Is Sonographic Morphology of Early Embryonic Complex Can Predict of Pregnancy Outcome?

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ABSTRACT
Background: There is a high rate of spontaneous abortion in the first trimester of pregnancy, affecting an estimated 30–40% of all implantations. A low implantation location, a large or irregular yolk sac, a weak decidual reaction, and a sluggish embryonic heart rate are just few of the many sonographic indicators of predictors of poor result that have been identified by many authors. The aim of the current study is to investigate the predictive value of abnormal gestational sac morphology at 6-8 week for the pregnancy outcome.
Patients and methods: The present study was a follow up observational study that included 188 patients aged 18-35 years, who presented at 6-8 weeks of gestation between May 2019 and February 2021 at Mansoura University Hospital's Antenatal Care Outpatient Clinic.
Results: Larger gestational sac was associated with abnormal pregnancy outcome, like abortion (2.25±0.58 cm), preterm labor (2.33±0.0 cm), intrauterine feal death (IUFD) (2.70±0.28 cm), intrauterine growth retardation (IUGR) (2.93±0.93 cm) and abruptio placenta (3.45±2.19 cm). Also, larger yolk sac was also associated with abnormal pregnancy outcome, like preterm labor (5.0±0.0 cm), IUGR (5.57±1.07 cm), and IUFD (5.50±0.71 cm). Moreover, higher fetal HR was associated with abnormal pregnancy outcome, like preterm labor (155.0±0.0 bpm), IUFD (157.50±3.53 bpm), and IUGR (171.0±4.58 bpm). **Conclusion:** Statistically highly significant correlations were found between both yolk sac size and fetal heart rate, and abnormal pregnancy outcome, despite the fact that there was no link between gestational sac size and an increased risk of a negative pregnancy outcome.
Keywords: Sonography, Morphology, Early embryonic complex, Pregnancy, Predictive outcome.

INTRODUCTION

Twenty-five to 30% of embryos are lost before the pregnancy is clinically identified, and 15% to 25% of clinical pregnancies spontaneously abort during the first trimester [1].

During embryonic development, the major viscera take shape. These structures mature and reach their full functional potential throughout gestation. In the context of a prenatal diagnosis, ultrasound is the gold standard [2,3]. Kratochwil and Eisenhut were the first to report the successful demonstration of an early intrauterine pregnancy using transvaginal ultrasonography (TVS) [3].

With TVS, a yolk sac and a Hypoechoic complex within the thickened Decidualized endometrium are among the earliest indicators of an intrauterine pregnancy (IUP). When a sonogram is performed on a pregnant woman, the secondary yolk sac is the first extraembryonic structure that may be seen [2].

When the mead sac diameter (MSD) is 5 to 6mm, a yolk sac is plainly visible using transvaginal sonography. When a gestational sac is bigger than 8 mm, it is standard practice to check on the yolk sac [4].

The normal appearance of the yolk sac is that of a spherical structure with an anechoic center surrounded by a homogeneous well-defined echogenic wall. So, the yolk sac is important, and then the embryo appears and the heart starts beating [5]. The presence of a yolk sac is definitive evidence of a genuine gestational sac [6].

A yolk sac's diameter is typically 2-5 mm between weeks 6-8 of pregnancy and continues to expand until week 10 of pregnancy [7]. When the mean gestational sac diameter is greater than 8 mm without a yolk sac, or greater than 16 mm without an embryo, a blighted ovum can be definitively diagnosed using transvaginal sonography. A blighted ovum can be diagnosed transabdominally if the gestational sac is larger than 20 mm without a yolk sac, or 25 mm without an embryo [8].

First, the yolk sac appears, then the embryo develops, and finally the heart begins to beat [9]. At around 5-6 weeks, a healthy resting fetal heart rate (FHR) is around 110 beats per minute (bpm). 9-10 weeks to get 170 bpm. After this, the average FHR will drop to: 150 beats per minute by week 14, 140 by week 20, and. Term-average heart rate of 130 beats per minute [10].

Fetal bradycardia refers to a low fetal heart rate, which is typically described as: FHR 100 bpm before 6 weeks gestation, or FHR 120 bpm between 6 and 7 weeks. Fetal tachycardia refers to an abnormally high heart rate in a developing baby and is typically classified as: Fetal tachycardia is defined as a heart rate in the fetus that is greater than 160 to 180 beats per minute, with a heart rate of around 170 being on the cusp of being considered [10].

