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Ovarian cyst formation following GnRH agonist administration in IVF cycles: incidence and impact

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BACKGROUND: The formation of functional ovarian cysts has been recognized as one of the side effects of GnRH agonist administration. The formation of cysts during IVF treatment may be of no clinical significance or may negatively influence its outcome. The objective of this study was to determine the incidence of ovarian cyst formation following GnRH agonist administration and to examine their effect on IVF outcome. METHODS: A prospective study of 1317 IVF patients who developed one or more functional ovarian cysts of ≥15 mm following GnRH agonist treatment was performed. Transvaginal ultrasonographic-guided cyst aspiration was carried out in 76 randomly allocated patients out of 122 patients who were found to have functional ovarian cysts before starting ovarian stimulation with gonadotropins. RESULTS: The incidence of follicular cyst formation was 9.3%. Cyst cycles in comparison with non-cyst cycles had significantly elevated day 3 basal FSH (mean ± SD of 8.3 ± 3.2 versus 5.3 ± 2.6 mIU/ml, *P* < 0.05) and required more ampoules of gonadotropins (46.3 ± 16.5 versus 35 ± 14.6, *P* <0.01). Furthermore, they showed a statistically significant decrease in the quality and number of oocytes retrieved, fertilization rate, number and quality of embryos, implantation and pregnancy rates, with a significant increase in cancellation and abortion rates. Patients with bilateral cysts had a significantly lower number of oocytes and embryos retrieved, with a lower proportion of metaphase II oocytes. They also had a higher proportion of poor quality embryos. Cyst aspiration was not associated with a significant difference in the above parameters. CONCLUSIONS: The incidence of cyst formation during GnRH agonist treatment is lower than previously reported. In such cases, the quality of oocytes and embryos were significantly compromised, with a significant increase in the cycle cancellation rate and a decrease in the implantation and pregnancy rates. Neither conservative management nor cyst aspiration improved the IVF outcome.

Key words: follicular ovarian cyst/GnRH agonist/*in vitro* fertilization/pregnancy rate

Background

One known complication of pituitary down-regulation using GnRH agonist in IVF treatment cycles is the formation of functional ovarian cysts (Feldburg *et al*., 1989; Rizk *et al*., 1990; Jenkins *et al*., 1992, 1993; Parinaud *et al*., 1992; Tarlatzis *et al*., 1994; Keltz *et al*., 1995; Segal *et al*., 1999; Biljan *et al*., 2000). The incidence of these cysts is reported to range between 8% and 53% (Feldburg *et al*., 1989; Parinaud *et al*., 1992; Keltz *et al*., 1995; Biljan *et al*., 2000).

Functional ovarian cyst formation had been reported following various IVF protocols (short and follicular or luteal long GnRH agonist protocols) (Rizk *et al*., 1990; Tarlatzis *et al*., 1994; Keltz *et al*., 1995), different types of GnRH agonist (short and long acting forms), the concomitant use of HMG (Parinaud *et al*., 1992) and in older women with decreased ovarian reserve (Keltz *et al*., 1995).

The precise mechanism by which these cysts are formed is unknown. Possible explanations include the initial transient flare up effect of the GnRH agonist on gonadotropins (Feldburg *et al*., 1989), insufficient suppression of the circulating gonadotropins to hypophyesectomy levels (Jenkins *et al*., 1992), the direct effect of GnRH agonist on the ovaries and steroidogenesis (Parinaud *et al*., 1992), and the serum progesterone level at the time of GnRH agonist administration (Jenkins *et al*., 1993).

It has been suggested that the formation of cysts during IVF treatment is of no clinical significance (Jenkins *et al*., 1992; Keltz *et al*., 1995; Segal *et al*., 1999) or to negatively influence its outcome (Feldburg *et al*., 1989; Parinaud *et al*., 1992; Tarlatzis *et al*., 1994; Biljan *et al*., 2000). We conducted this study to determine the incidence of functional ovarian cyst formation following GnRH agonist administration and to examine their effect on the outcome of IVF treatment.

