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Usefulness of Yolk Sac Diameter and Embryonic Heart Rate as Prognostic Factors of Gestational Outcome in Early Singleton Pregnancies

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ABSTRACT

Background: Within the gestational sac, the yolk sac is the first embryonic structure to be seen. The size, shape, and function of the yolk sacs, as well as the heart rates of the developing embryos, all play a role in the evaluation and prognosis of first-trimester pregnancy losses.

Objective: The purpose of this study was to determine if yolk sac diameter (YSD) and embryonic heart rate (HER) could be used to predict pregnancy outcomes.

Patients and Methods: 52 pregnant women at gestational age ranged between 6-12 weeks who were included in the study. Our prospective cohort study was carried out in Obstetrics and Gynecology Department at Fetomaternal Unit, Zagazig University Hospital and Fetomaternal & Ultrasound Units, Matrouh Maternity Hospital. Measurements of the embryo's crown-rump length as well as their heartbeat rate and the size and shape of the yolk sac were done.

Results: Normal sac diameter was seen in the great majority of YSD patients in the study groups (80.8 percent). Only one case of normal diameter YSD ended in miscarriage after the first trimester in all patients with normal YSD. A 98.1% success rate in predicting miscarriage was achieved by YSD, which had 97.6% sensitivity and 100% specificity. First-trimester pregnancy outcomes were accurately predicted by EHR with a sensitivity of 97.5% and a specificity of 100%.

Conclusion: Maternal risk variables including age, weight, or parity have no effect on the poor pregnancy outcome related with abnormal yolk sac diameter and embryonic bradycardia.

Keywords: Yolk sac diameter, Embryonic heart rate, Gestational outcome.

INTRODUCTION

Approximately 30% to 40% of human pregnancies terminate spontaneously in the first trimester following implantation. Abortion rates fall if a baby's heartbeat is discovered [(1)]. The yolk sac plays a significant role throughout organogenesis, supplying metabolic, immunological, endocrine, nutritional, and hemopoietic functions, and its peak functional activity occurs during the fourth and seventh weeks of development [(2)]. The properties of the gestational sac, the yolk sac, and the heartbeats of the embryo all appear to be linked to the health of the developing embryo [(1)].

Research on the yolk sac's structure and function has been conducted in a variety of ways. A higher percentage of pregnancies ended in miscarriage when the yolk sac was larger than 5 millimeters. Miscarriages occurred in 37.5% of pregnancies with larger yolk sacs and in 3.8% of pregnancies with irregular yolk sacs [(3)]. The incidence of problems decreases as the pregnancy progresses in the first trimester with a normal yolk sac. 94.2% of the time, a typical yolk sac can anticipate a normal outcome [(4)].

Within the gestational sac, the yolk sac is the first embryonic structure to be seen. A round anechoic region is usually visible from the fifth to the twelfth week of pregnancy; after that, it fades away [(5)]. In most cases, it is possible to detect the heartbeat of an embryo as early as five weeks of pregnancy. In this context, both Doppler investigations and motion mode (M-mode) can be helpful. Between 6 and 10 weeks of pregnancy, the fetal heart rate increased considerably, rising from 118 to 167 beats per minute [(6)].

First-trimester pregnancy losses are evaluated and prognosed by looking at yolk sac size, structure, and function, as well as heart rate during embryonic development. If a woman has bradycardia, a transvaginal ultrasonography can accurately show her EHR (Embryonic Heart Rate) and determine her pregnancy's fate [(7)].

An abnormally slow embryonic heart rate during the first six to nine weeks of pregnancy has been linked to 83.3% miscarriage rate, a heart rate of less than 100 beats per minute is considered abnormal [(8)].

The goal of this work was to determine if YSD and EHR could be used to predict pregnancy outcomes.

