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ASSISTED REPRODUCTION TECHNOLOGIES

Prognostic value of first IVF cycle on success of a subsequent cycle

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Abstract
Objective To determine whether a live birth or miscarriage in a previous IVF cycle is predictive of success in a subsequent cycle.
Design Retrospective study
Setting Private IVF unit
Patients 1141 couples having a second IVF cycle.
Intervention 3 groups; Group I: women who had a live birth in the first cycle, Group II those who had a miscarriage, Group III, women who had a negative pregnancy test in their first cycle.
Outcome measures Pregnancy (PR), Live birth (LBR) & miscarriage rates in the second cycle.
Results For women<than 40: PR was 46.4% (368/793), miscarriage rate was 29.9% and the LBR was 32.5% (258/793). Women in groups I & II had a statistically higher PR than those in group III 63.3% v 55.2% v 41.9% respectively. LBR was higher 45% v 37.8 v 29.6% respectively. Miscarriage rate was similar.

For women 40 years and older: The PR was 21.0% (73/348), miscarriage rate was 52.1% (38/73) and the LBR was 10.1% (35/348).There was no significant difference in PR among women in groups I, II & III. The LBR and miscarriage rates were similar in all groups.

Conclusion Young women who had a live birth and those who experienced an early miscarriage after IVF have a greater likelihood of achieving a live birth in a second cycle. Outcome of first IVF cycle however does not predict subsequent IVF success in older women.

Keywords IVF/ICS outcome · Assisted reproduction · Miscarriage · Prognosis

Capsule Whilst previous pregnancy (live birth or miscarriage) may be a positive marker for IVF success in young women, this may not be the case among women 40 years and over.

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Introduction

State funding for IVF in the UK is sparse. In spite of the recommendations by the National Institute of Health and Clinical Excellence [1], most health commissioners will only fund a single IVF cycle per couple [2]. Couples who wish to have further IVF treatment would usually have to self-fund. Previous IVF success may motivate a couple to invest on a further IVF cycle. Although a miscarriage is devastating, it may also be positively motivating to some couples who may be inclined to try again with the hope that the next cycle may be better. As IVF remains physically, emotionally and economically expensive, couples embarking on further treatment, seek guidance from clinicians to determine prognosis before investing in another cycle. Earlier studies suggest that women, who had a live birth or miscarriage in their first IVF cycle have better prognosis for success in a subsequent cycle compared to women who had a negative pregnancy test [3, 4]. These previous studies mainly focused on young women and the result may not be applicable to older women. In this study we reviewed treatment outcome to determine whether a live birth or miscarriage in a previous IVF cycle is predictive of success in a second cycle, and to determine if this is true for older women as well as for young women.

Materials and methods

We prospectively collect and store data of all patients undergoing IVF/ICSI in our unit in a Medical System for IVF (MedicalSys, London, UK). We analysed data on 1141 women who had their first and second IVF treatment cycles at the Lister Fertility clinic from January 2005 to December 2008. Three groups were identified based on the outcome of the first IVF treatment cycle. Group I consists of women who had a live birth in the first cycle, (n=75), Group II; those who had an early miscarriage in the first cycle (n=223), & Group III, consists of women who had a negative pregnancy test in their first cycle (n=843). Treatment outcomes of the second cycle were analysed and compared between the groups. Outcome measures include pregnancy, live birth and miscarriage rates. The women were further divided into 2 groups based on age (<40 and>40 years, and data was analysed to compare outcome between women in these age groups.

IVF stimulation

In brief, the IVF treatment protocol includes ovarian stimulation, with either recombinant FSH, human menopausal gonadotrophin or urinary FSH. Patients were down regulated with either Nafarelin or Buserelin at mid luteal phase. When follicles reached pre-ovulatory size (18 to 22 mm), 10,000 IU of hCG was administrated. Oocytes were aspirated using trans-vaginal ultrasound guidance 34 to 36 h after hCG administration. For fertilisation, standard insemination or ICSI was performed as clinically appropriate. Embryo culture was performed using a sequential micro-drop system at an atmosphere of 5–6% CO_2 at 37°C. SAGE sequential cleavage media (SAGE In-vitro Fertilization Inc. Trumbull, Connecticut) was used for embryos on day 1–3, and patients who met our criteria for extended culture continued to the blastocyst stage. 400 mg cyclogest pessary was administered to all the patients for luteal support. A pregnancy test was performed 2 weeks following embryo transfer and a transvaginal ultrasound scan at 6 weeks to determine the number of gestation.

