Ultrasonograph versus β-human chorionic gonadotropin titer for verification of termination of missed first trimester miscarriage

Aziza H. Nassef[a], Nahed H. Mohammed[a], Samar M. Ibrahim[b]

Introduction Miscarriage is one of the common complications of pregnancy. Up to 20% of recognized pregnancies will end in miscarriage. However, when women were followed with serial serum human chorionic gonadotropin (hCG) measurements, the actual miscarriage rate was found to be 31%. Many pregnancies are lost spontaneously before a woman recognizes that she is pregnant, and the clinical signs of miscarriage are mistaken for a heavy or late menses.
In some countries with low resources, ultrasound may be not available in all medical centers. So, confirmation of complete termination of first trimesteric miscarriage may be not possible, and these cases may present with complications of inadequate treatment. So, we need to study other method for verification of successful management such as β-hCG titter.

Objective The aim was to assess the usefulness of testing serum β-hCG titer to confirm the effective medical termination of the first trimester miscarriage.

Patients and methods A prospective study was conducted at the Department of Obstetrics and Gynecology at Al Zahraa university Hospital in the period between December 2017 and April 2018. A total of 34 pregnant women with first trimester miscarriage (7–13 weeks from the first day of last menstrual period) were submitted for medical termination of miscarriage, and each case was subjected to ultrasonography 7 days after termination of miscarriage (for measurements of endometrial thickness) and serum β-hCG at 3 and 7 days after termination of miscarriage.

Results Endometrial thickness decreased after termination of miscarriage (with cut-off value <15 mm). Moreover, β-hCG decreased after medical termination of miscarriage. In our study, receiver operating characteristics curve was used to define the best cut-off value of β-hCG, which was greater than 34 mIU/ml, with sensitivity of 90%, specificity of 70.8%, positive predictive value of 56.4%, and negative predictive value of 94.4%, with diagnostic accuracy of 83.5%.

Conclusion Measuring β-hCG level is an effective alternative to transvaginal ultrasound measurements of endometrial thickness to verify the completion of termination of early miscarriage.

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[a]Department of Obstetrics and Gynecology, Faculty of Medicine for Girls, Al Azhar University, Cairo, [b]Department of Obstetrics and Gynecology, Om El Masryeen General Hospital, Giza, Egypt

Correspondence to Aziza Hussien Nassef, MD in obstetrics & gynecology, El Shrouk city, 4th neighborhood 1133 building, Faculty of Medicine for Girls, Al Azhar University, 11837, Cairo, Egypt. Tel : +201013777336.
e-mail: aziza.nassef@gmail.com

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Introduction

Miscarriage, also known as spontaneous abortion and pregnancy loss, means spontaneous death of an embryo or fetus before survival [1,2]. Risk factors for miscarriage include an increased maternal age, previous miscarriage, exposure to tobacco smoke, obesity, diabetes, thyroid problems, and drug or alcohol use [3]. Approximately 80% of miscarriages occur in the first 12 weeks of pregnancy (the first trimester) [2]. The underlying cause in approximately half of the cases involves chromosomal abnormalities [4]. Diagnosis of a miscarriage may involve checking to see if the cervix is open or closed, testing blood levels of human chorionic gonadotropin (hCG), and an ultrasound (US) [5]. Other conditions that can produce similar symptoms include an ectopic pregnancy and implantation bleeding [2]. Miscarriage is one of the common complications of pregnancy, which occur in up to 20% of all recognized pregnancies. In some countries with low resources, US may not be available in all medical centers. So, confirmation of complete termination of first trimester miscarriage may be not possible, and these cases may present with complications of insufficient treatment. So, we studied other methods for verification of successful management such as β-hCG titer. Miscarriage is the most common complication of early pregnancy. Among women who know they are pregnant, the miscarriage rate is roughly 10–20%, whereas rates among all fertilization is ~30–50% [2]. In those under the age of 35 years, the risk is ~10%, whereas it is ~45% in those over the age of 40 years [2]. Risk begins to increase around the age of 30 years. Approximately 5% of women have two miscarriages [6]. Some recommend not using the term 'abortion' in discussions with those experiencing a miscarriage in an effort to decrease distress [7].