PATIENTS AND METHODS

This study was conducted in the period between June 2021 to December 2021 in the Obstetrics and Gynecology Department at Fetomaternal Unit, Zagazig University Hospital and Fetomaternal Unit & Ultrasound Unit, Matrouh Maternity Hospital. 52 pregnant women aged from 20 to 40 years old at gestational age ranged from six to twelve weeks were involved in the study.

Inclusion criteria:

Pregnancy of a singleton, an early ultrasound check with CRL was used if the LMP was unsure about the accuracy of the gestational age (GA), and action of the heart in the embryo is positive.

Exclusion criteria:

Past abortions or miscarriages, blighted ovum, patient having a well-documented history of uterine abnormalities, absent embryonic cardiac activity, and

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chronic diseases (cardiac diseases, diabetes, hypertension and SLE).

Ethical consent:

Zagazig University's Research Ethics Council approved the study as long as every participant signed informed consent form and submitted them to ZU-IRB#6891. We adhered to the Helsinki Declaration, which is the ethical norm for human testing established by the World Medical Association.

All patients were subjected to the following:

Full history: Personal, menstrual, contraceptive and obstetric history.

Clinical examination: General examination, abdominal examination and pelvic examination were done.

Trans abdominal/vaginal Ultrasound:

To assure intra uterine pregnancy, uterine wall tumors, detection of GA, adnexal swelling, and number of Sacs.

Ultrasound: Yolk Sac (YS):

The gestational sac appears during the fifth gestational week in a normal pregnancy. At 6 weeks of gestation, the embryo's YSD and GSD are around 3 and 10 mm, respectively. The YSD and GSD rise throughout pregnancy, but the yolk sac dissolves between 10 and 12 weeks [(9)]. A large yolk sac was described as one with a diameter greater than or equal to 5 millimeters, and a tiny yolk sac as one with a diameter less than or equal to 2 millimeters [(10)].

Embryonic heart rate (EHR) recording six to ten heartbeat cycles in M-mode ultrasonography allowed for transvaginal measurements. A person's heart rate can be calculated by multiplying the time interval between two cardiac cycles by 100 to arrive at a final figure [(11)].

A follow-up ultrasound or telephone interview was conducted at the end of the 12th week of pregnancy for all pregnancies. Miscarriage occurred naturally before or after the 12-week mark, which was a bad outcome.

Statistical analysis

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (IBM SPSS Inc., Chicago, IL, USA). Student T test and ANOVA were used. Multivariable regression analysis was used to calculate risk ratios. Analysis of differences between quantitative independent groups was done using t-tests or Mann Whitney, Kappa, and logistic regression. P value ≤ 0.05 was considered significant.

RESULTS

Age ranged from 21 to 40 with a mean of 25.8 ± 3.1 years, BMI ranged from 22.6 to 30 with a mean of 25.4 ± 2.4 kg/m^2. 76% (40) of patients have regular menses while only 24% (12) have irregular menses with a mean duration of 5.1 ± 1 days. Number of previous abortions ranged from 3-5 with a mean of 3 ± 0.7 with 76% of patients having more than 3 abortions. Also, the week of last abortion ranged from 6 to 13 weeks with a mean of 10.1 ± 3.1 weeks **(Table 1).**

In terms of YSD and GS diameter, the average was 39 ± 10.7 and 45 ± 13.7 mm, respectively. In the research groups, the vast majority of YSD had a normal sac diameter (80.8 percent) **(Table 2).**

Only one case of normal YSD ended in miscarriage after the first trimester, despite the fact that all other cases were normal **(Table 3).**

98.1% of miscarriages could be predicted using the YSD method, with 97.6% sensitivity and 100 % specificity **(Table 4, Figure 1).**

First-trimester pregnancy outcomes were accurately predicted by EHR with a sensitivity of 97.5 % and a specificity of 100% **(Table 5, Figure 2).**

All parameters were significant dependent predictors for pregnancy outcome except for parity **(Table 6).**

