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Obstetric outcomes of intramural leiomyomas in pregnancy

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Summary

Aim: The authors aimed to study larger intramural leiomyoma with a size of ≥ three cm on pregnancy outcome of singleton pregnancies compared with control group. *Materials and Methods:* The hospital records of all pregnancies followed between years of 2009 and 2013 were searched for the diagnosis of intramural leiomyoma in the second trimester ultrasonographic screening, past medical history, demographics, pregnancy follow up, and pregnancy outcomes of pregnant women. In the data analyses, 112 singleton pregnant women with intramural leiomyoma were included in the study group and 168 singleton pregnant women without leiomyoma were included in the control group. *Results:* The presence of pregnancy associated leiomyoma was found to be a risk factor for abortion (odds ratio (OR):12.6, 95% confidence interval (CI) 2.5−63.6) hospitalization for pain (OR: 19.6, 95% CI 5.8−66.5), premature rupture of membranes (OR: 6.7, 95% CI 1.4-32.4), oligohydramniosis (OR: 5.3, 95% CI 1.4−20.0), preterm birth (OR: 4.7, 95% CI 1.9−11.6), and breech presentation and other abnormal presentations (OR: 9.7, 95% CI 2.8−34.2) and neonatal intensive care need (OR: 3.0, 95% CI 1.2-7.5). No correlation with the rate of intrauterine growth restriction, intrauterine fetal death, placenta previa, abruption of placenta, and cesarean section was found. *Conclusions:* Pregnancy associated intramural leiomyoma is a risk factor for some perinatal complications and these results may be useful for prenatal counseling.

Key words: Intramural leiomyoma; Pregnancy; Obstetric outcome; Perinatal complication.

Introduction

Abnormal overgrowth of the smooth muscle cells in the uterus causes benign soft tissue masses called leiomyoma at a histopathological level. These masses do occur at any age, however are mainly prevalent in childbearing age. The prevalence of uterine leiomyoma in pregnancy varies between 2.7% and 10.7% [1-5]. The obstetric outcomes in women with leiomyoma are conflicting, and according to studies, different and discrepant outcomes were reported in literature. Leiomyoma in pregnancy can be associated with miscarriage, preterm birth, preterm premature rupture of membranes (PROM), intrauterine growth restriction (IUGR), intrauterine fetal death (IUFD), placenta previa, placental abruption, fetal malpresentation, labor dystocia, delivery by cesarean section, and postpartum hemorrhage [1-6].

In this present retrospective study the authors aimed to study larger intramural uterine leiomyoma with size of ≥ three cm on pregnancy outcome of singleton pregnancies compared with control group.

Materials and Methods

This study was a retrospective analysis of data. The hospital records of all pregnancies followed between years of 2009 and 2013 were searched for the diagnosis of intramural leiomyoma in the second trimester ultrasonographic screening, past medical history, demographics, pregnancy follow up, and pregnancy outcomes of pregnant women.

In the second trimester ultrasonographic screening at 15-24 weeks of gestation and the dimensions of the leiomyomas were measured and recorded in three dimensions. All pregnancies with intramural leiomyoma with size of ≥ three cm were included in the study group. Ones with subserosal and submucosal leiomyoma were excluded. To exclude potential effects of systemic diseases, multiple pregnancy on pregnancy outcome, ones with systemic diseases or multiple pregnancies were excluded. Pregnancies with proven chromosomal abnormalities or structural abnormalities were excluded as well from data analyses. In the second trimester, ultrasonographic screening at 15-24 weeks of gestation, pregnant women without leiomyoma, aged 30 to 40, were included in the control group. Likewise, ones with chromosomal abnormalities or structural abnormalities, systemic diseases or multiple pregnancies were excluded in the control group.

Specific demographic and perinatal outcomes were recorded including maternal age, parity, gestational age at ultrasound screening, presence of abortion (< 20 weeks), hospitalization for pain-pseudo, fetal presentation, mode of delivery, birth week, neonatal birth weight (grams), presence of IUGR, IUFD, placenta previa, placental abruption, preterm delivery (< 37 weeks, < 34 weeks, and <32 weeks), PROM, oligohydramniosis (without PROM), retained placenta, APGAR scores at one and five minutes, and neonatal intensive care need. Also all birth weights were transformed into birth weight centile according to normative references [7]. Data regarding demographic, obstetric, and perinatal outcomes were obtained from the present hospital database. In case of incomplete data, the authors contacted the patients by phone to complement their data.

