PRETERM LABOUR PATHOGENESIS AND MANAGEMENT

An Essay
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- **ACOG** American College of Obstetricians and Gynecologists
- **AF** Amniotic fluid
- **ATP** adenosine triphosphate
- **BMI** Body-mass index
- **BV** Bacterial Vaginosis
- **BCRCP** British Columbia Reproductive care programe
- **CAMP** cyclic adenosine monophosphate
- **CDMLK** calcium dependent myosin light chain kinase
- **CI** confidence interval
- **CL** cervical length
- **CNS** Central nervous system
- **COX** cyclooxygenase
- **CRH** Corticotropin-releasing hormone
- **CS** cesarean section
- **D&C** Dilatation and curettage
- **DES** Diethylstilboestrol
- **ECG** Electrocardiogram
- **ECM** the extracellular matrix
- **FDA** food drug administration
- **Ffn** Fetal fibronectin
- **GAG** Glucose AminoGlycans
- **GBS** Group B Streptococcal
- **HCG** Human chorionic gonadotropin
- **HMD** Hyaline membrane disease
- **HUAM** Human Uterine Activity Monitoring
- **ICU** intensive care unite
- **i.m** intramuscular
- **IgG** immunoglobin G
- **IL** Interleukin
- **IUGR** intrauterine growth retardation
- **i.v.** Intravenous
- **IVF** In vitro fertilization
- **IVH** Intra-ventricular hemorrhage
- **KD** Kib Dalton
- **LAHF** Low-amplitude high-frequency uterine activity

- **LEEP** Loop electrosurgical excision procedure
- **LBW** low birth weight
- **LMP** last menstrual period
- **LPs** lipopolysaccharide
- **LTs** Leukotriens
- **MCP** Monocytes chemo-attractant protein
- **MIAC** Microbial invasion of the amniotic cavity
- **MIP** Macrophage inflammatory protein
- **MFMU** Maternal-Fetal Medicine Units
- **NICHD** The National Institute of Child Health and Human Development
- **NICU** neonatal intensive care units
- **NIH** national institute of health
- **NO** nitric oxide
- **NOS** nitric oxide synthase
- **NPV** negative predictive value
- **NSAIDs** non steroidal anti-inflammatory drugs
- **PAF** Platelet activating factor
- **PDE4** potent phosphodiestrase 4
- **PGs** Prostaglandins
- **PhIGFBP-1** Phosphorylated insulin-like growth factor binding protein-1.
- **PPV** positive predictive value
- **PPROM** preterm premature rupture of membrane
- **PROM** premature rupture of membrane
- **PTB** Preterm birth
- **PTL** Preterm labour
- **RDS** Respiratory distress syndrome
- **ROP** Retinopathy Of Prematurity
- **RR** relative risk
- **SROM** spontaneous rupture of membranes
- **TAT** thrombin-antithrombin
- **TNFα** Tumor Necrosis Factor-α
- **TRH** thyrotropin releasing hormone
- **TVU** transvaginal ultrasound
- **UTI** urinary trypsin inhibitor
- **US** Ultrasonography
- **WHO** World health organization
- **ZAM** Zone of Altered Morphology

Chapter 1

IMPACT OF PRETERM LABOUR

DEFINITIONS:

Low birth weight is the term used to define infants who are born too small and **preterm** or **premature** birth are the terms used to define infants who are borne too soon. In 1990, **Ransom** wrote that in the United States ″Of the thousands of premature infants born, most are quietly laid away with little if any effort was being made for their rescue″. As the 20th century progressed, there was increasing awareness that preterm infants required special care units **(Cunningham et al., 2005).**

Prematurity become internationally visible as the most frequent cause of death in infancy. More recently, infant mortality has become a benchmark for international comparisons of health-care systems. In this regard, the United States has ranked poorly in 1995, the 25th in the world behind Japan, Singapore, Germany, and most of the Scandinavian countries. These countries with higher rate of preterm delivery have high rate of infant mortality **(Cunningham et al., 2005).**

The American Collage of Obstetrics and Gynecologists in 1995 defined preterm birth as these infants delivered prior to the completion of 37 weeks of gestation.

