Adverse obstetric outcomes associated with sonographically identified large uterine fibroids

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Study Objective: To determine the impact of sonographically identified large uterine fibroids (>5 cm in diameter) on obstetric outcomes.
Design: Retrospective cohort study.
Setting: University teaching hospital.
Patient(s): Women with singleton gestations (n = 95) noted to have uterine fibroids on obstetric ultrasonography from September 2009 through April 2010 and age-matched controls (n = 95).
Intervention(s): None.
Main Outcome Measure(s): Obstetric outcomes including short cervix, preterm premature rupture of membranes, and preterm delivery.
Result(s): Compared to women with no fibroids or small fibroids (≤5 cm), women with large fibroids (>5 cm) delivered at a significantly earlier gestational age (38.6 vs. 38.4 vs. 36.5 weeks). Short cervix, preterm premature rupture of membranes, and preterm delivery were also significantly more frequent in the large fibroid group, and were associated with number of fibroids >5 cm in diameter. Blood loss at delivery was significantly higher in the large fibroid group (486.8 vs. 535.6 vs. 645.1 mL), as was need for postpartum blood transfusion (1.1 vs. 0.0 vs. 12.2%).
Conclusion(s): Women with large uterine fibroids in pregnancy are at significantly increased risk for delivery at an earlier gestational age compared to women with small or no fibroids, as well as obstetric complications including excess blood loss and increased frequency of postpartum blood transfusion. (Fertil Steril® 2012;97:107–10. ©2012 by American Society for Reproductive Medicine.)
Key Words: Fibroid, leiomyoma, ultrasonography, pregnancy, short cervix, preterm delivery, premature rupture of membranes, blood transfusion

Uterine fibroids are the most common benign tumor of the female reproductive tract affecting 30%–70% of reproductive-age women (1). The incidence of uterine fibroids rises with increasing age, and they are most frequent among African American women (2). Uterine fibroids have a prevalence of 0.1%–10.7% in pregnancy (3, 4) and are associated with a 10%–40% obstetric complication rate (5, 6).

Prior research on obstetric outcomes in women with pregnancies complicated by uterine fibroids has produced inconsistent results. Moreover, findings may reflect an ascertainment bias because several retrospective studies identified women with fibroids on the basis of diagnosis codes or insurance records after delivery, rather than confirmation by antepartum obstetric ultrasonography (7). Nevertheless, evidence suggests that there is a trend toward delivery at an earlier gestational age in women with fibroids of any size (6, 8–12). Fibroids have also been reported to be associated with fetal malpresentation, intrauterine growth restriction, placenta previa, labor dystocia, placental abruption, delivery by cesarean section, retained placenta, and postpartum hemorrhage (PPH) (7).

We further investigated the impact of uterine fibroids on obstetric outcomes, specifically evaluating the impact of large uterine fibroids on the frequency of short cervix, preterm premature rupture of membranes (PPROM), preterm delivery (PTD), estimated blood loss (EBL) at delivery, and need for postpartum blood transfusion, as well as other adverse obstetric outcomes. Patients with uterine fibroids identified during routine obstetric ultrasonography were used in our analysis.

MATERIALS AND METHODS

This was a retrospective cohort study approved by the institutional review board of Wayne State University and the Detroit Medical Center that included women with singleton gestations who

Received June 8, 2011; revised October 7, 2011; accepted October 10, 2011; published online November 17, 2011.
V.I.S. has nothing to disclose. M.T. has nothing to disclose. A.S. has nothing to disclose. M.L.K. has nothing to disclose. T.B.J. has nothing to disclose. M.S. has nothing to disclose. E.E.P. has nothing to disclose. M.P.D. is a grant recipient from NICHD, Bio Sante, Boehringer Ingelheim, and Interlace Medical, serves as a consultant to Genzyme, Omrix, EMD Serono, Neomend, Boehringer Ingelheim, Auxogyn, Halt Medical, ZSX Medical, and Sanofi Aventis, and owns stock in SyntheMed and Neomend.
Preliminary data from this study were presented at the 66th Annual Meeting of the American Society for Reproductive Medicine, Denver, Colorado, October 23–27, 2010.
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Fertility and Sterility® Vol. 97, No. 1, January 2012 0015-0282/$36.00

doi:10.1016/j.fertnstert.2011.10.009

had uterine fibroids identified on routine obstetric ultrasonography during the first trimester screen (performed between and $10\frac{4}{7}$ and $13\frac{6}{7}$ weeks gestational age) or fetal anatomic survey (typically performed between 18 and 22 weeks gestational age) from September 2009 through April 2010, and who delivered at a gestational age greater than 20 weeks at a hospital of the Detroit Medical Center.

