Case Report

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Predictors of Preterm Labor

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Abstract

Preterm birth is caused by multiple etiologiesas individual and environmental factors which makes the prediction and prevention of preterm birthschallenging process in antenatal care. As underlying etiology of preterm labour is not completely clear, identification of risk factors and determining the individual risk for pregnant women have importance in obstetric management of women who may benefit from current treatment strategies, current screening tests for prediction of spontaneous preterm labour can bedivided into three categories : Risk factor assessment, cervical measurement and biochemical markers. Early interventions may be effective in reducing the risk of preterm birth.

Keywords: Preterm birth, Predictors, Cervical measurement, Biochemical markers.

INTRODUCTION

Preterm labour define as delivery before completing 37 weeks of gestation. Prediction and prevention of PB a challenging process in antenatal care. Preterm birth (PB) is one of the leading causes of neonatal mortality and its long term neurologic and developmental problems. It is related with cerebral palsy, bronchopulmonary dysplasia, retinopathy of prematurity, and many other morbidities.[1]

Causes of Preterm Birth

Premature birth may be iatrogenic or spontaneous. Iatrogenic premature birth is the result of a medical intervention due to fetal and/or maternal condition necessitating early delivery. By contrast, spontaneous premature birth often occurs despite best efforts to prolong the pregnancy. Upto 80 percent of premature births fall into this category. The major goal of the obstetrician in this regard is therefore to prevent preterm birth. Failing in this, it is crucial to delay preterm birth long enough to optimise the outcome for the fetus; for example, to allow for the transfer of the pregnant woman to a healthcare centre with appropriate neonatal facilities, to administer corticosteroids to enhance fetal lung maturation, and/or to give magnesium for fetal neuroprotection. A prerequisite for the success of prevention is the reliable prediction / identification of women at risk of preterm birth. Evidence suggests that spontaneous preterm labour

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and delivery are a heterogeneous condition with many triggers or precipitating factors including maternal genital tract haemorrhage, cervical dysfunction, idiopathic uterine contractions, infection, malnutrition, multifetal pregnancy, and spontaneous rupture of the fetal membranes. Four distinct mechanisms for the pathogenesis of preterm labour have been described and include premature activation of the fetal hypothalamic pituitary axis, mechanical stretch, inflammation/ matrix remodelling, and placental abruption. The temporal convergence of cervical effacement and dilatation, myometrial activation, and the rupture of fetal membranes are common to all spontaneous labour and in all placental mammals irrespective of the initiating trigger(s) or whether labour occurs at a term or at preterm gestation.[2]

Recent evidence also supports a role for fetal T-cell activation as a trigger for preterm labor and birth. The impairment of maternal regularly T-cell (Tregs) can lead to preterm birth, likely due to the loss of immunosuppressive activity resulting in unleashed effector T-cell responses. Homeostatic macrophages are essential for maintaining pregnancy and promoting fetal development, and the adoptive transfer of homeostatic M2-polarized macrophages shows great promise for preventing inflammation induced preterm birth.[3]

Inflammasomes are cytosolic multiprotein complexes that orchestrate inflammation in response to pathogens and endogenous danger signals. Inflammasome in the pathological inflammation are implicated in spontaneous preterm labor with acute histologic chorioamnionitis.[4]

With adequate sensitivity and high Negative predictive value (NPV), the TVS-UCA measurement can be considered as a useful tool for predicting preterm birth in threatened preterm labor. Moreover, both Uterocervical angle and Cervical length can be used to predict risks for preterm birth and support clinicians' decisions on using tocolytic agents in threatened preterm labor.[5]

Amniotic fluid cytokines have been implicated in the mechanisms of preterm labor and birth. Cytokines can be packaged within or on the surface of extracellular vesicles.

DISCUSSION

Prediction of Preterm Labor

Numerous methods of screening for preterm labor have been proposed, but none has fulfilled all the necessary criteria. These methods include the following.

