

The relation between abnormal yolk sac characteristics and miscarriage rate in first trimester of pregnancy

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Abstract

Background: The research included 200 pregnant women between the 7th and the 8th week of their pregnancy who were routinely seen at the hospital for prenatal follow-up visits. Participants were asked to recount their whole lives. Pregnant women were required to fill out a complete medical history form at their first visit at 5-7 weeks. There was a Case Recorded Form (CRF) for each participant, which was used to evaluate the YS features. First, individuals were asked whether they had had vaginal bleeding or other symptoms, and then YS features were checked again at 7 to 9 weeks (size, shape and echogenicity). This was the third and last appointment to the OB/GYN after 13 weeks of pregnancy. Pregnant women in their first trimester were the focus of this research, which assessed the accuracy of yolk sac features in predicting pregnancy outcomes. **Methods:** In March 2020, the research and ethical committee of the Faculty of Medicine approved the conduct of this prospective cohort study at Benha University Hospital. Between October 2020 and October 2021, the research team collected data on 200 pregnant women in their first trimester who went to the hospital for standard prenatal follow-up visits. Twenty women who refused to undergo transvaginal sonography testing were omitted from the study. Abortion rates increased significantly among women with abnormally big yolk sacs and abnormally tiny yolk sacs, but there was no statistically significant increase in abortion rates among women with abnormally small yolk sacs or abnormally shaped yolk sacs. YS diameter and echogenicity were found to be consistent with earlier investigations, although there was some disagreement about anomalous YS shape, which may be related to the small number of individuals with atypical yolk sac features. The present investigation found that instances with abnormally large yolk sacs and hyperechogenic centres had a statistically significant increase in the number of abortions. A substantial effect for the YS anomaly in the prediction of abortion was also shown in the current investigation. A big yolk and a hyperechogenic yolk sac are thus thought to be the most critical indicators for predicting early pregnancy loss among the yolk sac features. Additional research using a bigger sample size is required to assess the significance of the other criteria.

Key words: abnormal yolk sac, miscarriage, first trimester, pregnancy.

1. Introduction

Pregnancy loss before foetal viability (24 weeks gestation) is characterised as a miscarriage.. Expulsion of a foetus or embryo weighing 500 gms or less is what the WHO considers this to be [1].

There are several synonyms for abortion, such as miscarriage, early pregnancy failure, or early pregnancy loss, all of which describe the same thing [2].

When it comes to keeping track of an early pregnancy, finding the gestational sac via transvaginal ultrasound at 5 weeks is a key milestone [2].

When the gestational sac reaches 8 to 10 mm in diameter, the yolk sac should be seen as a spherical extra-amniotic structure. During the first trimester of pregnancy, the usual biometric value of the yolk sac diameter is an inner diameter of 3-6 mm [3].

For much of embryonic development, the yolk sac serves as a conduit between the mother and her foetus; it also serves as a source of nutrients, immunologic and endocrine activities, and hematolytic functions for the embryo [4].

The yolk-sac is located on the embryo's ventral side and is lined with endoderm, with a layer of mesoderm around it. It contains vitelline fluid, which the embryo may use for nutrition in the early stages of its development. [5].

With an anechoic centre and well-defined echogenic walls, the yolk sac is often an oval shape with an anechoic core [3].

The diameter of a yolk sac is said to expand consistently (0.1 mm) each day, according to research on the subject. As it turns out, the size of the yolk sac gradually rises from the fifth to the tenth gestational week. After then, the size of the yolk sac steadily decreases [6].

Pregnancies with a gestational age of 5 to 10 weeks are considered to have a normal yolk sac when the upper normal limit is 5-6 mm. A poor obstetric outcome, which often ends in embryonic mortality, has been linked to an excessively large yolk sac [7].

If the yolk sac is absent or its diameter is lower than the gestational age, the pregnancy may end in spontaneous abortion [8].

It is possible to see an echogenic ridge on sonograms of calcified yolk sacs only after the embryo is dead since the yolk sac would calcify within a few days of death [9].

Unrelated to a higher incidence of spontaneous abortion is an irregular yolk sac, which does not have a rounded or indented ridge [2].

However, another research found that the most relevant factor in early pregnancy loss was deformed shape [10].

