

# How Can the Maternal Age and the Basal Level of Serum FSH Predict the ICSI Outcome?

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## Abstract

**Background:** Age is an important factor affect female fertility, it is important to consider it while planning for intracytoplasmic sperm injection (ICSI). Basal follicular stimulating hormone(FSH) level can be an indicator of the ovarian reserve as the high level is associate with poor ovarian reserve and subsequently poor intracytoplasmic sperm injection outcome.

**Objective:** we aimed in this study to emphasize the role of age and basal serumfollicular stimulating hormone level in predicting the intracytoplasmic sperm injection outcome.

**Patients and Method:**a sixty sub-fertile couple were involved in this study. They were divided into two groups according to the age of female partner. Group 1  $\leq 35$  years old and group 2  $>35$  years old. We compared the difference in the basal follicular stimulating hormone level and theintracytoplasmic sperm injection outcome. Then we studied the association between the basal follicular stimulating hormone level and the intracytoplasmic sperm injection outcome.

**Results:** the study revealed that female  $\leq 35$  resulted in significantly better the intracytoplasmic sperm injection outcome.The no. of follicles, the no. of collected oocytes, no. of injected metaphase II oocytes (MII), no. of two pronuclei (2PN), total no. of embryos and no. of transferred embryos all were significantly higher in younger patients (P-value  $<0.05$ . The pregnancy rate was significantly higher in younger age group (47.5 % vs 25%, P-value = 0.04). there was a negative association between the basal follicular stimulating hormone level and the no. of follicles and no. of oocytes.

**Conclusion:** Maternal age is a good indicator for the success of the intracytoplasmic sperm injectionprocedure. The younger the female partner the better the intracytoplasmic sperm injection outcome. Basal level of follicular stimulating hormone is closely related to the ovarian reserve and subsequently the intracytoplasmic sperm injection outcome.

**Key words:** maternal age, basal FSH, ICSI.

## Introduction

The assisted reproductive techniques involve both intracytoplasmic sperm injection (ICSI) and in vitro

fertilization (IVF). In 1992 the Intracytoplasmic sperm injection (ICSI) was introduced to treat subfertility in couples due to severemale factor to allow fertilization and subsequent pregnancy whatever the semen characters were <sup>(1,2)</sup>. However, (IVF) or (ICSI) was also helpful to patients with tubal factor subfertility, unexplained subfertility as well as some cases of polycystic ovarian syndrome <sup>(3)</sup>.

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The age of female partner in assisted reproductive techniques (ART) cycles is an important influencing factor, the association between the advanced maternal age and the poor ART result is well known<sup>(4)</sup>. The diminishing ovarian reserve together with the decreased endometrial receptivity caused by aging are the possible explanation for this fertility reduction<sup>(5)</sup>, this is beside increasing the follicular disappearance starting after the 37 years old<sup>(6)</sup>. It is important to mention that advanced age is significant cause of increasing aneuploidy and spontaneous abortion rates<sup>(1)</sup>. Different responses to the controlled ovarian stimulation were obtained from women in the same age. Moreover, diminished ovarian reserve and poor IVF outcome have been noticed in women under the age of 35 years old<sup>(7)</sup>

Basal level (cycle day 2 or 3) of serum follicular stimulating hormone (FSH) has been studied as additional factor predicting the ICSI outcome<sup>(8)</sup>. Elevated basal level of serum FSH in sub-fertile women was associated with poor responses to the ovarian stimulation and subsequently lowering the pregnancy rate regardless the age<sup>(9)</sup>. Conversely other authors, mentioned that basal serum FSH level could be unreliable predictor for reproductive potential in older group of women as measuring FSH concentration represent an indirect ovarian reserve assessment<sup>(10,11)</sup>.

Basal FSH level and maternal age are associated with the ART outcome independently. They are related to the ovarian reserve phenomenon, which reflect the quality and quantity of remaining follicles in the ovary<sup>(12)</sup>.

In this study we aimed to estimate the role of maternal age and basal FSH level in predicting the ICSI outcome.