Patients and methods

Between January 2002 and December 2003, a total of 1317 infertile women underwent a single IVF treatment cycle using a standardized pituitary down-regulation protocol, namely long-luteal pituitary

down-regulation using the GnRH analogue triptorelin (Decapeptyl: Ipsen, Paris; France), which commenced on day 21 of the menstrual cycle. Patients with non-functional ovarian cysts were excluded.

A transvaginal ultrasound scan was performed and a blood sample was taken to measure estradiol (E_2) levels on the third day of bleeding following GnRH agonist administration. A functional ovarian cyst was defined as a thin-walled intraovarian sonolucent structure with a mean diameter of ≥15 mm and E_2 levels of ≥50 pg/ml.

Women who developed ovarian cysts were randomly divided into two groups: (i) group I underwent cyst aspiration (n = 76); and (ii) group II (n = 46) had no intervention. An algorithm of patients flow and allocation scheme for the study is summarized in Figure 1. Randomization was accomplished using a selection from a table of random numbers available in a standard statistics textbook.

Cyst aspiration under local anaesthesia was performed on the day of diagnosis. Ovarian stimulation with HMG was started in all patients on the third day of bleeding. Transvaginal ultrasound follow-up for follicular growth was commenced on day 8 of ovarian stimulation and repeated every 3–4 days thereafter. When at least three follicles reached a mean diameter of 17 mm, a single dose of 10,000 IU HCG was administered. After 36 hours, transvaginal-guided oocyte retrieval was performed under general anaesthesia.

Fertilization was considered successful after noting the presence of two pronuclei and second polar body 20–24 h after conventional IVF by adding ~10^5 motile spermatozoa/ml to droplets of medium each containing one oocyte or after ICSI.

Embryos were graded as previously described by Coskun *et al.* (1998). Good embryos included those with even-sized blastomeres and no obvious fragmentation or even-sized with <10% fragmentation or uneven-sized with no obvious or <10% fragmentation. Fair embryos included those with 10–30% fragmentation. Embryos with >30% fragmentations were considered poor.

Embryos were transferred 72 h following oocyte retrieval using a Wallace catheter (Marlow Surgical Technology, Willoughby, OH, USA). Progesterone pessaries (Cyclogest: Alpharma, Barnstaple, Devon, UK) were used for luteal phase support. Two weeks after embryo transfer, serum β-HCG was requested and pregnant women had an ultrasound scanning at 6 weeks gestation. Demonstration of intrauterine fetal pole with positive fetal heartbeat was defined as clinical pregnancy. The possibility of having a lower chance of pregnancy was explained to all patients with ovarian cysts who enrolled late and an informed consent was obtained. The department of obstetrics and gynaecology review board was informed of the findings.

Statistical analysis was presented as mean ± SD and percentages. Chi-Square test and Student- t test were used as appropriate. A P value of ≤ 0.05 was considered statistically significant.

Results

The demographic data of women with and without ovarian cyst formation after GnRH agonist administration are presented in Table I. A total of 1317 infertile women were recruited for IVF treatment. Their ages ranged between 21–43 years (mean ± SD: 31 ± 4.2 years). Duration of infertility ranged between 2–19 years (mean ± SD: 6 ± 4.2 years). Causes of infertility included anovulation, endometriosis, unexplained infertility, tubal and male factor. Of the 1317 women, 1195 had no evidence of ovarian cyst while the remaining 122 patients developed ovarian cysts (an incidence of 9.3%). The age and duration of infertility in patients with ovarian cysts did not differ significantly from those without cysts. There were no significant differences in the aetiology of infertility between the two groups.

