Postterm Births: Are Prolonged Pregnancies Too Long?

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"Postterm pregnancy" is defined by the World Health Organization as the end of gestation at ≥42 completed weeks' gestation, measured from the first day of the last menstrual period (LMP) and based on a 28-day cycle.[1] However, in reality, this definition is arbitrary, and there are no clear scientific data underpinning it. As pregnancies that last beyond 42 weeks have been associated with adverse events historically, they have been considered a separate at-risk group. It is clear that postterm births remain a common event worldwide, and management of postterm pregnancies is somewhat variable and therefore best-practice guidelines are lacking.

There are limited data across countries on long-term trends in the incidence of postterm births. Pregnancies were previously dated based on the LMP, but now rely on both LMP and early ultrasound scans, improving gestational age accuracy. Data from 81 singleton pregnancies after in vitro fertilization (where conceptions can be accurately timed) showed that ultrasound scans in the first 20 weeks underestimated gestation length by just 2.8 days (SEM 0.2), so that fetal age was determined to within 7 days in >95% of cases.[2] Thus, in Finland, for example, the incidence of postterm births dropped from 10.3% to 2.7% once ultrasound scans became the standard technique to date pregnancies.[3]

Nonetheless, postterm births are a common occurrence globally. The rate of postterm births varies considerably between and within countries, and in the developed world it ranges from 0.4% to 11%.[4-8] In Sweden, the incidence of postterm births is 7.5% compared with 5.6% for preterm births.[5,9,10] As a result, the Swedish birth registry recorded nearly 311 000 children born postterm in 1983-2006.[11] It is important to note that in many nations (particularly in poorer countries), mothers may not have access to ultrasound scans and will be unsure of the LMP date. Therefore, it is likely that the incidence of postterm births in many countries is higher than that officially recorded.

Etiology of Postterm Birth

The 2 most common factors associated with postterm birth are a first-degree relative born postterm and maternal obesity.[8,12-14] There is considerable evidence that maternal factors are associated with prolonged gestation in humans. Maternal genetic factors may account for 14%-30% of all postterm births.[8,14] Maternal gestational age correlated with the gestational age of the fetus,[15] indicating that mothers born postterm are more likely to give birth to postterm infants. Recently, from a cohort of 36 children born postterm, we observed that 90% of children had another family member born after 42 weeks' gestation, with 65% of children having a sibling and 29% having a mother also born postterm.[16] Similar evidence has been provided by parent–offspring data from Norway and Danish medical and twin registries.[8,14,17,18] Maternal obesity has also been associated with postterm birth, with a 1.4-fold increase in the risk of delivery beyond 41 weeks' gestation.[13]

Paternal factors are also associated with prolonged gestation in animal models. Studies in cattle suggest that the sire has a significant effect on length of gestation,[19,20] and "short gestation length semen" is currently marketed as a tool to maximize profits in the dairy industry.[21] A possible paternal effect has not been adequately studied in humans, but gestational age is better correlated among siblings born to the same parents than among siblings born to different fathers,[14] suggesting a possible paternal role in the length of human gestation. Although paternal body mass index did not alter the rate of postterm deliveries,[22] a linear relationship was observed between paternal gestational age and that of the offspring, which was confounded by the birth weight of the father.[15] Thus, it is possible that paternal factors may also be associated with postterm birth in humans.

The fetus itself can affect gestational length, as shown by the common occurrence of prolonged gestations among anencephalic infants[23] and infants born following in vitro fertilization using vitrified blastocysts.[24] Lunde et al suggested that fetal genetic factors could explain 11% of the variation in gestational length.[14] Environmental factors also have been associated with prolonged gestation.[25,26] Increased duration of pregnancy has been noted with fish oil supplementation.[27] Further, aspirin increased gestational length and the incidence of postterm births, due to the inhibitory effects on prostaglandins synthesis, which are important regulators of human gestation and labor.[28] It is important to stress that no human studies have elucidated the exact mechanisms (including genetic) leading to postterm birth, which is a likely result of the combination of the described factors.

LMP	Last menstrual period
SGA	Small for gestational age

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Perinatal and Neurologic Outcomes

Studies describing adverse neonatal outcomes following postterm birth do not distinguish between the effects of prolonged gestation itself from other factors (maternal and fetal) potentially responsible for both prolonged gestation and poorer outcomes.[29] For example, no studies have examined the possible effects of familial (with a postterm first-degree relative) vs nonfamilial (eg, maternal obesity) postterm pregnancy on perinatal outcomes.

Most of the earlier observational studies on the effects of postterm birth have focused on the immediate perinatal period. There is an increased rate of peripartum complications in association with prolonged gestation, including macrosomia, traumatic deliveries, postmaturity syndrome, intrapartum fetal distress, hypoxic encephalopathy, umbilical cord complications, fractures, peripheral nerve injury, pneumonia, and septicemia.[29-31] For a cohort of 27 000 women, it was found that the lowest risk for fetal death occurred at 38 weeks' gestation, and resuscitation was least likely at 39 weeks' gestation.[32] Another large study on singleton pregnancies in Sweden demonstrated an increased rate of fetal death beyond 40 weeks + 3 days.[33] Beyond 41 weeks' pregnancy, there are elevated risks for abnormal nonstress tests, respiratory distress, oligohydramnios, cesarean deliveries, and stillbirths.[34-36]

There is a higher risk of perinatal and obstetric complications in prolonged pregnancies, including increased rate of perinatal death[29,37] and stillbirth with signs of chronic hypoxia and malnutrition.[38] Retrospective analysis suggested that the rate of stillbirth was relatively low between 28 and 37 weeks gestation (at 0.19-0.45 per 1000 ongoing pregnancies), progressively increasing to 2.12/1000 pregnancies at 43 weeks.[39] In addition, mortality beyond birth (neonatal and postneonatal) increased 2-fold from 40 to 42 weeks.[39] A recent meta-analysis reported a minimal increase in meconium aspiration syndrome in postterm infants but no increase in perinatal mortality.[40]