Women with fibroids and their age-matched controls were identified by searching the departmental obstetric ultrasonography database. Age-matched women without uterine fibroids on routine obstetric ultrasonography during the same study period were randomly selected for inclusion. Charts were then reviewed in a systematic fashion to extract demographic and clinical characteristics for each patient, including maternal age, gravidity, parity, body mass index (BMI), race, medical history, substance use during pregnancy, and history of prior PTD (defined as delivery prior to 37 weeks' gestational age).

Based on prior studies, we defined fibroids as large if they measured >5 cm in diameter on ultrasonography (13). Additional ultrasonographic data were extracted and consisted of total number of fibroids, number of fibroids >5 cm in diameter, diameter of the largest fibroid, and location of fibroids >5 cm. Fibroid volumes were calculated using the following formula: length × width × diameter × $\pi/6$. Total fibroid volume was tabulated for each patient.

Obstetric outcomes were noted such as a shortened cervical length (defined as <25 mm on transvaginal ultrasonography at ≤32 weeks' gestational age), intrauterine growth restriction, placenta previa, placental abruption, gestational age at delivery, PTD, PPROM (defined as spontaneous rupture of membranes before 37 weeks' gestational age), fetal malpresentation, mode of delivery, EBL, retained placenta, PPH (defined as EBL >500 mL for vaginal delivery or >1,000 mL for cesarean delivery), need for blood transfusion, and length of hospital stay. Fetal outcomes such as infant birth weight, APGAR score at 1 and 5 minutes, and umbilical artery pH were also extracted from medical records.

Data were entered into an SPSS database (version 19.0 for Windows, SPSS Inc., Chicago, IL), and Student's independent samples *t* test, Pearson's chi-square test, and ANOVA were used to determine statistical significance. The Mann-Whitney *U* test was used for non-normally distributed measures. Student-Newman-Keuls was used for post hoc analysis. Total fibroid volumes were log transformed in order to normalize the data. A *P* value <.05 was considered statistically significant.

RESULTS

From September 2009 through April 2010, 95 women with singleton gestations had uterine fibroids documented on routine obstetric ultrasonography. Of the 95 women with sonographically identified fibroids, 42 (44.2%) were found to have large uterine fibroids measuring >5 cm in diameter. These women were, on average, 32.2 years of age with a mean gravidity of 3.8 and parity of 1.6. Compared to women with small or no sonographically identified fibroids, women with large fibroids were not statistically different with respect to maternal age, gravidity, parity, BMI, race, absence of past medical problems, substance abuse during pregnancy, or history of prior PTD (Table 1).

In the large fibroid group, the mean gestational age at time of ultrasonography was 20.3 weeks, which was not statistically different from gestational age at time of ultrasonography for women with small or no fibroids: 18.3 and 19.9 weeks, respectively (*P*>.05). In addition, women in the small fibroid group who had fibroids documented during first trimester screening (n = 7) were not found to have an increase in fibroid diameter to >5 cm on subsequent ultrasonographies to assess fetal anatomy. For women in the large fibroid group, a total of one to five fibroids were identified, of which one to three fibroids measured >5 cm in diameter. The mean diameter of the largest fibroid was 7.3 cm and ranged from 5.1 to 16.4 cm.

According to the results of the ANOVA used to compare women with no fibroids, small fibroids, and large fibroids, women with large fibroids delivered at a significantly earlier gestational age (38.6 vs. 38.4 vs. 36.5 weeks, *P*=.002). Women in the large fibroid group were also more frequently diagnosed with short cervix, PPROM, and PTD (Table 2). On the basis of a nonparametric statistical analysis, the total number of fibroids >5 cm was significantly associated with short cervix (*P*=.001), PTD (*P*=.005), and PPROM (*P*<.001). PPROM occurred in 100% of women with three fibroids >5 cm, 25% of women with two fibroids >5 cm, 8.3% of women with one fibroid >5 cm, and 1.9% with none (Fig. 1). Shortened cervical length (*P*<.001) and PTD (*P*=.015) were also significantly associated with the diameter of the largest fibroid (Fig. 2).

Similar results were obtained when fibroid size was assessed by fibroid volume. Total fibroid volume ranged from 0.9 to 1,141.3 cm^3 in the study population. Mean fibroid volume in the small fibroid group was 19.9 ± 20.3 cm^3 compared with 202.5 ± 263.3 cm^3 in the large fibroid group. Total fibroid volume was found to be significantly associated with earlier gestational age at delivery (Pearson correlation coefficient −0.29, *P*=.007), short cervix (*P*=.026), and PPROM (*P*=.002).