Cervical Assessment

Early cervical ripening and dilatation of the internal os of the cervix increase the risk of preterm delivery The positive predictive value for abnormal cervical findings is 25 to 30 percent for the high risk group and 4 percent for the low risk group. A cervical dilatation of more than 2 cm predicts PTD with a sensitivity of 60 percent.

Ultrasound examination of the length of the cervix

Transabdominal and transvaginal was compared with manual vaginal examination by Anderson et al. They found that normal examination of cervical effacement detected 71 percent of preterm births, but transabdominal ultrasonographic measurement of cervical length was not predictive. Both sensitivity and predictive value of cervical assessment are too low by the latter method for using the same as screening tool in unselected population.

Transvaginal sonography is considered superior to manual assessment of cervix as a predictor of PTD. A cervical length of less than 39 mm at 30 weeks has a sensitivity of 76 percent, specificity of 59 percent, while a cut-off at 30 mm had a sensitivity of 71 percent and positive predictive value of 86.6 percent.

Preterm labor is a heterogenous condition with numerous associated social and medical risk factors:

- Low socioeconomic class
- Previous preterm births
- Multiple pregnancy
- Cigarette smoking
- Alcohol and drug users
- Women doing heavy manual work during pregnancy
- General medical and obstetric disorders

Many attempts have been made to prepare some "risk scoring" in such condition. A modified risk scoring was devised by Creasy et al (1980) for predicting spontaneous preterm birth. In this system, scores of 1 to 10 are given to a variety of pregnancy factors such as socioeconomic status, reproductive history, complications. Women with scores of 10 or more are considered to be of high risk for preterm birth. According to screening at registration and at 26 to 28 weeks of high-risk women predicted 69 percent preterm labor. But centroversies exists over risk scoring system. Mercer BM et al (1996) in a recent study showed

that risk assessment failed to predict most women who have preterm birth.

Fetal Breathing Movement

Sonographically detected absence of fetal breathing movement predicts PTD within 48 hours with a sensitivity of 66.7 percent. Elevated prostanoids in amniotic fluid suppress fetal breathing movements.[6]

Signs and Symptoms of Preterm Labor:

- Menstrual like cramps
- Low, dull backache abdominal pressure
- Pelvic pressure
- Abdominal cramping (with or without diarrhoea)
- Increase or change in vaginal discharge (mucous, watery, light bloody discharge) Uterine contractions, often painless
- Cervical Changes

Cervical length can be used as a diagnostic factor. As cervical length decreases in mid-pregnancy, the risk of preterm birth has been shown to increase in a continuous fashion. Transvaginal ultrasound examination of the cervix is a reliable and reproducible method to assess cervical length.

Early asymptomatic dilation and effacement of the cervix (cervical insufficiency) may be associated with an increased likelihood of preterm labor and delivery. Interventions such as prophylactic cervical cerclage on sonographic recognition of a shortened cervical length (often defined as less than 2.5 cm) in low-risk women have not improved outcomes; however, placement of a cerclage in high-risk women (e.g., history of prior preterm birth) with a shortened cervix may be beneficial.

Other screening modalities in asymptomatic women, such as fetal fibronectin, bacterial vaginosis screening, and home uterine contraction.[7]

Biophysical and Biochemical Indices

Biochemical assays of serum oestradiol and progesterone have remained inconclusive and are not used anymore.

Fetal fibronectin as a biochemical marker has been studied extensively. Fibronectin is a protein and a component of the extracellular matrix of the membranes of the amniotic sac, particularly the choriodecidual junction. Mechanical stress caused by uterine contractions and cervical change can lead to choriodecidual disruption and lead to release of fibronectin into the cervicovaginal secretions. As gestational age advances in pregnancy, the predictive value of test decreases and is a better marker in TPL than in asymptomatic women. High concentrations (>50 ng/mL) of cervicovaginal secretion is associated with preterm delivery.

