Gynecology & Obstetrics
ISSN: 2161-0932

Farag et al., Gynecol Obstet (Sunnyvale) 2018, 8:8
DOI: 10.4172/2161-0932.1000481

Research Article Open Access

Ultrasonography and Pregnancy Outcome in Threatened Abortion: A Prospective Observational Study

Safaa Abdel Salam Ibrahim and Ahmed Mahmoud Farag*

Department of Obstetrics & Gynecology, Zagazig University, Egypt

***Corresponding author:** Ahmed Mahmoud Farag, Department of Obstetrics and Gynecology, Zagazig University, Egypt, Tel: +201000333162; E-mail: ahmed.farag@zu.edu.eg

Received date: June 29, 2018; **Accepted date:** September 5, 2018; **Published date:** September 20, 2018

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Abstract

Aim: To evaluate the role of ultrasound (US) as a predictor of pregnancy outcome in cases with threatened miscarriage.

Introduction: First trimester bleeding is a common anxious medical disorder. It may end with pregnancy loss or lead to adverse maternal and fetal outcomes. Certain sonographic parameters like (GSD, YSD, CRL, and FHR) could predict these outcomes.

Material and methods: A prospective study involving 500 women in their first trimester was divided into three groups: group I (130 women) in whom threatened abortion ended in abortion, group II (170 women) with threatened abortion and completed their pregnancy and group III (200 women) with normal pregnancy. US indicators included Gestational Sac Diameter (GSD), Yolk Sac Diameter (YSD), Crown-Rump Length (CRL), and Fetal Heart Rate (FHR). These patients were evaluated for the pregnancy outcomes.

Results: A significant difference was found between group I and the other two groups regarding FHR and CRL ($P<0.05$), while no significant difference was observed among the three groups regarding GSD or YSD. Compared to control group, the cases of group II had a higher incidence of premature rupture of membrane PROM (OR=9.9, $P<0.05$), gestational hypertension (OR=5.4, $P<0.05$), and placental abruption (OR=4.8, $P<0.05$).

Conclusion: FHR and CRL are good sonographic markers to predict pregnancy outcome in women with threatened miscarriage. FHR at 115 beat/minute yields the best predictivity and CRL at 22 mm yields the least predictive accuracy.

Keywords: Vaginal bleeding; Threatened abortion; Pregnancy outcome; Ultrasonography

Abbreviations: CRL: Crown-Rump Length; FHR: Fetal Heart Rate; GSD: Gestational Sac Diameter; IUGR: Intrauterine Growth Retardation; PROM: Premature Rupture of Membrane; US: Ultrasound; YSD: Yolk Sac Diameter

Introduction

The first trimester vaginal bleeding is a common medical problem, represents 15% to 25% of all pregnancies [1-3]. Threatened miscarriage is defined as any vaginal bleeding before 20 gestational weeks with or without abdominal pain, while the cervix is closed [4]. A threatened miscarriage is often associated with anxiety for the mother, family, and the physicians [2]. More than 50% of pregnancies with the first-trimester bleeding end in pregnancy loss. If the pregnancy continues, maternal and fetal outcomes may be affected [5-7].

Additionally, the first trimester vaginal bleeding assumes a role in the occurrence of late pregnancy complications [8-11]. The incidence of these complications such as Premature Rupture of Membrane (PROM), Low Birth Weight (LBW), placental abruption, pre-eclampsia has been reported in some studies as high as 5% to 10% [5-9].

Numerous sonographic signs have been described by various authors to predict pregnancy outcome. These signs included an excessively large, excessively small, or irregularly shaped gestational sac, a low implantation site, a large or irregular yolk sac, a weak decidual reaction, and a slow embryonic heart rate [10-14].

Other studies have been performed using ultrasound criteria and biochemical markers aiming to predict the outcome of pregnancy [8,15]. Various biochemical markers have been investigated in the past to predict the outcome of threatened miscarriage; however, the results have been conflicting [16]. A recent study published in 2017 [17] has shown that early pregnancy markers in patients with threatened abortion including the size of gestational sac, size and shape of yolk sac, and Fetal Heart Rate (FHR) are good predictors of pregnancy outcome.

