

## The Role of Beta hCG Value Measured on the 12<sup>th</sup> and 14<sup>th</sup> Days After Embryo Transfer in Determining Early Complications of Pregnancy

Embriyo Transferi Sonrası 12. ve 14. Günlerde Ölçülen Beta hCG Değerinin Gebelikte Erken Komplikasyonların Belirlenmesindeki Rolü

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### ABSTRACT

**Aim:** This study aimed to investigate the role of beta human chorionic gonadotropin (beta hCG) levels on post embryo transfer (ET) 12<sup>th</sup>- and 14<sup>th</sup>-day, and its folding after 48 hours in predicting live birth, abortion, and biochemical pregnancy.

**Material and Methods:** The study included 124 patients who had a positive pregnancy test after a fresh single day 3 ET at the in vitro fertilization (IVF) center between 2017 and 2021. The first beta hCG value was measured 12<sup>th</sup> day and the second 14<sup>th</sup> day after ET. The beta hCG fold was calculated by dividing the second beta hCG value by the first beta hCG value.

**Results:** The patients' IVF indications included unexplained (n=40, 41.1%), poor ovarian reserve (n=23, 25.0%), male factor (n=31, 29.8%), and tubal factor (n=3, 4.1%). Of the 124 patients, 97 (78.2%) had a fetal sac, 81 (63.5%) had a fetal heartbeat (FHB), and 70 (56.5%) had a live birth. The results indicated that the post-ET 14<sup>th</sup>-day beta hCG level was the best predictor of biochemical pregnancy. It has a high sensitivity (92.5%) and specificity (86.6%), with an optimal cut-off value of 175 U/L. The post-ET 14<sup>th</sup>-day beta hCG level was the best predictor of a live birth. The post-ET 14<sup>th</sup>-day beta hCG value of 214.5 U/L had an 82.7% sensitivity and 74.4% specificity to predict the FHB.

**Conclusion:** The beta hCG value, measured between the 12<sup>th</sup> and 14<sup>th</sup> days after ET, as well as the folding rate on these two days, can provide information about the pregnancy progression.

**Keywords:** Beta hCG; live birth rate; post embryo transfer; pregnancy outcome.

### ÖZ

**Amaç:** Bu çalışmanın amacı, embriyo transferi (ET) sonrası 12. ve 14. gündeki beta human chorionic gonadotropin (beta hCG) düzeylerinin ve 48 saat sonraki katlanmasının canlı doğum, düşük ve biyokimyasal gebeliği öngörmedeki rolünün araştırılmasıdır.

**Gereç ve Yöntemler:** Çalışmaya 2017 ve 2021 yılları arasında tüp bebek (in vitro fertilization, IVF) merkezinde taze tek 3. gün ET sonrası gebelik testi pozitif çıkan 124 hasta dahil edildi. İlk beta hCG değeri ET'den sonra 12. gün, ikincisi ise 14. gün ölçüldü. Beta hCG katlanması, ikinci beta hCG değerinin birinci beta hCG değerine bölünmesiyle hesaplandı.

**Bulgular:** Hastaların IVF endikasyonları arasında açıklanamayan (n=40, %41,1), kötü over rezervi (n=23, %25,0), erkek faktörü (n=31, %29,8) ve tubal faktör (n=3, %4,1) yer alıyordu. 124 hastanın 97'sinde (%78,2) gebelik kesesi, 81'inde (%63,5) fetal kalp atışı (fetal heartbeat, FHB) ve 70'inde (%56,5) canlı doğum gerçekleşti. Sonuçlar, ET sonrası 14. gün beta hCG düzeyinin biyokimyasal gebeliğin en iyi belirleyicisi olduğunu gösterdi. 175 U/L optimum kesim değeri ile yüksek bir duyarlılığa (%92,5) ve özgüllüğe (%86,6) sahipti. ET sonrası 14. gün beta hCG düzeyi canlı doğumun da en iyi belirleyicisiydi. ET sonrası 14. gün 214,5 U/L beta hCG değerinin FHB'yi öngörmedeki duyarlılığı %82,7, özgüllüğü ise %74,4 idi.

**Sonuç:** ET sonrası 12. ve 14. günler arasında ölçülen beta hCG değeri ve bu iki gündeki katlanma oranı gebeliğin seyri hakkında bilgi verebilir.

