

A Study to Evaluate the Yolk Size as Prognostic Factor of first Trimester Pregnancy Outcome: Prospective Observational Study

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Abstract

Aim: to evaluate the yolk size as prognostic factor of first trimester pregnancy outcome.

Materials and Method: This prospective observational study was performed in the department of Obstetrics and Gynecology, Lady Hardinge Medical College, New Delhi. This study was conducted in 230 pregnant women who had satisfied inclusion and exclusion criteria. Detailed history like chief complaints, past history, present history, and family history was taken. After that detailed examination- general physical examination, systemic examination, per speculum, and per vaginal examination was done. Gestational age was calculated by last menstrual period. Each participant was subjected to transvaginal ultrasonography. Philips HD 11xE model ultrasound machine was used which had transvaginal probe of frequency 6-9MHz. All scans were performed by a single sonographer. On sonography gestational sac diameter, mean yolk sac diameter, yolk sac size and shape, crown ramp length was measured.

Results: Total subjects participated in the study were 230, minimum and maximum ages were 19 years and 38 years respectively. Mean age was 27.68±4.38-year, maximum number of woman 128/230 (55.7%) were in the age group of 23-30 year. Out of 230 women small yolk sac (<3.5mm) was observed in 17(7.39%) women. Out of these 17 women with small yolk sac size, 13(76.47%) women had abortion and remaining 4 (23.52%) women had continued the pregnancy.

Conclusion: Suggested that pregnant women with large yolk sac had normal fetal outcome while patients with small yolk sac had more incidence of missed or spontaneous abortion. So, it showed that small and irregular shape yolk sac has poorer prognosis.

Keywords: yolk sac, outcome, sonography

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Introduction

An abnormality in the sonographic appearance of a yolk sac can predict subsequent embryonic death or abnormalities. The secondary yolk sac is the first extraembryonic structure that becomes sonographically visible within the gestational sac. During embryonic development, the yolk sac is the primary route of exchange between the embryo and the mother. The yolk sac also provides nutritional, immunologic, metabolic, endocrine, and hematopoietic functions until the placental circulation is established.[1] Therefore, the yolk sac is crucial in early embryonic life.

The yolk sac is the one of the most important conceptional structure evaluated sonographically in the first trimester. At present, the most important benefit of sonographic evaluation of the yolk sac is confirmation of an intrauterine pregnancy.[1,2] It has been hypothesized that sonographic features related to the shape, and size and internal structure of the yolk sac be associated with the gestational outcome.[1,3]

At the fourth week of embryologic development, the wall of the yolk sac consists of 3 thin cellular layers. The outermost layer is the ectoderm, which faces the exocoelomic cavity. The ectodermal layer is in fact a distinct layer of flattened cells. However, the innermost layer facing the yolk sac cavity is the endodermal epithelium, which is composed of a single layer of cuboidal epithelial cells. Located between two layers is the mesodermal layer, which is a very narrow tissue. This mesodermal layer consists of blood island formations in which hematopoietic layer, stem cells can be identified through tout a primitive capillary network. At this embryonic age, hematopoietic cells are also seen for the first time inside the embryonic body. Initially, the clusters of hematopoietic cells are located at the cephalic pole of the embryo, near the developing heart. By the

end of the fourth gestational week, primitive blood cells are widely scattered in embryonic blood vessels located in the primordium of the heart, mesonephros, and other embryonic organs.[4,5]

Yolk sac is the most important conceptional structure evaluated sonographically in first trimester. Yolk sac can be detected early by transvaginal sonography when the mean gestational sac diameter is 5-6mm. Normally the yolk sac appears as circular structure with anechoic center surrounded by a uniform well defined echogenic wall. Usually, inner diameter of yolk sac measures 3 mm to 5 mm. The yolk sac size progressively increases from beginning of fifth week of gestation to end of tenth week of gestation. Afterward the yolk sac size decreases gradually.[5,6]

The yolk sac is connected to the embryo by the vitelline duct. Actually, it is common to detect a dead embryo due to the absence of a yolk sac. In parallel, it is uncommon to observe a yolk sac and an empty amniotic sac without an embryo. The sequel of embryonic death is probably reabsorption of the very early embryo, the amnion and the yolk sac. The yolk sac performs important functions for embryonic development during organogenesis, On transvaginal sonography, absence of the yolk sac in the presence of an embryo is always abnormal and in general is associated with subsequent embryonic death[1,7].

