Term Complications and Subsequent Risk of Preterm Birth: Registry-Based Study

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ABSTRACT

Preterm birth in a previous pregnancy is associated with future preterm delivery. This suggests that underlying factors may play a role in an individual's pregnancies. However, whether there is a relationship between obstetric complications and poor infant outcomes in term pregnancies and future preterm delivery is unclear. The aim of this study was to investigate whether specific complications and poor outcomes during a first pregnancy increased the risk of preterm delivery in the second.

This was a population-based, prospective study, using data from the Medical Birth Registry of Norway. The main cohort was women who gave birth (living or stillborn) during a second delivery to a singleton child between 1999 and 2015. Excluded were women who had missing information in the registry on gestational age or birth weight, whose infant's gestational age fell outside the range of 20 to 46 weeks, or whose infants weighed more than 5 standard deviations above the mean for gestational week of birth. The main outcome was preterm birth (delivered between 20 and 36 weeks) after a first delivery at term with 1 or more of the following 5 complications: preeclampsia, placental abruption, stillbirth, neonatal death, or small for gestational age.

A total of 302,192 women met the inclusion criteria, including 284,225 women who had an at-term, first pregnancy. For each of the 5 complications, the risk of preterm birth in the second pregnancy was significantly increased. The absolute risk for subsequent preterm birth with none of the 5 complications in the first pregnancy was 3.1% (8202/265,043). In comparison, the absolute risks for subsequent preterm birth was 6.1% (688/11,225) after preeclampsia in the first pregnancy, 7.3% (41/562) after placental abruption, 13.1% (72/551) after stillbirth, 10.0% (22/219) after neonatal death, and 6.7% (463/6939) after small for gestational age. The unadjusted relative risk of preterm birth was 2.0 (95% confidence interval [CI], 1.8–2.1) after preeclampsia, 2.3 (95% CI, 1.7–3.1) after placental abruption, 4.2 (95% CI, 3.4–5.2) after stillbirth, 3.2 (95% CI, 2.2–4.8) after neonatal death, and 2.2 (95% CI, 2.0–2.4) after small for gestational age. Having any one of these 5 complications in the first pregnancy was associated with a relative risk of subsequent preterm birth of 2.0 (95% CI, 1.9–2.1) and an absolute risk of 6.2%. Having 2 or more complications was associated with a relative risk of 3.5 (95% CI, 2.9–4.2) and an absolute risk of 10.9%. Similarly, the links between complications and preterm delivery were seen in a reverse analysis: Preterm birth in the first pregnancy was strongly associated with an increased risk of complications in the second pregnancy.

In conclusion, women who experienced obstetric complications or poor infant outcomes during their first pregnancy were substantially more likely to experience preterm birth in a subsequent pregnancy. Relative risks for preterm birth in a second pregnancy were 2- to 4-fold higher after preeclampsia, placental abruption, stillbirth, neonatal death, or small for gestational age in the first pregnancy. The presence of one of these complications during the first pregnancy showed a 2-fold higher risk of subsequent preterm birth, whereas the presence of 2 or more of these complications showed a 3.5-fold higher risk.

EDITORIAL COMMENT

(Preterm birth is one of the leading causes of neonatal morbidity and mortality. Despite numerous efforts to reduce the preterm birth rate, one of the few interventions that has been shown in some studies to do so is progesterone, either the IM 17-hydroxy progesterone (17-OHP) or vaginal progesterone (N Engl J Med 2003;348:2379–2385; N Engl J Med 2007;357:462–469). For prophylaxis, this has really only been demonstrated to reduce the risk in women with a prior preterm birth and in one recent, large study, did not even reduce the risk in that population. A number of other risk factors have been examined. For example, there have been attempts to show a reduction in preterm birth in multiple gestations treated prophylactically with 17-OHP to no avail (N Engl J Med 2007;357:454–461).

Another avenue toward preterm birth prevention has been in prevention of iatrogenic preterm birth. There was a big push in 2008 to 2012 to...
discourage iatrogenic late preterm birth that led to a significant reduction in preterm birth during this period. Another etiology for preterm birth is delivery of a woman with preeclampsia with severe features. Thus, prevention of preeclampsia might also reduce preterm birth. Preeclampsia reduction has been demonstrated with prophylactic low-dose aspirin and, in recent studies, preterm birth as well (Am J Obstet Gynecol 2018;219:399.e1–399.e6).

Thus, such complicated pregnancies are a target for preterm birth reduction, both because of the higher rates, but also the morbidity and mortality from both the preeclampsia and the earlier deliveries with preeclampsia with severe features.

Although it is clear that delivery of a pregnancy complicated by preeclampsia with severe features, there is work to suggest that even those women with a history of preeclampsia of any kind have an increased risk of preterm birth in subsequent pregnancies. These findings have been extended to other pregnancy complications including fetal growth restriction and stillbirth as well.

The study abstracted above examined the risk of preterm birth in a subsequent pregnancy after the first pregnancy was complicated by preeclampsia, placental abruption, stillbirth, neonatal death, or small for gestational age. Certainly, placental function and overall placentation have a clear role in 4 of these conditions and may contribute to preterm birth in some fashion yet to be well understood. The authors found that the baseline risk of preterm birth in women with a prior, uncomplicated term birth was 3.1%. Having any of the listed risk factors increased the preterm birth risk at least 2-fold. Interestingly, when the authors examined the association in reverse temporality, having a preterm birth in the first pregnancy was associated with the 5 term complications of interest in the second pregnancy as well.

Is it that these 6 complications, preterm birth, and the other 5 have a universal, single etiology? This is unlikely. Rather, some of these associations are due to the management in subsequent pregnancies. For example, it is common in the setting of a prior stillbirth to begin antenatal testing, which can lead to a preterm delivery in order to prevent a recurrent stillbirth. This may also be true in the setting of a pregnancy complicated by prior fetal growth restriction or placental abruption. However, there may be some commonality for these pregnancy complications related to placentation and placental function, even for preterm birth. Given that there have been approaches to prevent recurrent preterm birth and preeclampsia with 17-OHP and low-dose aspirin (N Engl J Med 2017;377:613–622), respectively, one wonders if some benefits may be achieved by treating the other groups delineated in this study to achieve some benefit. Although low-dose aspirin is relatively easy to prescribe and take, 17-OHP has greater barriers in terms of both cost and ease of administration, but certainly, it deserves a prospective trial to ascertain whether there may be benefit.—ABC)