Estimated blood loss at delivery was found to be significantly greater in the large fibroid group compared with women in the small and no fibroid groups (*P*=.038) (Table 2). For women with large fibroids, mean EBL at delivery was 923.9 mL for cesarean section and 288.9 mL for vaginal delivery. Although more women in the large fibroid group were found to have PPH (12.2%) compared with those in the small fibroid (5.7%) or no fibroid (3.2%) groups, this was not found to be statistically significant (*P*=.120). However, need for postpartum blood transfusion was significantly more frequent in the large fibroid group (*P*=.001). Of women with large fibroids, 12.2% required blood transfusion prior to discharge, compared to 0.0% in the small fibroid group and 1.1% in the no fibroid group (Table 2). For those who received a blood transfusion in the large fibroid group, an average of 2.4 units of packed red blood cells were transfused, and 60% of transfusions were subsequent to cesarean section compared with 40% after vaginal delivery. Need for postpartum blood transfusion was also significantly associated with total fibroid volume (*P*<.005).

We did not find significant differences in women with large fibroids compared to those with small or no fibroids

TABLE 1

Demographic and clinical characteristics of women with large (>5 cm), small (≤5 cm), or no sonographically identified fibroids.

Characteristic	Large fibroids (n = 42)	Small fibroids (n = 53)	No fibroids (n = 95)	*P* value
Maternal age (y), mean ± SD	32.2 ± 5.5	31.6 ± 5.7	31.9 ± 5.6	.89
Gravidity, mean ± SD	3.8 ± 3.8	3.8 ± 2.3	4.6 ± 2.5	.16
Parity, mean ± SD	1.6 ± 1.3	2.0 ± 1.5	2.1 ± 1.7	.14
BMI (kg/m^2), mean ± SD	34.2 ± 13.6	34.6 ± 6.8	31.9 ± 7.9	.15
Race (%)				.32
African American	90.5	92.5	86.3	
Caucasian	4.8	1.9	10.5	
Other	4.8	5.7	3.2	
No past medical problems (%)	57.5	69.8	76.6	.08
Substance use (%)				.51
None	78.6	86.8	83.2	
Tobacco	7.1	7.5	8.4	
Illicit drugs	9.5	5.7	3.2	
Both	4.8	0.0	5.3	
Prior preterm delivery (%)	35.7	24.5	25.5	.40

Note: BMI = body mass index.

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with respect to intrauterine growth restriction, fetal malpresentation, placenta previa, placental abruption, mode of delivery (vaginal vs. cesarean delivery), retained placenta, infant birth weight, APGAR score at 1 and 5 minutes, umbilical artery pH, or length of hospital stay ($P>.05$).

Most large fibroids were located on the anterior (45.2%) and lateral (28.6%) walls of the uterus. Some (9.5%) large fibroids were located at the lower uterine segment or cervix and 15.8% were retroplacental. Of the fibroids whose type could be determined on the basis of sonographic images (n = 36), most large fibroids were found to be intramural (55.6%) and the remainder were noted to have subserosal (36.1%) or submucosal (8.3%) extension. Location of the large fibroids was not found to be associated with short cervix, PPROM, PTD, gestational age at delivery, EBL, or need for postpartum blood transfusion ($P>.05$), with the exception of large submucosal fibroids being significantly associated with short cervix ($P=.022$) and PPROM ($P=.022$) compared to intramural and subserosal fibroids. However, because there were only three women with large submucosal fibroids, it is difficult to draw conclusions from these findings.

DISCUSSION

Large uterine fibroids were significantly associated with delivery at an earlier gestational age compared to women with small or no fibroids. The mean age of delivery in the large fibroid group was 36.5 weeks compared with 38.4 weeks in the small fibroid group and 38.6 weeks in the no fibroid group. Preterm delivery was also more frequent in women with pregnancies complicated by large fibroids. Numerous studies have confirmed the association between uterine fibroids of any size and delivery at an earlier gestational age (6, 8–12). Although prior studies have not found an association between large uterine fibroids (>5 cm) and PTD (13, 14), our findings suggest that large uterine fibroids >5 cm in diameter have a significant impact on earlier gestational age at delivery. We also found that large uterine fibroids were significantly associated with short cervix and PPROM, and that total number of fibroids >5 cm were correlated with these occurrences. Consistent with these findings, total fibroid volume was also found to be significantly associated with earlier gestational age at delivery, short cervix, and PPROM. A decrease in uterine distensibility because of the presence of fibroids may contribute to these adverse obstetric outcomes.