Also the **WHO** has recommended that (preterm) is defined as gestational age less than 37 completed weeks of pregnancy or less than 259 days from the first day of the last menstrual period, which is further subdivided into:

Early preterm	>>> less than 34 week′s gestation.
Very early preterm	>>> less than 30 week′s gestation.
Extremely preterm	>>> less than 26 week′s gestation.

(WHO, 1993)

The obstetric precursors leading to preterm birth are:
(1) Delivery for maternal or fetal indications, in which labour is either induced or the infant is delivered by prelabour caesarean section.

(2) Spontaneous preterm labour with intact membranes
(3) Preterm premature rupture of the membranes (PPROM), irrespective of whether delivery is vaginal or by caesarean section. (**Robert L Goldenberg et al., 2008)**

With improved care of the preterm the Collaborative Group on Antenatal Steroid Therapy (1981) reported that the great mortality and serious morbidity from preterm birth is prior to 34 weeks **(Cunningham et al., 2005).**

In 1935, the American Academy of Paediatrics defined prematurity as live born infant weighing 2500 gm or less **(Cone, 1985).** These criteria were used widely until it became apparent that there were discrepancies between gestational age and birth weight because of restricted fetal growth. The Word Health Organization in 1961 added gestational age as a criterion for premature infants, and so distinction was made between low birth weight (2500gm or less) and prematurity (37 weeks or less).

The proportion of infants born before term has increased in the last 20 years. In Canada for instance births at 36 weeks gestation or less increased from 6.3% in 1981 to 6.8% in 1992. This increase has been attributed to changes in frequency of multiple births, increase in obstetrical interventions improved ascertainment of early preterm births and increased use of ultrasound for estimating gestational age **(Joseph et al., 1998).**

It is more logical to use gestational age than birth-weight as a threshold since:
1- Outcome is more closely related to gestational age especially before 30 weeks gestation.
2- Normal range of birth weight varies between populations and is dependent on number of factors such as hypertension and smoking.
3- Prior to delivery, an obstetrician can more accurately determine gestational age than estimated birth weight **(Gardner et al., 1995).**

MEASURING THE GESTATIONAL AGE:

The use of last menstrual period (LMP) in calculating the estimated day of confinement is based on the assumption that the cycles are always 28 days long and that ovulation occurs at mid-cycle. However LMP is uncertain or unsure in 20% of pregnant women and about 1/3 of all

women have cycles longer than 28 days **(Mittendrof et al., 1993),** and so fetal sonar biometry is an accurate way of assessing the predicated date of confinement **(Kramer et al., 1998).**

REGISTERATION:

The registration of preterm infant may be modified by a number of factors like: intensive care facilities, social and cultural factors cost of funerals, hospital charges for miscarriage, or confinement may also influence registration (**Lumley, 1993).**

INCIDANCE:

Preterm labour continues to be a major contributor to neonatal and infant morbidity. Recent data from the USA indicate that the number of preterm deliveries (including those associated with preterm labour) has risen in the last 20 years by 30% (from 9.4% to 12.5%). (**Rachel Marie, 2007).**

