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# Impact of Premature Progesterone Rise on Intracytoplasmic Sperm Injection Outcomes Using Gonadotropin-Releasing Hormone Antagonist Protocol

***Mohamed Ahmed Helmy*[1*], *Mahmoud Attia Seksaka* [1], *Eman Mahfouz Hafez*[1], *Walid Mohamed Sayed Ahmed Elnagar* [1]**

[1] *Obstetrics & Gynaecology Department, Faculty of Medicine, Zagazig University, Egypt.*

***Corresponding author :**
Name: **Mohamed Ahmed Helmy**
stetrics & Gynaecology Department, Faculty of Medicine, Zagazig University, Egypt.
E-mail: drmhmdhelmy14@gmail.com

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## ABSTRACT

**Background:** Premature progesterone rise (PPR) refers to an increase in serum progesterone (P4) levels on or before the human chorionic gonadotropin (hCG) trigger day. This work aimed to evaluate the impact of serum P4 levels on the day of hCG trigger on the outcomes of intracytoplasmic sperm injection (ICSI) cycles using the gonadotropin-releasing hormone (GnRH) antagonist protocol.

**Methods:** The prospective cohort study was conducted at the Cytogenetics and Endoscopy unit, Obstetrics & Gynaecology Department, Zagazig University, including 150 women having ICSI/fresh-embryo transfer (ET). Each patient had one trial of ICSI/fresh ET cycle. In the study, patients were subjected to controlled ovarian stimulation (COS) using a GnRH antagonist protocol. P4 levels were measured on the hCG trigger day (hCG-P4), and the results were correlated to the outcomes of the ICSI cycle.

**Results:** There was a statistically significant negative correlation between hCG-P4 and the top-quality embryo (TQE) rate. No significant association was found between hCG-P4 level and clinical pregnancy, ongoing pregnancy, or miscarriage. The cutoff for hCG-P4 predicting unsuccessful achievement of clinical pregnancy was ≥ 0.925 (p>0.05). Patients with hCG-P4 level ≥0.925 ng/ml had a significantly lower TQE rate than patients with hCG-P4 <0.925 ng/ml. There were significantly lower mature oocyte and TQE rates in patients with serum hCG-P4 level ≥1.5 ng/ml.

**Conclusion:** PPR was associated with significantly lower TQE, and hCG-P4 levels of ≥ 1.5 ng/ml were also associated with a significantly lower mature oocyte rate. However, it did not significantly affect pregnancy outcomes, either miscarriage, clinical or ongoing pregnancy rates.

**Keywords:** Progesterone; Gonadotropin-releasing hormone antagonist; Intracytoplasmic sperm injection; Human chorionic gonadotropin

## INTRODUCTION

Premature progesterone rise (PPR) refers to an increase in the serum progesterone (P4) level on or before the day of human chorionic gonadotropin (hCG) trigger for final oocyte maturation **[1]**. PPR during controlled ovarian stimulation (COS) for assisted reproductive technology (ART) and its impact on pregnancy and endometrial receptivity has been a subject of intense research over the last decades **[2]**. PPR is a common occurrence in stimulated cycles that is not avoided by administration of gonadotropin-releasing hormone (GnRH) analogous. It occurs with an incidence of about 38 percent of all COS cycles, regardless of the protocol type **[3]**.

A crosstalk between a viable blastocyst-stage embryo and a receptive synchronized endometrium is essential in successful embryo implantation. Whether low implantation and live birth rates observed when serum P4 is increased at the end of the follicular phase are attributable to an adverse effect on embryo viability, endometrial receptivity or both is still controversial **[4]**.

Most researchers have reported that elevated P4 harm the endometrium of fresh cycles, causing a decline in pregnancy rates. High P4 levels cause an accelerated endometrial maturation resulting in asynchrony between the implantation window and embryo transfer (ET) timing and consequently, lower rates of pregnancy **[5]**.

