatened preterm labor may include administration of tocolytics, corticosteroids and tertiary hospital transfer, only in retrospect can the diagnosis of true or spurious labor be established. Consequently, unnecessary and costly patient transfers, hospital admissions and medication administrations result.[2,3]

There is need to improve the accuracy of diagnosing preterm labor. Early cervical changes as revealed by ultrasound and biochemical findings in cervical secretions have been investigated. The former is restricted by the need for skilled operators and advanced ultrasound equipment.[4] Similarly, the 'gold standard' for biochemical markers, fetal fibronectin (fFN), is expensive and contraindicated in the setting of recent vaginal examination or sexual intercourse.[5]

Insulin-like growth factor binding protein-1 (*ph*IGFBP-1) is a phosphorylated protein synthesized in the uterine decidua. Disruption to the choriodecidual interface results in elevated levels in cervical secretions. Potentially contaminating body fluids with fFN—such as semen and urine—contain only trace quantities of *ph*IGFBP-1.[6] A commercial bed side test kit is available to detect *ph*IGFBP-1 in the cervical secretions of women presenting with threatened preterm labor. The Actim Partus test (Medix Biochemica, Kauniainen, Finland) is an immunochromatographic dipstick test based on monochromal antibodies for *ph*IGFBP-1. The test is similar in principle to a urine pregnancy test and does not require technical expertise. The cost per test is approximately one quarter that of fFN.

At the time we designed our study, data validating *ph*IGFBP-1 as a marker for preterm labor was limited by a paucity of studies, as well as variability in study designs and eligibility criteria. Nonetheless, available research suggested that a negative *ph*IGFBP-1 test would rule out imminent delivery in ~90 to 95% of patients.[7–11] The negative predictive value (NPV) of *ph*IGFBP-1 was therefore felt to be comparable to fFN, although there was little evidence directly comparing the two tests in the same population.[12]

Our prospective cohort study set out to examine the sensitivity, specificity, positive predictive value (PPV) and NPV of *ph*IGFBP-1 test in predicting preterm delivery in women with symptoms of preterm labor. Secondary objective was to compare the test characteristics of the *ph*IGFBP-1 and fFN tests.

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Methods

Population studied

Pregnant women were eligible to join the study if they attended the Foothills Medical Centre or Peter Lougheed Centre labor and delivery units with symptoms of preterm labor (symptoms of uterine activity judged by the assessing physician to be indicative of preterm labor) at 24^0 to 34^6 weeks gestation. Women were excluded if they had ruptured membranes, antepartum hemorrhage, active labor and suspected chorioamnionitis (defined by fever, abdominal pain, leukocytosis). Women who could not have a fFN test because they had a digital exam or sexual intercourse in the past 24 h were eligible to join the study and had an *ph*IGFBP-1 test, as described by the manufacturer.

Procedures carried out

Consenting women were treated according to usual hospital protocol, with the addition of a vaginal swab taken for *ph*IGFBP-1. According to the hospital fFN protocol, patients underwent a sterile speculum examination. At that time, swabs for both fFN and the *ph*IGFBP-1 test were taken from cervical secretions in the posterior vaginal fornix and external cervical os, respectively. A digital examination was also performed, and cervical dilation and effacement were recorded. The standard of care for fFN was to hold the swab for 1 h: in cases of unequivocal progression to labor the fFN swabs was discarded. fFN tests were read by laboratory personnel as per the current standard.

The *ph*IGFBP-1 test specimens were prepared by swirling the Dacron swab in a tube of extraction medium. Specimens were then frozen according to the instructions of the manufacturer (Medix Biochemica) for later testing by the study research nurse in the Department of Obstetrics and Gynaecology (blinded to the fFN result). The results of *ph*IGFBP-1 tests were unknown to the clinical or nursing staff involved in the care of the patient.

The *ph*IGFBP-1 test was analyzed according to the instructions of the manufacturer (Medix Biochemica) by thawing the frozen sample, and then placing the immunochromomatographic dipstick in the extraction medium until the liquid reached the result area. The dipstick was then removed, placed in the horizontal position and read. A positive test (equivalent to $>10\,\mu g\,l^{-1}$) was read as two blue lines—a control line and a positive line in the result area. If after 5 min the positive line was not visualized, the test was considered negative.

Data collection

Standardized data collection forms were used to collect all study data.