Data analysis was performed by using Statistical Package for

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Table 1. — *Demographic futures and obstetric outcomes of pregnant women with leiomyoma compared with pregnant women without leiomyoma.*

Parameters	Study group (n=112)	Control group (n=168)
Age (years)	34.4 ± 4.9	34.3 ± 2.7
Parity (n.)	1.2 ± 1.3	1.3 ± 1.0
Gestational age at ultrasound screening (weeks)	20.0 ± 2.9	19.6 ± 1.8
Birth week*	37.7 ± 2.5	38.8 ± 2.0
Neonatal birth weight (grams)*	3077 ± 575	3326 ± 556
Neonatal birth weight (percentile)	48.9 ± 25.4	50.1 ± 27.1
APGAR scores at 1 min*	7.4 ± 1.3	7.8 ± 1.0
APGAR scores at 5 min*	8.5 ± 1.2	9.1 ± 0.9

*Statistically significant $p \leq 0.01$.

Social Sciences (SPSS) version 11.5 software. Descriptive statistical methods (mean, standard deviation, and percentiles) were used to evaluate the data. Kolmogorov–Smirnov test was performed to determine whether or not parameters were normally distributed. Student's *t*-test, Pearson correlation, regression analyses, Mann-Whitney U test, and Chi square test were performed and odds ratios of risk estimations were determined via crosstabs. Results were evaluated with 95% confidence intervals, and $p < 0.05$ was considered to indicate significance.

Results

In the data analyses, 112 singleton pregnant women with leiomyoma were included in the study group and 168 singleton pregnant women without leiomyoma were included in the control group, in accordance with inclusion and exclusion criteria. Demographics related to these two groups are summarized in Table 1. Total of 144 intramural uterine leiomyoma mass were identified in 112 pregnancies. Mean diameter of the leiomyoma was 60.99 ± 30.95 mm (range 30.33−203.70). Determined locations of the leiomyoma in order of decreasing frequency was as following; anterior uterine wall (53.5%), posterior uterine wall (20.8%), isthmus (10.4%), fundus (8.3%), left lateral uterine wall (3.5%), and right lateral uterine wall (3.5%). The correlation analyses showed weak to moderate significant negative correlation between the diameter of leiomyoma and birth week (Pearson correlation coefficient: - 0.266 p = 0.006) (Figure 1). Calculated equation for birth weeks in relation to the diameter of leiomyoma was "birth weeks = - 0.016 x diameter of leiomyoma + 38.69". Though initial correlation analyses showed weak to moderate significant negative correlation between the diameter of leiomyoma and birth weight, when controlled with regression analyses for probable effect of birth week itself, size of leiomyoma had no significant effect on birth weight (p = 0.07). When compared with control group, pregnancies with associated intramural leiomyoma had significantly higher rates of preterm birth before gestational weeks of 34 and 37. However, percentiles related growth of the fetus represented with weight in this study was indifferent between control and, pregnancies with associated intramural leiomyomas. Likewise, intrauterine growth retardation rates were similar in both groups.

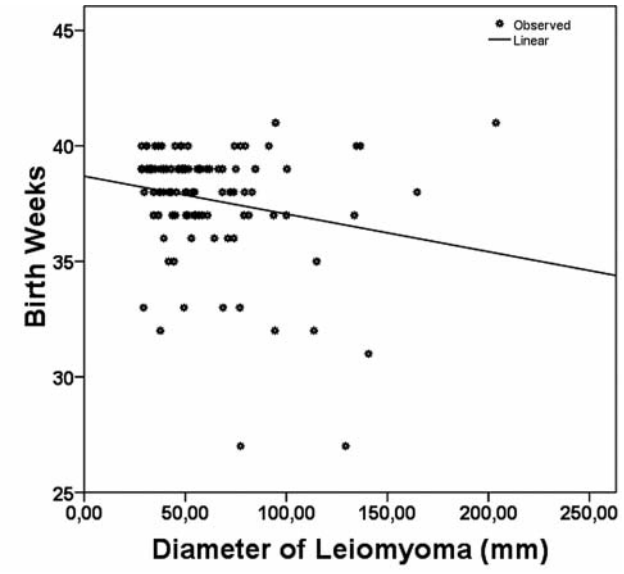

Figure 1. — Relationship between the diameter of leiomyoma and birth weeks.