However, in the case of embryo-endometrial crosstalk, the quality of the embryo is as important as the receptivity of the endometrium. Another hypothesis, therefore, is that the high P4 levels adversely affect the oocyte quality or the produced embryo. **[6]**. It has been suggested in the retrospective analyses by **Huang et al. [6],** and **Vanni et al. [7]** that high P4 levels at the end of COS may be associated with lower

top-quality embryo (TQE) rate.

PPR diagnosis varies between the reported studies. The absolute P4 concentration is used in many studies to diagnose PPR with arbitrarily defined cutoff concentrations varying from 0.8 to 2 ng/ml on the day of hCG administration **[8]**. This cutoff concentration is typically set to 1.5 ng/ml in several studies using modern serum P4 evaluation methods **[3, 9].** Numerous studies affirmed this cut-off by finding a marked distinction within the endometrial genes expression between patients with P4 serum concentrations over and below the 1.5 ng/ml level on the day of hCG administration **[10].** This work aimed to assess the effect of serum P4 levels on the hCG trigger day on intracytoplasmic sperm injection (ICSI)/fresh-ET cycles using the GnRH antagonist protocol.

## METHODS

The prospective cohort study was conducted at the Cytogenetics and Endoscopy unit, Obstetrics and Gynecology Department, Zagazig University, from January 2018 to November 2020. The total sample size was 150, which was calculated using OpenEpi software. Each patient was subjected to one trial of ICSI/fresh ET cycle. Of the 150 cases enrolled in the study, 141 were included in the final analysis after completing the ICSI/fresh-ET cycles within the study period. Nine patients were excluded because they either developed OHSS and the cycle was cancelled (n = 5), or they had no oocytes retrieved (n = 4) **(Figure 1)**. **Inclusion criteria** were patients age from 17 to 40, body mass index (BMI) between 18 and 30 Kg/m², no more than two previous failed IVF-ICSI attempts, day 3 basal FSH < 10 mIU/ml, and no intrauterine pathology (confirmed by transvaginal ultrasound (TVS) or hysteroscopy done before the trial). The **exclusion criteria** were patients age > 40, endometriosis stages III/IV (According to the revised American Society for Reproductive Medicine (r-ASRM) classification **[11]**), presence of azoospermia in the male partner that needs the extraction of testicular sperms, and cases with uterine anomalies or tumours. Patients were counselled about different diagnostic and treatment options, and written informed consents were signed. The research was accepted by the Institutional Review Board of the Faculty of Medicine-Zagazig University (IRB number: 4225/31-12-2017). The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans. The patients were subjected to detailed medical, reproductive, and family history, including infertility duration and results of any prior examination and treatment, menstrual history (Menarche age, cycle duration and characteristics) and obstetric history (gravidity, parity, the pregnancy outcome, and any associated complications). Complete **physical examination** was done, including BMI, signs of androgen excess, vaginal or cervical discharge or abnormality, the size, mobility, and the position of the uterus by vaginal and bimanual examination. Basal serum hormone levels, including luteinizing hormone (LH), follicle-stimulating hormone (FSH), estradiol (E2) and P4 levels were measured on 3rd day of the cycle. The antral follicle count (AFC) was measured by TVS on 3rd day of the cycle.

**Controlled Ovarian Stimulation**

Patients received COS using the GnRH antagonist protocol **[12]**. Women started with gonadotropin injections (Fostimon, IBSA or Merional, IBSA) on day two of the menstrual cycle and the GnRH antagonist (Cetrorelix, Serono) was started when one of the leading follicles was 14 mm in size. The antagonist was not given later than day 6 of stimulation. The ovarian response was closely monitored and when two follicles were ≥ 17-18 mm in size, 10,000 IU of hCG (Chorimon IBSA) was administered to mimic a natural-cycle LH surge. The GnRH antagonist was then continued until and including the day of the hCG trigger. Thirty-four to 36 hours later, women underwent TVS-guided oocyte pickup under intravenous (IV) sedation. Fertilization of oocytes was done in vitro by ICSI, and ET was done three days later. All embryos transferred were six or more cells and of A or B grade (Grade A: Cells are of equal size with no fragmentation seen; Grade B: Cells are of equal size with minor fragmentation only **[13]**). All women received luteal phase support with progesterone given as regular injections or as vaginal suppositories, which began on the evening of the day of oocyte pickup. Serum β-hCG levels were measured 14 days after oocyte pickup. All patients with β-hCG >10 IU/L were followed by serial β-hCG and/or serial TVS till the appearance of gestational sac and confirmation of clinical pregnancy. Patients with viable intrauterine pregnancy were followed up until 8 weeks gestation at which time they were referred to obstetric care.

