THE UNIVERSITY OF ARIZONA

COLLEGE OF MEDICINE PHOENIX

The Test Tube Baby: Out of Reach or Out of Luck?

A Retrospective Look at the Impact of Basal FSH and Age on In Vitro Fertilization Success in a Clinic Operating Without Laboratory Value Thresholds or Age Limits?

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Introduction

As global rates of assisted reproductive technology (ART) utilization and success increased over the years, factors were assessed in order to determine ways to both increase successful outcomes and reduce expensive repeat therapies for clients who would likely not benefit. Two of the most consistent factors evaluated and found to affect ART success are advancing age and basal level of follicle stimulating hormone (FSH).

It is important to understand the impact of age on ART success rates as the age of first birth is postponed in many women in America. In fact, in the early 2000s, nearly 20% of all women utilizing ART in America were over 40 years old.

The level of FSH is traditionally low in women with normal fertility. An elevated FSH has been interpreted in many studies to indicate a diminished ovarian reserve, which has been extrapolated to women seeking IVF as a poor prognostic factor. However, it is unclear what, if any, cutoff should be applied to in vitro fertilization therapy.

This study assessed the impact of age and FSH on in vitro fertilization outcomes at The Arizona Center for Fertility Studies in Scottsdale, AZ, an ART clinic, that does not have treatment thresholds based on age or laboratory FSH values.

Methods

This was a retrospective study of IVF patients at the clinic between the years 1999- 2007. There was no cutoff for age or FSH level.

Outcomes were defined as confirmed intrauterine gestation, and live birth. The data was compiled and analyzed in Microsoft Excel and ANOVA as a tool on EXCEL. The probability level for statistical significance was taken to be $p<0.05$.

Among the 1,388 cycles included in this analysis, the mean age of the patients was 35.13 ± 4.9 years (mean ± SD). The mean maximal basal FSH detected on cycle day 1-4 in this analysis, was 11.6 ± 6.98 mIU/mL.

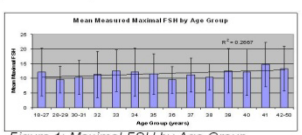

Figure 1: Maximal FSH by Age Group

Results

The maximal basal FSH by age group showed no significant change as age increased (Figure 1). Interestingly, there were two age groups, 36 and 38 year olds, that had a significantly lower maximal FSH than the rest of the age groups ($p<0.05$ when compared to all other ages).

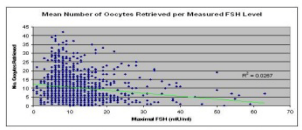

Figure 2: Number of Oocytes Retrieved by FSH level

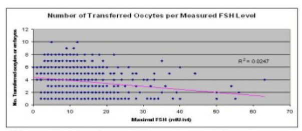

Figure 3: Number of Transferred Oocytes Per Measured FSH Level

Outcomes by Age

The pregnancy rate (PR) as determined by ultrasound confirming an intrauterine gestation showed a decrease as age increased above 35. At ages 36, and then at age 40, the pregnancy rates decreased significantly ($p<0.05$, and $p<0.001$ respectively) (Table 1).

The live birth rate(LBR) also decreased with increase in age, much the same way that pregnancy rate decreased. There was no difference in the live birth rates between the years 18- and 37.

At ages 38 and then over the age of 40, the LBR decreased significantly. ($p<0.05$, and $p<0.001$ respectively).

Outcomes by FSH level

The number of oocytes and transferred embryos decreased as FSH level increased (Figures 2 and 3). Interestingly, there was no significant difference between pregnancy rates or live birth rates between the five FSH groups (P-value =0.06 for all groups)(Table 2).

Table 1: Cycle Outcome Based on Age

Age, years	No. cycles N = 1388	%	No. oocytes retrieved	No. oocytes or embryos transferred	Pregnancy Rate (%)	Live Birth Rate(%)
18-27	90	6.48	$14.29 \pm 7.79^{\chi}$	3.43 ± 1.81^{1}	41.1^{a}	38.9^{f}
28-29	85	6.12	$13.21 \pm 7.52^{\chi}$	4.02 ± 1.69^{1}	32.9^{a}	27.1^{f}
30-31	148	10.66	$13.1 \pm 7.5^{\chi}$	4.04 ± 1.86^{1}	29.05^{a}	27.7^{f}
32	97	6.98	$11.9 \pm 8.1^{\chi}$	3.55 ± 1.96^{1}	28.8^{a}	24.7^{f}
33	106	7.63	$11.06 \pm 6.6^{\psi}$	3.96 ± 1.77^{1}	31.1^{a}	29.2^{f}
34	97	6.98	$10.52 \pm 6.59^{\psi}$	4.11 ± 2.03^{1}	34^{a}	28.8^{f}
35	115	8.28	$10.13 \pm 6.2^{\phi}$	3.79 ± 2.07^{1}	20^{b}	18.2^{g}
36	68	4.89	$10.29 \pm 6.6^{\psi}$	4.15 ± 2.04^{1}	19.1^{c}	17.6^{g}
37	97	6.98	$11.74 \pm 8.68^{♀}$	4.18 ± 2.17^{1}	24.7^{b}	20.6^{g}
38	94	6.77	$9.21 \pm 6.6^{\Upsilon}$	3.74 ± 2.14^{1}	22.3^{c}	18^{h}
39	106	7.63	$7.07 \pm 4.09^{\Upsilon}$	3.98 ± 2.11^{1}	19.8^{c}	16.9^{h}
40	98	7.06	$8.98 \pm 5.58^{\Upsilon}$	4.57 ± 2.49^{1}	14.3^{d}	13.2^{i}
41	71	5.11	$6.78 \pm 5.32^{\Upsilon}$	3.5 ± 2.25^{1}	7^{e}	7.0^{j}
42-50	116	8.35	$4.65 \pm 3.55^{\Upsilon}$	2.88 ± 1.92^{2}	6^{e}	3.4^{j}

