

An ultrasonographic study to evaluate the correlation of calcified yolk sac with spontaneous abortion



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ABSTRACT

Background: The yolk sac is a small, membranous structure, which is situated outside the embryo and has a variety of functions during embryonic development. The yolk sac plays an important role in critical biological functions during early gestation, which includes primitive hematopoiesis as well as production of germ cells. It can be visualized between 6 and 12 weeks of pregnancy by ultrasonography as a regularly rounded extra-amniotic structure when the gestational sac reaches dimensions of 8–10 mm. On sonography, the yolk sac appears as a round structure which has an anechoic center bordered by a regular well-defined echogenic rim. Thus, a normal yolk sac is a yolk sac with echogenic rim and hypoechoic center, whereas yolk sac with hypoechoic rim or hyperechoic center is considered as calcified yolk sac. **Aim and Objectives:** To study the correlation of calcified yolk sac with spontaneous abortion in the first trimester of pregnancy. **Materials and Methods:** We studied 144 pregnant females who were in their first trimester of pregnancy, referred by the department of obstetrics and gynecology. The echotexture of yolk sac was observed by transvaginal sonography and its correlation with spontaneous abortion. **Results:** Yolk sac was present in 140 cases (97.22%), and in 4 cases (2.78%), it was absent. Out of 140 cases, it was calcified in two cases and normal in 138. All the cases in which there was absence of yolk sac or calcified yolk sac resulted into spontaneous abortion. **Conclusion:** Accurate recognition of the normal and abnormal sonographic findings related to yolk sac can be used to anticipate the course of pregnancy which may be used as good tool in clinical practice to predict whether a pregnancy is going to have a good or a poor outcome.

Key words: Calcified yolk sac; Pregnancy; Spontaneous abortion; Transvaginal sonography; Yolk sac

INTRODUCTION

Ultrasonography is an essential diagnostic imaging modality in the field of obstetrics and is being extensively used for the evaluation of pregnancy.¹ The first-trimester ultrasonography aims to visualize viability, establish pregnancy dating, and evaluate fetal gross anomaly.² The basic ultrasound markers for normal pregnancy are intrauterine gestational sac, morphologically

normal embryo, crown-rump length, cardiac activity, and yolk sac.³ About 30–40% of pregnancies fail after implantation, and only 10–15% manifest with clinical symptoms. The threatened and spontaneous abortions are the most common complications of early pregnancy.^{4,5}

The yolk sac is the first extra-embryonic structure that becomes sonographically visible within the gestational sac. It acts as the primary route of exchange between

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the human embryo and the mother before the placental circulation is established. The yolk sac is responsible for critical biologic functions during early gestation.⁶ The yolk sac provides nutrition and gas exchange between the mother and the developing embryo, before the placenta is formed. It is also the main organ of embryonic blood cell production through blood islands near the yolk sac.⁷ Other functions of the yolk sac include the production of stem cells and primitive macrophages, production of germ cells, metabolic regulation, and synthesis of proteins such as albumin, alpha-fetoprotein, and apolipoproteins.^{8,9} The yolk sac also contributes to the formation of the umbilical cord.¹⁰ Sonography shows the yolk sac as a round structure that is made up of an anechoic center bordered by a regular well-defined echogenic rim. Normal yolk sac shape has an echogenic rim and hypoechoic center, whereas yolk sac with hypoechoic rim or hyperechoic center is considered as calcified yolk sac.^{11,12}

Aims and objectives

This study aims to study the correlation of calcified yolk sac with spontaneous abortion in the first trimester of pregnancy.

MATERIALS AND METHODS

The present study was done in the Department of Anatomy, Department of Radiology, and Department of Obstetrics and Gynaecology at Era's Lucknow Medical College and Hospital, Lucknow, India, on 144 pregnant women in their first trimester of pregnancy of gestational age 6–12 weeks. The machine used was Logiq Pro 5 by GE Healthcare with a TVS probe of 7–12 MHz. All ultrasounds were performed by a single radiologist to avoid interobserver variation. All the patients who had structural anomalies, medical disorders, having molar pregnancy, or who refused for transvaginal sonography (TVS) or were unwilling for follow-up were excluded from the study.

The patients were asked to empty their urinary bladder. The endovaginal transducer was covered with a sterile condom lubricated with gel before use and the patient was placed in the lithotomy position. The yolk sac was identified and its echotexture was observed. If the internal structure of a yolk sac had echogenicity rather than being totally anechoic, it was described as a calcified yolk sac. The patients were followed till 20 weeks of gestation.