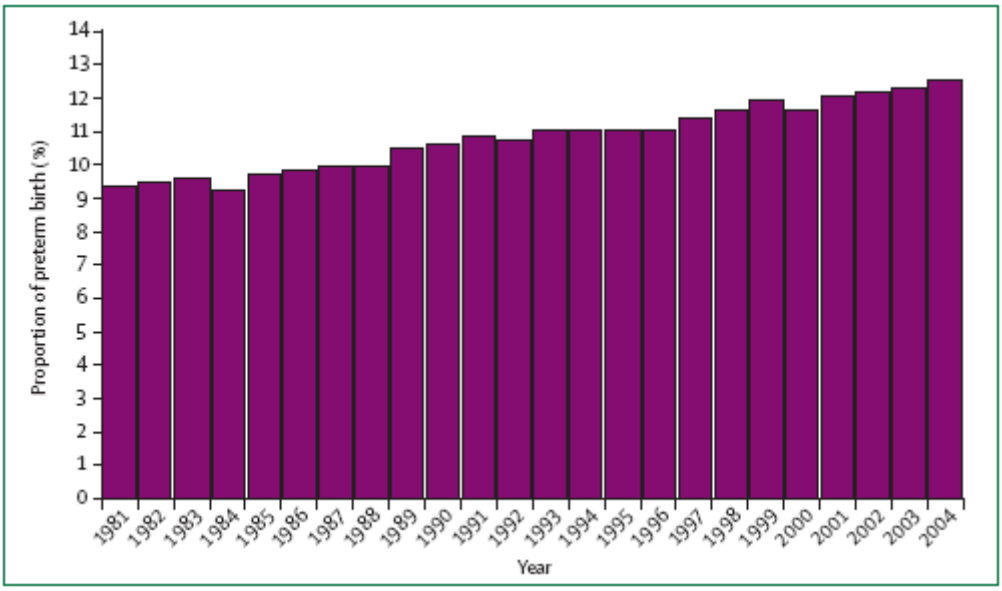

Figure 1.1: **Percentage of all births classified as preterm in the USA, 1981–2004**
Source: Martin JA, Kochanek KD, Strobino DM, Guyer B, MacDorman MF. Annual summary of vital statistics—2003.
Pediatrics 2005; **115:** 619–34.

Ananth et al., 2006, subdivided Preterm births according to gestational age: about 5% of preterm births occur at less than 28 weeks' (extreme prematurity), about 15% at 28–31 weeks' (severe pre maturity), about 20% at 32–33 weeks' (moderate pre maturity), and 60–70% at 34–36 weeks' (near term).

Table (1.1): shows the estimated numbers of preterm labour by region (**Villar & Ezcurra, 1994).**

Region	Total no. of births 1990(x1.000)	Incidence of preterm birth (%)	Total no. of expected preterm birth/year(x1.000)
Latin	12.442	7.74	963
Africa	28.438	9.98	2.809
Asia	84.122	9.26	7.789
North America	4.513	10.60	478
Europe	6.385	5.88	375
Former USSR	5.065	9.20	465
Oceania	503	5.80	29
Total world	141.468	″	12.908

As shown in table (1.1) the incidence of preterm birth worldwide varies between 5.8% for Oceania based solely on hospital deliveries in Australia and Newzeland and 10.6% of a sample of over 4.000.000 in North America (**Villar & Ezcurra 1994).**

Thirty seven precent of preterm of black women of low socioeconomic status, 50% of white women of upper middle class socioeconomic class, and possibly 75% of low risk selected South American women, are eligible for intervention therapy. On this basis it is estimated that nearly 5.5 million women in preterm labour worldwide are potentially treatable **(Villar & Ezcurra., 1994).** Of these women who are potentially treatable, intervention is only likely to be successful if they present in early labour to a hospital capable of and skilled in the use of intervention agents. This immediately excludes at least 10% of women who arrive in advanced labour and another 50% whose spontaneous preterm labour occurs at 35 week of gestation **(Tucker et al., 1991).**

Table (1.2): Estimated number of ″potentially treatable″ women in preterm labour by world region **(Villar & Ezcurra 1994).**

Region	Total no. of births 1990(x1.000)	Institutional Deliveries (%)	Incidence of preterm birth (%)	No. of Treatable women preterm labour(x1.000)
Latin	12.442	66	7.74	635.5
Africa	28.438	34	9.98	955.2
Asia	84.122	33	9.26	2.570.0
North America	4.513	95	10.60	454.4
Europe	6.385	95	5.88	356.6
Former USSR	5.065	95	9.20	442.6
Oceania	503	80	5.80	23.3
Total world	141.468	-		5.437.6

ECONOMIC IMPACT AND COST OF PREMATURITY:

The principal short term cost is that of neonatal ICU, which will be high with lower gestational age at delivery and lower birth weight. The largest component of this cost is the nursing and medical staff, and clearly the longer the stay in the neonatal ICU, the greater the cost. Additional costs treatment such as ventilation, artificial surfactant, and recombinant arises from erythropoietin, and surgical procedures **(Hall et al., 1997).**

