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Review Global burden of prematurity

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SUMMARY

The global burden of preterm birth (PTB) includes the morbidity and mortality of babies born before 37 completed weeks of gestation. Prematurity has been the leading worldwide cause of neonatal mortality for at least a decade, but has now also become the leading cause of childhood mortality through age five years. Globally, each year, 15 million babies are born preterm, which is estimated to be about 11% of all deliveries. Preterm birth appears to be increasing in most countries. This review will address the epidemiology, rates, and etiology of PTB around the globe as well as survival by gestational age and interventions and preventative measures known to improve outcomes in high-burden countries.

1. Introduction

Keywords:

Prematurity

Preterm birth

Preterm delivery

Neonatal mortality

Neonatal morbidity

Childhood mortality

Currently, about half the world's births occur at home without access to skilled care during or immediately after birth, and in many low- and middle-income countries (LMICs) those births that occur in a facility are attended by poorly trained physicians, midwives, and/or nurses with limited equipment or ability to provide goodquality obstetric and neonatal care [1]. It is in these settings that most of the world's preterm infants are born, and it is for these reasons, among others, that the global burden of prematurity is so high.

Preterm birth is defined by the World Health Organization (WHO) as delivery before 37 completed weeks of gestation, with extremely PTB defined as occurring at less than 28 weeks, very preterm delivery occurring between 28 and 32 weeks, and moderate to late PTB occurring from 32 through 36 weeks [2]. These distinctions are important clinically as there are very large increases in morbidity and mortality as the gestational age decreases among preterm births, and the obstetric management often differs at different stages of pregnancy. There are also important economic considerations as deliveries at earlier gestational ages are associated with a greater cost [3].

Determining that a PTB has occurred is a challenge in many settings where ultrasound is not readily available for pregnancy dating. The gestational age distributions derived from other dating

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methods such as last menstrual period (LMP) or fundal height data are significantly different than those derived from ultrasound, and are often not usable for clinical management or population studies. Therefore, gestational age is often estimated using the proxy measure of birth weight. In low-resource settings, this increases inaccuracy where pregnancies may be more likely to be affected by intrauterine growth restriction (IUGR) or small for gestational age, confounding the methodology of assigning presumed gestational age [4]. Current collaborative efforts are underway by the World Health Organization (WHO) and partners to better and more specifically define gestational age and PTB with special attention to those settings where ultrasound is not readily available, as those tend to be the locations where the majority of PTB occur. Preterm birth is a critical global problem because of its impli-

cations for morbidity and mortality, as well as its socio-economic liability. The publication of new data on neonatal and childhood mortality rates and causes has shifted at least part of the focus of the world community from communicable diseases in the population aged under five years to prediction, prevention, and management of PTB. Worldwide, PTB accounts for 965,000 deaths in the neonatal period, and an additional 125,000 deaths in children aged one to five years, representing the leading cause of both neonatal and childhood mortality [5]. Measures of the global burden of prematurity include not only concrete metrics such as the neonatal and childhood mortality rates attributed to PTB, but also the associated psychosocial, economic, and physical burdens and morbidities affecting mothers, infants, and communities at large. Sequelae of PTB can be lifelong with long-term poor outcomes in surviving premature infants including an increased risk of cerebral palsy, impaired learning and visual disorders, and increased chronic disease in adulthood [3].





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This review reports on the global burden of PTB by epidemiologic measures, including the rates of PTB around the world, by addressing the leading etiologies of PTB in those settings, and by commenting on specific interventions and preventative measures which would improve outcomes in the highest risk areas.

2. Epidemiology

Understanding the global burden of PTB is limited by the availability and quality of data. The estimated rates of PTB around the world are qualified by the fact that, in many LMIC, vital registries and routine health surveillance data collection are often poor. Additionally, whereas there are WHO guidelines regarding the classification of PTB, the determination of gestational age poses a huge challenge, as do outcomes such as stillbirth and early neonatal mortality, which may be defined differently in different regions, preventing clean comparisons of pregnancy outcomes across regions. The contribution of PTB to stillbirth and vice versa is not an entirely clear relationship. In the USA and other high-income countries (HICs), >80% of the stillbirths are preterm, and half of all stillbirths occur from 20 to 28 weeks. For comparison, in LMIC only about half of all stillbirths occur at preterm gestations.

