

Management of a woman with a previous spontaneous preterm birth

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Abstract

Preterm birth is an important cause of neonatal morbidity and mortality, and is associated with long term adverse health consequences. Worldwide close to 15 million babies are born preterm each year, and there are no signs that the rate of preterm birth is slowing. A history of a previous spontaneous preterm birth is a significant risk factor for a subsequent spontaneous preterm birth; identifying these women provides an opportunity to optimize care in future pregnancies. Interventions such as progesterone and cervical cerclage appear to be beneficial in women at high risk of preterm birth; however uncertainties remain as to how best to screen women, the optimal treatment regimen, and whether these treatments improve perinatal outcomes. Tests that accurately identify asymptomatic women who go on to deliver preterm are lacking. Research is underway to develop biomarkers that can accurately predict women who will deliver preterm. However, without effective strategies that diminish rates of preterm birth and improve perinatal outcomes, the clinical role of these tests is less well defined.

Keywords Cervical cerclage; cervical length; fetal fibronectin; preterm birth; prevention; progesterone

Introduction

Preterm birth is defined as birth occurring prior to 37 weeks gestation. Worldwide, every year close to 15 million babies are born preterm. Despite extensive ongoing research into causes, predictors and treatments for preterm birth, there is no evidence that rates of preterm birth are falling. In fact, a recent systematic review of preterm birth rates suggested that worldwide, preterm birth rates are stable or increasing.

The consequences of preterm birth include increased risk of mortality, and short and long-term respiratory and gastrointestinal

complications and neurodevelopmental disability. Furthermore, being born preterm increases the risk of developing chronic diseases in adulthood, including obesity, type II diabetes, hypertension and cardiovascular disease. The consequences of prematurity are most grave for those born at the earliest gestations, with the majority of long term adverse outcomes occurring at gestations of less than 33 weeks. For example, perinatal mortality is 2% for those babies born at 32 weeks, but approaches 90% for those born at 23 weeks.

Preterm birth may be broadly considered as either medically indicated or spontaneous. Indicated preterm birth accounts for approximately one third of preterm deliveries, and occurs when complications arise that put mother or fetus at risk unless delivery is expedited, for example: severe intra-uterine growth restriction, massive antepartum haemorrhage, or severe preeclampsia. The remainder of preterm births are considered spontaneous, and include those which are preceded by preterm pre-labour rupture of membranes. The processes culminating in spontaneous preterm labour can be initiated by a wide range of aetiologies such as infection, uterine stretch, placental ischaemia, haemorrhage and other inflammatory stimulus. Spontaneous preterm birth represents a final common pathway of a heterogeneous group of conditions. This is likely to explain why, despite considerable healthcare advances, successful prediction and prevention of spontaneous preterm birth has remained so elusive – as each predictor or intervention is likely to only identify or improve outcomes for a subset of cases.

There are many risk factors for preterm birth, however a prior history of spontaneous preterm birth is the most significant and consistently identified clinical risk factor, and the identification of women with a history of preterm birth gives an opportunity to optimise care for subsequent pregnancies. This article will review and discuss risk assessment and management of pregnancies where there is a history of a prior preterm birth.

Predicting recurrent preterm birth

Mrs PT is a 32 year-old G3P1 who attends your clinic pre-pregnancy. Her notes document an elective early surgical termination in her first pregnancy, and a previous delivery at 27 weeks, with her baby spending time in the neonatal unit. She is considering becoming pregnant again, but is extremely anxious given her history. She wants to know the likelihood of this baby being born preterm again.

At present, risk scoring tools based on clinical history alone perform poorly. However, details of the circumstances leading to the previous preterm birth may aid prediction and so a full history and case note review of the previous births is important to assess future risk. It may identify areas where there is opportunity to reduce or eliminate risk factors for recurrent preterm birth as well as other pregnancy complications.

Number and timing of previous deliveries

The risk of recurrent spontaneous preterm birth reflects the aetiology of the previous preterm birth, the number of previous preterm births, and the severity of prematurity. The likelihood of having a preterm birth in a given pregnancy increases with the

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number of previous preterm births, with a reducing chance of delivery after 33 weeks of 83, 86 and 68% after one, two or three prior preterm births. Risk of preterm birth also increases as the gestational age of previous preterm births declines, with the greatest risk for those with a previous delivery at less than 28 weeks gestation. If the previous preterm delivery was an indicated delivery, the risk of recurrence will be related to the recurrence risk of the condition leading to the indicated delivery; however a history of previous indicated preterm birth is also associated with an increased risk of spontaneous preterm birth in subsequent pregnancy. Presumably this is due to a shared aetiology – such as placental ischaemia – between pregnancy complications such as preeclampsia and preterm birth. The timing of the last pregnancy should also be reviewed, as risk of early delivery increases with reducing interpregnancy interval (IPI). An analysis of 6181 women with a previous preterm birth demonstrated that after adjusting for confounding factors, those with an IPI of <6 months had the highest increase in risk of preterm delivery (44% increase in risk of recurrent preterm birth), IPIs of 6–12 months had a modest increase, and there was no increase in risk of recurrent preterm birth with IPIs of 12–18 months, compared to the risk of those with an IPI of 18 months or more.