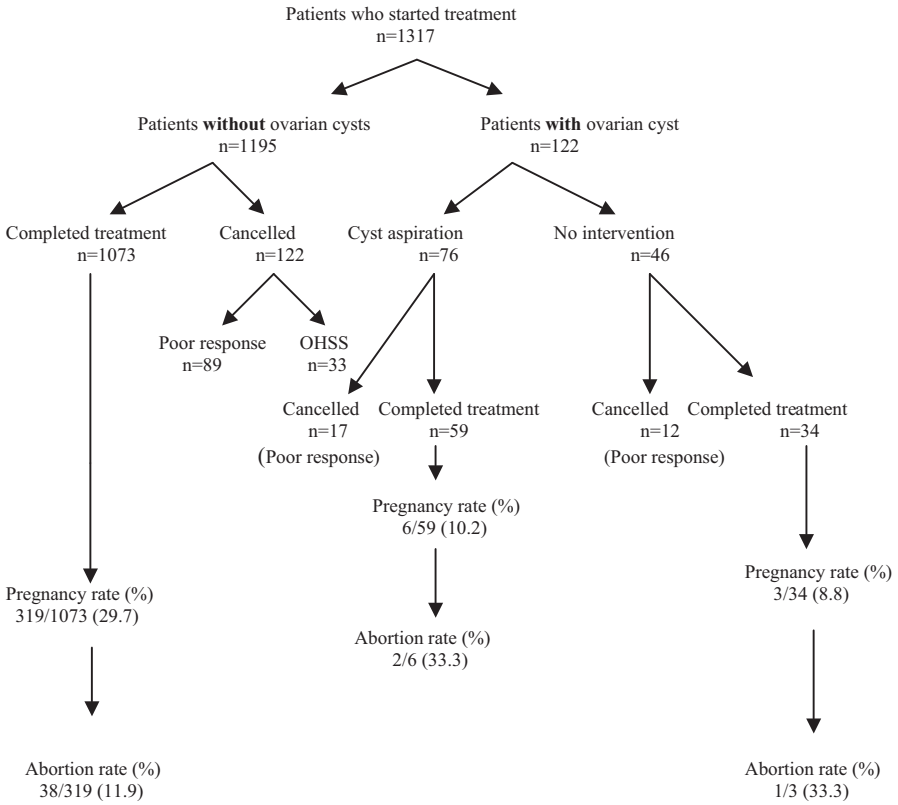

Figure 1. Algorithm of patient flow and allocation scheme for the study.

Table I. Demographic data of IVF patients who developed ovarian cysts after GnRH agonist administration and those who did not

	Patients with ovarian cysts (n = 122)	Patients without ovarian cysts (n = 1195)
Age (years)	31.8 ± 5.2	30.6 ± 4.7
Duration of infertility (years)	6.4 ± 4.2	6.1 ± 3.7
Cause of infertility		
Tubal	14 (15.1)	187 (14.5)
Anovualtion	17 (18.3)	213 (16.5)
Male factor	35 (37.6)	513 (39.8)
Endometriosis	23 (27.7)	341 (26.5)
Unexplained	4 (4.3)	34 (2.6)

Values are expressed as mean ± SD. Values in parentheses are percentages.

Table II. Cycle characteristics and outcome in patients with and patients without ovarian cyst formation following GnRH agonist administration

	Patients with ovarian cysts (n = 122)	Patients without ovarian cysts (n = 1195)
Day 3 FSH (mIU/ml)	8.3 ± 3.2	5.3 ± 2.6*
E2 levels on day of diagnosis (pg/ml)	180 ± 30.6	56 ± 21.7**
Days of stimulation with HMG	16.2 ± 3.9	13.2 ± 4.1*
No. of ampoules of HMG	46.3 ± 16.5	35 ± 14.6**
No. of follicles > 14 mm	5.6 ± 2.8	11.2 ± 4.1***
No. of oocytes retrieved	5.2 ± 1.99	10.1 ± 3.1***
Metaphase II oocytes	(30.8)	(76.2)**
Fertilization rate (%)	(47.8)	(72.8)*
No. of day 2 embryos	3.7 ± 1.6	7.3 ± 3.2**
Grades of embryos		
Good (%)	(16.4)	(55.2)**
Fair (%)	(19.7)	(19.1)
Poor (%)	(63.9)	(25.7)***
No. of embryos transferred	2.1 ± 1.3	2.7 ± 1.4
Cancellation rate (%)	29/122 (23.8)	122/1195 (10.2)***
Implantation rate (%)	(4.2)	(13.7)**
Pregnancy rate (%)	9/93 (9.6)	319/1073 (29.7)***
Abortion rate (%)	3/9 (33.3)	38/319 (11.9)*

Values are expressed as mean ± SD. Values in parentheses are percentages.
*P < 0.05; **P < 0.01; ***P < 0.001.