Patients and methods

An informed consent was obtained from all patients. This study was approved by the medical ethics of the committee of faculty of medicine for girls, Al Azhar university, Cairo, Egypt. an informed consent was obtained from all participants. The study included 34 pregnant women recruited from the obstetrics outpatient clinic of Al Zahraa University Hospital. They were accidently discovered to have missed miscarriage during routine first trimester US with or without mild vaginal bleeding, or mild abdominal pain. All patients fulfilled the inclusion criteria, which were maternal age 25–41 years old, gestational age from 7 to 13 weeks from the first day of last menstrual period and confirmed by ultrasonography, and absence of dilation of internal cervical os or severe vaginal bleeding. Exclusion criteria were as follows: (a) signs of sepsis (fever and leukocytosis); (b) contraindication to misoprostol as bronchial asthma; (c) allergy to prostaglandin or misoprostol; (d) ectopic pregnancy; (e) hydatidiform mole; (f) incomplete or inevitable abortion; (g) medical disorder as hypertension, diabetes mellitus, thrombocytopenia, or cardiac disease; and (h) if the case is hemodynamically unstable. The cases were admitted to the hospital and subjected to complete history taking, general examination, abdominal examination, local examination, and routine laboratory investigations. Quantitative β-hCG was measured by ELISA test using a commercial kit (Immunotech Beckman Counter Co. Czech Republic, France). Transvaginal US was done (using Logic BV5, Logic V5, Alkan medical, Cairo, Egypt) to exclude ectopic pregnancy, confirm the diagnosis of missed miscarriage, detect fetal pole, and measure crown rumb lengh (CRL) and mean gestational sac diameter. Then termination of missed miscarriage was induced by misoprostol tablets (800 μg) was inserted per vagina repeated after 3 h or (600 μg) sublingual every 3 h (two doses) depending on the amount of vaginal bleeding according to FIGO classification, 2017. Follow-up of all patients was done by serum β-hCG titer (3 days and 7 days after termination) and by transvaginal US (7 days after termination) for measuring endometrial thickness for verification of the effectiveness of the medical termination of miscarriage (Figs 1).

Results

A total of 34 pregnant women having missed abortion (7–13 weeks) were evaluated by transvaginal US. Then, they were subjected to medical termination. The mean age was 29±4.4 years, and the mean BMI was 25.9±2.6.

There were 10 (29.41%) cases with failed medical termination, and these were diagnosed by US, where the ultrasonographic appearance were either incomplete abortion with endometrial thickness more than 15 mm or retained products of conception (Figs 2). These cases necessitated surgical intervention. A total of 24 (70.59%) cases had succeeded medical treatment (Tables 1–5).

Receiver operating characteristics curve was used to define the best cut-off value of β-hCG (7 days after termination), which was greater than 34, β-hCG (7 days after termination) was 90% sensitive, 70.8% specific, with positive predictive value of 56.4%, and negative predictive value of 94.4% (Figs 3).

Table 1 Demographic data distribution of the cases

Demographic data	Total (*N*=34) [*n* (%)]
Age (years)	25–41 (29±4.41)
Gestational age	7–13 (8.13±1.47)
BMI (weight/height^2)	20–32 (25.9±2.6)
Gravidity	0–8 (4.32±1.54)
Type of previous delivery	
Nulliparous	7 (20.6)
CS	9 (26.5)
NVD	18 (52.9)
Previous abortion	
0	9 (20.9)
1	17 (50.0)
2	8 (23.5)
Education	
High school	2 (5.9)
Middle school	13 (38.2)
Primary education	13 (38.2)
Illiterate	6 (17.6)

CS, cesarean section; NVD, normal vaginal delivery.

Table 2 Comparison between the levels of β-human chorionic gonadotropin before and 3 days and 7 days after medical termination of miscarriage

	β-hCG (mIU/ml) (mean±SD)	Mean difference	Paired sample *t*-test	*P* value
Before	16 950.29±23 492.13			
After 3 days	867.22±2105.04	−16 083.07	11.683	<0.001**
After 7 days	253.88±877.38	−16 696.41	17.914	<0.001**

This table shows highly statistically significant difference between before, after 3 days, and after 7 days of β-hCG values in the patient group. hCG, human chorionic gonadotropin.

Discussion

Misoprostol can be used in miscarriage as an available effective medical alternative to surgical treatment such as suction evacuation. In the current study, success rate of medical termination was 70.59%. However, Ngoc *et al.* [8] found 92.9% verification of termination of miscarriage success rate after administration of 800-μg misoprostol. Fiala *et al.* [9] reported a 98.2% success rate in their study using mifepristone 600 mg and misoprostol 400 μg orally followed 3 h later by a second dose of 400 μg misoprostol if the woman had not started to bleed. Confirming a completion of abortion at the follow-up visit should be done. In the current study, transvaginal US was done before and 7 days after the medical treatment for all cases. US confirmed the effectiveness of medical treatment in 70.59% of cases. β-hCG was measured at 3 days and 7 days after termination. Receiver operating characteristics curve was used to define the best cut-off value of β-hCG (7 days after termination), which was less than 34 mIU/ml, with sensitivity of 90%, specificity 70.8%, positive predictive value of 56.4%, and negative predictive value of 94.4%, with diagnostic accuracy of 83.5%. This means that measuring β-hCG titer is as effective as transvaginal US in verification of the effectiveness of medical treatment of miscarriage. Fiala *et al.* [9] found that the value at second week for β-hCG was 98.5% and 89.8% for US (differences between both results were owing to the different timing, as it was done after 2 weeks in Fiala's study). Clark *et al.* [10] reported that using