Several studies have investigated the role of ultrasound parameters in threatened abortion and its predictive value in pregnancy outcome, but few such studies used the combination of these parameters.

In the clinical context of diagnostic algorithms on this subject, there is a perceived knowledge gap regarding the shortage of information and the significance of late pregnancy outcomes. We conducted a prospective study to evaluate the prognostic value of sonographic parameters Gestational Sac Diameter (GSD), Yolk Sac Diameter (YSD),

Crown-Rump Length (CRL), and FHR and the impact of first trimester vaginal bleeding on maternal and perinatal outcomes.

Patient and Methods

Study population

In this prospective observational study, we examined patients diagnosed with a threatened miscarriage (patients presented with vaginal bleeding with or without cramping during the first 20 weeks of gestation with a closed cervix and documented heartbeats during the ultrasonographic examination) during the period from January 2017 to January 2018.

Inclusion criteria

- Normal Body Mass Index (BMI); 18-25 kg/m^2
- Sure of dates (previous regular cycles with a known 1st day of LMP)
- Previous regular cycles (inter-cycle variation ≤ 7 days)
- The absence of cervical pathology
- A single pregnancy

Exclusion criteria

- Pregnant females with chronic systemic disease (i.e. chronic hypertension, diabetes mellitus, and thrombophilia)
- Those on antiepileptic or antipsychiatric drugs
- Multiple pregnancies
- History of trauma or surgery during the current pregnancy
- Smokers

This yielded a final cohort of 300 pregnant women. We divided our patients into two groups: group I included 130 women with threatened abortion and ended in pregnancy loss and group II included 170 women with threatened abortion and completed their pregnancy.

We also carefully selected 200 women with normal pregnancy as group III (the control group). The characteristics of the patients in the three groups were presented in Table 1.

Ethical consideration

The present study was approved by the institutional review board. All patients were informed about the study and provided written informed consent. The study was performed in accordance with the ethical principles of the Declaration of Helsinki.

Patient management

We subjected all participants for full history taking, complete general examination, and ultrasound examination. Gestational age was calculated according to the first day of last menstrual cycle and was confirmed by ultrasound. All patients were registered and followed up prospectively at antenatal clinics.

We noted the amount of bleeding at each visit. If we found spotting, it was considered as light. If the bleeding was similar to patients' menstrual bleeding or more, it was considered heavy. All patients were delivered at the same hospital and evaluated for the outcome.

The outcome included primary and secondary outcomes. The primary outcome was pregnancy loss before 20-weeks' gestation. The secondary outcome was the occurrence of late pregnancy complications either maternal or fetal complications.

	Group I (n=130)		Group II (n=170)		Group III (n=200)		P value
	Mean	SD	Mean	SD	Mean	SD	
Maternal age (years)	28.9	4.2	29.8	6.5	30.5	6.7	> 0.05
BMI (kg/m^2)	27.9	2.9	26.4	3.1	26.5	2.5	> 0.05
Parity							> 0.05
Nullipara	87	66.9	113	66.5	131	65.5	
Multipara	43	33.1	57	33.5	69	34.5	
Previous one pregnancy loss	18	13.8	25	14.7	27	13.5	> 0.05
GA at bleeding onset (weeks)	6.8	2.5	7.5	2.2	-	-	> 0.05
Vaginal spotting	5.9	1.9	4.8	1.6	-	-	< 0.05 *
Heavy vaginal bleeding	7.5	2.1	1.4	0.3	-	-	< 0.05 *

Table 1: Characteristics of studied groups at presentation.