**Anahtar kelimeler:** Beta hCG; canlı doğum oranı; embriyo transferi sonrası; gebelik sonucu.

## INTRODUCTION

Beta human chorionic gonadotropin (beta hCG) released by trophoblasts is detected in the blood 6-8 days after fertilization. It has been shown that 12-16 days after in vitro fertilization (IVF) treatment, its level is predictive of pregnancy outcome. In general, elevated initial serum beta hCG levels indicate a good prognosis (1).

Approximately 22% of IVF pregnancies result in miscarriage. Patients undergoing IVF experience intense anxiety and stress during their first pregnancy test. Identifying an accurate predictor of pregnancy following embryo transfer (ET) can reduce patient stress (2). Many studies based on the fetal yolk sac, which is one of the fetal transvaginal ultrasonography findings, as well as the size of the fetal sac and the doubling of the beta hCG test, have made significant contributions to the literature in determining pregnancy outcomes. For example, Deaton et al. (3) discovered that the presence of a yolk sac between 22 and 32 days after ET indicated fetal cardiac activity development in 94% of patients, whereas its absence was associated with 100% spontaneous abortion. However, none of these ultrasonographic findings can be detected before the fifth or sixth week of pregnancy. There are a few studies (4-6) looking into the relationship between the initial beta hCG result and live birth, and there is no ideal cut-off value for clinical and live birth predictions.

In this study, we aimed to investigate the role of post-ET 12<sup>th</sup>- and 14<sup>th</sup>-day beta hCG levels and their fold in two days to predict early pregnancy outcomes by determining possible cut-off values.

## MATERIAL AND METHODS

After approval from the University of Health Sciences Hamidiye Scientific Research Ethics Committee, İstanbul on 08.04.2022 date and 22/209 number, medical records are retrospectively collected from patient files. The study only included patients with positive IVF results and excluded multiple pregnancies and ETs due to elevated beta hCG levels, as well as ectopic and heterotopic pregnancies.

A retrospective study was conducted on 124 patients, who tested positive for pregnancy after a fresh single day 3 ET at the IVF center of Dr. Ali Kemal Belviranlı Obstetrics and Gynecology Hospital, Konya, between 2017 and 2021. The first beta hCG measurement was taken on the 12 days after ET, followed by a second measurement two days later. Patients with beta hCG levels greater than 5 U/L are considered to have a positive pregnancy. The same hospital's Medical Biochemistry Laboratory performed beta hCG measurements using an immunometric sandwich assay with the Immulite 2000 system (Siemens Medical Solutions Diagnostics, Flanders, NJ). The assay's sensitivity was 0.4 mIU/mL. The increase in the beta hCG measurement was observed after 48 hours and control was requested to examine the gestational sac (GS) in response to this increase. Patients with GS were invited to check the fetal heartbeat (FHB) 10 days later. Those with a visible FHB on ultrasound were considered clinically pregnant; babies born before 20 weeks and weighing less than 500 g were recorded as abortions; and babies born after 24 weeks were recorded as live births. Biochemical pregnancy is defined as a decrease in beta hCG levels without the presence of an intrauterine or extrauterine GS (7).

The patients' demographic data included age, body mass index (BMI), basal follicle stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2) levels, infertility duration, and cause of infertility were recorded. While the short antagonist protocol was initiated for 114 patients, the files revealed that the long agonist protocol was initiated for 10 patients.

In the short antagonist protocol, medication was started on the second day of menstruation. Recombinant FSH (Gonal F, Merck Serono, Italy) or urinary human menopausal gonadotropin (Menogon, Ferring, Germany) doses were determined individually based on the patient's BMI and the causes of infertility. When the follicle diameter reached 13-14 mm, an antagonist (Cetrorelix, Merck Serono, Germany) injection was administered flexibly. In the long protocol, a gonadotropin releasing hormone (GnRH) analog was started during the previous cycle's mid-luteal period (usually the 21<sup>st</sup> day), and gonadotropins were added after pituitary-ovarian suppression (usually 10 days after agonist use). Both drugs were administered concurrently until the day of the hCG injection. When an optimal cohort of large antral follicles is observed on ultrasound (at least three follicles >18 mm), ovulation is triggered by a single hCG injection (Ovitrelle, Merck Serono). Oocytes were collected after 34-36 hours of hCG injection. All patients underwent the intracytoplasmic sperm injection (ICSI) procedure. To provide luteal phase support, the patients received 600 mg/day of intravaginal progesterone capsules (Progestan 200 mg soft capsule, Koçak Farma, İstanbul). When the pregnancy was confirmed by a positive beta hCG test (>5 U/L), luteal phase support was maintained until the 10<sup>th</sup> gestation week.

### Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 20.0 (Armonk, NY: IBM Corp.). Kolmogorov-Smirnov and Shapiro-Wilk tests and histograms were used to determine whether the distribution of continuous variables was normal. Mean and standard deviation values were reported for normally distributed variables. For non-normally distributed variables, median, minimum, and maximum values were presented. The independent sample t-test was used to assess differences between two groups for normally distributed continuous variables, and the Mann-Whitney U test was used for continuous variables that did not show a normal distribution. In the analyses of categorical variables, the chi-square test was used to evaluate the relationships along with number and percentage values. Receiver operating characteristic (ROC) curve analysis was performed to determine the optimal threshold values of hCG levels used to predict biochemical pregnancy, positive FHB, and live birth. A two-way p-value of 0.05 was taken as a significance level.

## RESULTS

The study included 124 patients who underwent IVF and had positive beta hCG values. The mean age of the patients was 29.7±5.3 (range, 20-43) years. The IVF indications of the patients were unexplained (n=40, 41.1%), poor ovarian reserve (n=23, 25.0%), male factor (n=31, 29.8%), and tubal factor (n=3, 4.1%). Patients have beta hCG values measured for the first time 12 days after ET and for the

second time 2 days after the first test. Of 124 patients included, 97 (78.2%) had a fetal sac, 81 (63.5%) had a FHB, and 70 (56.5%) had a live birth (Table 1).

There were no significant differences between the two groups of GS positive and GS negative in terms of basic demographic and clinical parameters such as age, BMI, FSH, LH, and E2. There were also no significant differences in infertility duration ( $p=0.161$ ) and IVF indications ( $p=0.584$ ) between the two groups. The first and second beta hCG values, as well as their ratio, were significantly higher in the GS positive group ( $p=0.001$ ). The GS positive group had significantly higher positive fetal heart activity at 82.5% ( $n=80$ ) compared to the rate of 3.7% ( $n=1$ ) in the GS negative group ( $p=0.001$ ). The live birth rate was 72.2% ( $n=70$ ) out of the 97 GS positive patients (Table 2).

When assessed according to the presence of FHB, the FHB positive group showed significant differences in first and second beta hCG levels (193.2 U/L vs 51.7 U/L,  $p=0.001$  and 567.8 U/L vs 141.2 U/L,  $p=0.001$ , respectively) and second to first beta hCG ratio (2.67 vs 2.05,  $p=0.003$ ) compared to the FHB negative group. However, a small but statistically significant difference was also found in BMI (24 kg/m<sup>2</sup> vs 25 kg/m<sup>2</sup>,  $p=0.010$ ). No significant difference was found between FHB positive and negative groups in terms of age, FSH, LH, E2 values, and duration of infertility (Table 3).

Age, FSH, LH, and E2 were similar in the labor and abortion groups. BMI (23.5 kg/m<sup>2</sup> vs 24 kg/m<sup>2</sup>,  $p=0.035$ ) and duration of infertility (5 years vs 6 years,  $p=0.026$ ) were significantly lower in the labor group than in the abortion group. The first and second beta hCG measurements were significantly higher in pregnancies that ended in labor compared to those that ended in miscarriage (both  $p<0.001$ ). In addition, the beta hCG ratio was higher in labor than in miscarriage (2.65 vs 2.29,  $p=0.005$ , Table 4).

The performance of beta hCG level to predict biochemical pregnancy, FHB positivity, and live birth outcomes

following ET was presented in Table 5. It reveals that for the detection of biochemical pregnancy, the beta hCG level measured on post-ET day 14 offers the highest predictive accuracy. A cut-off value of 175 U/L provided a sensitivity of 92.5% and a specificity of 86.6% with an area under the curve (AUC) of 0.952 (95% CI, 0.910-0.993,  $p=0.001$ ). The second to first beta hCG ratio and beta hCG level on post-ET day 12 also showed significant predictive value, but the highest AUC value and sensitivity were obtained for the day 14 measurement. In the assessment of a positive FHB, which is an important early marker of viable pregnancy, again the beta hCG measurement on post-ET day 14 proved to be highly predictive. A cut-off value of 214.5 U/L was associated with a sensitivity of 82.7%, a specificity of 74.4%, and an AUC of 0.837 (95% CI, 0.761-0.914,  $p=0.001$ ). The beta hCG ratio and beta hCG