Statistical analysis

The study parameters include age, parity, weight, gestational age in weeks, and appearance of yolk sac on sonography. The collected data were analyzed by usual methods of statistical analysis using SPSS 20.0

(SPSS Inc., Chicago, IL) software package. Results were expressed as mean±standard deviation or percentage; where appropriate. Student's t-test was used in numerical value between two groups. Spearman correlation test, Chi-square test, and Fisher's exact test were utilized to detect the correlations between the variables, whereas the odds ratios and corresponding 95% confidence intervals were used to estimate miscarriage risks. Two-tailed P<0.05 was accepted to be statistically significant.

RESULTS

This is a prospective observational study carried out in the Department of Anatomy in collaboration with the Department of Radiology and Department of Obstetrics and Gynaecology at Era's Lucknow Medical College and Hospital, Lucknow. A total of 144 singleton pregnant female patients belonging to gestational age of 6–12 weeks coming to Obstetrics and Gynaecology O.P.D. were enrolled for this study.

Table 1 shows the mean, median, and range of demographic characteristics such as maternal age (in years), parity, weight (kg), and gestational age. The mean, median, and range for maternal age were 26.96±3.16, 27.0, and 20–35. Similar data for parity were 1.1±0.75, 1.00, and 0–3. For weight and gestational age, the mean was 55.46±9.89 and 7.76±1.39; median was 55.00 and 7.00; and range was 20–35, 0–3, 37–72, and 6–11, respectively.

In the present study, yolk sac was present in 140 cases (97.22%), and in 4 cases (2.78%), it was absent.

Out of 140 cases, it was calcified in two cases and normal in 138.

All the cases in which there was absent yolk sac or calcified yolk sac resulted into spontaneous abortion.

DISCUSSION

In a normal pregnancy, it is possible to observe the yolk sac between 6 and 12 weeks of pregnancy. The appearance of the yolk sac is of significant clinical use in the evaluation

Table 1: Demographic characteristics of the study population

Characteristics	Mean±Standard deviation	Median	Range
Maternal age (years)	26.96±3.16	27.0	20–35
Parity	1.1±0.75	1.00	0–3
Weight (kg)	55.46±9.89	55.00	37–72
Gestational age (GA) in weeks	7.76±1.39	7.00	6–11

of early pregnancy, and therefore, its presence would have to routinely precede visualization of the embryo.¹³

TVS is rapidly becoming the diagnostic procedure of choice when the patient has to be evaluated in very early pregnancy. The previous reports have shown that TVS can identify early pregnancy and can correlate certain growth parameters of the pregnancy with the menstrual history. The cases in which the yolk sac was not identified earlier than identification of the embryo or abnormal yolk sac appearance visualized at initial sonography were always associated with a poor pregnancy outcome.

Hence, the absence of a yolk sac and the presence of degenerative changes such as numerous calcifications that have decreased translucency of the yolk sac are indicative of pregnancies that may result in spontaneous abortion.¹⁴

Yolk sac prevalence and its correlation with pregnancy outcome

The present study demonstrates the fact that visualization of yolk sac is crucial for a normal pregnancy outcome. In the present study, the yolk sac was not visualized in 2.78% of the cases (Table 2, Figures 1 and 2). In studies carried by Xie et al.,¹⁵ non-visualization of yolk sac was reported in 0.67% of cases, which is much lower than what has been seen in the present study. While in the studies done by Heller and Cameron,¹⁶ Jose and Latheef,⁹ Moradan and Forouzeshfar,¹⁷ and Shetty et al.,¹⁸ different

percentages of non-visualization of the yolk sac were found as 11%, 20.3%, 4.54%, and 4.3%, respectively, which were much higher than the findings of the present study. In the present study, all cases showing absence of yolk sac resulted in abortion. Similar findings were reported by Heller and Cameron,¹⁶ Jose and Latheef,⁹ and Moradan and Forouzeshfar.¹⁷ Thus, these studies strongly support the findings of the present study that a yolk sac should always be present in normal pregnancies.

Contrary to the present study, Shetty et al.,¹⁸ depicted the fact that the detection of the yolk sac is not an early predictor of pregnancy outcome and they concluded that the absence of the yolk sac was not consistently predictive of a spontaneous abortion.

In the present study, all cases with absent yolk sac ended up in abortion, while in the study done by Shetty et al.,¹⁸ only 75% of the cases with absent yolk sac ended in spontaneous abortions.

Yolk sac appearance and its correlation with pregnancy outcome

In the present study, yolk sac was observed to be calcified in 1.4% of cases (Table 3, Figure 3, and Graph 1). In the study carried by Jose and Latheef,⁹ a higher percentage of yolk sac calcification was observed, that is, 2.8% of the cases. This may be due to lower sample size in the present study or may be due to ethnic variations.