Approximately 30-40% of all implantations are lost to spontaneous abortion, and the vast majority of these abortions occur within the first trimester [6]. If fetal cardiac activity has been established, however, the chance of a spontaneous abortion is reduced to 2-5% [7].

At 6 weeks of pregnancy, antenatal sonography with a transvaginal transducer can typically detect the embryonic heartbeat, and the heart rate can be examined

using M-mode ultrasonography. Severe bradycardia of the embryo has been linked to miscarriage in the past [11].

Pregnancy outcomes can be predicted with a high degree of accuracy based on the timing and appearance of key structures such as the gestational sac, yolk sac, fetal heart, and vascularity (decidual vascularity). A low implantation location, a large or irregular yolk sac, a weak decidual reaction, and a sluggish embryonic heart rate are just few of the many sonographic indicators of predictors of poor result that have been identified by many authors [12].

The aim of this study was to investigate the predictive value of abnormal gestational sac morphology at 6-8 week for the pregnancy outcome.

PATIENTS AND METHODS

The present follow up observational study included 186 patients outpatient clinic for antenatal care. The patients were recruited from antenatal care outpatient clinic in Mansoura University Hospital during the period between May 2019 and February 2021.

Inclusion criteria: Age: 18-35 years who come to our Antenatal Clinic between the sixth and eighth week of pregnancy. women who have experienced per vaginal bleeding at any point during their current pregnancy. Patients who are pregnant and who have abnormal sonographic markers like, a retro chorionic or retro placental collection; a small or irregular gestational sac; a large or calcified yolk sac; a slow FHR.

Exclusion criteria: Pregnant aged <18 years and >35 years. History of congenital mal formation and recurrent abortion. Patient with extra uterine pregnancy and multiple pregnancy. Patient with major comorbid disease e.g., COVID-19 virus infection, tuberculosis, hepatitis, diabetes, long-term hypertension. Individuals treated with antipsychotic and antiepileptic medications. Patients refusing sharing in a study. Patients who refuse to continue in this study. Patients with lost follow up.

Methods:

Women who met inclusion and exclusion criteria were recruited from the Department of Obstetrics and Gynecology for transvaginal sonography during their first trimester of pregnancy. We took a thorough medical history to rule out any preexisting conditions, including those treated surgically, that would alter our results, excluding all participants without complete health and wellness. The checkup is over with; A singleton pregnancy with no complications throughout pregnancy. Participants had to be between 6 and 8 weeks along in their pregnancies, and the study excluded women with uterine or cervix abnormalities or known medical conditions associated with an unfavorable pregnancy outcome (such as anemia or hyperthyroidism).

Scanning technique:

The Samsung HD 16 (South Korea) by GE Healthcare with a TVS probe operating at 7-12 MHz was used for this study. This sonogram was performed with the patient's bladder completely empty. The patient was given an in-depth explanation of the procedure, and their agreement was obtained. Before insertion, a sterile condom was placed over the transvaginal transducer, and the device was lubricated with gel.

A modest Trendelenburg tilt was performed in the opposite direction, placing the patient in the dorsal position. Patient was instructed to loosen up her pelvic floor. Six to eight centimeters of the transducer were placed in the vagina. The scans were performed in the coronal and sagittal planes. TVS was completed in a methodical fashion.

Scans of the uterus, adnexa, and call-de-sac were performed in that order. Diameter, form, and contour of the gestational sac, as well as appearance and shape of the yolk sac, were determined; the YSD was measured by inserting callipers into the sac at its inner boundary; a normal YSD falls within a range of 2-5 mm. Yolk sacs were classified as either large (diameter >5mm) or small (diameter 2 mm). Patients were monitored all the way through labor and delivery; a heart rate of less than 110 was considered to be abnormal.

After 12-14 weeks, a second trans-abdominal ultrasound was planned for all study participants to rule out structural abnormality using assessment of Abdominal circumference, Head circumference, femoral Length, BPD as well as Doppler).

Thereafter, at weeks 28 and 32, another scan is performed to check on the baby's development and, if necessary, to detect IUGR or oligohydramnios using the Method of Ultrasound Measurement of Fetal Dilation and Translucency (Head circumference, BPD, Abdominal circumference, femoral Length), in addition to unusual Doppler measurements. Patients were monitored till delivery to learn about the health of their unborn children.

Ethical consent:

An approval of the study was obtained from Mansoura University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of participation in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

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. Number and percentage descriptions were used to describe qualitative information. After checking normality with the Kolmogorov-Smirnov test, quantitative data were summarized using the median (minimum and maximum) for non-parametric data and the mean, standard deviation (SD), for parametric data. Two different groups were compared using a parametric

test, specifically the Student's t-test. We compared two unrelated groups using the Mann-Whitney U test (a non-parametric test). P-value ≤0.05 was considered significant.

