Can Embryonic Heart Rate and Yolk Sac Size Predict First-Trimester Pregnancy Outcome in Women With Threatened Abortion?

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Abstract: Objective: To evaluate the role of embryonic heart rate (EHR) and yolk sac diameter (YSD) as predictors of the first trimester pregnancy outcomes in women with threatened abortion. **Patients and Methods:** The current prospective cohort study was conducted at Ain Shams University Maternity Hospital during the period between January 2008 and December 2009. The study included 300 pregnant women presenting to the outpatient clinic with first trimesteric threatened abortion between 6-7 weeks gestation. All women had a transvaginal ultrasound using 5 MHz transvaginal probe and with a capability of B-mode and M- mode scanning. After documentation of the fetal viability, the fetal heart rate was measured by M-mode in all cases. The calculation of the embryonic heart rate (EHR) was done by recording the time interval for at least three waves, which inform us about the number of heart beats per minute and then it had been registered. The yolk sac diameter (YSD) was estimated by putting the calipers on the inner more limits of the longer diameter. All women were followed up weekly till completion of 12 weeks and by then, all women were divided into 2 groups: Group (I):Included women who miscarried spontaneously at any time from enrollment till the end of 12 weeks. Women who continued their pregnancies till the end of 12 weeks were included as group II. **Results:** A total of 300 pregnant women were finally analyzed. Out of all included women, 271 women (90.4%) continued their pregnancy till the end of 12 weeks (Group II), while the remaining 29 women were miscarried (group I). There was no statistical significant difference between both groups regarding demographic characteristics. The mean EHR and the mean YSD were significantly lower in group I when compared to group II. Cutoff value of EHR at 128 beat per minute (bpm) was associated with sensitivity of 88.3%, specificity of 100%, PPV of 100% and NPV of 82.6%, while, YSD at a cutoff value of 2.9 mm was associated with sensitivity of 70.6%, specificity of 82.8%, PPV of 87.7% and NPV of 78.9% to predict fate of pregnancy by the end of trimester. **Conclusion:** EHR of 128 bpm is suggested to be an excellent parameter to predict fate of pregnancy by the end of first trimester and YSD of 2.9 mm is also suggested to be used as a very good parameter to predict fate of pregnancy by the end of trimester.

1. Introduction

Out of all clinical pregnancies, fetal loss occurs in approximately 15–20% of them. Reduction of this percentage to 3-4% is observed after authentication of embryonic heart rate (EHR). Approximately half of women who have threatened miscarriage in early pregnancy will miscarry [1]. At 6 weeks of gestation EHR can be detected using prenatal sonography, moreover the EHR can be measured via M-mode**.** Previous study have demonstrated that a slow EHR at 6–7 weeks gestation was conjoined with a high percentage of first-trimester fetal loss, and that fetal loss often occurs immediately after the slowness of EHR [2]. It is preferable to perform transvaginal sonography 1 week after slowness of EHR. Follow-up ultrasound is advisable approximately 1 week after detection of a slowness, to affirm early diagnosis and to avoid the happening of vaginal bleeding at an unsuitable time and place and to reduce the period of concern and anxiety for the

couples [3]. Yolk sac is the first sure embryonic structure detected by ultrasound and usually seen as a round anechoic area within the gestational sac between the 5th and 12th week of pregnancy [4].EHR bradycardia and absence of yolk sac or even a smaller yolk sac diameter than anticipated for any gestational age can predict a poor fetal outcomes during the first trimester [2].The aim of the current study was to evaluate the role of EHR and YSD as predictors of the first trimester pregnancy outcomes in women with threatened miscarriage.

2. Patients and methods

The current prospective cohort study was conducted at Ain Shams University Maternity Hospital during the period between January 2008 and December 2009. The study included 300 pregnant women presenting to the outpatient clinic in the first trimester of their pregnancy. The study had been approved by the ethical research committee of

obstetrics and gynecology department, Ain Shams University. An informed consent was signed by every patient before participating in the study and after thorough explanation of the purpose and procedures of the study. Women with multiple pregnancies and women who had negative embryonic cardiac pulsation were excluded from the study. Gestational age was calculated at the time of enrollment according to date of last menstrual period and was confirmed by obstetric ultrasound examination. All women had a transvaginal ultrasound using (SONOACE 400-Medison, Korea) with 5 MHz transvaginal probe and with a capability of B-mode and M- mode scanning. Obstetric ultrasound estimation of gestational age was determined by measuring gestational sac diameter and embryonic crown-rump length. After documentation of the fetal viability, the fetal heart rate was measured by M-mode in all cases. The calculation of EHR was done by recording the time interval for at least three waves, which inform us about the number of heart beats per minute and then it had been registered. The yolk sac diameter (YSD) was estimated by putting the calipers on the innermost limits of the longer diameter. All women were followed up weekly till completion of 12 weeks and by then, all women were divided into 2 groups: Group (I):Included women who miscarried spontaneously at any time from enrollment till the end of 12 weeks. Women who continued their pregnancies till the end of 12 weeks were included as group II.