**Hormone assay**

P4 levels were measured on the hCG trigger day. Blood samples were drawn 1 to 2 hours before hCG administration, in plain (red-top) tubes. Samples were subjected to centrifugation at 3,000 g for 10 minutes to separate the serum. Samples were transferred to

the laboratory within 1 hour of collection. Laboratory results were given to the investigators as they became available. The results were correlated to the outcomes of the ICSI cycle.

**Measurements of Outcomes**

The main outcomes assessed in this study were the clinical pregnancy rate per initiated cycles (diagnosed by ultrasound detection of one or more gestational sacs) **[14]** and the ongoing pregnancy rate per initiated cycles (patients who were followed until ten weeks of gestation) **[15]**. Other outcomes were the numbers of oocytes retrieved, the mature oocyte, the TQE and the implantation rates.

## STATISTICAL ANALYSIS

Data analysis was conducted using the Statistical Package for the Social Sciences software (SPSS version 20.0). Quantitative variables were described using their means and standard deviations. Categorical variables were described using their absolute frequencies and were compared using the Chi-square test when appropriate. Kolmogorov-Smirnov (distribution-type) and Levene (homogeneity of variances) tests were used to verify parametric tests assumptions. To compare quantitative variables between two groups sample t-test (for normally distributed data) and Mann Whitney test (for discrete and not normally distributed data) were used. To assess the correlation between two continuous variables which are not normally distributed spearman rank correlation coefficient was used. ROC curve analysis was used to assess the best cutoff of specific parameters in diagnosing health problems. The level of statistical significance was set at $P<0.05$. A highly significant difference was present if $p\leq0.001$.

## RESULTS

One hundred fifty women were recruited to the study and 141 were included in the final analysis after completing the ICSI/fresh-ET cycles within the study period. Nine patients were excluded; five patients developed OHSS, and the cycle was cancelled, and four patients had no oocytes retrieved **(Figure 1)**. The study population mean age was 31.62 ± 6.303 years ranging from 19 to 40 years. The mean BMI was 24.6 ± 3.2 Kg/m$^2$. The majority of patients 119 (84.4%) came with primary infertility and 22 (15.6 %) patients with secondary infertility. Concerning etiology of infertility, male factor was responsible for 68 (48.2%) cases whereas, 29 (20.6%) had unexplained infertility. Thirty-five (24.8%) cases had female factors such as tubal problems (16.3%), anovulation (2.8%), and decrease ovarian reserve (5.7%). Concerning the pregnancy rate in our study, 35.5% attained clinical pregnancy, 32.6% had ongoing pregnancy till ten weeks gestation, while the percentages of miscarriage and biochemical pregnancy were 2.8 and 1.4% respectively **(Table 1)**. The AFC ranged from 8 to 20 with mean follicular count 13.633±3.47. FSH dose during stimulation ranged from 1350 to 5100 IU with mean 2789, and E2 levels measured on the day of hCG trigger ranged from 237 to 7817 pg/ml with a median of 1580 pg/ml. Serum P4 level on hCG administration day (hCG-P4) ranged from 0.05 to 2.74 ng/ml with a median of 0.98 ng/ml. The number of mature oocytes ranged from 0 to 20, with a median 8, representing 85.7% of total oocytes. The median of the good quality embryos number was four, and the fertilization rate was 70% **(Table 2)**.

