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Can slow early embryonic heart rate measurement predict first trimester miscarriage?

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Abstract: Background and objective: Miscarriage is the most common adverse pregnancy outcome which has detrimental psychological consequences for the woman and her partner, this study aimed to confirm the relation between the first trimester miscarriage and slow EHR at 6^{th} (6^{0-6}) weeks of gestational age to predict miscarriage **Patients and Methods:** This was a prospective observational cohort study was conducted at the department of Obstetrics and Gynecology, Al-Azhar university hospital (New Damietta) during the period from October 2017 to January 2019 and included 90 pregnant women who had slow EHR (80-100) b/pm at 6^{th} weeks gestational age and the relation between slow embryonic heart rate and first trimester demise was recorded and statistically analyzed. **Results:** A Total of 90 early (6^{+0} to 6^{+6th} weeks) pregnant women with slow embryonic heart rate 80-100 b/pm included in the study The mean embryonic heart rate at booking visit was nearly 92 b/pm and EHR in majority of cases was between 95-99 b/pm, There is highly significant relation between incidence of abortion and the slowing EHR where p-value <0.001. **Conclusion:** it was concluded that slow embryonic heart rate is one of the earliest predictors for first trimester fetal demise and so early follow up by ultra sound is recommended and this help the clinician to make the diagnosis of fetal demise quickly to avoid the occurrence of vaginal bleeding at an inconvenient time and place.
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Keywords*:* Miscarriage**,** embryonic heart rate**,** first trimester demise.

1. Introduction

Miscarriage is the most common adverse pregnancy outcome which has detrimental psychological consequences for the woman and her partner and delays successful childbearing ***(1).***

The human heart begins beating at a rate near the mother's (75-80) b/pm then increases for the first month, peaking at (165-185) b/pm during 9th week. This acceleration is approximately 3.3 b/pm per day, or about 10 b/pm every three days, an increase of 100 b/pm in the first month, so it increases from 110 b/pm at 6 weeks to 175 b/pm at 9 weeks in a nearly-linear fashion. After 9 weeks, the FHR decreases throughout the remainder of the pregnancy. This phenomenon is likely due to the evolving parasympathetic system ***(2)*** With advances in computer technology, hardware, and software, ultrasound has become the modality of choice for many medical specialties, such as obstetrics and gynecology ***(3).***

With the use of 7.5 MHz trans-vaginal probes, more detailed structures of the fetal heart could be identified. The atrial and ventricular walls were visualized at the end of week 8, and the atrioventricular valves at the end of week 10 ***(4)***

Previous studies on the embryonic heart rate (HER) normally measured about 100-200 beat per minute (b/pm) when it is first visible on sonography at approximately 5 weeks gestation. the rate increases progressively over the subsequent 2-3 weeks ***(5)***

Another one showed that FHR < 90 at 6-8 weeks of GA has been associated with poor outcome and < 70 has been associated with pregnancy loss ***(6).***

while evidence of abnormal EHR may indicate poor prognosis and higher risk of spontaneous miscarriage, routine assessment of EHR may be used as a prognostic tool for miscarriage ***(7).***

Fetal demise often occurs within 1 week after the slow FHR and almost always occurs by the end of the first trimester **(8)**.

So, the present study aimed to confirm the relation between the first trimester miscarriage and slow EHR at 6^{th} (6^{0-6}) weeks of gestational age to predict miscarriage risk.

2. Patients and Methods

This was a prospective observational cohort study was conducted at the department of Obstetrics and Gynecology, Al-Azhar university (New Damietta) during the period from October 2017 to January 2019 and included 90 pregnant women who had slow EHR (80-100) b/pm at 6^{th} weeks.

Sample size: The calculated sample size of the study was **79** participants at 5% level of significance and 80% power of the study, using sample size online

calculator based on outcome of pregnancy with slow FHR at 4-6th weeks of GA ***(6)***. The sample size will be increased to **90** participants to increase the study power.

Inclusion criteria:

Age: 18-35 years old, Singleton pregnant women., Intra-uterine pregnancy.

Spontaneous pregnancy, Gestational age: 6th weeks confirmed by reliable regular last menstrual period andultrasound CRL measurement, EHR (80-100) b/pm by trans-vaginal ultrasound.

Exclusion criteria: Maternal bradycardia or any medical disorder, Non-viable fetuses, Threatened abortion, Medications other than folic acid supplement.

Intervention:

After selection, counseling, explaining the procedure to all participants an informed written consent was taken from allparticipants in the study and the local ethics committee approved this study, all participants were submitted to thorough full history taking at the booking visit at 6th weeks GA.