Abnormalities in the yolk sac are linked to spontaneous abortions, according to this study. Finally, we consider the following abnormalities in the yolk sac to be aberrant enough to warrant a different classification: This research aims to evaluate the accuracy of yolk sac features in predicting pregnancy

outcome in pregnant women in the first trimester in women with a diameter less than 2 mm or more than 5 mm, as well as degenerative alterations and an echogenic yolk sac [10].

2. Patients and Methods

This prospective cohort study was conducted at Benha university hospital after obtaining approval from the research and ethics committee of the Faculty of Medicine in march 2020.

A total of 200 women in the first-trimester of pregnancy and who attended the hospital for routine antenatal follow-up visits between october 2020 and october 2021 were consecutively recruited for the study. Twenty women who refused to have examinations by transvaginal sonography were excluded.

2.1. Inclusion criteria

1. Pregnant women aged 18-45 year-old
2. Healthy pregnant women at 5-7 weeks (namely 5 weeks-6 days to 7 weeks-6 days) by last menstrual period.
3. Pregnant women who fulfilled the creteria of reliable dates of last menstrual period.

2.2. Exclusion criteria

1. Pregnant women who rejected examination by transvaginal sonography.
2. Pregnant women who did not have regular cycle before pregnancy.

2.3. The following procedures were completed for each participant

Participants signed informed permission forms after being fully briefed on the study's scope. Those taking part in the clinical trial were made aware of their rights and the nature of the study, as well as its aims, advantages, and dangers. The following conditions were imposed on all participants:

Participants were asked to recount their whole lives. Pregnant women were required to submit a thorough medical history on their first consultation. Patient number, age, medical, surgical, obstetric, and menstrual histories, including the last menstrual period (LMP), were all entered on a case recorded form (CRF) for each participant.

2.4. General examination

Weight, height, and BMI measurements; as well as vital statistics such as blood pressure, pulse rate, respiration rate, and temperature (BMI). Ultrasonographic scans of the chest, heart, and abdomen are included in this procedure.

Benha University Hospital's Department of Obstetrics and Gynecology employed a two-dimensional transvaginal ultrasound Voluson 730 PRO.,T.V prob:4-9 MHZ to measure the gestational sac's diameter and features. All of the aberrant yolk sac features were evaluated by the same sonographer in all of the images. In the first trimester, pregnant women had two-dimensional transvaginal ultrasonography for the following purposes:-

- Confirmation of the presence of intrauterine pregnancy.
- Assessment of the gestational sac criteria (size, shape & location).
- The yolk sac criteria (size, shape & echogenicity)

All visit were scheduled as the following:

- Over 200 people attended their first visit at 5-7 weeks. look at the following YS traits: (size, shape and echogenicity).
- There were 150 participants in the second visit, which took place from 7-9 p.m.
- After asking participants whether they had had vaginal bleeding or any other worrisome symptom, then assessing YS features, 38 cases were lost and 12 instances had an abortion (size, shape and echogenicity).
- So, among a total of 200 trial participants, 52 instances were lost in fellow up, and 148 women went on to complete the study to determine the foetal viability at the third visit at 13 weeks of gestation.

Techniques and Equipment

After excluding pregnant women who rejected to participate in the study, the remaining 200 women were assessed using Voluson 730 PRO.,T.V prob:4-9 MHZ transvaginal probe (figure 13). The urinary bladder was empty while the patients were evaluated sonographically.

During the sonographic examination, the size, shape and echogenicity of the yolk sacs were assessed carefully. Then embryonic cardiac activity was noted. Afterwards, the gestational age was specified by measurement of the crown- rump length. Alternatively, the measurement of the gestational sac diameter could be used if CRL still not detected.

The yolk sac diameter was determined by placing the calipers on the inner limits of the longer diameter. Any yolk sac with totally smooth and non-deformed margins was defined as having regular shape, and any yolk sac with mainly wrinkled margins, indented walls, or both was identified as having an irregular shape. The echogenicity of the yolk sac was detected by comparing it to fluid inside the sac (normal YS is hypochoic center with hyperechoic rim) ⁽²⁾.



Fig. (1) voluson 730 PRO.

This is a picture of voluson730 PRO sonographic equipment with a 4- to 9-MHz transvaginal probe.

Subject confidentiality

All evaluation forms reports and other records had not included personal data to maintain subject confidentiality

Sample Size:

The required sample size had been calculated using the program of STATA Data analysis and statistical software version 10.0.

