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ORIGINAL ARTICLE

Human chorionic gonadotropin cutoff value determined by receiver operating characteristic curve analysis is useful but not absolute for determining pregnancy outcomes

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KEYWORDS

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Viable pregnancy;
Non-viable pregnancy

Abstract *Objective:* To assess the clinical value of a single early human chorionic gonadotropin (HCG) assay (day 14 post embryo transfer) in assisted reproductive technology (ART) pregnancies. *Design:* Retrospective study. *Settings:* The Assisted Reproductive Unit at Jordan University Hospital, Amman, Jordan. *Patients:* During 2009–2011, a total of 248 embryo transfer cycles resulting in pregnancy, defined as serum HCG concentration of $\geqslant 10$ IU/l, were included. *Interventions:* None. *Materials and methods:* Pregnancies were classified as viable (live fetus at 24 weeks gestation) or non-viable (biochemical pregnancy, miscarriage, ectopic pregnancy). Receiver operating characteristic (ROC) curve analysis was used to evaluate the cutoff value of HCG with maximal sensitivity and specificity to differentiate between viable and non-viable pregnancies. *Results:* The median HCG concentration was 264 IU/l in viable pregnancies and 120 IU/l in non-viable pregnancies ($p < 0.001$). The median HCG concentration was 222 IU/l in singleton pregnancies, 389 IU/l in twin pregnancies and 809 IU/l in triplet pregnancies ($p < 0.001$). An HCG value of 145 IU/l emerged as the most suitable cutoff point to predict viable pregnancy. *Conclusion:* HCG cutoff values determined by a ROC curve analysis are useful but not absolute for discriminating between

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viable and non-viable pregnancy outcomes on day 14 after embryo transfer. So it is important to continue routine monitoring of ART pregnancy outcomes.

1. Introduction

Human chorionic gonadotropin (HCG) is produced by the trophoblast, a layer of tissue on the outside of the blastocyst that provides the embryo with nutrients and later forms part of the placenta and the fetal membranes (1). HCG is a glycoprotein dimer with a molecular weight of 37 kDa. HCG consists of a 145 amino acid β-subunit, which is unique to HCG, and a 92 amino acid α-subunit, which is identical to that of luteinizing hormone (LH), follicle-stimulating hormone (FSH), and thyroid-stimulating hormone (TSH) (2). HCG plays various key functions during pregnancy such as implantation, placenta development, and uterine and fetal growth (2).

Viable pregnancies follow an exponential rise in HCG during the first seven weeks of pregnancy and then decline slowly from the 10th week until term (2). HCG concentration shows a wide range among pregnancies, which can be the result of poor dating of pregnancy or the different doubling rates of HCG among different trophoblast cells (2,3).

Patients undergoing assisted reproductive techniques (ART) such as in vitro fertilization (IVF) are a group, in which the date of ovulation is known exactly; an injection of HCG is given to prepare for oocyte retrieval. These patients are very anxious to hear the prognosis, and thus early prediction of pregnancy outcome is very important for them. In addition, early prediction can allow a more efficient treatment and in cases of unfavorable outcomes it can reduce the risks associated with these pregnancies (4).

Early pregnancy loss is similar for singleton pregnancies conceived naturally or through ART (5). Spontaneous loss of at least one gestation occurred in about 25% of singleton pregnancies, 35% of twin pregnancies, and 55% of triplet pregnancies (5–7). It was suggested that 0.7% of ART cycles resulted in ectopic pregnancy (8). Clayton and coworkers found that the standard IVF resulted in 2.2% rate of ectopic pregnancy, compared to only 0.9% risk of ectopic pregnancy in spontaneous pregnancies. In addition, they found that ectopic pregnancy is higher in patients with tubal factor (9).

Single assay of serum HCG has been used to predict the outcome of the pregnancy (viable versus non-viable) well before it can be visualized by transvaginal ultrasound (US) scan (3,10–13). Different studies have determined the cutoff value of HCG that can discriminate viable from non-viable pregnancies (4,14,15). However and ideally, each ART center should analyze its own data to determine HCG cutoff value based on its experience (3). Thus, the aim of the current study is to find a correlation between HCG level measured at day 14 post embryo transfer and pregnancy outcome at our ART center.

2. Material and methods

2.1. Subjects

This study was performed at the Assisted Reproductive Unit at Jordan University Hospital, Amman, Jordan. Patients were identified from patient's registry at the unit. Between January 2009 till December 2011, data from 248 embryo transfer (ET) cycles resulting in pregnancy were collected. Information regarding the age of the female patients, cause of infertility, serum HCG level, and outcome of pregnancy was collected. Conception was defined as HCG serum concentration higher than 10 IU/l (4).

2.2. In vitro fertilization protocol

The participating patients underwent IVF and embryo transfer according to the protocols described by (16,17). Participating women who underwent fresh IVF cycles used either long down regulation using [gonadotrophin releasing hormone agonist (GnRHa) (Decapeptyl 3.75 mg)] in the mid luteal phase of the preceding cycle or short down regulation protocol using [gonadotrophin releasing hormone agonist (GnRHa) (Decapeptyl 0.1 mg)]. Controlled ovarian stimulation was performed using purified urinary gonadotrophin (Menogon, Ferring, Germany, or Fostimon, IBSA, Switzerland, or Merional, IBSA, Switzerland). Transvaginal US was used to monitor the IVF cycles. When three or more of the follicles had a diameter exceeding 18 mm, 10,000 IU units of HCG (Choriomon, IBSA, Switzerland or Pregnyl, Organon, USA) were administered intramuscularly (IM) to induce ovulation. Oocyte aspiration was performed approximately 36–38 h after HCG was given using a standard transvaginal US-guided approach. Embryo transfer was performed 3 days after oocyte aspiration and a maximum of three embryos were transferred. All patients included in this series received progesterone support for at least two weeks as vaginal suppositories (800 mg daily) (Cyclogest, Actavis UK Limited, or Utrogestan, Besins Healthcare, Belgium) starting one day after oocyte aspiration. HCG was not used for luteal support.

2.3. HCG assay

Serum HCG concentrations were measured by Chemiluminescent Microparticle Immunoassay (CMIA) for the quantitative and qualitative determination of total beta human chorionic gonadotropin (βHCG) in human serum (ARCHITECT; Abbot Laboratories, Abbot Park, IL, USA). The HCG assay was performed inside our hospital on day 14 post embryo transfer for all the patients. Blood results that were not obtained by day 14 after ET were not included in the study.