*Review Article*

# Magnitude of Problems of Prematurity- National and Global Perspective: A Review

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## Introduction

Preterm birth, defined as childbirth occurring at less than 37 completed weeks or 259 days of gestation, is a major determinant of neonatal mortality and morbidity and has long-term adverse consequences for health[1–3]. Children who are born prematurely have higher rates of cerebral palsy, sensory deficits, learning disabilities and respiratory illnesses compared with children born at term. The morbidity associated with preterm birth often extends to later life, resulting in enormous physical, psychological and economic costs[4,5] .

Of all early neonatal deaths (deaths within the first 7 days of life) that are not related to congenital malformations, 28% are due to preterm birth.[6] Preterm birth rates have been reported to range from 5% to 7% of live births in some developed countries, but are estimated to be substantially higher in developing countries[7]. These figures appear to be on the rise.[8] Events leading to preterm birth are still not completely understood, although the aetiology is thought to be multifactorial. It is, however, unclear whether preterm birth results from the interaction of several pathways or the independent effect of each pathway. Causal factors linked to preterm birth include medical conditions of the mother or foetus, genetic influences, environmental exposure, infertility treatments, behavioural and socioeconomic factors and iatrogenic prematurity[8].

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Approximately 45–50% of preterm births are idiopathic, 30% are related to preterm rupture of membranes (PROM) and another 15–20% are attributed to medically indicated or elective preterm deliveries[9,10].

Preterm birth rates available from some developed countries, such as the United Kingdom, the United States and the Scandinavian countries, show a dramatic rise over the past 20 years[11]. Factors possibly contributing to but not completely explaining this upward trend include increasing rates of multiple births, greater use of assisted reproduction techniques, increases in the proportion of births among women over 34 years of age and changes in clinical practices, such as greater use of elective Caesarean section.

In developing countries, accurate and complete population data and medical records usually do not exist. Furthermore, estimates of the rate of preterm birth in developing countries are influenced by a range of factors including varying procedures used to determine gestational age, national differences in birth registration processes, heterogeneous definitions used for preterm birth, differences in perceptions of the viability of preterm infants and variations in religious practices such as local burial customs, which can discourage the registering of preterm births[12]. These issues make measurement of preterm birth and comparisons across and between developing countries difficult.

It is estimated that 9.6% of all births were preterm in 2005, which translates to about 12.9 million births definable as preterm (Table-I). Approximately 85% of this burden was concentrated in Africa and Asia, where 10.9 million births were preterm. About 0.5 million preterm births occurred in Europe and the same number in North America, while 0.9 million occurred in Latin America and the Caribbean.

**Table-I**

*Preterm birth rates, number of preterm births by United Nations geographical region/subregion and percentage of births covered by the estimates in a systematic review of the worldwide incidence of preterm birth*[13]

| Region/subregion[a] | Preterm births | Preterm birth rate | | | Percent coverage |
|---|---|---|---|---|---|
| | No. in 000s | 95% CI[b] | % | 95% CI[b] | of estimates[c] |
| World total | 12 870 | 12 228-13 511 | 9.6 | 9.1–10.1 | 85.8 |
| More developed countries | 1 014 | 982-1 046 | 7.5 | 7.3–7.8 | |
| Less developed countries | 7 685 | 7 109-8 261 | 8.8 | 8.1–9.4 | |
| Least developed countries | 4 171 | 3 891-4 452 | 12.5 | 11.7–13.3 | |
| Africa | 4 047 | 3 783-4 311 | 11.9 | 11.1–12.6 | 72.7 |
| Eastern | 1 686 | 1 481-1 891 | 14.3 | 12.5–16.0 | |
| Middle | 602 | 535-669 | 11.6 | 10.3–12.9 | |
| Northern | 407 | 290-523 | 8.7 | 6.2–11.2 | |
| Southern | 228 | 191-265 | 17.5 | 14.6–20.3 | |
| Western | 1 125 | 1 036-1 215 | 10.1 | 9.3–10.9 | |
| Asia | 6 907 | 6 328-7 486 | 9.1 | 8.3–9.8 | 90.9 |
| Eastern | 724 | 650-798 | 3.8 | 3.4–4.1 | |
| South-central | 4 467 | 3 944-4 991 | 11.4 | 10.0–12.7 | |
| South-eastern | 1 271 | 1 062-1 480 | 11.1 | 9.3–13.0 | |
| Western | 396 | 290-501 | 7.9 | 5.8–9.9 | |
| Central | 49 | 21-77 | 3.8 | 1.6–5.9 | |
| Europe | 466 | 434-498 | 6.2 | 5.8–6.7 | 94.8 |
| South America | 591 | 524-658 | 7.9 | 7.0–8.8 | |
| North America[d] | 480 | 479-482 | 10.6 | 10.5–10.6 | 100 |
| Oceania | | | | | 91.0 |
| Australia/New Zealand | 20 | 20-20 | 6.4 | 6.3–6.6 | |
| Rest of Oceania | 16 | 11-20 | 6.4 | 4.6–8.2 | |