Cycle characteristics and outcome of conventional IVF and ICSI treatments in patients with and without ovarian cyst are summarized in Table II. Of the remaining 1195 patients, 89 (6.7%) were cancelled because of poor response and 33 (2.5%) because of ovarian hyperstimulation syndrome (OHSS). Twenty-nine cycles of the 122 ovarian cyst group were cancelled because fewer than three follicles of ≤14 mm were observed on days 13–16 of stimulation. Women with ovarian cysts demonstrated significantly higher levels of day 3 FSH ($P \leq 0.05$) and E_2 levels ($P \leq 0.01$), more days of HMG stimulation ($P \leq 0.05$) and number of HMG ampoules required ($P \leq 0.01$), and higher abortion and cancellation rates ($P \leq 0.05$ and $P \leq 0.001$, respectively), compared with those without ovarian cysts. In contrast, women without ovarian cysts had a significantly higher number of retrieved oocytes ($P \leq 0.001$), fertilization rate ($P \leq 0.05$), number of day 2 embryos ($P \leq 0.01$), number of good embryos ($P \leq 0.01$), implantation rate ($P \leq 0.01$) and pregnancy rate ($P \leq 0.001$) compared with those with ovarian cysts.

The cycle characteristics and outcome of women who developed unilateral and bilateral ovarian cysts are presented in Table III. Patients with bilateral ovarian cysts (25.4%) had a significantly higher E_2 level and a higher proportion of poor quality embryos ($P < 0.05$) than those in the unilateral group. Furthermore, the number of follicles of ≥14 mm, number of oocytes retrieved and number of day 2 embryos were significantly lower compared with the unilateral cyst group. There were no significant differences between the two groups in terms of cancellation rate, number of embryos transferred, fertilization, pregnancy and abortion rates.

Of the 122 women with ovarian cysts, 76 (62.3%) underwent ovarian cyst aspiration. There were no significant differences in the average size of the cysts or the E_2 levels on the day of diagnosis between the aspirated and the non-aspirated group. The 'cyst aspiration' group showed no significant difference in the number of HMG stimulation days or in the number of ampoules required compared with the 'no-aspiration' group. There were no significant differences in terms of cancellation rate, number of oocytes retrieved, fertilization rate, quality of embryos, number of embryos transferred, pregnancy and abortion rates (Table IV).

Discussion

To our knowledge, this is the largest study conducted to examine the incidence of functional ovarian cyst formation following GnRH agonist administration and the effect of these cysts on the outcome of conventional IVF and ICSI treatment. Furthermore, this is the first study that examines the outcome of IVF treatment in relation to unilateral and bilateral cyst formation.

In our study, the incidence of ovarian cyst formation following GnRH agonist treatment was 9.3%. Using the same criteria of functional ovarian cysts of ≥15 mm and E_2 levels of ≥50 pg/ml, other investigators had reported a higher incidence—33.3% as reported by Keltz *et al.* (1995), 14.5% by Tarlatzis *et al.*

Table III. Ovarian cyst distribution with cycle characteristics and outcome

	Unilateral (n = 91)	Bilateral (n = 31)
Age (years)	31.7 ± 5.1	31.9 ± 4.9
Day 3 FSH	8.2 ± 3.3	8.3 ± 3.6
E2 levels on day of diagnosis (pg/ml)	166 ± 27.7	273 ± 31.3*
Days of stimulation with HMG	15.9 ± 4.1	16.1 ± 4.2
No. of ampoules of HMG	44 ± 17.1	46 ± 16.6
No. of follicles > 14 mm	6.4 ± 2.9	3.7 ± 1.2**
No. of oocytes retrieved	5.3 ± 1.9	3.1 ± 1.5**
Metaphase II oocytes (%)	(46.5)	(16.7)***
Fertilization rate (%)	(49.2)	(46.4)
No. of day 2 embryos	4.4 ± 2.1	2.8 ± 1.6***
Grades of embryos		
Good (%)	(19.5)	(13.3)
Fair (%)	(31.5)	(7.9)
Poor (%)	(54.8)	(73)*
No. of embryos transferred	2.2 ± 1.4	2 ± 0.8
Cancellation rate (%)	17/91 (18.6)	9/31 (29)
Implantation rate (%)	(4.5)	(3.9)
Pregnancy rate (%)	7/71 (9.9)	2/22 (9.1)
Abortion rate (%)	2/6 (33.3)	1/3 (33.3)

Values are expressed as mean ± SD. Values in parentheses are percentages.
*P < 0.05; **$P \leq 0.01$; ***$P \leq 0.001$.

