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Original Research Article

## Evaluation of yolk sac size and embryonic heart rate in first trimester and pregnancy outcome

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### ABSTRACT

**Background:** Accurate differentiation between normal pregnancy and pregnancy loss in early gestation remains a clinical challenge-previous studies have described the association between embryonic well-beings and the characteristics of gestational sac. The aim of the study was to evaluate the yolk sac size and embryonic heart rate as a prognostic factor for the first trimester pregnancy outcome.

**Methods:** This was a prospective cohort observational study. It included 52 pregnant women in their first trimester from 6 week till 12 weeks gestation. Transvaginal sonographic examination after explanation and agreement of each patient. All pregnancies were followed for their pregnancy outcome after completion of 12 weeks. The adverse outcome was spontaneous miscarriage occurring before or at 12 weeks of gestation. These patients allocated into four study groups: according to gestational age at presentation and pregnancy outcome. Group I included women who were examined during (6-7 weeks+6 days). Group II included women who were examined during (8-9 weeks+6 days). Group III included women who were examined during (10-12 weeks). Group IV included women who had their pregnancies resulted into first trimester spontaneous miscarriage.

**Results:** The validity of YS diameter regarding the prognosis of first trimester pregnancy outcome shows that; YSD had 100% specificity and 97.8% sensitivity in prediction of miscarriage. Regarding embryonic heartbeat, there was a statistically significant difference between group IV and the other groups. There was embryonic bradycardia in the miscarriage group. EHR had a sensitivity of 97.5% and specificity of 100% in prediction of first trimester pregnancy outcome.

**Conclusions:** Abnormal yolk sac diameter, in the form of small, enlarged, absent or irregular yolk sac, and embryonic bradycardia are associated with poor pregnancy outcome.

**Keywords:** Yolk sac, First trimester, Pregnancy outcome

### INTRODUCTION

Miscarriage is defined as the expulsion of a fetus or embryo from the uterus prior to 20 weeks of gestation or less than 500 g birth weight. Approximately 15 to 20% of the pregnancies are terminated by miscarriage. The common causes of spontaneous miscarriage during the first trimester are chromosomal abnormalities of the embryo/fetus, advanced mother age, uterine anomalies, teratogen and mutagen agents, maternal diseases, placenta anomalies, maternal trauma, endocrine, and immune

diseases.<sup>1</sup> The yolk sac (YS) is the primary source of exchange between the embryo and mother before the placental circulation is established. It first appears at about 5 weeks gestation and is visualized by ultrasound when the mean gestational sac diameter exceeds 8 to 13 mm.<sup>2</sup>

Accurate differentiation between normal pregnancy and pregnancy loss in early gestation remains a clinical challenge. Previous studies have described the association between embryonic well-beings and the characteristics of gestational sac.<sup>3</sup>

Studies reporting reference ranges from embryonic heart rate (EHR), gestational sac diameter (GSD) or yolk sac diameter (YSD) have examined small numbers of either spontaneously conceived pregnancies in women with certain LMP or in vitro fertilization pregnancies and report their values in relation to gestational (GA) or embryonic CRL.<sup>4</sup> As the use of vaginal sonography is increasing during the first trimester, we are able to demonstrate embryonic heart activity during the six-post menstrual week, and thus calculate the embryonic heart rate-many previous studies have related embryonic bradycardia with abortion.<sup>5</sup> In consistent and few reports have argued that a slow FHR at 6-8 weeks appears to be associated with subsequent fetal demise. A single observation of an abnormally slow heart rate does not necessarily indicate subsequent embryonic death, but a continuous decline of EHR activity might inevitably be associated with miscarriage.<sup>6</sup> The pregnancies with a YS diameter >5 mm had a significantly higher risk of miscarriage. But the risk of miscarriage was statistically similar between the pregnancies with regular yolk sacs and those with irregular yolk sacs as miscarriage occurred in 37.5% of pregnancies with enlarged yolk sacs and 3.8% of pregnancies with irregular yolk sacs.<sup>7</sup>

Studies suggested that a slow embryonic heart rate early in pregnancy (6-9 weeks of gestation) is associated with a high rate of subsequent fetal demise as embryonic heart rate <100 bpm is abnormal with miscarriage rate 83.3%.<sup>8</sup>

### **Aim**

The aim of the study was to evaluate the YS size and embryonic heart rate and to examine whether these parameters could serve as a prognostic factor for the first trimester pregnancy outcome.