Assessment of the yolk sac should be part of a complete first-trimester sonographic examination. An abnormality in the sonographic appearance of yolk sac may predict subsequent embryonic death or abnormalities. Therefore, accurate recognition of the normal and abnormal sonographic findings related to the yolk sac may be used to anticipate the course of pregnancy.

Materials and Methods

This prospective observational study was performed in the Department of Obstetrics and Gynecology, Lady Harding Medical College and Hospital, New Delhi, India

. This study was conducted in 230 pregnant women who had satisfied inclusion and exclusion criteria.

Sample size estimation

(Researchers have reported the abortion figures in Indian population to lie between 9.8% (Sebastian et al., 2014)⁸ to 20% (Abortion: Facts and Figures, 2011)⁹. Therefore, assuming 15% as the incidence of abortion and 5% margin of error, the minimum required sample size at 5% level of significance was 196 patients).

Inclusion Criteria:

- Singleton pregnancy.
- With period Gestation ≤ 10 week on ultrasonography.
- Embryo with positive cardiac activity on ultrasonography.

Exclusion Criteria

- Women having bleeding per vagina with pregnancy of ≤ 10 week were excluded from study.

Methodology

This prospective observational study was conducted in the department of Obstetrics and Gynecology, Lady Hardinge Medical College, New Delhi, Cases were selected out of a cohort of women attending the Gynae OPD who had early pregnancy. 230

women with pregnancy ≤ 10 week were included in the study. Detailed history like chief complaints, past history, present history, and family history was taken. After that detailed examination- general physical examination, systemic examination, per speculum, and per vaginal examination was done. Gestational age was calculated by last menstrual period. Each participant was subjected to transvaginal ultrasonography. Philips HD 11xE model ultrasound machine was used which had transvaginal probe of frequency 6-9MHz. All scans were performed by a single sonographer. On sonography gestational sac diameter, mean yolk sac diameter, yolk sac size and shape, crown ramp length was measured.

Yolk sac diameter was measured in three dimension. Yolk sac diameter- yolk sac diameter < 3.5 mm considered as cut-off value. Women were followed till the end of 14 week of pregnancy. Result of ultrasonography was correlated with pregnancy outcome in first trimester of pregnancy.

Statistical methods:

The quantitative variables were evaluated using unpaired t-test. The qualitative variables were compared using Chi-square test. ROC curves were made to find the critical values of quantitative variables to predict abortion. Sensitivity, specificity, PPV, NPV was calculated for the critical values. A p-value < 0.05 was assumed statistically significant. Statistical Package for Social Sciences (SPSS) version 15.0 was used for analysis.

Results

Table 1: Age distribution

Age group	Number of subjects	Percentage
< 20 YEARS	4	1.7
20-30 YEARS	128	55.7
>30 YEARS	98	42.6
Total	230	100.0

Total subjects participated in the study were 230, minimum and maximum age were 19 years and 38 years respectively. Mean age was 27.68 ± 4.38 years, maximum number of woman 128/230 (55.7%) were in the age group of 23-30 year.

Table 2: Distribution based on fetal indices

Indices	N	Minimum	Maximum	Mean	Std. Deviation
POG (weeks)	230	6	10	7.98	1.019
CRL(cm)	230	0.40	4.80	2.3197	.92318
FHR(b/m)	230	78	176	152.70	25.735
Yolk sac(mm)	230	2.07	8.2	5.1132	.91213

Period of gestation varied from 6 week to 10 week with mean of 7.8 ± 1.02 week. Yolk sac size 5.1132 ± 0.91213

Table 3: Area under ROC curve

Area under the curve (AUC)	Standard error	Asymptotic 95% Confidence Interval		P value
		Lower Bound	Upper Bound	
0.868	0.046	0.777	0.959	<0.001

Based on ROC analysis cut off value of yolk sac size that predict the abortion was <3.548 mm

Table 4: Validity of yolk sac size in predicting abortion

Validity	Values
Sensitivity (%)	76.47 (69.28 – 96.24)
Specificity (%)	93.89 (78.73 – 89.22)
PPV (%)	50.0 (37.08 – 54.41)
NPV (%)	98.03 (94.42 – 99.06)
Accuracy (%)	92.60 (79.48 – 94.17)

Sensitivity in prediction was 76.47%, specificity 93.89%, positive predictive value 50.0%, negative predictive value 98.03% and accuracy was 92.60%.