Table IV. Cycle characteristics and outcome of IVF patients who underwent functional ovarian cyst aspiration and those who did not

	Cyst aspiration group (n = 76)	No-cyst aspiration group (n = 46)
Cyst diameter (mm)	22 ± 6	21 ± 6
E_2 levels on day of diagnosis (pg/ml)	178 ± 26.8	183.5 ± 25.9
Days of stimulation with HMG	14.4 ± 3.3	16.4 ± 4.3
No. of ampoules of HMG	42.2 ± 12.7	45.3 ± 19.4
No. of follicles > 14 mm	5.4 ± 3.1	5 ± 2.9
No. of oocytes retrieved	5.6 ± 1.8	5.2 ± 2.1
Metaphase II oocytes (%)	(32)	(29)
Fertilization rate (%)	(50.9)	(44.7)
No. of day 2 embryos	3.8 ± 1.5	3.5 ± 1.3
Grades of embryos		
Good (%)	(15.9)	(16.9)
Fair (%)	(25.5)	(13.9)
Poor (%)	(58.6)	(69.2)
No. of embryos transferred	2.1 ± 1.4	2.1 ± 1.2
Cancellation rate (%)	18/76 (23.7)	11/46 (23.9)
Implantation rate (%)	(4.3)	(4.1)
Pregnancy rate (%)	6/59 (10.2)	3/34 (8.8)
Abortion rate (%)	2/6 (33.3)	1/3 (33.3)

Values are expressed as mean ± SD. Values in parentheses are percentages.

(1994), and 52.9% by Biljan *et al.* (2000). Even when a diameter criterion of ≥20 mm was considered, a higher incidence was reported by Feldberg *et al*. (1989). These investigators suggested that the incidence of functional ovarian cyst formation is affected by woman's age, ovarian reserve, type of GnRH agonist, and the time and route of GnRH agonist administration. In view of the larger sample size in this study, we speculate that the lower incidence of cyst formation observed in this study is a more accurate account of this event.

The precise mechanism by which cysts are formed is still unclear. The mechanism by which functional ovarian cyst development during GnRH agonist treatment can affect the outcome of IVF, leading to poor follicular recruitment, decreased number of oocytes, low implantation and pregnancy rate, and increased cancellation rate is also unclear. Jenkins *et al.* (1993) found that women who developed ovarian cysts after GnRH agonist administration had elevated serum E_2 levels and high concentrations of E_2 in the aspirated cyst fluid; they concluded that these cysts are functional follicular cysts. Biljan *et al.* (2000) suggested that the increased serum levels of E_2 observed in these patients was probably caused by a passive diffusion from the cyst into the circulation. It has been found that this aberrant rise in serum E_2 after GnRH agonist down-regulation may cause imperfect pituitary suppression of bioactive gonadotropins, with subsequent effects on oocyte quality and implantation (Penzias *et al*., 1994). In agreement with this suggestion, patients in our study who developed ovarian cysts had significantly higher E_2 levels compared with those in the 'non-cyst' group.

It has been postulated that these cysts might affect the IVF results mechanically by reducing the space for growing follicles or by impairing the ovarian blood supply (Fiszbajn *et al*., 2000). In our study, patients who had bilateral ovarian cyst formation had a significantly lower number of oocytes and higher number of poor quality embryos compared with the unilateral cyst group.

The activation of the endocrine–paracrine pathway has been suggested as another mechanism by which functional ovarian cysts may affect IVF results (Penzias *et al*., 1994; Ghosh and Sengupta, 1998). In a similar study to this one but with smaller sample size, Keltz *et a.* (1995) noted cyst formation in 26 out of 78 cycles (33.3%). In their series, patients with ovarian cysts compared with the no-ovarian cysts group had significantly higher cancellation rate and showed significant decrease in the number of retrieved oocytes, total number of embryos, fertilization and pregnancy rates. 'Cyst cycles' were associated with significantly higher basal levels of FSH.