Table (1): Demographic data, Menstrual and obstetric history of the studied cases

	n = 52
Age (years)	
Mean ± SD	25.8 ± 3.1
Range	21-40
Weight(kg)	
Mean ± SD	65.8 ± 8.1
Range	58-83
Height(cm)	
Mean ± SD	160.8 ± 4.2
Range	153-167
Body mass index	
Mean ± SD	25.4 ± 2.4
Range	22.6-30
Duration of mens (days)	
Mean ± SD	5.1 ± 1
Range	4-7
No. of previous Pregnancy losses	
Mean ± SD	3 ± 0.7
Range	3-5
Regularity of cycle	
Regular	40 (76%)
Irregular	12 (24%)
Gravidity	
3	12 (24%)
> 3	40 (76%)
Parity	
0	27 (51.9%)
1	25 (48.1%)
Week of last abortion	
Mean ± SD	10.1 ± 3.1
Range	6-13

Table (2): Ultrasound findings, distribution of yolk sac diameter (YSD) in the studied group

	n = 52
YSD (mm) Mean ± SD Range	 39 ± 10.6 16-62
GS diameter (mm) Mean ± SD Range	 45 ± 13.7 26-61
Weeks of gestations Mean ± SD Range	 9.9 ± 1.6 6-12

YSD	Frequency	%
Normal	42	80.8
Irregular	2	3.8
Absent	1	1.9
Enlarged	4	7.7
Small	3	5.8
Total	52	100

Table (3): Correlation of YSD with first trimester outcome:

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

Table (4): Validity of YSD in predicting pregnancy outcomes in the first trimester

	YSD		Specificity	Sensitivity	NPV	PPV	Accuracy
	Normal	Abnormal					
Miscarriage	1	10	100%	97.6%	90.9%	100	98.1%
Continue preg	41	0					

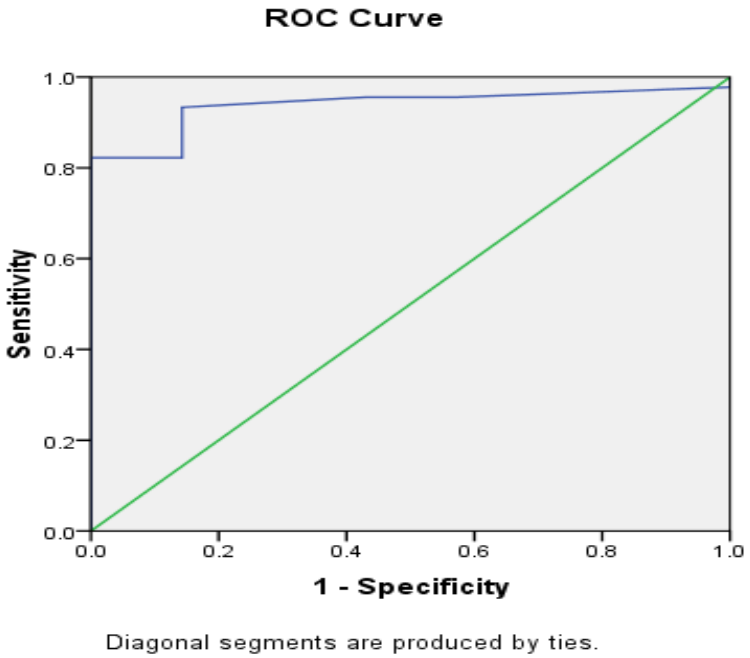

Figure (1): ROC curve for predicting miscarriage using YSD data

Table (5): Pregnancy outcomes in the first trimester can be accurately predicted using the embryonic heart rate (EHR)

EHR*bpm			Sensitivity	Specificity	PPV	NPV	Accuracy
	+ ve	-ve					
>100	39	0	97.5%	100%	100%	92.3%	98.1%
≤100	1	12					