Ultrasound examination

All ultrasound examinations of this study were done and reviewed by a single radiologist experienced in obstetric sonography to reduce the observational bias. Logiq-5 Sonography Machine from GE was used for sonographic evaluation. We performed transvaginal sonography for all patients using a high-frequency endovaginal probe (5/7.5 MHz) with real-time sector scanner after the patient voided urine. Transabdominal ultrasound scanning was done for all patients using a low-frequency probe (3/3.5 MHz) with real-time sector scanner. Ultrasound examination included: early scan for measurement of GSD (Figure 1), FHR (Figure 2), CRL and YSD (Figure 3); 11-14 weeks' scan; 20 weeks scan to rule out any structural abnormality; 28, 34, and 38 weeks' scans, and when necessary to look for IUGR, oligohydramnios and abnormal Doppler findings. Finally, followed up till delivery to find out the fetal outcome.

At 7 weeks' gestation, we measured CRL as the greatest length of the embryo as it cannot be visualized at this age. After 7 weeks, we measured CRL in a sagittal section of the embryo and avoided inclusion of the yolk sac [18]. We calculated FHR as beats per minute (b/min) by the software of the ultrasound machine after measurement by electronic calipers of the distance between two heart waves. FHR of less than 100 beats per minute at 7 weeks or earlier was classified as slow [19]. We measured GSD as the mean of three perpendicular diameters with the calipers sited at the inner edges of the trophoblast [20]. Yolk Sac Diameter (YSD) was determined by placing calipers on the inner limits of the longer diameter. Size of the sac, shape, echogenicity of the rim and center of the sac, its number and degenerative changes such as calcification were evaluated. YS having a diameter of 3 mm to 6 mm, rounded shape, the absence of degenerative changes, and the presence of echogenic rim and

hypoechoic center were considered normal. Any deviation from above parameters was considered abnormal [21].

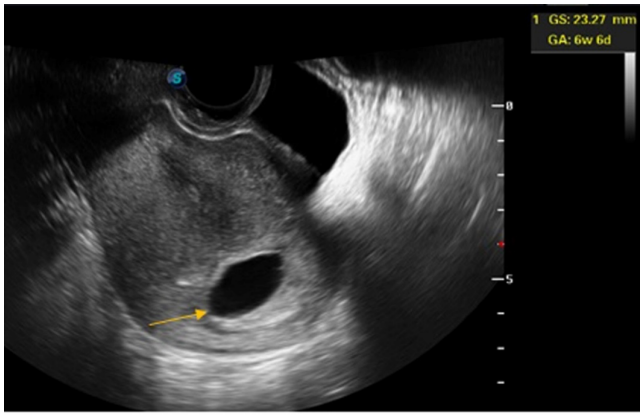

Figure 1: Normal GS (yellow arrow) in a patient with vaginal bleeding at 7 weeks' gestational age.

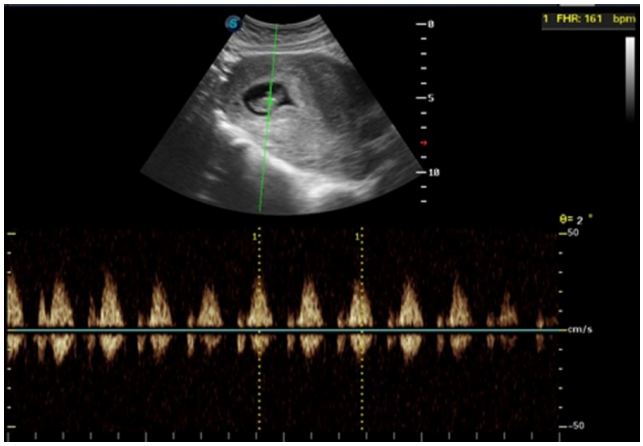

Figure 2: Normal regular FHR in a patient with vaginal bleeding at 8 weeks' gestational age.

Gestational age was calculated by modified Naegele's rule. LMP derived gestational age was compared with ultrasound derived gestational age using CRL and marked discrepancy of one or more weeks led to exclusion of participants from the study.