Table 3 Endometrial thickness distribution 7 days after termination of miscarriage in all cases

Endometrial thickness (mm)	Number of cases (*N*=34) [*n* (%)]
<15	24 (70.6)
>15	10 (29.4)

The mean of endometrial thickness (mm) in all cases was 8–29 (15.18±5.97).

Table 4 Comparison between endometrial thickness less than 15 mm and greater than 15 mm according to β-human chorionic gonadotropin of the study group

	Endometrial thickness (mm) (mean±SD)		*t*-test	*P* value
	<15 mm	>15 mm		
β-hCG (mIU/ml) 7 days after termination	35.04 ±38.04	779.10 ±1544.23	5.818	0.022
Decline of β-hCG (mIU/ml) before and after 7 days	99.37 ±0.65	98.71 ±1.61	3.014	0.092

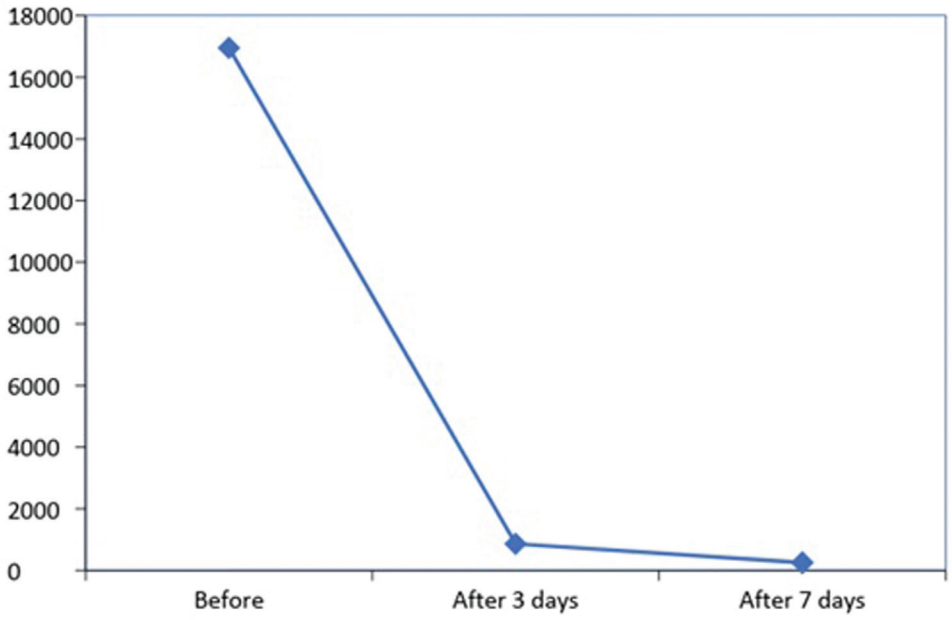
This table shows statistically significant difference between endometrial thickness less than 15 mm and greater than 15 mm according to β-hCG values of the cases. hCG, human chorionic gonadotropin.

Table 5 Diagnostic performance of β-human chorionic gonadotropin (mIU/ml) in discrimination of endometrial thickness (mm)

Cut-off value of endometrial thickness (mm).	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Diagnostic accuracy (%)
>34	90	70.8	56.4	94.4	83.5

