Review

Women's Health

In vitro fertilization for endometriosis-associated infertility

Endometriosis is an enigmatic disease affecting 10–15% of reproductive aged women and is encountered in 25–35% of women suffering from infertility. IVF is an effective tool to overcome endometriosis-associated infertility when expectant management or surgery fails. Direct IVF should be envisioned if the female age is greater than 38 year and infertility is long lasting. Likewise, semen characteristics or tubal status that is incompatible with natural conception mandates going straight to IVF. IVF, not only bypasses the distortion of pelvic anatomy associated with advanced stage endometriosis, but also removes gametes from a hostile peritoneal environment. In this article, we address the impact, if any, of endometriosis and endometriomason IVF outcome, whether surgical treatment of early-stage disease, endometriomas or deep infiltrating endometriosis would enhance pregnancy rates in IVF, which protocol to employ for controlled ovarian hyperstimulation for IVF and finally the impact, if any, of controlled ovarian hyperstimulation for IVF on progression of endometriosis.

Keywords: controlled ovarian stimulation • embryo quality • endometriosis • endometrioma • IVF outcome • oocyte quality

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Does endometriosis *per se* affect IVF results?

It is still controversial whether endometriosis *per se* is associated with lower pregnancy rates in women undergoing IVF. Previous reports on the IVF outcome in women with endometriosis have been conflicting. In minimal-mild endometriosis, lower success rates were reported compared with various nonendometriosis control groups [1–4], whereas no difference was reported in others [5–8]. In late-stage disease, the results have also been conflicting and reported poor [9–11] or similar pregnancy outcomes [12–15].

The 2002 meta-analysis by Barnhart *et al.* [16] concluded that endometriosis was associated with significantly less fertilization and implantation rates and hence significantly less pregnancy rates compared with tubal factor controls after adjusting for stimulation regimen, publication date and female age. A more recent meta-analysis also reported significantly less implantation and clinical pregnancy rates in stage III–IV disease compared with the controls with no endometriosis [17]. However the live birth rate in stage III–IV disease was comparable to the controls. In contrast to the 2002 Barnhart meta-analysis, in early-stage disease (stage I–II), the implantation, clinical pregnancy and live birth rates are comparable to the controls. The results of this meta-analysis, however, are in contrast to the 2011 registry data from Society for Assisted Reproductive Technology; both live birth rates per cycle commenced and implantation rates are comparable to tubal factor controls [18]. A recent study enrolling 1074 patients with different stages of endometriosis and 1171 patients with tubal factor controls also concluded that endometriosis *per se* was not associated with inferior pregnancy rates [19].

In a single-center retrospective case–control study, we recently analyzed whether the presence of endometriosis *per se* was

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associated with inferior pregnancy rates in women undergoing IVF (unpublished data). A total of 571 consecutive patients (842 cycles) with endometriosis were included; 86 patients (129 cycles) had minimal-mild disease and the remaining 485 patients (713 cycles) had moderate-severe disease. Two hundred and nine patients (330 cycles) with laparoscopically confirmed tubal factor infertility not harboring endometriosis and hydrosalpinx served as the control group. Primary outcome measures were implantation and live birth rates. Secondary outcome measures were response to follicle-stimulating hormone (FSH) stimulation, fertilization rate, embryo quality, clinical pregnancy and miscarriage rates. Although there were statistically significant differences in some of the baseline demographic features, ovarian response parameters and embryological data, the implantation and live birth rates were comparable among the minimal–mild, moderate–severe disease and control groups. Female age, antral follicle count and number of embryos transferred were noted to be significant independent predictors of live birth rate. However, neither the presence nor the extent of endometriosis had any detrimental effect on IVF pregnancy rates. This conclusion was compatible with the results of our two previous studies [15,20].

