The effect of amniocentesis on preterm delivery rate in women with uterine myoma

S. Buyukkurt[1], A. Yuksel[2], G. Seydaoglu[3], R. Has[2], O. Kadayifci[1]

[1]Department of Obstetrics and Gynecology, University of Cukurova School of Medicine, Adana
[2]Department of Obstetrics and Gynecology, Istanbul University, Istanbul Faculty of Medicine, Istanbul
[3]Department of Biostatistics, University of Cukurova School of Medicine, Adana (Turkey)

Summary

Objectives: To evaluate the effect of genetic amniocentesis on the preterm delivery rate in women with uterine myoma. *Methods:* The volume of each fibroid and the relation to the placenta, myometrium and uterine corpus were recorded. Amniocentesis was performed by an experienced operator, if indicated. *Results:* During the study 14,579 pregnant women were examined and 234 had complications of uterine myomas (1.61%). Forty-three women delivered prematurely (19.46%). The results revealed that multifocal fibroids in relation to the myometrium, uterine myoma subjacent to the placenta, total myoma volume greater than 150 cm^3 are statistically significant independent risk factors for preterm delivery, while amniocentesis was not found to be an independent risk factor for preterm delivery. *Conclusions:* Although having uterine myoma is a fairly known cause of preterm delivery, second trimester genetic amniocentesis does not seem to have any additional adverse effect on the preterm delivery rate in women with uterine myomas.

Key words: Uterine myoma; Amniocentesis; Preterm delivery.

Introduction

Women of the modern epoch tend to delay pregnancy until after their professional career or modern assisted reproductive technologies permit them to become pregnant even in advanced ages. A large demographic analysis conducted in Turkey and another study by Jacobsson *et al*. demonstrated that maternal age at first pregnancy has been increasing in the last decades [1, 2].

Uterine myoma or uterine fibroid is a frequently seen benign tumor of the female pelvis. Clinically the fibroid may be asymptomatic or may be the source of some gynecological or obstetrical problems. Preterm delivery is still the major cause of neonatal mortality and morbidity, and having myomas is reported to be a risk factor for this condition [3-6]. Uterine fibroids are more frequent after the fourth decade. Borgfelt and Andolf stated that the prevalence of myomas was 3.3% in women aged 25 to 32 years old and 7.8% for women aged 33 to 40 years old [7]. Qidwai *et al*. reported that the prevalence of uterine myoma is 1.4% and 5.6% in women younger and older than 35 years old, respectively [3].

Amniocentesis is a widely performed invasive procedure in prenatal diagnosis all over the world. Advanced maternal age is the most common indication for the amniocentesis, which is also the era when myoma prevalence increases. Positive trisomy screening tests and congenital abnormalities are the other frequent indications for amniocentesis. As the number of women who wish to have a child in advanced maternal age is increasing, the prevalence of pregnancies complicated by uterine myoma with the need for genetic amniocentesis is also rising. Recently Salvador *et al*. concluded in a retrospective study that the gestational age at delivery was similar in women with uterine myomas who underwent amniocentesis [8].

The aim of this study was to evaluate prospectively the impact of amniocentesis on preterm delivery in pregnancies complicated by uterine myoma from the point of view of number, volume, localization and relation with the placenta.

Methods

The study was conducted in the prenatal diagnosis unit of Istanbul University, Istanbul Faculty of Medicine between April 1, 2004 and May 31, 2008. All ultrasonographic (US) examinations and invasive procedures were performed by two expert physicians. A second trimester routine sonographic screening was performed on all pregnant women including fetal biometry, amniotic fluid volume assessment, screening for fetal structural abnormalities and placental localization.