The primary outcome measure is the spontaneous abortion rate.

According to a previous study, the prevalence of yolk sac anomalies was expected to be approximately 12%.

According to a previous studies, the spontaneous abortion rate associated with normal or anomalous yolk sacs were expected to be approximately 3.6% and 63.6%, respectively⁽¹⁰⁾.

Consequently it was estimated that a sample of **200 patients** would yield 24 (12%) patients with abnormal yolk sacs and 176 (88%) patients with normal yolk sacs.

The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following:

Probability (P-value)

- P-value <0.05 was considered significant.
- P-value <0.001 was considered as highly significant.
- P-value >0.05 was considered insignificant.

So in this study, the yolk sac characteristics of 200 consecutive pregnant women with normal body mass index was evaluated.

The abortion rate in was assumed to be identical and to equal 3.6% under the null hypothesis. Under the alternative hypothesis, the abortion rate was assumed to equal 3.6% or 63.6% in patients with normal or abnormal yolk sacs, respectively.

3. Results

Table (1) showing US of YS findings among the study participants in the 1st visit

		Study participants (n =200)
YS (mm)	Mean ± SD	3.37 ± 1.44
	Range	1 – 10
YS size	Absent	1 (0.5%)
	Small < 2 mm	2 (1%)
	Normal 2 – 5 mm	184 (92%)
	Large >5 mm	13 (6.5%)
Shape	Regular	191 (95.5%)
	Irregular	9 (4.5%)
Echogenicity	hyperechogenic	5 (2.5%)
	hypoechoogenic	195 (97.5%)

YS size in the study participants ranged from 1 to 10 mm with a mean value of 3.37 ± 1.44 mm.

YS size was small in 2 (1%) case, normal in 184 (92%) cases and large in 13 (6.5%) cases.

YS shape was regular in 191 (95.5%) cases and irregular in 9 (4.5%) cases.

YS echogenicity was hyperechogenic in 5 (2.5%) cases and hypoechoogenic in 195 (97.5%) cases.

Table (2) showing US of YS findings among the study participants in the 1st follow up visit.

		Study participants (n =150)
YS (mm)	Mean ± SD	4.2 ± 1.67
	Range	1 – 7
YS size	Small < 2 mm	1 (0.67%)
	Normal 2 – 5 mm	139 (92.67%)
	Large >5 mm	10 (6.67%)
Shape	Regular	143 (95.33%)
	Irregular	7 (4.67%)
Echogenicity	hyperechogenic	4 (2.67%)
	hypoechoic	146 (97.33%)

In the 1st follow up visit , YS size ranged from 1 to 7 mm with a mean value of 4.2 ± 1.67 mm.

YS size was small in 1 (0.67%) case, normal in 139 (92.67%) cases and large in 10 (6.67%) cases.

YS shape was regular in 143 (95.33%) cases and irregular in 7 (4.67%) cases.

YS echogenicity was hyperechogenic in 4 (2.67%) cases and hypoechoic in 146 (97.33%) cases.

Table (3) Comparison between cases with normal yolk sac and cases with abnormal yolk sac regards incidence of abortion.

Variable	Abnormal YS (n=21)		Normal YS (n=127)		P
	No	%	No	%	
Pregnancy fate at 12wks:					
<i>Viabile</i>			122	96.1	<0.001**
<i>Abortion</i>	6	28.6	5	3.9	<0.001**
	15	71.4			

Table 3 shows that there were statistical significance increase in frequency of abortion among cases who had abnormal yolk sac in comparison to normal cases.

Table (4) showing accuracy of size and echogenicity of YS in prediction of abortion.

	Sens.	Spec.	PPV	NPV	Acc.	P
Large YS size	33.33	99.17	90	86.96	66.25	<0.001
Hyperechogenic YS	14.81	100	100	84.8	57.4	0.033

Large YS size and hyperechogenic YS are good predictors for abortion with sensitivity of 33.33% and 14.81% and specificity of 99.17%, and 100% respectively (p <0.001 and =0.033 respectively).

Table (5) showing pregnancy outcome findings in the study participants at the end of first trimester.