The detrimental impact, if any, of endometriosis on IVF outcome would be expected to be on embryo 'quality' and/or endometrial receptivity. The effect of endometriosis on embryo quality is controversial; detrimental [21] and no detrimental effects [22] have been reported. Egg donation using sibling oocytes is an excellent model to evaluate the impact of endometriosis on endometrial receptivity. Recipients effected with stage III–IV endometriosis (n = 25 patients) sharing sibling oocytes with control recipients (n = 33 patients) not harboring endometriosis have been reported to have comparable implantation and live birth rates [23] concluding that endometriosis is not detrimental to endometrial receptivity. However, in a more recent prospective cohort study, employing the sharing sibling oocytes model, the impact of endometriosis on implantation, pregnancy and live birth rates in menopausal recipients was evaluated [24]. Of the total 240 menopausal recipients, 120 had endometriosis and the remaining 120 controls had no endometriosis. The implantation (23.81 vs 31.48%; p = 0.019) and pregnancy (45.00 vs 58.33%; p = 0.039) rates were significantly lower in the endometriosis group compared with the control group. The conclusion was that in oocyte donation cycles, a recipient's history of endometriosis might have a negative impact on implantation, pregnancy and live birth rates, even in menopausal women.

Does surgical treatment of early-stage disease improve subsequent IVF outcome?

Enhancement of IVF outcome by surgical ablation or resection of endometriotic implants in the absence of endometrioma is controversial. One randomized controlled trial (RCT) reported the effect of laser ablation of endometrial implants at the time of gamete intrafallopian transfer procedure. Carbon dioxide laser ablation of endometriotic implants at the time of gamete intrafallopian transfer was performed in patients with stages I–IV endometriosis in the study group and no treatment was performed in control group. Destruction of endometrial implants did not seem to improve cycle outcome and pregnancy rates; however, pregnancy rates in the study group in subsequent cycles who failed to conceive were higher [25].

A recent Norwegian study, retrospectively analyzed IVF outcomes in patients with stage I/II endometriosis who either underwent complete surgical resection of lesions prior to IVF procedure or diagnostic laparoscopy only [26]. Surgical resection significantly improved implantation (30.9 vs 23.9%; p = 0.02) and live-birth (27.7 vs 20.6%; p = 0.04) rates. However, the study is retrospective with its inherent selection bias. Furthermore, no difference in day 3 embryo quality was noted before and after surgical treatment of all stages of endometriosis [27]. Well-designed RCTs are warranted before one can state that surgical treatment of early-stage disease prior to IVF is beneficial.

Is the presence of endometrioma associated with inferior pregnancy rates in IVF?

Endometriomas are present in 20–40% of women with endometriosis. It is difficult to truly assess the effect of endometrioma *per se* on IVF outcome, since most of the patients with these lesions are likely to have concomitant peritoneal disease and/or deep infiltrating endometriosis (DIE) that could have independent effects. The effect of the size of the endometrioma *per se* has also not been evaluated as an independent variable.

A higher incidence of pregnancy loss, a decreased number of oocytes harvested, as well as an adverse effect on embryo quality in patients with endometrioma have been reported [28]. In contrast, no adverse on any outcome measure has also been reported [6].

It is still controversial whether the presence of an endometrioma is associated with diminished ovarian reserve. Previous studies have evaluated indirectly the effect of endometriomas on ovarian reserve by comparing the number of oocytes collected from endometrioma-containing ovaries with contralateral ovaries following ovarian stimulation in IVF cycles [29–32]. While Esinler *et al.* [30] and Almog *et al.* [29] reported

similar numbers of oocytes being collected from ovaries containing endometriomas and ovaries without endometriomas. Somigliana *et al.* [31] reported that the number of co-dominant follicles was significantly decreased in ovaries containing an endometrioma. The number of oocytes collected was not reported by Somigliana *et al.* [31]. In a more recent study [32], the same group reported similar number of follicles >15 mm in diameter on the day of human chorionic gonadotropin (hCG) administration between the affected and nonaffected sides, contradicting their previous report. More recently, serum anti-Mullerian hormone (AMH) levels were compared between women with endometrioma(s) and similarly aged women who do not have ovarian cysts; an endometrioma-related loss of ovarian reserve was clearly noted [33]. Serial assessment of ovarian reserve (e.g., AMH, antral follicle count) without surgery in patients with endometrioma is warranted to delineate if endometrioma cause a progressive decrease in ovarian reserve. Unfortunately, there is no such study, yet. Comparison of endometrioma-related decrease in AMH with that of surgery-related decrease (in AMH) would also be of great interest.

Does cystectomy of endometriomas improve subsequent IVF outcome?