### **METHODS**

This was a prospective cohort observational study conducted during the period from November 2019 till May 2020. 52 pregnant women in their first trimester from 6 weeks till 12 weeks gestation. These women fulfill to inclusion criteria and agree to participate in this study after explanation informed written consent was taken from each patient.

#### ***Inclusion criteria***

Pregnant women in their first trimester between 6-12 weeks, singleton pregnancy and positive heart motion seen in the embryo were included. If the LMP not sure, early ultrasound examination using CRL was used to detect accurate GA.

#### ***Exclusion criteria***

Patients with following criterias were excluded- (a) pregnant women with any problem during pregnancy e.g. vaginal bleeding, abdominal cramps; (b) pregnant patient

with medical disorders that may be a risk of miscarriage like diabetes chronic hypertensive disorder, connective tissue disorders; (c) patient don't like to continue in the study; and unwilling for follow-up; (d) patient with known uterine anomalies; (e) patients refusing transvaginal sonography. After taking a written informed consent from every patient; each patient was subjected to the following: (a) history; (b) examination; and (c) scanning technique.

EHR measurements were obtained transvaginally using M-mode sonography, after the recording 6-10 heartbeat cycles. The calculation of the heart rate was made by measuring the time interval of two cardiac cycles. All pregnancies were followed for their pregnancy outcome after completion of 12 weeks by either a subsequent ultrasound scan or a telephone interview. The adverse outcome was spontaneous miscarriage occurring before or at 12 weeks of gestation.

#### ***Statistical analysis***

Data were analyzed using Statistical Program for Social Science (SPSS) version 19.0. Quantitative data were expressed as meant standard deviation (SD). Qualitative data were expressed as frequency and percentage.

### **RESULTS**

This was a prospective cohort observational study carried out in the outpatient clinic of radiology department in Maternity hospital of Benha University hospital. During the period from November 2019 till May 2020. The study involved 52 pregnant women in their first trimester starting from 6-week gestation, all patients were followed for their pregnancy outcome after completion of 12 weeks.

These patients allocated into four study groups: according to first gestational age at presentation and second to pregnancy outcome. The first group (group I): women who were examined during (6-7 weeks+6 days). The second group (group II): women who were examined during (8-9 weeks+6 days). The third group (group III): women who were examined during (10-12 weeks). The fourth group (group IV): women who is their pregnancies resulted into first trimester spontaneous miscarriage. There were no statistical differences in the age, parity and BMI in the studied groups. There was no statistical difference between all groups; except miscarriage group (group IV). The vast majority of YSD in the studied groups had normal sac diameter (80.8%). All normal YSD continued beyond first trimester only one case of normal diameter end in miscarriage. There was a positive significant correlation between YSD and gestational age in miscarriage group (group IV) while nonsignificant correlation in other groups. YSD had 97.6% sensitivity and 100% specificity in prediction of miscarriage with total accuracy of 98.1%. EHR of miscarriage group IV was highly significant lower than that of other groups. There was a highly significant correlation between EHR and G.A in miscarriage group IV. No correlation was found between EHR and G.A in the

remaining other three groups. EHR had a sensitivity of 97.5% and specificity of 100% in the prediction of first trimester pregnancy outcome, with a total accuracy of 98.1%.

**Table 1: Demographic characteristic of the studied groups.**

Characteristics	Group I N=23	Group II N=11	Group III N=7	Group IV N=11	F	P value	Sig.
<b>Age (years)</b>							
X±SD	27.0±1.6	27.9±2.3	27.7±1.4	26.7±1.5	1.14	0.33	NS
Range	25-30	25-31	25-30	25-30			
<b>Parity</b>							
X±SD	2.2±0.7	2.3±0.7	1.9±0.7	2.3±0.8	0.7	0.53	NS
Range	1-3	1-3	1-3	1-3			
<b>BMI (kg/m<sup>2</sup>)</b>							
X±SD	26.8±1.9	26.5±1.9	25.7±1.7	26.3±1.7	0.69	0.56	NS
Range	24-29	24-30	24-29	24-29			

**Table 2: YSD in mm according to gestational age in weeks.**

Groups	N	YSD X±SD (range)	P value
<b>I</b>	23	4.3±2.4 (1.25-8.96)	0.54 (NS)
<b>II</b>	11	4.9±2.7 (1.6-8.38)	
<b>III</b>	7	4.893±1.9 (2.78-8.65)	
<b>IV</b>	11	2.0±0.4 (1.7-2.53)	

Note: \*P value when compare group I with II or III or IV.