US diagnosis of the uterine myoma was performed in the presence of a spherical or ellipsoid mass at least 1 cm in maximal diameter with different echogenicity from the surrounding myometrium. The fibroids were investigated regarding their localization in the uterus and their relation between the placenta and myometrium. The myoma was characterized as *retroplacental* if it was superposed totally or partially to the placenta and was called *away from placenta* if not in touch with the placenta. Fibroids were named *subserous, intramural* or *submucous* depending on their relationship to the myometrium. Finally, localization was noted as *corporal* or *lower uterine segment* in relation to the uterine corpus. Three dimensions (sagittal, axial, and transverse) of the myoma were measured in centimeters and the volume was calculated in centimeters cube (cm^3).

According to previous reports, myoma localization which is less related to the obstetric complication is defined as sub-

Revised manuscript accepted for publication April 20, 2009

serous, away from placenta, corporal, smaller and single [6, 9]. These localizations and characteristics were accepted to be less related with obstetric complications.

Amniocentesis was performed (if necessary), between the 16th and 20th gestational weeks under continuous sonographic guidance using the free-hand technique with a 20-gauge needle for amniocentesis. Anesthesia, antibiotic prophylaxis or tocolyticis were not used in any patient. Transplacental passage was avoided when possible and was also recorded if it occurred.

Exclusion criteria from the study included any fetal structural abnormality, chromosomal abnormality, polyhydramnios, oligohidramnios, isoimmunization, spontaneous abortion and multiple pregnancies. History of abortion in recent pregnancies, threatened abortion in the present pregnancy, maternal age, parity, gestation age at examination, gestation age at delivery and birthweight were recorded. Preterm delivery was defined as a birth occurring between the 24th and 37th week of gestation. Premature rupture of membranes was defined as the absence of contractions one hour after rupture of the membranes regardless of gestational age.

For each continuous variable, normality was checked. Comparisons were applied using the Student's *t*-test for data normally distributed. If the data was not distributed normally, an appropriate non-parametric test was chosen such as the Mann-Whitney U test. A logistic regression model was constructed to assess the independent factors on preterm delivery. We included variables with probability values < 0.1 in univariate analysis in the model as confounders. The results are presented as prevalence of odd ratios and their 95% confidence intervals. Statistical analyses of the groups were performed using the Statistical Package for the Social Sciences (SPSS) for Windows 15.0. Results are presented as mean ± SD and median (min-max).

This study was approved by the ethics committee of Istanbul University, Istanbul Faculty of Medicine.

Results

During the study period 14,579 pregnant women were examined and 234 had uterine myomas (1.6%). One hundred and thirty-five women had single (57.7%), 36 had two (15.38%), 27 had three (11.5%) and 36 had at least four (15.4%) uterine myomas and the mean total volume was 392.96 ± 812.86; 606.34 ± 1399.51; 790.34 ± 1494.56 and 1214.46 ± 1574.40, respectively. Total myoma volume was < 150 cm^3 in 117 women (50%), 150-300 cm^3 in 33 women (14.10%) and > 300 cm^3 in 84 women (35.90%). In 151 of the women none of the fibroids were in contact with the placenta (64.53%), whereas at least one of the rest was in touch with placenta.

Five pregnancies were terminated because karyotype analysis was revealed as abnormal. Eight patients (three had amniocentesis and five did not) who had spontaneous abortions before the 24th week of gestation were also excluded from the study. One hundred and twenty-five (56.6%) of the remaining 221 had amniocentesis, whereas 96 (43.4%) did not. The most common indication for genetic amniocentesis was maternal age. Only 21 women who had amniocentesis were age 34 or younger (16.8%). During the amniocentesis placing the amniocentesis needle through the myoma or placenta was avoided. While no patient had transmyomatic amniocentesis, nine had transplacental amniocentesis. The mean gestational age at delivery for this small subgroup was 37.22 ± 1.92.

Only one patient of the 221 women presented with placental abruption at the 36th week of gestation. She did not undergo amniocentesis and two of her four uterine myomas were subjacent to the placenta. She delivered a 2,650 g healthy boy by cesarean section.