There are theoretical advantages and disadvantages of resecting an endometrioma(s) before IVF. Theoretical advantages of surgery before IVF include avoidance of pelvic abscess and rupture of an endometrioma, avoidance of occult malignancy (≈0.8%), avoidance of retrieval difficulties and contamination of the follicular aspirate with endometrioma content and finally avoidance of endometriosis progression. Possible disadvantages of surgery before IVF include decreased ovarian reserve, cost, major (≈1.4%) and minor (≈7.5%) complications of operative laparoscopy in even experienced hands and finally increased time to conception.

While addressing the impact of resection of endometriomas before IVF, one should consider several variables that may affect IVF cycle outcome. These include different patient profiles, diameter of endometrioma, bilaterality, time from surgery to IVF and finally and most importantly the surgical technique employed for the resection of endometrioma. Regarding different patient profiles, patients with endometrioma with no previous history of surgery, surgically resected endometrioma with no recurrence at the time of IVF and finally surgically resected endometrioma with recurrence at the time of IVF may, at least from ovarian reserve point of view, represent different prognostic subgroups. These prognostic variables should be controlled in studies evaluating the impact of pre-IVF surgery on IVF outcome.

In a case–control report, Garcia-Velasco and colleagues [34] showed that surgery for ovarian endometriosis failed to augment outcome of ART versus expectant management. In the systematic review and meta-analysis by Tsoumpou *et al.* [35], surgical removal of endometrioma or expectant management was compared; five studies were included. No significant difference in controlled ovarian hyperstimulation (COH) response parameters as well as clinical pregnancy rates was noted between the treated and untreated groups.

An RCT noted that ovarian surgery led to a longer stimulation, higher doses of gonadotrophins required and a lower number of oocytes retrieved after IVF compared with no surgery before IVF [36]. However, clinical pregnancy rates were comparable between the two groups.

A recent Cochrane review analyzing RCTs to determine the effectiveness of surgery in women with endometriomas prior to undergoing IVF also showed no evidence of an effect on reproductive outcomes [37].

Surgery for endometriomas could cause harm, particularly in women with bilateral disease, impaired ovarian reserve or who had previous surgery for endometriomas [38]. Aboulghar and co-workers [9] stressed that surgery for ovarian endometriosis could deteriorate ovarian response to the point of causing cycle cancellation. Importantly, cessation of cycles may not be recognized when only the pregnancy rates per retrieval are assessed. In an analysis of the pros and cons of surgery for endometriomas [38], criteria in favor were an intact ovarian reserve, no previous ovarian surgery, unilateral disease and rapid growth. Conversely, past history of surgery, diminished ovarian reserve and bilateral endometriomas favored avoidance of surgery [38].

The rule of no surgery before ART comes with exceptions. These include the presence of hydrosalpinges, severe associated pelvic pain and when endometriomas are excessively large or doubts exist about their exact nature [38].

Does surgery for DIE improve subsequent IVF outcome?

Endometriomas are often associated with DIE, which raises the issue of their concomitant surgical treatment before ART. Bianchi *et al.* [39] reported that thorough laparoscopic excision of deep infiltrating endometriosis improves IVF outcome.

DIE was recently reported in a retrospective study to be a determinant factor of cumulative pregnancy rate after intracytoplasmic sperm injection/IVF cycles in patients with endometriomas [40]. In this study, a total of 103 patients were included; 30 had isolated endometrioma and the remaining 73 had endometrioma with associated DIE. Of interest, the total number of endo-

metriomas and size of the largest endometrioma and bilaterality had no impact on clinical pregnancy rates. The clinical pregnancy rate per patient for women with isolated endometriomas and women with endometriomas and associated DIE was 82.5 and 69.4%, respectively (p = 0.009). Using multivariable analysis, associated DIE (odds ratio [OR]: 0.2; 95% CI: 0.06–0.6; p = 0.008) was an independent factor associated with a lower pregnancy rate.

In a recent study, a nomogram to predict the clinical pregnancy rate in patients with endometriosis was built based on the patients' characteristics [41]. A training cohort of 94 consecutive patients (141 ICSI–IVF cycles) was used to form the nomogram and was validated in a cohort of 48 patients (83 ICSI–IVF cycles). Female age, serum AMH level and the number of previous IVF/ICSI attempts were also significant predictors of clinical pregnancy. The presence of DIE was noted to be the strongest factor of the clinical pregnancy rate in the model (OR: 1/4 0.26; 95% CI: 0.07–0.9 [P 1/4 0.006]). The pregnancy rates per patient in women with and without DIE were 58 and 83%, respectively (p = 0.03).

