Research Paper

Volume : 4 | Issue : 8 | Aug 2015 • ISSN No 2277 - 8179

Predictive Factors in Fresh in Vitro Fertilization-Embryo Transfer (Ivf-Et) Cycles

Medical Science

KEYWORDS : Predictive factors, Infertility, In vitro fertilization,Clinical pregnancy

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ABSTRACT

Introduction

Infertility affects approximately 13-14% of reproductive-aged couples. Initially, In vitro fertilization-embryo transfer (IVF-ET) was advocated for the treatment of patients with bilateral tubal block but now it has become the treatment option for patients with a variety of fertility problems including unexplained infertility, male factor infertility, endometriosis, cervical factor infertility and failed ovulation induction. Various predictive factors affecting the chances of pregnancy in a fresh IVF-ET program have been studied but there is still no consensus.

Objective

To identify the predictive factors affecting the outcome of a fresh IVF-ET cycle

Study Design

A hospital based prospective study

Material and Methods

A total of 135 infertile women between 20-40 years with a normal uterine cavity on office hysteroscopy and undergoing fresh IVF cycles from Januaty 2014 to December 2014 were included in the study. Patients were put on either long GnRH agonist ,short agonist or antagonist protocol for IVF followed by oocyte retrieval and embryo transfer in the same cycle .Primary outcome was clinical pregnancy defined as the presence of one or more intrauterine gestational sac at six weeks on transvaginal sonography (TVS).Various parameters were compared between the pregnant and the non pregnant group.

Results

Out of 135 women, 57(42.22%) became pregnant.Patients in the pregnant group were younger(29.67±2.76 years v/s 30.94±4.29years) and had low body mass index (BMI) as compared to the non pregnant group although the difference was not statistically significant. Patients in the pregnant group had comparable hormonal profile but higher antral follicle count(AFC) than the non pregnant group. The number of follicles formed, oocytes retrieved and embryos formed (14.86±2.52v/s11.42±3.16; 12.54±2.30v/s6.87±2.63; 10.02±1.92v/s4.47±1.81) were significantly higher in the pregnant group as compared to the non pregnant group. Average number of embryos transferred in the pregnant group was 2.61±0.56 while in the other group was 1.90±0.59 and the difference was significant. Endometrial thickness and vascularity indices were similar between the two groups.

Conclusion

Female age, duration of infertility, AFC, number of oocytes retrieved, number of embryos formed and transferred areuseful predictorsof pregnancyafter IVF. However, further large and better quality studies are necessary to identify the actual predictive factors affecting the cycle outcome.

INTRODUCTION

Since the reports of the first IVF baby born in 1978 with the efforts of Steptoe and Edwards, IVF has become a major treatment option for infertile couples when all other fertility treatments have failed but still it remains a challenge with low success rates on the first attempt. Various factors affecting the success rate of IVF include female age, body mass index(BMI), infertility duration, hormone levels, ovarian reserve, number of eggs retrieved, endometrial thickness and pattern, number and quality of embryos transferred etc.. An individualized, patient-centered approach to controlled ovarian hyperstimulation is a key factor in optimizing results of an IVF cycle which includes careful selection of stimulation protocols, adjusting gonadotropin dose according to response so as to avoid hypo or hyper response, careful cycle monitoring and appropriate timing for hCG injection. Although many studies have been done to identify predictors of IVF outcome, there is still no real consensus**.** **(**1,2) Both clinical and laboratory procedures are being constantly improved to increase the success rate of IVF. The objective of this study was to determine the factors affecting the success of a fresh IVF cycle.

MATERIAL AND METHODS

This was a prospective study conducted at the IVF unit of Obstetrics and Gynecology Department of Institute of Kidney Diseases and Research centre-Institute of Transplantation Sciences (IKDRC-ITS), Civil hospital, Ahmedabad from Jan 2014 to Dec 2014. A total of 135 women attending the hospital for vitro fertilization treatment were enrolled in the study. Inclusion criteria were fresh IVF-ET cycles, age 20-40 years and a normal uterine cavity on office hysteroscopy. Exclusion criteria were presence of a systemic disease, uterine anomalies, known endometrial pathology, cryopreserved cycles and cycles with donor oocytes.

An informed consent was obtained from all the women participating in the study. Detailed evaluation of the female and male partner was done. Day 2 hormonal profile included serum FSH, LH, estradiol, TSH and prolactin levels. Baseline transvaginal ultrasonography (TVS)was done using Volusen E8 USG machine with 7.5 MHz transvaginal probe to rule out presence of ovarian cyst, any adnexal or uterine pathology and to assess ovarian size, volume and antral follicle count (AFC).Office hysteroscopy was done in all the patients prior to IVF to confirm normal uter-

ine cavity.

