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The Level of Serum Progesterone on the day of HCG Administration in Assisted Reproduction Cycles

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Abstract

Introduction: During stimulated IVF- ET cycle spontaneous LH surge occur in about 20 – 50 % of cycle stimulated with gonadotropin without the pituitary suppression of GnRH agonist. This has been related to maturation and recovery of oocyte together decrease fertilization and implantation rate, this spontaneous LH surge is associated with increase in serum progesterone , so without pituitary suppression with GnRH , the rise of serum progesterone in the per ovulatory period may indicate the occurrence of spontaneous of LH surge, the aim of study is to indicate cutoff point of progesterone in the day of HCG administration. **Method:** This was a retrospective, non-interventional cohort study of patients undergoing ICSI at Tiba infertility center in Babylon, from period 2015 - 2019, all patient age from 20 – 45 years old under long protocol, had at least one grade I embryo transferred, total amount of patients was 1457. At second day of menstrual cycle we stimulate by used recombinant FSH, measured on second day of menstruation serum FSH, LH and estrogen levels, transvaginal ultrasound used to monitored the follicles. when follicle became 14 mm in size we used antagonist. 3 or more follicles gotten 18 mm in diameter. Activation gave either hCG alone or mixture of hCG and agonist. After 14 days from embryo transfer we checked HCG and after that after 10 days transvaginal ultrasound was done. **Results:** In our study showed the significant association between positive pregnancy outcome and progesterone level at day of HCG trigger were 79.2 % of female with positive pregnancy at progesterone level < 1.5, while 9.3 % of female with positive pregnancy at progesterone level > 2.5, There is a significant differences of LH at day of HCG activate rendering to progesterone level day of HCG activate, progesterone level (< 1.5) had more chief level at day of HCG activate with mean and SD (5.38 ± 2.52), and reduction when the level progesterone rise. **Conclusion:** pregnancy cannot depend on progesterone level at day when HCG administration for assisted reproduction cycles treated with GnRH agonists and gonadotrophins. So cutoff point of progesterone can reach to above 1.5 ng/ ml and expected of pregnancy at this level.

Key word: *serum progesterone , HCG , IVF, estrogen, HCG trigger.*

Introduction:

During stimulated IVF- ET cycle spontaneous LH surge occur in about 20 – 50 % of cycle stimulated with goDDuring stimulated IVF- ET cycle spontaneous LH surge occur in about 20 – 50 % of cycle stimulated with gonadotropin without the pituitary suppression of GnRH agonist (1,2). This has been related to maturation and recovery of oocyte together decrease fertilization and implantation rate (3–5), this spontaneous LH surge is associated with increase in serum progesterone , so without pituitary suppression with GnRH , the rise of serum progesterone in the per ovulatory period may indicate the occurrence of spontaneous of LH surge (6), with the use of GnRH agonist to suppress pituitary gonadotropin increase in serum progesterone in the day of HCG administration has been reported sporadic cases (7), in such cases the usage of plasma progesterone as a conception predictor is controversial with some studies reported that peri- ovulatory rise in progesterone has negative outcome, some studies reported that peri-ovulatory rise in progesterone has negative outcome in pregnancy rate during assisted reproductive cycle (8,9), while other studies disagree and consider the rise in progesterone in the daytime of HCG management as unconnected to the proportion of pregnancies in assistant reproductive cycles(7), premature progesterone elevation during IVF cycles and its effect of endometrium respectively (10–12), the exact mechanism of peri-ovulatory plasma progesterone increase during stimulation IVF cycle is not fully clear as the rise proceeds the HCG administration for the final maturation of

oocyte and is not associated with LH surge during IVF cycles relatively high dose of exogenous FSH require to achieve multiple follicular maturation (13), some study contribute the premature progesterone elevation FSH stimulation (14,15). Recently publish study on sample of humen ovary cortices shows that FSH stimulate the enzymatic activity of 3B- HSD which are salting increase conversion of progenenolone to progesterone (16). Different cutoff points have been used to difine the progesterone elevation during stimulation IVF cycle that is range from 0.8 – 2 ng / ml (10,17), significant decrease in pregnancy rate with 1.5 ng/ ml or above progesterone level at the day of HCG administration (18,19). The aim of study is to indicate cutoff point of progesterone in the day of HCG administration.