**Table 1.** Demographic and clinical characteristics of the patients

Age (year)	29 (8) [20-43]
BMI (kg/m <sup>2</sup> )	24 (2) [20-29]
Duration of infertility (year)	5 (5) [1-23]
FSH (U/L)	7 (4) [4-16]
LH (U/L)	9 (5) [3-15]
E2 (ng/L)	45 (20) [15-88]
Post-ET 12 <sup>th</sup> -day beta hCG (U/L)	144.3 (208.7) [9.3-880.1]
Post ET 14 <sup>th</sup> -day beta hCG (U/L)	392.5 (550.7) [0.9-2213.5]
Beta hCG ratio	2.55 (1.15) [0.07-9.77]
GS Positivity, n (%)	97 (78.2)
Clinical pregnancy, n (%)	81 (65.3)
Pregnancy outcomes, n (%)	
Chemical pregnancy	26 (21.0)
Abortion	28 (22.6)
Live birth	70 (56.5)

BMI: body mass index, FSH: follicle stimulating hormone, LH: luteinizing hormone, E2: estradiol, ET: embryo transfer, hCG: human chorionic gonadotropin, GS: gestational sac, descriptive statistics for continuous variables were presented as median (interquartile range, 75<sup>th</sup>-25<sup>th</sup> percentile) [minimum-maximum]

**Table 2.** Comparison of clinical and demographic characteristics of IVF treatments according to the GS status

	GS positive (n=97)	GS negative(n=27)	p
Age (year)	29 (8) [20-43]	31 (9) [21-42]	0.100
BMI (kg/m <sup>2</sup> )	24 (2) [20-29]	24 (3) [21-29]	0.193
Duration of infertility (year)	5 (4) [1-23]	6 (6) [1-15]	0.161
FSH (U/L)	7 (3) [4-15]	8 (6) [4-16]	0.133
LH (U/L)	9 (5) [3-15]	9 (6) [4-15]	0.626
E2 (ng/L)	45 (15.5) [15-88]	45 (24) [15-88]	0.887
Post-ET 12 <sup>th</sup> -day beta hCG (U/L)	189.6 (226.1) [27.9-880.1]	33.5 (47.8) [9.3-175.5]	<b>0.001</b>
Post ET 14 <sup>th</sup> -day beta hCG (U/L)	514.0 (495.8) [80.4-2213.5]	48.6 (131.0) [0.9-486.8]	<b>0.001</b>
Beta hCG ratio	2.70 (0.92) [1.63-9.77]	1.08 (1.59) [0.07-4.52]	<b>0.001</b>
Fetal cardiac activity, n (%)	80 (82.5)	1 (3.7)	<b>0.001</b>
IVF indication, n (%)			
Unexplained	40 (41.2)	11 (40.7)	
Poor ovarian reserve	23 (23.7)	8 (29.6)	
Male factor	31 (32.0)	6 (22.2)	0.584
Tubal factor	3 (3.1)	2 (7.4)	
Pregnancy outcome, n (%)			
Miscarriage	27 (27.8)		
Live birth	70 (72.2)		

BMI: body mass index, FSH: follicle stimulating hormone, LH: luteinizing hormone, E2: estradiol, ET: embryo transfer, hCG: human chorionic gonadotropin, GS: gestational sac, IVF: in vitro fertilization, descriptive statistics for continuous variables were presented as median (interquartile range, 75<sup>th</sup>-25<sup>th</sup> percentile) [minimum-maximum]

