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Estradiol level on day two and day of trigger: A potential predictor of the invitro fertilization success

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Abstract

Background and objective: Infertility is defined as not getting pregnant after 12 months of unprotected sex for women under 35 or 6 months for those over 35. Ten to fifteen percent of couples struggle to conceive. All cases of infertility are evaluated; however, evaluations should be conducted sooner if there is a male factor or if the female has endometriosis, tubal illness, oligomenorrhea, or amenorrhea. Investigation includes an assessment of ovulatory function, ovarian reserve, uterinecavity, tubalpatency, and a semen analysis, diagnostic laparoscopy, hormone levels estradiol, the number of ovarian antral follicles have role in successful pregnancy in IVF cycles. It is generally known that a particular quantity of estradiol per follicle is necessary for pregnancy to occur. The purpose of this study was to evaluate the effects of IVF on the normal level of E2 in follicular day (12.5-166 pg/ml) and ovulation day (85.5-498 pg/ml) in relation to the estradiol level.

Methods: Because it depended on a few indications (questionnaire), the retrospective study of 50 infertile women at the YAD infertility center in Erbil, Kurdistan Region, Iraq, was analyzed.

Results: In this research the median age was 33 years, and their mean age (SD) was 32.6 (5.9) years. Their average body mass index was ≥ 30 at 28%, although their rate was 34%.Over 38% of women have no history of pregnancy, which is also more common in multigravidas than in primigravidae. In contrast, 23% of nulliparous women are infertile, and 46% of infertile women are nulliparous compared to primiparous and multiparous women. While the success rate was highest for the type of oocyte (M II) (89.7%) compared to 65% for the other types, the mean estradiol level on day 2 of the cycle was 46.9%, and the mean estradiol level on the day of HCG administration was also higher among women with successful biochemical pregnancies than those with failed pregnancies.

Conclusion: The estradiol 2nd day of cycle and the trigger day was found to have influence on IVF success.

Keywords: Estradiol; Day 2; Day of hCG trigger; Invitro fertilization.

Introduction

Approximately 10% to 15% of couples will have difficulties getting pregnant. Infertility is defined as no conception after 12 months of unprotected sexual intercourse in women less than 35 or six months in women 35 years and more.[1] According to World Health Organization the term primary infertility is used when a woman has never conceived and secondary infertility who have had at least one successful conception in the past.[2] Infertility diagnosis include the evaluation of sperm quality; hormones, and analysis of imaging of the uterus and fallopian tubes. According to the medical diagnosis, infertility may be treated by reproductive surgery, prescribing hormones or applying infertility technologies.[3] There are several causes of infertility that include Sexually transmitted disease (STD) like Chlamydia trachomatis and Neisseria gonorrhoea, Mycoplasma

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genitalium.[4] DNA damage reduces fertility in female oocytes, as caused by smoking.[5] Diabetes mellitus, thyroid disorders, undiagnosed and untreated celiac disease, and adrenal disease.[6] Hypothalmic pituitary factors, hyperprolactinemia, hypopituitarism, and presence of anti-thyroid antibodies.[7] Immune infertility due to the anti-sperm antibodies. Another major cause of infertility in women may be the inability to ovulate. Malformation of the eggs for example, polycystic ovarian syndrome in which eggs only partially developed within the ovary and there is an excess of male hormones. Some women are infertile because their ovaries do not mature and release eggs. Other factors that can affect women chances of conceiving include being overweight or underweight or her age as female fertility declines after the age of 30.[8]

Techniques that involve manipulation of oocytes outside the body are termed assisted reproductive technology (ART) with invitro fertilization (IVF) as the most common form. The term 'in Vitro means outside a living organism as oocytes mature in vivo in the ovary and embryos develop into pregnancy in the uterus, but the oocytes are fertilized in a petri dish. IVF is now widely applied for the treatment of infertility due to irreparable tubal, endometriosis, male factor, and unexplained infertility. Women who cannot use their oocytes due to primary ovarian insufficiency (POI) or age-related decline in oocyte number can now become successfully pregnant utilizing donor oocyte IVF.[9] Many factors affect IVF outcome like cause of infertility, age, subfertility duration, parity, life style factors,[10] oocytes retrieved,[11] endometrial thickness,[12] the number of embryos transferred,[13] quality of blastocysts,[14] hormons and sperm quality. Elevated basal follicle-stimulating hormone (FSH), low number of antral follicles and premature luteinization may negatively affect ART outcomes.[15]

Estrogen is one of the crucial female steroid hormones and plays a key role in regulating physiological and cellular functions of various tissues including reproductive organs, also estrogen orchestrates the cycle of uterine epithelium with another steroid hormone, progesterone, for successful uterine implantation after puberty.[16] Some studies have shown that the ratio of serum estradiol (E2) level to the number of follicles on the day of human chorionic gonadotrophin (hCG) administration, a ratio abbreviated as E2/fol (follicle), provides a useful index for predicting IVF/ ICSI-Etoutcomes.[17]

This study was conducted to evaluate the outcome of IVF in relation to estrogen levels. Considering that the typical levels of E2 are 12.5-166 pg/ml on follicular day and 85.5-498 pg/ml on ovulation day.