Ultrasonographic assessment of the cervix as a predictor of preterm labour is currently gaining popularity. Cervical length can be assessed with ultrasound accurately and the gradual effacement of the cervix can be detected. There is controversy regarding whether abdominal or transvaginal ultrasound is better for measuring the cervical length. Transabdominal ultrasound needs full bladder and hence may falsely note elongated cervix due to compression of cervix by full bladder. The critical length by abdominal ultrasound (with partially full bladder) is 2.5 cm. Cervix measuring shorter than this may need intervention with cerclage. Routine universal screening for cervical length by ultrasound is not recommended, it may be performed in high-risk patients starting from 16-18weeks as before that the interpretation is difficult.

Cervical dilatation may be a better predictor of preterm labour but cannot beaccurately assessed with ultrasound. Different signs like 'Y', 'U' and ballooningof the bag of membranes into cervical canal show different stages of cervical effacement and dilatation.The positive predictive values of different markers are in the range of 25-30%. It appears that cervical assessment and uterine activity monitoring may be more accurate than other methods.[8]

Fetal fibronectin

Fetal fibronectin is a glycoprotein variant of the fibronectin family present in amniotic fluid, placenta and the extracellular substance of the decidua. Its synthesis and release is increased by the mechanical and inflammatory events which occur prior to the onset of labour. Fibronectin is often described as 'leaking' from disruption to the fetal membranes and decidua in the lower pole of the uterus associated with the early biochemical events of parturition. However, it is also an inflammatory response gene, and therefore concentrations of fibronectin in vaginal fluid can be considered to also be a marker of inflammation (which may be pathological or a normal part of the onset of labour at term).

Fetal fibronectin may normally be detected in vaginal secretions at levels in excess of 50 ng/mL. up to 20 weeks' gestation and again after 36 weeks' gestation. Detection up to 20 weeks is possible because the amniochorion is not fully fused with the

decidua until that time. Detection closer to term is a feature of the normal mechanical and biochemical events leading to normal term labour. The presence of fibronectin in vaginal secretions at levels above 50 ng/mL between 20 and 36 weeks is therefore not normal and may be used to predict a risk of preterm labour.[13,14] When originally introduced as a commercial test, fibronectin analysis was principally intended to be used in women who present with preterm contractions to differentiate those with a risk of imminent delivery. However, it is now being increasingly used to predict risk in women who are asymptomatic but at risk for other reasons, in particular cervical shortening. The currently available bedside testing kits allow quantification of the concentration of fibronectin in the vaginal fluid, which has improved the predictive performance of the test. So, for example, women with a cervical length below 25 mm between 22 and 28 weeks, but with a fetal fibronectin concentration of less than 10 ng/mL, will have a risk of preterm birth before 34 weeks of less than 10%; this rises to over 50% if the fibronectin concentration is greater than 200 ng/mL.[9]

Future approaches to prediction of preterm labour.

Identification of a single biomarker to predict spontaneous preterm labour poses a significant challenge due to heterogeneity of clinical presentations and biochemical mechanism involved in preterm birth. Simultaneous quantification of multiple biomarkers, including demographic/risk factors, cervical length and biochemical markers represent a promising approach to improving diagnostic efficiency.[10]

CONCLUSION

The ability to accurately predict and therefore prevent preterm labour and birth remains one of the crucial challenges facing modern obstetrics. A single biomarker or even in combination if found for prediction of PB, can decrease hospital cost and restrict treatment.Preconceptionalcounselling regarding risk factors for preterm birth may further reduce the risk. No single biomarker will achieve desired predictive efficiency due to multifaceted etiology of preterm birth. Many findings such as maternal risk factors, USG markers and biomarkers in maternal serum amniotic fluid or cervical length can be effective in predicting preterm birth. More research is needed to develop new strategies to identify women who may benefit from prophylactic therapy.

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