Prevention of preterm labour

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Abstract

Preterm labour complicates 3—4% of all pregnancies and its causes are multifactorial. The incidence is rising and it is more common in the economically deprived populations and communities in the rich countries. The recurrence rate is doubled after one previous preterm delivery. Secondary preventive measures have not been shown to be as effective as primary measures. A concerted multidisciplinary effort to eliminate risk factors for inducing preterm labour such as early marriage, smoking, short inter-pregnancy intervals, domestic violence and under nutrition will significantly reduce the incidence while optimisation of medical disorders pre-pregnancy and during pregnancy will result in a reduced incidence.

Keywords cervical length; enhanced antenatal care; oncofetal fibronectin; premature rupture of fetal membranes; preterm birth; preterm labour; progesterone; tocolysis; ultrasound

Introduction

Preterm labour (PTL) is defined by the World Health Organisation (WHO) as the onset of labour after the gestational age of viability and before 37 completed weeks or 257 days of pregnancy. It is clinically confirmed by demonstrable uterine contractions associated with documented cervical changes. Threatened preterm labour is diagnosed when there are documented uterine contractions without cervical changes.

Every year about 15 million babies are born prematurely and preterm birth (PTB) remains the biggest cause of neonatal death. It is also one of the commonest causes of under- 5 deaths. About 50% of preterm births follow spontaneous onset of labour, 30% after premature rupture of fetal membranes and the remaining 20%, iatrogenic due to maternal and fetal medical indications. There is evidence that the preterm birth rate is increasing in all countries where there are reliable data. In the UK, the rate is about 7.9%.

Key reasons for the rise in the number of preterm deliveries include a rise in multiple pregnancies from reproductive techniques, widespread obesity with its associated comorbidities of hypertension and diabetes and an increased incidence of sexually transmitted infections. Whilst an improved understanding of some of the underlying mechanisms and advances in technologies have culminated in the introduction of new tools for both the diagnosis of preterm labour and the management of extremely preterm babies, many controversies remain about the optimal methods for the prevention and care of women presenting in preterm labour.

Globally the need to address the impact of preterm births has become crucial as recent statistics indicate that the millennium development goals (MDGs) number 4 of reducing the under- 5 mortality by two-thirds will not be achieved due primarily to failure to reduce neonatal deaths from prematurity.

The burden of preterm labour

About 1 million babies die from complications of preterm birth and in most developed countries, about 70% of neonatal deaths are attributable to prematurity. The babies that survive are at an increased risk of disabilities involving neurological, respiratory and mobility functions. These incapacities exact a heavy financial toll on the affected countries, families, healthcare and educational systems. The cost of prematurity remains high for many developed countries with high level neonatal and ongoing care of premature babies. In the United States for example, the annual cost associated with preterm infants is over 26 billion dollars. In the UK, an Oxford research group reported in 2009, that the public cost of premature babies, in terms of their health needs, education and time off work taken by caring parents was about 939 million pounds per year. This figure fails to capture the psychological and emotional burden as well as the challenging family dynamics created in the event of an unexpected preterm birth of a baby.

Fifty percent of long-term neurological morbidity in the high income nations is linked directly to preterm delivery. Prolonging pregnancies even for several weeks significantly reduces newborn risks, and gestational age is the essential determinant of most perinatal outcomes. As an example, for a fetus delivered in the peri-viable gestational age, as few as 5 extra days could double chances of survival and also greatly increase 'neurologically intact survival'.

Causes of preterm labour

The pathophysiological mechanisms that underlie PTL are poorly understood, but some clinical and laboratory evidence suggest that a host of multiple factors trigger pathogenic processes leading to a final common pathway for the initiation of uterine contractions that result in spontaneous preterm labour (Figure 1). In about 50 % of cases, a definitive risk factor cannot be identified. A history of previous PTL is probably the most significant risk factor, followed by multiple pregnancies. For example, a previous history of PTB increases the recurrence risk to 15%, 2 previous PTBs to 30 % and then 3 previous PTBs to 45%. The risk of PTL in a multiple pregnancy is 10 times that of a singleton pregnancy. Associations between PTB and young or advanced maternal age, short inter-pregnancy intervals, low BMI, black ethnicity, smoking and excessive alcohol intake have also been established.

Apart from PPROM and "idiopathic" PTL, the two most common maternal conditions associated with PTB are pregnancy-induced hypertension and antepartum haemorrhage. This may either be spontaneous or iatrogenic in the interest of either the mother or to rescue the fetus from an adverse environment.