Methods

Study design: A retrospective study was conducted, with data obtained through the review of patient files and the completion of a prepared questionnaire. Data was gathered by monitoring women undergoing IVF-ET until they achieved pregnancy. A history and physical examination were conducted, estradiol and other hormone levels were assessed, transvaginal sonography for antral follicle count was performed on the second day, and estrogen levels together with endometrial thickness were evaluated on the ovulation day of the cycle. BHCG levels on days 10 to 12 post-embryo transfer.

Study setting

A sample of 50 infertile women was conveniently selected following the inclusion and exclusion criteria. From YAD Infertility Center. Erbil, Kurdistan Region, Iraq. Study period: March 1, 2018, to March 1, 2020. The inclusion criteria encompassed adults aged above 18 and under 45 years. Primary infertility, secondary infertility, and participants who consented to engage. Exclusion criteria encompassed individuals under 18 years of age, those over 45 years, and patients with systemic disorders such as Cushing's

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syndrome, Addison's disease, and congenital adrenal hyperplasia (CAH). Unrepaired uterine abnormality. Declined to engage in the study and Cryopreserved embryo.

Ethical consideration: The study proposal received approval from the ethics committee of the College of Medicine at Hawler Medical University. A facilitation letter was acquired from the Erbil Directorate of Health (DOH). The information remains confidential.

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) program for Windows version 26 was employed for data entry and analysis. Descriptive statistics were utilized to ascertain general data, while the chi-square test of association was applied as necessary to evaluate data normality and to compare percentages and rates.

A *P* value of less than 0.05 was deemed statistically significant.

Results

Fifty infertile women were included in the study. Their mean age (SD) was 32.6 (5.9) years, the median was 33 years, and the age range was 20-43 years. Table 1 show that 28% of the women were aged 30-39 years and 14% aged 40-44 years. The table shows that more than one third (34%) of the sample were obese. 46% were nulliparous (Table 1).

Table 1 Basic characteristics of the studied sample

	No.	%
Age (years)		
20-24	5	10.0
25-29	10	20.0
30-34	14	28.0
35-39	14	28.0
40-44	7	14.0
BMI (Kg/m^2)		
< 25	12	24.0
25-29	21	42.0
≥ 30	17	34.0
Parity		
Nulliparous	23	46.0
Primiparous	12	24.0
Multiparous	15	30.0
Total	50	100.0

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It is evident in Table 2 that more than one third (38%) of the women had primary infertility, and the duration of infertility was less than five years in 30% of the sample. Regarding the etiology of infertility, it was due to polycystic ovary syndrome in 38% of cases, 22% due to male factors, and 40% due to other causes.

The mean estradiol level in day 2 of the cycle was 46.9 pg/ml among women with successful biochemical pregnancy compared with 44.0 pg/ml among women with a failed pregnancy, but the difference was not significant (*P* = 0.697) as presented in Figure 1

Table 2 The pattern of infertility

	No.	%
Type of infertility		
Primary	19	38.0
Secondary	31	62.0
Duration of infertility (years)		
< 5	15	30.0
5-9	24	48.0
≥ 10	11	22.0
Etiology of infertility		
Polycystic ovary syndrome (PCOS)	19	38.0
Male factor	11	22.0
Others	20	40.0
Total	50	100.0

