The relationship between preeclampsia and intrauterine growth restriction in twin pregnancies

Nathan S. Fox, MD; Daniel H. Saltzman, MD; Sandip Oppal, MD; Chad K. Klauser, MD; Simi Gupta, MD; Andrei Rebarber, MD

OBJECTIVE: Preeclampsia and intrauterine growth restriction (IUGR) are correlated in singleton pregnancies. The objective of this study was to estimate their relationship in twin pregnancies.

STUDY DESIGN: Cohort of 578 patients with twin pregnancies delivered by 1 maternal fetal medicine practice from 2005-2013. Patients with chronic hypertension, monochorionic-monoamniotic placentation, twin-twin transfusion, and major congenital anomalies were excluded. Standard definitions were used for gestational hypertension and preeclampsia. We defined IUGR as any twin birthweight less than the 5th percentile for gestational age, as well as any twin birthweight less than the 10th percentile for gestational age.

RESULTS: The incidence of preeclampsia was 14.9%, the incidence of birthweight <10% was 50.0%, and the incidence of birthweight <5% was 27.5%. Comparing patients with and without preeclampsia, the rate of birthweight <5th percentile did not differ (27.9% vs 27.4%, $P = .929$), nor did the rate of birthweight <10th percentile (48.8% vs 50.2%, $P = .815$). We had 80% power with an alpha error of 5% to show a difference in the likelihood of IUGR <10th percentile from 50% to 66% and a difference in the likelihood of IUGR <5th percentile from 27% to 42% in patients without and with preeclampsia.

CONCLUSION: In patients with twin pregnancy, there is no correlation between preeclampsia and IUGR. This suggests that in twin pregnancies, as opposed to singleton pregnancies, the pathophysiology may differ between these 2 common conditions.

Key words: IUGR, placenta, preeclampsia, twin

Cite this article as: Fox NS, Saltzman DH, Oppal S, et al. The relationship between preeclampsia and intrauterine growth restriction in twin pregnancies. Am J Obstet Gynecol 2014;211:x-ex-x-ex.

Patients with twin pregnancies are at increased risk of many pregnancy complications compared with singleton pregnancies.[1-3] Because twins account for 3.3% of all live births in the United States,[4] it is important to have a good understanding of these complications in these high-risk pregnancies. Two common complications of twin pregnancies are preeclampsia[5-7] and intrauterine growth restriction (IUGR).[8-11]

In singleton pregnancies, there is a strong association between preeclampsia and IUGR. Several studies showed that the presence of preeclampsia is associated with a 2 to 4-fold increase in the risk of IUGR.[12,13] Similarly, pregnancies complicated by IUGR are at increased risk of developing preeclampsia, and the likelihood of developing preeclampsia is positively correlated with the severity of the fetal growth restriction.[14,15] There is also evidence that the biologic pathways leading to preeclampsia and IUGR are similar. For example, first and second trimester abnormal uterine artery Doppler measurements demonstrating increased impedance to flow is associated with an increased risk of developing of preeclampsia as well as IUGR.[16,17] Also, several first and second trimester maternal serum markers for aneuploidy are associated with both preeclampsia and IUGR,[18] as are various serum angiogenic factors such as sFlt-1 and PlGF.[19] Finally, there is evidence that low dose aspirin started early in pregnancy in at-risk patients can reduce the risk of both preeclampsia and IUGR.[20]

Despite the large pool of evidence supporting an association between preeclampsia and IUGR in singleton pregnancies, there is limited data regarding this association in twin pregnancies. The strength of this association, or lack thereof, in twin pregnancies could influence our management of these pregnancies when either preeclampsia or IUGR develops, and may also increase our understanding of the pathophysiology of these 2 common complications in twin pregnancies.

The objective of this study was to estimate the association between preeclampsia and IUGR in twin pregnancies.

Materials and Methods

After Biomedical Research Alliance of New York Institutional Review Board approval was obtained, the charts of all patients with twin pregnancies and live births of both twins >24 weeks delivered by a single maternal-fetal medicine

From Maternal-Fetal Medicine Associates, PLLC (Dr Oppal), and the Department of Obstetrics, Gynecology, and Reproductive Science (Drs Fox, Saltzman, Klauser, Gupta, and Rebarber), Icahn School of Medicine at Mount Sinai, New York, NY.

Received Feb. 18, 2014; revised April 24, 2014; accepted May 24, 2014.