When presence of pregnancy associated leiomyoma was evaluated as a risk factor for clinical parameters related to pregnancy and fetal outcome, it was found to be a risk factor for abortion, hospitalization for pain, PROM, oligohydramniosis, preterm birth, breech or other abnormal presentation, and neonatal intensive care need as shown in Table 2. No correlation with the rate of IUGR, placenta previa, IUFD, retained placenta, and cesarean section was found. Perioperative complications were myomectomy (n=2), hysterectomy due to postpartum hemorrhage (n=1), and Bakri balloon (n=1) in pregnancies with intramural leiomyoma.

Discussion

Uterine leiomyoma do occur at any age, however are mainly prevalent in childbearing age. The prevalence of uterine fibroids in pregnancy varies between 2.7% and 10.7%, depending upon the trimester of assessment and the size threshold [1-5]. In one study, 4% of 12,708 pregnant patients had fibroids with a diameter > three cm [1]. In another study, 2.7% of 15,104 consecutive pregnant patients had fibroids > one cm [2]. Stout *et al.* [3] reported a similar prevalence of 3.2% in 64,047 women undergoing ultrasound screening in the second trimester. Laughlin *et al.* [4] observed 10.7% of women had a fibroid of ≥ 0.5 cm in

Table 2. — *Obstetric and fetal outcomes for pregnant women with leiomyoma compared with pregnant women without leiomyoma.*

Clinical parameters	Study group (N=112)	Control group (N=168)	Odds ratio (95 % CI)
Abortion (< 20 weeks)	6 (5.4%)	1 (0.6%)	9.4 (1.1−79.6)*
Hospitalization for pain-pseudo	28 (26.4%)	3 (1.8%)	19.6 (5.8−66.5)**
PPROM	8 (7.5%)	2 (1.2%)	6.7 (1.4−32.4)**
Oligohydramniosis (without PROM)	9 (8.8%)	3 (1.8%)	5.3 (1.4−20.0)**
Preterm birth < 32 weeks	6 (5.7%)	3 (1.8%)	3.3 (0.8−13.4)
Preterm birth < 34 weeks	10 (9.4%)	4 (2.4%)	4.3 (2.0−13.9)**
Preterm birth < 37 weeks	18 (17%)	7 (4.2%)	4.7 (1.9−11.6)**
Intrauterine growth restriction	9 (8.5%)	9 (5.4%)	1.6 (0.6−4.3)
Placenta previa	3 (2.8%)	1 (0.6%)	4.8 (0.5−47)
Abruption of placenta	2 (1.9%)	1 (0.6%)	3.2 (0.3−35.6)
Intrauterine fetal death	-	1 (0.6%)	N/A
Retained placenta	-	1 (0.6%)	N/A
Breech or other abnormal presentation	16 (15.1%)	3 (1.8%)	9.7 (2.8−34.2)**
Cesarean section	61 (57.5%)	86 (51.5%)	1.3 (0.8−2.1)
Primary Cesarean section	39 (46.4%)	43 (34.7%)	1.6 (0.9−2.9)
Neonatal intensive care need	14 (13.2%)	38 (4.8%)	3.0 (1.2−7.5) *

*Statistically significant $p < 0.05$. **Statistically significant $p \leq 0.01$.

4,217 women undergoing ultrasound screening in the first trimester of pregnancy.

Due to pregnancy, increases in estrogen and progesterone levels and uterine blood flow are believed to affect fibroid growth, but reported volumetric changes during pregnancy are in conflict [4, 8-10]. In one study, 31.6% of pregnant women with leiomyoma were reported to increase statistically between the first and the third trimesters [9]. In accordance with this study, even a higher rate of volumetric increase was reported as 71.4% between the first and second gestational periods and 66.6% between the second and third trimesters [9]. However, in another study, reduction in leiomyoma size during pregnancy was reported to be 55.1% with a mean decrease in mass volume of 35 ± 4%. Interestingly the rest (44.9%) was reported to have volume increase with a mean increase of 69 ± 11% in the same study [11]. Postpartum resolution of fibroids was reported as 36% and postpartum ultrasonographic volume reduction ratio was reported as 79%, with a median change of 0.5 cm. This volume reduction in diameter was more significant in the uterine leiomyoma located in the submucosa and ones in lower segment of uterus [4].