Statistical Methods

Statistical analysis was performed using statistical package for social sciences (SPSS®) for Windows® version 15.0. Normally distributed numerical data were presented as mean and standard deviation (SD) and between-group differences were compared using the unpaired student's t-test. Categorical data were presented as number and percentage and inter-group differences are compared using the Pearson chi square test (for nominal data) or the chi square test for trends (for ordinal data). Associations between measured variables and miscarriage were estimated using receiver operator characteristic (ROC) curves. Validity of study parameters was evaluated in terms of sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). Significance level was set at 0.05.

3. Results

A total of 300 pregnant women were finally analyzed, flow chart of the participants is shown in figure-1. Demographic characteristics of all included women are shown in table-I. At the time of enrollment, the mean EHR of all included women was 130.3±13.4 beat per minute (bpm), while the mean YSD was 3.91±1.3mm. Out of all included women, 271 women (90.4%) continued their pregnancy till the end of 12 weeks (Group II), while the remaining 29 women were miscarried (group I). There was no statistical significant difference between both groups regarding demographic characteristics (table-II).The mean EHR and the mean YSD were significantly lower in group I when compared to group II (table III). In group II, there were a significant correlation between gestational age and both EHR and YSD, while in group I, there was no significant correlation between gestational age and both EHR and YSD. Cutoff value of EHR at 128 bpm was associated with sensitivity of 88.3%, specificity of 100%, PPV of 100% and NPV of 82.6%, so EHR at 128 bpm was highly sensitive and highly specific test to differentiate between women who continued pregnancy till the end of 12 weeks and those who aborted at the end of the same period in women presented with first trimester threatened miscarriage. YSD at a cutoff value of 2.9 mm was associated with sensitivity of 70.6%, specificity of 82.8%, PPV of 87.7% and NPV of 78.9%, so YSD at 2.9 mm was moderate sensitive and moderate specific test to differentiate between women who continued pregnancy till the end of 12 weeks and those who miscarried at the end of the same period in women presented with first trimester threatened miscarriage. ROC curve analysis demonstrated that EHR is an excellent parameter to predict fate of pregnancy by the end of first trimester (area under the ROC curve: 0.912, $p < 0.001$) figure (II). Also, YSD was found to be a very good parameter to predict fate of pregnancy by the end of first trimester (area under the ROC curve: 0.848, $p < 0.001$) figure (III).

Table (I): Demographic characteristics of all included women

	Mean ±SD	Range
Age (years)	32.3±5.6	25.0-35.0
BMI (Kg/m^2)	29.5±6.2	19.9-46.3
Gestational age at enrollment (weeks)	8.3±2.1	6.0-10.0
Duration of marriage (years)	6.1±2.3	2.0-8.0
	Number	%
Parity • Primigravida • Multigravida	228 72	76.0 24.0
Previous miscarriages	10	3.3

SD: Standard deviation
BMI: Body mass index

Table (II): Comparison between group I and group II as regards demographic characteristics

	Group I (Number=29)	Group II (Number=271)	$t^\wedge/\chi^{2\#}$	P
Age (years)	32.4±5.9	31.4±5.1	0.878^	0.380
BMI (Kg/m^2)	29.7±6.3	27.6±6.7	1.702^	0.089
Gestational age at enrollment (weeks)	7.83±2.2	8.35±2.4	1.120^	0.263
Duration of marriage (years)	5.63±2.3	6.15±2.4	1.113^	0.266
Parity • Primigravida • Multigravida	 25 (68.2%) 4 (13.8%)	 201 (74.7%) 68 (25.3%)	1.885#	0.170
Previous miscarriages	1 (3.4%)	9 (3.3%)	0.001#	0.971

BMI: Body mass index   ^ Analysis using Independent t-test   # Analysis using Chi square test

Table (III): Comparison between group I and group II as regards embryonic heart rate and yolk sac diameter

	Group I	Group II	t^	P
Heart rate (bpm)	119.1±12.9	131.5±13.5	4.720	**<0.001**
Yolk sac diameter (mm)	2.13±1.1	4.1±1.4	7.335	**<0.001**

bpm: beat per minute   ^ Analysis using independent t-test

Table (IV): Correlation between gestational age and both embryonic heart rate and yolk sac diameter in both groups

