The Epidemiology of Low Birthweight

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Abstract

In this paper, I review the epidemiology of low birthweight (LBW). I begin by defining LBW and emphasizing the distinction between infants who are born early (preterm) and those who are born small for their gestational age (SGA). I then review data on the global burden of preterm birth and SGA and the evidence bearing on whether ‘one size fits all’, i.e. whether a single birthweight (or birthweight for gestational age) cutoff is appropriate for different regions and population subgroups. I summarize what is known about the etiologic determinants of preterm and SGA birth, how they differ among countries of varying socioeconomic development and prevalence of risk factors, and how they are changing over time. I conclude with a critical appraisal of LBW prevention as a public health priority and argue that reducing fetal and infant mortality is a more important and achievable target for intervention.

Definitions

The World Health Organization (WHO) defines low birthweight (LBW) as a weight at birth <2,500 g. But birthweight is known to be determined by two separate, if not entirely independent, processes: (1) the duration of gestation and (2) the rate of fetal growth [1]. Thus, LBW can arise through one or both of two mechanisms. Infants who are born ‘too soon’ are referred to as preterm, which WHO defines as a gestational age at birth <37 completed weeks [2]. Infants can also be LBW because they are born ‘too small’ for their age (small for gestational age, SGA), which has several definitions, the most common of which is a birthweight below the 10th percentile of gestational age based on an appropriate reference [3].
Figure 1 shows the relationship among LBW, SGA birth, and preterm birth (PTB). As the figure illustrates, all LBW infants are preterm, SGA, or both. But the figure also makes it clear that infants can be born preterm without having LBW. In the Canadian birthweight for gestational age reference [4], for example, many infants born between 34 and 36 completed weeks have a birthweight ≥2,500 g. Similarly, infants can be SGA without having LBW; the 10th percentile for Canadian infants born at 40 completed weeks (i.e. at term) is about 3,000 g (3,079 g for boys, 2,955 g for girls), while the majority of SGA infants born at 38 weeks or later weigh ≥2,500 g [4].

The importance of distinguishing preterm birth from SGA is evident from the contrast in temporal trends between preterm birth and LBW, as illustrated by figure 2, which is based on data from Canada over a quarter of a century. After slight declines in the rates of preterm birth and LBW in the early 1980s, LBW remained stable or decreased slightly over the next 20 years, while preterm birth increased steadily. This reflects an increase in weight for gestational age [5], along with the increased incidence of preterm birth in the population [6, 7].
Since about 2000, however, rates of LBW and preterm birth have risen in parallel and, in the most recent years, have also fallen in parallel, reflecting the end of the temporal trend towards increasing birthweight for gestational age and an apparent true decrease in preterm birth.

In addition to these differences in prevalence and temporal trend, preterm and SGA infants have very different prognoses for survival, morbidity, and development [8]. Preterm birth is the world’s leading cause of infant mortality [9]. SGA infants are at increased risk of stillbirth and infant mortality [10], but much recent literature has focused on long-term associations with chronic diseases of adulthood, including hypertension, type 2 diabetes, and coronary heart disease [11].

These considerations underline why it is important to distinguish between preterm birth and SGA as causes of LBW and why it is inappropriate to use LBW as a population health indicator to compare geographic differences in countries or regions, or trends over time. Of course, the ability to distinguish between SGA and preterm birth depends on reasonably valid estimates of gestational age at birth, and of weight at or soon after birth. In many poor rural areas of the world, particularly in South Asia and sub-Saharan Africa, many women are not seen regularly during the course of pregnancy, and births occur in the home. Thus, reasonably accurate measures of gestational duration and size at birth are not available for a very large fraction of births in those regions.

The Global Burden of LBW

The limited value of LBW prevalence as an indicator of maternal and child population health has been recognized by the World Health Organization. For example, in WHO’s World Health Report of 2005 [12], which focused on maternal and child health, tabulated indicators included numbers of births, cesarean delivery, maternal mortality, stillbirth, and neonatal mortality, but not LBW. This is in line with WHO’s emphasis on the Millennium Development Goals (MDGs), particularly MDG 4 and 5, which bear on reducing young child and maternal mortality, respectively.