		Viable (n =128)	Abortion (n =20)	P value
YS size	Absent	-	1 (5%)	-
	Small < 2 mm	1 (0.78%)	1 (5%)	0.249
	Normal 2 – 5 mm	126 (98.43%)	10 (50%)	<0.001*
	Large >5 mm	1 (0.78%)	8 (40%)	<0.001*
YS shape	Regular	125 (97.65%)	19 (95%)	0.439
	Irregular	3 (2.34%)	1 (5%)	
Echogenicity	hyperechogenic	1 (0.78%)	4 (20%)	0.001*
	hypoechoic	127 (99.2%)	16 (80%)	

Participants with normal YS size, and hypoechoic YS who had viable pregnancy were significantly higher than those who had abortion pregnancy (p <0.001).

Participants with large YS size, and hyperechogenic YS who had abortion pregnancy were significantly higher than those who had a viable pregnancy (p <0.001).

There was no significance difference in YS shape between cases who had viable pregnancy or abortion pregnancy.

4. Discussion

Hyperechogenic centres were linked to the detection of abortion rates in this study, but abnormal yolk sac shape was not linked to abnormal first-trimester pregnancy outcomes.

When it comes to the size of the yolk sac, larger yolk sacs (>5 mm) were linked to a higher rate of abortion, whereas smaller yolk sac diameters were not.

p value 0.001** was found to be associated with an abortion rate of 71.4 percent for abnormal yolk sac characteristics and a rate of 3.9 percent for normal yolk sac characteristics in the current study's findings table [4].

There is agreement with these findings with Ashoush et al. [11], Mordan et al [12]

According to Berdahl and Blame et al [8], Ashoush and Jaiswal J et al [11] and Jaiswal J et al [13], the current study found a significant increase in the abortion rate for large YS by sensitivity 33.3 percent and accuracy 66.2 percent [13].

When it comes to the first trimester, I disagree with Prashant Adiga et al [14] who found that the range of 2 to 5mm reasonably guarantees pregnancy viability. The fact that more than half of the cases were terminated isn't necessarily a sign of a bad outcome. Because of the larger sample size, this discrepancy may exist.

This study found no statistically significant increase in the abortion rate for YS (2mm) in agreement with Singh et al. [15] but disagreed with Ghali et al. [16], who found that a YS with a diameter less than 2 standard deviations below the mean could predict an abnormal outcome with a sensitivity and specificity of 15 percent and 95 percent, respectively, while Varelas et al.

In terms of YS shape, the current study found that irregular shapes were not statistically significant. In agreement with Tan and others [2] Though they disagreed with the findings of Mordan et al. [10] who found an association between abnormal yolk sac characteristics and spontaneous abortion, Srivastava et al. [17] found a highly significant correlation between yolk sac shape and spontaneous abortion, and Das et al. [18] found that abnormal yolk sac morphology had a significant impact on the foetal prognosis. In cases where the yolk sac was hyperechoic and irregular, there was a high rate of foetal death.

Having a large and distorted yolk sac are two of the most common causes of early pregnancy loss. On the level of a large YS, this study agrees with the current study, but it disagrees with the latter in regards to an irregular YS shape.

In accordance with Varelas et al., the present investigation found that the absence of a yolk sac in one instance was related with an increased abortion rate by 100%. [6].

Echogenicity was shown to be related with a 57.3 percent rise in the risk of abortion in the present research, which agrees with Mordan et al [10].

According to Ashoush et al. [11] anomalies of YS diameters were connected with abortion rates rather than

shape or echogenicity. However, the findings of this research differ. As AHMED et al. [19] observed, the patterns of YS anomalies are significantly related to early embryonic morphological abnormalities. about 40% of the time is there an abnormally echogenic yolk sac can be seen.

The use of high-quality ultrasound scanners is a clear strength of the present investigation. Because of this, it is quite probable that the scans used in this investigation were of high quality.

Yet another problem is that even though the sample size determined for this research was adequate, a low incidence of some yolk sac anomalies such YS uneven form and small size precluded the drawing of any clinically meaningful conclusions.

5. Conclusion

The present investigation found that instances with abnormally large yolk sacs and hyperechogenic centres had a statistically significant increase in the rate of abortion. A substantial effect for the YS anomaly in the prediction of abortion was also shown in the current investigation. A big yolk and a hyperechogenic yolk sac are thus thought to be the most critical indicators for predicting early pregnancy loss among the yolk sac features. Additional research using a bigger sample size is required to assess the significance of the other criteria.

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