Controversies in diagnosis of preterm labour

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Despite scientific advances, efforts to prevent preterm birth can be disappointing. Obstetric care must focus on strategies to improve the outcome of preterm infants. The major goal is to delay preterm birth long enough to allow the transfer of women about to deliver preterm to a facility with a neonatal intensive care unit and to administer corticosteroids to enhance fetal lung maturation. A prerequisite for the success of this strategy is the reliable identification of women who will give birth preterm. Although symptoms of preterm labour strongly suggest preterm birth, contractions—even if combined with cervical effacement and dilation—do not reliably predict preterm birth. The diagnosis of true preterm labour that will eventually lead to preterm birth has been facilitated by the use of transvaginal cervical ultrasonography and by the detection of fetal fibronectin (FFN) in cervicovaginal secretions. The main clinical value of these tests is that preterm birth is very unlikely if the results of both tests are negative. This may help to avoid unnecessary transfer, hospitalisation and treatment of women with false preterm labour. The detection of phosphorylated insulin-like growth factor binding protein-1 in cervicovaginal secretions, or elevated levels of inflammatory markers, like interleukin-6, interleukin-8 and tumour necrosis factor-α (TNF-α), also predict preterm birth in symptomatic women. These markers, however, are not routinely used to predict preterm birth in women with symptoms of preterm labour.

INTRODUCTION

Even though efforts to prevent preterm birth have been disappointing, modern obstetric care has been more successful in preparing the unborn child for a preterm birth. The transfer of women about to give birth preterm to a facility with a neonatal intensive care unit, the administration of corticosteroids to enhance fetal lung maturation and tocolysis to delay birth long enough so that these preparations can be completed are interventions with proven benefit to the preterm infant. A prerequisite for the success of this strategy is the reliable identification of women who will have a preterm birth. A test to identify women about to give birth preterm should be both highly sensitive (i.e. all preterm infants should be identified) and highly specific (i.e. antenatal transfer, administration of corticosteroids and tocolysis should be avoided in women who will ultimately give birth at term).

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If preterm birth is preceded by spontaneous preterm labour, clinical signs and symptoms (such as contractions, increased pressure or discharge) strongly suggest imminent delivery. These clinical signs and symptoms, in combination with the findings of a digital vaginal examination (such as changes in cervical consistency, effacement or dilation) are often sufficient to make a diagnosis of preterm labour.

In many cases, women with symptoms suggestive of preterm labour—even if combined with cervical effacement and dilation—will not have a preterm birth, so that a clinical diagnosis of preterm labour is often unreliable.

The problem in correctly identifying symptomatic women who will ultimately give birth preterm can be exemplified by the results of clinical studies in which women with suspected preterm labour were included. Only 3% of the women with suspected preterm labour who were included in studies of fetal fibronectin (FFN) testing delivered within 7–10 days, and only 21% delivered before 37 weeks of gestation.1

Fortunately, the diagnosis of true preterm labour that will eventually lead to preterm birth has been facilitated by the use of three tests that have been introduced into routine obstetric care in the last two decades: the detection of FFN or phosphorylated insulin-like growth factor binding protein-1 in cervicovaginal secretions, and transvaginal cervical ultrasonography.

In a systematic review of symptomatic women, the mean sensitivity and specificity of FFN testing to predict a delivery within seven days after testing was 77% and 87%,2 with corresponding 95% confidence intervals (CIs) of 67–88% and 84–91%, respectively. As in asymptomatic women, FFN was more predictive as a short term marker than as a long term marker for preterm birth. Mean sensitivity rates for the outcomes of birth within 14 days, 21 days or before 34 weeks of gestation were 74%, 70% and 63%, with corresponding mean specificity rates of 87%, 90% and 86%, respectively. The 95% CIs for these
outcomes widened considerably, indicating larger heterogeneity within the results of the studies included in the review.

The typical clinical performance of FFN testing in symptomatic women has been calculated using pre- and post-test probabilities. From a median pretest probability of 3% for a delivery within 7–10 days after testing, the positive and negative post-test probabilities were 14.4% and 0.8%, respectively. In this way, positive and negative post-test probabilities were neither high nor low enough to rule in or out true preterm labour.

Phosphorylated insulin-like growth factor binding protein-1 has been shown to predict preterm birth in symptomatic women. For the outcomes of birth within seven days after testing or before 35 weeks of gestation, sensitivity rates were 94% and 100%, and specificity rates 85% and 82%, respectively. These results are promising but need to be reconfirmed by more studies in different populations.

Inflammatory markers that can be detected in cervicovaginal secretion and that have been shown to be significantly associated with preterm birth include interleukin (IL)-6, IL-8 and tumour necrosis factor-α (TNF-α). These markers are not currently used in routine practice. As in asymptomatic women, future clinical research using inflammatory markers may deepen our understanding of the role of infection in preterm labour.

In contrast to FFN testing, for which a common cutoff value of 50 ng/mL was used in the great majority of diagnostic studies, the evaluation of cervical ultrasonography in symptomatic women is complicated by the use of a variety of criteria to define abnormal results. Different cutoff values for cervical length were found to be optimal in individual studies, and various criteria were used to define dilatation of the internal cervical os.

Optimal cutoff values for cervical length in symptomatic women were found to range between 18 and 30 mm. Sensitivity and specificity rates at these optimal cutoff values ranged between 68% and 100% and between 44% and 79%, respectively. The corresponding performance rates for a dilated internal cervical os using various criteria ranged from 70% to 100% and from 54% to 75%, respectively.

Because optimal test results were achieved at different cutoffs, it is difficult to propose an overall optimal cutoff value. In women in preterm labour, a high sensitivity rate would be the primary target and a lower specificity rate would be tolerated in most clinical settings, resulting in more women being admitted to hospital. A cervical length of 30 mm or less or a dilatation of the internal cervical os would have detected 80–100% or 70–100% of women who subsequently delivered preterm. Both parameters appear to be reasonably sensitive criteria for true preterm labour, but suboptimal specificity must be expected.

Even though a series of studies of FFN testing and cervical ultrasonography in both asymptomatic and symptomatic women have been published, only sparse data about the performance of a combination of FFN testing and cervical ultrasonography in symptomatic women exist.

Preterm birth rates for all combinations of both tests are available from one study, which included symptomatic women at 24–34 weeks of gestation with singleton pregnancies. The pretest probability of a delivery before 37 weeks of gestation in this study was 26.3%, which is comparable to other studies that included women with suspected preterm labour (Table 1). Positive tests of both markers, either alone or in combination, raised the post-test probability for a delivery before 37 weeks of gestation to 52.4%, which has only moderate clinical significance. A negative result on both tests lowered the probability to 5.6%. This is less than the preterm delivery rate that would be expected in the general population, suggesting that symptomatic women with both a negative FFN test and a normal result of cervical ultrasonography carry a risk of preterm birth that is even lower than the average risk in the general population.

**CONCLUSION**

The diagnosis of true preterm labour that will eventually lead to preterm birth has been facilitated by the use of transvaginal cervical ultrasonography and by the detection of FFN in cervicovaginal secretions. Both tests do not reliably rule in true preterm labour and a substantial proportion of women will not give birth preterm even if both tests are positive. The main clinical value of these tests is that preterm birth is very unlikely if the results of both tests are negative as the risk of preterm birth drops below the baseline risk of preterm birth found in the general population. This may help to avoid unnecessary transfer, hospitalisation and treatment of women with false preterm labour.

**References**