At baseline, information was collected about the characteristics of the women, including pregnancy history, and gestational age (GA) of the pregnancy. GA was determined by last menstrual period and/or first trimester ultrasonography (reported in the patient chart). GA at baseline was used to calculate GA at birth, in order to avoid any bias from later determining GA at birth. The results of the first and second cervical exams were documented. The fFN test result was recorded from the patient chart.

Data on the subsequent course of pregnancy were extracted from the maternal and neonatal charts after the mother and her baby were discharged from hospital.

Main data items

The main data items were defined as follows:

- *ph*IGFBP-1 test: positive ($\geqslant 10\,\mu g\,l^{-1}$) versus negative ($<10\,\mu g\,l^{-1}$) test, as recommended by Lembet *et al*.[11] and the manufacturer of the test (Medix Biochemica).
- fFN test: positive ($\geqslant 50\,ng\,ml^{-1}$) versus negative ($<50\,ng\,ml^{-1}$), as defined by the manufacturer (Adeza Biomedical Corporation, Sunnyvale, CA, USA).
- GA at delivery: defined as premature (<37 weeks)[13] versus not premature ($\geqslant 37$ weeks), based on the assessment of GA at baseline. The use of cut-off of GA at 37 weeks was based on review of other studies of *ph*IGFBP-1 and fFN test characteristics.

Statistical considerations: data analysis and sample size

Analyses were carried out using SAS (version 9.2, SAS Institute, Cary, NC, USA). Descriptive statistics were calculated as appropriate for baseline and outcome data.

Estimating the study results for the primary question involved calculating the sensitivity, specificity, PPV and NPV and likelihood ratio positive (LR+) and negative (LR−) for the *ph*IGFBP-1 test (plus 95% confidence interval (CI) for each), in identifying women who deliver at <37 weeks (primary outcome), and for delivery within 7 and 14 days of the test. Similar tests of sensitivity, specificity, PPV, NPV, LR+ and LR− were also calculated for the fFN test.

For comparing of the results of the *ph*IGFBP-1 test and fFN test, data were analyzed only for women who had both tests done. Comparisons examined the overlap of 95% CIs of sensitivity, specificity, PPV, NPV, LR+ and LR− for the two tests. A paired analysis was carried out using the McNemar test to estimate agreement between the two test results.

A sample size calculation before our study based on the primary study question established that a sample of 360 women, and assuming that data would be unavailable for 30% of cases, meant that a sample of 250 cases would provide useful estimates of sensitivity, specificity, PPV and NPV. For example the *a priori* estimate of NPV was 0.89, and the estimated 95% CI was 0.85 to 0.93: the lower 95% CI estimates were considered to include clinically useful values.

Ethics

The study was approved by the University of Calgary Conjoint Health Research Ethics Board (ethics ID #18 605).

Results

Consenting women provided 366 swabs for the study from October 2005 to May 2009: 15 swabs were excluded because they were collected outside the eligible GA, and two because women were mistakenly entered twice in the study. The characteristics of the 349 included women are shown in Table 1. Median GA at the time of recruitment was 29^{6} weeks (interquartile range 4^{6} weeks). *ph*IGFBP-1 swabs were negative for 258 (73.9%) women. fFN swabs were negative for 260 (74.5%) and not done, either because of ineligibility for swab, or discard of swab following clarification of clinical status, for 61 (17.5%).

Table 2 shows the delivery characteristics and neonatal outcome. Outcomes were available for all women. The median GA at delivery was 39^{1} (interquartile range 2^{3}), with 57 (16.3%) women delivering at <37 weeks gestation, 6 (1.7%) within 7 days and 9 (2.6%) within 14 days of the initial test. The majority of women had a spontaneous vaginal delivery (182, 52.1%). The median birth weight was 3208 g (interquartile range 712), and 295 (79.7%) neonates went to a newborn nursery.

Table 3 shows the sensitivity, specificity, PPV, NPV, LR+ and LR− for delivery <37 weeks gestation, the primary outcome, for the *ph*IGFBP-1 test. The results were: sensitivity 0.39 (95% CI 0.26 to 0.51); specificity 0.76 (0.72 to 0.81); PPV 0.24 (0.15 to 0.33); and NPV 0.86 (0.82 to 0.91). Table 3 also shows sensitivity, specificity, PPV and NPV for delivery within 7 and 14 days of the index *ph*IGFBP-1 test. The results for fFN are shown in Table 4. Both tests have high NPVs for each of these outcomes, but sensitivity is poor for both tests.