History of cervical surgery or trauma/uterine instrumentation

Women undergoing excisional treatment for cervical dysplasia have an increased risk of preterm birth compared to women who have not had these procedures, although the mechanism/s mediating this increase in risk are unclear. One hypothesis is that these procedures reduce the mechanical support of the cervix which may then increase susceptibility to cervical incompetence, or spontaneous loss of the cervical mucous plug leading to ascending infection. Cervical conization has the most consistent and largest association with preterm birth. Women with a history of conization are 2–3 times more likely to have a preterm birth than healthy controls, and those conceiving within 2–3 months of conization or large conization (>1 cm depth) may have the greatest risk. Recent meta-analyses have also demonstrated an increased risk of preterm birth with other excisional therapies – such as large loop excision of the transformation zone (LLETZ) (RR 1.70 compared to healthy controls). Although many studies within the meta-analyses use healthy controls as the comparison group, an increased risk of preterm birth with all excisional therapies remains – albeit attenuated – when women undergoing cervical treatment are compared to those who had been diagnosed with precancerous lesions, but not treated. This suggests that the increase in risk may be in part due to the underlying pathology of the precancerous lesion, as well as the cervical procedure itself.

It is unclear as to whether cervical dilation and curettage – for the management of miscarriage or surgical termination of pregnancy – increases the risk of spontaneous preterm birth in subsequent pregnancies. Whilst some large cohort studies have found no significant difference in rates, more recent good quality studies have demonstrated a small but significant increase in risk of spontaneous preterm birth after these procedures, with odds ratios of up to 1.8 with evidence that the risk of preterm birth in

subsequent pregnancies rises with the number of procedures performed.

Presence of congenital uterine anomalies

Congenital uterine anomalies are found more commonly in women with a history of second trimester loss or preterm birth, with a prevalence of up to 25% – compared to 6% in women from an unselected population. The risk of preterm birth varies with the type of uterine anomaly; women with a uterine didelphys or a septate uterus have the highest risk with up to 33% of pregnancies ending in preterm delivery. It has long been thought that the increased rate of preterm birth results from a reduced volume and distensibility of the uterine cavity, however it is most likely that women with uterine anomalies may also have a cervical anomaly which contributes to cervical insufficiency in pregnancy.

Use of assisted reproductive technologies

Several systematic reviews have shown an increase in risk of preterm delivery in women undergoing IVF treatment compared to those who conceive naturally, with the risk of preterm delivery doubling for delivery prior to 37 weeks, and tripling for delivery prior to 33 weeks for singleton pregnancies. It is unclear whether this increase in risk evolves from the fertility treatment itself, underlying maternal factors associated with infertility, or iatrogenic bias in the care of these pregnancies.

Demographic, socioeconomic, psychosocial and lifestyle factors

Women who are obese or significantly underweight pre-pregnancy are at increased risk of preterm delivery, as well as other pregnancy complications. A large meta-analysis of data from over one million women found that women from developed countries with a pre-pregnancy BMI <18.5 kg m⁻² are more likely to have a preterm birth – either spontaneous or indicated – compared to women with a BMI in the normal range (RR 1.22). Women with a BMI of ≥35 kg m⁻² also appear to be at increased risk of indicated preterm birth (OR 1.5–1.8), which may be partially explained by an increased prevalence of chronic disease (such as hypertension or diabetes) in this population.

Race and ethnicity are important risk factors for preterm birth. After adjusting for risk factors such as age, education and parity, black women have a two to three-fold higher risk of preterm birth compared to non-black women. The aetiology of this association is unclear, but is possibly interlinked with other lifestyle factors and/or social disparities; rates of preterm birth are increased amongst socioeconomically deprived women, women who have high levels of anxiety or perceived stress or low levels of support, are at the extremes of maternal age, and those who smoke, consume alcohol, and use illicit drugs during pregnancy.

Pre-conception strategies to reduce risk of preterm birth

What advice should be given and what medical or surgical interventions are available pre-conception that could reduce the risk of preterm delivery?

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