Statistical analysis

Data are presented as the mean ± standard deviation (SD) and were processed and analyzed using the statistical software SPSS 10 (SPSS, Chicago, IL, USA). The significance of the difference between each parameter in patients and controls was assessed by the nonparametric Mann-Whitney test for unpaired samples. The diagnostic performance of sonographic parameters was estimated. The Odds Ratio (OR) with 95% Confidence Interval (CI) was calculated. A p-value ≤0.05 was considered statistically significant.

Results

Study population

We did not find a significant difference among the three studied groups regarding age, parity, Body Mass Index (BMI), gestational age at bleeding onset or number of previous abortions. There is a statistically significant difference among the three studied groups regarding heavy vaginal bleeding Table 1.

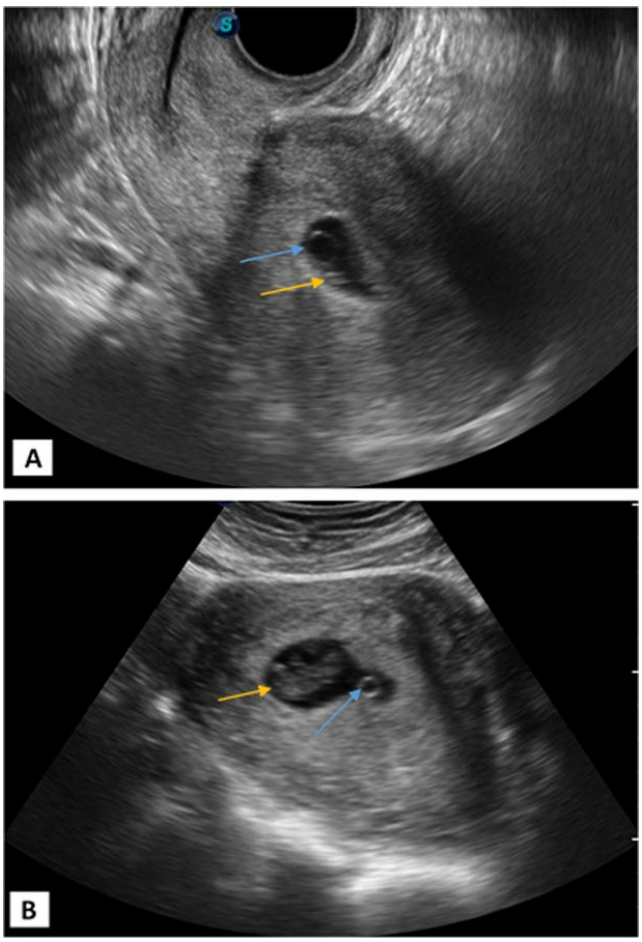

Figure 3: (A) Normal fetal pole (yellow arrow) and YS (blue arrow) in a patient with vaginal bleeding at 6 weeks' gestational age. (B) Normal fetal pole (yellow arrow) and YS (blue arrow) in a patient with vaginal bleeding at 9 weeks' gestational age.

Sonographic markers

The study of sonographic markers showed a statistically significant difference between Group I and the other two groups regarding FHR and CRL; while there was no significant difference among the three groups regarding GSD or YSD Table 2.

Maternal pregnancy outcome in group II and III

The pregnancy outcome complications are summarized in Table 3. We found that the first trimester vaginal bleeding increases the risk of

PROM by ten-folds (95% CI: 6.3% to 15.1%). There is a statistically significant difference (P<0.05) between two groups as regard gestational hypertension, and placental abruption, and. On the other hand, the difference in Preterm labor (PTL), placenta previa, preeclampsia, and Cesarean section (CS) delivery between the two groups was not statistically significant.

	Group I (n=130)		Group II (n=170)		Group III (n=200)		P value
	Mean	SD	Mean	SD	Mean	SD	
FHR (beats/min)	98.8	24.5	157.8	18.8	166.5	15.3	< 0.05*
GSD (mm)	48.3	28.8	52.5	29.1	57.8	32.2	> 0.05
YSD (mm)	33.2	21.2	45.5	22.1	45.4	22.9	> 0.05
CRL (mm)	14.2	15.5	13.5	16.6	9.2	15.7	< 0.05*
SD=standard deviation; GA=gestational age; BMI=body mass index; *=statistically significance							

Table 2: Ultrasound markers of the studied groups.

