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Review

The epidemiology, etiology, and costs of preterm birth

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SUMMARY

After decades of rising preterm birth rates in the USA and other countries, recent prematurity rates seem to be on the decline. Despite this optimistic trend, preterm birth rates remain higher in the USA, where nearly one in every eight infants is born early, compared to other developed countries. The prevention of preterm birth is considered a public health priority because of the potential to reduce infant and childhood morbidity and mortality related to this condition. Unfortunately, progress has been modest. One of the greatest challenges in studying this outcome is that preterm birth is a complex condition resulting from multiple etiologic pathways. Recently, experts have developed innovative frameworks for classifying and studying preterm birth based on phenotype. These proposed classification systems have only recently been adopted, but a different perspective on a longstanding problem has the potential to lead to new discoveries.

1. Introduction

Preterm birth (PTB), defined as delivery prior to 37 weeks of gestation, is considered one of the leading health indicators of a nation [1], as it is the most frequent cause of neonatal death and the second most frequent cause of death in children aged <5 years worldwide [2]. Furthermore, those infants who do survive have higher rates of long-term morbidity, including neurologic and developmental disabilities, compared to infants born full term [3]. The development of effective preventive measures to reduce the incidence of PTB is, thus, urgently needed. This requires a thorough understanding of the epidemiology of the condition as well as familiarity with the previously studied factors thought to be related to pathogenesis. But perhaps most importantly, progressive approaches to studying this longstanding public health problem are essential.

2. Recent trends in preterm birth rates

During the latter part of the 20th century, an alarming increase in the PTB rate occurred in the USA as well as in other countries worldwide [4,5]. Multiple factors were thought to have contributed to the rising PTB rate including higher average maternal age, more frequent use of assisted reproductive technologies, an increase in non-infertility-related multiple gestations (multiple gestation will be discussed elsewhere in this volume), and higher rates of preterm inductions and cesarean deliveries [6]. However, since 2006, when the PTB rate in the USA peaked at 12.8%, the fraction of births that are preterm has been declining [4,7] (Fig. 1). Indeed, the PTB rate in 2013 (11.4%) was the lowest reported in the USA since prior to 2000. Although the PTB rate in the USA exceeds that of other developed countries [5,8], similar temporal changes in prematurity rates have been observed in European countries [9]. Understanding the factors that have caused this shift in the directionality of trend in the rate of preterm deliveries over the past decade may be important to the future prevention of PTB.

Preterm births are often analyzed based on gestational age at delivery and clinical presentation. There is an inverse relationship between gestational age at delivery and the risk of neonatal morbidity and mortality [10,11]. Whereas infants born in the very early (<28 weeks), early (28^{+0}–31^{+6} weeks), and moderate (31^{+0}–33^{+6} weeks) preterm periods comprise the smallest proportion of births (0.7%, 1.2%, and 1.5% of all births in the USA in 2013, respectively) these infants experience disproportionately higher rates of prematurity-related complications. Most preterm deliveries (8.0% of all births) occur in the late preterm (34^{+0}–36^{+6} weeks) period [4] (Fig. 2). Although morbidity and mortality rates are relatively low among late-preterm infants compared to those

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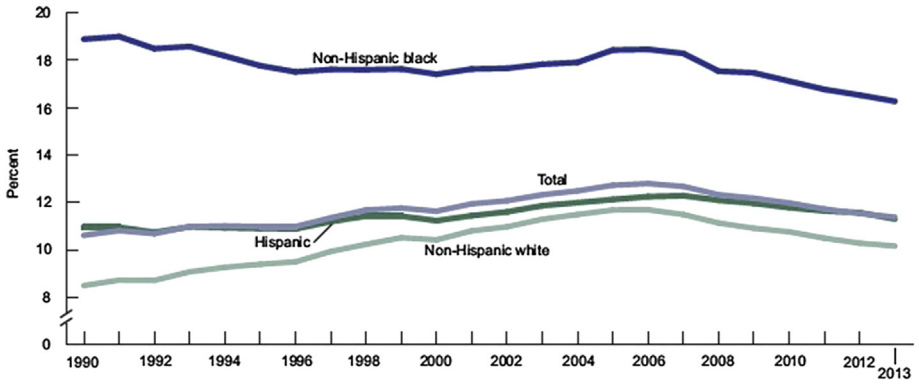

Fig. 1. Preterm birth rates, by maternal race and Hispanic origin: USA, 1990–2013. Source: Martin et al. [4].