Materials and Method

This was a retrospective, non-interventional cohort study of patients undergoing ICSI at Tiba infertility center in Babylon, from period 2015 - 2019, all patient age from 20 – 45 years old under long protocol, had at least one grade I embryo transferred, total amount of patients was 1457. At second day of menstrual cycle we stimulate by used recombinant FSH, measured on second day of menstruation serum FSH, LH and estrogen levels, transvaginal ultrasound used to monitored the follicles. when follicle became 14 mm in size we used antagonist. 3 or more follicles gotten 18 mm in diameter. Activation gave either hCG alone or mixture of hCG and agonist. After 14 days from embryo transfer we checked HCG and after that after 10 days transvaginal ultrasound was done, pregnancy occur when at least one gestational sac and detectable cardiac pulse. Progesterone measurement on the day of hCG administration. Samples were tested with electrochemiluminescence immunoassay. Statistical analysis: Progesterone 1.5 ng/ ml; this cut-off on the day of hCG administration. Comparisons were made by Student's t test and Chi square analysis where applicable. P <0.05 was considered statistically significant

Results:

In our study showed the significant association between positive pregnancy outcome and progesterone level at day of HCG trigger were 79.2 % of female with positive pregnancy at progesterone level < 1.5, while 9.3 % of female with positive pregnancy at progesterone level > 2.5 as show in table 1.

Table 1: Association between progesterone level at day of HCG trigger and pregnancy outcome (age 20-45)

Study variables	Pregnancy		Total	X2	P-value
	Positive	Negative			
Progesterone level at day of HCG trigger					
Less than 1.5	570 (79.2)	537 (72.9)	1107 (76.0)		
1.5- 2	52 (7.2)	75 (10.1)	127 (8.7)		
> 2- 2.5	31 (4.3)	39 (5.3)	70 (4.8)	8.226	0.042 *
More than 2.5	67 (9.3)	86 (11.7)	153 (10.5)		
Total	720 (100.0)	737 (100.0)	1457 (100.0)		

*p value ≤ 0.05 was significant.

In our study the distribution of patients with infertility according to pregnancy outcome. Those patients those get pregnant represent (49.4%) of study sample. (age 20-45).

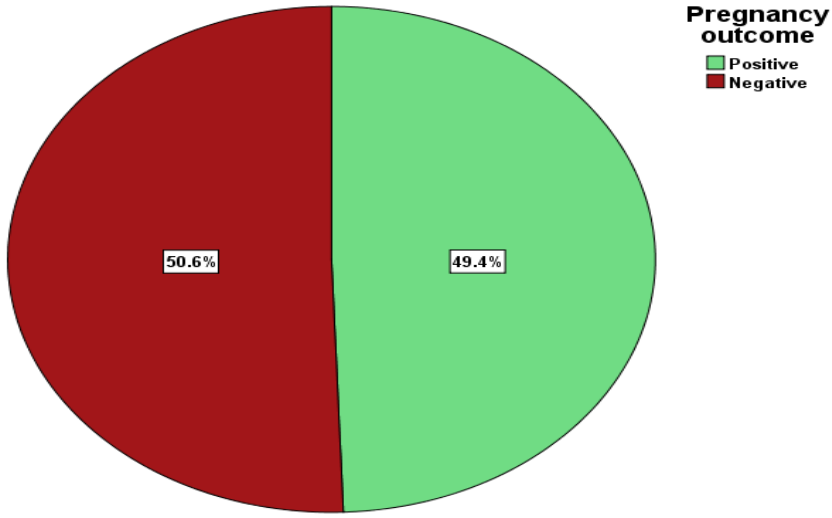

Figure 1: Show distribution of patients with infertility according to pregnancy outcome