Table 5 shows the comparison of test characteristics between fFN and *ph*IGFBP-1 swab results in predicting preterm births (<37 weeks) for those who had both the *ph*IGFBP-1 and fFN swabs. fFN is marginally more specific and better at predicting positive outcome than *ph*IGFBP-1, but there is not a significant difference for sensitivity or NPV.

Table 6 examines the agreement between *ph*IGFBP-1 and fFN test results within subjects, finding that for individual patients the *ph*IGFBP-1 swab was more likely to give a positive result than fFN swab: 28.1 versus 9.7%, $P<0.001$.

Discussion

Our study, undertaken in 349 women attending a labor and delivery unit with symptoms of preterm delivery, between 24^{0} and 34^{6} weeks gestation, found that the sensitivity of *ph*IGFBP-1 test in predicting preterm delivery at <37 weeks gestation was 0.39, specificity 0.76, PPV 0.24 and NPV 0.86. The results were similar for predicting birth within 7 and 14 days. That is, the test was relatively specific and predicted the majority of women who would not go on to deliver a preterm infant. In our study, the NPV of *ph*IGFBP-1 did not differ greatly from that of the fFN test.

Table 1 Patient characteristics at time of recruitment preterm labor visit

Characteristic	*Mothers,* n = *349*
Mean maternal age (s.d.)	29 (s.d. 5.0)
	Range 17–46
Nullip	151 (43.3%)
Previous preterm delivery	56 (16.1%)
Conception	
Spontaneous	323 (92.6%)
Infertility treatment	15 (4.3%)
Unknown	11 (3.2%)
Smoking during pregnancy	39 (11.2%)
Number of fetuses	
Single	327 (93.7%)
Multiple	20 (5.7%)
Unknown	2 (0.6%)
Hypertension during pregnancy	21 (6.0%)
Cerclage	1 (0.3%)
Uterine abnormality	10 (2.9%)
Median gestational age at PT labor visit (IQR)	29^{+6} (IQR 4^{+6})
	Range 24–34
Intercourse before test	8 (2.3%)
Bleed	7 (2.0%)
Cervical exam dilation	
0–1 cm	260 (74.5%)
1–2 cm	52 (14.9%)
2–3 cm	2 (0.6%)
Unknown	35 (10.0%)
Treated with steroids	56 (16.0%)
Treated with tocolytics	8 (2.3%)
Admitted	47 (13.5%)
Median length of overnight stay (days) if admitted	3 (IQR 4)
	Range 0–34
Other L&D visits for PT labor	
None	221 (63.3%)
1	60 (17.2%)
2	32 (9.2%)
⩾3	29 (8.3%)
Unknown	7 (2.0%)
Result of phIGFBP-1 test	
Positive	91 (26.1%)
Negative	258 (73.9%)
Result of fFN test	
Positive	28 (8.0%)
Negative	260 (74.5%)
Not run/not done	61 (17.5%)

Abbreviations: fFN, fetal fibronectin; IQR, interquartile range; L&D, labor and delivery; *ph*IGFBP-1, insulin-like growth factor binding protein-1; PT, preterm.

Table 2 Characteristics at delivery

Characteristic	*Mothers,* n = *349*
Median gestational age at delivery (IQR)	39^{+1} (IQR 2^{+3}) Range 28–43
Gestational age <37 weeks at delivery	57 (16.3%)
Mode of delivery	
Spontaneous vaginal delivery	182 (52.1%)
Operative delivery	52 (14.9%)
Cesarean section	115 (33.0%)
Neonatal outcomes	*Babies*, n = *370*
Median birth weight, g (IQR)	3208 (IQR 712) Range 928–4715
Median APGAR scores (IQR)	
1 min ($n = 2$ missing)	8 (IQR 1)
5 min ($n = 2$ missing)	9 (IQR 0)
Admission	
Newborn nursery	295 (79.7%)
Special care nursery	26 (7.0%)
Neonatal intensive care unit	40 (10.8%)
Unknown	9 (2.4%)

Abbreviation: IQR, interquartile range.