CI, confidence interval; PI, prediction interval.

[a] Countries categorized according to United Nations classification.

[b] Whereas PIs were calculated for country estimates based on the model, CIs were derived for the regional/subregional aggregate estimates that utilized data from studies as well as modelled estimates.

[c] Refers to the proportion of live births for which data were available and model-based estimates were not generated.

[d] Excluding Mexico, which is included under Latin America.

**Etiology of Preterm Birth**

Yet many of the cases are idiopathic; causes of preterm birth are many folds. Most of the causes of preterm birth are related to mother health. Here are the some recognized causes:[14]

1. Prior Obstetric/Gynaecologic History
   Prior Preterm Birth
   Cervical surgery (eg cone biopsy, Loop Electro-surgical Excision Procedure (LEEP), etc)
   Multiple dilatation and evacuation
   Uterine anomalies
2. Maternal Demographics
   Age <17 years & >35 years
   Single marital status
   Lower socio-economic status
   Short inter-pregnancy interval (eg, <6months)
   Other social factors (eg, less education, poor access to care, physical abuse, acculturation)

3. **Current pregnancy characteristics**
   Assisted reproductive techniques (e.g., IVF)
   Multiple gestations
   Fetal disease (e.g., chromosomal anomaly, structural anomaly, growth restrictions, etc)
   Vaginal bleeding (eg, 1st and 2nd trimester, placenta previa, abruption)
   Poly or oligohydramnios
   Maternal medical conditions (eg Hypertension, Diabetes, thyroid disease, asthma)
   Maternal abdominal surgery
   Psychological (eg stress, depression)
   Adverse behaviours
      Smoking (eg tobacco)
      Heavy alcohol consumption
   Cocaine
   Heroin
4. Infections
   Bacterial vaginosis
   Trichomoniasis
   Chlamydia Gonorrhoea
   Syphilis
   UTI
   Severe viral infections
   Intrauterine infections
5. **Short cervical length (between 14 and 28 weeks)**
6. **Positive fetal Fibronectin between 22 to 34 weeks**
7. **Uterine contraction**

**Where and when does preterm birth happen?[15]**
Over 60% of preterm births occur in Africa and south Asia, but preterm birth is truly a global problem; countries with the highest numbers include Brazil, India, Nigeria and the United States of America. Of the 11 countries with preterm birth rates over 15%, all but two are in sub-Saharan Africa. In the poorest countries, on average, 12% of babies are born too soon compared with 9% in higher-income countries. Within countries, poorer families are at higher risk.

The 10 countries with the greatest number of preterm births where Bangladesh is placed at 7th[16]:

India: 3 519 100
China: 1 172 300
Nigeria: 773 600
Pakistan: 748 100
Indonesia: 675 700
The United States of America: 517 400
Bangladesh: 424 100
The Philippines: 348 900
The Democratic Republic of the Congo: 341 400
Brazil: 279 300

The 10 countries with the highest rates of preterm birth per 100 live births:

Malawi: 18.1 per 100
Comoros: 16.7
Congo: 16.7
Zimbabwe: 16.6
Equatorial Guinea: 16.5
Mozambique: 16.4
Gabon: 16.3
Pakistan: 15.8
Indonesia: 15.5
Mauritania: 15.4

Of 65 countries with reliable trend data, all but three show an increase in preterm birth rates over the past 20 years. Possible reasons for this include better measurement, increases in maternal age and underlying maternal health problems such as diabetes and high blood pressure, greater use of infertility treatments leading to increased rates of multiple pregnancies, and changes in obstetric practices such as more caesarean births before term.

