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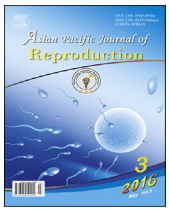

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Effect of polycystic ovaries on *in vitro* fertilization and intra-cytoplasmic sperm injection treatment outcome

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ABSTRACT

Objective: The reproductive performance of women with polycystic ovaries (PCO) with regular ovulatory menstrual cycles undergoing *in vitro* fertilization and intra-cytoplasmic sperm injection (IVF/ICSI) treatment has not been well described. This study aimed to investigate the outcome of IVF/ICSI in ovulatory women with PCO.

Methods: A retrospective cohort study of women aged ≤ 42 years with infertility and regular ovulatory menstrual cycles who underwent their first IVF/ICSI cycle using the long down regulation protocol at IVF Australia-EAST in Sydney between 2000 and 2011. A pre-treatment baseline transvaginal pelvic ultrasound (TVS) had been performed by a single tertiary level diagnostic ultrasound center. Patients were divided into either group NO (normal ovaries) or group PCO according to the pre-treatment TVS. The primary outcome measure was live birth rate per patient.

Results: A total of 200 patients (135 in group NO and 65 in group PCO) were included in the data analysis. There was no difference in live birth rate per patient between the two groups (25.2% vs 26.2%) with both raw (*OR* [95% *CI*] = 1.05 [0.54–2.07]) and logistic regression adjusted (for maternal age) (Adjusted *OR* [95% *CI*] = 0.99 [0.50–1.98]) data.

Conclusions: The presence of PCO in ovulatory women did not adversely affect IVF/ICSI outcome at our unit. However, the results are not conclusive and further large, well-designed prospective cohort studies are required in order to confirm our findings.

1. Introduction

Polycystic ovary syndrome (PCOS), which is characterized by features of ovulatory dysfunction, hyperandrogenism and polycystic ovaries (PCO) has been shown to affect a striking 12%–21% of Australian reproductive-age women [1–3]. The reproductive performance of women with PCOS undergoing *in vitro* fertilization and intra-cytoplasmic sperm injection (IVF/ICSI) treatment has been well described in a large systematic review and meta-analysis of nine observational studies comparing 458 women with PCOS (793 cycles) with 694 matched controls (1 116 cycles) [4].

In contrast, there are very few studies analyzing IVF/ICSI outcome in women with regular ovulatory menstrual cycles with PCO. Ultrasound evidence of PCO affects approximately 20%–30% of the female population [5–7] and up to 34% of women attending fertility clinics [8]. Although the presence of PCO may be considered a normal variant, data suggest that subtle endocrine disturbances, similar to those that are found in PCOS, may be uncovered in up to 1/3 women with ovulatory PCO [9]. The aim of this study was to assess the success rate of women with regular ovulatory menstrual cycles who have ultrasound evidence of PCO undergoing IVF/ICSI treatment.

2. Materials and methods

2.1. Patients

This retrospective cohort study included all patients with various causes of infertility undergoing their first cycle of IVF/ICSI treatment at IVF Australia-East between January 2000 and

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2011 and who had a transvaginal pelvic ultrasound (TVS) performed by a single tertiary level diagnostic ultrasound center (Warren and McNally Diagnostic Ultrasound Group, Royal Hospital for Women, Sydney, Australia) prior to embarking on their treatment cycle.

All patients met the following inclusion criteria: (i) aged 42 years or less at the time of commencement of IVF/ICSI treatment, (ii) infertility, (iii) regular ovulatory menstrual cycles (iv) normal uterine cavity assessed by ultrasound, hysterosalpingogram or hysteroscopy, (v) first stimulated cycle of IVF/ICSI, and (vi) long down regulation protocol. Exclusion criteria consisted of: (i) oocyte donor treatment cycle, (ii) presence of hydrosalpinges, (iii) presence of stage four (severe) endometriosis, and (iv) past history of myomectomy. This study was approved by the IVF Australia Ethics Committee.