Table 3 Sensitivity, specificity, PPV, NPV, +LR and −LR for *ph*IGFBP-1

Results for phIGFPBP-1 test (n = *349*)	*Primary outcome: preterm delivery <37 weeks*	*Delivery within 7 days of swab*	*Delivery within 14 days of swab*
Sensitivity	22/57 (0.39)	2/6 (0.33)	4/9 (0.44)
95% CI	0.26–0.51	0.00–0.71	0.12–0.77
Specificity	223/292 (0.76)	254/343 (0.74)	253/340 (0.74)
95% CI	0.72–0.81	0.69–0.79	0.70–0.79
Positive predictive value	22/91 (0.24)	2/91 (0.02)	4/91 (0.04)
95% CI	0.15–0.33	0.00–0.05	0.00–0.09
Negative predictive value	223/258 (0.86)	254/258 (0.98)	253/258 (0.98)
95% CI	0.82–0.91	0.97–1.00	0.96–1.00
LR+	1.63	1.28	1.74
95% CI	1.11–2.41	0.41–4.04	0.82–3.69
LR−	0.80	0.90	0.75
95% CI	0.65–1.00	0.51–1.59	0.41–1.34

Abbreviations: CI, confidence interval; LR, likelihood ratio; NPV, negative predictive value; *ph*IGFBP-1, insulin-like growth factor binding protein-1; PPV, positive predictive value.

Table 4 Sensitivity, specificity, PPV, NPV, +LR and −LR for fFN

Results for fFN test (n = *288*)	*Preterm delivery <37 weeks*	*Delivery within 7 days of swab*	*Delivery within 14 days of swab*
Sensitivity	15/46 (0.33)	2/6 (0.33)	4/8 (0.50)
95% CI	0.19–0.46	0.00–0.71	0.15–0.85
Specificity	229/242 (0.95)	256/282 (0.91)	256/280 (0.91)
95% CI	0.92–0.97	0.87–0.94	0.88–0.95
Positive predictive value	15/28 (0.54)	2/28 (0.07)	4/28 (0.14)
95% CI	0.35–0.72	0.00–0.17	0.01–0.27
Negative predictive value	229/260 (0.88)	256/260 (0.98)	256/260 (0.98)
95% CI	0.84–0.92	0.97–1.00	0.98–1.00
LR+	6.07	3.62	5.83
95% CI	3.10–11.89	1.10–11.88	2.64–12.87
LR−	0.71	0.73	0.55
95% CI	0.58–0.87	0.42–1.29	0.27–1.09

Abbreviations: CI, confidence interval; fFN, fetal fibronectin; LR, likelihood ratio; NPV, negative predictive value; PPV, positive predictive value.

A review of the medical literature found 13 studies that reported sensitivity, specificity, PPV and NPV (with or without LR− and LR+) of *ph*IGFBP-1.[8–12,14–21] (Supplementary material). The published reports vary widely, in terms of study size (from 36 to 349 women with symptoms of preterm labor), the definition of symptomatic preterm labor, and the prevalence of preterm labor (from 4.1 to 50.0%), making it difficult to comment on differences and similarities between studies. In general, sensitivity was found to be less than specificity, and NPV was higher than PPV. Few LR+ and LR− tests were reported, but suggest that *ph*IGFBP-1 is not a highly relevant clinical test.

In a recent review of fFN testing, the current 'gold standard' biochemical test for predicting birth within 7 days, the authors also found it difficult to compare the results of different studies.[22] They reported that the sensitivity, specificity, PPV and NPV vary according to the prevalence of outcome, size of study and patient inclusion criteria (for example, using symptoms or cervical length as the inclusion criteria). Other characteristics, such as date of testing, other interventions (for example, tocolysis) and blinding of test result also affected test results. Despite the problems with comparing the studies they identified, the authors of the review came to the conclusion that fFN testing was of limited value as a short-term predictor of preterm birth in symptomatic patients.[22] Unfortunately, the review did not address the utility of the fFN test in excluding women who would not go on to deliver prematurely (that is, the NPV).

