20th World Congress in Fetal Medicine

The first trimester risk of preterm preeclampsia predictsion of timing of spontaneous birth

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Objective

The screening for preterm preeclampsia (PE) proposed by the Fetal Medicine Foundation (FMF) effectively predicts the major form of placental dysfunction, which is also a potential precursor of spontaneous preterm birth (sPTB), as demonstrated by lower mean birthweight centile of premature neonates and by lower risk of sPTB after low-dose aspirin prophylaxis. Prediction of gestational age (GA) at spontaneous birth is challenging, particularly when attempted in the first trimester. The aim of our study was to assess the extent to which the risk of PE calculated by the FMF model may predict gestational age (GA) at onset of spontaneous delivery.

Methods

This was a monocentric, retrospective study carried out selecting three groups of PE risk: very high-risk (group 1: >1/50), high-risk (group 2: from 1/50 to 1/100) and low-risk (group 3: ≤1/1000). In all patients, the risk for PE was calculated prospectively in the first trimester by the combined test for PE, with a standardized protocol according to the FMF algorithm. Cases with PE risk ≥ 1/100 underwent 150 mg daily aspirin prophylaxis from first trimester to 36 weeks. Only cases with spontaneous onset of delivery (labour with intact membranes or preterm prelabour rupture of membranes) were included (primary outcome). The following conditions were excluded from analysis: preeclampsia, induction of labour, elective or prelabour caesarean section. A survival analysis was carried out with Kaplan-Maier estimator based upon the three study groups with different risks for preterm PE. Log-rank and Breslow tests were applied to compare GA at spontaneous birth in the study groups, in different phases of gestation. Instantaneous GA-related smoothed hazard estimates were also calculated for each study group.

Results

A sample of 305 cases was collected, including 72 in group 1, 109 in group 2 and 124 in group 3. There were 16 cases of PE excluded from analysis (of which 10 in group 1, 6 in group 2 and 0 in group 3). Spontaneous onset of delivery in group 1, 2 and 3 occurred below 37 weeks in 28%, 24% and 2.4% and below 35 weeks in 8%, 6% and 0, respectively. The survival analysis showed different rates of spontaneous birth without PE in the study groups, at paired gestational ages and across all stages of pregnancy. A greater difference among groups was shown below 37 weeks (Breslow test: p-values<0.05 (from <0.001 to 0.02) for all the comparisons) and a lower difference above 37 weeks (Log-rank test: group 1 vs 2: p-value=ns; group 3 vs 1 or 2: p-values<0.001). Overall, the greater the risk of PE at first trimester, the earlier GA at spontaneous birth. Smoothed estimates of instantaneous hazard for spontaneous delivery onset showed that group 3 had a very low-risk until 37 weeks with a shoulder effect and a subsequent rapid progression, whereas risk evolution in group 1 and 2 was smoother with risk rise starting at 35-36 weeks. Most cases of group 1-2 delivered before 40 weeks (75%) vs 55% of group 3.

Conclusion

This study improves understanding around the natural onset of human parturition. Major findings: i) strong indirect relationship between GA at spontaneous birth (without PE) and risk of PE; ii) low risk of sPTB in patients at low-risk of PE and high in patients at high-risk of PE; iii) significant risk progression for spontaneous birth (term or preterm) across GA, directly related to the risk of PE. Future studies may assess both sPTB prediction and definition of optimal GA for delivery based upon the individual PE risk as well as the common basis of PE and sPTB within a generalized framework.