A negative impact of ovarian cysts on folliculogenesis was recently reported by Segal *et al.* (1999). A higher incidence of ovarian cyst formation was reported in their series (51.8%), but their cyst diameter criterion was ≥10 mm. The pregnancy rate in the 'cyst cycles' was 24% versus 41% in the 'non-cyst cycles'. In our study, the pregnancy rate was 9.7% versus 29.7%. This discrepancy is possibly because our patients were at a higher risk of being poor responders as manifested by their significantly elevated basal FSH levels. This study was disadvantaged by the smaller sample size of 137 patients compared with 1317 in our study.

In contrast, other studies have reported no detrimental effect due to functional cyst formation following GnRH agonist treatment (Feldburg *et al*., 1989; Ron-El *et al*., 1989; Herman *et al*., 1990; Parinaud *et al*., 1992; Tarlatzis *et al*., 1994; Biljan *et al*., 2000; Owj *et al*., 2004). Furthermore, they have demonstrated no difference in the incidence of cyst formation in different GnRH agonist type groups. Tarlatzis *et al.* (1994) studied 141 women using three different types of GnRH agonist in the long protocol and reported an overall functional cyst formation incidence of 14.5%; they concluded that the presence of such cysts did not interfere with induction of ovulation or achievement of pregnancy. In a recent study, Biljan *et al.* (2000) observed cyst formation in 27 out of 51 (52.9%) cycles. Similar to the findings of our study, in their series patients who developed ovarian cysts required a significantly longer time to achieve pituitary suppression and higher doses of gonadotropins. In contrast, the implantation and pregnancy rates were significantly lower in our study, whilst Biljan *et al.* (2000) reported no difference in the pregnancy rates between the cyst and non-cyst groups. This discrepancy may be related to the smaller size of their study.

In a more recent study by Owj *et al.* (2004), unexpected results were found when comparing 39 women who developed ovarian cysts with 42 who did not. Owj *et al.* (2004) found that the number of oocytes, MII oocytes retrieved and embryos was significantly higher in the ovarian-cyst group compared with controls. Their study lacked a possible explanation of the mechanism.

In order to improve folliculogenesis and IVF outcome, different approaches have been described for the management of women with follicular ovarian cyst development following GnRH agonist administration. These include conservative management with prolonged down-regulation (Feldburg *et al*., 1989; Thatcher *et al*., 1989; Ron-El *et al*., 1989; Keltz *et al*., 1995; Segal *et al*., 1999; Biljan *et al*., 2000; Owj *et al*., 2004) and progesterone therapy during pituitary desensitization (Engmann *et al*., 1999).

Aspiration of functional ovarian cysts has been advanced as an alternative to improve IVF outcome. Consistent with our findings, no significant difference was demonstrated in the number of retrieved oocytes, embryo quality, fertilization rate, implantation and pregnancy rates between women whose cysts were aspirated and those whose cysts were not (Rizk *et al*., 1990; Parinaud *et al*., 1992; Tarlatzis *et al*., 1994).

In summary, the current study demonstrates that the incidence of ovarian cyst formation following GnRH agonist administration before controlled ovarian hyperstimulation for the purposes of IVF treatment is 9.3%. This may reflect the true incidence because of the larger sample size of this study. Cyst formation was associated with relatively higher basal FSH levels and lower IVF success rates. When functional ovarian cysts were present, the cycle cancellation rate, the number and quality of oocytes and embryos, and the implantation and pregnancy rates were negatively affected to a statistically significant degree as compared with 'non-cyst' cycles. Furthermore, when such cysts were present bilaterally as opposed to being present unilaterally, the number and quality of oocytes and embryos were further compromised, but without a significant affect on the implantation and pregnancy rates. Cysts aspiration before ovarian stimulation was of no added benefit.

