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Original article

Outcome of First Trimester Pregnancy in Cases with Impending Embryonic Demise

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ABSTRACT

Background: Miscarriage is the most common adverse pregnancy outcome which has detrimental psychological consequences for the woman and her partner and delays successful childbearing. Normal embryonic heart rate is about [100-200] bpm at 5 weeks gestation then it increases progressively over the subsequent 2-3 weeks. Fetal demise often occurs within one week after the slow embryonic heart rate and always occurs by the end of the first trimester.

Aim of the work: The aim of the present study was to investigate the relation between first trimester miscarriage and slow embryonic heart rate at sixth week of gestational age and other risk factors of miscarriage.

Patients and methods: A prospective observational cohort study was conducted in the department of Obstetrics and Gynecology, Al-Azhar Faculty of medicine [Damietta] during the period from September 2017 to September 2018 on 90 pregnant women who had slow embryonic heart rate [80-100] bpm at sixth week of gestational age. All were submitted to full history taking, clinical and ultrasound examination and followed up till the end of their pregnancy and outcome was documented.

Results: Percentage of aborted cases at the 8th week of gestational age was [38.9%], while, [20%] at the 10th week and [15.4 %] at 13th week. Whom fetus had a heart rate less than 90 were at risk 23.8 times for experiencing abortions more than other females.

Conclusion: Slow embryonic heart rate is one of the earliest predictors for the first trimester fetal demise and it is one of the newest studies.

Keywords: Embryonic; Heart rate; Miscarriage; Gestational age; Pregnancy.

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INTRODUCTION

Heart's function is the first sign of independent fetal activity explored with non-invasive techniques such as ultrasound [U/S] [1]. Previous studies on the EHR normally measured about 100-200 beat per minute [b/m] when it is first visible on sonography at approximately 5 weeks gestation. The rate increases progressively over the subsequent 2-3 weeks [2]. FHR < 90 b/m at 6-8 weeks of GA has been associated with poor outcome and < 70 b/m has been associated with pregnancy loss [3].

Fetal demise often occurs within 1 week after the slow FHR and almost always occurs by the end of the first trimester [4]. Thus, when a slow heart rate is seen at 6th weeks, a follow-up US performed approximately 1 week later will often reveal that cardiac activity has ceased. If the embryonic heart is still beating on the follow-up US scan, the heart rate may still be slow or it may be normal. Our study was done to confirm that principle and get accurate percentage of miscarriage to those cases, also follow up cases with specific data throughout the first trimester and see if most cases are lost within 1 week or not. Also find out relation between some factors with slow EHR and miscarriage.

AIM OF THE WORK

The aim of the present study was to confirm the relation between first trimester miscarriage and slow embryonic heart rate at 6th weeks of gestational age and other risk factors of miscarriage.

PATIENTS AND METHODS

This was a prospective observational cohort study conducted in the department of Obstetrics and Gynecology, Al-Azhar University [New Damietta] during the period from September 2017 to September 2018 on 90 pregnant women who had slow EHR [80-100] bpm at 6th weeks GA.

Inclusion criteria:

18-35 years old women with 6th weeks [confirmed by reliable regular last menstrual period; regular is defined as three consecutive cycles each 21-35 days length, average amount, no blood clots and reliable is defined by accurate date not preceded by combined oral contraception pill, breast feeding or pregnancy in the last 3 months and ultrasonographic CRL measurement [0.3-0.8] cm] normal, singleton, intra-uterine,

Spontaneous pregnancy. EHR [80-100] b/m by TVS.

Exclusion criteria:

Maternal bradycardia or any medical disorder. Non-viable fetuses. Threatened abortion. Pregnancies complicated with a vanishing twin. Medications other than folic acid supplement.

Methods:

After selection, counseling, explaining the procedure to all participants, obtaining an informed written consent to participate in the study and the local ethics committee approved this study, all participants were submitted to thorough history taking at the booking visit at 6th weeks GA at which each woman was included only once.

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.