Blood loss at delivery was estimated to be significantly higher in women with large fibroids compared to women without fibroids. In agreement with this finding, the need for postpartum blood transfusion was also increased in the large fibroid group. Although there was a trend toward increased frequency of PPH in women with large fibroids, it

TABLE 2

Differences in obstetric outcomes in women with large fibroids (>5 cm) compared to those with small (≤5 cm) or no fibroids.

Outcome	Large fibroids (n = 42)	Small fibroids (n = 53)	No fibroids (n = 95)	*P* value
GA at delivery, mean ± SD (wk)	36.5 ± 5.0	38.4 ± 2.9	38.6 ± 2.2	.002
EBL, mean ± SD (mL)	645.1 ± 437.7	535.6 ± 316.7	486.8 ± 275.6	.038
Short cervix at ≤32 wk GA (%)	14.3	1.9	3.2	.012
PPROM (%)	14.3	1.9	2.1	.004
Preterm delivery (%)	16.7	3.8	6.3	.050
Postpartum blood transfusion (%)	12.2	0.0	1.1	.001

Note: GA = gestational age.

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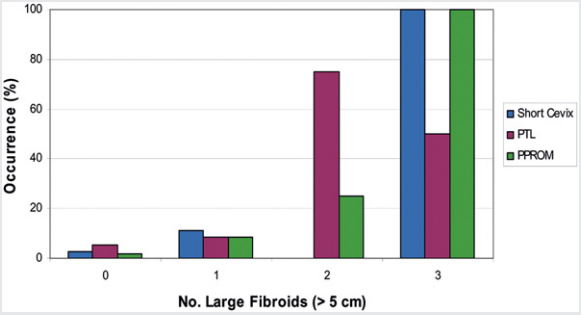
FIGURE 1



Occurrence of short cervix, preterm delivery (PTD), and preterm premature rupture of membranes (PPROM) by total number of large fibroids (>5 cm).

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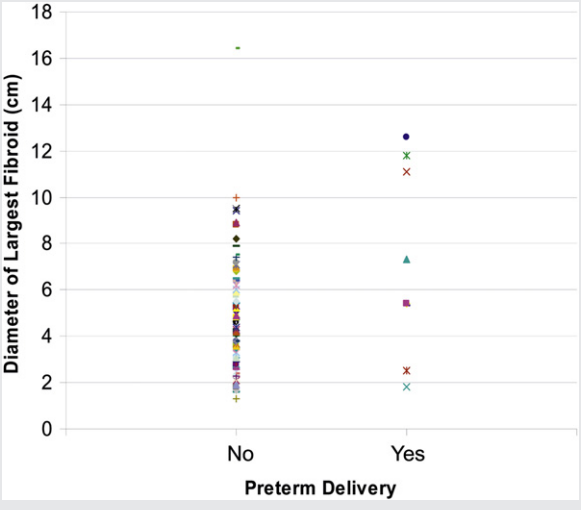
did not reach statistical significance. Others have found an association between PPH >1,000 mL and fibroids ≥5 cm (13). However, Qidwai et al. did not find an association between fibroids ≥10 cm and severe PPH (EBL >1,000 mL for vaginal delivery or >1,500 mL for cesarean section) (11). Of note, these studies used different definitions for PPH.

Though several reports have suggested that uterine fibroids are associated with an increased rate of cesarean section (6, 8, 10, 11), we did not find a difference in mode of delivery in women with large fibroids compared to those with small or no fibroids. This is in agreement with findings published by Stout et al. in which women with fibroids >5 cm did not have an increased risk of cesarean section when compared with women with fibroids ≤5 cm (adjusted odds ratio of 1.1, 95% confidence interval = 0.9–1.4) (14). Interestingly, Vergani et al. found an increased rate of cesarean section before the onset of labor in women with fibroids ≥5 cm but not during labor (13).

FIGURE 2



Occurrence of preterm delivery (PTD) by diameter of the largest fibroid (cm).

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Our findings are limited by the fact that this was a retrospective cohort study. However, in identifying women for inclusion on the basis of the documentation of uterine fibroids on routine obstetric ultrasonography, ascertainment bias was minimized. We also accounted for the effect of maternal age on obstetric outcomes by using age-matched controls not found to have uterine fibroids on obstetric ultrasonography during the same study period.

Uterine fibroids have been associated with a multitude of adverse obstetric outcomes. We have found, however, that large uterine fibroids in particular are associated with short cervix, PPROM, delivery at an earlier gestational age, increased blood loss at delivery, and need for postpartum blood transfusion. Women with fibroids larger than 5 cm in diameter, therefore, should be counseled regarding the increased likelihood of these unfavorable obstetric outcomes. We believe it is premature, however, to make specific recommendations regarding the value of myomectomy prior to conception in such women.

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