Correlation between hCG-P4 and the parameters in our study revealed a statistically significant positive correlation with the total number of oocytes retrieved. On the other hand, there was a statistically significant negative correlation with the TQE rate. The mature oocyte rate and the fertilization rate correlated negatively with hCG-P4 level; however, this correlation was nonsignificant **(Table 3)**. In the current study, no significant association was found between hCG-P4 level and attaining clinical pregnancy, ongoing pregnancy, or miscarriage **(Table 4)**. After receiver operating characteristic (ROC) curve analysis in the current study, we found that the cutoff for hCG-P4 predicting unsuccessful achievement of clinical pregnancy was ≥ 0.925 with area under the curve (AUC) 0.492, sensitivity 52.6%, specificity 50.9%, positive predictive value (PPV) 66.2%, negative predictive value (NPV) 37% and accuracy 52% ($p>0.05$) **(Table 5)**. Patients with hCG-P4 level ≥0.925 ng/ml had a significantly higher number of oocytes retrieved and a significantly lower TQE rate than patients with hCG-P4 <0.925 ng/ml. Also, we found a significantly lower mature oocyte and TQE rates in patients with serum hCG-P4 level ≥1.5 ng/ml **(Table 6)**.

**Table 1.** Distribution of the patients regarding demographic data and clinical characteristics

| | N=141 | % |
|---|---|---|
| Age (year)<br>Mean ± SD<br>Range | <br>31.62 ± 6.303<br>19 – 40 | |

| | N=141 | % |
|---|---|---|
| BMI (Kg/m$^2$)<br>Mean ± SD<br>Range | <br>24.6 ± 3.2<br>18.7-29.8 | |
| Infertility<br>Primary<br>Secondary | <br>119<br>22 | <br>84.4<br>15.6 |
| Type of infertility<br>Male<br>Female:<br>Anovulation<br>Decrease ovarian reserve<br>Tubal<br>Unexplained<br>Combined (Male & female factors) | <br>68<br>35<br>**4**<br>**8**<br>**23**<br>29<br>9 | <br>48.2<br>24.8<br>**2.8**<br>**5.7**<br>**16.3**<br>20.6<br>6.4 |
| Abnormal Semen Analysis<br>Asthenospermia<br>Oligospermia<br>Oligo-Asthenospermia<br>Oligo-Teratozoospermia | N=77<br>8<br>18<br>47<br>4 | <br>10.4<br>23.4<br>61<br>5.2 |
| Clinical pregnancy rate<br>Ongoing pregnancy rate<br>Miscarriage<br>Biochemical pregnancy<br>Biochemical pregnancy + miscarriage | 50<br>46<br>4<br>2<br>6 | 35.5%<br>32.6%<br>2.8%<br>1.4%<br>4.3% |

**Table 2.** AFC, serum hormones levels, oocytes retrieved, embryos quality, fertilization & implantation rates among the studied patients among the studied patients

| | Mean ± SD | Median*(Range) |
|---|---|---|
| AFC | 13.633 ± 3.477 | 8 – 20 |
| Basal FSH | 4.202 ± 0.793 | 3.2 – 8.3 |
| Basal LH | 6.451 ± 1.046 | 4.1 – 8.4 |
| Basal E2 | 44.378 ± 2.2 | 40.5 – 48.26 |
| Basal P4 | 0.825 ± 0.184 | 0.1 – 1.2 |
| FSH dose | 2789.1 ± 941.485 | 1350 - 5100 |
| Trigger E2 | 2068.171 ± 1730.853 | 1580 (237 – 7817) |
| P4 on hCG day | 1.089 ± 0.592 | 0.98 (0.05 – 2.74) |
| Total number of oocytes retrieved | 9.68 ± 6.3 | 9 (1 – 30) |
| Number of mature oocytes | 7.913 ± 4.489 | 8 (0 – 20) |
| Mature oocyte rate | 87.162 ± 19.777 | 85.714% (0 – 100%) |
| Number of TQE | 4.993 ± 3.418 | 4 (0 – 17) |
| TQE rate (%) | 94.75 ± 13.49 | 100 (30 – 100) |
| Number of ET | 2.31 ± 0.8 | 3 (0 – 4) |
| Implantation rate (%) | 15.6 ± 24.5 | 0 (0 – 100)<br>(25 – 100[a]) |
| Fertilization rate (%) | 68.38 ± 22.29 | 70 (0 – 100)<br>(24 – 100[b]) |