There is a dramatic difference in survival of premature babies depending on where they are born. For example, over 90% of extremely preterm babies (<28 weeks) born in low-income countries die within the first few days of life; yet less than 10% of babies of this gestation die in high-income settings.

**Categories of Preterm Delivery**
Preterm births can be categorized as those undertaken because of a specific indication or as spontaneous preterm births. Indicated preterm births occur when a health care provider delivers a baby because of medical or obstetrical complications that jeopardize the health of the mother or the fetus. Spontaneous preterm births occur as a consequence of spontaneous preterm labor or preterm rupture of fetal membranes before the onset of labor.

**Mechanisms of Preterm Labor**
Preterm parturition is not necessarily the result of premature physiologic activation of processes that normally occur at term; rather, preterm labor commonly results from pathologic processes[17,18]. Regardless of when parturition occurs in gestation, the process

itself is generally heralded by synchronous changes in the myometrium and cervix that permit expulsion of the fetus. The molecular processes underlying parturition were recently comprehensively reviewed by Smith[19].

**Pathophysiology of Preterm Birth**

Spontaneous preterm birth is a physiologically heterogeneous syndrome[18]. The cascade of events that culminate in spontaneous preterm birth has several possible underlying pathways. Four of these pathways are supported by a considerable body of clinical and experimental evidence: excessive myometrial and fetal membrane overdistension, decidual hemorrhage, precocious fetal endocrine activation, and intrauterine infection or inflammation[18,20]. These pathways may be initiated weeks to months before clinically apparent preterm labor. The processes leading to preterm parturition may originate from one or more of these pathways; for example, intrauterine infection or inflammation and placental abruption often coexist in preterm births[21-24]. Decidual hemorrhage and intrauterine infection share several inflammatory molecular mechanisms that contribute to parturition[25]. The etiologic heterogeneity of preterm birth adds complexity to therapeutic approaches. Although the ultimate clinical presentation of women with preterm labor may appear to be homogeneous, the antecedent contributing factors probably differ considerably from woman to woman.

Certain clinical presentations and risk factors preferentially predispose the maternal–fetal unit to preterm birth in a pathway-specific fashion. For example, women with multifetal pregnancies are at particular risk for preterm birth, presumably owing to pathologic uterine overdistention. Women with preterm rupture of membranes or preterm labor at a very early gestational age (e.g., 24 to 28 weeks) are at increased risk for having underlying intrauterine infection; the precise nature of such predispositions is not known at this time.

**Diagnosing Preterm Delivery**

Serial endo-cervical ultrasound measuring the cervical length and also presence or absence of fetal fibronectin may help in detecting preterm labour. If it cervix length is more than 3 cm and fibronectin is absent, suggest no premature labour in next two weeks or so.

**Diagnosis of Acute Preterm Labor**

For decades, the clinical diagnosis of preterm labor has been based on the presence of regular, painful uterine contractions accompanied by cervical dilatation or effacement. If framed as screening criteria for the outcome of "preterm birth," such factors generally demonstrate poor sensitivity and specificity. The identification of women with preterm contractions who will actually deliver preterm is an inexact process. A systematic review showed that in approximately 30% of patients, preterm labor resolved spontaneously[26]. In subsequent studies, 50% of patients who were hospitalized for preterm labor actually delivered at term[27]. The inability to distinguish accurately between women in "true" preterm labor and those in "false" labor has greatly hampered the assessment of therapeutic interventions, since up to 50% of untreated (or placebo-treated) subjects do not actually deliver preterm.