### Patients and Method

This is a retrospective cohort study was done in the sub-fertility center of AL-Sader Medical city in Iraq- Al Najaf governorate. It involved retrieving data of sub-fertile couples who were referred to the center by their gynecologist for ICSI procedure during the

period from October 2017 to May 2019. The study involved randomly collected 60 couples with different causes of sub-fertility (male factor = 36, tubal factor = 4, unexplained factor = 10 and anovulatory cause = 10). For the female patients age, type of infertility (primary infertility: the patient had never get pregnant previously or secondary infertility: the patient had get pregnant at least once regardless the fate of the pregnancy) and duration of infertility were recorded. The female age ranged from 21 years old till 44 years. The female gynecological, medical and surgical history were taken into account. On the menstrual cycle day 2 (CD2) baseline transvaginal ultrasound (TVUS) was done to assess uterus, endometrium and ovarian condition. Blood sample was collected in the second day of the menstrual cycle for the measurement of basal level of serum FSH, serum estradiol (E2) and serum luteinizing hormone (LH) level.

Male partners were evaluated by seminal fluid analysis; biopsy was done for azoospermic patients. Sever endometriosis, anatomical uterine abnormalities, female age > 44, cancelled cycles and male partner with testicular atrophy were excluded. The whole study was clarified to the patients and an informed verbal consents were taken. The patients were grouped according to the maternal age into two groups: Group 1 ≤ 35 and Group 2 > 35. The ICSI outcome was compared between the two groups. CD2 serum FSH level was measured and the correlation between it and the ICSI outcome and patients age were analyzed.

**Ovarian Stimulation, Oocytes Pick up and ICSI:** The patients were involved in controlled ovarian hyperstimulation (COH) programs using recombinant follicular stimulating hormone +/- human menopausal gonadotropin (HMG) with pituitary desensitization by agonist /antagonist protocols which were chosen according to the patient's age, body mass index (BMI) and cause of subfertility. Follicular maturation was followed by US and serial measurement of serum E2. Ova pick up was performed under general anesthesia guided by transvaginal ultrasound 36 hour after ovulation trigger with 0.1 mg decapeptyl (gonadotropin releasing hormone

GnRH agonist) or 10000 IU of pregnyl (the human chorionic gonadotropin Hcg). In the ICSI procedure the good quality metaphase II (MII) oocytes were injected and incubated in special media. The fertilization was assessed 16\_18 hr. after injection by identifying the two pronuclei(2PN). On the day 2 or 3 post injection the top quality embryos were transferred, not more than 3 embryos. The number and quality of picked up oocytes and the ICSI outcome in form of number of 2PN, number and quality of embryos, number of transferred embryos, fertilization rate, cleavage rate and pregnancy rate all recorded and statistically explained.

## Statistical Analysis

The data analysis was done using Microsoft Office Excel 2016 and the SPSS 21 program (Statistical Package for social sciences). The categorical data were represented as number and percentage while numeric data were represented as mean  $\pm$ SE. The difference between two numeric variables was studied by independent sample t-test and the association of categorical data analyzed by Chi-Square test. Pearson's correlation test shows the correlation between variables. The significant P value is  $< 0.05$ .

## Results

**Table 1: Demographic data of the patients.**

Variables		Value
Total number of couples		60
Age in years		31.3 $\pm$ 0.8 6.1042
Type of sub-fertility	Primary n (%)	45 (75%)
	Secondary n (%)	15(25%)
Duration of sub-fertility in years		8.26 $\pm$ 0.26
Cause of subfertility	Male factor (%)	36 (60%)
	Unexplained (%)	10 (16.7%)
	Tubal (%)	4 (6.7%)
	Anovulatory (%)	10 (16.7%)
Type of protocol	Agonist (%)	28(46.7 %)
	Antagonist (%)	32(53.3%)
Basal FSH (mlu/ml)		6.22 $\pm$ 0.36
Basal LH (mlu/ml)		4.2 $\pm$ 0.31
Basal E2 (pg/ml)		38.89 $\pm$ 2.3

**Table 2: Comparing the day 2 serum FSH and ICSI outcome between the patients according to the age.**

Variables	Age ≤ 35 (N=40)	Age > 35 (N=20)	P value
FSH (mlu/ml)	5.79 ± 0.37	7.07 ± 0.37	0.09
No. of preovulatory follicles	12.97 ± 0.91	7.9 ± 1.26	0.002
No. of collected oocytes	10.9 ± 0.126	7.500 ± 0.90	0.033
No. of injected MII	9.27 ± 0.88	6.200 ± 1.21	0.048
No. of 2PN	7.02 ± 0.58	3.800 ± 0.80	0.002
Total no. of embryos	6.55 ± 0.5546	3.7 ± 0.78	0.04
Grade I embryos	1.8 ± 0.33	1.1 ± 0.31	0.12
Grade II embryos	3.61 ± 0.46	1.7 ± 0.5	0.01
Low quality embryos	0.74 ± 0.18	0.9 ± 0.49	0.7
Fertilization rate %	75.6 ± 3.99	65.30 ± 7.64	0.5
cleavage rate %	92 ± 2.88	88.12 ± 6.87	0.1
No. of transferred embryos	2.71 ± 0.1	1.9 ± 0.25	0.02
Pregnancy rate %	47.5 % (19/40)	25% (5/20)	0.04