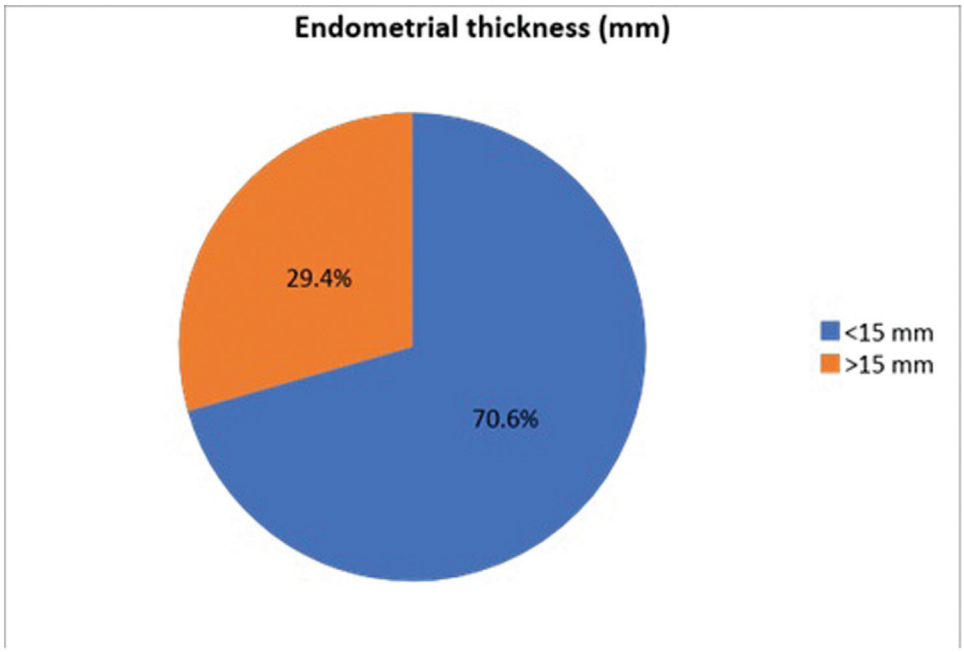
NPV, negative predictive value accuracy; PPV, positive predictive value.

Figure 1



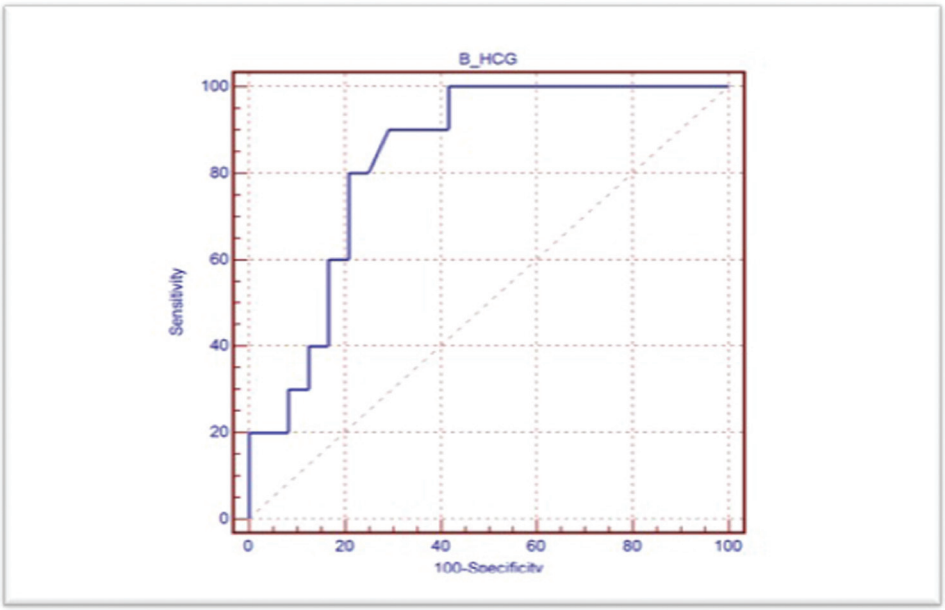
Line chart of β-hCG levels before and 3 day after and 7 days after termination of miscarriage.

Figure 2



Pie chart of endometrial thickness distribution of the cases (7 days after termination).

Figure 3



Receiver operating characteristic curve showing diagnostic performance of β-hCG in discrimination of endometrial thickness (mm).

pretreatment and post-treatment serum β-hCG measurement with sonograms, only when indicated, had similar outcome to using mandatory pretreatment and postsonograms. Clark *et al.* [10] used sonography, only when indicated, as in cases of no successful medical abortion, no β-hCG decline by at least 80%, or in cases with uncertain history. Fielding *et al.* [11] stated that if clinicians monitor β-hCG levels to identify any ectopic or continuing pregnancies, medical abortion can be safely performed without sonography.

Conclusion

Measuring β-hCG level is as effective as transvaginal US measurement of endometrial thickness to verify the completion of termination of early miscarriage. The best cut-off value of β-hCG (7 days after termination) was less than 34 mIU/ml, with sensitivity of 90%, specificity of 70.8%, positive predictive value of 56.4%, and negative predictive value of 94.4%, with diagnostic accuracy of 83.5%.

Recommendations

In low-resource places, we can use β-hCG titer for verification of completion of termination of miscarriage (especially when US or the sonographer is not available).

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Nil.

Conflicts of interest

There are no conflicts of interest.

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