All trans-vaginally ultrasonic examinations to measure embryonic heart rate were performed by the same operator by using SonoaceR5 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 and the average values obtained from two measurements were utilized for statistical analysis. Measuring heart rate was done as follow: first, button on M -mode was switched, arrow was put on beating chamber, 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.

Statistics analysis: Data were analyzed with 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 was fixed at 5% level. The results was considered non-significant when the probability of error is more than 5% [p > 0.05], significant when the probability of error is less than 5% [p < 0.05] and highly significant when the probability of error is less than 0.1% [p < 0.001].

RESULTS

In the present study, cases enrolled at the 6th week of GA were middle- aged females with the most are below thirty years, overweight and more than half cases had no history of miscarriage with mean fetal heart rate nearly 92 b/m [table-1].

As regard vaginal bleeding and lower abdominal pain, all cases enrolled to this study at the 6th week had started without both, then after two weeks at 8th week of GA, [57.8%] of cases had unfortunately experienced vaginal bleeding while [45.5] experienced pain, but after another two weeks [at 10th], percentage had hopefully decreased significantly in bleeding [40%] but remained nearly the same in pain. Finally, at the end of the study [13th] percentage also decreased significantly in pain [22.7%] and not significant in bleeding. As regard miscarriage, [38.9%] of cases had aborted at the 8th week of GA and percentage decreased significantly at the 10th week [20%] then decreased insignificantly at 13th week. The total percent of miscarriage was [58.9 %] [Table-2].

Percentage of aborted cases was greater than not aborted by very high significance value in all groups of FHR classifications [Table-3]

Number of cases >30 years who had aborted was less significantly than those were ≤30 years and number of obese patients aborted was more than who did not abort but with no significant difference, meanwhile number of patients who had previous miscarriage aborted was more those did not abort with highly significant difference [Table-4].

Table [5] revealed that, previous abortion and slow heart rate were the good predictors of early pregnancy loss among studied populations.

Table [1]: Demographic and obstetric data of the studied group [n=90]

	No	%	Mean ± SD	Range
Age / years				18-35
≤30 y	79	87.8%	23.58±5.03	
>30 y	11	12.2%		
BMI			26.64±3.95	19-36
Obesity				
Yes	17	15.6%		
No	76	84.4%		
History of previous miscarriage				
Yes	37	41.1%		
No	53	58.9%		
FHR			91.84±4.70	80-99
80-84	4	4.4		
85-89	21	23.3		
90-94	26	28.9		
	39	43.4		

Table [2]: Comparison of vaginal bleeding rate, lower abdominal pain and abortion at different follow up durations

		8 th week [n=90]	10 th week [n=55]	13 th week [n=44]	total	p-value
Bleeding	Yes	52 [57.8%]	22 [40%]	15 [34%]		P1=0.037* P2=0.01* P3=0.546
	No	38 [42.2%]	33 [60%]	29 [66%]		
Pain	Yes	41 [45.5%]	25 [45.6%]	10 [22.7%]		P1: 0.991 P2: 0.011* P3: 0.018*
	No	49 [54.5%]	30 [54.4%]	34 [77.3%]		
Abortion	Yes	35 [38.9%]	11 [20%]	7 [15.9%]	53 [58.9%]	P1: 0.017* P2: 0.007* P3: 0.599
	No	55 [61.1%]	44 [80%]	37 [84.1%]	37 [41.1%]	

P1: Comparison between 8th and 10th weeks; P2: comparison between 8th and 13th week; P3: comparison between 10th and 13th weeks.

