Guest Article

Prediction and prevention of preterm labour

N. N. Roy Chowdhury
Sr. Consultant Obstetrician and Gynaecologist, Calcutta Medical Research Institute, Calcutta.

Dr. N. N. Roy Chowdhury

Pre-term (premature) labour is defined as labour before 37 completed weeks of gestation. About 6-8 percent of all deliveries are preterm and of these about two-thirds occur between 34 and 37 weeks of gestation. Prematurity is the major cause of principal morbidity and mortality to 75% of all perinatal deaths. When lethal anomalies are excluded, 85 per cent of neonatal deaths are in preterm infants.

Despite advances in perinatal medicine in recent decades, the problem of preterm delivery continues to frustrate satisfactory reproductive outcome with little progress made in reducing the incidence of preterm births. The problem of preterm delivery has actually increased in recent years as other causes of adverse perinatal oucome have decreased and it remains one of the most serious problems facing obstetricians and neonatologists.

Incidence of premature labour

The incidence of premature labour (Berkowitz, 1993) varies in various studies as reported by different authors.

Name of Author	Year	Place	Incidence
Butler et al	1963	Edinburgh	3.4%
Wynn and Wynn	1970	East Germany	3.3%
		England	6.4%
Rush et al	1976	England	5.1%
Caritis et al	1979	U.S.A	9.8%
P.K. Devi	1980	India	12-18%
Dutta	1992	India	5-10%
Dawn	1992	India (Calcutta)	16%

Of all preterm deliveries about 70 percent occur following induced or spontaneous labour associated with obstetric complications as: severe pre-eclampsia, antepartum haemorrhage, intrauterine growth retardation, fetal anomalies and premature rupture of the membranes. Thus the incidence of spontaneous, otherwise uncomplicated, preterm labour is only about 2-3 percent (James et al, 1988).

Etiology

Most premature deliveries occur for unknown causes. Premature delivery may occur with the following conditions:

1. Uterine malformations e.g. double uterus.
2. Incompetent cervical os:
   which is associated with recurrent early deliveries, often in the second trimester.

3. Multiple gestation :
   The more fetuses present, the earlier delivery occurs.
4. Premature rupture of membranes and amnionitis. The major causes of morbidity in this condition are prematurity and infection.
5. Acute illness in the mother may precipitate preterm delivery. These may be: acute septic fever, acute pyelonephritis, diarrhoea, dysentery, malaria, acute appendicitis, toxoplasmosis and abdominal operations.
   Chronic diseases may be:
   Hypertension, nephritis, diabetes, decompensated heart disease, severe anaemia.
6. Pregnancy complications: such as pre-eclampsia, antepartum haemorrhage.
7. Low socio-economic class.
8. Iatrogenic:
   Elective induction with wrong estimation of gestational period.
9. Idiopathic (Majority)
   * Premature effacement of the cervix with hyperirritable uterus and early engagement of the head.
   * If previous infant was premature the current pregnancy has a 3 to 4 times greater chance of being premature.
   * Teen age pregnancy
   * Closely spaced pregnancies.

Main et al, 1985 sub-divided preterm deliveries into four groups:

1. Spontaneous labour of unknown causes: 38% of all preterm deliveries and 35% of all preterm early neonatal deaths.
2. Spontaneous labour with maternal and / or fetal complications.
3. Multiple pregnancy
4. Elective delivery: 23.3% of preterm deliveries were spontaneous, unexplained and suitable for tocolytic therapy to defer labour.

Fuchs, 1976 reported that 30% of all preterm deliveries represented a failure of tocolytic treatment.

Perinatal mortality and morbidity

Rapid advances in perinatal and neonatal medicine in developed countries have in recent decades led to improved survival or preterm infants given below (Kingdom et al, 1995).

Duration of Pregnancy	Survival Rate
23 weeks	20%
24 weeks	56%
25 weeks	44%
26 weeks	54%
27 weeks	65%
28 weeks	94%
29 weeks	94%

According to Copper, 1990 from 29 to 34 weeks of gestation the incidence of neonatal mortality ranged from:

Incidence of Morbidity	Nature of Morbidity
80%	Respiratory Distress Syndrome (RDS)
Other complications are: 50%	Patent ductus arteriosus
Intraventricular haemorrhage : 31.5%	Sepsis
Retinopathy : 25.2%	Necrotizing enterocolitis

The longterm problems for infants born preterm are :

* Refractive errors, myopia, hypermetropia
* Strabismus
* Hearing loss - 15%
* Physical and neurological disabilities
* Intellectual impairments
* Behavioural problems

Prediction of preterm labour

Numerous methods of screening for preterm labour have been proposed but none has fulfilled all the necessary criteria. These methods include (Anderson, 1990):

* Risk scoring
* Cervical assessment
* Uterine activity monitoring
* Cervico-vaginal fibronectin
* Biochemical markers
* Mediators of inflammation and infection

Risk scoring

Preterm labour is a heterogeneous condition with numerous associated social and medical risk factors e.g.:

* Low socio-economic 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 but in vain. The construction and validity of formal risk scores appears to offer a low positive predictive value having large difference in different populations (Hibbard, 1987).