References

Biljan MM, Lapensee L, Mahutte NG, Bissonnette F, Hemmings R and Tan SL (2000) Effect of functional ovarian cysts detected on the 7th day of gonadotropin-releasing hormone analogue administration on the outcome of IVF treatment. Fertil Steril 74,941–945.

Coskun S, Roca, GL, Elnour A, al Mayman H, Hollanders JM and Jaroudi KA (1998) Effect of reducing insemination time in human *in vitro* fertilization and embryo development by using sibling oocytes. J Assist Reprod Genet 15,605–608.

Engmann L, Maconochie N, Bekir J and Tan SL (1999) A prospective randomized study to assess the effect of progesterone therapy during pituitary desensitization with GnRH agonist in the prevention of functional cyst formation. Am J Obstet Gynecol 181,576–582.

Feldburg D, Ashkenazi J, Dicker D, Yeshaya A, Goldman GA and Goldman JA (1989) Ovarian cyst formation: A complication of gonadotropin-releasing hormone agonist therapy. Fertil Steril 51,42–44.

Fiszbajn GE, Lipowicz RG, Elberger L, Grabia A, Papier SD, Brugo- Olmedo SP and Chillik CF (2000) Conservative management versus aspiration of functional ovarian cysts before ovarian stimulation for assisted reproduction. J Assist Reprod Genet 17,260–263.

Ghosh D and Sengupta J (1998) Recent developments in endocrinology and paracrinology of blastocyst implantation in the primate. Hum Reprod Update 4,153–168.

Herman A, Ron-El R, Golan A, Nahum H, Soffer Y and Capsi E (1990) Follicle cysts after menstrual versus midluteal administration of gonadotropin-releasing hormone *in vitro* fertilization. Fertil Steril 53,854–858.

Jenkins JM, Davies DW, Anthony F, Wood P, Gadd SG, Waston RH and Masson GM (1992) The detrimental influence of functional ovarian cyst during in-vitro fertilization cycles. Human Reprod 7,776–780.

Jenkins JM, Anthony FW, Wood P, Rushen D, Masson GM and Thomas E (1993) The development of functional ovarian cyst during pituitary down-regulation. Hum Reprod 8,1623–1627.

Keltz MD, Jones EE, Duleba AJ, Polcz T, Kennedy K and Olive DL (1995) Baseline cyst formation after luteal phase gonadortopin-releasing hormone agonist administration is linked to poor *in vitro* fertilization outcome. Fertil Steril 64,568–572.

Owj M, Ashrafi M and Baghestani AR (2004) Ovarian cyst formation and *in vitro* fertilization outcome. Int J Obstet Gynecol 87,258–259.

Parinaud J, Cohen K, Oustry P, Perineau M, Monrozies X and Reme JM (1992) Influence of ovarian cysts on the results of *in vitro* fertilization. Fertil Steril 58,1174–1177.

Penzias AS, Lee G, Seifer DB, Shamma FN, DeCherney AH, Reindollar RH and Jones EE (1994) Aberrant estradiol flare despite gonadotropin-releasing hormone-agonist- induced suppression is associated with impaired implantation. Fertil Steril 61,558–560.

Rizk B, Tan SL, Kingsland C, Steer C, Mason BA and Campbell S (1990) Ovarian cyst aspiration and the outcome of *in vitro* fertilization. Fertil Steril 54,661–664.

Ron-El R, Herman A, Golan A, Raziel A, Soffer Y and Capsi E (1989) Follicle cyst formation following long-acting gonadotropin releasing hormone analogue administration. Fertil Steril 52,1063–1066.

Segal S, Shifren JL, Isaacson KB, Leykin L, Chang Y, Pal L and Toth TL (1999) Effect of baseline ovarian cyst on the outcome of *in vitro* fertilization-embryo transfer. Fertil Steril 71,274–277.

Tarlatzis BC, Bili H, Bontis J, Lagos S, Vatev I and Mantalenakis S (1994) Follicle cyst formation after administration of different gonadotrophin-releasing hormone analogues for assisted reproduction. Hum Reprod 9,1983–1986.

Thatcher SS, Jones EE and DeCherney AH (1989) Ovarian cysts decrease the success of controlled ovarian stimulation and *in vitro* fertilization. Fertil Steril 52,812–816.

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