# Effect of fibroids on cumulative probability of pregnancy in women taking follicle maturing drugs without assisted reproductive technology

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## Summary

*Purpose:* To determine if the presence of uterine fibroids adversely affect in vivo conception rates.

*Methods:* Pelvic ultrasound evaluation of the presence or absence of fibroids in consecutive infertility patients not treated with assisted reproductive technology in a two-year period. Conception outcome noted. Data analyzed according to the presence or absence of fibroids.

*Results:* No difference in cumulative probability of pregnancy after five months was seen in patients with or without the presence of fibroids. There were no confounding variables found that could have skewed the pregnancy rates in one direction or the other.

*Conclusion:* In general the presence of fibroids do not adversely affect conception outcome for in vivo pregnancies. However, since the majority of the fibroids were small (< 6 cm) and were not submucosal and did not compress the endometrial cavity, larger studies are needed to address specific subtypes and circumstances on pregnancy outcome.

*Key words*: Uterine fibroid; Infertility; Pregnancy rates.

## Introduction

Uterine fibroids (leiomyomata) are the most common tumors found in women. The occurrence increases with age; they occur in 20-50% of women over the age of 30 years [1]. The effect of their presence on fertility potential is still subject to controversy. There have been several studies with various conclusions about the influence of fibroids and subsequent pregnancy rates (PRs) and implantation rates following in vitro fertilization-embryo transfer (IVF-ET). Farhi *et al.*, found that impaired implantation is associated with uterine leiomyomata only in cases where uterine inner-cavity abnormalities coexist [2]. Stovall *et al.*, found that patients with intramural or subserosal uterine leiomyomata have reduced implantation.

However, they did not distinguish between the two types of leiomyomas [3]. Eldar-Geva *et al.*, found that PRs and implantation rates were lower in patients with intramural and submucosal fibroids even in the absence of distortion of the uterine cavity but not subserosal fibroids [4].

Ramzy *et al.*, found that uterine corporeal myomata, not encroaching on the cavity and < 7 cm in diameter do not affect the implantation or miscarriage rates in IVF with or without intracytoplasmic sperm injection (ICSI) [5]. The objective of our study was to investigate the influence of uterine myomata on cumulative probability of pregnancy in patients not requiring IVF-ET but needing follicle maturing drugs to correct ovulatory dysfunction. The key clinical factors for assessing the potential negative effects of uterine leiomyomata include the site of the fibroids (both height and depth within the uterus), size of the fibroids, number of fibroids, and the presence or absence of endometrial compression.

## Materials and Methods

All patients seeking treatment at the Pennsylvania satellite of the Cooper Center for IVF beginning January, 1997 to December, 1998 underwent an ultrasound screening to detect the presence of uterine leiomyomata.

A total of 168 consecutive patients ≤ 40 years old were enrolled in this study. There were 34 patients with fibroids (20.2%). Patients were excluded if they did not have a minimum of at least three treatment cycles (unless pregnancy occurred first), if they had prior myomectomies or had uterine cavity abnormalities other than endometrial compression. Patients in the study were taking follicle maturing drugs to correct ovulatory dysfunction (anovulation or luteal phase defects with oocyte release before follicle maturation).

Pelvic ultrasound was carried out routinely on all patients before the treatment cycle. Those with uterine myomata had detailed sonographic evaluation starting with a transabdominal scan with full bladder to be followed by transvaginal ultrasound after voiding. Scanning of the uterus was carried out in two planes (sagittal and coronal) at the level of maximum width. Each leiomyoma was measured in three dimensions (length, width, and height) and the mean diameter of each leiomyoma was calculated. Ultrasonography was performed with a multifrequency transducer on an ATL Apogee 800 ultrasound system (Advanced Technology Laboratories, Bothell, WA). The location of the leiomyomata was categorized by depth in the uterus (intramural, subserosal, or submucosal). Life table analysis was used to predict the cumulativee probability of pregnancy for the first five cycles of treatment. Log-rank tests were used to

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compare the cumulative PRs by presence of fibroids within each age group. Rates were computed for positive pregnancy test, clinical pregnancy (gestational sac observed) and delivery rates (live birth).

## Results

The women who had fibroids were on average older than women in the control groups (35.5±2.7 versus 32.7±3.8, $p < .05$). However, both groups had similar histories with respect to parity and gravida; 27% of the fibroid group and 18% of the control group had never been pregnant; 41% of the fibroid group and 37% of the control group had never given birth to a child.

A summary of the life table analysis is presented in Tables 1, 2 and 3. The cumulative probability of having a positive pregnancy test after five cycles of treatment was 44% in the fibroid group and 46.6% in the control group (p=NS, log-rank test). Comparable rates for clinical pregnancy and delivery were 35.4%, 33.4% in the fibroid group and 46.6%, 43.6% in the control group, respectively (p=NS, log-rank test).

Table 1. — *Life Table Analysis for Cumulative Probability of Pregnancy.*

| Fibroid Group | | | |
|---|---|---|---|
| Cycle | # patients treated | # of pregnancies (positive beta-hCG) | Cumulative probability of pregnancy (95% confidence interval) |
| 1 | 34 | 2 | .06 (-.02-.14) |
| 2 | 32 | 4 | .18 (.05-.30) |
| 3 | 28 | 2 | .24 (.09-.38) |
| 4 | 23 | 5 | .40 (.23-.57) |
| 5 | 16 | 1 | .44 (.26-.61) |
| Control Group | | | |
| Cycle | # patients treated | # of pregnancies (positive beta-hCG) | Cumulative probability of pregnancy (95% confidence interval) |
| 1 | 132 | 6 | .05 (.01-.08) |
| 2 | 126 | 13 | .14 (.08-.20) |
| 3 | 113 | 13 | .24 (.17-.32) |
| 4 | 92 | 13 | .35 (.27-.43) |
| 5 | 67 | 12 | .47 (.38-.56) |

p = NS, Log-rank test.