The patients were examined to determine preterm delivery. Forty-three of the 221 women delivered prematurely (19.5%). Demographic features of the women are shown in the Table 1. Maternal age, gestational age at the time of examination, parity, and previous history of abortion were all similar for the preterm and term groups.

Tables 2 and 3 show the comparisons of distribution of the fibroids from the point of view of number and volume, respectively, between the term and preterm groups. As all myomas were classified according to the relationship with the myometrium, the uterine corpus, and placenta each condition was evaluated. There were not any significant differences between the distributions

Table 1. — *Patient demographics*.

	Preterm delivery (n = 43) Mean ±(SD) Med (min-max)	Term delivery (n = 178) Mean ±(SD) Med (min-max)	Significance
Maternal age	34.00 ± 4.80	35.30 ± 4.00	0.12
Gestational age	34 (23-43)	36 (24-44)	0.09
at examination	19.40 ± 4.20	18.70 ± 2.80	
Parity	18 (10-30)	18 (12-29)	0.25
	0.50 ± 0.80	0.60 ± 0.80	
Number of previous	0 (0-4)	0 (0-5)	0.18
abortions	0.90 ± 1.80	0.80 ± 1.20	
	0 (0-9)	0 (0-10)	

Table 2. — *Comparison of preterm and term deliveries from the point of view of the number of myomas*.

	Preterm delivery Mean ±(SD) Med (min-max) n	Term delivery Mean ±(SD) Med (min-max) n	*p*
Distribution of the fibroids in relation to the uterine wall			
– Submucous	1.00 ± 0.00	1.10 ± 0.40	0.3
	1.00 (1,00-1.00)	1.00 (1-2)	
	1	8	
– Subserous	1.10 ± 0.40	1.50 ± 0.80	0.2
	1 (1-2)	1 (1-4)	
	16	66	
– Intramural	1.90 ± 1.60	2.10 ± 2.00	0.2
	1 (1-9)	1 (1-12)	
	40	133	
Distribution of the fibroids in relation to the uterine body			
– Lower uterine segment	1.70 ± 1.40	1.70 ± 1.80	0.7
	1 (1-6)	1 (1-12)	
	14	60	
– Corporal	1.60 ± 0.90	2.00 ± 1.70	0.02
	1 (1-4)	1 (1-10)	
	43	147	
Distribution of the fibroids in relation to the placenta			
– Retroplacental	1.20 ± 0.50	1.30 ± 0.60	0.1
	1 (1-3)	1 (1-3)	
	26	58	
– Away from the placenta	1.80 ± 1.50	2.20 ± 2.00	0.1
	1 (1-9)	1 (1-12)	
	31	149	

Table 3. — *Comparison of preterm and term deliveries in relation to myoma volume*.

	Preterm delivery Mean ±(SD) Med (min-max) n	Term delivery Mean ±(SD) Med (min-max) n	*p*
Distribution of fibroids in relation to the uterine wall			
– Submucous	325.01 ± 0.00 325.10 (325.10-325.10) 1	358.95 ± 636.37 132.91 (8.58-1903.18) 8	0.3
– Subserous	588.28 ± 629.23 334.68 (32.00-2142.00) 16	1006.96 ± 1527.09 380.58 (3.54-7047.94) 66	0.5
– Intramural	480.57 ± 1071.06 180.41 (8.40-6541.04) 40	288.03 ± 539.42 97.04 (5.15-2966.40) 133	
Distribution of fibroids in relation to the uterine body			
– Lower uterine segment	482.33 ± 541.69 218.82 (21,50-1766.40) 14	474.30 ± 727.42 140.87 (6.29-3091.20) 60	0.5
– Corporal	489.10 ± 1039.81 217.60 (8.40-6541.04) 43	564.68 ± 1165.61 120.64 (3.54-7047.94) 147	0.5
Distribution of fibroids in relation to the placenta			
– Retroplacental	660.54 ± 1181.34 229.18 (12.54-5706.08) 26	575.4 ± 1114.3 135.8 (9.98-5734.2) 58	0.3
– Away from the placenta	305.0 ± 376.8 169.8 (8.40-1581.2) 31	535.9 ± 1021.7 135.1 (3.54-7047.9) 149	0.1

Table 4. — *Multiple regression analysis of the preterm deliveries*.