In its 2009 The State of the World’s Children [13], UNICEF estimated the world birth prevalence of LBW from 2000 to 2007 based on the most recent year’s data available in each country and region. The region-specific birth prevalence ranged from 6% in the East Asia and Pacific region, and 7% in industrialized countries to 27% in South Asia. To my knowledge, the last time WHO estimated the international SGA birth prevalence was in 1998 [3], based on the threshold <10th percentile from the Williams et al. [14] (California) reference curve, as occurring in 30 million newborns per year, or 20.8% of all births. Of
the total number of SGA infants, 75% were estimated to be born in Asia, with another 20% in Africa and 5% in Latin America. Figure 3 is taken from the WHO report [3] and shows the prevalence of newborn infants born between 1985 and 1995 who were both SGA and LBW.

Because preterm birth is a far more important cause of neonatal and infant mortality than intrauterine growth restriction [1], both WHO and the March of Dimes have focused more recently on preterm birth, despite the difficulty in ascertaining gestational age at birth in many low- and middle-income countries [9, 15]. Figure 4 is a world map showing estimated country-specific prevalences of preterm birth in 2005; 12.9 million births, or 9.6% of all births worldwide, were estimated as being preterm, 85% of whom were concentrated in Africa and Asia [9]. The lowest estimated rates were seen in Europe and Australia.

**Does One Size Fit All?**

One question that frequently emerges in public health circles when discussing international comparisons of birthweight distributions is whether the prevalence of LBW (or the prevalence of SGA) should be based on a single birthweight cutoff or a single birthweight for gestational age reference, or whether different
The need for sex-specific birthweight for gestational age standards is generally accepted because in every region in the world, newborn girls weigh less than newborn boys [16]. These sex differences have also been noted as early as the first trimester in ultrasound measurements obtained in nonselected populations. Despite their smaller size in utero and at birth, girls have lower stillbirth and infant mortality rates than do boys, and thus it is reasonable to infer that their ‘smallness’ relative to boys is physiologic, rather than pathologic.

But other widely recognized differences in birthweight, or birthweight for gestational age, are not so clearly classified as physiologic (‘normal’) or pathologic. For example, birthweights are higher and LBW rates lower in rich countries than in low- and middle-income countries [10]. Within countries, robust differences have been reported according to ethnicity, parity, maternal height, maternal prepregnancy BMI, and plurality (singleton vs. multiple gestation) [1]. Despite these robust differences, there is little agreement as to which of these differences are physiologic versus pathologic.

We carried out a study related to ethnic differences in birthweight for gestational age in the Canadian province of British Columbia [17]. We examined live and stillbirths in 1981–2000 and compared 4 ethnic groups of infants with substan-
tial prevalence in the British Columbia population: Chinese, South Asian, First Nations (‘American Indians’), and other (predominantly Caucasian). We found a substantially higher prevalence of SGA (based on a single, internal standard for the province) among South Asians at all gestational ages. For the Chinese population, SGA rates were not different from those of First Nations or others until term when they resembled rates among the South Asian population. SGA rates were actually lowest at term in the First Nations populations, who are well-known to have higher birthweights for gestational age [18, 19]. Yet despite these differences, gestational age-specific perinatal mortality rates were lowest among the Chinese, next lowest among the South Asian population, and highest among First Nations. Results for the Chinese and South Asian groups are likely to be affected by the ‘healthy migrant’ bias, but such a bias does not seem to protect them against higher SGA rates. It is difficult to understand how that bias would simultaneously lead to higher SGA rates and lower perinatal mortality rates. We therefore inferred that the lower weights of South Asian and Chinese infants were likely to be ‘physiologic’ [17].

In a more recent study based on the Swedish National Birth Register (which includes data on maternal height), we observed higher perinatal mortality rates in women of short stature and in primiparous (vs. multiparous) women [20]. Using marginal structural models to avoid the collider stratification bias that can occur in regression models including a causal intermediate, those higher mortality rates were ‘explained’ by the lower birthweight for gestational age among short and primiparous women. In other words, the smaller size seemed to be largely responsible for the higher perinatal mortality rates, suggesting that the smaller size of infants born to short or primiparous women can indeed be considered ‘pathologic’ [20].

It is also important to emphasize that at preterm gestational ages, all fetal growth references based on birthweight for gestational age are biased, because infants born at these pathologic (preterm) gestational ages tend to be significantly undergrown compared with the population of normal fetuses who remain in utero at those gestational ages [21]. Thus, increasingly, fetal growth at birth is evaluated based on ultrasound-derived estimates of fetal weight [22]. Two large international studies are currently under way to develop new reference curves of fetal weight for gestational age based on repeated ultrasound measurements in pregnancy.