Values are expressed as mean ± SD. Values in parentheses are percentages.
1 denotes $p=0.06$
2 denotes $p<0.001$ when compared to all other age groups.
χ denotes $p=0.2$
ψ denotes $p<0.05$ when compared to age groups 18-27, 28-29, 30-31, and 32.
ϕ denotes $p<0.01$ when compared to age groups 18-27, 28-29, 30-31, and 32.
♀ denotesa $p=0.17$ when compared to age groups 18-27, 28-29, 30-31, and 32.
Υ denotes $p<0.001$ when compared to age groups 18-27, 28-29, 30-31, and 32.
a denotes a $p=0.46$
b denotes $p=0.06$ when compared to age groups 18-27, 28-29, 30-31, 32, 33 and 34.
c denotes $p<0.05$ when compared to age groups 18-27, 28-29, 30-31, 32, 33 and 35.
d denotes $p<0.01$ when compared to age groups 18-27, 28-29, 30-31, 32, 33 and 35.
e denotes $p<0.001$ when compared to age groups 18-27, 28-29, 30-31, 32, 33 and 35.
f denotes $p=0.3$
g denotes $p<0.1$ when compared to age groups 18-27, 28-29, 30-31, 32, 33 and 34.
h denotes $p<0.05$ when compared to age groups 18-27, 28-29, 30-31, 32, 33 and 35.
I denotes $p<0.01$ when compared to age groups 18-27, 28-29, 30-31, 32, 33 and 35.
j denotes $p<0.001$ when compared to age groups 18-27, 28-29, 30-31, 32, 33 and 35.

Table 2: Cycle Outcome Based on Mean Maximal FSH

Basal FSH	# of cycles	Age	No. oocytes retrieved	No. oocytes or embryos transferred	Pregnancy Rate (%)	Live Birth Rate (%)
<5	125	35.2±4.34	11.35 ± 7.78^{1}	4.15 ± 2.28^{1}	16.8^{a}	12.0^{b}
6-10	644	$34.7 \pm 4.87^{*}$	11.60 ± 7.28^{1}	4.1 ± 2.03^{1}	26.7	22.9
11-15	379	35.6±4.91	$8.88 \pm 6.2^{**}$	$3.70 \pm 2.02^{*}$	24.0	21.6
16-20	128	35.3±5.00	$9.14 \pm 7.15^{\Psi}$	3.56 ± 1.85^{2}	21.9	21.1
>20	112	35.54±5.4	$8.30 \pm 6.98^{**}$	$2.89 \pm 1.77^{**}$	17.8	17.8

Values are expressed as mean ± SD. Values in parentheses are percentages.
1 denotes a $p=0.7$.
* denotes P-value <0.05 when compared to FSH groups <5, and 6-10.
2 denotes $p=0.05$ when compared to FSH groups <5, and 6-10.
**** denotes $p<0.001$ when compared to FSH groups <5, and 6-10.**
Ψ denotes $p<0.01$ when compared to FSH <5 and 6-10.
a denotes $p=0.06$ for all age groups
b denotes $p=0.07$ for all age groups

Discussion

This data analysis revealed that increasing age in this population does correlate with decreasing successful outcomes in IVF defined as confirmed intrauterine gestation and live births. Once a woman reaches 38 years of age, her pregnancy rate and live birth rate becoming significantly lower than that of younger patients ($p<0.05$). The ages of 40 and 42 also indicate more significant decreases in pregnancy rate and live birth rate compared to women under the age of 35. This finding is similar to many studies that have identified age as a factor impacting IVF outcomes.

This data analysis revealed that while basal FSH can result in lower numbers of oocytes retrieved and transferred, there was no affect on pregnancy rate and live birth rate. This was an interesting finding as it was surmised that an elevated FSH would represent decreased ovarian reserve which has been identified in literature as being a poor indicator for IVF success.

The highest basal FSH to result in a live birth was 44 mIU/mL. This finding is consistent with the literature that reports that young age can overcome elevated FSH levels. For patients over the age of 40, the highest measured FSH level that resulted in a live birth was 15 mIU/mL. Thus older patients with normal or moderate levels of FSH are able to have successful outcomes with IVF, and younger patients with elevated levels of FSH are able to overcome this poor prognostic factor and give birth.

Conclusion

The data analysis revealed that increasing age in this population does correlate with decreasing successful outcomes in IVF. At ages 36 and 40 years, there are significant reductions in pregnancy rate. At ages 38 and 40, there are significant reductions in live birth rate.

Interestingly, there were no significant differences in pregnancy rate or live birth rate based on basal FSH level.

In this clinic's population, age but not FSH level is an important factor affecting IVF outcomes.