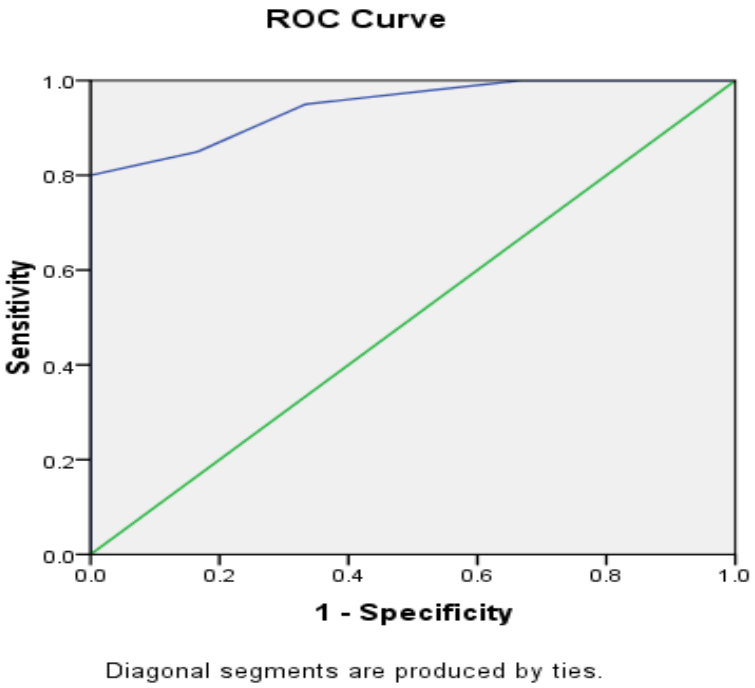

Figure (2): Predicting miscarriage using EHR's ROC curve

Table (6): Dependent predictors contributing together to predict pregnancy outcome

Score		P
Maternal age	**7.89**	**0.005***
BMI	**13.71**	**0.001****
GA	**11.00**	**0.001****
parity >3	**2.49**	**0.511**
EFH > 100	**122**	**0.001****
YSD	**31.42**	**0.0001****

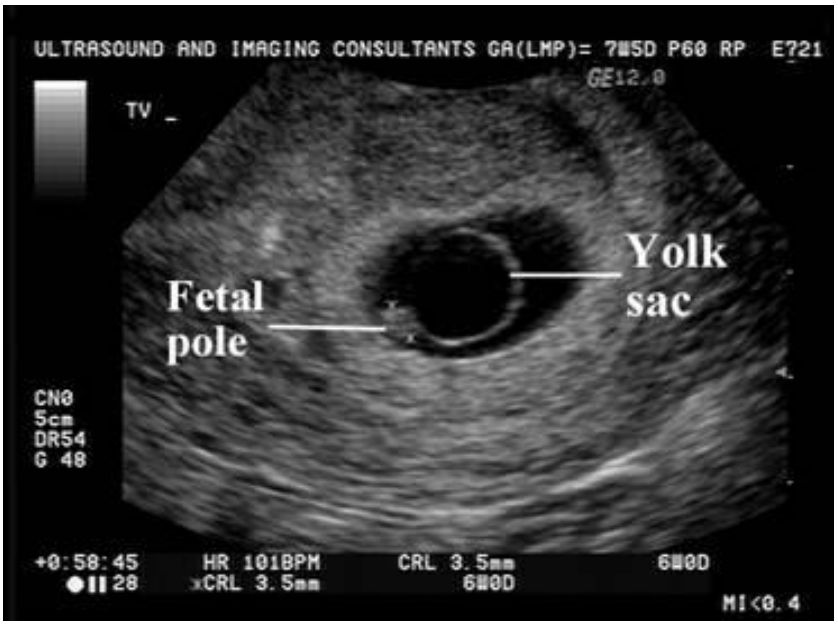

Figure (3): At 6 weeks and 1 day, a transvaginal ultrasound showed an embryo with heart activity and a big yolk sac.