The mean differences of age (years) according to pregnancy outcome including (positive and negative).There were significant differences between means of age between these two groups (N= 1457, t= -7.316, and P=<0.001*). Were 30.9% get pregnant at age 20-40 years as show in fig (2)

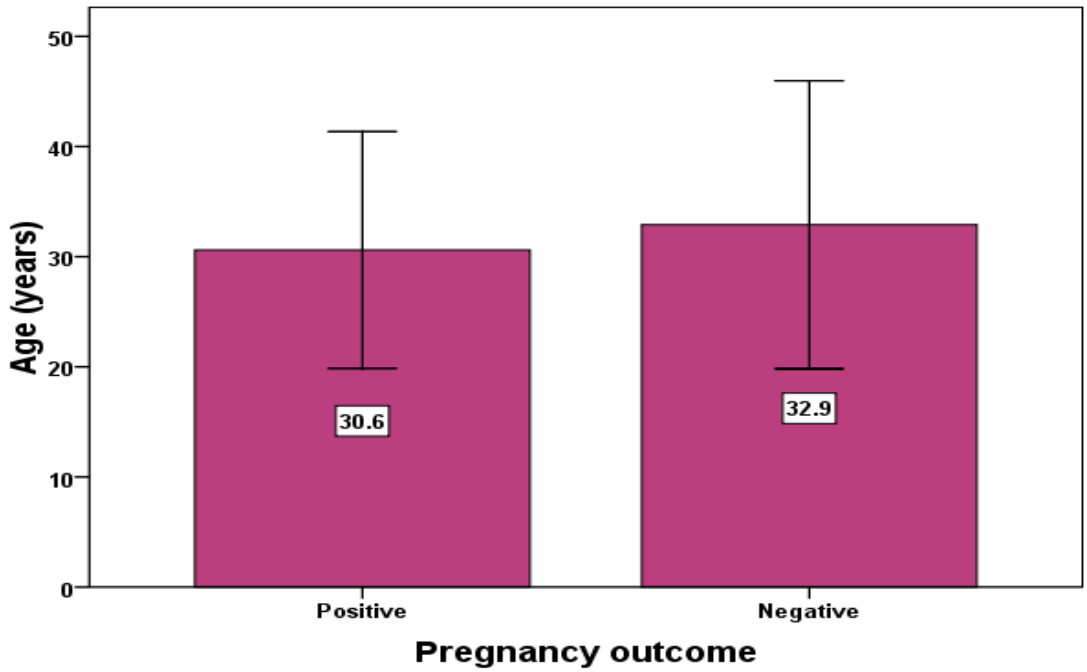

Figure 2: The mean differences of age according to pregnancy outcome.

The mean significant differences of estrogen at day of HCG activate rendering to progesterone level day of HCG activate, progesterone level (>2 - 2.5) had more predominant level at day of HCG trigger with mean and SD (2625.73 ± 65.62), as show in table 2.

Table 2: The mean differences of estrogen at day of HCG trigger according to progesterone level day of HCG trigger.

Progesterone level at day of HCG trigger	N	Mean	SE	P-value
Less than 1.5	1107	1870.16	23.20	<0.001*
1.5 - 2	127	2231.16	72.35	
>2 - 2.5	70	2625.73	65.62	
> 2.5	153	1849.71	72.50	
Total	1457	1935.78	21.00	

There is a significant differences of LH at day of HCG activate rendering to progesterone level day of HCG activate, progesterone level (< 1.5) had more main level at day of HCG activate with mean and SD (5.38 ± 2.52), and decrease when the level progesterone increase as show in table 3. while in table 4; There is no significant differences of LH at day of HCG activate rendering to progesterone level day of HCG activate, progesterone level (< 0.9) .