Table [3]: Relation between abortions and fetal heart rate [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%]	$\chi^2=33.19$	<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 \pm SD	89.5 \pm 3.9	95.16 \pm 3.629	t=6.89	<0.001**

Table [4]: Relation between abortions and other parameters

Item	Study group [n=90]		χ^2	p-value	
	Abortions [n=53]	No abortion [n=37]			
Age / years	≤ 30 y	43 [81.1%]	36 [97.3%]	5.3	0.021*
	> 30 y	10 [18.9%]	1 [2.7%]		
Obesity	Yes	11 [20.8%]	3 [8.1%]	2.65	0.103
	No	42 [79.2%]	34 [91.9%]		
Previous miscarriage	Yes	31 [58.5%]	6 [16.2%]	16.08	<0.001**
	No	22 [41.5%]	31 [83.8%]		

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 > 30 y [r]	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**

DISCUSSION

Miscarriage is the most common adverse pregnancy outcome which has detrimental psychological consequences for the woman and her partner and delays successful childbearing^[5]

Previous studies showed that FHR <90 b/m at [6th-8th] weeks of GA has been associated with poor outcome and <70 b/m has been associated with pregnancy loss^[3,6] and considered it advantageous to make the diagnosis quickly to avoid the occurrence of vaginal bleeding at an inconvenient time and place and to minimize the period of concern and uncertainty for the parents. For these reasons, a follow-up US is advisable approximately 1 week after detection of a slow early embryonic heartbeat^[8].

The aim of this study was to evaluate the outcome of first trimester pregnancy in relation to slow EHR. The mean age of studied group was [23.58], the larger percent were equal or below thirty years. More than half of the sample in this study had no history of previous miscarriage which unlike Mellerup et al.^[6] study who reported that [52.5%] of sample were at "previous one abortion".

Results of that table showed that symptoms of threatened abortion and abortion percentage decrease with advancing gestational age after first detection of slow FHR at 6th week, and the total percent of miscarriage was [58.9] which was less than Arleo and Troiano^[7] who reported value near 80%, but it was because their GA tested [< 6.1 weeks] was earlier and our results are comparable to Doubilet and Benson^[8] [60.6%] which worked on same GA as the present study.

The 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 6th week which can be used as an early predictor of miscarriage and that agreed with Kosus et al.^[9] who said that while evidence of abnormal embryonic heart rate [EHR] may indicate poor prognosis and higher risk of spontaneous miscarriage, routine assessment of EHR may be used as a prognostic tool for miscarriage.

As regard classification of slow FHR in our study, we made it in four groups [80-84, 85-89, 90-94, and

95-99 b/m] 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 first 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, Baba et al.^[10] was in line with our results regarding obesity, as they couldn't find an association between weight status and miscarriage.

Risk of abortion in women above 30 was 8.4 folds more than below and equal to 30 years while in history of previous miscarriage was 7.2 folds. In Doubilet and Benson^[8], pregnancies with normal embryonic heart rate served as a control group which we should have had in the present study and other pregnancies were divided into two study group, slow [subdivided into slow and very slow] and the borderline embryonic heart rate but this study classified slow FHR to four groups and there were significant percentages of abortions in all of them, then it calculated risk of abortion according to FHR; high risk for miscarriage [< 90] bpm was 13 folds more than moderate risk for miscarriage [≥ 90] bpm.

These results were comparable with Doubilet and Benson^[11] study, which showed that a very high rate of first-trimester demise was [< 80] bpm at [6⁰⁻²th] weeks gestation or [< 100] bpm at [6³⁻⁷] weeks, a moderately high rate of demise was [80-89] bpm at [6⁰⁻²] weeks or [100-109] bpm at [6³⁻⁷] weeks, a mildly elevated rate of demise was [90-99] bpm at [6⁰⁻²] weeks or [110-119] bpm at [6³⁻⁷] weeks and lower demise rates was [≥ 100] bpm at [6⁰⁻²] weeks or [≥ 120] bpm at [6³⁻⁷] weeks.

The most significant predictors for abortion were history of previous abortion and FHR as pregnant females with history of previous abortion were 5.3 times more at risk for abortion than other females and whom fetus had a heart rate less than 90 were at risk 23.8 times for experiencing abortions more than other females.

Conclusion: The present concluded that slow embryonic heart rate in early pregnancy could be a good predictor for the first trimester fetal

miscarriage and the first one to start very early at 6th week. In addition, history of previous miscarriage is a risk factor for miscarriage.

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