Analysis of the receiver operating characteristic (ROC) curve is used to determine the diagnostic performance of a test, or the accuracy with which it can separate diseased cases from healthy ones. The curve was used to detect sensitivity and specificity, while positive predicative value (PPV), negative predictive negative (NPV), and accuracy were computed using cross tabulation. Independent variables of binary outcomes were predicted using a binary stepwise logistic regression analysis. Predictors that performed well in univariate analysis were added to the regression model via the Enter technique. The odds ratios were adjusted, and the 95% confidence intervals were determined.

RESULTS

Table 1 demonstrates age, gravidity, and parity of the studied cases. The mean age of the studied females ranged from 18-35 years. The median gravidity was 2.0 (range: 1.0-5.0). The median parity was 1.0 (range: 0.0-4.0).

Table (1): Age, gravidity and parity of cases.

Total number =188	
Age/years Mean ± SD	(18-35)
Gravidity Median (range)	2.0 (1.0-5.0)
Parity Median (range)	1.0 (0.0-4.0)

Table 2 reveals ultrasound findings of the studied females at 6-8 weeks. The mean diameter of gestational sac age was 2.047 (SD 0.57) cm. The mean yolk sac diameter was 4.47 (SD 0.84) cm. The mean FHR was 140.19 (SD 13.48) bpm.

Table (2): Ultrasound findings of the studied females at 6-8 weeks.

Ultrasound findings	Total number =188
Gestational sac/cm	2.047 ± 0.57 2.04 (1.06-5.0)
Yolk sac	4.47 ± 0.84 4.6 (2.0-8.0)
HR	140.19 ± 13.48 142.0 (89.0-188.0)

Table 3 illustrates pregnancy outcome distribution among the studied females. Normal pregnancy outcome was reported in 91.5% of the studied females. 4.3% of the studied cases had abortion, 1.1% had abruption placenta, and 0.5% had preterm labor. IUGR and IUFD were reported in 1.1% and 1.6% of the studied females, respectively. No congenital anomalies were reported in any of the studied cases.

Table (3): Pregnancy outcome distribution among studied females.

Outcome of pregnancy	N=188	%
Normal	172	91.5
Abortion	8	4.3
Abruptio placenta	2	1.1
IUFD	2	1.1
Preterm labor	1	.5
IUGR	3	1.6
Congenital anomalies	zero	zero

Table 4 demonstrates association between abnormal pregnancy outcome and the studied female characteristics. According to the current results, a statistically significant correlation was found between age of the studied females and abnormal pregnancy outcome **(P<0.05)**, while no statistically significant correlations were found between the mean values of neither gravidity nor parity and abnormal pregnancy outcome of the studied cases **(P>0.05)**.

Table (4): Association between abnormal pregnancy outcome and studied female characteristics.

Variable	Normal outcome N=172	Abnormal outcome N=16	test of significance
Age/years	24.43 ± 4.39	27.81 ± 3.75	t=2.98 P=0.003*
Gravidity	2.0 (1.0-5.0)	2.0 (1.0-5.0)	z=0.238 P=0.812
Parity	1.0 (0.0-4.0)	1.0 (0.0-4.0)	z=0.736 P=0.462

Table 5 reveals association between abnormal pregnancy outcome and ultrasound findings among the studied females at 6-8 weeks. According to the current results, a statistically significant correlation was found between the mean diameter of gestational sac and abnormal pregnancy outcome **(P<0.05)**, while no statistically significant correlations were found between the mean values of neither yolk sac diameter nor fetal HR and abnormal pregnancy outcome of the studied cases **(P>0.05)**.

Table (5): Association between abnormal pregnancy outcome and ultrasound findings among studied females at 6-8 weeks:

Variable	Normal outcome N=172	Abnormal outcome N=16	Test of significance
Gestational sac/cm	1.99 ± 0.51	2.59 ± 0.89	t=4.12 P<0.001*
Yolk sac	4.45 ± 0.66	4.73 ± 1.93	t=1.26 P=0.211
HR	140.67 ± 9.67	135.06 ± 34.21	t=1.59 P=0.112

t: Student's t test *statistically significant if p<0.05, parameters described as mean ± SD.