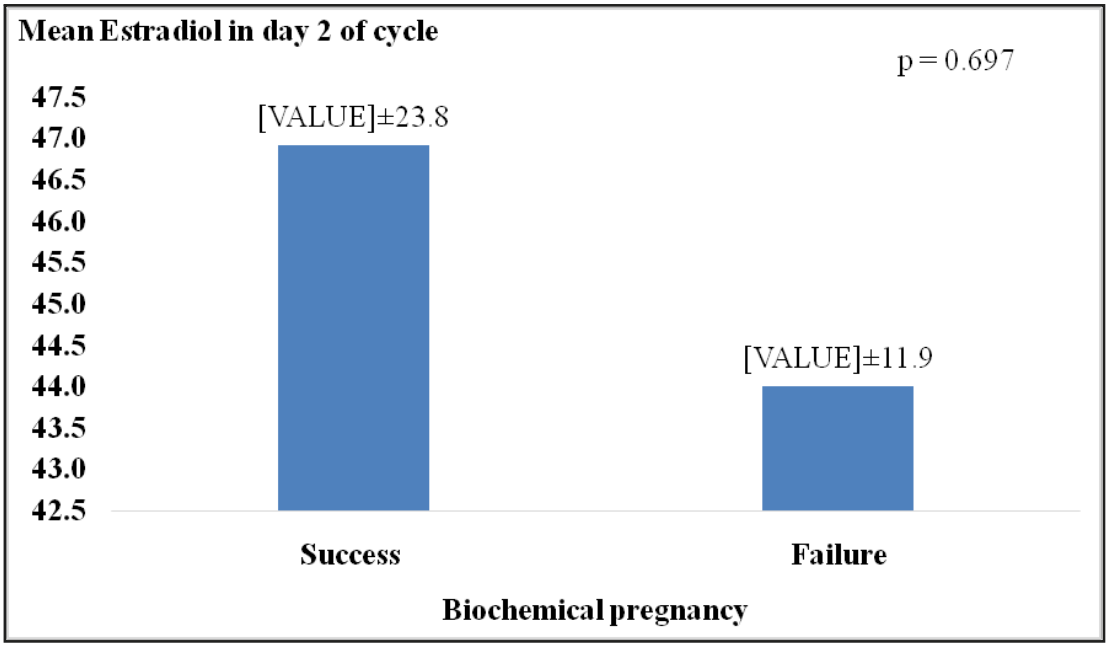

Figure 1 Mean estradiol by the outcome of biochemical pregnancy

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The mean estradiol level on the day of HCG administration was also higher among women with successful biochemical pregnancies than that among women with failed pregnancies (1818 pg/ml vs 1239 pg/ml respectively) but the difference was not significant (*P* = 0.086) as presented in Figure 2.

It is evident in Table 3 that the only factor that was significantly associated with the success of biochemical pregnancy was type of oocyte, where it is evident that the rate of success was highest in M II (89.7%) compared with 65% among the other types. There was only one patient with M I which ended with failure (*P* = 0.018).

No significant association was detected between success of biochemical pregnancy with the following factors: age (*P* = 0.518), BMI (*P* = 0.230), gravidity (*P* = 0.762), parity (*P* = 1.000), duration of infertility (*P* = 0.675), type of embryo (*P* = 1.000), type of infertility (*P* = 1.000), and etiology of infertility (*P* = 0.206).

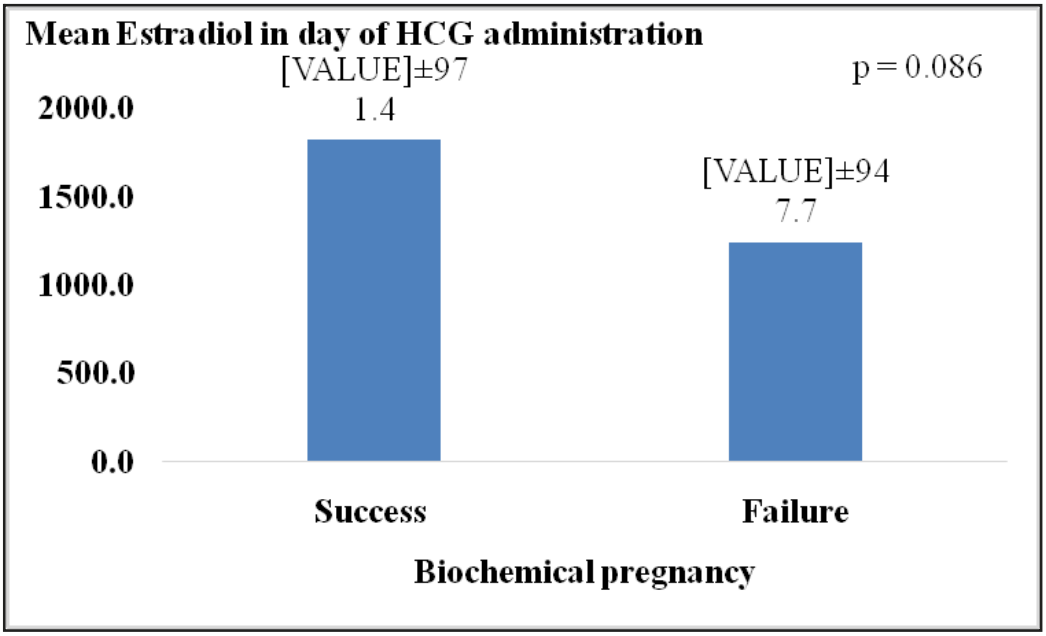

Figure 2 Mean estradiol in day of HCG administration by biochemical pregnancy outcome

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Table 3 Rate of biochemical pregnancy by the studied factors