Table 2. — *Life Table Analysis for Cumulative Probability of Clinical Pregnancy.*

| Fibroid Group | | | |
|---|---|---|---|
| Cycle | # patients treated | # of pregnancies (gestational sac) | Cumulative probability of pregnancy (95% confidence interval) |
| 1 | 34 | 2 | .06 (-.02-.14) |
| 2 | 32 | 3 | .15 (.03-.27) |
| 3 | 28 | 2 | .21 (.07-.35) |
| 4 | 23 | 3 | .31 (.15-.47) |
| 5 | 16 | 1 | .35 (.18-.53) |
| Control Group | | | |
| Cycle | # patients treated | # of pregnancies (gestational sac) | Cumulative probability of pregnancy (95% confidence interval) |
| 1 | 132 | 6 | .05 (.01-.08) |
| 2 | 126 | 13 | .14 (.08-.20) |
| 3 | 113 | 13 | .24 (.17-.32) |
| 4 | 92 | 13 | .35 (.27-.43) |
| 5 | 67 | 12 | .47 (.38-.56) |

p = NS, Log-rank test.

Table 3. — *Life Table Analysis for Cumulative Probability of Delivery.*

| Fibroid Group | | | |
|---|---|---|---|
| Cycle | # patients treated | # of pregnancies (live births) | Cumulative probability of pregnancy (95% confidence interval) |
| 1 | 34 | 1 | .03 (-.03-.09) |
| 2 | 32 | 3 | .12 (.01-.23) |
| 3 | 28 | 2 | .18 (.05-.32) |
| 4 | 23 | 3 | .29 (.13-.45) |
| 5 | 16 | 1 | .33 (.16-.51) |
| Control Group | | | |
| Cycle | # patients treated | # of pregnancies (live births) | Cumulative probability of pregnancy (95% confidence interval) |
| 1 | 132 | 5 | .04 (.01-.07) |
| 2 | 126 | 12 | .13 (.07-.19) |
| 3 | 113 | 11 | .21 (.14-.28) |
| 4 | 92 | 13 | .33 (.24-.41) |
| 5 | 67 | 11 | .44 (.34-.53) |

p = NS, Log-rank test.

Table 4. — *Conception Outcome Within Fibroid Group (< 40 years old).*

| | Pregnant (n=14) | Not-pregnant (n=20) |
|---|---|---|
| Age | 35.4±2.7 | 35.6±2.8 |
| # Fibroids | 1.2±.42 (1-2) | 2.0±1.8 (1-5) |
| Mean diameter of smallest fibroid | 1.41±.73 | 1.85±1.45 |
| < 3 cm | 14 | 17 |
| 3-6 cm | 0 | 2 |
| > 6 cm | 0 | 1 |
| Mean diameter of largest fibroid | 14.8±7.1 | 27.8±22.1 |
| < 3 cm | 14 | 13 |
| 3-6 cm | 0 | 5 |
| > 6 cm | 0 | 2 |
| Site of fibroid | | |
| IM | 10 (71.4%) | 9 (45.0%) |
| SS | 4 (28.6%) | 9 (45.0%) |
| SM | 0 | 2 (10%) |
| Compression of endometrium | | |
| Yes | 1 (7.1%) | 7 (35.0%) |
| No | 13 | 13 |

p = NS.

Patients with fibroids who conceived were similar in age, number of fibroids, site of fibroid and size of fibroid to those that did not conceive (Table 4). In the group that did not conceive, there were more cases in which the fibroid compressed the endometrium (35% versus 7.1%), however it was not statistically significant.

## Discussion

Uterine leiomyomas are encountered more frequently today in infertile patients because of the rising age of patients admitted for infertility therapy. This rise is caused by the tendency of women to delay marriage and childbearing to first accomplish advanced education and careers [6]. Sonographic monitoring of infertile women allows the physician to detect small uterine fibroids early

in the patient's treatment. The question is whether the physician should consider surgical treatment of these fibroids if detected. The IVF literature did not make it clear as to whether fibroids that do not compress the uterine cavity negatively affect the chance of conception. This study was performed to see if evaluating fibroids in non-IVF cycles could provide more insight into this question. The fibroids in this study were predominately < 3 cm and either intramural or subserosal. Our data demonstrate that small uterine fibroids do not interfere with pregnancy following five cycles of treatment with ovulation inducing drugs. Similar results were previously reported by Ramzy *et al.* [5] and by Farhi *et al.* [2] in IVF cases.

Based on the results of this study, we concluded that patients presenting with small fibroids and no previous history of myomectomy or uterine cavity abnormalities other than endometrial compression, can be advised to proceed with ovulation therapy, without the need for any intervention for treatment of the small fibroids. There were not enough cases during the study period to make valid conclusions about fibroids > 6 cm. Similarly there were insufficient submucosal fibroids in this study to conclude that they do not negatively affect conception. These data do corroborate those IVF studies concluding that the presence of small intramural or subserosal fibroids not impinging on the endometrial cavity do not adversely affect conception following IVF-ET [2, 5, 7, 8].

Though one might argue that there may be a trend for lower clinical and viable pregnancy rates in the group with fibroids, it should be remembered that the group with fibroids were significantly older.

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