Neonatal outcome in group II and III

The neonatal complications are presented in Table 3. We found that the risk of LBW infant increases by two times (OR=2; 95% CI: 1.3 to 3.2%) in pregnancy with the first trimester vaginal bleeding. There is a statistically significant difference (P<0.05) between two groups as regard LBW and IUGR. The Apgar score at 5 min <7 was more frequent in case groups (17%) than in the control groups (5.1%) (P<0.05). The risk of Neonatal Intensive Care Unit (NICU) admission increases by five times in case groups.

	Group II (n=170)		Group III (n=200)		P value	Odd ratio	95% CI
	n	%	n	%			
PROM	40	23.5	7	3.5	<0.05*	9.9	6.3-15.1
Gestational Hypertension	10	5.8	3	1.5	<0.05*	5.1	2.6-10.5
Placental abruption	6	3.5	2	1	<0.05*	4.8	1.8-12.9
Pre-eclampsia	10	5.8	9	4.5	>0.05	1.7	0.9-3.1
Placenta previa	3	1.8	2	0.1	>0.05	3.8	9.1-12.3
PTL	32	18.8	34	17	>0.05	1.4	0.8-1.5
CS delivery	87	51.1	107	53.5	>0.05	1.3	0.8-1.4
Birth weight < 2 kg	20	11.7	14	7	< 0.05*	2.1	1.2-3.2
IUGR	11	6.4	5	2.5	< 0.05*	2.8	1.6-6.3
Apgar score at 5min < 7	29	17	10	5	< 0.05*	4.2	2.5-6.6
NICU admission	32	18.8	9	4.5	< 0.05*	5.1	3.4-7.8

Table 3: Maternal and neonatal outcome in Group II and III.

The relationships of late pregnancy complications and early abnormal sonographic parameters

We found patients with abnormal early sonographic markers especially large YSD and fetal tachycardia, have a higher incidence of complications like PROM, PTL, IUGR, placental abruption or pre-eclampsia Table 4.

	FHR (n=16)		CRL (n=7)		GSD (n=2)		YSD (n=7)	
	n	%	n	%	n	%	n	%
PROM	8	50	2	28.5			2	28.5
Gestational hypertension	1	6.5	1	14.28			1	14.28
Placental abruption			1	14.28			1	14.28
Pre-eclampsia							1	14.28
Placenta previa	5	31						
IUGR	2	12.5	3	42.8	2	100	2	28.5
CS delivery	4	25	2	28.5			4	57.2
PTL	12	75	5	71.5	2	100	3	42.8

Table 4: Late pregnancy complications in relation to early abnormal sonographic parameters.

Diagnostic performance of sonographic parameters in determining abortion

The diagnostic performance of the sonographic parameters is summarized in Table 5. We found that FHR >115 b/min had a 98.5% sensitivity, a 99.2% specificity, an 89.5 PPV, and a 92.8 NPV reflecting the sound cardiac development and correlate with good pregnancy outcome.

Parameter	Sensitivity (%)	Specificity (%)	PPV	NPV	OR (95%CI)
FHR (100 b/min)	98.5	99.2	89.5	92.8	20.2 (3.2-65.3)

CRL (9 mm)	46.9	42.3	35.5	33.9	5.5 (1.5-56.4)
GSD (50 mm)	39.8	90.3	57.5	89.3	4.5 (2.1-33.5)
YSD (42 mm)	32.3	95.5	63.1	88.1	16.2 (2.31-98.6)

Table 5: Diagnostic performance of sonographic parameters in determining abortion.