Leiomyoma have been associated with a number of pregnancy complications, but mechanisms by which leiomyoma increase the risk of adverse obstetric outcomes are unknown. Speculations as to distensibility of the uterus, physical obstruction, efficacy of contraction patterns, inflammation, changes in the endometrial structure, and molecular signaling all have been postulated [3]. In literature, the obstetric outcomes in women with leiomyoma are conflicting. Different studies with different cut-off diameters or methods reported various pregnancy related problems like abruptio placentae, pelvic pain, abortion, breech presentation, placenta previa, PROM, preterm birth IUGR, IUFD, cesarean section rate, and postpartum hemorrhage with varying and conflicting ratios [1-6, 11]. In the present study, pregnancies with intramural leiomyoma with size of ≥ three cm included and cases with subserosal and submucosal leiomyoma excluded. This is the most striking difference between the present study and the previously published studies.

In the present study, we showed that the presence of leiomyoma was associated with higher rates of abortion (5.4% compared with 0.6%, OR:9.4 [95% CI 1.1−79.6)], hospitalization for pain (26.4% compared with 1.8%, OR:19.6 [95% CI 5.8−66.5)], PPROM (9.4% compared with 1.3%, $p \leq 0.01$ OR: 7.7 [95% CI 2.7−21.6)], oligohydramniosis without PROM [7.5% compared with 1.2%, OR:6.7 (95% CI 1.4−32.4)] preterm birth [(for < 34 weeks 9.4% compared with 2.4%, OR: 4.3 (95% CI 2−13.9)] and [for < 37 weeks 17% compared with 4.2%, OR: 4.7 (95% CI 1.9−11.6)], breech presentation, other abnormal presentations [15.1% compared with 1.8%, OR: 9.7 (95% CI 2.8−34.4)], and neonatal intensive care need [13.2% compared with 4.8%, OR:3.0 (95% CI 1.2−7.5)]. Despite this the authors detected higher rate of preterm birth for < 32 weeks in pregnancies with leiomyoma, however there was no significance. In addition, we found significant negative correlation between the diameter of leiomyoma and birth week (Pearson correlation coefficient: - 0.266, $p = 0.006$).

Exacoustos and Rosati [1] reported incidence of threatened abortion, threatened preterm delivery, abruption of placenta, and pelvic pain that were significantly more frequent in patients with leiomyoma. Pelvic pain was found to be related to leiomyoma with volumes of 200 cm^3 and with heterogeneous echo patterns and cystic areas in leiomyoma mass. The

present study further confirms higher pain risk related to pregnancy associated leiomyoma and the need of hospitalization for pain. However, in the present study, leiomyoma was shown to have no effect on the mode of delivery, abortion, preterm birth, and PROM. In the Exacoustos and Rosati study, 32 of 492 patients had either myomectomy or hysterectomy for uterine leiomyoma [1]. A similar surgery rate at birth was present in the current study (3 /112).

Qidwai *et al.* [2] reported that the presence of leiomyomata was associated with increased risks for cesarean delivery (OR 1.64, 95% CI 1.28–2.11), malpresentation (OR 1.64, 95% CI 1.11–2.40), malposition (OR 1.59, 95% CI 1.18–2.15), preterm delivery (OR 1.45, 95% CI 1.08–1.96), severe postpartum hemorrhage (OR 2.57, 95% CI 1.54–4.27), and placenta previa (OR 1.86, 95% CI 1.02–3.39), but they determined that PROM, placental abruption, operative vaginal delivery, chorioamnionitis, and endomyometritis were not associated with leiomyoma. Whereas Stout *et al.* [3] reported that breech presentation (5.3% compared with 3.1%, adjusted OR 1.5, 95% CI 1.3–1.9), placenta previa (1.4% compared with 0.5%, adjusted OR 2.2, 95% CI 1.5–3.2), cesarean delivery (33.1% compared with 24.2%, adjusted OR 1.2, 95% CI 1.1–1.4), placental abruption (1.4% compared with 0.7%, adjusted OR 2.1, 95% CI 1.4–3.0), preterm PROM (3.3% compared with 2.4%, adjusted OR 1.3, 95% CI 1.0 –1.7), preterm birth less than 37 weeks (15.1% compared with 10.5%, adjusted OR 1.5, 95% CI 1.3–1.8), less than 34 weeks (3.9% compared with 2.8%, adjusted OR 1.4, 95% CI 1.0 –1.8), and IUFD in women with a fetus with growth restriction (3.9% compared with 1.5%, adjusted OR 2.5, 95% CI 1.2–5.0) were significantly associated with the presence of leiomyomas. Unlike other studies, the present authors did not find an association between leiomyoma and the rate of IUGR, IUFD, placental abruption, and placenta. Similarly, Ciavattini *et al.* [7] reported that no correlation with IUGR and placental abruption was found.