All the women were put on either long GnRH agonist, short agonist or antagonist protocol for IVF and controlled ovarian hyperstimulation was done with recombinant follicle-stimulating hormone (rFSH) or human menopausal gonadotrophin (HMG) starting on day 2 or 3 of the cycle. Usual starting dose was 150-225 IU and further dose adjustment was done according to the patient's response to stimulation which was evaluated by serial TVS examinations. When at least three follicles with a diameter of ≥18 mm had reached, purified urinary human chorionic gonadotrophin (hCG) injection 10,000 IU was administered intramuscularly for final oocyte maturation and trigger. Number of follicles, endometrial thickness, pattern and vascularity were assessed by transvaginal ultrasound on the day of hCG injection. Oocyte retrieval was performed 34–36 h after hCG administration and embryos transfer was done on day 3 after oocyte retrieval followed by luteal phase support with vaginal micronized progesterone capsules 200mg thrice daily .Serum β hCG values > 50 m IU/ml after 14 days of embryo transfer were considered as positive for pregnancy .In this study, the outcome of interest was clinical pregnancy defined as presence of one or more intrauterine gestation sac on TVS at 6–7 weeks of gestation. All other cycle outcomes were classified as non pregnant.

STATISTICAL ANALYSIS

Statistical analysis was done using data analysis software system SPSS V20. Continuous data were expressed as mean ± SD. P-value <0.05 was considered statistically significant. Independent T - Test , Mann-Whitney test and Chi Square test were used to calculate statistically significant value. i.e. P-value. NS represented non-significant difference between two groups.

RESULTS

Out of 135 women undergoing fresh IVF-ET cycle, 57(42.22%) became pregnant. Baseline characteristics of the patients in pregnant and non pregnant group are shown in table1.Patients in the pregnant group were younger than in the non pregnant group (29.67±2.76 years v/s 30.94±4.29years) though the difference was not statistically significant. Mean BMI in the pregnant group was 24.42±2.08 Kg/m^2 while in the non pregnant group was 25.09±2.99 Kg/m^2. Majority of the patients had primary infertility in both the groups but patients in the non pregnant group had significantly longer duration of infertility.

Baseline hormonal profile of the patients in both the groups is shown in table 2.Mean FSH (6.24±1.83 v/s 6.80±2.98 IU/mL) and LH (3.85±1.51 v/s 4.13±2.23 IU/mL) levels were comparable between the two groups. The total antral follicle count (AFC) in the pregnant group (15.96±2.01) was significantly higher than in the non pregnant group (11.53±2.82).The total gonadotropin dose required for stimulation per day was significantly lower in the pregnant group .The duration of stimulation was also lower in the pregnant as compared to non pregnant group (9.61±0.92 v/s 10.01±1.42 days) although the difference was not significant. There was a significant difference in number of follicles formed, number of oocytes retrieved, number of embryos formed (14.86±2.52v/s 11.42±3.16, 12.54±2.30v/s6.87±2.63, 10.02±1.92v/s4.47±1.81)between the two groups. Average number of embryos transferred in the pregnant group was 2.61±0.56 while in the other group was 1.90±0.59 and the difference was significant. (Table 3)

The mean endometrial thickness and volume were comparable between the two groups .Endometrial vascularity indices like vascularization index(VI), flow index(FI) and vascularization flow index(VFI) as calculated by 3 D power Doppler histogram were not significantly different in the two groups as shown in table 4.Out of 135 women, long GnRH agonist protocol for stimulation was used in 70 (51.85%), short agonist protocol in 35(25.92%) and antagonist protocol in 30 (22.22%) women. Pregnancy rate in the long protocol was 41.42% which was higher than the short protocol (40%) but lower than the antagonist protocol (46.66%).

The most common indications for IVF were tubal factor in 53 (39.25%) patients followed by male factor in37 (27.4%) and ovulatory dysfunction in 25(18.5%) patients (Table 5).

DISCUSSION

Various advances in assisted reproductive technologies have led to a significant improvement in the efficacy of these treatments over the past decades. Initially , IVF was advocated as a treatment for women with severe tubal disease but with improved efficacy ,the indications for IVF have expanded and now, it is the most effective treatment option for couples with multifactorial infertility problems.(3)

A large number of studies have reported on the factors predicting chances of pregnancy after IVF but there is still no consensus .Identification of the predictive factors affecting cycle outcome can help to prevent overtreatment and still maximizing the chances of pregnancy.