Colorectal endometriosis is one of the most severe forms of DIE and there is currently no consensus about indications for surgery for infertility associated with colorectal endometriosis. Mathieu d'Argent *et al.* [42] reported pregnancy rates after a first ICSI–IVF cycle to be similar in patients with colorectal endometriosis and in patients with tubal or male infertility raising the issue about the legitimacy of surgery. Conversely, [43] underlined that IVF results increased after removal of DIE and that the pregnancy rate was higher in patients undergoing colorectal resection compared with patients undergoing limited surgery leaving *in situ* colorectal endometriosis. In a recent multicenter study, cumulative pregnancy rate after ICSI–IVF in patients with colorectal endometriosis was reported [44]. A total of 75 patients were included, the cumulative pregnancy rate per patient after three ICSI–IVF cycles was 68.6%. The cumulative pregnancy rate differed considerably mainly depending on the presence of adenomyosis, AMH serum level and patient age.

Operative surgery for DIE is not without major and minor complications. Despite the above-mentioned data, one cannot recommend surgery, before IVF to enhance pregnancy rates, especially in patients without chronic pelvic pain. Future RCTs are warranted to delineate the role of surgery before IVF in patients with DIE.

Which COH protocol to employ in IVF?

Controlled ovarian hyperstimulation is an integral part of an IVF cycle. Four available retrospective studies concluded that reproductive outcome of patients with endometriosis is improved if downregulation with GnRH agonists (GnRHa) is used for a period of about 2–3 weeks before COH [6,45–47]. However, the available retrospective studies have limited power and there is no RCT.

There is no prospective study comparing the long and the short GnRHa protocols in patients with endometriosis. In the short protocol GnRHa is commenced in the early follicular phase, usually on day 2 of the cycle, followed by gonadotropins 1 day later. In the ultrashort agonist protocol the agonist is administered only on days 2, 3 and 4 of the cycle and gonadotropins are commenced on day 3 of the cycle. In a retrospective study, Tan *et al.* [47] compared the cumulative conception rates in patients with endometriosis undergoing IVF with the use of the long, short and ultrashort regimens and a significantly higher cumulative conception rate was reported with the long agonist protocol compared with those treated with a short or ultrashort protocols (50.3%; 95% CI: 35.9–66.6 vs 8.3%; 95% CI: 1.2–46.1).

Extension of the 2–3-week period of GnRHa administration is defined as prolonged downregulation, so called long protocol. The goal of prolonged downregulation in women with endometriosis is to extinguish the disease prior to the IVF cycle. Although one study [46] concluded that the reproductive outcome in women with endometriosis undergoing IVF is not improved after prolonged downregulation with GnRHa before starting ovarian stimulation, the majority of retrospective studies [6,45,47] reported higher pregnancy rates in patients treated with long protocol.

In a prospective cohort study, 162 Chinese women surgically diagnosed as having moderate or severe endometriosis were enrolled [48]. In group 1 (97 cycles), the patients received the traditional luteal long pituitary downregulation protocol. In group 2 (52 cycles) monthly GnRHa depot was used twice and, COH was initiated within 35 days of the last injection; in group 3 (75 cycles) monthly GnRHa depot was used three-times, COH was initiated within 35 days of the last injection. Patients in group 2 and 3 consumpted significantly higher doses of gonadotropins for ovarian stimulation (p < 0.001); the duration of stimulation was also significantly longer (p < 0.05). The number of oocytes harvested and good quality embryos were lower in group 3 than in groups 1 or 2 (p < 0.05). The implantation rate was significantly higher in group 2 than in group 1 (p < 0.02). The authors concluded that a 2-month treatment with a GnRHa prior to IVF produced a trend toward an increase in the implantation rate in women with stages III and IV endometriosis.