**Table 3: Distribution of YSD in the studied groups.**

YSD	Frequency	Percentage (%)
<b>Normal</b>	42	80.8
<b>Irregular</b>	2	3.8
<b>Absent</b>	1	1.9
<b>Enlarged</b>	4	7.7
<b>Small</b>	3	5.8
<b>Total</b>	52	100

**Table 4: Correlation of YSD with first trimester outcome.**

YSD	Abortion	Continued beyond 12 weeks	Total	P value
<b>Normal</b>	1	41	42	<0.001
<b>Enlarged</b>	4	0	4	
<b>Irregular</b>	2	0	2	
<b>Absent</b>	1	0	1	
<b>Small</b>	3	0	3	
<b>Total</b>	11	41	52	

Note: p<0.001 HS.

**Table 5: Correlation between gestational age (G.A) and YSD.**

Variables	R value	P value	Sig.
<b>Group IV: GA and YSD</b>	0.53	<0.05	Sig.
<b>Other: GA and YSD</b>	0.1	>0.05	NS

**Table 6: Validity of YSD in prognosis of first trimester pregnancy outcome.**

Validity of YSD	YSD		Sensitivity	Specificity	PPV	NPV	Accuracy
	Normal	Abnormal					
<b>Continue pregnancy</b>	41	0	97.6%	100%	100%	90.9	98.1%
<b>Miscarriage</b>	1	10					

**Table 7: Embryonic heart rate (EHR) in beats per minute (bpm) according to gestational age.**

Groups	EHR (bpm) X±SD (range)	P value
I	129.5±21.2 (95-150)	
II	142.0±12.7 (125-160)	0.09
III	143.0±13.0 (130-150)	0.09*
IV	98.3±10.7 (90-120)	<0.001

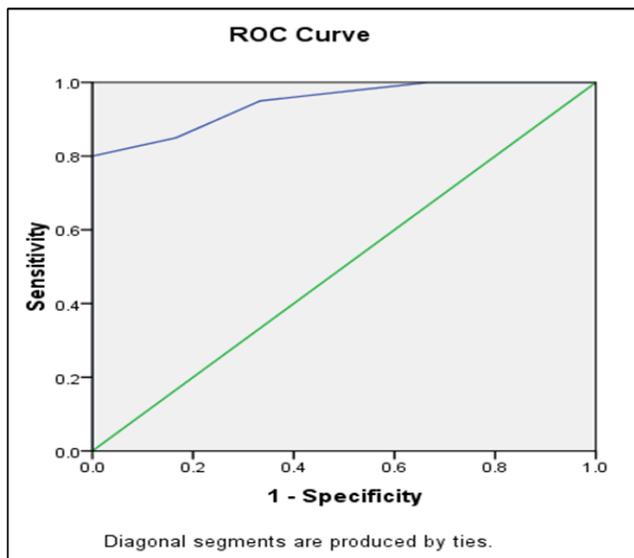
Note: \*P value when compare group I with II or III or IV.

**Table 8: Correlation between embryonic heart rate (EHR) and gestational age (G.A).**

Variables	R value	P value	Sig.
Group I-III: EHR and G. A	0.15	>0.05	NS
Group IV: EHR and GA	0.86	<0.001	HS

**Table 9: Validity of embryonic heart rate (EHR) in prediction of first trimester pregnancy outcome.**

EHR* (bpm)			Sensitivity	Specificity	PPV	NPV	Accuracy
	Positive	Negative					
>98	39	0	97.5%	100%	100%	92.3%	98.1%
≤98	1	12					