	Group I		Group II	
	r^	p	r^	p
Embryonic heart rate (bpm)	0.137	0.381	0.541	<0.001*
Yolk sac diameter (mm)	0.107	0.427	0.432	<0.001*

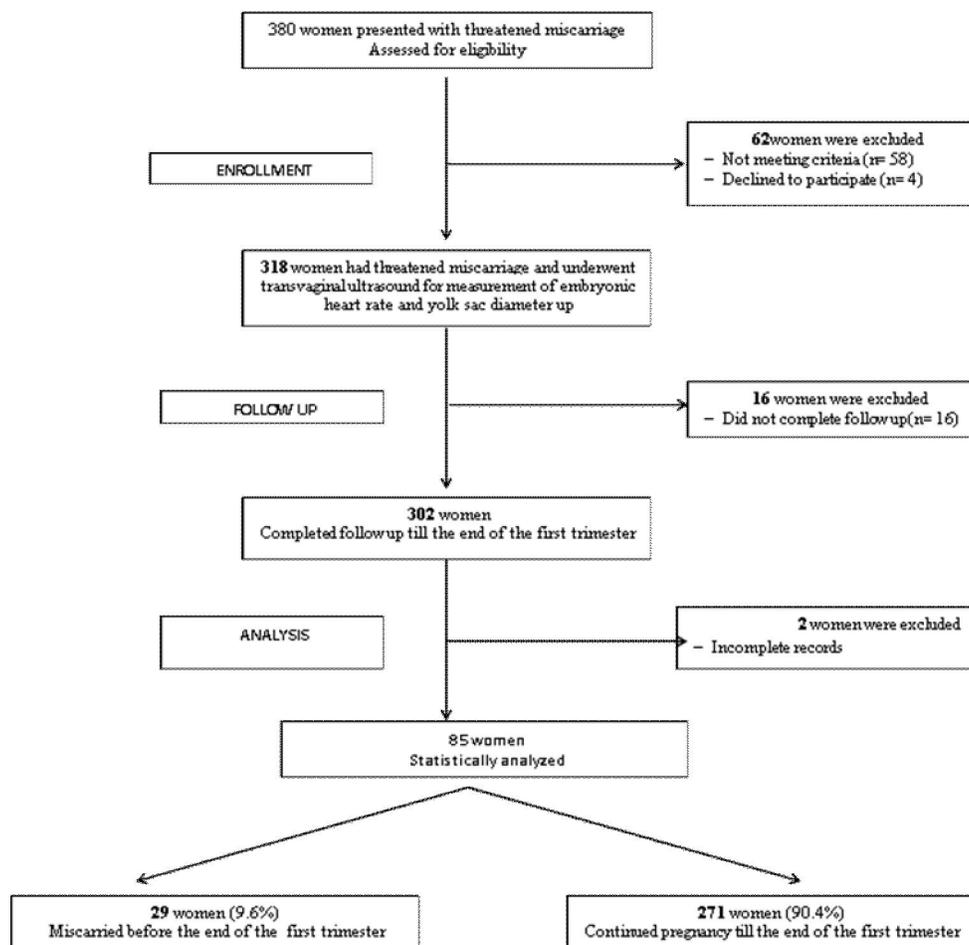bpm: beat per minute   ^ Analysis using Pearson correlation test

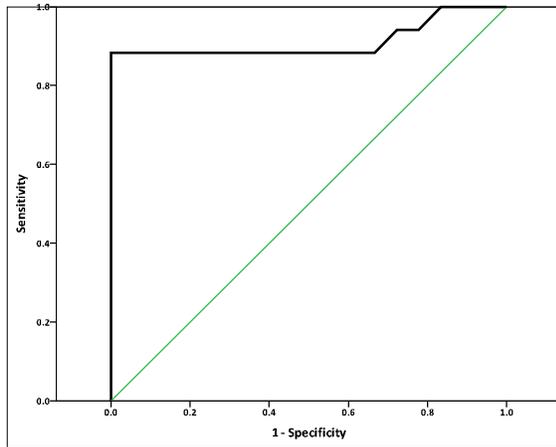Figure I: patients flow chart

Figure II: Receiver operator characteristic curve to determine predictive value of embryonic heart rate to predict fate of pregnancy by the end of first trimester
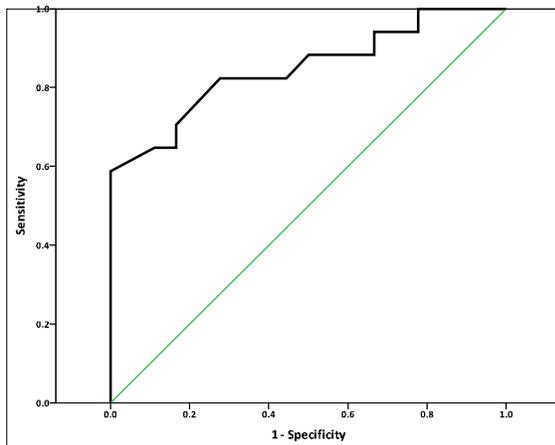

