

Late Preterm Birth: Appreciable Risks, Rising Incidence

Western countries have experienced a sharp rise in the occurrence of preterm birth in recent decades.¹⁻³ The reasons for this rise are well documented and include more frequent obstetric intervention (particularly induction of labor), a higher rate of twinning, mostly because of the use of ovulation stimulation and assisted reproductive techniques with multiple embryo transfer, and delayed childbearing, because older mothers, even those who deliver singletons, are at increased risk of preterm birth.

The recent rise in preterm birth has occurred throughout the industrialized world, but has been particularly marked in the United States.² Part of the reason that the United States has such a high incidence of preterm birth is the extremely high rate among African-Americans. Another, less well-appreciated reason is that US preterm birth statistics, unlike those of most other high-income countries, are based on menstrual-based gestational age estimates, rather than ultrasound scanning estimates. All states except California also record a clinical estimate of gestational age, which (at least until recently) did not specify the basis for the estimate. The clinical estimate provides rates of preterm birth that are more similar to, albeit still somewhat higher than, those of other industrialized countries.⁴ Finally, the high incidence of preterm birth in the United States, even among Caucasian mothers, is certainly at least partly caused by higher rates of obstetric intervention in general and labor induction in particular. More frequent obstetric intervention in the United States compared with other high-income countries may be related to the medico-legal climate, closer fetal surveillance, and the wish to avoid potentially avoidable obstetric disasters, particularly stillbirth.

Most of the increase in preterm birth in the United States and elsewhere is attributable to increases in late preterm birth, primarily between 34 and 36 weeks of gestation.⁵ Advances in neonatal care, including intensive care, have markedly improved survival throughout the preterm gestational age range. But these advances may have led many obstetricians and neonatologists to consider late preterm births to be risk-free. Although the absolute risks are extremely low in such infants, my colleagues and I have shown that even 34- to 36-week infants are at increased risk for mortality in both the neonatal and post-neonatal periods.⁶ The relative risks (versus infants born at term) are modest compared with infants born at <32 weeks, but the much larger and increasing numbers of births at late preterm ges-

tational ages translate into a non-negligible impact on overall infant mortality.

Relatively few studies have examined morbidity outcomes in late preterm births. Some reports have noted short-term risks, but only recently has the issue of possible long-term risks been addressed. It is in this latter context that the current study by Petrini et al⁷ fills an important gap in our knowledge. In an analysis of a large sample of infants followed within the Northern California Kaiser Permanente Medical Care Program, the authors report 3-fold increased risks of cerebral palsy and modestly but significantly increased risks of developmental delay, mental retardation, or both in children who were born at 34 to 36 weeks.

This study has several important strengths: a large sample size, high follow-up rates, and an assessment of the effect of false-positive diagnoses of the long-term neurologic outcomes, with a sensitivity analysis based on plausible ranges of false-positive diagnoses. However, the study also has several weaknesses, the most important of which is the lack of information on whether the labors that led to preterm birth were spontaneous or induced and on the presence or absence of important pregnancy complications associated with preterm birth, including pregnancy-induced hypertension (including pre-eclampsia), pre-gestational and gestational diabetes mellitus, and antepartum hemorrhage. Whether labor was induced or spontaneous, we have no way of knowing whether late preterm birth or the underlying reasons for its occurrence (eg, the aforementioned pregnancy complications, poor fetal growth, reduced fetal movements, or oligohydramnios) were the cause of the observed increased long-term neurocognitive risks. Nor does the study include data on other potentially confounding factors, such as maternal smoking during pregnancy or the use of infertility treatments. Finally, as the authors themselves note, the relatively advantaged population included in the Kaiser HMO system may limit the generalizability of their results. It is possible that the observed risks are underestimates of those that would be observed in a less-advantaged population.

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Reprint requests: Michael S. Kramer, MD, The Montreal Children's Hospital, 2300 Tupper St (Les Tourelles) T-118, Montreal, Quebec, Canada H3H 1P3. E-mail: michael.kramer@mcgill.ca.

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In conclusion, Petrini et al⁷ have provided important new information about the long-term prognosis of infants born at late preterm gestational ages. Pediatricians and other providers of care to late preterm infants should be more vigilant for potential neurocognitive problems in their follow-up of such infants. But this new information should also give us cause for concern about ovulation stimulation and multiple embryo transfer, and particularly about the rising rate of labor induction. We need to pose the question of whether more frequent induction might be doing more harm than good. Future observational studies with clinically detailed databases from HMOs and other health care systems should attempt to fill gaps with respect to additional potentially confounding factors—particularly pregnancy complications, labor induction, and other underlying maternal and fetal causes of preterm birth. It may be, however, that the issue of how much labor induction is too much can be adequately addressed only with a randomized trial of labor induction at 34 to 36 weeks for specific maternal or fetal indications. In the meantime, obstetricians, pediatricians, and other care providers should inform pregnant women of the long-term risks associated with late preterm birth and should take those risks into account when making decisions about ovulation stimulation, multiple embryo transfer, and labor induction.

Michael S. Kramer, MD

Departments of Pediatrics and of Epidemiology and Biostatistics
McGill University Faculty of Medicine
Montreal, Quebec
Canada

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