All cases had been followed up till the end of first trimester on three visits, first one was at 8th weeks, second one was at 10th weeks and third one was at 13th weeks (the end of first trimester). In those three visits, GA was confirmed by measuring CRL. We also asked every visit including booking one about vaginal bleeding or pain at that current period. We compared between all groups as regard first trimester outcome which is "demise" if by anytime during first trimester, an US scan demonstrated that cardiac activity was no longer present and "alive" if at 13.0 weeks, an ultrasound scan documented that the patient was still pregnant.

Measurements:

All trans-vaginally ultrasonic examinations to measure embryonic heart rate were performed by the same operator by using Sonoace R5 model 7.5MHz, (Samsung Medison co., Ltd., Seoul, Korea) ultrasound machine. patient was placed in dorsal lithotomy position, doctor on the right of her, the probe used was covered by glove and lubricant (gel) was inside and outside the glove then introduced gently into vagina. EHR was measured by M-Mode, at least ten regular cardiac cycles, the calculation of the heart rate was made by measuring the time interval of two cardiac cycles andthe average values obtained from two measurements were utilized for statistical analysis. Measuring heart rate was done as follow: first fetal heart was detected, arrow was put on beating chamber, button on M -mode was switched, sit first wave and then the successive second one, measured the distance between both waves to detect accurate fetal heart rate. We confirmed 6th weeks GA by measuring Crown Rump Length of the fetal pole (3-8) mm which was measured from the cranial to caudal end of the body with the fetus in neutral position and the results were statistically analyzed.

Statistical analysis

Data were analyzed using **SPSS** version 21. The normality of data was first tested with one-sample Kolmogorov-Smirnov test, Qualitative data were described using number and percent. Association between categorical variables was tested using Chi-square test and at different duration was tested using Mcnemar test. Continuous variables were presented as Mean (SD). The two groups were compared with Student t- test while paired groups were compared by paired t-test test. Significant variables entered into Logistic regression model using Wald statistical technique to predict the most significant determinants and to control for possible interactions and confounding effects. p-value, Significant when the probability of error is less than 5% ($p < 0.05$).

3. Results

The study were included 90 early (6^{+0} to 6^{+6th} weeks) pregnant women with slow embryonic heart rate 80-100 b/pm, The included pregnant women were middle- aged, overweight, more than half of patients had previous history ofmiscarriage. table 1, The mean fetal heart rate at booking visit was nearly 92 b/pm and EHR in majority of cases was between 95-99 b/pm table 2, Almost one third of cases had aborted two weeks after slow EHR table 3, There is highly significant relation betweenincidence of abortion and the slowing EHR where p-value <0.001. table 4, after Univariate Logistic regression analysis the following were independent predictors for abortions; Age more than >30 y (OR=8.4), history of previous abortion (OR=7.28) and FHR <90 (OR=13.42).

After Multivariate Logistic regression analysis and adjusting confounding factors the following were the most significant predictors for abortion; history of previous abortion (OR=5.3) and FHR <90 (OR=23.8). This means pregnant females with history of previous abortion were 5.3 times more at risk for abortion than other females. Also, pregnant females which had fetus with heart rate less than 90 were at risk 23.8 times for experiencing abortions more than other females table 5.

Table (1): Demographic data of the studied patients

Item	Study group (n=90)	
	No	%
Age / years ≤30 y >30 y	 79 11	 87.8% 12.2%
Mean ± SD Range	23.58±5.03 18-35	
BMI Mean ± SD Range	 26.64±3.95 19-36	
Obesity Yes No	 17 76	 15.6% 84.4%
Previous miscarriage Yes No	 37 53	 41.1% 58.9%

Table (2): FHR among the studied groups

FHR	Study group (n=90)	
	No	%
80-84	4	4.4
85-89	21	23.3
90-94	26	28.9
95-99	39	43.4
Mean ± SD Range	91.84±4.70 80-99	

Table (3): Comparison of abortion at different durations

Abortion	Abortion 8th (n=90)	Abortion 10th (n=79)	Abortion 13th (n=65)	Total
Yes	27 (30%)	14 (17.7%)	9 (13.8%)	53 (58.9%
No	63 (70%)	65 (82.3%)	56 (86.2%)	37 (41.1%)
p-value		P1=0.063	P2=0.018*	-
			P3=0.527	

Table (4): Relation between abortions and FHR

FHR	Study group (n=90)		Test of significance	p-value
	Abortions (n=53)	No abortion (n=37)		
80-84	3 (5.7%)	1 (2.7%)	χ^2=33.19	<0.001**
85-89	20 (37.7%)	1 (2.7%)		
90-94	20 (37.7%)	6 (16.2%)		
95-99	10 (18.9%)	29 (78.4%)		
Mean ± SD	89.5±3.9	95.16±3.629	t=6.89	<0.001**