**Table 3.** Comparison of clinical and demographic characteristics according to the status of FHB

	FHB positive (n=81)	FHB negative (n=43)	p
Age (year)	29 (8) [20-43]	300 (10) [21-42]	0.575
BMI (kg/m <sup>2</sup> )	24 (2.5) [20-28]	25 (3) [21-29]	<b>0.010</b>
Duration of infertility (year)	5 (3.5) [1-23]	6 (6) [1-16]	0.108
FSH (U/L)	7 (3) [4-15]	7 (5) [4-16]	0.769
LH (U/L)	9 (5) [4-15]	9 (6) [3-15]	0.910
E2 (ng/L)	45 (15) [15-88]	49 (29) [15-88]	0.559
Post-ET 12 <sup>th</sup> -day beta hCG (U/L)	193.2 (229.8) [27.9-880.1]	51.7 (91.6) [9.3-398.6]	<b>0.001</b>
Post ET 14 <sup>th</sup> -day beta hCG (U/L)	567.8 (533.3) [64.0-2213.5]	141.2 (231.5) [0.9-1694.0]	<b>0.001</b>
Beta hCG ratio	2.67 (0.86) [1.63-9.77]	2.05 (2.23) [0.07-5.62]	<b>0.003</b>
<b>IVF indication, n (%)</b>			
Unexplained	35 (43.2)	16 (37.2)	0.695
Poor ovarian reserve	18 (22.2)	13 (30.2)	
Male factor	24 (29.6)	13 (30.2)	
Tubal factor	4 (5.0)	1 (2.3)	
<b>Pregnancy outcome, n (%)</b>			
Miscarriage	11 (13.6)		
Live birth	70 (86.4)		

BMI: body mass index, FSH: follicle stimulating hormone, LH: luteinizing hormone, E2: estradiol, ET: embryo transfer, hCG: human chorionic gonadotropin, FHB: fetal heartbeat, IVF: in vitro fertilization, descriptive statistics for continuous variables were presented as median (interquartile range, 75<sup>th</sup>-25<sup>th</sup> percentile) [minimum-maximum]

**Table 4.** Comparison of pregnancies resulting in birth and abortive pregnancies

	Birth (n=70)	Abortion (n=54)	p
Age (year)	29 (8) [21-42]	30 (9) [20-43]	0.298
BMI (kg/m <sup>2</sup> )	23.5 (2) [20-28]	24 (3) [21-29]	<b>0.035</b>
Duration of infertility (year)	5 (3) [1-23]	6 (6) [1-16]	<b>0.026</b>
FSH (U/L)	7 (3) [4-15]	7 (5) [4-16]	0.471
LH (U/L)	9 (4) [4-15]	9 (4.25) [3-15]	0.286
E2 (ng/L)	45 (17.25) [24-88]	48.5 (21) [15-86]	0.328
Post-ET 12 <sup>th</sup> -day beta hCG (U/L)	210.0 (208.5) [36.4-880.1]	55.5 (111.6) [9.3-398.6]	<b>&lt;0.001</b>
Post ET 14 <sup>th</sup> -day beta hCG (U/L)	586.3 (520.6) [101.0-2213.5]	146.4 (282.6) [0.9-1694.0]	<b>&lt;0.001</b>
Beta hCG ratio	2.65 (0.90) [1.63-9.77]	2.29 (1.88) [0.07-5.62]	<b>0.005</b>

BMI: body mass index, FSH: follicle stimulating hormone, LH: luteinizing hormone, E2: estradiol, ET: embryo transfer, hCG: human chorionic gonadotropin, descriptive statistics for continuous variables were presented as median (interquartile range, 75<sup>th</sup>-25<sup>th</sup> percentile) [minimum-maximum]

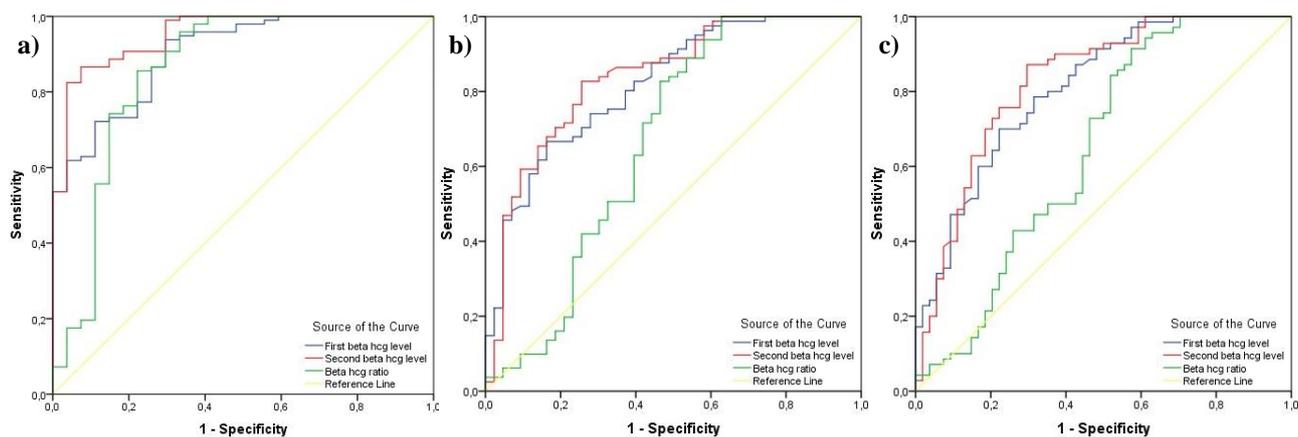
**Table 5.** Evaluation of the performance of beta hCG values in predicting biochemical pregnancy, fetal heartbeat, and live birth outcomes after embryo transfer