**Problems of prematurity in the Neonatal Period**

- Need for resuscitation at birth
- Respiratory
  - Respiratory distress syndrome
  - Pneumothorax
  - Apnoea and Bradycardia
- Hypotension
- Patent DuctusArteriosus
- Temperature Control
- Nutrition
- Metabolic
  - Hypoglycaemia
  - Hypocalcaemia
  - Electrolyte Imbalance
  - Osteopenia of Prematurity
- Infection
- Jaundice
- Intracranial Haemorrhage
- Retinopathy of Prematurity
- Anaemia of Prematurity
- Bronchopulmonary Dysplasia (Chronic lung disease of prematurity)
- Inguinal Hernia

All these are problems faced by the neonatologist in the Special Care Baby Unit (SCBU) but, when the baby is eventually discharged from hospital and goes home with the family that is not the end of problems. The baby who is just slightly premature will probably have few or no long-term problems but those who are very premature and who have a stormy start to life often suffer many and serious problems.

Because mortality rates have fallen substantially over the last few decades with improved neonatal care, the focus for perinatal interventions is to reduce long-term morbidity, especially the prevention of brain injury and abnormal brain development. The premature baby faces a number of problems (these may be accentuated if there is also intrauterine growth restriction (IUGR)):

**Long-term outcome of premature babies**

Morbidity is inversely related to gestational age; however, there is no gestational age (including term) that is wholly exempt[28]. Severe problems such as cerebral palsy, blindness and deafness may affect as many as 10 to 15% of significantly premature babies.

About 1 in 4 preterm babies with birth weight below 1.5 kg has peripheral or central hearing impairment, or both[27]. Infants who undergo early screening and treatment for retinopathy of prematurity (ROP) have improved long-term functional and structural outcomes compared with those who receive conventional screening and treatment[29,30]. However, the increased survival of lower birthweight infants has increased the prevalence of aggressive, posterior ROP that may be unresponsive to conventional treatment. In a multicentre study, 66% of preterm babies under 1.25 kg developed ROP, but only 6% required treatment[31].

Preterm babies with extremely low birth weight (birth weight 500-999 g) children have more hospital readmissions and other health problems in the early years after discharge than do normal birth weight (birth weight>2499 g) children. Respiratory illnesses, including lower respiratory infections, are the dominant cause for hospital readmission[32].

Cognitive and neuromotor impairments at 5 years of age increase with decreasing gestational age. Many of these children need a high level of specialised care[33]:

- About half of infants born at 24-28 weeks of gestation have a disability at 5 years, similar to the proportion observed in the UK-based EPICure study.
- Over 30% had developmental co-ordination disorder (DCD) compared with 6% of class mates.
- The preterm children were significantly more likely be overactive, easily distractible, impulsive, disorganised and lacking in persistence. They also tended to overestimate their ability.
- Attention deficit hyperactivity disorder (ADHD) was found in 8.9% of the preterm children and 2% of controls.

**Prevention**

Interventions to reduce the morbidity and mortality of preterm birth can be primary (directed to all women), secondary (aimed at eliminating or reducing existing risk), or tertiary (intended to improve outcomes for preterm infants)[34]. Most efforts so far have been tertiary interventions.

- Primary - problems of social deprivation, poor maternal nutrition and substance abuse must all be addressed. Smoking should cease and, as explained in the article on fetal alcohol syndrome, alcohol consumption should be avoided as there may be no safe lower limit.
- Secondary - antenatal care is important and should be easily accessible to all women.
- Tertiary - interventions when complications arise in regionalised care, treatment with antenatal corticosteroids, tocolytic agents and antibiotics.

**Conclusion:**

Preterm Birth is a common pregnancy outcome associated with much of the pregnancy related mortality and short and long term morbidity in infant and children. PTB is far more common in the developing countries than the developed world. Important risk factors include multiple pregnancy, prior PTB, and maternal malnutrition. Maternal infection/inflammation, especially of the chorioamnionism, is associated with the majority of early spontaneous PTB. The risk factors in Table 1 should be reviewed in each woman of reproductive age, and each pregnant woman. Only by identifying the risk factors can appropriate risk-specific interventions be applied. Additional research that defines the mechanisms by the risk factors are related to PTB is crucial. Better understanding of these mechanisms should allow clinicians to design appropriate interventions so that the incidence of PTB and related fetal and neonatal morbidity and mortality will be reduced.

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