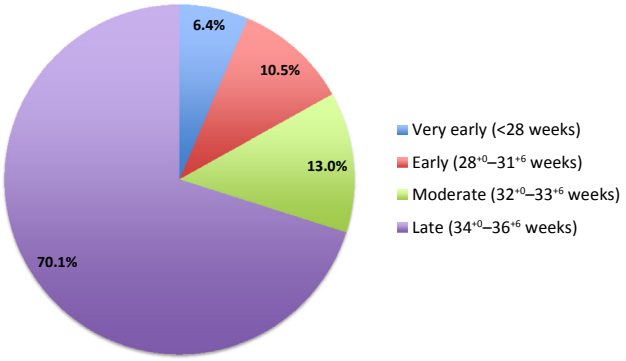

Fig. 2. Distribution of preterm births in the USA in 2013.

born at earlier gestational ages, they still exceed those of infants born full-term [12,13]. A collective acknowledgement of these risks has led to initiatives to reduce non-medically indicated late PTBs and changes in the management of some pregnancy complications favoring a later timing of delivery [13–15]. It has been speculated that the recent overall decline in preterm deliveries is attributable in part to a reduction in late PTBs. Late PTBs decreased by 15.8% from 2005 to 2012 in singleton gestations, but preterm deliveries <32 weeks and between 32^{+0} and 33^{+6} weeks also declined during that time-period [7].

The clinical presentation of PTBs is widely described as being either 'spontaneous' or 'indicated'. Women with spontaneous PTB present with preterm rupture of membranes or preterm labor with cervical dilation. In contrast, indicated PTBs are initiated by the obstetric care provider for maternal or fetal complication in the absence of labor or membrane rupture. The increase in PTB prior to 2006 was largely the result of a rise in the number of indicated preterm deliveries [16]. In contrast, the decline in preterm deliveries since 2006 has been attributed to a decrease in both spontaneous and indicated PTB. Using US birth certificate data, Gyamfi-Bannerman and Ananth reported that from 2005 to 2012, the number of indicated PTBs among women with singleton gestations declined by 17.2%, whereas spontaneous PTBs also decreased by 15.4% [7].

Systematic bias may also have an effect on reported PTB rate trends in the USA. The primary source of national data about prematurity rates comes from birth certificates. Unfortunately, these data are associated with a risk of misclassification [17,18]. Compared to the 1989 birth certificate version, the 2003 revision was designed to improve the quality of the data [19]. For example, the 2003 version specifically collects information regarding induction and augmentation of labor, which has been used to classify births as indicated or spontaneous [7]. However, adoption of the 2003 revision has been slow. It is anticipated that it will be used in all states by 2016 [20]. Even after the use of the 2003 revision became widespread, concerns remained regarding the validity of the estimate of gestational age at the time of delivery. Until 2014, official gestational age for natality data was based on the date of the last normal menstrual period (LMP). However, alternative measures of gestational age, termed the "clinical estimate" (1989 revision) and the "obstetric estimate" (2003 revision) based on the birth attendant's final estimate of gestational age, have also been collected [21]. A comparison of these estimates of gestational age suggests that LMP-based data may overestimate the PTB rate. Based on the obstetric estimate, the national PTB rate was only 9.6% in 2013 compared to 11.4% based on maternal LMP. The obstetric estimate, which incorporates all perinatal factors including ultrasound data, is expected to have higher validity than LMP data, which may be inaccurate due to poor maternal recall and individual variation in menstrual cycle length [22]. In contrast, early ultrasound dating is considered the most accurate method of determining gestational age [23,24]. It is anticipated that the national PTB rate will be reported as being lower than in prior years beginning in 2014 because of the adoption of this new approach to estimating gestational age. Although the absolute PTB rates are lower using the obstetric estimate, trends can still be analyzed. The differences in percent distributions between the obstetric estimate and LMP-based data were consistent from 2007 to 2013 [21], which implies that the recent observed decline in prematurity rates based on LMP-based data is real.

3. Racial disparities in preterm birth

One of the most persistent findings in the study of the epidemiology of PTB is that rates of PTB vary according to women's racial and ethnic background. This disparity is most clearly evident in the relatively heterogeneous US population. In 2013, 16.3% of pregnant non-Hispanic black women delivered prior to 37 weeks compared to only 10.2% of non-Hispanic white women and 11.3% of Hispanic women. Additionally, the early PTB rate (<32 weeks) in non-Hispanic black women was more than twice the rate seen in non-Hispanic white women [4]. This large difference in PTB rates has been observed for decades; however, the recent decline in PTB rates occurred in all racial groups [7]. In fact, the 2013 PTB rate in non-Hispanic black women was the lowest recorded since 1981 [4].

Although there is a tendency to group all black women together as a single racial group, PTB rates appear to vary among US black women according to their ancestry and nativity. Howard and