Table 2 shows that when we divided the patients according to the age, the group whom age was younger than 35 years old had lower CD2 serum FSH and better ICSI outcome. The no. of follicles, the no. of collected oocytes, no. of injected MII, no. of 2PN, total no. of embryos, no. of transferred embryos and pregnancy rate all were significantly higher in patients group younger than 35 years old.

**Table 3: Correlation between basal FSH with patients age and ICSI outcome.**

Variables	Correlation coefficient	P- value
Age	0.18	0.14
No. of preovulatory follicles	-0.33*	0.01
No. of collected oocytes	-0.26*	0.04
No. of injected MII	-0.21	0.1
No. of 2PN	-0.21	0.1
Total no. of embryos	-0.19	0.1
Grade I embryos	0.02	0.8
Grade II embryos	-0.2	0.1

**Cont... Table 3: Correlation between basal FSH with patients age and ICSI outcome.**

Low quality embryos	-0.04	0.7
Fertilization rate	-0.06	0.6
Cleavage rate	0.03	0.8
No. of transferred embryos	-0.16	0.2
Pregnancy rate %	-0.01	0.9

Table 3 show the correlation between the CD2 serum FSH and the ICSI outcome. The CD2 serum FSH correlate negatively with no. of follicle and no. of collected oocytes.

### Discussion

Female age and basal FSH level are independently associated with IVF outcome<sup>(7)</sup>. The increased maternal age and its effect on the reproduction is a subject of interest because it affects negatively oocytes and embryos quality and pregnancy rate<sup>(13,14)</sup>. In addition to that the rates of obstetrical and maternal complication such as maternal death, prematurity, fetal and early neonatal death, and caesarian section deliveries<sup>(15)</sup>.

The elevated basal FSH in many women discourage the option of ICSI/IVF as treatment option for them. This is due to that the high basal FSH is associated with lower assisted reproduction treatment results<sup>(16)</sup>. The age and elevated serum level of basal FSH in women are used as predictive criteria associated with diminished fertility<sup>(17)</sup>. In this study we re-evaluated the association between the ICSI outcome and the maternal age and basal FSH level.

The study showed significantly better ICSI outcome in women younger than 35 years old. This is probably due to the better oocytes quality and better ovarian reserve in young women. The no. of follicles, no. of oocytes, the no. of injected oocytes, no. of 2PN (fertilized oocytes), no. of embryos and pregnancy rates were all significantly higher in younger group of patients. Many studies were in agree with this results<sup>(12,15, 18, 19,20, 21,22)</sup>. On the other hand, the level of basal serum FSH was higher in older women group but still the difference was not significant may be due to the minimum differences in the age of

the individuals between both groups. The higher level of FSH in older women is indicative of decreased ovarian reserve. A study reported that there were no significant differences in level of FSH with age<sup>(23)</sup>. When we studied the association of the basal serum FSH level and the ICSI outcome, there was significant negative correlation between the FSH level and the no. of follicles and the no. of collected oocytes. This is because the FSH secretion from the pituitary gland increases with diminished ovarian reserved and women with high basal FSH frequently have lower no. of collected oocytes. There were studies which were in agreement with our finding in that the elevated FSH level is associated with poor ICSI outcome<sup>(7,12,24)</sup>.

### The limitation for this study

**Conclusion:** the maternal age is a cornerstone factor affecting the outcome of ICSI. The basal FSH is a good indicator of the ovarian reserve. Both of age and basal FSH are a good predictor for the success of the ICSI procedure.

**Conflict of Interest:** Non.

**Source of Funding:** Self-Funding.

**Ethical Clearance:** We obtained the ethical approval for our study from the institutional ethical committee. The patients were voluntarily participated in the study after they understood the aim of the research and verbal consents were taken from them. The participants were award that their information would remain strictly

confidential and would be used for research purpose only.

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