Table 6 illustrates validity of ultrasound findings in prediction of abnormal pregnancy outcome among the studied females. According to the current results, only gestational sac diameter could significantly predict abnormal pregnancy outcome (p=0.001, AUC=745, with 81.2% sensitivity, 20.6% specificity, and 71.8% accuracy at a cut-off point 2.135), while each of yolk sac diameter and fetal HR could not.

Table (6): Validity of ultrasound findings in prediction of abnormal pregnancy outcome among studied females.

Variable	AUC (95% CI)	P-value	Cut off point	Sensitivity	Specificity	PPV	NPV	Accuracy
Gestational sac/cm	745 (0.617-0.873)	0.001	2.135	81.2	20.6	70.9	97.6	71.8
Yolk sac	589 (0.383-0.795)	0.240	4.89	62.5	70.9	16.7	95.3	70.2
HR	494 (0.260-0.728)	0.939	154.5	50.0	90.1	32.0	95.1	86.7
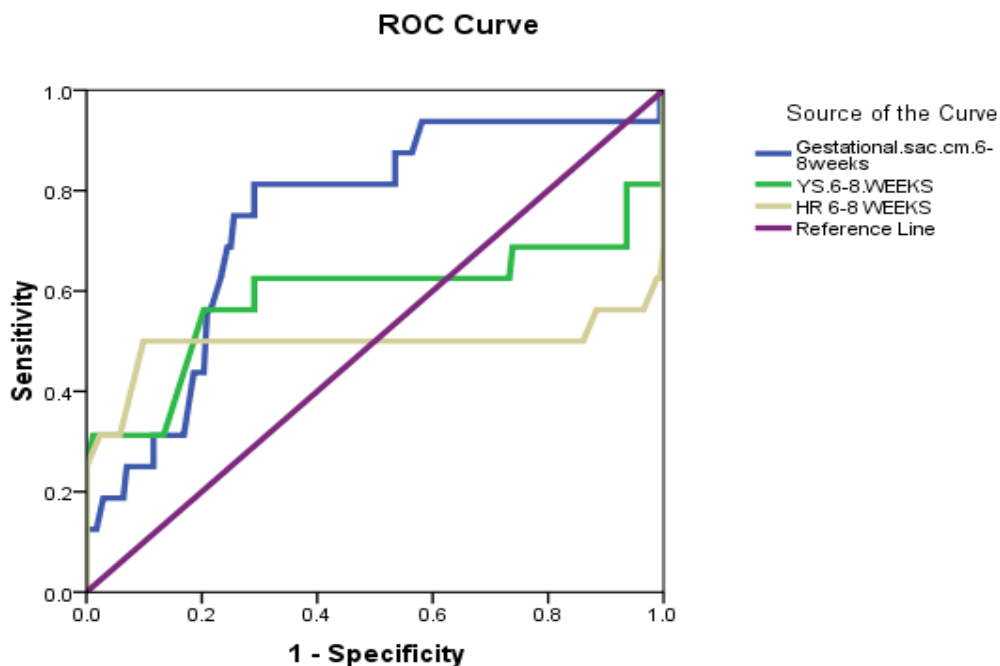
Figure (1): Receiver operating characteristics curve for gestational sac, yolk sac and HR at 6-8 gestation in prediction of abnormal pregnancy outcome.

Table 7 reveals association between abnormal pregnancy outcome and ultrasound findings. According to the current results, larger gestational sac was associated with abnormal pregnancy outcome, e.g. abortion (2.25 ± 0.58 cm), preterm labor (2.33 ± 0.0 cm), IUFD (2.70 ± 0.28 cm), IUGR (2.93 ± 0.93 cm) and abruptio placenta (3.45 ± 2.19 cm). As well, larger yolk sac was also associated with abnormal pregnancy outcome, e.g. preterm labor (5.0 ± 0.0 cm), IUGR (5.57 ± 1.07 cm), and IUFD (5.50 ± 0.71 cm). Moreover, higher fetal HR was associated with abnormal pregnancy outcome, e.g. preterm labor (155.0 ± 0.0 bpm), IUFD (157.50 ± 3.53 bpm), and IUGR (171.0 ± 4.58 bpm).

Table (7): Association between abnormal pregnancy outcome and ultrasound findings.

Variable	Normal outcome	Abortion	Abruption	IUFD	Preterm labor	IUGR
	N=172	N=8	N=2	N=2	N=1	N=3
Gestational sac/cm	1.99±0.43	2.25±0.52	3.45±0.73	2.70±0.28	2.33±0.01	2.93±0.61
Yolk sac	4.45±0.65	4.61±1.1	3.0±0.01	5.50±0.71	5.0±0.01	5.57±1.07
HR	140.67±9.67	111.63±32.51	142.50±17.68	157.50±3.53	155.0±0.01	171.0±4.58

Parameters described as mean ± SD.