	β	Odds Ratio (OR)	CI (95.0%)	Significance
Amniocentesis	-0.44	0.64	0.26-1.58	0.33
Age > 35	0.34	1.41	0.55-3.64	0.48
Myoma localization in relation to the myometrium				
– Subserous	Ref			0.01
– Intramural	0.78	2.17	0.76-6.19	0.15
– Submucous	-0.60	0.55	0.03-9.62	0.68
– Multifocal	-1.94	0.14	0.02-0.89	0.04
Myoma localization in relation to the uterus				
– Corpus	Ref			0.93
– Lower uterine segment	-0.10	0.91	0.31-2.64	0.86
– Both	0.25	1.28	0.28-5.84	0.75
Myoma localization in relation to the placenta				
– Away from the placenta	Ref			0.03
– Retroplacental	0.99	2.70	1.09-6.71	0.03
– Both	1.33	3.79	1.06-14.95	0.05
Myoma number				
– 1	Ref			0.58
– 2	0.57	1.76	0.26-11.78	0.56
– 3	0.16	1.18	0.19-7.42	0.86
– ≥ 4	1.08	2.95	0.47-18.52	0.25
Myoma volume (cm^3)				
– < 150	Ref			0.03
– 150-300	1.42	4,12	1.29-13.17	0.02
– > 300	1.03	2.80	1.09-7.20	0.03
Threatened abortion	0.78	2.20	0.63-7.57	0.22

β: Beta coefficients.

for each variable, except one. Only number of myomas located in the uterine corpus was significantly lower in the preterm group compared to the term group.

The multiple regression analysis of the preterm deliveries is shown in Table 4. According to this analysis having multifocal fibroids in relation to the myometrium, having at least one uterine myoma subjacent to the placenta, and having a total myoma volume between 150 cm^3 and 300 cm^3 and > 300 cm^3 are risk factors for preterm delivery. Nevertheless, performing amniocentesis was not an independent risk factor for preterm delivery in women with uterine myomas (OR: 0,64). Maternal age greater than 35, the presence of threatened abortion in the present pregnancy, presence of submucous or intramural fibroids, myoma localization in relation to the uterus, and having multiple uterine myomas were the other parameters which did not increase the risk for preterm delivery.

Discussion

Today, women have the tendency to postpone childbearing until after their professional carriers or until new assisted reproductive technologies give them the chance of pregnancy even in advanced ages. Additionally, in the last three decades ultrasound has become an essential tool of obstetric units which allows diagnosing even asymptomatic or small myomas. Uterine fibroid is a benign tumor of the female pelvis. It may be asymptomatic or may be the cause of infertility, early pregnancy loss, premature delivery, obstructed delivery or postpartum bleeding. Its incidence rises with age. Sonographic studies report the incidence of uterine myoma throughout pregnancy as between 0.3% and 3.3% [7, 8, 10, 11]. The consequence of this situation is confronting more pregnancies complicated with uterine myomas today. In this report the incidence of uterine myomas detected sonographically during pregnancy revealed 1.61%. This finding is comparable to previous retrospective studies.

The effect of uterine myoma on pregnancy outcome has been investigated by many authors. Muram *et al*. reported that retroplacental myoma is a risk factor for several complications [11]. While Rice *et al*. [12] and Exacoustòs and Rosati [9] stated that a fibroid subjacent to the placenta is a risk factor for ablation placenta. They could not show that it increases the risk of preterm delivery. On the other hand, two other studies showed that the localization of the myoma in relation to the placenta had no sway on pregnancy outcome [6, 13]. However our study revealed that if a woman with a myoma or myomas all subjacent to the placenta or with multiple myomas with at least one subjacent to the placenta, had a significantly increased risk of preterm delivery. The OR was 2.70 and 3.79, respectively (95% CI; 1.09-6.71; $p < 0.05$ and 95% CI; 1.06-14.95; $p < 0.05$, respectively).