*Median was calculated for non-parametric data
[a] Range in cases with successful implantation
[b] Range in cases with successful fertilization

**Table 3.** Correlation between hCG-P4 level with the studied parameters

| Parameters | hCG-P4 | |
|---|---|---|
| | **r** | **p** |
| Total number of oocytes retrieved | 0.227 | 0.005* |
| Number of mature oocytes | 0.223 | 0.006* |
| Mature oocyte rate | -0.111 | 0.176 |

| Parameters | hCG-P4 | |
|---|---|---|
| Number of TQE | 0.085 | 0.304 |
| TQE rate | -0.297 | <0.001** |
| Fertilization rate | -0.137 | 0.094 |
| Implantation rate | 0.009 | 0.915 |

*p<0.05 is statistically significant
**p≤0.001 is statistically highly significant
r Spearman rank correlation coefficient

**Table 4.** The relation between the pregnancy rate and hCG-P4 level

| Outcomes | hCG-P4 | | | |
|---|---|---|---|---|
| | **Median** | **Range** | **Z** | **p** |
| Clinical pregnancy<br>Yes<br>No | <br>0.91<br>1.1 | <br>0.22-1.86<br>0.05 –2.74 | -0.165 | 0.869 |
| Biochemical pregnancy + miscarriage<br>Yes<br>No | <br>0.91<br>1.02 | <br>0.22 - 1.9<br>0.05 –2.74 | -0.249 | 0.769 |
| Ongoing pregnancy<br>Yes<br>No | <br>1.02<br>0.925 | <br>0.4 – 1.86<br>0.05 –2.74 | -0.744 | 0.457 |

Z Mann Whitney test

**Table 5.** Performance of hCG-P4 in predicting unsuccessful achievement of clinical pregnancy among the studied patients

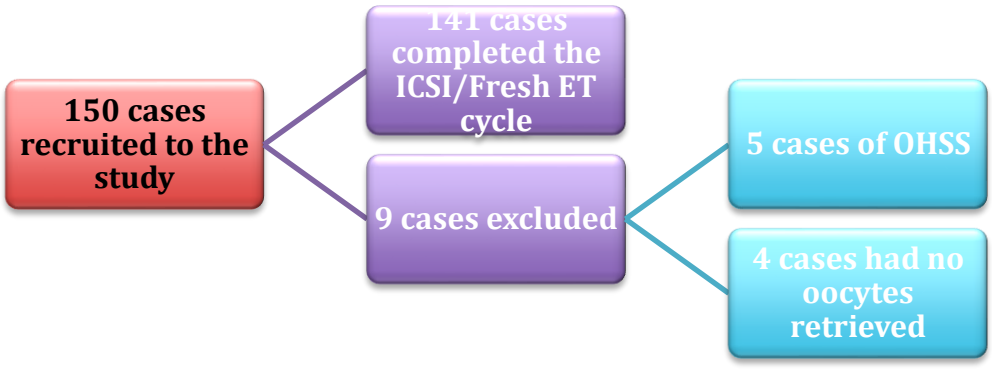
| | Cutoff | AUC | Sensitivity | Specificity | PPV | NPV | Accuracy | p |
|---|---|---|---|---|---|---|---|---|
| hCG-P4 | ≥0.925 | 0.492 | 52.6% | 50.9% | 66.2% | 37% | 52 | 0.869 |