The long-term GnRHa suppression before IVF was evaluated in a Cochrane review [49] including three RCTs [50–52]. The clinical pregnancy and live birth rates per woman were significantly higher in women receiving ultra-long protocol GnRHa compared with the control group (OR: 4.28; 95% CI: 2.00–9.15; OR: 9.19; 95% CI: 1.08–78.22, respectively). The authors concluded that the administration of GnRHa for a period of 3–6 months prior to IVF or ICSI in women with endometriosis increased the odds of clinical pregnancy by fourfold. However, more RCTs with live birth as the primary end point are warranted. Furthermore, RCTs stratifying to the stage of endometriosis and comparisons between different types of GnRHa and length of treatment are needed. The administration of extended GnRHa to patients with decreased ovarian reserve may further diminish ovarian response to subsequent gonadotropin treatment. Hence, vitrification of all embryos after stimulation and transferring in a thaw cycle following extended GnRHa treatment for endometrial preparation may be more appropriate. Obviously, RCTs are warranted to test this hypothesis.

Which specific subgroup of patients with endometriosis should be offered such extended suppressive treatment has not been defined given the associated increased expense and time delay before pregnancy can occur. In a recent pilot RCT, whether endometrial expression of the integrin $\alpha_v\beta_3$ vitronectin could predict which endometriosis patient subgroup would benefit from pre-IVF cycle prolonged GnRHa therapy was evaluated [53]. Thirty-six IVF candidates with regular menses, surgically confirmed endometriosis and normal ovarian reserve were included. All patients underwent endometrial biopsy 9–11 days post-LH surge to evaluate $\alpha_v\beta_3$ integrin expression. After assessing the $\alpha_v\beta_3$ vitronectin expression, patients were randomized either to receive depot leuprolide acetate 3.75 mg every 28 days for three doses before COH or to proceed directly to COH and IVF. Contrary to what is expected, integrin-positive patients administered prolonged GnRHa had higher pregnancy rates that did not reach statistical significance. The value of a negative integrin biopsy in predicting an ongoing pregnancy after prolonged GnRHa therapy was only 44.4%. The evaluation of integrin expression seems to have little value in selecting which patients would benefit from extended GnRHa treatment. Limited sample size or by the fact that patients in the control group moved directly to IVF after endometrial biopsy, whereas study group patients did not undergo stimulation for IVF for 3 months may be confounder factors. The performance of an endometrial biopsy alone may improve implantation rates due to the localized injury, particularly in patients with a history of implantation failure [54].

There is paucity of data on whether other means of ovarian suppression, such as oral contraceptives (OC), may be similarly effective to improve IVF outcome. De Ziegler *et al.* recently evaluated the role of a 6–8 week course of OC pretreatment in IVF outcome in patients with either surgically diagnosed endometriosis or those with sonographic suspicion of the presence of endometriosis [55]. OC-pretreatment for 6–8 weeks was associated with higher pregnancy rates per retrieval than in controls (35 vs 12.9%; $p = 0.01$). This impact was greater in the subgroup of patients with presumed endometriomas. The drawbacks of this study are its retrospective design with its inherent limitations, lack of documentation of endometriosis in all patients and that control patients were both significantly older and had higher baseline FSH levels.

There is only one study, an RCT, on comparing GnRH agonist or antagonist administration for COH in patients with endometriosis [56]. The number of metaphase-II oocytes was significantly less with the use of GnRH antagonists in subgroup of patients with resected endometrioma ($p < 0.0001$) or active endometrioma ($p < 0.01$), whereas it was comparable in patients with stage I–II disease. However, the clinical pregnancy and implantation rates appear to be comparable with the use of GNRH agonists or antagonists.

Letrozole is an interesting drug that may be employed in COH for IVF. High endometrial aromatase P450 mRNA expression has been reported to be associated with poor IVF outcome [57]. In theory, aromatase inhibitors may inhibit aberrant endometrial aromatase expression resulting in a change in intracellular balance of estrogen and progesterone action. This may restore progesterone action resulting in upregulation of HOXA10 and hence upregulation of $\alpha_v\beta_3$ as well as downregulation of estrogen receptors, both resulting in improved endometrial receptivity. In concordant with this hypothesis, in a retrospective cohort study, lack of endometrial $\alpha_v\beta_3$ integrin expression was noted to be associated with a poor prognosis for IVF that might be improved with letrozole co-treatment [58]. The administration of letrozole 5 mg daily for days 2–6 of gonadotropin stimulation resulted in cycle outcome that were similar to patients who were integrin receptor positive and not treated with this agent. A lack of randomization of integrin-negative patients to similar protocols with or without the use of letrozole is the main drawback of this study.