DISCUSSION

In the current study, there were four cases of YS growth, one of irregular or absent YS, and one of both. For the first trimester, the YSD (Yolk Sac Diameter) was a reliable predictor of the outcome. Observing YS is critical to a healthy pregnancy, according to the findings of this study. Only one normal YSD instance out of 41 had an abortion rate of 2.5%. This is in agreement with **Doublet *et al.*** [12] and **Srivastava *et al.*** [4].

1.9% of the time, the YS was not visible in our investigation. This is in accordance with **Xie and Chen** [13] who stated that YS was not visible in 0.67% of the cases. However, **Shetty *et al.*** [14] found YS in 4.5% and 4.3% in their cases. A smaller sample in our study may explain why these results are higher than ours. Thus, the findings of the present investigation are supported by prior studies, which show that YS is always present in normal pregnancies.

Only 13.4% of patients in this study had aberrant YSD (big or small). This finding resembled somewhat that of **Srivastava *et al.*** [4] where it was 11.2%, 10%, and 11.4%, respectively. Consequently, these research show that a small YS is substantially linked to miscarriage.

After 12 weeks in the current trial, none of the patients with an enlarged YS were still experiencing symptoms. A whopping 36.3% of situations. This is in agreement with the finding of **Tan *et al.*** [10] who found that 37.5% of their aborted cases had enlarged YS. According to **Srivastava *et al.*** [4] visualization of a large size YS is a predictor of poor pregnancy outcome.

Small YSD is linked to poor first-trimester outcomes, as our findings showed, and this is in line with **Varelas *et al.*** [15]. Unusual YS sizes were detected in 5.7 percent of patients, which was slightly greater than the 3.7 % found by the study of **Jose *et al.*** [16]. According to these findings, a small YSD is related with an increased risk of a poor first trimester outcome **Varelas *et al.*** [15].

3.8% of the participants in this study had abnormal (irregular) YS. **Moradan and Forouzeshfar** [17] found irregular YS in 18.1% of their cases. This may be due to a large sample size of their cases 193 cases of them versus 52 cases of ours. Thus, distorted (irregular) shape of YS is an important factor in prediction of poor first trimester outcome.

Benson and Doubilet [18] found that if the embryonic heart rate was 70 BPM or less the miscarriage rate was 100%, and if ranged 70-79 BPM miscarriage rate was 91%, if ranged 80-90 BPM miscarriage rate was 79%. They concluded that, patients with slow EHR < 120 BPM in first trimester, threatened miscarriage may eventually be at risk for pregnancy loss.

When comparing the EHRs of women who had miscarried with those who carried on with their pregnancies, a statistically significant difference (bradycardia) emerged.

Premature fetal death can be predicted by fetal bradycardia, which is a symptom of a breakdown of the cardiovascular system. A chromosomal defect that was linked to fetal bradycardia may potentially be to blame [19].

According to the results of this study, the miscarriage group had an embryonic heart rate (EHR) of 98.3± 10.7 bpm. This is in accordance with **Oztekin** [20], where he discovered that, regardless of gestational age, an early first trimester heart rate of less than 100 pbm (6-18 weeks) indicated a poor prognosis (source).

Maged and Mustafa [21] examined 150 pregnant women in the 5th to 12th week of a singleton pregnancy. They found that the probability of miscarriage was raised if the EHR was below the cut-off point of 110 BPM.

Pregnancies that ended in miscarriage had a markedly lower EHR than those that progressed past the first trimester. The bulk of past research have discovered such a decline [22]. According to our observations, this is correct. This notion, however, has not been proven by certain researchers [23]. It's possible that they looked at a different demographics in this study (threatened miscarriage).

This study was one of the few to assess yolk sac dimensions and embryonic heart rate at the same time during the first trimester of pregnancy. A poor first-trimester outcome was found to be linked to abnormalities in the YSD gene and embryonic bradycardia in this study.

CONCLUSION

Maternal risk variables including age, weight, or parity have no effect on the poor pregnancy outcome related with abnormal yolk sac diameter and embryonic bradycardia. .

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