In addition to our study, three small studies have made within-patient comparisons of *ph*IGFBP-1 testing and fFN testing in women with symptoms of preterm labor. In a prospective study undertaken in the Singapore, 94 women presenting with symptoms of preterm labor at 24 to 34 weeks gestation were recruited, and bedside tests for *ph*IGFBP-1 and fFN were carried out, with clinician and patient blinded to test result. Both *ph*IGFBP-1 and fFN had high NPV in predicting birth within 48 h, 7 and 14 days. The authors commented that both bedside tests were effective for the

Table 5 Comparison of test characteristics between *ph*IGFBP-1 and fFN test results in predicting preterm births (<37 weeks) for those who had both the *ph*IGFBP-1 and fFN tests ($n = 288$)

	phIGFBP-1	*fFN*
Sensitivity	0.39	0.33
(95% CI)	(0.25–0.53)	(0.19–0.46)
Specificity	0.74	0.95
(95% CI)	(0.68–0.80)	(0.92–0.97)
PPV	0.22	0.54
(95% CI)	(0.13–0.31)	(0.35–0.72)
NPV	0.86	0.88
(95% CI)	(0.82–0.91)	(0.84–0.92)
LR+	1.50	6.07
(95% CI)	(0.99–2.28)	(3.10–11.89)
LR−	0.82	0.71
(95% CI)	(0.65–1.05)	(0.58–0.87)

Abbreviations: CI, confidence interval; fFN, fetal fibronectin; LR, likelihood ratio; NPV, negative predictive value; *ph*IGFBP-1, insulin-like growth factor binding protein-1; PPV, positive predictive value.

Table 6 Agreement of *ph*IGFBP-1 and fFN test results

	+ve phlGFBP-1	*−ve phlGFBP-1*	*Total*	*McNemar's test* P-*value*
+ve fFFN	23 (8.0%)	5 (1.7%)	28 (9.7%)	<0.001
−ve fFN	58 (20.1%)	202 (70.1%)	260 (90.3%)	
Total	81 (28.1%)	207 (71.9%)	288 (100.0%)	

Abbreviations: fFN, fetal fibronectin; *ph*IGFBP-1, insulin-like growth factor binding protein-1.
Analysis was restricted to women who had both tests done.

prediction of preterm delivery.[12] In a Turkish prospective study of 51 women with regular uterine contractions tested between 24 and 35 weeks gestation, sensitivity, specificity PPV, NVP, LR + and LR− for delivery <35 weeks and delivery within 7 days were approximately equivalent for *ph*IGFBP-1 and fFN tests. The ability of both tests to predict early delivery was improved when combined with a cervical length of <25 mm.[18] A final recent Canadian study conducted both *ph*IGFBP-1 testing and fFN testing on 62 women with a clinical diagnosis of preterm labor between 24 and 34 weeks. fFN test result was known by clinical staff, but they were blind to *ph*IGFBP-1 result. The study reported very poor sensitivity and PPV for *ph*IGFBP compared with fFN testing for delivery within 2 weeks, <34 and <37 weeks, although specificity and NPV were similar for the two tests.[15] Audibert *et al*.[15] pointed out that their study was small and stressed the need for adequately powered prospective studies to investigate *ph*IGFBP-1 as a marker of preterm delivery. Our much larger study ($n = 349$) used a study design similar to Audibert's in that the labor and delivery staff were blinded only to the *ph*IGFBP-1 test result. This should, if anything, produce more favorable findings for fFN testing (as found by Audibert) because the result of the test would be expected to contribute to the clinical management of individual women, including hospital admission, transfer or administration of medication. Results of *ph*IGFBP-1 testing could not contribute to clinical decisions because the results were unknown to clinical staff. In our study, differences were not found between the results of tests for birth <37 weeks, or <7 or 14 days. Thus, studies in which *ph*IGFBP-1 and fFN tests results are directly compared, despite significant differences in design, are consistent in finding that NPV, the characteristic of testing that is considered most useful in supporting clinical decision-making, does not differ significantly between *ph*IGFBP-1 and fFN testing. Unfortunately, sensitivity, another clinically important test characteristic, is poor for both *ph*IGFBP-1 and fFN testing.

The utility of tests for preterm labor lies in being able to identify women who will not go on to deliver early. A negative test would be used to avoid unnecessary treatments, such as tocolysis, magnesium sulfate and steroids, and could avoid protracted hospital stays.[6] In particular, such a test could be of particular utility in rural and remote areas to prevent the unnecessary and distressing transport of women away from their homes.[23] Published research about *ph*IGFBP-1 is consistent in reporting that the test will identify the majority of women who will not have a preterm birth (Table 6), although a negative test will not exclude every woman who will go on to deliver preterm.

