Human chorionic gonadotropin as a Predictor of outcome in assisted reproductive technology pregnancies

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اندازه گیری هورمون گونادوتروپین جفتی به عنوان یک روش پیشگویی کننده حاملگی در روش های حاملگی کمک شده (ART)

خلاصه:

مقدمه و هدف:

در دوره های کمک باروری شده (ART= Assited reproductive technology) ،افزایش میزان سرمی HCG ، ۱۶ روز پس از تخمک گذاری بعنوان نشانه حاملگی شناخته می شود. هدف این مطالعه بررسی میزان پیشگوئی مقدار HCG درنتیجه حاملگی می باشد.

روش مطالعه:

این یک مطالعه گذشته نگر در زنانی است که با روش ART در بیمارستان منتصریه درمان شده و حامله شده بودند. با اندازه گیری HCG در روز ۱۶ تخمک گذاری ارتباط آن را با نتیجه حاملگی (سقط یا پیشرفت حاملگی به بعد از بیست هفتگی) مورد بررسی قرار دادیم.

نتایج:

میزان HCG بعنوان فاکتور مهم پیش آگهی حاملگی بود. سن مادر تأثیر کمی در نتیجه حاملگی داشت. حمایت فاز لوتئال و نوع درمان در پیش آگهی حاملگی تأثیری نداشت. مقدار HCG پائین (۲۵-۵۰Iu/L) همراه با میزان کم حاملگی موفق بود (کمتر از ۲۵٪). در حالیکه مقادیر HCG در حد ۲۰۰Iu/L و بیشتر در ۹۶٪ موارد منجر به حاملگی موفق شد.

نتیجه گیری:

اندازگیری HCG یک بار در روز ۱۶ تخمک گذاری می تواند به عنوان یک فاکتور پیش گوئی کننده در نتیجه حاملگی مورد استفاده قرار گیرد.

کلید واژه ها:

حاملگی ـ هورمون گنادوتروپین جفتی ـ حاملگی کمک شده.

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Introduction:

Diagnosis of pregnancy has both emotional and practical implications for the pregnant woman and her family. Early diagnosis with knowledge of prognostic outcome has the potential to reduce the stress often associated with the uncertainty of outcome in assisted reproductive technology treatment (ART).

The pregnancy test under evaluation was obtained from a single blood test taken 16 days after ovulation which is assayed for levels of hCG.

Human chorionic gonadotropin is secreted from the implanting blastocyst and appears in maternal blood approximately 6-8 days after fertilization.

Studies by Heriner et al and Guth et al both Found a correlation between the levels of serum hCG (serum sample taken on day 16 after ovulation) and pregnancy outcome. Some studies that suggest a relationship between serum progesterone levels of an early pregnancy and outcome have also been undertaken (2). For the patient, ART treatment is often stressful, and waiting for pregnancy test results can be a time of tension and uncertainty (3).

Information provided by physicians to patients may be inconsistent or nonspecific causing further stress and uncertainly. For example: patients may be told that they are pregnant, but their levels are a little low; or simply "Congratulations. You are pregnant." It would be better if we obtained hCG levels at this time quantitationly, and obtained reliable predictive information about pregnancy outcome. This could be used to improve patient care .

The aim of this study was to assess the predictive value on pregnancy outcome based on serum hCG level 16 days after ovulation. Other factors such as treatment method, ovarian stimulation, luteal support, and age were also inculded in the analysis.

Materials and Methods:

Data form Montasarieh IVF Center was the basis of analysis.

The ART treatment included in vitro fertilization (IVF), Intracytoplasimc sperm injection (ICSJ), intrauterine insemination (IUI), Ovulation induction (OI), and intercourse timing.

Serum collected 16 days after ovulation (following any of the above ART cycles) was assayed for hCG level by the same laboratory, by the method of radio immunoassay.

Data from all patients who had a positive pregnancy (hCG > 25 Iu/L) test after ART during 1999-2002 were reviewed. Patients who had a positive pregnancy test 16 days after ovulation were selected for further analysis.

The timing was considered critical because of the day to day rising of hCG at an exponential rate. The data were analysed with use of stata to predict a binary outcome: Ongoing pregnancy or miscarriage, the effect of hCG, age, stimulation, luteal support and treatment type were also analyzed.

Results :

Of the 250 cases reviewed, 50 patients were excluded because blood was not taken exactly 16 days after ovulation.

Serum samples taken 16 days after ovulation were positive for pregnancy (hCG>25Iu/l)in 200 cases.

Subjectd included in the analysis had undergone a variety of treatment types. (Table 1).

Treatment types of stimulation included clomiphen citrate (50-150mg). Clomiphen citrate plus hMG, (75-375 Iu/day) luteal support of either progesterone pessaries (25 mg/twice a day) or progesterone injection (100 mg/day) or hCG injection (5000 IU) every 3-4 days until 10 weeks of pregnancy.

The mean maternal age was 29 years (range 19-35); 60 subjects were >30 years of age.

The hCG levels ranged from 25 to 9800 Iu/L. All hCG> 300 Iu/L resulted in pregnancies.

The effect of hCG was clearly the major determining factor of pregnancy outcome. Human chorioic gonadotropin levels of <50 Iu/L were associated with a low probability of ongoing pregnancy <25%), whereas high levels >200 Iu/L , were associated with a >96% chance of ongoing pregnancy(Table 2).