Recent studies evaluated the size of the myoma by measuring the diameter or volume. Total myoma volume was evaluated by Exacoustòs and Rosati and they found that total myoma volume greater than 200 cm^3 is a risk factor for placental abruption. Nonetheless, they found that the presence of uterine myomas did not affect the preterm delivery rate [9]. Rice *et al*. also evaluated the size of uterine myomas regarding the largest diameter. They concluded that as the myoma becomes larger, the rate of complications rises concordantly [12]. In contrast, in two recent studies the authors did not find any associ-

ation between myoma size and preterm delivery [3, 13]. Our results revealed that total myoma volume between 150 and 300 cm^3 and > 300 cm^3 is associated with increased risk of prematurity. The OR was 4.12 and 2.80, respectively (95% CI; 1.29-13.17; $p < 0.05$ and 95% CI; 1.09-7.30; $p < 0.05$).

Exacoustòs and Rosati stated that women with multiple myomas have an increased risk for abortion, but they did not investigate the effect of multiple myomas on preterm delivery [9]. In another study, having multiple myomas was found to be a risk factor for malpresentation, placental retention and premature uterine contractions [6]. Conversely, in other studies the investigators could not demonstrate any relationship between the number of myomas and preterm delivery [3, 13]. Our results underlined that the number of uterine myomas did not increase the risk of preterm delivery. While the OR for having two, three or more uterine myomas is 1.76; 1.18 and 2.95 correspondingly, it did not reach significance level (95% CI; 0.26-11.78; $p = 0.56$, 95% CI; 0.19-7.42; $p = 0.86$ and 95% CI; 0.47-18.52; $p = 0.25$).

Like uterine myomas, the risk of chromosomal abnormality and the need of second trimester genetic amniocentesis also rise with age. In our study group 104 of the women who had amniocentesis were aged 35 or older (83.2%). This study did not demonstrate an increased preterm delivery rate in pregnancies complicated by uterine myomas when performing second trimester genetic amniocentesis (OR: 0.64; 95% CI; 0.26-1.58; $p = 0.33$). Previously Salvador *et al*. evaluated the effect of amniocentesis in pregnant women with uterine myomas in a retrospective study. They composed three groups of women who had uterine myomas and underwent amniocentesis *(cases)*, women who did not have uterine myomas and underwent amniocentesis *(amnio only)* and women who had uterine myomas and did not undergo amniocentesis *(myoma only)*. They reported that the mean gestational age at delivery was 37.6 ± 5.1 and 37.1 ± 5.3 in the group of cases and myoma only respectively, which were not statistically significant [8].

While it should be avoided, in nine women an anterior placenta obliged the operator to perform the procedure transplacentally. However it is difficult to draw a conclusion from this small subgroup, but we should note that the mean gestational age was 37.22 ± 1.92. This finding is appropriate to the report of Bombard *et al*. They underlined that transplacental amniocentesis should be done by an experienced operator, far away from the cord insertion [14].

In this report we aimed to evaluate prospectively the effect of amniocentesis on the preterm delivery in women with uterine myomas. With the increasing age of the obstetric population, uterine fibroids will be more frequently detected during pregnancy. While there is a wide discrepancy in the results of the studies evaluating the effect of myoma through the pregnancy, the authors conclude that performing second trimester amniocentesis is not a risk factor for preterm delivery in women with uterine myomas.