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 25-30% for the high risk group and 4% for the low risk group. A cervical dilatation of >2 cm predicts PTD with a sensitivity of 60%.

Ultrasound examination of the length of the cervix - trans abdominal and transvaginal was compared with manual vaginal examination. They found that normal examination of cervical effacement detected 71% of P.T. 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 a screening tool in unselected population.

Transvaginal sonography is considered superior to manual assessment of cervix as a predictor of PTD. A cervical length of <39 mm at 30 weeks has a sensitivity of 76%, specificity of 59%, while a cut-off at 30 mm had a sensitivity of 71% and positive predictive value of 86.6% (Buckshee & Malhotra, 1997).

Uterine activity monitoring

It is controversial whether uterine activity monitoring allows earlier detection of the onset of preterm labour at all. Rather early intervention with tocolytic treatment in selected cases and increased nursing support may give better result in such condition. There is as yet no reliable standard method to differentiate the "genuine PTL with impending PTD and false labour". A sudden increase in uterine activity precedes the clinical diagnosis of PTL by 12-48 hours. Clinically significant contractions missed by self palpation could be identified by tocodynamometry with a sensitivity of 57-86% in predicting PTL.

Fetal breathing movement

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

Biochemical markers of preterm labour

It is not yet clear whether the molecular mechanism involved in preterm activation of myometrium and cervical ripening are same as in term labour, nor it is clear whether

the predisposing factors exert their influence on uterine action through a common pathway or multiple independant mechanism.

The possible biochemical markers of preterm delivery are:

1. Cervico-vaginal fetal fibronectin
2. Cervico-vaginal cytokines - Interleukin - 1
   Tumour necrosis factor (TNF)
3. Serum and cervico-vaginal proteases
4. Markers of maternal and/or fetal stress
   a. Serum corticotrophin releasing hormones (CRH)
   b. Plasma, urinary, salivary estradiol and/or estriols.

Cervico-vaginal fibronectin

The presence of fetal fibronectin in cervico-vaginal secretion is a specific predictor of preterm labour having sensitivity of 68-81.7% and a specificity of 72-82.5% and positive and negative predictive values of approximately 30% and 90% respectively. This investigation is technically complicated due to possibility of contamination with amniotic fluid. For this there is as yet no reliable U.K. data on this screening method.

Role of oxytocin

The myometrium becomes progressively more sensitive to oxytocin administration thus making it an important factor in initiation of labour (Niebyl, 1978).

Role of oestrogen and progesterone

The oestrogen and progesterone are incriminated in the mechanism of term as well as preterm labours. Increase in oestrogen progesterone ratio is a pre-requisite for initiation of labours.

Relaxin

It is a hormone found in corpus luteum of pregnancy and decidua. The exact role of this hormone is not yet known. Mac Lenan, (1980) found some evidence of it in the role of cervical ripening and effacement of the cervix.

Mediators of inflammation and infection

Some cases of preterm labour are caused by systemic or intrauterine infections, but the exact incidence, specific organisms and pathogenesis are poorly understood. In the majority of cases of preterm labour the pathophysiology is far from clear.

C-reactive protein (CRP) has been studied in women with preterm labour with and without preterm rupture of the membrane. While death, it is not of predictive value for preterm labour. There is no definitive evidence of a causal relationship between bacterial vaginosis and preterm labour nor it is clear that screening for it will accurately help to identify subsequent cases of preterm labour.

In preterm labour associated with intrauterine infection, amniotic fluid cultures may be positive but that may not be helpful in the prediction of preterm labour.

Conclusion

Preterm labour and delivery have a signficant impact on perinatal outcome. There is as yet hardly any reliable predicting factor and satisfactory medical treatment for the prevention or treatment of preterm labour. Clinical predictors of incipient preterm labour have been found to have poor sensitivity and specificity values. The epidemiology of this condition suggests that some efficient theraputic option may give benefit in a significant proportion of preterm labour. The solution of this problem demands sound scientific investigations along with rigorous clinical appraisal.

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