Objectives—Abnormal placentation is an important factor in the pathogenesis of preeclampsia. As a result of diminished blood flow, the incidence of preeclampsia might be higher in patients with laterally located placentas compared to patients with centrally located placentas. The objective of this study was to evaluate the relationship between placental location and the development of hypertensive disorders of pregnancy.

Methods—Patients with singleton pregnancies who were seen in our ultrasound unit and delivered at our institution from October 2014 to April 2015 were included. The incidence of hypertensive disorders was compared in those with a lateral placental location and those with centrally located placentas (placental locations other than lateral). Baseline characteristics and pregnancy outcomes were compared between groups. The χ² test, Fisher exact test, Mann-Whitney U test, and t test were used when appropriate. \( P < .05 \) was considered significant.

Results—We included 464 patients; 411 (88.57%) had centrally located placentas, and 53 (11.42%) had laterally located placentas. The incidence of hypertensive disorders of pregnancy was similar between groups (21% versus 19%; \( P = .71 \)). Gestational age at delivery (\( P = .73 \)), and small for gestational age (\( P = .96 \)) were also similar between our study groups.

Conclusions—In our study, there was no difference in the rate of hypertensive disorders of pregnancy between patients with central and laterally located placentas.

Key Words—central placentas; gestational age at delivery; growth restriction; lateral placenta; obstetrical complications; placental location; preeclampsia

The incidence of hypertensive disorders of pregnancy has increased over the last 2 decades and complicates about 5% to 10% of all births in the United States. Hypertensive disorders of pregnancy are important causes of prematurity, obstetric morbidity, and maternal mortality around the globe.\(^1\)\(^-\)\(^3\)

Although the etiology of preeclampsia remains uncertain, abnormal trophoblast invasion with vascular remodeling and consequent increased resistance in the spiral arteries has been implicated in the pathogenesis of this condition. Such changes may predispose to hypoxia-reperfusion injury in the placenta, which leads to generation of an excess load of free radicals and reactive oxygen species in the maternal systemic circulation, creating an alteration between the angiogenic and antiangiogenic factors and vasodilators and vasoconstrictors.\(^4\)\(^-\)\(^6\)

Uterine perfusion is supplied by the uterine and ovarian arteries. Each uterine artery supplies its corresponding side of the uterus, has a substantial number of branches, and has anastomoses with the
Materials and Methods

This work was a retrospective cohort study performed at the Department of Obstetrics and Gynecology of the University of Tennessee Health Science Center. Approval was obtained from the University of Tennessee Health Science Center Institutional Review Board and Regional One Health Office of Medical Research. We included patients with singleton pregnancies who were seen in our ultrasound unit for an anatomy survey (18–36 weeks’ gestation) between October 2014 and April 2015 and who delivered at our institution. We excluded multiple pregnancies, cases of persistent placenta previa, persistent low-lying placentas, those with morbidly adherent placentas, fetal anomalies, and those with incomplete delivery information. In the cases in which multiple ultrasound examinations were performed, the placental location was obtained from the last available sonogram.

Medical records were reviewed to obtain baseline information on all participants, including age, ethnicity, gravidity, parity, body mass index, medical and obstetric histories, and placental location. Delivery information was then obtained, including gestational age (GA) at delivery, birth weight, Apgar scores, and the diagnosis of hypertensive disorders of pregnancy.

Our participants were divided into 2 groups according to the placental location. All placentas located on the anterior, posterior, or fundal uterine wall were classified as central; all placentas located on the right or left uterine wall were classified as lateral.

Our primary outcome, the occurrence of hypertensive disorders of pregnancy, was compared in cases with central placentas and those with lateral placentas. Our secondary outcomes, the occurrence of a small-for-gestational-age (SGA) neonate and GA at delivery, were compared between our study groups.

Sample size calculations showed that 295 participants were needed to detect a doubling of the incidence of hypertensive disorders of pregnancy in our population with 80% power and a 95% confidence interval (CI). Baseline characteristics were compared among exposure groups.

The diagnosis of hypertensive disorders of pregnancy included gestational hypertension, preeclampsia without severe features, preeclampsia with severe features, and chronic hypertension with superimposed preeclampsia, and it was made in accordance with the American College of Obstetricians and Gynecologists Task Force on Hypertension in Pregnancy. For the purpose of our study, pregnancies with chronic hypertension were not included in the hypertensive disorders group. SGA was defined as having a birth weight below the 10th percentile for GA.

Our results were presented as number (percent) and mean ± standard deviation with odds ratios (ORs) and 95% CIs. All data were analyzed with SPSS Statistics version 24.0 software for Windows (IBM Corporation, Armonk, NY). Differences between the groups were assessed with the χ² test, Fisher exact test, Mann-Whitney U test, and Student t test when appropriate. The Levene test for equality of variances was used. Logistic regression was used to control for potential confounders. P < .05 determined statistical significance.

Results

Of the 622 pregnancies that presented to our ultrasound unit, 158 were excluded (Figure 1). Therefore, a total of 464 patients were included in our study; 411 (88.57%) had centrally located placentas, and 53 (11.42%) had laterally located placentas. A comparison of the baseline characteristics between the study groups is presented in Table 1.