Table (5): Logistic regression analysis of independent predictors of abortions

Independent predictors	Univariate Logistic regression analysis			Multivariate Logistic regression analysis	
	B	OR (95% CI)	p-value	OR (95% CI)	p-value
Age / years ≤30 y **(r)** >30 y	2.12	8.4 (1.02-18.6)	0.048*	1.2 (0.8-8.1)	0.128
Previous abortion Yes No **(r)**	1.98	7.28 (2.6-20.4)	<0.001**	5.3 (1.39-20.5)	0.015*
FHR **<90** **≥90 (r)**	2.59	13.42 (2.9-26.6)	0.001*	23.8 (4.1-39.5)	<0.001**

OR: odds ratio, (r): reference group

4. Discussion

Miscarriage is the most common adverse pregnancy outcome which has detrimental psychological consequences for the woman and her partner and delays successful childbearing ***(1).***

Previous studies showed that FHR <90 at (6^{th} -8) weeks of GA has been associated with poor outcome and <70 has been associated with pregnancy loss***(6).***

The aim of this study was to evaluate the outcome of first trimester pregnancy in relation to slow EHR.

The present study was a prospective observational cohort study, conducted at Al-Azhar university hospital (New Damietta) during the period from September 2017 to January 2018. It included 90 pregnant women who had fetal bradycardia (80-100) b/pm at the 6^{th} week.

This (cut off) of embryonic heart rate was chosen according to results of (***7)***in which normal EHR at 6^{th} week was (140±40) b/pm with minimum value100 b/pm which differs from***(6)***<109 b/pm.

Edward (5) study, was more precise than ours, as it divided 6^{th} week to 3 and 4 days but we wanted a general result about the 6^{th} week, it shows that EHRs associated with: increase the risk of demise at the end of the first trimester: (<100) b/pm at (6^{0-3}) weeks or (<120) b/pm at (6^{0-3} -7.0) weeks.

The risk of death is approximately 100% (<80) b/pm at (6^{0-3}) weeks or (<100) b/pm at (6^{0-3} -7.0) weeks.

In the present study, mean age of studied group was (23.58) with range (18-35) years old, the larger percent were equal and below thirty years. This mean was lower than that in ***(9***) at which mean ages were (25.4 ±3.2, 25.0± 3.6, 25.3 ±3.8) for (control, placebo, study) groups respectively, with range (17-35). As regard our targeted outcome, miscarriage, almost one third of cases had aborted at the 8^{th} week of Gestational age, decreased insignificantly after another two weeks (10^{th}) then decreased insignificantly again at 13^{th} week with total percent 58.9 which was less than ***(10)***study (near 80%) but it is due to decreased their GA tested (< 6.1 weeks) and close to the result (60.6%) of (Doubilet & Benson, 2005)which worked on our same GA. Previous results shows that generally risk of miscarriage decrease by going forward in GA and the most serious period is the first two weeks after detection of slow FHR at 6^{th} week of GA which we can use as a predictor of miscarriage.

As regard classification of slow FHR in our study, we made it in four groups and studied percentage of abortion in each, which were significantly more than continuation of pregnancy. We studied association between risk factors and probability of abortion in 1st trimester with slow heart rate. We found that age and previous miscarriage had significant relation with abortion while obesity had not. In a research was done to study risk factors of early spontaneous abortions among Japanese. ***(11)*** was in line with our results regarding obesity, as he couldn't find an association between weight status and miscarriage. Regarding previous miscarriage, the present study showed the majority of study sample have previous abortion with significant difference and increase 7 folds more than no previous abortion cases. This result agrees with (***12),*** they reported that most of the sample was reported at "previous one abortion", and they are accounted 105 (52.5%) of the study sample Regarding EHR, we can classify our results to: High risk for miscarriage: <90 b/pm which 13folds more than, Moderate risk for miscarriage: ≥90 b/pm. These results agreed with **(13)** study which showed that heart rates associated with: a very high rate of first-trimester demise:

(<80) b/pm at (6^{0-2}) weeks gestation or (<100) b/pm at (6^{3}–7) weeks a moderately high rate of

demise, (80–89) b/pm at (6^{0-2}) weeks or (100–109) b/pm at (6^{3}–7) weeks a mildly elevated rate of demise (90–99) b/pm at (6^{0-2}) weeks or (110–119) b/pm at (6^{3}–7) weeks lower demise rates:100 or more b/pm at (6^{0-2}) weeks or 120 or more b/pm at (6^{3}–7) weeks**.**

5. Conclusion and recommendations

The present study conclude that slow embryonic heart rate is one of the earliest predictors for first trimester fetal demise and early follow up by ultra sound is recommended and this help the clinician to make the diagnosis of fetal demise quickly to avoid the occurrence of vaginal bleeding at an inconvenient time and place.

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