**Figure 1: ROC curve of EHR in prediction of miscarriage.**

## DISCUSSION

Miscarriage is defined as the expulsion of a fetus or embryo from the uterus prior to 20 weeks of gestation or less than 500 g birth weight. Approximately 15 to 20% of the pregnancies are terminated by miscarriage. The common causes of spontaneous miscarriage during the first trimester are chromosomal abnormalities of the embryo/fetus, advanced mother age, uterine anomalies, teratogen and mutagen agents, maternal diseases, placenta anomalies, maternal trauma, endocrine and immune diseases.<sup>9</sup> The YS is the first extra embryonic structure that becomes sonographically visible within the gestational sac

and acts as the primary route of exchange between the human embryo and the mother before placental circulation is established. YS is normally visible by TVS by the end of the fifth week of pregnancy, increases gradually in diameter between the 5<sup>th</sup> and 8<sup>th</sup> weeks, grows slower until 11<sup>th</sup> weeks and then decreases.<sup>10</sup>

In the present study we find that enlarged YS (4 cases), irregular or abscent YS (one case each) were highly significant associated with fetal loss. This suggesting that measurement of the YSD was a reliable prognostic factor for the first trimester outcome. The present study demonstrates the fact that visualization of YS is crucial for a normal pregnancy outcome. One case only out of 41 cases of normal YSD aborted 2.5%. This in agreement within our study the YS was not visualized in one case 1.9% of cases; this is in agreement with Xie et al who reported non-visualization of YS in 0.67% cases.<sup>11</sup> However, abscent YS in 4.5% and 4.3% in their cases. These finding is higher than our finding which may be explained by small sample size of our study. Thus, these studies strongly support the finding of the present study, that YS should always be present in normal pregnancies.<sup>12</sup>

In the present study abnormal YSD (enlarged or small) was present in 13.4% of cases. This was approximately like finding of Srivastava et al which were 11.2%, 10% and 11.4% respectively.<sup>13</sup> Thus, these studies support that abnormal diameter of YS is strongly associated with miscarriage.

In the present study, small YS size was found in 5.7% of cases which was slightly higher (3.7%) than found by Jose et al.<sup>14</sup> These finding support that small YSD is associated with adverse first trimester outcome.<sup>14</sup>

In this study abnormal (irregular) YS size was found in 5.7% of cases which was slightly higher (3.7%) that found by Jose et al.<sup>14</sup>

In this study, there was a statistically high significant difference between embryonic heart rate (EHR) in the miscarriage group (bradycardia) and other groups who continued their pregnancies (Table 7).

Fetal bradycardia is a sign of impending fetal death reflecting the forth coming collapse of the cardiovascular system. It may be also due to underlying chromosomal abnormality which was associated with fetal bradycardia.<sup>15</sup>

In the present study EHR was  $98.3 \pm 10.7$  bpm in the miscarriage group. This was with agreement of Ozgur et al who concluded in his study that a heart rate lower than 100 pbm in early first trimester 6-18 weeks will indicate a poor prognosis irrespective of gestational age.<sup>16</sup>

Maged et al studied 150 women with threatened miscarriage with singleton pregnancy between 5th and 12l week.<sup>17</sup> They reported that FHR below cut off 110 bpm it increased risk of miscarriage.

Mohamady et al enrolled 100 cases with threatened miscarriage between 7-13 week of gestations.<sup>18</sup> The FHR was significantly different ( $p < 0.001$ ) between the miscarried and those continuing pregnancy. The mean FHR for the continued group was  $156.9 \pm 20$  bpm and for the miscarried group was  $122 \pm 9$  bpm.

A significant decrease of EHR was observed in pregnancies that resulted in miscarriage when compared to the ones that continued beyond the first trimester. Such a decrease was found in most previous studies.<sup>19</sup> This in agreement of our findings. However, some researchers have failed to prove this hypothesis.<sup>20</sup> This maybe they studied different population (threatened miscarriage).

This study was one of few which simultaneously evaluate yolk sac diameter and embryonic heart rate during the first trimester. The result of this study showed that abnormal or absent YSD and embryonic braducardia was associated with poor prognosis of first trimester outcome. Limitation of the study was the small number of patients in the study group.

## CONCLUSION

Abnormal yolk sac diameter, in the form of small, enlarged, absent or irregular yolk sac, and embryonic bradycardia are associated with poor pregnancy outcome independent of maternal risk factors such as age, body mass index or parity.

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