Figure III: Receiver operator characteristic curve to determine predictive value of yolk sac diameter to predict fate of pregnancy by the end of first trimester

4. Discussion

To the best of our knowledge, the current study is one of the largest studies that evaluated the role of EHR and YSD as predictors of the first trimester pregnancy outcomes in women with threatened miscarriage. After analyzing our results, EHR was confirmed to be an excellent parameter to predict the fate of pregnancy by the end of first trimester. . Cutoff value of EHR at 128 bpm was associated high sensitivity and high specificity to differentiate between women who continued till the end of first trimester and women who miscarried at the end of the same period. Moreover, YSD was a very good parameter to predict fate of pregnancy by the end of first trimester and YSD of 2.9 mm can be used as moderate sensitive and moderate specific test to differentiate between women who continued till the end of first trimester and women who miscarried at the end of the same period. *Lindsay et al.* concluded

that miscarriage occurred with yolk sac size larger than 5.6 mm and a YSD greater than two standard deviations (SDs) above the mean in comparison to the mean gestational sac diameter allowed anticipation of an abnormal first trimester pregnancy outcome with a sensitivity of 15.6%, a specificity of 97.4%, and a positive predictive value of 60.0% [5]. *Stampone et al.* examined 101 normal cases and 16 miscarriages with gestational ages of less than 12 weeks and abnormal YSD was statistically significant ($p < 0.001$) in spontaneous miscarriage when compared to normal pregnancy with a sensitivity of 68.7%, a specificity of 99%, a PPV of 91.6% and a NPV of 95.2%. These conclusions authenticated that a measurement of the yolk sac very early in pregnancy may be a useful prognostic factor of pregnancy outcome [6]. While, *Kucuk et al.* enrolled 219 normal women and 31 miscarriages with gestational ages of less than 12 weeks and predicted the miscarriage by yolk sac size±2SD. Moreover, they concluded that an abnormal shaped yolk sac allowed anticipation of an abnormal first trimester pregnancy outcome with a sensitivity of 29%, a specificity of 95%, a PPV of 47% and a NPV of 90.5%, but our study did not study the shape of the yolk sac [7]. Also, other investigators examined 70 normal women and 35 miscarriages with gestational age of less than 12 weeks and predicted the miscarriage by yolk sac size±2SD and recommended that women at risk of poor pregnancy outcome should undergo a routine transvaginal sonography before 12 weeks gestation to evaluate their yolk sac, moreover women with an abnormal yolk sac should be followed-up strictly to diagnose any abnormalities in the fetus before 24 weeks gestation [8]. *Rowling et al.* selected pregnant women with gestational age of less than 13 weeks and the results authenticated that live birth may occur with no yolk sac in the 8-mm gestational sac size [9]. One study authenticated that embryonic death occurred when yolk sac size showed regression in women with gestational age between 7-10 weeks. However, *Kurtz et al.* had 163 normal cases and 49 miscarriages with gestational ages less than 12 weeks and they concluded that detection of yolk sac is not a predicting sign of early pregnancy outcome. A more recent study concluded that EHR and YSD continuously increase in healthy pregnancies during the first trimester. Bradycardia of EHR and nonappearance of yolk sac or even a smaller yolk sac diameter than wonted for any gestational age are prognosticators of poor first trimester pregnancy [2]. The strengths of the current study included current study is one of the largest studies that evaluated the role of EHR and YSD as predictors of the first trimester pregnancy outcomes in women with threatened miscarriage (high risk

group) and the use of non invasive methods (ultrasound) for measurement of these predictors. Limitations of the current study included the selection of the women with threatened miscarriage only without inclusion of low risk women, the measurement of YSD only without comment on yolk sac shape and lastly the short term follow up as follow up of the women were stopped at the end of the first trimester and we did not correlate the studied parameter with neonatal outcomes.

5. Conclusion:

As early as 6-7 weeks gestation, EHR of 128 bpm measured is suggested to be an excellent parameter to predict fate of pregnancy by the end of first trimester and YSD of 2.9 mm is also suggested to be used as a very good parameter to predict fate of pregnancy by the end of trimester.

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