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Severe intrahepatic cholestasis of pregnancy is a risk factor for preeclampsia in singleton and twin pregnancies

TO THE EDITORS: We welcomed the evidence-based report by Raz et al[1] describing a relationship between intrahepatic cholestasis of pregnancy (ICP) and preeclampsia. They tested a plausible hypothesis that elevated serum bile acids (the hallmark of ICP) are a risk for preeclampsia. Common inflammatory processes may link these 2 obstetric conditions.[2,3] The authors used 2 study groups: (1) gravid women with uncomplicated and ICP-affected pregnancies whose information was culled from a retrospective cohort to identify the targeted association and (2) an important smaller prospective group to confirm that bile acids are not elevated in pregnancies that are affected by preeclampsia. In contrast to the authors' evidence-based primary conclusion, in the absence of data, the death of 1 twin in their study group was ascribed to ICP-related adverse perinatal outcome. As an alternate explanation, we suggest that the fetal death in this study may be related to the 18% discrepant growth between the female twins. To support the assertion that the stillbirth was associated with ICP, the authors cite a report of alleged similar unexplained stillbirths.[4] However, rather than identify ICP as a cause for unexplained stillbirth, this cited report describes 32- and 34-week gestations with abnormal intrapartum fetal heart tracings that continued for >30 minutes before fetal death occurred. It is certainly possible that elevated bile acids were directly related to the fetal heart rate abnormalities that were documented in the article referenced by the authors. However, we would contend that these intrapartum deaths should not be described as unexplained stillbirths attributed to ICP. ■

Shadi Rezai, MD
Isamarie Lora, MD
Cassandra E. Henderson, MD, CDE
Department of Clinical Obstetrics and Gynecology
Weill Cornell Medical College
Lincoln Medical and Mental Health Center
Bronx, NY
Cassandra.henderson@nychhc.org

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REPLY

We thank Henderson et al for the interest shown in our study and would like to offer our comments in reply.

In our study, we had 1 case of intrauterine fetal death (IUFD) in a woman with dichorionic diamniotic twins' pregnancy and severe intrahepatic cholestasis of pregnancy (ICP) at 30 weeks of gestation. The patient had been under observation, which included routine fetal monitoring 3 times per a day, in our Department for 1 week before this event. Importantly, a pathologic fetal heart rate monitoring of the dead fetus was documented several hours after a normal heart monitoring of both twins.

In their letter, Henderson et al suggest that this case of IUFD may be related to the 18% difference in fetal growth between the fetuses. Being that the accepted definition for growth discrepancy is 20% of the larger twin's weight (in this case 1675 g) and that the dead fetus weighted 1369 g, which is compatible with the 56th weight percentile for gestational age, both intrauterine growth restriction (IUGR) and discrepancy do not exist in this case. Moreover, although IUGR is associated with increased perinatal death in twins in all gestational ages, growth discordance alone is not.[1]

Indeed, as Henderson et al rightfully stated, whether or not ICP is associated with increased risk of fetal death is debatable, but the evidence that supports the true existence of such a connection is accumulating, mostly for singleton pregnancies. Geenes et al[2] recently showed in their prospective case-control study that women with severe ICP were at increased risk for stillbirth.