Table 3: The mean differences of LH level at day of HCG trigger according to progesterone level day of HCG trigger.

Progesterone level at day of HCG trigger	N	Mean	SE	P-value
Less than 1.5	1107	5.38	2.52	<0.001*
1.5 - 2	127	3.60	0.32	
>2 - 2.5	70	3.43	0.50	
> 2.5	153	2.47	0.23	
Total	1457	4.83	1.91	

Table 4: Association between progesterone level at day of HCG trigger and pregnancy outcome (age 20-45)

Study variables	Pregnancy		Total	X2	P-value
	Positive	Negative			
Progesterone level at day of HCG trigger					
Less than 0.9	358 (49.7)	353 (47.9)	711 (48.8)		
0.9-below 1.5	210 (29.2)	184 (25.0)	394 (27.0)		
1.5- 2	56 (7.8)	75 (10.1)	131 (9.0)	8.144	0.086
> 2- 2.5	31 (4.3)	39 (5.3)	70 (4.8)		
More than 2.5	65 (9.0)	86 (11.7)	151 (10.4)		
Total	720 (100.0)	737 (100.0)	1457 (100.0)		

*p value ≤ 0.05 was significant.

Discussion

During IVF/ICSI and embryo transfer, the rise of progesterone in late follicular parts of cycles has controversial affect (7,8,10,12), in our study significant association between positive pregnancy outcome and progesterone level at day of HCG trigger were 79.2 % of female with positive pregnancy at progesterone level < 1.5, while 9.3 % of female with positive pregnancy at progesterone level > 2.5, similar to study done by Jawa Ashmita and similar the study done by Ze Wu in China (20,21). In our study the distribution of patients with infertility according to pregnancy outcome. Those patients those get pregnant represent (49.4%) of study sample. (age 20-45), The pregnancy rate in 45% (65/143) in study done by Kinnari Vilaschandra Amin (22). The mean differences of age (years) according to pregnancy outcome including (positive and negative).There were significant differences between means of age between these two groups (N= 1457, t= -7.316, and P=<0.001*). Were 30.9% get pregnant at age 20-40 years, similar to study done by Jawa and study done by Ze Wu in China (20,21). In our study mean significant differences of estrogen at day of HCG trigger according to progesterone level day of HCG trigger, progesterone level (>2 - 2.5) had more predominant level at day of HCG trigger with mean and SD (2625.73 ± 65.62) , in difference to study done by Francisca Martínez; no significant differences in progesterone /estrogen ratio between conception and no conception cycles (23). Un obvious mechanism responsible for increasing plasma progesterone, exposure to FSH lead to increase sensitivity of granulosa cells (GCs) to LH this occur after hMG treatment this lead to premature Latinization even low plasma LH (24). IVF-ET have been lesser during the existence of pre-hCG rise in plasma P, lead to decrease embryo and oocyte quality, when increase in plasma progesterone the oocyte got from follicular have this rising lead to pregnancy rate decrease (24,25). So in our study 1107 women get pregnancy when level of progesterone < 1.5 ng/mL, 127 get pregnant in level of 1.5- 2 ng/mL, 70 get pregnant in level of >2 - 2.5 ng/mL, and the no. increase in level > 2.5 ng/mL to 153 women get pregnant. a premature elevation of progesterone 0.9 ng/mL was observed in 62% of 166 IVF cycles pretreated with GnRH-a. We do not see an obvious explanation for the discrepancy between Loughlin's results and hose reported by other investigators (24).

Conclusion

Pregnancy cannot depend on progesterone level at day when HCG administration for assisted reproduction cycles treated with GnRH agonists and gonadotrophins. So cutoff point of progesterone can reach to above 1.5 ng/ ml and expected of pregnancy at this level.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

Conflict of Interest: The authors declare that they have no conflict of interest.

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