Given the similarity between *ph*IGFBP-1 and fFN in predicting which women will not have a preterm birth, authors have highlighted the benefits of *ph*IGFBP-1. Unlike fFN, *ph*IGFBP-1 testing is not affected by urine or seminal plasma, and therefore can be used after recent sexual intercourse or in the presence of urine.[6,22] The cost of the *ph*IGFBP-1 is less than the fFN test.[10,18] In our health zone, where at present ~720 fFN tests are processed by the laboratory service each year, the use of *ph*IGFBP-1 bedside testing 870 women (substituting for fFN, plus use in additional women who had a recent vaginal exam or sexual intercourse as recommended by the manufacturer), would save approximately $70 000 per year in testing costs. A full economic evaluation would be needed to determine whether this strategy would be cost-effective from a health service perspective.

From both methodological and clinical points of view, it is important to consider whether testing, either for *ph*IGFBP-1 or fFN, offers an increase in diagnostic accuracy beyond clinical assessment. To assess this, the pre- and post-test probabilities should be compared. In our study, the pretest probability of not having a preterm delivery, or NPV, was 84% (292/349). The post-test negative probabilities for the *ph*IGFBP-1 test and the fFN test were 86% (95% CI 82 to 91%) and 88% (95% CI 84 to 92%), respectively. This minimal change in negative probability from pre to post test is not clinically important. Our results are similar

to another study that examined the added value of either *ph*IGFBP-1 or fFN in women with preterm labor. In that study, the pretest probability of not delivering at < 37 weeks was 70%[15] and the post test NPVs were 65% for *ph*IGFBP-1 and 65% for fFN. Therefore, it appears that adding either test to the clinical assessment of patients with symptoms of preterm labor, did not increase the ability to correctly identify women who would not have a preterm birth. This finding could explain why fFN has failed to change clinical practice in studies where clinicians were randomized to know the test results of fFN tests versus being blinded to the results.[24–26]

Further research is clearly needed to identify a test that would be more effective than either *ph*IGFBP-1 or fFN in correctly identifying women who will not deliver preterm or within a defined period. Until the time when a better test is available, institutions and clinicians must decide whether the use of either test is clinically justified in women with symptoms of preterm labor.

Conflict of interest

The authors declare no conflict of interest.