In a retrospective case–control study design, we compared microdose-flare-up protocol (84 patients; 121 cycles) with letrozole-GnRH antagonist protocol (113 patients; 192 cycles) in patients with endo-

metriosis and poor ovarian response (unpublished data). Letrozole-antagonist protocol was associated with significantly better implantation, clinical pregnancy and live birth rates per embryo transfer compared with the microdose protocol concordant with the theory that letrozole may correct endometrial receptivity defects (unpublished data). Although the results are encouraging, it is difficult to draw definite conclusions and well-designed powerful RCTs are warranted.

IVF have any impact on the progression of endometriosis?

Since endometriosis is an estrogen-dependent disease, COH for IVF may theoretically lead to a higher recurrence rate of endometriosis. In a retrospective cohort study, a total of 67 patients with stage III–IV disease underwent pelvic reconstructive surgery and subsequently started fertility treatment with either IVF only (n = 39), both IVF and IUI in different cycles (n = 11) or IUI only (n = 7) [59]. The cumulative endometriosis recurrence rate (CERR) based on histologic or cytologic proof of disease was calculated by using life-table analysis. The overall CERR was 31% and was significantly lower in women treated with IVF only (7%) or women treated with both IVF and IUI in different cycles (43%) than in those treated with IUI only (70%) after 21 months. Lower CERR following IVF compared with IUI suggests that temporary exposure to higher estradiol levels in women during COH for IVF is not a major risk factor for endometriosis recurrence.

Similarly, in a more recent retrospective study, IVF procedures did not seem to influence the likelihood of endometriosis recurrence [60]. No worsening in endometriosis symptom scores or changes in size of either endometriomas or peritoneal nodules evaluated by serial transvaginal ultrasound examinations in the 3–6 months after an IVF cycle [60]. Twenty-two percent of the patients reported improvement, whereas 11% reported worsening of symptoms during this follow-up. Furthermore, the number of IVF cycles and the responsiveness to COH were not associated with the risk of disease recurrence.

Conclusion

Taken as a whole, endometriosis *per se* is not associated with worse IVF outcome; in other words, patients with endometriosis should expect similar age-based outcomes from IVF as nonendometriosis patients. One exception for this contention may be the one with significantly diminished ovarian reserve necessitating aggressive stimulation resulting in a compromised number of oocytes and embryos.

There is inconclusive evidence to recommend pre-IVF surgical resection of peritoneal endometriosis to enhance IVF outcome. However, the data are more encouraging from a small number of retrospective studies addressing the effects of resecting DIE. Precycle endometrioma resection does not enhance IVF outcome; such surgery may only be considered in the presence of severe pelvic pain attributable to mass, rapid growth, suspicious sonographic features and concern for rupture in pregnancy due to size.

Prolonged course of GnRH agonist administration appears to be beneficial. However, the ideal candidate for such extended course of GnRH agonist treatment has not been defined. Such treatment may be considered in the subsets of infertile women with prior implantation failure particularly after transfer of good quality embryos. There are limited data on the beneficial effect of OC pretreatment.

There is paucity of data on the use of GnRH antagonists in IVF. Letrozole may be a promising agent to enhance pregnancy rates although RCTs are warranted.

Executive summary

- Endometriosis is an enigmatic disease affecting 25–35% of women suffering from infertility.
- IVF is an effective treatment for endometriosis-associated infertility.
- Although still controversial, endometriosis *per se* may not be associated with worsened IVF outcome.
- There is insufficient evidence to recommend surgical resection of endometriosis prior to IVF to enhance IVF outcome.
- Surgical resection of endometrioma prior to IVF does not enhance IVF outcome; such surgery may only be considered in the presence of severe pelvic pain, rapid growth, suspicious sonographic features and concern for rupture/leakage in pregnancy due to size.
- Limited number of retrospective studies suggests that resecting deep infiltrating endometriosis may improve subsequent IVF outcome.
- Prolonged course of GnRH agonist administration in patients with endometriosis may improve IVF outcome.
- There is paucity of data on the use of oral contraceptive treatment before downregulation and GnRH antagonist co-treatment.
- Letrozole may be a promising agent to enhance pregnancy rates in IVF.

Future perspective

With the progress of individualised management protocols in patients undergoing IVF, including controlled ovarian stimulation, triggering final oocyte maturation, luteal phase support and laboratory handling, the live birth rates achieved may be expected to be improved. Better understanding of the pathophysiology of endometriosis may further contribute to the success of IVF.

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