Assisted Reproduction – The Role of Maternal Age

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Summary: The aim of this study is to evaluate the effect of maternal age on the outcome of in vitro fertilisation – embryo transfer (IVF-ET). Hundred women aged 25- 45 years were evaluated. Results showed that the number of oocytes retrieved, the number of oocytes fertilised, the clinical pregnancy rate and live birth rate steadily decreased in women aged 36 years and above in comparison to those aged 25 to 30 years. Hence, the success rates of IVF declined significantly in women aged 36 years and above. The absence of pregnancy in women aged 40 years and above suggest that these women are unlikely to benefit from IVF.

Introduction

Pregnancy rates are known to decline with increasing maternal age after standard IVF-ET treatment (Padilla & Gorai, 1989), and standard IVF-ET using intracytoplasmic sperm injection (Abdelmassih et al, 1996). Nevertheless, it is still somewhat controversial whether maternal age during IVF has an effect on oocyte production, oocyte quality, number and quality of embryos transferred, and uterine receptivity.

Embryo implanting ability and survival gradually decline after 30 years of age. After 40 years of age, this decline is more than two-thirds (Hull et al, 1996). Although many studies have shown that there is no difference in fertilisation rates of younger and older women (Romeu et al, 1987), significant differences have been consistently found in their pregnancy outcome (Penzias et al, 1991). All these factors were evaluated in this study.

Material and Methods

160 IVF cycles were conducted in hundred women aged 25 to 45 years (mean age 35 ± 4.6) at the Assisted Conception Unit, Mahavir Hospital and Research Centre, Hyderabad from April 1995 to December 1997. The characteristics of the study group are shown in Table 1.

Table –1.

Characteristics of the couples who underwent IVF (n=100)

Age of women (years)	35 ± 4.5 (25-45)
Female Infertility Factor:	70
Tubal pathology	59
Endometriosis	11
Male Infertility Factor	30

The patients were down regulated with LHRH analogue (Busereline acetate, Suprefact, Hoechest, Frankfurt Germany), until the day of hCG administration. Estradiol E2 levels were measured by radioimmunoassay (RIA). When E2 levels fell to less than 50 pmols/L (conversion factor to SI Units 3.671), the patients were stimulated with pure FSH (Metrodin, Laboratories Serono, U.K.). Follicular development was monitored by daily ultrasound (US) and E2 measurements. An injection of 10,000 IU of hCG (Profassi, Laboratories Serono, U.K.) was given when the leading follicle reached 18 mm. Transvaginal follicular aspiration under ultrasound guidance was carried out 34 hours after hCG administration. Uterine ET s were performed 2 days later. Currently, the number of embryos replaced are two for women less than 30 years of age and three for women over 30 years of age, to minimize the risk of multiple pregnancies in younger women. All patients were given luteal phase support with progesterone, beginning on the day of transfer. We defined a clinical pregnancy as the presence of a gestational sac by US.

Results

In the present study, the number of oocytes retrieved, the number of oocytes fertilised, the clinical pregnancy rates and the pregnancy outcome following IVF, were found to decrease steadily with increasing maternal age. The difference was statistically significant between the two age groups-25 to 30 years and 36 years and above. The results of couples who underwent IVF are given in Tables 2-4.

The number of oocytes retrieved declined rapidly from a mean of 21 in the age group 25 to 30 years to a mean of 2

Table – II
Results of couples who underwent IVF (n=100)

Characteristics	Range	Mean (SD)
No. of oocytes retrieved	0-42	18 (8.5)
No. of oocytes fertilised	0-32	14 (6.2)
No. of embryos transferred	0-5	3 (1.5)
No. of embryos implanted	0-3	0.6 (0.7)

Table – III
Pregnancy outcome (n=100)

Characteristics	Number of Patients	% of Patients
Positive pregnancy test	30	30
Clinical pregnancy	22	22
Live births	13	13
No response	35	35

Table – IV
Effect of age on the outcome of IVF.

	Age Groups (years)			
Characteristics	25-30	31-35	36-40	40-45
No. of oocytes retrieved	0-42 (21)*	0-30 (15)	0-11 (5.5)	0-4 (2.0)
No. of oocytes fertilised	0-32 (16)**	0-22 (11)	0-5 (2.5)	0-2 (1.0)
No. of positive pregnancies	13	9	2	1
No. of clinical pregnancies	9***	7	2	0

Values represent the range
Values in parentheses represent mean values
* $p < 0.5$ ** $p < 0.05$ *** $p < 0.005$ (level of significance between age groups 25-30 and 36 –40 years).

in the age group 40 to 45 years ($p<0.5$).

Likewise, the number of oocytes fertilised also declined from a mean of 16 to a mean of 1 in these two age groups. These two factors have contributed significantly towards the low rate of success of IVF in the latter age group.

In the age group 30 to 40 years, the number of oocytes retrieved and the number fertilised decreased markedly in those aged 36 years and above. This again resulted in lower pregnancy rates in this group. However, in women aged 31 to 36 years, the results of IVF were encouraging, so far as the number of clinical pregnancies demonstrated, but the live birth rates were far lower than the age group 25 to 30 years.

Discussion

It has been shown that women aged 40 years can achieve similar fertilisation rates as their younger counterparts (Romeu et al, 1987) despite having fewer eggs retrieved as a consequence of ovarian depletion. However pregnancy rates have been consistently much lower in these women (Scott et al, 1995). We categorised the women according to age to see if there was a change in effect.

The observation of lower pregnancy rates (PR) in women more than 35 years of age could also be attributed to low quality and degenerative changes in oocytes. It has recently been shown that the age related decline in fertility might be due to degenerative changes in oocytes (Alvin et al, 1997). In the same study, it has been concluded that, a decline in the number of oocytes recovered with age may be of less importance than the decline in oocyte quality.

In another study, a total of 2931 cycles of IVF and 1826 cycles of GIFT were analysed using autologous eggs (Bopp et al, 1995). For patients undergoing IVF, the cancellation rate for initiated cycles, as a result of poor response, showed significant differences among the age groups-38.3% in women aged 29 to 39 years, 49.5% in women aged 40 to 43 years and 69.5% in women aged 44 to 45 years.

In our study, the number of clinical pregnancies in women aged 40 to 45 years was nil. The highest success rate was seen in women aged 25 to 30 years.

Conclusions

In our study, the success rate of IVF declined significantly in women aged 36 years and above. Women aged 40 years and over did not benefit from IVF. Hence it can be concluded that the success rates of IVF are significantly influenced by maternal age. It is essential to stress that couples should consult a qualified infertility specialist before an advanced maternal age adds to the problem of infertility. Thus, timely referral and consultation would help both the couple and the specialist achieve a high degree of success using IVF-ET.

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