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References

1 Slattery M, Morrison J. Preterm delivery. *Lancet* 2002; **360**(9344): 1489–1497.
2 Gilbert WM, Nesbitt TS, Danielsen B. The cost of prematurity: quantification by gestational age and birth weight. *Obstet Gynecol* 2003; **102**(3): 488–492.
3 Mistry H, Dowie R, Franklin RC, Jani BR. Costs of neonatal care for low-birthweight babies in English hospitals. *Acta Paediatr* 2009; **98**(7): 1123–1129.
4 Leitich H, Brunbauer M, Kaider A, Egarter C, Husslein P. Cervical length and dilatation of the internal cervical detected by vaginal ultrasonography as markers for preterm delivery: a systematic review. *J Obstet Gynecol* 1999; **181**: 1465–1472.
5 Honest H, Bachmann LM, Gupta JK, Kleijnen J, Khan KS. Accuracy of cervicovaginal fetal fibronectin test in predicting risk of spontaneous preterm birth: systematic review. *BMJ* 2002; **325**(7359): 301–310.
6 Rutanen EM. Insulin-like growth factors in obstetrics. *Curr Opin Obstet Gynecol* 2000; **12**: 163–168.
7 Goldbenberg RL. The management of preterm labor. *Obstet Gynecol* 2002; **100**: 1020–1037.
8 Akercan F, Kazandi M, Sendag F, Cirpan T, Mgoyi L, Terek MC *et al.* Value of cervical phosphorylated insulinlike growth factor binding protein-1 in the prediction of preterm labor. *J Reprod Med* 2004; **49**: 368–372.
9 Elizur SE, Yinon Y, Epstein GS, Seidman DS, SchiV E, Sivan E. Insulin-like growth factor binding protein-1 detection in preterm labor: evaluation of a bedside test. *Am J Perinatol* 2005; **22**: 305–309.
10 Kwek K, Khi C, Ting HS, Yeo GS. Evaluation of a bedside test for phosphorylated insulin-like growth factor binding protein-1 in preterm labour. *Ann Acad Med Singapore* 2004; **33**: 780–783.
11 Lembet A, Eroglu D, Ergin T, Kuscu E, Zeyneloglu H, Batioglu S *et al.* New rapid bed-side test to predict preterm delivery: phosphorylated insulin-like growth factor binding protein-1 in cervical secretions. *Acta Obstet Gynecol Scand* 2002; **81**: 706–712.
12 Ting H-S, Chin PS, Yeo G, Kwek K. Comparison of bedside test kits for prediction of preterm delivery: phosphorylated insulin-like growth factor binding protein-1 (pIGFBP-1) test and fetal fibronectin test. *Ann Acad Med Singapore* 2007; **36**: 399–402.
13 Beck B, Wojdyla D, Say L, Pilar Betran A, Merialdi M, Harris Requejo J *et al.* The worldwide incidence of preterm birth: a systematic review of maternal mortality and morbidity. *Bull World Health Organization* 2010; **88**: 31–38.
14 Altinkaya O, Gungor T, Ozat M, Danisman N, Mollamahmutoglu L. Cervical phosphorylated insulin-like growth factor binding protein-1 in prediction of preterm delivery. *Arch Gynecol Obstet* 2009; **279**: 279–283.
15 Audibert F, Fortin S, Delvin E, Djemli A, Brunet S, Dubé J. *et al.* Contingent use of fetal fibronectin testing and cervical length measurement in women with preterm labor. *J Obstet Gynaecol Can* 2010; **32**(4): 307–312.
16 Azlin M, Bang H, An L, Mohamad A, Mansor N, Yee B *et al.* Role of phIGFBP-1 and ultrasound cervical length in predicting pre-term labor. *J Obstet Gynaecol* 2010; **30**: 456–460.
17 Brik M, Hernandez A, Pedraz C, Perales A. Phosphorylated insulin-like growth factor binding protein-1 and cervical measurement in women with threatening preterm birth. *Acta Obstet Gynecol Scand* 2010; **89**: 268–274.
18 Eroglu D, Yanik F, Oktem M, Zeyneloglu HB, Kuscu E. Prediction of preterm delivery among women with threatened preterm labor. *Gynecol Obstet Invest* 2007; **64**: 109–116.
19 Paternoster D, Muresan D, Vitulo A, Serena A, Battaglirin G, Dell'Avanzo M *et al.* Cervical phIGFBP-1 in the evaluation of the risk of preterm delivery. *Acta Obstet Gynecol Scand* 2007; **86**: 151–155.
20 Rahkonen L, Unkila-Kallio L, Nuutila M, Sainio S, Saisto T, Rutanen EM *et al.* Cervical length measurement and cervical phosphorylated insulin-like growth factor binding protein-1 testing in prediction of preterm birth in patients reporting uterine contractions. *Acta Obstet Gynecol Scand* 2009; **88**(8): 901–908.
21 Tanir HM, Sener T, Yildiz Z. Cervical phosphorylated insulin-like growth factor binding protein-1 for the prediction of preterm delivery in symptomatic cases with intact membranes. *J Obstet Gynaecol Res* 2009; **35**(1): 66–72.
22 Sanchez-Ramos L, Delke I, Zamora J, Kaunitz A. Fetal fibronectin as a short-term predictor of preterm birth in symptomatic patients, a meta-analysis. *Obstet Gynecol* 2009; **114**: 631–640.
23 Kornelsen J, Grzybowski S. Is local maternity care an optional service in rural communities? *J Obstet Gynaecol Can* 2005; **27**(4): 329–331.
24 Grobman WA, Welshman EE, Calhoun EA. Does fetal fibronectin use in the diagnosis of preterm labor affect physician behaviour and health care costs? A randomized trial. *Am J Obstet Gynecol* 2004; **191**: 235–240.
25 Berghella V, Hayes E, Visintine J, Baxter JK. Fetal fibronectin testing for reducing the risk of preterm birth. *Cochrane Database Syst Rev* 2008; **(4)**: CD006843.
26 Vis JY, Wilms FF, Oudijk MA, Bossuyt PM, van der Post JA, Grobman WA *et al.* Why were the results of randomized trials on the clinical utility of fetal fibronectin negative? A systematic review of their study designs. *Am J Perinatol* 2011; **28**(2): 145–150.

Supplementary Information accompanies the paper on the Journal of Perinatology website (http://www.nature.com/jp)