**Table 6.** The relation between the hCG-P4 cutoff in our study (≥0.925 ng/ml) & the cutoff suggested in previous studies (>1.5 ng/ml) and the studied parameters

| Parameters | hCG-P4 | | Z/t /$\chi^2$ | p | hCG-P4 | | Z/t /$\chi^2$ | p |
|---|---|---|---|---|---|---|---|---|
| | ≥0.925 N=72 | <0.925 N=69 | | | ≥1.5 N=32 | <1.5 N=109 | | |
| | Median (range) | Median (range) | | | Median (range) | Median (range) | | |
| Total number of oocytes retrieved | 11 (1 – 30) | 6 (1 – 21) | -4.29 | <0.001** | 10.5 (1 – 22) | 9 (1 – 30) | -0.781 | 0.435 |
| Mature oocyte rate | 85.66 ± 16.53 | 88.74 ± 22.71 | -0.953 | 0.342 | 86.5 ± 13.82 | 87.36 ± 21.25 | -2.57 | 0.014* |
| TQE rate | 91.69 ± 14.42 | 98.03± 11.66 | -2.938 | 0.004* | 92.49 ± 13.5 | 96.81 ± 10.33 | -2.85 | 0.003* |
| Fertilization rate | 68 (0 – 100) | 74 (0 – 100) | -1.219 | 0.223 | 67 (0 – 100) | 75 (0 – 100) | -0.935 | 0.35 |
| Implantation rate | 0 (0 – 67) | 0 (0 – 100) | -0.158 | 0.847 | 0 (0 – 50) | 0 (0 – 100) | -0.722 | 0.47 |
| Clinical pregnancy (n; %) | 24 (33.3%) | 26 (37.7%) | 0.17 | 0.68 | 9 (28.1%) | 41 (37.6%) | 0.675 | 0.411 |
| Biochemical pregnancy + miscarriage (n; %) | 2 (2.8%) | 4 (5.8%) | Fisher | 0.267 | 2 (6.3%) | 4 (3.7%) | Fisher | 0.654 |
| Ongoing pregnancy (n; %) | 24 (33.3%) | 22 (31.9%) | 0.227 | 0.634 | 9 (28.1%) | 37 (33.9%) | 0.135 | 0.713 |

*p<0.05 is statistically significant
**p≤0.001 is statistically highly significant
Z Mann Whitney test
t independent sample t-test
χ2 Chi-square test

**Figure 1.** Flowchart of the studied cases




## DISCUSSION

Rise in serum P4 levels are found at the end of the follicular phase in many cases, despite the wide use of GnRH analogues in COS cycles for ART **[16]**. For several years, the clinical effect of this was highly controversial, with some research that found no link between P4 levels and pregnancy rates. **[17]**, while some reported a negative effect on the outcomes of the cycle when serum P4 levels rise on the day of hCG trigger **[18, 19]**.

Currently, many studies have shown that elevated P4 has a detrimental impact on the endometrium. There is, however, minimal evidence available regarding the impact on embryo development and the rate of TQE associated with elevated P4 levels **[20]**.

The meta-analysis evaluating studies including frozen embryo transfers by **Venetis et al. [9]** and the studies by **Healy et al. [21]** and **Yang et al. [22]** showed no association between increased P4 in the corresponding stimulation cycle with the pregnancy rate in the subsequent cryopreserved ET cycles. The results of these studies give indirect evidence of a negative impact of P4 rise on endometrial receptivity, not the oocyte or embryo quality.

On the other hand, the retrospective analyses by **Huang et al. [6],** and **Vanni et al. [7]** demonstrated that increased serum P4 levels at the end of stimulation may be associated with lower embryo quality. This finding was also supported by **Simon et al. [23]** and **Racca et al. [24]**.

In the current study, we found a statistically significant positive correlation between hCG-P4 and the total number of oocytes retrieved. On the other hand, a statistically significant negative correlation with the TQE rate was observed.

Similarly, a study conducted by **Tanada et al. [25]** assessed the impact of high hCG-P4 levels on ART outcomes and found that increased serum P4 levels might adversely affect the oocyte maturation and the formation of TQE.

A retrospective study of **Huang et al. [6]** that included 4,236 fresh IVF cycles found that hCG-P4 was negatively related to the TQE rate in IVF cycles. They observed that when serum P4 levels were >2.0 ng/ml, the TQE rate was reduced significantly. However, they noted that further studies are required to detect the mechanism by which adverse effects are caused by high P4 levels.