Etiology of LBW

The major known causes of preterm birth probably do not appear to vary much among rich, middle-income, and low-income countries [1]. The leading identified causes of spontaneous (i.e. not induced or delivered by prelabor ce-
sarean section) include multiple birth, genitourinary tract infection, pregnancy-induced hypertension/preeclampsia, low prepregnancy BMI, incompetent cervix, cigarette smoking, prior history of preterm birth, abruptio placentae, prolonged standing and lifting at work, and cocaine use in pregnancy [1]. Most cases of spontaneous preterm birth remained unexplained, however, but nonspontaneous preterm births (those resulting from labor induction or prelabor cesarean delivery) are becoming increasingly large contributors to preterm birth, particularly in high-income countries [6, 23, 24]. In the United States, for example, preterm birth rates have increased to about 11–12%, with much of the increase over the last 20 years attributable to increased obstetric intervention [24].

Unlike the situation for preterm birth, the causes of SGA birth differ considerably among countries and regions [1]. Cigarette smoking is probably accountable for the largest fraction of SGA births in those countries where a sizeable fraction of women smoke during pregnancy. Other causes include low gestational weight gain, low prepregnancy BMI, primiparity, short stature, pregnancy-induced hypertension/preeclampsia, congenital anomalies, other genetic factors, and alcohol/drug use. In low-income countries where smoking during pregnancy is rare or nonexistent, nutritional factors (low gestational weight gain, low prepregnancy BMI, and short stature) account for a much larger fraction of the prevalence of SGA birth [1]. In endemic areas, malaria is another important cause of SGA birth, particularly among primiparous women [1]. Maternal morbidity due to common respiratory and gastrointestinal infections is also likely to contribute to SGA occurrence in such settings [1].

Few interventions have been shown to reduce the risk of preterm birth. Based on the most recent Cochrane reviews, effective interventions include intensive counseling to reduce cigarette smoking [25] and progesterone treatment of women with short cervix or prior history of preterm birth [26]. Reduced risk of SGA birth has been demonstrated with balanced energy/protein supplementation [27], intensive counseling to reduce smoking [25], and malaria prophylaxis [28, 29].

**Prevention of LBW: A Public Health Priority?**

LBW is highly associated with infant (and especially neonatal) mortality in both rich and poor countries [8, 30]. Moreover, countries with the highest infant mortality rates are also those with the highest apparent rates of LBW [10]. Because many developing countries cannot afford the technologies (e.g. neonatal
intensive care units) required to reduce mortality among LBW infants, the conventional ‘wisdom’ is that poor countries should emphasize prevention of LBW as a public health priority [31–33].

We carried out a study comparing temporal trends in infant mortality and LBW in several countries in the Americas (the United States, Canada, Argentina, Uruguay, and Chile) between the late 1980s and the late 1990s [34]. With the exception of Chile, which reported a slight reduction in their LBW rate, all of the other study countries reported increases in LBW, yet substantial reductions in infant mortality, over the decade. The countries’ infant mortality rates were highly correlated with their LBW rates in the late 1980s (Spearman r = +0.80) but much less closely correlated in the late 1990s (r = +0.25). The risk of infant mortality was negatively associated with the proportion of infant deaths occurring among LBW infants. The RR per SD increase in that proportion was 0.68 (95% confidence interval 0.67–0.68) in the late 1980s and diminished even further to 0.47 (95% CI 0.46–0.47) in the late 1990s.

Infant, and particularly neonatal, mortality is affected far more by preterm birth than by SGA birth [1]. Moreover, modifiable determinants such as maternal nutrition, smoking, and malaria affect SGA birth to a much larger degree than preterm birth [1]. To my knowledge, no country has successfully reduced its infant (or neonatal) mortality rate by preventing LBW. Yet many countries have succeeded in substantially lowering their infant and neonatal mortality without reducing their rates of LBW or preterm birth [7, 35–37]. In fact, because of increased obstetric intervention, preterm birth rates are rising in many high- and middle-income countries [6, 23, 24, 38]. Thus, prevention of LBW, and especially preterm birth, are elusive goals with limited success thus far. In my opinion, the major public health priorities should focus on the MDG goals of reducing maternal and young child (especially neonatal) mortality and on reducing stillbirth. Prevention of LBW has proved difficult and is not necessary to reduce neonatal mortality or stillbirth; though a laudable long-term public health goal, far more research is required to achieve it.

**Disclosure Statement**

The author declares that no financial or other conflict of interest exists in relation to the content of the chapter.
References