2.2. IVF/ICSI treatment

All patients had IVF/ICSI treatment using the long down regulation protocol with gonadotropin releasing hormone (GnRH) agonist commenced in the mid-luteal phase (or 15 d after starting the combined oral contraceptive pill [OCP] for OCP pre-treated cycles) either as a nasal spray (nafarelin acetate; Pharmacia Australia), 200 μg twice daily, or as a subcutaneous injection (leuprorelin acetate; Abbott Australasia, Cronulla, NSW, Australia), 1 mg daily for at least 10 d, until pituitary down-regulation was confirmed by a serum estradiol (E2) level of <120 pmol/L. Follicle-stimulating hormone (FSH) injections (Gonal F; Merck Serono Laboratories, Frenchs Forest, NSW, Australia; or Puregon; MSD Laboratories, Lane Cove, NSW, Australia) were then commenced for ovarian stimulation, with the starting dose being determined by the individual clinician according to the patient's age, BMI and the presence or absence of PCO on ultrasound. Daily FSH injections and the GnRH agonist were continued until the day of human chorionic gonadotropin (hCG) trigger injection (Profasi or Ovidrel; Merck Serono Laboratories, Sydney) when 2 or more follicles at least 17 mm diameter were seen on ultrasound. Transvaginal egg collection was timed 36 h following the hCG trigger injection.

Two to four hours following egg collection, the oocytes were either inseminated (IVF) or injected (ICSI) with prepared sperm and fertilization was confirmed 16–18 h later. Depending on whether the patient was having an embryo cleavage or blastocyst stage transfer, the embryos were transferred transcervically on day 2/3 or day 5 after egg collection, respectively. Patients were given vaginal progesterone (Progesterone pessaries 100 mg, Macquarie Street Pharmacy, Sydney, NSW, Australia or Crinone gel, Serono Laboratories, Frenchs Forest, NSW, Australia) beginning on the day after egg collection and continuing daily until the pregnancy test with serum βhCG 16 d following egg collection.

Biochemical pregnancy was defined as a positive βhCG at the time of the pregnancy test. Clinical pregnancy was defined by the presence of an intrauterine gestational sac and live fetus on TVS at 7 weeks gestation. Ongoing clinical pregnancy was defined as a clinical pregnancy continuing past 12 weeks gestation. Live birth was defined as the delivery of a live baby beyond 20 weeks gestation. Severe ovarian hyperstimulation syndrome (OHSS) was defined as OHSS requiring hospital admission.

2.3. Pelvic ultrasound assessment

All patients had a TVS in the follicular phase of the menstrual cycle by a single ultrasound practice specialized in gynecological imaging (Warren and McNally Diagnostic Ultrasound Group) prior to commencing their treatment cycle. The ultrasound machine used was an Ultrasound Systems, GE Logiq 9 Systems (General Electric Medical Systems, Milwaukee, Wisconsin, USA). In addition, the ultrasound images of all patients had been digitally stored (ALI Ultrapacs) and were re-reviewed by a sole reviewer from the single ultrasound practice (Author GM) who was sub-specialized in gynecological sonography.

All patients' ultrasounds were assessed for the presence of PCO according to the Rotterdam criteria: presence of 12 or more follicles in either ovary measuring 2–9 mm in diameter, and/or increased ovarian volume (≥10 mL) [2].

2.4. Primary outcome

The primary outcome measure was live birth rate per patient.

2.5. Secondary outcome

The secondary outcome measures were (i) ongoing clinical pregnancy rate per patient, (ii) clinical pregnancy rate per patient, (iii) biochemical pregnancy rate per patient, (iv) miscarriage rate per biochemical pregnancy and patient, (v) multiple pregnancy rate per clinical pregnancy and patient, (vi) ovarian stimulation response, and (v) severe OHSS rate per patient.

2.6. Statistical analysis

Continuous variables were tested for normal distribution using Kolmogorov–Smirnov test and subsequently analyzed using either the independent samples *t*-test (normally distributed data) or Mann–Whitney *U* test (skewed data) to compare two means (normally distributed data) or medians (skewed data), where appropriate. Categorical variables were analyzed using the Chi-square test or Fisher's Exact Test where appropriate. Statistical significance was assumed when $P < 0.05$. Statistical analysis was performed using SPSS version 21 (SPSS Inc., Chicago, IL).

3. Results

A total of 200 patients undergoing their first stimulated cycle of IVF/ICSI were included in the data analysis. One hundred and thirty five patients had normal ovaries (group NO) and 65 patients had PCO (group PCO) on baseline pelvic ultrasound.

Table 1 compares the baseline demographic and clinical variables between the patients with normal or PCO on ultrasound and demonstrates no differences between the two groups in terms of treatment type (IVF or ICSI), treatment year, the time between TVS and IVF/ICSI treatment cycle, the duration of infertility, body mass index, cause of infertility, gravidity, and the number of patients who smoke. However, the PCO group was younger compared to the NO group.

The IVF/ICSI treatment cycle outcomes between the patients with normal and PCO are compared in Table 2. There was no difference seen in any of the ovarian response parameters,