In this study a pregnancy was defined as a positive serum or urine HCG test and a sac on ultrasound scan, or an ectopic pregnancy. Miscarriage was defined as pregnancy loss following ultrasound confirmation of an intrauterine gestation sac. A live birth was defined as a pregnancy resulting in a viable infant. Twins were counted as one live birth. The study was approved by the local ethics committee.

Data analysis

Data was collected in Medical System for IVF (MedicalSys, London, UK) and analysed by Statistics Package for Social Sciences (SPSS, Surrey, UK). Descriptive statistical analysis was performed initially to examine the normal distribution of all continuous variances for parametric statistical tests. Chi-square Cross Tabulation test was used to analyse the significant difference in pregnancy rates and live birth rates between the groups. Statistical significant was set at $P<0.05$.

Results

1141 women embarked on a second IVF cycle; 441 got pregnant (Pregnancy rate (PR)=38.7%). Women in groups I (live birth in first cycle) & II (miscarriage in first cycle) had

Table 1 Treatment outcome in 2nd IVF cycle in women who failed to achieve a positive pregnancy in 1st IVF cycle compared with those who miscarried or had a live birth after their 1st IVF cycle

	Not pregnancy in 1st cycle (Group 3)	Miscarriage in 1st Cycle (Group 2)	Live birth (Group 1)	*P*-value
Number of patients	843	223	75	NA
Basal FSH levels IU/L±SD	7.26±6.9	6.11±5.2	7.13±2.1	NS 0.17
Mean age±SD	37.9±4.4	36.9±4.2	36.6±3.9	NS 0.46
Average no. of oocytes collected±SD	8.28±5.9	9.05±5.4	10.1±6.1	NS 0.11
Average no of normal fertilized embryos±SD	6.18±3.7	6.65±2.6	7.11±3.9	NS 0.21
Average no of embryos transferred±SD	1.63±0..85	1.66±0.75	1.67 ±).71	NS 0.67
Pregnancy rate (%)	**34.5%** (291/843)	**48.0%** (107/223)	**57.3%** (43/75)	0.001
Miscarriage rate (%)	33.7% (98/291)	33.6% (36/107)	32.6% (14/43)	NS 0.907
Live birth rate (%)	**22.9%** (193/843)	**31.8%** (71/223)	**38.7%** (29/75)	0.001

NS=difference not statistically significant ($P>0.05$)

NA=not applicable.

Table 2 Treatment outcome in 2nd IVF cycle in women aged <40 years, who failed to achieve a positive pregnancy in their 1st IVF cycle compared with those who miscarried or had a live birth after their 1st IVF cycle

	Not pregnancy in 1st cycle	Miscarriage in 1st Cycle	Live birth	*P*-value
Number of patients	561	172	60	NA
Basal FSH levels IU/L±SD	6.10±5.4	4.97±4.6	5.92±2.5	NS
Mean age±SD	35.2±3.4	34.8±3.5	33.4±3.8	NS
Average no. of oocytes collected±SD	9.16±6.1	9.34±5.5	11.7±6.0	NS
Average no of fertilized embryos±SD	7.21±2.8	6.95±1.5	8.01±3.1	NS
Average no of embryos transferred±SD	1.43±0.79	1.76±0.48	1.78±0.41	NS
Pregnancy rate (%)	41.9% (235/561)	55.2% (95/172)	63.3% (38/60)	<0.001
Miscarriage rate (%)	29.4% (69/235)	31.6% (30/95)	28.9% (11/38)	NS
Live birth rate (%)	29.6% (166/561)	37.8% (65/172)	45.0% (27/60)	0.015

NS difference not statistically significant (*P*>0.05)

NA not applicable

a higher PR than those in Group III (negative pregnancy test in first cycle). 57.3% (43/75), vs 48.0% (107/223), vs 34.5% (291/843) respectively; (p=0.00). There was also a statistically significant difference in the live birth rate (LBR) between the 3 groups. Women in Groups I & II had a higher LBR in their second cycle compared to those in III; 38.7%(29/75) vs 31.8% (71/23) vs 22.9% (193/843) respectively (p=0.01). The rate of miscarriage in the second cycle was not significantly different in the 3 groups (32.6% v 33.6% v 33.7% respectively). (Table 1)

When only women age less than 40 were considered Of 1141 women in the study, 793 were age<40 years. In this cohort, the PR was 46.4% (368/793), miscarriage rate was 29.9% and the LBR was 32.5% (258/793). Women in groups I & II had a statistically higher PR than those in group III (63.3% v 55.2% v 41.9% respectively (p=0.00). Similarly the LBR was higher (45% v 37.8 v 29.6% respectively, p=0.015). There was however no difference in the miscarriage rate in the 3 groups. (28.9% v 31.6% v 29.4% respectively). (Table 2).