Various studies have suggested that there is an age-related decline in the success of IVF. With increasing age, there is a progressive decline in the ovarian reserve with decrease in both the quantity and quality of oocytes and this may negatively affect the success of IVF.(4) In our study ,patients in the pregnant group were younger as compared to the non pregnant group though the difference was not significant . The chances of achieving a successful pregnancy decreases with increasing BMI. As such, women with high BMI have a higher risk of reproductive failure and lower chances for successful embryo implantation after IVF. (5)In our study also, patients in the pregnant group had low BMI as compared to the non pregnant group.

Maseelall et al revealed that AFC is better than basal FSH as a predictor of ovarian response and IVF outcome. (6) Various studies have shown negative association between the chance of pregnancy and female age, duration of infertility and basal FSH levels. The association with the age was stronger than that with duration of infertility. (7, 8)

Studies by Ottosen et al. and Sabatini et al. showed that the chances of pregnancy were significantly lower in women with FSH more than 10 IU than in women with FSH concentrations of less than 10 IU.(9,10) However in our study, FSH levels were not significantly different between the two groups. The chances of pregnancy increase with increase in the number of oocytes retrieved. (11)These results are similar to that of our study.

Several randomized controlled trials have shown that transfer of more than 2 embryos doubles the chances of pregnancy but also increases the risk of multiple pregnancy as compared to single embryo transfer .(12)The number of embryos transferred has a positive correlation with the chances for successful embryo implantation and pregnancy outcome and these results are similar to our study .(13)Various studies have been done to assess the role of endometrial blood flow in predicting the chances of pregnancy but the results are conflicting.In our study, endometrial vascularity as assessed by 3 D power Doppler was similar between the pregnant and the non pregnant group. These results are similar to Ernest et al who showed that endometrial and sub endometrial vascularity on the days of HCG and embryo transfer were not predictive of pregnancy .(14)

CONCLUSION

Female age, infertility duration, AFC, number of oocytes retrieved, number of embryos formed and number of embryos

Volume : 4 | Issue : 8 | Aug 2015 • ISSN No 2277 - 8179

transferred can be useful as predictors of IVF cycle outcome. However further large studies are required to establish the definitive predictive factors affecting the outcome of an IVF-ET cycle.

Table. 1 Baseline characteristics

	Pregnant (N=57)	Non pregnant (N=78)	P- value
Age(Years)	29.67±2.76	30.94±4.29	0.18 (NS)
BMI(Kg/m^2)	24.42±2.08	25.09±2.99	0.13 (NS)
Duration of infertility (years)	5.70±2.04	8.04±4.52	<0.01*
Type of infertility			
Primary	45 (78.94%)	57 (73.07%)	0.43 (NS)
Secondary	12 (21.05%)	21 (26.92%)	

*represents significant difference between these groups.

Table 2 .Baseline (Day2) hormonal profile

	Pregnant (N=57)	Non pregnant (N=78)	P value
FSH(IU/mL)	6.24±1.83	6.80±2.98	0.21 (NS)
LH(IU/mL)	3.85±1.51	4.13±2.23	0.39 (NS)
TSH(μg/dl)	1.94±0.94	2.24±1.22	0.12 (NS)
Prolactin(ng/ml)	10.66±4.73	12.85±6.25	0.03*
Estradiol (pg/ml)	41.09±15.95	44.19±31.08	0.49 (NS)

*represents significant difference between these groups.

Table 3 .Cycle characteristics

	Pregnant (N=57)	Non pregnant (N=78)	P value
AFC	15.96±2.01	11.53±2.82	<0.01*
Dose of gonadotropins/ day(IU)	238.16±28.78	254.81±38.87	<0.01*
Days of stimulation	9.61±0.92	10.01±1.42	0.25 (NS)
No. of follicles	14.86±2.52	11.42±3.16	<0.01*
No. of oocytes retrieved	12.54±2.30	6.87±2.63	<0.01*
No. of embryos formed	10.02±1.92	4.47±1.81	<0.01*
No. of embryos transferred	2.61±0.56	1.90±0.59	<0.01*

*represents significant difference between these groups.

Table 4 .Endometrial thickness and vascularity indices

	Pregnant (N=57)	Non pregnant (N=78)	P value
Endo thickness (mm)	8.07±0.73	8.28±1.51	0.79 (NS)
Endo vol.(cm^3)	2.62±1.41	2.38±1.16	0.24 (NS)
VI(%)	3.48±4.61	2.97±3.82	0.35 (NS)
FI(0-100)	24.01±3.39	23.32±3.61	0.26 (NS)
VFI(0-100)	0.95±1.33	0.83±1.12	0.39 (NS)

Table 5.Indications for IVF

Indication	Total number (N=135)	Percentage (%)
Tubal factor	53	39.25%
Ovulatory dysfunction	25	18.5%
Hypogonadotropic hypogonadism	3	2.22%
Unexplained	10	7.40%
Male factor	37	27.40%
Combined factors	7	5.18%

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