However, according to a recent guideline from the World Association of Perinatal Medicine, there is no conclusive evidence that induction of postterm pregnancies before 42 weeks' gestation improves fetal, maternal, and neonatal outcomes (compared with expectant management).[41] A randomized controlled trial did not find any effects on perinatal mortality or morbidity when comparing labor induction against serial antenatal monitoring in postterm pregnancies.[42] Two meta-analyses showed that labor induction at 41 weeks did not alter stillbirth rates in comparison with expectant management, but other findings on neonatal morbidity and postnatal mortality were inconsistent.[43,44] Even though the 2003 meta-analysis of 16 randomized controlled trials found no improvements in neonatal intensive care unit admission rates, meconium aspiration, Apgar scores, or perinatal mortality,[43] a 2011 meta-analysis showed that induction led to fewer postnatal deaths with a reduction in neonatal morbidity from meconium aspiration and macrosomia.[44] Conversely, a recent Canadian study suggested that induction of labor at 41 weeks' gestation in uncomplicated low-risk postterm pregnancies increased severe neonatal morbidity (especially among infants born to multiparous women).[45] Thus, the optimal management of postterm pregnancies is still unclear.[40]

Neurologic Outcomes in Childhood

Postterm birth is associated with adverse neurologic and neurodevelopmental outcomes in childhood. An increased incidence of epilepsy in infancy is noted following instrumental and cesarean deliveries in postterm children.[46] A population-based study in Norway revealed an increase in the incidence of cerebral palsy in children born at or after 42 weeks' gestation.[47]

Postterm birth is also associated with behavioral and emotional problems, including attention-deficit/hyperactivity disorder in early childhood.[48] A small study suggested that IQ in children born after 41 weeks' gestation was lower than their siblings born at term.[49] However, other early childhood studies on IQ and developmental milestones have yielded conflicting results.[50-53]

Long-term Metabolic and Cardiovascular Effects

Two recent studies reported adverse metabolic outcomes in postterm children and adolescents. In a Swedish cohort with detailed longitudinal height and weight data from birth to 16 years of age, nearly one-half of postterm boys were overweight or obese at age 16 years compared with 13% of term boys.[54] This difference in body mass index was evident at 3 years of age and became progressively greater as these boys aged, so that postterm adolescent boys were on average 11 kg heavier than their term counterparts.[54] Notably, this difference was not due to parental obesity.[54]

More recently, data on prepubertal children born postterm demonstrated a 34% reduction in insulin sensitivity, increased insulin secretion, and reduced glucose-mediated glucose uptake.[16] Body composition analysis using dual-energy x-ray absorptiometry showed that postterm children had more body fat and increased abdominal adiposity.[16] Further, postterm children had other early markers of the metabolic syndrome, including reduced nocturnal blood pressure dip, higher leptin concentrations, lower adiponectin concentrations, a less favorable lipid profile, and higher uric acid concentrations.[16] Surprisingly, the range of adverse metabolic outcomes in postterm children greatly exceeds those previously noted in small for gestational age (SGA) or preterm children. In addition, a recent large study in Taiwan has noted the increase in the incidence of exercise-induced wheeze and asthma in children born postterm.[55]

Long-term growth and metabolism in those born postterm had never been examined before these studies. Our data[16,54] showed metabolic similarities between infants born SGA and

those born postterm. Term infants born SGA have physiologic stress characterized by poor weight gain due to uteroplacental insufficiency, largely in the last trimester of pregnancy.[56,57] Similarly, postterm children may be exposed to physiologic stress due to abnormally long gestation or late pregnancy uteroplacental insufficiency, although at birth postterm infants are not as thin as those born SGA.[54] Placenta from postterm pregnancies have abnormal histologic features that are similar to SGA placenta, including apoptotic changes, diffuse calcifications, chorionic villus degeneration, infarcts, increased necrosis, and decreased perfusion surface.[58-62]

SGA infants are at increased risk of developing abdominal (particularly visceral) obesity, insulin resistance, type 2 diabetes mellitus, and the metabolic syndrome in late adult life.[63-67] In addition, young adults born SGA have an increased incidence of the metabolic syndrome and show changes in associated inflammatory markers.[68-70] Similarly, we showed that postterm children had higher concentrations of uric acid, which is also a marker of cardiovascular disease, metabolic syndrome, and type 2 diabetes mellitus.[71] As a result, the recent evidence suggests that the postterm offspring may be similarly at increased risk of developing metabolic and cardiovascular diseases later in life.[16,54]

To Induce or Not to Induce?

The recent findings in postterm children raise important questions regarding the management of prolonged pregnancies. As previously noted, the definition of prolonged pregnancy is not based on clear scientific evidence showing maternal and/or perinatal adverse outcomes. Current international recommendations are to allow the mothers to make an informed decision regarding the management of their own prolonged pregnancies.[41] However, informed decision is complicated by the lack of clear evidence in the outcomes of either management strategy (ie, induction of labor vs serial antenatal surveillance).[41] Thus, the number of postterm deliveries continues to be significant.

In light of the recent evidence, prolonged pregnancies beyond 42 weeks are associated with risk factors for long-term adverse health outcomes in the offspring. However, it is important to note that the underlying factors associated with the observed metabolic changes in postterm children are unclear. They may not be a result of prolonged gestation per se but rather may be associated with fetal and/or parental genetic factors that also lead to delayed parturition. Larger multicenter studies are needed to clarify the long-term risks associated with postterm birth. Such studies would better inform the management of prolonged pregnancies. ■

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