Discussion

The outcome of the first trimester vaginal bleeding is a subject of debate. This study of singleton pregnancies with documented embryonic cardiac activity proved that early sonographic measures of FHR, CRL, GSD, and YSD are good sonographic parameters for the prediction of pregnancy outcome in women with threatened abortion, and should be routinely documented in all early pregnancy scans. We established a risk assessment table based on various combinations of early pregnancy sonographic parameters. The table will help to predict the pregnancy outcome.

Several previous studies have examined whether different sonographic parameters measured in early pregnancy have a significant role in the prediction of pregnancy outcome but few studies discuss the combination of these parameters. In our study, we found a statistically significant difference between threatened miscarriage cases who ended with pregnancy loss or completed their pregnancy and those with a normal pregnancy in relation to sonographic markers as FHR and CRL. The sensitivity and specificity of these markers especially FHR with a cutoff value of 115 bpm can help us to decide which women with threatened miscarriage are likely to continue their pregnancy and which ones will abort. Thus, helping to modify management given to both groups of patients. This result was similar to the result of [22] which reported that the first elevation of the FHR from 115 bpm at the 5th week of gestation to 170 bpm at the 9th week of gestation coincides with the morphological development of the heart. Also, similar to the result of Leylek [23] which documented the higher incidence of abortion in cases with low FHR reflecting poor cardiac development. However, some other previous studies had higher cutoff values: [24] showed the best cutoff value of FHR for the continuation of pregnancy was 128 bpm. Dede et al. [25] found that an FHR value below 130 bpm had 81.4% sensitivity and 85.1% specificity for predicting abortion. Chitacharoen and Herabutya [26] reported that FHR values below 120 bpm predicted early abortion with a sensitivity of 54.2% and false-positive rate of 5%. In our study, the best cutoff for FHR in the prediction of abortion was 115 bpm with 98.5% sensitivity and 99.2% specificity.

In a study of 188 pregnancies, Wie et al. [27] concluded that GSD below the 5th percentile and YSD below the 2.5th percentile or above the 97.5th percentile had an OR of 4.87 (P=0.018) and 15.86 (P<0.001) respectively for abortion. These findings are parallel to our results.

In the current study, the CRL cutoff value of 22 mm was obtained with a sensitivity of and specificity of 46.9% and 42.3%, respectively. On the other hand, Abuelghar et al. [28] found that 56.6% of women who experienced abortion had CRL below the 5th percentile with a sensitivity of 56.6% and specificity of 81.9%.

In our study, we did not find a significant difference between the three study groups regarding GSD or YSD. This finding contradicts the result of the study performed by Bamniya et al. [17], which found that the incidence of pregnancy loss with large YSD and smaller GSD was 78.57% and 14.28% respectively. Moreover, Oh et al. [29] reported that mean GSD was significantly smaller in pregnancies ending in abortion (4.5 mm vs 8.2 mm; P<0.001). Also, Tan et al. [14] established that the pregnancies with YSD ≥5 mm had a significantly higher risk of miscarriage (p=0.005) [29].

In this study, none of the demographic features revealed considerable assistance for the prediction of pregnancy loss. This finding might be owing to slight variations in ages among the examined women. Thus, the statistical analysis could not evaluate the impact of demographic features on the pregnancy outcome.

Papaioannou et al. [30] reported that first trimester bleeding increased the risk of PTL. Other previous studies [31,32] showed that the possibility of PTL is more in pregnant women with the first trimester bleeding due to many placental disorders. Thus, such pregnancies developed IUGR and LBW newborn. In our study, we found that the first trimester bleeding increases the risk of PROM by ten-fold (95% CI: 6.3–15.1%).

A systematic review performed by Saraswat et al. [33] revealed no effect of the first trimester bleeding on the rout of delivery which is concordant with our result.

In conclusion, the CRL and FHR are good sonographic indicators for the prediction of outcome in women with threatened miscarriage. The FHR at 115 bpm yields the best predictive accuracy, and the CRL at 22 mm gives the least predictive accuracy among studied markers. The incidence of maternal and fetal complications increased in cases with threatened miscarriage who completed the pregnancy.

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