Coronado *et al.* [5] reported independent associations between uterine leiomyoma and first trimester bleeding (OR 1.82, 95% CI 1.05–3.20), dysfunctional labor (OR 1.85, 95% CI 1.26–2.72), breech presentation (OR 3.98, 95% CI 3.07–5.16), and placental abruption (OR 3. 87, 95% CI 1.63–9.17). In one study, increased risk of malpresentation (OR 2.9; 95% CI 2.6–3.2), cesarean (OR 3.7; 95% CI 3.5–3.9), and preterm delivery (OR 1.5; 95% CI 1.3–1.7) are reported by Klatsky *et al.* [6]. Similarly in another study, size of uterine leiomyoma were compared in 95 singleton pregnancies with pregnancy associated uterine leiomyoma and larger leiomyoma (> five cm) and were also found to be associated with earlier gestational age, short cervix, preterm PROM, preterm delivery, blood loss at delivery, and need for postpartum blood transfusion [12].

In a study concerning the natural growth pattern of uterine leiomyoma during pregnancy, in which 36 pregnant women with uterine leiomyoma were followed, uterine leiomyoma with the volume ≥ 200 cm^3 were found to have a higher incidence of complications compared to ones with uterine leiomyoma with the volume ≤ 100 cm^3 [8]. Lam *et al.* [13] evaluated 121 patients for their pregnancy associated uterine leiomyoma; preterm delivery was related to multiplicity of the uterine leiomyoma. Study suggested that the location of leiomyoma had no significant effect on the rate of preterm delivery. However, ones with uterine leiomyoma in the lower part of uterus had higher cesarean section rate, postpartum hemorrhage, and greater estimated blood loss compared to the body of the uterus. Presence as well as increasing size of uterine leiomyoma was associated with higher incidence of hemorrhage, estimated blood loss, and admissions for related pain. Mean estimated blood loss was found to be higher in subserosal and intramural uterine leiomyoma. Michels *et al.* [14] reported that women with leiomyoma were at increased risk (RR, 1.27; CI, 1.17–1.37) for cesarean birth particularly, those with larger tumor volumes. However, the present study included leiomyoma with a size of ≥ three cm that are suggested as large leiomyoma in the previous study and we did not detect any significant difference in the rate of cesarean section between ones with leiomyoma and ones without leiomyoma.

Lai *et al.* [15] compared the rates of neonatal outcomes between the group of women with leiomyoma and the group of women without leiomyoma. They reported leiomyoma were significantly associated with preterm delivery, PROM, IUFD, and low Apgar scores, but not with IUGR, shoulder dystocia, presence of meconium, umbilical cord pH < 7, neonatal jaundice (hyperbilirubinemia), and sepsis. In the present study, we found significantly lower Apgar scores and higher rate of neonatal intensive care need in pregnancies with intramural leiomyoma but no correlation with the rate of IUGR and IUFD was found.

In conclusion, pregnancy associated intramural leiomyomas do have negative effect on pregnancy outcome and are a risk factor for abortion, hospitalization for pain, PROM, oligohydramniosis, preterm birth, breech presentation, and neonatal intensive care need, but IUGR, IUFD, placenta previa, abruption of placenta, retained placenta, and cesarean section were not associated with leiomyoma. These results are important for prenatal counseling of women with intramural leiomyoma.

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