The discrimination for miscarriage was 75% when hCG was <50 Iu/L, compared to 4% when hCG levels were >200Iu/L. Age was shown to be an independent determinant but much weaker than hCG. In the <30 years group, the chance of ongoing pregnancy was as high as 100% when the hCG was >200 Iu/L (140 from 200 were patients <30years). In women aged >30 years the levels needed to be substantially higher in the region of 300 Iu/L for an 60% chance of ongoing pregnancy. (60 from 200 patients were >30 years).

Discussion:

This study confirms the hypothesis that serum levels of hCG in samples taken 16 days after ovulation are powerful predictors of good or poor pregnancy outcome.

The strength of the relationship was sufficient to allow its use at a clinical level for the prediction of pregnancy outcome to the exclusion of all other markers.

Serum from all subjects was collected 16 days after ovulation. In early pregnancy,hCG increases rapidly (5).

Therefore, a test using serum hCG as a marker requires standardization of the number of days after ovulation at which the serum is collected. Serum is generally tested for hCG at approximately 14-16 days after ovulation following ART, although pregnancy can be detected with the most sensitive assays available at 8 days (7). In this study, the use of samples taken at 16 days was chosen to allow for accurate early detection with a good degree of pregnancy outcome prediction. These results are in general agreement with previous studies of hCG in early pregnancy.

Schmidt et al (6) examined 390 IVF pregnancies, collecting serum on day 16 after ovulation and anlyzing it for hCG. The results suggested that the hCG of nonviable pregnancies was markedly lower than those that were to progress beyond the first trimester. Heiner et al (1) and Guth et al (3) also analyzed serum for hCG levels; and both found it to be of predictive value.

In Heiner's study, serum from 134 subjects was collected 14, 15, or 16 days after ovulation; and Guth's included 111 subjects whose serum was taken on day 14. Because hCG was a comparable marker of pregnancy outcome for all ART treatment modalities, the results of this study demonstrate that these measurements are useful for all patients embarking on ART cycles, not just those who have IVF.

It is well documented that age is a contributing factor to pregnancy loss (8). Hansen (9) reviewed several studies and concluded that there was a substantially greater risk of spontaneous abortions for women aged >40. Gillian et al (10) also identified an increase in spontaneous abortions in older women. Therefore, age was considered in the analysis of data.

Age proved to be a significant factor; and analysis according to age subgroups revealed a significantly poorer outcome at each level of hCG for patients older than 30 years despite the smaller number of subjects in the older age group. Because we do not do ART in any women above 30 years of age, we divided women upon base of age into two groups above and under 30 years.

Luteal support, hormonal stimulation, and treatment types were included in the analysis, but the results demonstrated that they had no predictive value.

The results of the patient survey clearly indicated that predictive information is highly desired. The ART can be stressful for patients and their families (4), and our results indicate that providing information is of value to most and may relieve some of the anxiety and uncertainty surrounding treatment outcome.

A pregnancy test described in the context of probability of ongoing pregnancy may be helpful. If the possibility of miscarriage is high, patients, although disappointed, are able to prepare themselves emotionally.

From the data presented, it is clearly beneficial to both staff and patients to be able to make predictions about pregnancy outcome at this early stage. Informed patients will experience reduced anxiety and confusion, and medical follow-up can be tailored to individual needs.

Heiner et al (1) also state that providing predictive information may alleviate anxiety for patients and assist clinicians in providing appropriate medical follow up as required.

Conclusion:

In conclusion, a single serum sample taken and assayed 16 days after ovulation, following ART treatment, is clinically useful in predicting pregnancy outcome.

This is valuable information for both patients and practitioners because it does reduce anxiety and provide a basis for early pregnancy management and monitoring .

The findings of this study could be included in a patient information sheet because the relationship between the level of hCG, age, and the predictive value of pregnancy outcome is comprehensible to patients. This study included all ART treatment cycles; therefore, this information can be used for all patients in units where a variety of ART procedures are practiced.

TABLE 1: Distribution of treatment types

Treatment Types	No. of Patients (%)
Ovulation induction	18 (9%)
Intercoursc timing	16 (8%)
IUI	110 (55%)
IVF	30 (15%)
ICSI	26 (13%)

TABLE 2: Summary of outcome by hCG levels

hCG (IU/L)	No of women	Ongoing pregnancy Rate(%)	Miscarriage Rate (%)
25-50	4	<25	>75
50-100	16	25	75
100-199	27	73	27
200-299	48	96	4
>300	105	100	0

Abstract:

Objective :
After assisted reproductive technology (ART) cycles, elevated serum hCG at 16 days after ovulation is used as an endocrine marker of pregnancy. The goal of this study is to determine whether serum hCG level obtained 16 days after ovulation is a reliable predictor of pregnancy outcome.

Material & Method :
This is a retrospective study in women who have achieved pregnancy through ARJ treatment, in Montaserieh Hospital (IVF center). Analysis of data using logistic regression (stata) to predict a binary outcome: Ongoing pregnancy or miscarriage. Pregnancy was defined as progression to >20 weeks' gestation. Miscarriage included spontaneous abortion, blighted ovum, or ectopic pregnancy.

Results :
Human chorionic gonadotropin (hCG) was found to be the main determinant of pregnancy; age had minor effects; whereas luteal support and treatment types were nonpredictive. Low hCG levels between 25-50Iu/L were associated with a low probability of ongoing pregnancy (<25%), whereas levels of 200IU/L and higher predict a >96% chance of ongoing pregnancy.

Conclusions :
A single serum hCG level 16 days after ovulation provides a useful predictor of pregnancy outcome.

Key Words :
Pregnancy outcome, Human chorionic gondotropin- assisted reproductive technology.

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