Table 8 demonstrates univariate and multivariate analysis for predictors of abnormal pregnancy outcome among the studied females. According to the current results, gestational sac diameter (cm) at 6-8 weeks, of the women who were evaluated, can be utilized as a predictor of an unsatisfactory pregnancy outcomes [OR: 4.47 (95% CI 1.86 - 10.78), p=0.001] only with univariate analysis.

Table (8): Univariate and multivariate analysis for predictors of abnormal pregnancy outcome among studied females.

Variable	Univariate analysis		Multivariate analysis		
	P-value	crude odd ratio (95% CI)	β	P-value	Adjusted odds ratio 95% CI
Gestational sac/cm at 6-8 weeks	0.001*	4.47 (1.86-10.78)	0.292	0.804	1.34 (0.133-13.45)

Model χ²=49.11   P<0.001* Constant=34.39
Overall % predicted=98.9%

Table 9 reveals distribution of studied cases according to abnormal ultrasound findings at 6-8 weeks. According to the current results, gestational sac was normal in size (16-24 mm) in most cases (66.5%), but larger in 18.1% of cases, and smaller in 15.4% of cases. As well, normal yolk sac size (4-6 mm) was reported in the majority of the studied cases (76.6%), while it was larger in 14.9% of cases, but smaller in 8.5% of cases. As regards FHR, it was normal (110-160 bpm) in the vast majority of cases (95.2%), while tachycardia was reported in 2.1% of cases, and bradycardia in 2.7% of cases.

Table (9): Distribution of studied cases according to abnormal ultrasound findings at 6-8 weeks.

Variable	N=188	%
Gestational sac		
Small	29	15.4
Normal (16-24 mm)	125	66.5
Large	34	18.1
Yolk sac		
Small	16	8.5
Normal (4mm-6mm)	144	76.6
Large	28	14.9
Heart rate		
Bradycardia	5	2.7
Normal (110 bpm-160bpm)	179	95.2
Tachycardia	4	2.1

Table (10) displays association between abnormal ultrasound findings and abnormal pregnancy outcome. According to the current results, statistically highly significant correlations were found between both yolk sac size and FHR, and abnormal pregnancy outcome

(p<0.001), Despite the fact that there was no link between gestational sac size and an increased risk of a negative pregnancy outcome **(p>0.05)**.

Table (10): Association between abnormal ultrasound findings and abnormal pregnancy outcome.

Variable	Total number	Findings Normal N=172	Abnormal N=16	Test of significance
Gestational sac Normal Small Large	125 29 34	115(92.0) 28(96.6) 29(85.3)	10(8) 1(3.4) 5(14.7)	p=0.263
Yolk sac Normal Small Large	144 16 28	138(95.8) 11(68.8) 23(82.1)	6(4.2) 5(31.2) 5(17.9)	p<0.001*
Heart rate Normal Bradycardia Tachycardia	179 5 4	172(96.1) 0 0	7(3.9) 5(100) 4(100)	p<0.001*

DISCUSSION

Results of the current study found that the mean age of the studied females ranged from 18-35 years. The median gravidity was 2.0 (range: 1.0-5.0). The median parity was 1.0 (range: 0.0-4.0).

Regarding the ultrasound findings of the studied females at 6-8 weeks gestation, the mean diameter of gestational sac age was 2.047 (SD 0.57) cm, the mean yolk sac diameter was 4.47 (SD 0.84) cm, while the mean FHR was 140.19 (SD 13.48) bpm.

As regards pregnancy outcome distribution among the studied females, the current results found that normal pregnancy outcome was reported in 91.5% of the studied females, 4.3% of the studied cases had abortion, 1.1% had abruptio placenta, and 0.5% had preterm labor. In addition, IUGR and IUFD were reported in 1.1% and 1.6% of the studied females, respectively. Moreover, no congenital anomalies were reported in any of the studied cases.

In addition, a statistically significant correlation was found between the mean diameter of gestational sac and abnormal pregnancy outcome, while no statistically significant correlations were found between the mean values of neither yolk sac diameter nor fetal HR and abnormal pregnancy outcome of the studied cases.

Results of the current study are in accordance with the results of the study conducted by **Das and Roy** [13], in which 21% of cases (50/100) were aborted, however only 2% of those instances (4% of total cases)

had yolk sacs smaller than 2 mm, while in the current investigation, abortion was identified at greater yolk sac sizes.