When only women age 40 years or older were analysed Of 1141 women, 348 were age >=40 years. The PR in this older cohort was 21.0% (73/348), miscarriage rate was 52.1% (38/73) and the LBR was 10.1% (35/348).

There was no significant difference in PR among women in groups I, II & III (33.3 v 23.5 v 19.9% p=0.44). The LBR was similar in the three groups (13.3 v 11.8 v 9.6% respectively). There was no difference in the miscarriage rates in the three groups (Table 3).

Discussion

IVF treatment is stressful and costly. The emotional stress may even be greater in women who achieve pregnancy but

Table 3 Treatment outcome in 2nd IVF cycle in women aged >=40, who failed to achieve a positive pregnancy in 1st IVF cycle compared with those who miscarried or had a live birth after their 1st IVF cycle

	Not pregnancy in 1st cycle	Miscarriage in 1st Cycle	Live birth	*P*-value
Number of patients	282	51	15	NA
Basal FSH levels IU/L±SD	9.02±6.9	6.10±4.2	11.97±2.6	NS
Mean age±SD	42.07±2.4	41.58±1.3	40.4±1.2	NS
Average no. of oocytes collected±SD	6.53±5.0	7.96±4.9	7.80±5.6	NS
Average no of fertilized embryos±SD	4.13±2.2	5.63±2.2	4.31±3.1	NS
Average no of embryos transferred±SD	1.77±1.02	1.95±0.75	1.93±0.45	NS
Pregnancy rate (%)	19.9% (56/282)	23.5% (12/51)	33.3% (5/15)	NS
Miscarriage rate (%)	51.8% ((29/56)	50.0% (6/12)	60.0% (3/5)	NS
Live birth rate (%)	9.6% (27/282)	11.8% (6/51)	13.3% (2/15)	NS

NS difference not statistically significant (P>0.05)

NA not applicable

unfortunately suffer miscarriage. There is a tendency for such couple to pull resources together to try a further IVF with the hope that outcome will be better. This expectation is not unfounded as studies have shown that women who achieve a pregnancy (whether this is a live birth or a miscarriage) in a previous IVF cycle have a better chance of conceiving in subsequent cycles [3, 4]. Our data supports this assertion and is consistent with these previous studies. From our data, women who had a live birth or suffered a miscarriage following their first IVF cycle had a live birth rate of 38.7% and 31.8% respectively, significantly higher than 22.9% for women who had a negative pregnancy test following their fist IVF. However this assertion seems to apply only to young women. Among our young women age below 40, those who had a live birth or suffered a miscarriage following their first IVF had a significantly higher chance (45% and 37.8% respectively) of having a live birth in a subsequent IVF cycle compared to 29.6% among women who had a negative pregnancy test in the first cycle. Interestingly our results suggests that among older women (>=40 years), the situation is different. A miscarriage or even a live birth in a first IVF cycle does not confer a better prognosis in the second cycle. In this older cohort, we did not find any significant difference in pregnancy or live birth rates in women in all three groups. This finding is consistent with results from one previous study [5]. Although the authors from this also included data from thaw transfer cycles, as well as data from gamete intrafallopian transfer, their results were similar to ours and showed that an early pregnancy loss is not predictive of a successful delivery in subsequent IVF cycles for women older than 40 years. This observation is important when counseling women prior to subsequent IVF cycles.

Sneeringer et al. [5], suggested that the differences in the findings for younger and older women may be due to the different aetiologies for infertility between these two groups. They suggest that whilst an early pregnancy loss may represent a proven ability to become pregnant in younger women with varied aetiologies of infertility, for older women where the aetiology is usually diminished ovarian reserve, early pregnancy loss does not select for a group with a more favourable prognosis in this older cohort.

We did not find any significant difference in the rate of miscarriage among women in the three groups. Women who had a miscarriage in their first IVF are not at increased risk of suffering a further miscarriage in a subsequent cycle compared to women who had a live birth.

In conclusion, whilst previous pregnancy (miscarriage or live birth) may be a positive marker for success in a subsequent cycle in young women, this may not be the case among women over 40 years of age. In this older cohort, a live birth or previous pregnancy loss is not predictive of a successful delivery in a subsequent IVF cycle. This information should enable clinicians to effectively counsel couples and guide them as they make informed decisions prior to committing more resources towards further IVF cycles.

Conflict of interest All the authors declare no conflict of interest.

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