Other short-term costs include additional time spent in the hospital by parents possibly with loss of earning and travelling costs to and from the unit often for a long period of time **(Griffen, 1993).**

PRETERM LABOUR, PERINATAL MORTALITY AND MORBIDITY:

Perinatal mortality compromises neonatal mortality [death of any live born in the first 28 days after birth], plus deaths in the last trimester [stillbirth]. It is found that no infants less than 22 weeks gestation survived, but survival rates increased sharply to about 77% at 28 weeks, 96% at 32 weeks, and >99% at 36 weeks. Gestational age-specific neonatal mortality rates for 3386 live-born infants between 1982 and 1986, decreased from 100% at 23 weeks to about 10% at 29weeks, with little additional improvement through 34 weeks. Also the probability of neonatal death before 26 weeks exceeds 75 %.**(Lopez Bernal A et al, 2007).**

The last trimester of pregnancy is necessary for the maturation of the fetal lungs and other organs in preparation for extra uterine life. If this process is interrupted by an early delivery the chances of survival of the newborn are severely decreased. The mortality rate is higher at lower gestational ages. For example it increases from 2 ‰ (two per thousand deliveries) at 37–40 weeks, to 18 ‰ at 32–36 weeks and 216 ‰ at 24–31 weeks (**Lopez Bernal A et al, 2007).**

Despite considerable improvements in special care baby units the perinatal mortality rates in the UK remain steady, and there is a wide range of both short-term and long-term morbidity and handicap in the surviving infants (**Lopez Bernal A et al, 2007).**
Based on the best obstetrical assessment of gestational age, death, severe infant morbidity, or both were great before 26 weeks gestation and almost universal before 24 weeks gestation. The chances of survival increase appreciably at or above 1000g birth weight **(Fanaroff et al., 1995).**

It is also reported that survival is possible for infants weighing 500-750g. Many of these extremely low birth weight infants; however were growth restricted and therefore of more advanced maturity. For example, survival of a 380g infant has been reported, but the gestational age was confirmed to be 25 weeks. Clearly, expectation for neonatal survival is primarily influenced by gestational age and maturity rather than birth weight alone (**Ginsberg et al., 1990).**

*MORBID CONDITION ASSOCIATED WITH PRETERM LABOUR:

1- Respiratory distress syndrome [RDS]:

The major and most frequent cause of morbidity in preterm neonates is hyaline membrane disease [HMD], caused by lack of surfactant formation in distal bronchiole and alveoli (**Lewis et al., 1996).** they also found that the incidence of HMD at 34 weeks of gestation to be [14.9%], a percentage very similar to the incidence reported by **Robertson et al.** in **1992** [22.5%], both of them are lower than those of **Konte et al.** in 1986 who found an incidence of [22.5%] during this week of gestation. The incidence of HMD was very low between 35 and 36 weeks of gestation
(Lewis et al. 1996).

Antepartum fetal asphyxia accounted for at least 34% of the fetal asphyxia in the pregnancies that were delivered preterm. Predictive criteria that led to intervention and diagnosis included clinical risk factors and, particularly, abnormal fetal assessment tests. The 50% incidence of moderate to severe asphyxia in the antepartum preterm pregnancy compares with 15% in term pregnancies. Moderate to severe asphyxia occurred with equal frequency with early and delayed intervention. So, fetal asphyxia in pregnancies those were delivered preterm is present frequently before onset of labour. Abnormal fetal assessment tests are valuable predictors of antepartum fetal asphyxia. The increased frequency of moderate and severe asphyxia in preterm pregnancy implies a greater likelihood of long-term morbidity or death **(Low et al., 1995).**

Boy are more prone than girls to develop these problems and white infants are more severely affected than black infants (**Hulsely et al., 1993)**.

The important preventive therapy is the administration of exogenous surfactant and antenatal corticosteroids which are responsible for much decrease of hyaline membrane disease as a cause of neonatal death, and were used as prophylaxis of preterm infants at risk of RDS (**Long et al., 1995).**