Similarly, in consistence with the current results, in the study by **Das and Roy** [13], 3 pregnancies were identified with a big yolk sac (more than 6 mm), and two of those pregnancies ended in abortion. One had a normal, 7 mm morphology and was born at 10 weeks gestation, while the other had an abnormal, 8mm morphology and was born at 5 weeks. In contrast, another 7mm yolk sac with normal shape at 10 weeks gestation made it to term. As a result, a big yolk sac is a portent of a negative obstetric outcome.

Furthermore, the current results illustrated that only gestational sac diameter could significantly predict abnormal pregnancy outcome (p=0.001, AUC=745, with 81.2% sensitivity, 20.6% specificity, and 71.8% accuracy at a cut-off point 2.135), while each of yolk sac diameter and FHR could not.

The current work also could demonstrate that larger gestational sac was associated with abnormal pregnancy outcome, like abortion (2.25 ± 0.58 cm), preterm labor (2.33 ± 0.0 cm), IUFD (2.70 ± 0.28 cm), IUGR (2.93 ± 0.93 cm) and abruptio placenta (3.45 ± 2.19 cm). As well, larger yolk sac was also associated with abnormal pregnancy outcome, like preterm labor (5.0 ± 0.0 cm), IUGR (5.57 ± 1.07 cm), and IUFD (5.50 ± 0.71 cm). Moreover, higher FHR was associated with abnormal pregnancy outcome, like preterm labor (155.0 ± 0.0 bpm), IUFD (157.50 ± 3.53 bpm), and IUGR (171.0 ± 4.58 bpm).

The current prospective observational study highlights the importance of seeing the yolk sac and measuring its size and form as a predictor of abortion and other poor pregnancy outcomes.

Xie et al. [14] found that in 0.6% of ultrasonography examinations, the yolk sac was not seen. However, we were able to document yolk sac size and shape in every case here. In the studies done by **Jose et al.** [9], **Heller and Cameron** [15], **Moradan and Forouzeshfar et al.** [16], and **Shetty et al.** [17], researches indicated significantly greater rates of non-visualization of the yolk sac (11%, 4.54%, 20%, and 4.3%) than previous studies had reported.

Similar findings were reported by **Jose et al.** [9], **Heller and Cameron** [15], and **Moradan and Forouzeshfar et al.** [16]. Thus, these other studies provide significant support for the conclusion reached in this observational study, which is that a yolk sac is always present in normal pregnancies.

In contrast to the current investigation, **Kurtz et al.** [18] and **Shetty et al.** [17] showed that the lack of the yolk sac was not consistently predictive of a spontaneous abortion and that identification of the yolk sac was not an early predictor of pregnancy outcome. Only 75% of instances with a missing yolk sac resulted in spontaneous abortions in the study by **Shetty et al.** [17].

In the study by **Selvi** [19], Abnormalities in yolk sac size were observed in 72% of cases in the current investigation. **Adiga et al.** [20] and **Küçük et al.** [21] revealed that 10% and 11.2% of patients, respectively, had an aberrant size of the yolk sac. Similar results were seen in the study by **Jose et al.** [9], where an abnormally large yolk sac was present in 5.6% of cases.

About 96% of instances with aberrant yolk sac size resulted in abortion, as reported by **Selvi** [19], Abortions caused by an abnormally large yolk sac were shown to occur in 64.5% and 35.7% of pregnancies in studies by **Adiga et al.** [20] and **Küçük et al.** [21]. In contrast to the results of **Selvi's** study, the percentages reported in the previous paragraphs in other investigations were significantly lower [19]. The smaller sample size of the latter study may explain the discrepancies in percentages and results.

In addition, the current study demonstrated that gestational sac diameter (cm) at 6-8 weeks can be used as a predictor of abnormal pregnancy outcome among the studied females [p=0.001, OR: 4.47 (95% CI 1.86-10.78)], only with univariate analysis.

According to the current results, gestational sac was normal in size (16-24 mm) in most cases (66.5%), but larger in 18.1% of cases, and smaller in 15.4% of cases. As well, normal yolk sac size (4-6 mm) was reported in the majority of the studied cases (76.6%), while it was larger in 14.9% of cases, but smaller in 8.5% of cases. As regards fetal HR, it was normal (110-160 bpm) in the vast majority of cases (95.2%), while tachycardia was reported in 2.1% of cases, and bradycardia in 2.7% of cases.