Result/Measurement	Cut-off	Sensitivity	Specificity	AUC	95% CI	p
<b>Biochemical Pregnancy</b>						
Post-ET 12 <sup>th</sup> -day beta hCG	43	70.3	93.8	0.901	0.840 - 0.962	<b>0.001</b>
Post ET 14 <sup>th</sup> -day beta hCG	175	92.5	86.6	0.952	0.910 - 0.993	<b>0.001</b>
Beta hCG ratio	2.06	77.7	85.5	0.855	0.750 - 0.959	<b>0.001</b>
<b>Fetal Heartbeat</b>						
Post-ET 12 <sup>th</sup> -day beta hCG	58.6	87.7	55.8	0.818	0.741 - 0.895	<b>0.001</b>
Post ET 14 <sup>th</sup> -day beta hCG	214.5	82.7	74.4	0.837	0.761 - 0.914	<b>0.001</b>
Beta hCG ratio	2.19	80.2	53.5	0.661	0.546 - 0.776	<b>0.003</b>
<b>Live Birth</b>						
Post-ET 12 <sup>th</sup> -day beta hCG	145.5	77.7	70.0	0.808	0.732 - 0.885	<b>0.001</b>
Post ET 14 <sup>th</sup> -day beta hCG	216	70.3	87.1	0.828	0.753 - 0.904	<b>0.001</b>
Beta hCG ratio	1.91	42.5	91.4	0.646	0.542 - 0.749	<b>0.005</b>

ET: embryo transfer, hCG: human chorionic gonadotropin, AUC: area under the curve, CI: confidence interval

level on post-ET day 12 also showed significant predictive value, but the highest AUC value was obtained from the day 14 measurement. Prediction of live birth outcomes revealed that both post-ET day 12 and day 14 beta hCG levels, and also beta hCG ratio had significant prognostic value. In particular, the post-ET day 14 beta hCG level

with a cut-off value of 216 U/L was labeled as a critical predictor of live birth, showing a sensitivity of 70.3%, a specificity of 87.1%, and an AUC of 0.828 (95% CI, 0.753-0.904, p=0.001). The highest performance to predict all three results was at the post-ET beta hCG level that was measured on day 14 (Figure 1).



**Figure 1.** Receiver operating characteristic curve of first beta hCG, second beta hCG, and second to first beta hCG ratio to predict a) biochemical pregnancy, b) fetal heartbeat, and c) live birth

## DISCUSSION

HCG is secreted by trophoblasts during the blastocyst stage, and its primary function is to keep the corpus luteum intact until the placenta matures enough to take over progesterone production. HCG is a heterodimeric glycoprotein composed of alpha and beta subunits derived primarily from syncytiotrophoblast cells. The beta subunit determines hCG's biological specificity (8). Years ago, it was known that a beta hCG of more than 100 mIU on the estimated menstrual date predicted a viable pregnancy (9). Patients, particularly in IVF pregnancies, are frequently required to take serum beta hCG tests to monitor the progress of conception, which increases the number of visits and thus causes psychological and financial stress. To reduce patient anxiety and costs, follow-ups must be tailored to individual serum beta hCG values. We aimed to present the ideal beta hCG cut-off values in IVF cycles that resulted in pregnancy, as well as any early pregnancy complications that may occur so that clinicians could guide their patients.

In this study, we discovered that beta hCG levels measured on the 12 and 14 days after day 3 single ET, as well as fold changes, were significantly higher in the live birth patient group than the biochemical pregnancy group. There are useful studies in the literature that attempt to predict the course of pregnancy by taking single or multiple beta hCG measurements during IVF cycles (10-14).