Acknowledgments

The authors wish to thank Güssün GÜNEŞ, the health service librarian of the Suna Kıraç Library of Koç University, for her kind help in getting manuscripts; to Gülru VARDAROĞLU BÜYÜKKURT for her helpful comments on the English version, and to Çağla SARITÜRK for her help in statistical analyses.

References

[1] Koc I., Ozdemir E.: "Fertility". In: Hacettepe University Institute of Population Studies, Turkey Demographic and Health Survey, 2003. Hacettepe University Institute of Population Studies, Ministry of Health General Directorate of Mother and Child Health and Family Planning, State Planning Organization and European Union. Ankara, Turkey. 2003, 4, 55. Available from http://www.hips.hacettepe.edu.tr/tnsa2003/data/English/chapter04.pdf [Accessed February 13, 2009].

[2] Jacobsson B., Ladfors L., Milsom I.: "Advanced maternal age and adverse perinatal outcome". *Obstet. Gynecol.,* 2004, *104,* 727.

[3] Qidwai G.I., Caughey A.B., Jacoby A.F.: "Obstetric outcomes in women with sonographically identified uterine leiomyomata". *Obstet. Gynecol.,* 2006, *107,* 376.

[4] Koike T., Minakami H., Kosuge S., Usui R., Matsubara S., Izuni A. *et al*.: "Uterine leiomyoma in pregnancy: its influence on obstetric performance". *J. Obstet. Gynecol. Res.,* 1999, *25,* 309.

[5] Rosati P., Exacoustòs C., Mancuso S.: "Longitudinal evaluation of uterine myoma growth during pregnancy: a sonographic study". *J. Ultrasound Med.,* 1992, *11*, 511.

[6] Lev-Toaff A., Coleman B.G., Arger P.H., Mintz M.C., Arenson R.L., Toaff M.E.: "Leiomyomas in pregnancy: Sonographic study". *Radiology,* 1987, *164,* 375.

[7] Borgfeldt C., Andolf E.: "Transvaginal ultrasonographic findings in the uterus and endometrium: low prevalence of leiyomyoma in a random sample of women age 25-40 years". *Acta Obstet. Gynecol. Scand.,* 2000, *79,* 202.

[8] Salvador E., Bienstock J., Blakemore K.J., Pressman E.: "Leiomyomata uteri, genetic amniocentesis, and the risk of second-trimester spontaneous abortion". *Am. J. Obstet. Gynecol.,* 2002, *186*, 913.

[9] Exacoustòs C., Rosati P.: "Ultrasound diagnosis of uterine myomas and complications in pregnancy". *Obstet. Gynecol.,* 1993, *82,* 97.

[10] Katz V.L., Dotters D.J., Droegemueller W.: "Complications of uterine leiomyomas in pregnancy". *Obstet. Gynecol.,* 1989, *73,* 593.

[11] Muram D., Gillieson M., Walters J.H.: "Myomas of uterus in pregnancy: Ultrasonographic follow-up". *Am. J. Obstet. Gynecol.,* 1980, *138,* 16.

[12] Rice J.P., Kay H.H., Mahony B.S.: "The clinical significance of uterine leiomyomas in pregnancy". *Am. J. Obstet. Gynecol.,* 1989, *160,* 1212.

[13] Davis J.L., Ray-Mazumder S., Hobel C.J., Baley K., Sassoon D.: "Uterine leiomyomas in pregnancy: A prospective study". *Obstet. Gynecol.,* 1990, *75,* 41.

[14] Bombard A.T., Powers J.F., Carter S., Schwartz A., Nitowsky H.M.: "Procedure-related fetal losses in transplacental versus nontransplacental genetic amniocentesis". *Am. J. Obstet. Gynecol.,* 1995, *172,* 868.

Address reprint requests to:
S. BUYUKKURT, M.D.
Çukurova Üniversitesi Tıp Fakültesi Kadın Hastalıkları ve Do um Anabilim Dalı
01330 Adana (Turkey)
e-mail: selimbuyukkurt@gmail.com