Consistent with the current study, **Selvi** [19] found that 71.4% of abortions were caused by a yolk sac that was either swollen or larger than normal (by roughly 2 standard deviations above normal). Abortion occurred in 37.5% and 80% of cases, respectively, in which an expanded yolk sac was identified in investigations by **Adiga et al.** [20] and **Tan et al.** [22], compared to other research.

Additionally, roughly six cases with increased yolk sac diameter advanced past 20 weeks of gestation in the study of **Selvi** [19]. According to the results of this analysis, around 17% of cases may still develop. With this, there have been no occurrences of persistently inflated yolk sacs after 20 weeks.

From the findings of this work, it can be concluded that statistically highly significant correlations were found between both yolk sac size and fetal HR, and abnormal pregnancy outcome, while no statistically significant correlation was found between gestational sac size and abnormal pregnancy outcome.

As regards FHR, it was normal (110-160 bpm) in the vast majority of cases (95.2%), while tachycardia was reported in 2.1% of cases, and bradycardia in 2.7%

of cases. Moreover, fetal HR was associated with abnormal pregnancy outcome, e.g. preterm labor (155.0±0.0 bpm), IUFD (157.50 ± 3.53 bpm), and IUGR (171.0 ± 4.58 bpm).

FHR activity was analyzed for its potential to predict the outcome of the pregnancy. Studies can be roughly classified into two groups: those that look at fetal loss following proven fetal cardiac activity, and those that look at FHR in connection to outcome [23].

As early as weeks 5 and 6, doctors are able to see the embryonic heart beating, and they also know that the average heart rate rises steadily from that point until week 9, when it stabilizes at a lower rate than the rest of the pregnancy [20].

According to the study by **Abd Ellatif et al.** [2], six women with poor FHRs underwent genetic amniocentesis. Two of the fetuses tested positive for trisomy 21 via karyotype analysis, indicating a much higher incidence (33%) of aneuploidy.

The authors also showed a correlation between low FHRs and abortion rates; although they did not do any karyotype analysis or genetic amniocentesis. Having a healthy-looking fetus with a yolk sac of the appropriate size and an embryonic heart rate of above 100 beats per minute was linked to a high likelihood of a successful pregnancy outcome in the study's analysis of the first trimester [2].

Similarly, **Varelas et al.** [24] examined the significance of first trimester embryonic heart rate (EHR) and yolk sac diameter (YSD) as predictors of subsequent pregnancy outcomes. The 219 female participants in the prospective cohort study. They discovered that pregnancies that lasted longer than 12 weeks were substantially linked with the EHR and YSD. Furthermore, spontaneous abortion pregnancies showed statistically significant decreases in EHR, decreases in YSD, or the absence of a yolk sac.

In the study by **Abd Ellatif et al.** [2], The area under the ROC curve for combining GA and EHR was 0.971 (p <0.001), while the area under the ROC curve for combining GA and YSD was 0.858 (p <0.001). Both combinations were highly predictive of the outcome of the first trimester of pregnancy. During the first three months of a healthy pregnancy, both EHR and YSD rise steadily. Pregnancy outcomes can be predicted to be poor in the first 12 weeks of pregnancy if the embryo has a bradycardia, the yolk sac is absent, or the yolk sac diameter is significantly lower than expected for the gestational age.

In conclusion, pregnancy outcomes may be predicted with high accuracy using noninvasive first trimester ultrasound measurements of GS shape, YS diameter, and FHR. Normal Gestational sac, normal yolk sac and normal embryonic heart rate are both good predictors for successful pregnancy outcome. Amongst the two parameters EHR is more specific in predicting an adverse outcome of pregnancy. As our study was performed on a low risk population, identification of abnormal gestational sac shape, yolk sac diameter or EHR allows us to closely monitor the index pregnancy and predict occurrence of complications.