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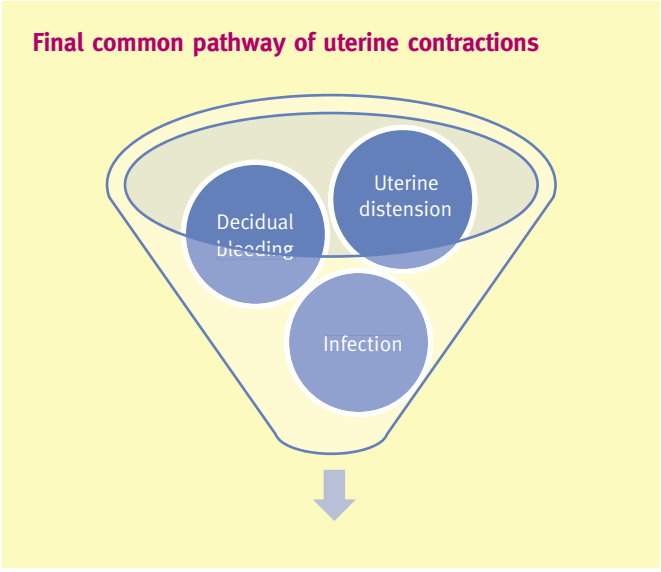

Figure 1

Infections such as bacteria vaginosis (BV), human immunodeficiency virus (HIV), syphilis, periodontal disease, subclinical chorioamnionitis and UTI have been associated with PTB. Non-infectious causes such as vaginal bleeding, abnormal uterine distention and pathological weakness and dilatation of the cervix may all trigger PTL by stimulating the release of pro-inflammatory markers.

Primary prevention

Primary prevention of PTB involves the provision of interventions before and between pregnancies which enhance the mother's health and reduce risks of her or the baby succumbing to preventable adverse pregnancy conditions. In the past, this aspect of women's health received less attention but awareness is now growing. It comprises of interventions aimed at identifying and improving the 'biochemical, behavioural and social risks of women's health or pregnancy outcomes through prevention and management'. These interventions can be grouped under preconception care, enhanced antenatal care, reducing multiple births and infections, optimizing the management of medical disorders and progesterone prophylaxis.

(a) Preconception care

A recent WHO commissioned report on PTB titled ''Born too soon – the 'Global Report' outlines comprehensive measures to prevent PTB. These measures start from preconception right through the pregnancy. Preconception care initiatives, include education on smoking cessation, better family planning and inter-pregnancy spacing, economic empowerment programs which alleviate poverty, community – based interventions like teenage HPV vaccination, micronutrient food supplementation and partner education to reduce domestic violence.

There is growing evidence that these social policy interventions do reduce the risk of PTB, the most effective being primary and secondary education of girls, increasing the legal age of marriage, pre-pregnancy weight optimization, screening and treating mental health disorders and other medical conditions such as chronic hypertension and diabetes mellitus. Policies relevant in developed countries include smoking cessation programs, prevention of domestic violence and increased engagement with deprived and marginalized communities. There is moderate to strong evidence of the effectiveness of a number of these interventions.

(b) Enhanced antenatal care

This care is designed to reduce or eliminate complications in women with documented potential risks to their pregnancies. The women receive the basic recommended antenatal care package by the National Institute for Clinical Effectiveness (UK) (NICE) as well as interventions targeted at improving healthy behaviours, promoting early identification of danger signs and increasing the women's knowledge about pregnancy complications such as antepartum haemorrhage and early warning signs of PTL. Regular antenatal visit is emphasised and those requiring multidisciplinary care on account of medical co-morbidities receive extra attention.

(c) Reducing multiple births

National policies to regulate assisted reproductive techniques (ART) and reduce multiple pregnancies are essential. The Human Fertilisation and Embryology Act (HFEA) in the UK in 2008 set out a national policy to reduce multiple pregnancy rates by encouraging all fertility centres to adopt the single embryo transfer policy. This was followed by new guidelines from the British Fertility Society and the Association of Clinical Embryologists on single embryo transfer, which have also been widely accepted. Women who carry multiple pregnancies whether conceived spontaneously or by ART require close clinical monitoring. Others with the diagnosis of cervical weakness in previous pregnancies need prior identification and plans made to institute early treatment such as elective cervical cerclage or cervical pessary.

(d) Reducing infections

Although the association between PTB and infections is still poorly understood, it is generally acknowledged that maternal infection plays a significant role in the pathogenesis. Goldberg et al. reported that 80% of women presenting with PTL before 30 weeks had evidence of amniotic fluid infection compared to 30% who deliver after 37 weeks. There is also evidence of activation of inflammatory mediators characterized by elevated concentrations of cytokines (IL-6, IL-1, IL-8, and TNF) but there is limited clarity on how these inflammatory agents are linked with the onset of labour.

A number of clinical trials using antenatal screening to identify and treat asymptomatic Bacteria Vaginosis and bacteriuria as well as periodontal disease have shown conflicting findings of benefit. While one Cochrane review of moderate quality studies showed that antenatal screening and treatment may be of value, another reported that current knowledge does not provide adequate evidence as to which antimicrobial agents are most suitable for intra-uterine infections. The ORACLE trial demonstrated, not only the lack of benefit of prophylactic antibiotics in women presenting with PTL, but also the potential harm of treatment in the neonate. The most recent Cochrane review on this subject confirmed that the only subgroup of women who