Slow rising serial chorionic gonadotropins predict poor pregnancy outcome despite sonographic viability

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Summary

Purpose: To determine the prognosis of women with slow rising beta-hCG levels when viability is detected by ultrasound.

Methods: Serum beta-hCG levels were obtained every two to three days in the early first trimester. Doubling-time (DT) of beta-hCG levels was defined as DT exceeding 3.2 days. Sonography was performed at eight weeks and then after 12 weeks.

Results: There were 158 consecutive pregnancies evaluated and 111 (70%) had normal rising beta-hCG levels, viable ultrasound at eight weeks, and viable pregnancies after 12 weeks. There were 22 pregnancies with slow rising beta-hCG levels (13.9%) with 16 (72.7%) showing viability at eight weeks but not after the first trimester. A sac-crown rump length discrepancy with a sac smaller than normal was found in 11 of these 16 (68.7%) women.

Conclusions: Patients with slow rising beta-hCG levels should not be given an optimistic prognosis even if viability is demonstrated at eight weeks.

Key words: Slow rising beta-hCG levels; Fetal viability; Sonography.

Introduction

Up to 20% or more pregnancies demonstrating fetal heart activity by ultrasonography subsequently abort [1-4]. Other data show that dropping, slow rising, or low levels of serum beta human chorionic gonadotropin (hCG) may also be indicative of spontaneous abortion (SAB) [5-8].

Early normal pregnancies are usually characterized by serum beta hCG doubling times varying from 1.4 to 3.5 days [7, 9-14]. Serial beta hCG determination provides more accurate information than data based on single hCG levels [11, 14-16]. There are data supporting the concept that in some women the exponential rate of increase of serum hCG in early normal pregnancy is constant [7, 9, 11-13], whereas others suggest that the beta hCG levels decrease with increasing hCG concentration and gestational age [14, 15, 17, 18].

Failure to demonstrate a proper rise of serum beta hCG has been found to be associated with increased risk of SAB [6, 10, 16]. Though both early pregnancy monitoring with serial chorionic gonadotropin determination and real-time sonography have been determined to be reliable indicators that an intrauterine pregnancy will progress to viability [16], no study to date has addressed the question of the prognosis of patients with a prolonged doubling time in early pregnancy but who demonstrate fetal heart activity. The study presented here was established to address this question so that a physician could properly counsel a woman warned of a possible abnormal pregnancy based on the rate of rise of beta hCG levels but who demonstrates fetal viability at eight weeks.

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Materials and Methods

A random selection of single pregnancies from 12/95 to 8/00 in infertile women not as a result of in vitro fertilization or gamete intrafallopian transfer were evaluated for the rate of rise of the sera beta hCG levels. Treatments included progesterone therapy for luteal phase defects, follicle maturing drugs for anovulation or release of oocytes before follicle maturity, treatment for cervical mucus abnormalities, e.g., guaifenesin or intrauterine insemination, hCG for luteinized unruptured follicle syndrome, and progesterone therapy for recurrent spontaneous abortion. Only patients with high sera beta hCG levels during the early first trimester were included. Patients from our suburban Pennsylvania infertility center were used for the investigation.

Doubling times of beta hCG levels were calculated according to the formula doubling time = $1n(2)*(t2-t1)/1n(hCG2-hCG1)$ where t1 is time after conception of the first beta hCG, t2 is time after conception of the second beta hCG, and hCG1 and hCG2 are the corresponding beta hCG levels [12]. Based on the literature [11, 14-16], we considered a patient as having a slow rising beta hCG if the doubling time exceeded 3.2 days.

Ultrasonography was performed at eight weeks and then again at 12-14 weeks. Transvaginal ultrasound exam performed at eight weeks included measurements of the mean gestational sac diameter (average length, width, depth from inner wall to inner wall), crown rump length and embryonic heart rate. A sac crown rump length discrepancy was reported if the corresponding gestational age derived from the sac average was > 1 week earlier than the age determined by the crown rump length. The patients were classified into two groups based on the beta hCG DTs: group 1 – normal DT < 3.2 days; group 2 – increased DT, DT ≥ 3.2 days. Chi-square analysis was used to compare the pregnancy outcomes in both groups. A p value of .05 was used.

Results

There were 158 pregnancies evaluated. Normal rising beta hCG levels were found in 136 (86.0%) (group 1) and slow rising levels in 22 (14%) (group 2). A comparison of pregnancy outcome by DT levels is presented in Table 1. Viable pregnancies past the first trimester were found in 111 (81.6%) group 1 patients vs 0% in group 2 patients ($p < .05$).

Despite the zero viability rates after the first trimester seen in group 2 patients, 16 (72.7%) women showed viability at eight weeks. The calculated doubling time for 14 women with normal doubling times and viable pregnancies at eight weeks but non-viable after the first trimester was 2.0 vs 6.2 for the 16 group 2 patients with viability at eight weeks ($p < .05$). The mean doubling times for the 11 group 1 patients with non-viability after eight weeks was 2.4 vs 7.2 for those group 2 patients not demonstrating viability at eight weeks ($p < .05$).

For the 16 women with slow rising beta hCG levels the sac was lagging behind the crown-rump length by at least one week in 11 (68.7%). This is in contrast to only two of 111 (1.8%) with normal rising beta hCG levels and viable pregnancies past the first trimester ($p < .05$). Fourteen of the 125 (11.2%) patients with normal rising beta hCG levels and viability at eight weeks did not complete the first trimester and only one out of 14 (7.1%) showed a sac size/crown-rump length discrepancy ($p < .05$).

Table 1. — *Comparison of pregnancy outcome by doubling time of serum beta-hCG levels.*

	Normal rising beta hCG DT < 3.2 Days	Slow rising beta hCG DT ≥ 3.2 Days
Live birth	111 (81.6%)	0 (0.0%)
Fetal heart motion, SAB	14 (10.3%)	16 (72.7%)
No fetal heart motion	11 (8.1%)	6 (27.3%)

p <. 05, chi-square.

Discussion

Previous data found that gestational sacs that are too small for dates predict subsequent pregnancy loss even when viability is seen [19-21]. Though the majority of patients with slow rising beta hCG levels and viability did demonstrate a small sac size, still 31.3% would have only been predicted by the slow rising sera beta hCG levels.

These data suggest that women with slow rising beta hCG levels should not be given an optimistic prognosis even if viability is demonstrated at eight weeks. Despite an extensive search of the literature, we could not find a previous study addressing the question of which is the more important prognostic finding: a slow rising beta-hCG or viability on ultrasound at eight weeks without a crown rump length/sac size discrepancy? Our data suggest the answer is the slow rising beta hCG level.

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