		Biochemical pregnancy		
		Success	Failure	
	N	No. (%)	No. (%)	*P*-value
Age (years)				
20-24	5	4 (80.0)	1 (20.0)	
25-29	10	9 (90.0)	1 (10.0)	
30-34	14	12 (85.7)	2 (14.3)	
35-39	14	10 (71.4)	4 (28.6)	
40-44	7	4 (57.1)	3 (42.9)	0.518*
BMI (Kg/m^2)				
< 25	12	11 (91.7)	1 (8.3)	
25-29	21	17 (81.0)	4 (19.0)	
≥ 30	17	11 (64.7)	6 (35.3)	0.230*
Parity				
Nulliparous	23	18 (78.3)	5 (21.7)	
Primiparous	12	9 (75.0)	3 (25.0)	
Multiparous	15	12 (80.0)	3 (20.0)	1.000*
Duration of infertility (years)				
< 5	15	13 (86.7)	2 (13.3)	
5-9	24	18 (75.0)	6 (25.0)	
≥ 10	11	8 (72.7)	3 (27.3)	0.675*
Type of embryo				
G1	28	22 (78.6)	6 (21.4)	
G2	6	5 (83.3)	1 (16.7)	
Others	16	12 (75.0)	4 (25.0)	1.000*
Type of oocyte				
M I	1	0 (0.0)	1 (100.0)	
M II	29	26 (89.7)	3 (10.3)	
Others	20	13 (65.0)	7 (35.0)	0.018*
Type of infertility				
Primary	19	15 (78.9)	4 (21.1)	
Secondary	31	24 (77.4)	7 (22.6)	1.000*

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Discussion

According to the findings, 28 percent of the women were between the ages of 30 and 39 years old. The age of the woman was found to be a protective factor of the live birth in the IVF cycle. The pregnancy rates in IVF-ET treatment are nearly 30–35 percent. Additionally, it was uncovered that the success of in vitro fertilization (IVF) is dependent on a number of factors, including the age of the woman, the quality of the embryo, and the endometrial receptivity.[19,20] In recent research, it was shown that more than 34.0% of women who were infertile had a body mass index (BMI) of 30 or above. This finding is in conformity with the World Health Organization (WHO), which deems a person to be obese if their BMI is 30 or more. These current findings have supported such findings. According to reports, women who have a higher body mass index (BMI) also have a lower incidence of conception and a higher rate of abortion (AR), and they typically face various reproductive difficulties with their reproductive health.[21,22]

More than one third of the women had secondary infertility these results indicated that the present of many causes of infertility like an infection that lead to adhesion that effect on tubal function, previous surgery and endometriosis. This current study showed the duration of infertility was less than five years in 30% of the sample The woman's age and the duration of infertility have a major impact on fertility rates.[23] Polycystic ovarian syndrome occupy 38% of causes, male factor 22% and other causes represent largest part.

The present study found that the mean estradiol level on day 2 of the cycle was 46.9pg/ml among women with successful biochemical pregnancy compared with 44.0 pg/ml among women with a failed pregnancy, this result agrees with many previous studies that indicated that serum E2 plays an important role in oocytes/ follicular maturation and preparation of the uterus for implantation.[24] About the role of total E2 value as well as estradiol/follicle ratio (E2/fol) and estradiol/oocytes (E2/O) ratio concerning IVF outcome.[25] In IVF protocol, E2 increased tenfold in the natural cycle, however, significant deviation from the physiologic level of E2 has a detrimental effect on the endometrium, embryoimplantation, and subsequently on pregnancy rate. Early follicular phase E2 levels have been used to predict the outcome of IVFcycles, such that serum E2 levels <100 pg/mL appear to have worse outcomes than those >100.[26]

The increased level of serum estradiol on the day of HCG administration in recent results was higher among women with successful biochemical pregnancy than that among women with failed pregnancy (1818 pg/ml vs 1239 pg/ml respectively, as result of the arrested oocyte maturation. A positive feedback mechanism might be used to stimulate immature oocytes and immature oocytes might be picked up at this time,[27]summarising that higher E2 levels before hCG administration predicted more oocytes retrieved, but a consensus was not reached on its impact on oocyte/ embryo.

The ratio of the oocyte (M II) was highest at 89.7 % due to an increase of E2 tittering on the day of HCG, the results agree with the previous results that indicated that the numbers of oocytes and MII oocytes received and the implantation and clinical pregnancy rate increased gradually as serum E2 levels increased up to 5000 pg/ ml,but these parameters began to decline at concentrations above 5000pg/mL. The findings of the study, which revealed that a higher blood estradiol level on the day of HCG was connected with a greater number of oocytes and embryos, as well as high-grade embryos that were suitable for transfer or cryopreservation techniques.[28]

Conclusion

According to the findings of this research, the concentration of estradiol on the trigger day and on the second day of the menstrual cycle, which is the day that

is down-regulated, was found to have a substantial influence on the success rate of in vitro fertilization and embryo transfer.

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Competing interests

The authors declare that they have no competing interests.

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