Despite the obstacles to determining accurate rates of PTB around the world, the WHO and partners published national, regional, and worldwide estimates of PTB rates from 2010 [3]. This article included data from national registries, reproductive health surveys, and published and unpublished studies to estimate PTB rates and trends over the previous 20 years. Based on data from 184 countries, the global average PTB rate in 2010 was estimated to be 11.1%, ranging from about 5% in northern Europe to 18% in sub-Saharan Africa [3]. The highest PTB rates in 2010 occurred in southeastern Asia, south Asia, and sub-Saharan Africa. Nine of the 11 countries with the highest rates are in Africa [3]. Furthermore, 60% of all PTBs were estimated to have occurred in sub-Saharan Africa and south Asia accounting for just over nine million of the almost 15 million PTBs that occurred worldwide in 2010, yielding a PTB rate of 12.8% in those settings [3]. Figures 1 and 2 illustrate the global burden of PTB in 2010.

By the same analysis, the 10 countries with the highest number of PTBs were India (23.6% of the global total of PTBs with a PTB rate of 13% of all live births), China (7.8%, 7.1%), Nigeria (5.2%, 12.2%), Pakistan (5.0%, 15.8%), Indonesia (4.5%, 15.5%), USA (3.5%, 12.0%), Bangladesh (2.8%, 14.0%), Philippines (2.3%, 14.9%), Democratic Republic of Congo (2.3%, 14.9%), and, in tenth place, Brazil, with 2.3% of the global total of PTBs and a PTB rate of 9.2% [3].

This analysis illustrates very clearly that a majority of PTBs are occurring in LMICs. The implications of this finding are that the global burden of PTB is falling more heavily on countries with fewer resources to manage the medical, social, and economic complexities of caring for premature infants. Evidence of this fact comes from another WHO-led analysis on the updated global, regional, and national causes of childhood mortality, which showed that the leading cause of neonatal death was complications of prematurity, accounting for nearly a million of the greater than six million deaths in children aged <5 years who died in 2013 [5]. Furthermore, these analyses suggest that the global burden of PTB is increasing [6]. Unfortunately, the proportion of childhood mortality associated with PTB is not achieving the reductions that have been seen over the last decade with infectious causes [3,5].

3. Survival by gestational age and/or birth weight

As mentioned previously, the burden of PTB includes not only the delivery itself and how that affects the mother and infant in the moment, but also, and probably more importantly, the ongoing challenges faced by mothers and neonates during the postpartum period, especially in terms of survival, and then over the long term with attention to lifelong morbidities resulting from prematurity.

Most PTBs - about 84% or 12.5 million - occur after 32 completed weeks of gestation [3]. Whereas the great majority of infants born in this gestational age range survive in HICs, neonates in LMICs are less fortunate. Ninety percent of infants born before 28 weeks of gestational age survive in HICs as compared to 10% in lowincome countries [4]. Research has shown that many of these neonates would survive with supportive care and that intensive care is not essential for survival in many cases; interventions to improve neonatal survival will be discussed in a separate section [4]. Data from HICs prove that neonatal survival improves with an increase in gestational age. For example, a study conducted in the USA found that survival was better for older infants and for the heavier newborns within each gestational age category [7]. At less than 29 weeks gestational age, female infants survived better than males with singletons also doing better than multiples [7]. The same study showed that the greatest improvement in survival occurred between 25 and 26 weeks, and that by 30 weeks of gestation, survival rates were >90%, increasing by <1% per week thereafter until term [7]. A similar picture was seen in a study evaluating



Fig. 1. Estimated preterm birth rates by country for the year 2010. Reproduced from Blencowe et al. [2], with permission.

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