Table 5: Total adverse outcome as per the yolk sac size

YOLK SAC	CONTINUING		TOTAL	P VALUE
	YES	NO		
< 3.5 MM	4	13	17	<0.001
	23.5%	76.5%	100.0%	
≥ 3.5 MM	200	13	213	
	93.9%	6.1%	100.0%	
TOTAL	204	26	230	
	88.7%	11.3%	100.0%	

Out of these 17 women with small yolk sac size, 13(76.5%) women had abortion and remaining 4 (23.5%) women had continued the pregnancy.

Discussion

An abnormality in the sonographic appearance of a yolk sac can predict

subsequent embryonic death or abnormalities. The secondary yolk sac is the first extraembryonic structure that becomes sonographically visible within the gestational sac. During embryonic development, the yolk sac is the primary route of exchange between the embryo and the mother. The yolk sac is the one of the

most important conceptional structure evaluated sonographically in the first trimester. At present, the most important benefit of sonographic evaluation of the yolk sac is confirmation of an intrauterine pregnancy.[1,2] It has been hypothesized that sonographic features related to the shape, and size and internal structure of the yolk sac is associated with the gestational outcome.[1,3]

In present study out of 230 women, small yolk sac ($<3.5\text{mm}$) was observed in 17(7.39%) women. Out of these 17 women with small yolk sac size, 13(76.47%) women had abortion and remaining 4(23.52%) women had continued the pregnancy. Out of 230 subjects, irregular shape of yolk sac was observed in 2(0.86%) women and both these women had abortion. Mean value of yolk sac size in women who had abortion was $3.5487\pm 1.27\text{mm}$ as compared to $5.3126\pm 0.619\text{mm}$ in women who had continued pregnancies. The difference between two groups was statistically significant ($p<0.001$), with a sensitivity of 76.47%, a specificity of 93.89%, a positive predictive value of 50% and a negative predictive value of 98.03% suggesting that pregnant women with large yolk sac had normal fetal outcome while patients with small yolk sac had more incidence of missed or spontaneous abortion. So, it showed that small and irregular shape yolk sac has poorer prognosis. These results were consisted with the study done by VarelasFK1, et al. In their study they observed that the EHR and YSD were significantly correlated to advancing gestational age ($p<0.001$) in pregnancies continuing beyond 12 weeks. Pregnancies that resulted in spontaneous abortion exhibited a statistically significant lower EHR ($p<0.001$), smaller YSD ($p=0.001$).[1] Lynos et al in a study observed that a yolk sac diameter more than two standard deviations (SDs) above the mean when compared with the mean gestational sac diameter allowed prediction of an abnormal pregnancy outcome with a sensitivity of 15.6%, a specificity of 97.4%,

and a positive predictive value of 60.0%. A yolk sac diameter more than two SDs below the mean allowed prediction of an abnormal outcome with a sensitivity of 15.6%, a specificity of 95.3%, and a positive predictive value of 44.4%. No pregnancy with a normal outcome had a YS diameter of greater than 5.6 mm at less than 10 weeks menstrual age. In six patients, the YS diameter was greater than 5.6 mm. All six had an abnormal outcome[6]. Of seven patients with abnormal YS shape at initial sonography, three had abnormal YS shape at follow-up examinations. All three had an abnormal outcome.[6] In a study by Stampone et al reported that a yolk sac of abnormal size was statistically significant ($p < 0.001$) in spontaneous abortion (SA) versus normal pregnancy outcome, with a sensitivity of 68.7%, a specificity of 99%, a positive predictive value of 91.6% and a negative predictive value of 95.2%. Results of their study were more or less comparable to present study.[10]

Conclusion

Mean value of yolk sac size in women who had abortion was $3.5487\pm 1.27\text{mm}$ as compared to $5.313\pm 0.6196\text{mm}$ in women who had continued pregnancies, with a sensitivity of 76.47%, a specificity of 93.89%, a positive predictive value of 50% and a negative predictive value of 98.03% suggesting that pregnant women with large yolk sac had normal fetal outcome while patients with small yolk sac had more incidence of missed or spontaneous abortion. So, it showed that small and irregular shape yolk sac has poorer prognosis.

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