Uterine Leiomyomas and Their Effect on In Vitro Fertilization Outcome: A Retrospective Study

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Purpose: The effect of uterine leiomyomas on the outcome of in vitro fertilization (IVF) treatment has been controversial. This study was undertaken to clarify influence of fibroids on IVF success, in a large population with age and other potential confounding variables controlled for in the analysis.

Methods: A population of 141 patients with and 406 without leiomyomata undergoing their first IVF cycle was studied.

Results: The association between uterine leiomyomas and assisted reproduction treatment outcome was not statistically significant (OR = 0.73, 95% CI: 0.49–1.19, p = 0.21) after controlling for age and other risk factors. Also, fibroids neither affected the risk of spontaneous abortion (OR = 1.06, 95% CI: 0.44–2.60) nor the risk of ectopic pregnancy (OR = 0.78, 95% CI: 0.08–8.02). Location of fibroids (intramural vs. submucosal/subserosal) and their size had no significant effect on pregnancy outcome.

Conclusions: Results from our analyses indicated that in vitro fertilization outcome was not affected by the presence of uterine leiomyomas. Therefore, in patients with normal uterine cavities and fibroids less than a certain size (i.e., <7 cm), undergoing myomectomies as a prerequisite for assisted reproduction treatment is seriously questionable.

KEY WORDS: Assisted reproduction cycle; effect on in vitro fertilization outcome; fibroids; myomectomy; uterine leiomyomas.

INTRODUCTION

The association between infertility and uterine leiomyomas (fibroids), the most common benign pelvic tumors in women of reproductive age, has yet to be clearly defined (1). There is an increased prevalence of infertility and miscarriages in women having fibroids, with size and location being the two most important factors (2). Reduced sperm transport efficiency for fertilization because of distortion of the uterine cavity, vascular changes, and irritation of the endometrium, resulting in poor implantation and mechanical obstruction of the uterine tubes are some of the possible mechanisms by which fibroids may cause infertility (2–5). Higher pregnancy rates and lower rates of spontaneous abortions have been reported after myomectomy (4) which further supports this idea.

The incidence of fibroids increases with age (1). Because of a growing patient population of older women undergoing in vitro fertilization (IVF), uterine fibroids and their effect on the outcome of assisted reproduction is of great interest. However, this issue still remains controversial. Implantation rates with leiomyomas may be reduced only in those with uterine cavity deformation (6). This study found no significant effect on IVF outcome as long as there was no change in uterine contour. Ramzy et al. (7) found fibroids to have no effect on implantation and miscarriage rates in IVF and intracytoplasmic sperm injection (ICSI) procedures unless the leiomyomas were >7 cm in size and caused distortion of the endometrial cavity (7). However, others found that intramural and submucosal fibroids considerably reduce the pregnancy and implantation rates even with a normal endometrial cavity (8). Consistent results of impaired pregnancy and delivery rates in patients with...
leiomyomas undergoing their assisted reproduction cycles were presented by Stovall et al. (9).

The purpose of our study was to help clarify this controversy by examining a much larger patient population than those previously reported for the effect of uterine leiomyomas on in vitro fertilization outcome, with age and other potential confounding variables accurately controlled for in the analyses.

MATERIALS AND METHODS

Medical records from Brigham and Women's Hospital (BWH), of IVF patients diagnosed with uterine leiomyomas and who were undergoing their first assisted reproduction cycle between January 1997 and December 1998 were analysed retrospectively. Baseline pelvic ultra-sonography results were used to determine presence, size, and location of fibroids. All ultrasounds and laboratory studies were performed at BWH. As part of the standard fertility evaluation, a hysterosalpingogram, hysteroscopy, or sonohysteroscopic study was approved by the Partner's Healthcare System Human Research Committee for medical records review.

Of the 587 patients initially reviewed, 40 patients were excluded from the study because their outcomes were associated with donor eggs, gestational carriers, frozen embryos, GIFT and ZIFT procedures. The remaining 547 IVF patients were divided into two groups: 141 patients with fibroids (exposed) and 406 without (unexposed). Patients with prior myomec-tomies, whose ultrasound showed no fibroids were considered unexposed at the time of the study. This study was approved by the Partner’s Healthcare System Human Research Committee for medical records review.

Stimulation Protocols

Controlled ovarian hyperstimulation was performed with luteal down-regulation. The standard IVF protocol was as follows: Leuprolide acetate (Lupron, TAP Pharmaceuticals, Deerfield, IL; 1.0 or 0.5 mg depending on prior gonadotropin response), was begun either a week after documentation of urinary LH surge, or on the day after a midluteal progesterone determination, and was continued until at least Day 2 of menses. Following appropriate down-regulation gonadotropin therapy was begun with either purified FSH (Fertinex, Serono Laboratories, Norwell, MA), recombinant FSH (Follistim, Organon, West Orange, NJ; Gonafal-F, Serono Laboratories, Norwell, MA) or human menopausal gonadotropins (Humegen, Organon, West Orange, NJ).

Follicle growth monitoring, achieved with use of ultrasonography and measurement of serum estradiol, was begun on stimulation Day 6, and then performed every 1–3 days, as indicated. A dose of 10,000 IU of hCG (Profasi, Serono, Norwell, MA) was administered intramuscularly when two follicles reached a maximal diameter of >20 mm (mean 16.5 mm) with estradiol ≥500 pg/mL.

Transvaginal oocyte retrieval was performed 36 hours after hCG administration. Luteal progesterone supplementation was initiated the day after oocyte retrieval and achieved by one of three regimens: 1) daily intramuscular progesterone (50 mg); 2) daily vaginal gel (8% progesterone; Crinone, Wyeth-Ayerst, Philadelphia, PA); or 3) twice daily vaginal progesterone suppositories (50–100 mg). Embryo transfer was performed 3 or 5 days after retrieval.

Statistical Analyses

Unconditional multiple logistic regression was used to derive odds ratios (ORs) of IVF outcome associated with uterine leiomyoma and to calculate 95% confidence intervals (CIs), while controlling for age (continuous) and eight other risk factors: number of days stimulated, number of eggs retrieved, number of follicles stimulated, number of fertilized eggs, number of cells per embryo, number of cells in embryos transferred, year of treatment (1997 vs. 1998), and physician’s diagnosis of the primary cause of infertility (using indicator terms for adhesions/tubal factor/pelvic inflammatory disease (PID), anovulatory/oligoovulation/poly cystic ovarian syndrome (PCOS), cervical factor/DES/immunological/ovarian cancer, endometriosis, male factor, unexplained, uterine factor, and not indicated).

Three separate analyses were run using a modified dichotomous outcome variable: 1) pregnancy (reference category) versus “pregnancy ending in either 1) livebirth, 2) spontaneous abortion, or 3) ectopic pregnancy.” The same set of risk factors was controlled for in each of the three analyses.

In a separate analysis, consisting of the subset of women with fibroids (n = 141), we added indicator terms for uterine leiomyoma locations (intramural vs. submucosal/subserosal) and sizes to determine whether these factors had any independent effect on IVF outcome, after controlling for the same set of potential confounders. To maximize the number of women in each of the exposure groups, sizes were divided into quartiles (<1.05 cm, 1.05–1.5 cm, 1.6–2.3 cm, >2.3 cm). In all logistic regression models,