

First-trimester bleeding with falling HCG

Don't assume miscarriage

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Family physicians often use quantitative human chorionic gonadotropin (HCG) testing to assess first-trimester bleeding. While we anticipate a range of normal results for any given week in the first trimester, we predict an approximate doubling over 48 hours in a normal pregnancy during the first trimester. Human chorionic gonadotropin tends to peak at about 10 weeks' gestation before declining and stabilizing. When HCG levels plateau prematurely or fail to rise as expected, we consider that the pregnancy might not be viable.

This case report points to a wide range of normal values for HCG rate of rise and time to peak, making interpretation based on HCG activity alone challenging for family physicians.

Case description

Mrs S.C., a 28-year-old primiparous woman, was diagnosed at a walk-in clinic with a 6-week pregnancy. She was referred to our clinic for prenatal care, and an appointment was made for about 12 weeks' gestation. Several weeks later, however, she returned to the walk-in clinic because of postcoital spotting that had lasted 1 day. There was no associated cramping. Her estimated gestational age (EGA) by confident dates was 8 weeks, 5 days. Her examination revealed blood in the vaginal vault, but was otherwise normal with no cervical dilation or pathology. Quantitative HCG test results showed her HCG level was 167 343 IU/L. She was asked to repeat the test the next day; results showed a level of 131 681 IU/L.

She was asked to come to our clinic for further evaluation. While awaiting her appointment, her HCG test was repeated again, 48 hours after the second test (EGA 9 weeks, 1 day). Results showed a further drop to 115 104 IU/L. She was seen in our clinic several days later (EGA 9 weeks, 5 days) with no further bleeding or pain. Results of examination were normal. Results of a follow-up HCG test, however, showed her levels had dropped yet again to 104 177 IU/L. Prenatal laboratory workup also determined that she was Rh-negative.

Based on the 3 consecutive HCG drops, I initiated a difficult discussion with the patient. I discussed the

progressive decline in HCG as representing, in all likelihood, a nonviable pregnancy. As usual in these circumstances, I addressed the issues of guilt, blame, and grief associated with miscarriage. We discussed management options, including chemical induction, dilation and curettage, and watchful waiting. The patient opted to wait for spontaneous completion of her miscarriage. Finally, I referred her for treatment to suppress the immune response, in light of her Rh-negative status.

Before receiving treatment the following week, a confirming ultrasound was obtained. At 10 weeks, 6 days EGA, ultrasound scans revealed a viable 11-week pregnancy. This experience understandably resulted in an emotional roller coaster for my patient, who graciously but decidedly transferred her care to another physician.

Discussion

Human chorionic gonadotropin is a glycoprotein produced by the trophoblasts of the developing placenta. It is detectable in maternal serum within a few days of implantation. The literature points to wide variability in HCG levels at any given point during pregnancy.¹⁻¹⁰ It consistently demonstrates, however, an increasing doubling time as pregnancy progresses. The average doubling time for HCG levels during the first 6 weeks from conception (8 weeks gestational age) is 1.94 days.¹ This increases to an average of 4.75 days between 6 and 8 weeks from conception (8 to 10 weeks gestational age)¹; HCG levels then begin to plateau, reaching an average peak of about 100 000 IU/L before declining and stabilizing at approximately 20 000 IU/L.² This generally occurs at 10 to 14 weeks gestation, at which point HCG levels become less helpful in the evaluation of first-trimester bleeding.¹¹

Variation in serum HCG applies not only to serum levels, but to the rate of rise and the time to peak as well. At the end of 6 weeks from the last menstrual period, serum HCG has been shown to vary from 440 to 142 230 IU/L among women whose pregnancies resulted in normal term deliveries.³ Among women presenting with an initial HCG level lower than 5000 IU/L, a rise of as little as 53% over a 2-day period has been associated with normal pregnancy.²

A slow rate of rise or a drop in HCG levels during the first 8 to 10 weeks of pregnancy represents death of trophoblastic tissue and can indicate ectopic or nonviable

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intrauterine pregnancy.³ Serial quantitative HCG values are, therefore, helpful in management of threatened early pregnancies. Correlation of HCG levels with transvaginal ultrasound scans contributes to management as well.^{12,13} Ultrasound, however, is not always readily available in this type of situation.

Family physicians are generally familiar with the concept of a 2-day average doubling time for HCG values in a normal first-trimester pregnancy. It is less well known, however, that the data from which this concept is derived come primarily from women with initial HCG values lower than 5000 IU/L presenting at less than 10 weeks from their last menstrual period.² While a 2-day doubling time is a dependable marker up to 8 weeks gestational age, normal HCG activity is less clearly defined beyond that point, and the usually accepted doubling times might not apply.¹ Because there are few recent guidelines and reviews in the literature specifically addressing use of HCG levels in the evaluation of possible first-trimester pregnancy loss, family physicians might find themselves at a disadvantage when confronted with this issue.

Conclusion

Wide variation in first-trimester HCG levels, coupled with uncertain HCG activity patterns at values greater than 5000 IU/L should give pause to family physicians managing late first-trimester bleeding. Transvaginal or transabdominal ultrasound should be employed early in the management of these pregnancies. Decisions based solely on the pattern of HCG activity late in the first trimester might result in misinformation and in mismanagement of patients. ❁

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EDITOR'S KEY POINTS

- Human chorionic gonadotropin (HCG) levels are frequently used to assess first-trimester bleeding. It is commonly expected that HCG levels will double over 48 hours during the first trimester of a normal pregnancy.
- There is wide variation in HCG levels, however, particularly late in the first trimester and with values greater than 5000 IU/L. The author cautions that HCG levels should not be relied on as the sole determinant of the viability of a pregnancy. Correlation of HCG levels with ultrasound scans is a key component of assessment.

POINTS DE REPÈRE DU RÉDACTEUR

- On se sert souvent des niveaux de gonadotrophine chorionique humaine (HCG) dans l'évaluation d'un saignement au premier trimestre. On s'attend généralement à ce que le niveau de HCG double sur une période de 48 heures durant le premier trimestre d'une grossesse normale.
- Il y a toutefois d'importantes variations du niveau de HCG, notamment vers la fin du premier trimestre, les valeurs pouvant alors excéder 5000 IU/L. Les auteurs suggèrent de ne pas se fier aux seuls niveaux de HCG pour déterminer la viabilité d'une grossesse. L'évaluation idéale devrait associer échographie et niveaux de HCG.

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