On the other hand, **Tsai et al. [26]** found that in patients with higher hCG-P4 levels, the number of oocytes retrieved and TQE rate were statistically significantly higher. **Liu et al. [27]** found that the number of oocytes retrieved showed a substantial increase with higher P4 levels with no significant relation to the TQE rate. The retrospective study by **Kofinas et al. [28]** including 238 patients undergoing preimplantation genetic testing and subsequent frozen ET, found that elevated P4 more than 1.5 ng/ml on hCG day did not have an effect on the number of oocytes collected or the available number of embryos for biopsy.

No significant association was found between hCG-P4 level and attaining clinical pregnancy, ongoing pregnancy, or miscarriage in the current study. The same result was published in the prospective study conducted by **Saharkhiz et al. [29]** including 107 women using both the agonist and antagonist protocols and the prospective study by **Hajishafiha et al. [30]** which included 249 women undergoing IVF/ICSI using the GnRH agonist protocol. In both studies, they found that a significant rise in hCG-P4 levels did not decrease the pregnancy rate or increase the miscarriage rate.

Over the past years, different cutoff values for raised P4 in ART cycles have been suggested, ranging from 0.8 to 2.0 ng/ml **[31]**. In the meta-analysis by **Venetis et al. [9],** P4 levels ≥0.8 ng/ml have already demonstrated a strong negative association with pregnancy rates. Results reported by **Tsai et al. [26]** showed that, following the ROC analysis, the P4 cutoff value that differentiated between successful and unsuccessful achievement of clinical pregnancy was 1.94 ng/ml.

After ROC analysis in the current study, we found that the cutoff for hCG-P4 predicting unsuccessful achievement of clinical pregnancy was ≥ 0.925 with AUC 0.492, sensitivity 52.6%, specificity 50.9%, PPV 66.2%, NPV 37% and accuracy 52% ($p>0.05$). We divided the patients in our study into two

groups, one group, including patients with serum hCG-P4 <0.925 ng/ml and the other, including patients with P4 ≥0.925 ng/ml. We found that patients with hCG-P4 level ≥0.925 ng/ml had a significantly higher number of oocytes retrieved and a significantly lower TQE rate than patients with hCG-P4 <0.925 ng/ml. No significant difference between the two groups regarding miscarriage, fertilization and implantation rates, clinical and ongoing pregnancy rates.

Many studies supported the hCG-P4 cutoff level of 1.5 ng/ml by finding a marked difference in the expression of the endometrial genes between patients with P4 serum levels above and below this threshold on the hCG day **[10]**. A retrospective study of 4032 cycles by **Bosch et al. [3]** showed significantly reduced pregnancy rates in patients with P4 levels ≥1.5 ng/ml, regardless the protocol used or the ovarian response. The same cutoff was also supported by the study of **Vikas and Swati [32]** who found a significant decrease in clinical pregnancy rates in patients with P4 ≥ 1.5 ng/ml and the study of **Huang et al. [33]** who observed that hCG-P4 levels greater than 1.5 ng/ml might adversely affects fertilization.

We assessed the relationship between the cutoff level of 1.5 ng/ml and our studied parameters. We divided the patients in our study into two groups (hCG-P4 <1.5 ng/ml and ≥1.5ng/ml), and we found significant lower mature oocyte and TQE rates in patients with serum hCG-P4 level ≥1.5 ng/ml, with no significant difference between the two groups regarding miscarriage, fertilization and implantation rates, clinical and ongoing pregnancy rates.

## CONCLUSION

We concluded that premature progesterone rise (PPR) was associated with significantly lower top-quality embryos (TQE), and progesterone levels ≥ 1.5ng/ml on hCG administration day were also associated with a significantly lower mature oocyte rate. However, it did not significantly affect pregnancy outcomes, either miscarriage, clinical or ongoing pregnancy rates.

- Conflict of Interest: None.
- Financial Disclosures: None.

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