The rate of hypertensive disorders of pregnancy between the central and the lateral placenta groups was not statistically significantly different (87 [21%] versus 10 [19%]; OR, 0.87; 95% CI, 0.4–1.8; P = .71). Our results remained similar after logistic regression to control for chronic hypertension (P = .84). For our secondary outcomes, the occurrence of SGA (84 [20%] versus 11 [21%]); OR, 1.02; 95% CI, 0.48–2.03; P = .96) and GA at delivery (38.24 ± 2.51 versus 38.06 ± 2.84 weeks;...
P = .73) were not statistically different among the central and lateral placenta groups. Our secondary outcome results remained not statistically different after logistic regression was performed to control for chronic hypertension: SGA (P = .98) and GA at delivery (P = .80).

Because the prevalence of chronic hypertension between our study groups trended toward statistical significance and is an important clinical risk factor for the development of hypertensive disorders of pregnancy, a secondary analysis was performed excluding participants with chronic hypertension. Fifteen of the patients with chronic hypertension in the central placenta group and 2 of the ones with chronic hypertension in the lateral placenta group were complicated by hypertensive disorders of pregnancy. Therefore, the occurrence of hypertensive disorders of pregnancy (72 [20%] versus 8 [16%]; OR, 0.74; 95% CI, 0.33–1.60; P = .47), SGA (75 [21%] versus 10 [20%]; OR, 0.94; 95% CI, 0.42–1.90; P = .84), and GA at delivery (38.42 ± 2.32 versus 38.13 ± 2.83; P = .41) remained not statistically different among the central and lateral placenta groups after such an analysis.

**Discussion**

Our study showed no difference in the development of hypertensive disorders of pregnancy between pregnancies with lateral placentation and those with other placental locations. The rate of SGA neonates and the GA at delivery were also not different in our study.

Similar studies have shown conflicting results; some have shown no association of preeclampsia, FGR, and other adverse outcomes with a lateral placenta, but some have shown an increased risk of adverse outcomes with lateral placentation. Among those reporting an increased risk of adverse outcomes, in a study from Italy, Liberati et al reported a nonsignificantly higher incidence of FGR and pregnancy-induced hypertension in patients with lateral placetas (P = .31); however, their lateral placenta group included 65% of their study population. In an article from Germany, Gonser et al reported an increased risk of preeclampsia in their patients with lateral placentas (28% versus 3%; risk ratio, 3.1); however, their lateral placenta group was 3 times greater than the control group. Similar results were found in a study of 300 patients by Kofinas et al, who found an increased risk of preeclampsia and FGR in patients with unilateral placentas; they also seemed to have a higher rate of lateral placentas. In all 3 of these studies, the rate of lateral placentas was a lot higher than in our study.

Two other studies found an increased risk of preeclampsia. In a study of 1057 participants from Turkey, the authors reported an increased risk of preeclampsia (4.5% versus 1.6%; P = .027) and other adverse outcomes, such as FGR, preterm delivery, low Apgar scores, and neonatal intensive care unit admissions, in the lateral placenta group (P < .05). In that study, lateral placentas were seen in 12% of their population, a similar proportion as in our study (11%). In another study of more than 16,000 pregnancies from Hong Kong in 2011, Fung et al found an increased risk of preeclampsia,
preterm birth, and cesarean delivery in patients with a lateral placental location compared to other placental locations.

On the other hand, Antsaklis et al19 did not find an increased incidence of preeclampsia in lateral placentas, and similarly, in a 2007 study that included 3336 patients from Western Australia and Mississippi, Magann et al20 reported an increased number of Apgar scores of less than 7 at both 1 and 5 minutes after birth but no association with preeclampsia, FGR, preterm birth, and other adverse obstetric outcomes with a high lateral placental location; however, they included low lateral placentas in a different group. In a study primarily assessing the relationship between placental location and neonatal weight, Devarajan et al21 did not find an increased incidence of preeclampsia in their lateral placenta group. Our results were similar to those from the last 3 studies.

Our study had strengths and limitations. Our study’s strengths were as follows: first, our study’s ultrasound examinations were completed in a maternal-fetal medicine referral ultrasound unit with a high incidence of preeclampsia and FGR; second, we believe that our rate of lateral placentas (11%) was more representative of the general population and similar to recent research (6%–12%)17,18,21,22 than the higher lateral placentation rates reported in older studies14–16,19; and third, our results remained similar after controlling for chronic hypertension by logistic regression and after excluding the cases with this condition. Among our limitations, our retrospective design had well-known biases. In addition, our ultrasound examinations were performed from 18 to 36 weeks’ gestation; thus, we could have missed cases of placental migration. Also, our 2-group classification of placental locations could be seen as a limitation, as lateral implantation in the fundus and lower uterine segment may have a different blood supply, questioning the accuracy of our assessment of pregnancy outcomes of lateral placentation. However, this categorization has been used by other investigators21 and can be reproduced in future studies. Finally, our study might not represent the general population because it took place at a single institution.

In conclusion, in our study, we did not find an association between the placental location during second-trimester obstetric ultrasound examinations and the development of hypertensive disorders, SGA, and the GA at delivery, suggesting that the increased vascular resistance in the uterine arteries associated with lateral placentation may not always translate into hypertensive disorders. We acknowledge the need for more-diverse population studies and larger prospective trials to corroborate our findings.

References