REFERENCES

1. **Sfakianaki A, Monteagudo A, Timor-Tritsch I (2018):** Pregnancy of Unknown Location, Early Pregnancy Loss, Ectopic Pregnancy, and Cesarean Scar Pregnancy}. Obstetric Imaging: Fetal Diagnosis and Care, 1:236-46.
2. **Kratochwil E, Eisenhut L (1967):** The earliest evidence of fatal heart action by ultrasound. Obstetrics Frauenheilkd, 27:176-80.
3. **Abd Ellatif E, Ahmad A, Halawa M (2018):** 3Yolk Sac Size and Shape, Gestational Sac Diameter and Embryonic Heart Rate as Prognostic Factors for First Trimesteric Outcome. The Egyptian Journal of Hospital Medicine, 73(9):7418-28.
4. **Srivastava G, Nagwani M, Pasricha N et al. (2016):** Size of yolk sac by ultrasonography and its correlation with pregnancy outcome. Int J Anat Res., 4(1):2052-7.
5. **Brezinka C (2019):** The yolk sac–an important marker in early pregnancy ultrasound. Journal for Gynecological Endocrinology/Austria, 29(1):28-32.
6. **Suguna B, Sukanya K (2019):** Yolk sac size \& shape as predictors of first trimester pregnancy outcome: A prospective observational study. Journal of Gynecology Obstetrics and Human Reproduction, 48(3):159-64.
7. **Wu W, Ji Q, Guo B et al. (2019):** Clinical value of serum homocysteine, folate, and ultrasonography detection of yolk sac in predicting the outcome of threatened abortion. Pteridines, 30(1):10-5.
8. **Bottomley C (2017):** Ultrasound to diagnose and predict early pregnancy outcome. Early Pregnancy, 17:196-207.
9. **Jose L, Abdul Latheef N (2015):** Sonographic evaluation of yolk sac. International Journal of Scientific & Engineering Research, 6(5):11-5.
10. **Hornberger L, Sahn J (2017):** Rhythm abnormalities of the fetus. Heart, 93:(10):1294-300.
11. **Quarello E, Lafouge A, Fries N et al. (2017):** Basic heart examination: feasibility study of first-trimester systematic simplified fetal echocardiography. Ultrasound in Obstetrics & Gynecology, 49 (2):224-30.
12. **Sukenik-Halevy R, Sukenik S, Koifman A et al. (2016):** Clinical aspects of prenatally detected congenital heart malformations and the yield of chromosomal microarray analysis. Prenatal Diagnosis, 36(13):1185-91.
13. **Das S, Roy P (2018):** Yolk sac and its effects on fetal prognosis. International Journal of Reproduction, Contraception, Obstetrics and Gynecology, 7(12):4895-900.
14. **Xie Y, Chen M, Chen S (2014):** Prediction of pregnancy outcomes with combined ultrasound scanning of yolk sacs

and serum CA125 determinations in early threatened abortion. Clin Exp Obstet Gynecol., 41(2):186-9.

15. **Heller R, Cameron S (2015):** Termination of pregnancy at very early gestation without visible yolk sac on ultrasound. J Fam Plann Reprod Health Care, 41(2):90-5.

16. **Moradan S, Forouzeshfar M (2012):** Are abnormal yolk sac characteristics important factors in abortionrates?. International Journal of Fertility and Sterility, 6(2):127-30.

17. **Shetty A, Hegde D, Shetty B *et al.* (2015):** Yolk Sac Abnormalities –Is it a Reliable Indicator of Abortions? – A Prospective Study in the Population Residing in Rural Setup of Mangaluru, Karnataka, India. J Pharm Biomed Sci., 05(05):380-4.

18. **Kurtz A, Needleman L, Pennell R *et al.* (1992):** Can detection of the yolk sac in the first trimester be used to predict the outcome of pregnancy? A prospective sonographic study. AJR Am J Roentgenol., 158: 843-7.

19. **Selvi R (2019):** Prospective study in Predicting Pregnancy Outcome using Yolk Sac Parameters in First Trimester. The Tamil Nadu Dr.M.G.R. Medical University. http://repository-tnmgrmu.ac.in/id/eprint/11312

20. **Adiga P, Selvi C, Rai L *et al.* (2015):** Evaluation of yolk sac diameter and embryonic heart rate as prognostic factors of gestational outcome in early singleton pregnancies. Scholars Journal of Applied Medical Sciences, 3(2):543-50.

21. **Küçük T, Duru N, Yenen M *et al.* (1999):** Yolk sac size and shape as predictors of poor pregnancy outcome. J Perinat Med., 27: 316-20.

22. **Tan S, Tangal N, Kanat-Pektas M *et al.* (2014):** Abnormal sonographic appearances of the yolk sac: which can be associated with adverse perinatal outcome? Med Ultrason, 16(1):15-20.

23. **Arleo E, Troiano R (2011):** Outcome of early first-trimester pregnancies (< 6.1 weeks) with slow embryonic heart rate. AJR Am J Roentgenol., 197(1):252-5.

24. **Varelas F, Prapas N, Liang R *et al.* (2008):** Yolk sac size and embryonic heart rate as prognostic factors of first trimester pregnancy outcome. EJOG., 138:10-3.