In this study, we discovered that the first (post-ET day 12) beta hCG value was 58.6 U/L, and the second (post-ET day 14) beta hCG value was 214.5 U/L, which predicted the FHB. Poikkeus et al. (15) found that a beta hCG level of 76 mIU/mL predicted a viable pregnancy with a sensitivity of 80% and a specificity of 82% when measured 12 days after ET. This value is slightly higher than found in this study. Bjercke et al. (16) found 55 IU/L, Qasim et al. (17) found 42 mIU/ml, and Sugantha et al. (18) found 50 IU/L, which are consistent with the findings in this study for a viable pregnancy.

Another retrospective study by Urbancsek et al. (19) found that the beta hCG value after IVF treatment was 50 IU/L for ongoing pregnancies and 135 IU/L for multiple pregnancies. In a retrospective study investigating the relationship between pregnancy and serum beta hCG value on the post-ET 12<sup>th</sup>-day, the mean serum beta hCG value

was reported as 126 IU/L in single viable pregnant women, while 31 IU/L in nonviable pregnant women (19). In this study, we discovered a beta hCG level of 43 IU/L, with a sensitivity of 70.3% and 93.8% specificity to differentiate a nonviable pregnancy on the post-ET 12<sup>th</sup>-day.

Sung et al. (20) discovered that the cut-off value for postovulatory 12<sup>th</sup>-day beta hCG levels to predict live birth was 40.5 mIU/mL, with 75.2% sensitivity and 72.6% specificity. In addition, they discovered that a postovulatory 14<sup>th</sup>-day beta hCG level of 104.5 mIU/mL predicted a live birth with 80.3% sensitivity and 74.1% specificity. Hughes et al. (21) discovered that when beta hCG levels "doubled" in 48 hours, a live birth occurred in 80.7% of IVF cycles, and when beta hCG levels "reached 100" 15 days after oocyte retrieval, a live birth occurred in 81.6% of IVF cycles. In this study, post-ET 14<sup>th</sup>-day beta hCG was the most accurate predictor of live birth, with an optimal cut-off value of 216 IU/L. Similar to the present study, Grin et al. (22) found that the best value for predicting live birth for beta hCG measured on the 14 and 16 days after fresh ET is 211 IU/L (sensitivity 84%, specificity 76.2%) and 440 IU/L (sensitivity 86.0%, specificity 72.5%), respectively.

The second to first beta hCG ratio had the lowest prediction rate, with a cut-off value of 1.91 for live births. Sung et al. (20) discovered that the beta hCG changes in biochemical pregnancy, early pregnancy loss, and live birth groups were  $2.0 \pm 1.3$ ,  $3.0 \pm 1.0$ , and  $3.1 \pm 0.8$  fold, respectively. Our study revealed that the fold changes for biochemical pregnancy, clinical pregnancy, and live birth were 2.06, 2.19, and 1.91, respectively. In our study, the beta hCG folding rate for live birth was lower than that of Sung et al. (20). They also discovered that the post-ET 14<sup>th</sup>-day sensitivity of serum beta hCG levels to predict ongoing pregnancy was 72.2% and 73.6%, respectively. When the initial beta hCG value was taken as 347 mIU/ml, we discovered that the post-ET 14<sup>th</sup>-day beta hCG cut-off value for live birth was 216 IU/L.

Kathiresan et al. (23) discovered that the proposed optimal thresholds predictive for live birth were 94 IU/L post-ET 12<sup>th</sup>-day; the likelihood of live birth on day 3 ET with beta hCG levels  $>94$  IU/L was 79%. The beta hCG level in this study, which was measured on the post-ET 12<sup>th</sup>-day and

can predict live birth, was 145.5 IU/L, with a sensitivity of 77.7% and a specificity of 70%.

The limitation of this study was the fact that studied with a small number of patients. The strength of the study was the exclusion of multiple ETs and pregnancies, which could cause a false beta hCG increase.

## CONCLUSION

It is critical to be able to predict the correct probabilities of pregnancy in IVF patients while reducing their anxiety. The earliest predictor of pregnancy outcomes in IVF cycles is early beta hCG measurement, which represents trophoblastic mass and function. This study yielded reliable data that can assist clinicians with beta hCG results and beta hCG ratio on the 12<sup>th</sup> and 14<sup>th</sup> days following ET. Because live birth is the desired outcome in IVF pregnancies, clinical and laboratory parameters that predict live birth are critical. The post-ET 14<sup>th</sup>-day beta hCG level was discovered as the best predictor of live birth with a higher sensitivity.

**Ethics Committee Approval:** The study was approved by the Hamidiye Scientific Research Ethics Committee of the University of Health Sciences (08.04.2022, 22/209).

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