The authors have no conflicts of interest to report.

Presented at the annual meeting of the Society for Maternal-Fetal Medicine, New Orleans, LA, Feb. 3-8, 2014.

Reprints: Nathan S. Fox, MD, Maternal Fetal Medicine Associates, PLLC, 70 East 90th St., New York, NY 10128. nfox@mfmnyc.com.

0002-9378/$36.00 • © 2014 Mosby, Inc. All rights reserved. • http://dx.doi.org/10.1016/j.ajog.2014.05.035

practice between June 2005 (when our electronic medical record was established) and June 2013 were reviewed. We excluded patients with chronic hypertension (defined as prepregnancy hypertension, or hypertension diagnosed before 20 weeks of gestation[21]), monochorionic-monoamniotic placentation, twin-twin transfusion syndrome, and patients with major congenital fetal anomalies discovered before or after birth.

Baseline characteristics and pregnancy outcomes were obtained from our computerized medical record. Gestational age was determined by last menstrual period and confirmed by ultrasound in all patients. The pregnancy was redated if there was a >5 day discrepancy up to 14 weeks or a >7 day discrepancy after 14 weeks. If the pregnancy was the result of in vitro fertilization (IVF), gestational age was determined from IVF dating.

Standard definitions were used for the diagnosis of gestational hypertension and preeclampsia.[21] We used 2 definitions of IUGR for twin pregnancies: (1) either twin with a birthweight less than the 10th percentile for gestational age; (2) either twin with a birthweight less than the 5th percentile for gestational age. We chose birthweight, as opposed to sonographic estimated fetal weights, to remove the known error associated with estimated sonographic measurements, as well as not to miss any diagnoses of IUGR because of lack of ultrasound immediately before delivery. To define birthweight percentiles for gestational age we used standard tables for singleton pregnancies.[22] We chose singleton tables as they are the standard tables used for twins in the United States in defining growth restriction and determining neonatal outcomes.[23-25]

In our practice, expectant management of patients with preeclampsia does not differ in twin pregnancies, as compared with singleton pregnancies. Patients with mild preeclampsia are delivered at 37 weeks, and patients with severe preeclampsia without contraindications to expectant management are delivered at 34 weeks.[21] All patients with twin pregnancies have their blood pressure routinely checked in our office every 2-4 weeks until 28 weeks, then every 2 weeks until 36 weeks, and then every week until delivery. Ultrasound for fetal growth is done every 4 weeks for dichorionic twins and every 2 weeks for monochorionic twins. Uncomplicated dichorionic twin pregnancies are delivered at approximately 38 weeks and uncomplicated monochorionic twin pregnancies are delivered at approximately 37 weeks. The recommendation for low-dose aspirin was not uniform over the study period.

TABLE 1
Baseline characteristics of the population

Characteristic	Value
Number of patients	578
Maternal age	34.1 ± 6.5
Chorionicity	
Dichorioic-Diamniotic	86.9%
Monochorionic-Diamniotic	13.1%
Conception	
Spontaneous	23.7%
Ovulation induction	11.6%
In vitro fertilization	64.7%
Egg donor	8.8%
Multifetal reduction	7.3%
White race	87.9%
Nulliparity	61.8%
Uterine anomaly	2.8%
Anticoagulation	4.7%
Prepregnancy BMI, kg/m^2	23.4 ± 4.5
Obesity (prepregnancy BMI ≥30 kg/m^2)	8.3%
Gestational age at delivery	35.8 ± 2.5
Any diabetes	8.7%
Preeclampsia	
Total	14.9%
<32 wks	0.7%
32-34 wks	2.6%
>34 wks	11.6%
Any newborn weight <10th percentile	50.0%
Any newborn weight <5th percentile	27.5%

Mean ± SD, or %.

BMI, body mass index.

Fox. Preeclampsia and IUGR in twin pregnancies. Am J Obstet Gynecol 2014.

We compared the likelihood of IUGR in patients with and without preeclampsia. We also compared the likelihood of gestational hypertension and preeclampsia in patients with and without IUGR. Becauuse we planned on including every patient over the course of the study period, the power analysis was done post hoc. Student *t* test, χ^2, and Pearson correlation were used when appropriate (SPSS for Windows 16.0, Chicago, IL). A *P* value of < .05 was considered significant.

FLA 5.2.0 DTD ■ YMOB9845_proof ■ 17 June 2014 ■ 8:56 pm ■ ce