In the present study, all the cases showing calcified yolk sac resulted into abortion (Table 4). Similar findings were observed by Jose and Latheef⁹ and Harris et al.,⁸ according to whom, all cases of the sonographic demonstration of yolk sac calcification were associated with the first-trimester intrauterine embryonic demise. Yolk sac calcification may reflect typical dystrophic changes or be

Table 2: Prevalence of yolk sac in the study population		
	Yolk Sac	
	(n)	%
Present	140	97.22
Absent	4	2.78
Total	144	100

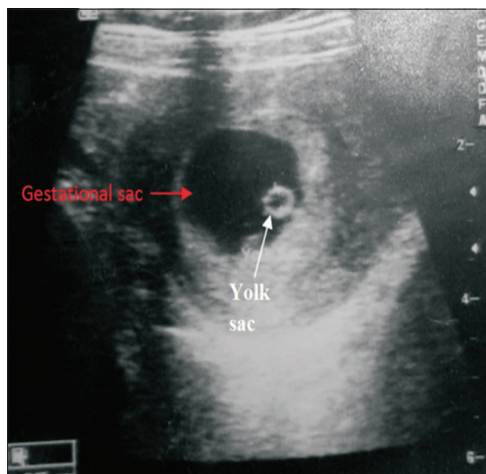


Figure 1: Gestational sac with yolk sac

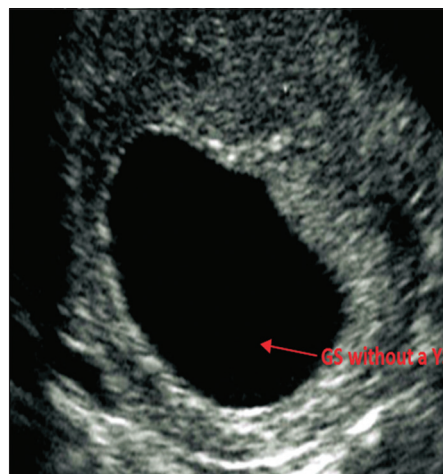


Figure 2: Gestational sac without yolk sac

Table 3: Frequency of different appearances of yolk sac

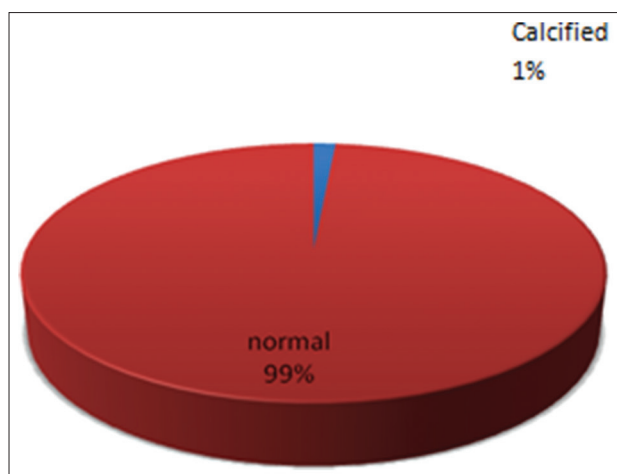
Appearance of yolk sac	Frequency (n)	Percent
Calcified	2	1.4
Normal	138	98.57
Total	140	100.0

Table 4: Frequency of various pregnancy outcomes

Yolk sac appearance	Outcome		Total	P value
	Abortion	Continued beyond 20 weeks		
Calcified	2	0	2	<0.001
Normal	0	138	138	
Total	2	138	140	



Figure 3: Calcified yolk sac (white arrow point calcified yolk sac)



Graph 1: Frequency of appearances of the yolk sac

more specifically related to a yolk sac calcium-binding protein. The calcification could be related to low oxygen perfusion. Since the yolk sac is irrigated by an end artery, this organ may be highly susceptible to ischemia, which may

be caused, either by the poorly developed villous vessels associated with embryonic maldevelopment or by maternal (environmental) factors.^{8,9,11}

Limitations of the study

One of the limitation of our study was a small sample size. We should have included minor congenital anomaly scan which is done at approximately 13 weeks. The cause of abortion might have been congenital anomaly too. So, further study is needed to sort out whether abnormal yolk sac was due to congenital anomaly or vice versa.

CONCLUSION

Yolk sac is a very important landmark which is usually neglected in ultrasounds for a normal pregnancy. Thus, assessment of the yolk sac should be part of a complete first-trimester sonographic examination. Its non-visualization is an important predictor of spontaneous abortion as well as if there is abnormality in the sonographic appearance, it predicts subsequent embryonic death. Therefore, accurate recognition of the normal and abnormal sonographic findings related to the yolk sac can be used to anticipate the course of pregnancy which may be used as good tool in clinical practice to predict whether a pregnancy is going to have a good or a poor outcome. More specifically, an abnormal yolk sac is identifiable on ultrasound at least 7 days before a spontaneous abortion, most of which occur during the first trimester. This finding is crucial in pursuing a more active line of management if required as well as helps in counseling of patients during a spontaneous abortion.

ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee.

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