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Original Research Article

Yolk Sac Diameter as a Prognostic Marker for First Trimester Pregnancy Outcome: A Prospective Observational Study

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Abstract:

Background: Early pregnancy loss is a common obstetric complication, with the majority of miscarriages occurring during the first trimester. Transvaginal ultrasonography plays a vital role in early pregnancy assessment, and yolk sac diameter (YSD) is one of the earliest measurable sonographic parameters. Abnormalities in yolk sac size may reflect early embryonic compromise and predict adverse pregnancy outcomes.

Objectives: To evaluate yolk sac diameter as a prognostic factor for first-trimester pregnancy outcome and to determine its predictive accuracy for adverse outcomes.

Methods: This prospective observational study included 105 pregnant women with confirmed intrauterine singleton pregnancies between 5 and 10 weeks of gestation. Transvaginal ultrasonography was performed to measure yolk sac diameter, along with assessment of gestational sac, crown–rump length, and embryonic cardiac activity. Yolk sac diameter was categorized as normal (3–6 mm) or abnormal (<3 mm or >6 mm). Participants were followed until completion of 12 weeks of gestation, and pregnancy outcomes were classified as viable or non-viable. Statistical analysis was performed to assess the association between YSD and pregnancy outcome and to calculate diagnostic performance indices.

Results: Out of 105 pregnancies, 90 (85.7%) resulted in viable outcomes, while 15 (14.3%) ended in first-trimester pregnancy loss. Abnormal yolk sac diameter was significantly associated with adverse pregnancy outcome ($p < 0.001$). The sensitivity, specificity, positive predictive value, and negative predictive value of abnormal YSD for predicting non-viable pregnancy were 73.3%, 86.7%, 47.8%, and 95.1%, respectively. A significant positive correlation was observed between yolk sac diameter and gestational age, crown–rump length, and gestational sac diameter.

Conclusion: Yolk sac diameter is a simple, non-invasive, and reliable ultrasonographic parameter for predicting first-trimester pregnancy outcome. Normal YSD is strongly associated with pregnancy viability, while abnormal values indicate increased risk of early pregnancy loss.

Keywords: Yolk Sac Diameter, First-Trimester Pregnancy, Transvaginal Ultrasonography.

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Introduction

Early pregnancy loss is one of the most common complications of pregnancy and the majority of miscarriages occur in the first trimester of pregnancy. Timely identification of risk pregnancies is important for appropriate counselling and follow-up and clinical decision making. Transvaginal ultrasonography has been established as a cornerstone in the evaluation of early pregnancy and is useful for visualization of the gestational sac, yolk sac, embryo, and cardiac activity of the embryo as early as five weeks of gestation. Among these parameters, the yolk sac is the first extra-embryonic structure to be visualised and plays an important role in embryonic nutrition, haematopoiesis and metabolic exchange during early development [1].

Under normal circumstances, the yolk sac is seen as a round echogenic ring with an anechoic center and shows a predictable growth in size with advancing gestation. Deviations from normal yolk sac diameter of abnormally reduced or enlarged size as well as morphological abnormalities have been increasingly associated with adverse pregnancy outcomes [2,3]. Several observational and prospective investigations

have found an increase in yolk sac diameter beyond accepted gestational norms to be linked with a significantly increased risk of first trimester pregnancy loss 4-6. Similarly, small or irregular yolk sac has also been demonstrated to be correlated with poor embryonic development and early pregnancy failure [7,8].

The prognostic significance of yolk sac diameter when measured with other early ultrasound parameters like embryonic heart rate and crown--rump length has been highlighted recently [9-11]. Abnormal yolk sac measurements have been found to precede abnormal embryonic cardiac activity or growth parameters, and therefore yolk sac abnormalities could represent an early indicator of embryonic compromise [12,13]. Multiple studies performed from 2023 to 2025 have provided more convincing clinical relevance of yolk sac diameter as an independent predictor of pregnancy outcome with significant statistical association of abnormal yolk sac size with miscarriage rates [14-16].

Despite the increasing evidence, there is still variability in the suggested cut-off values for the abnormal yolk sac diameter and a variation in study design, population characteristics, and definitions of outcome. This variability emphasises the importance of further evaluation and standardisation of yolk sac measurements in early pregnancy evaluation.[17,18] Knowledge of the prognostic importance of yolk sac diameter could help clinicians to early risk-stratify, which may help to optimise follow-up strategy and deliver accurate prognostic information to expectant mothers.

The present study aims to evaluate yolk sac diameter as a prognostic factor for the first trimester pregnancy outcome in an attempt to add to the existing body of evidence and help optimize the role of early ultrasonographic markers in the prediction of pregnancy viability.

Materials and Method

The research is a prospective observational study carried out in the Department of Obstetrics and Gynecology of one of the tertiary care teaching hospitals in a 18 month's time. One hundred five pregnant women reporting during the first trimester were recruited sequentially with an informed written consent. Ethical approval of the study by the Institutional Ethics Committee was obtained before start of the study.

The study included pregnant women whose intrauterine singleton pregnancy between 5 and 10 weeks of gestation was confirmed through the last menstrual period and supported by ultrasonographic results. Exclusion of women with multiple pregnancies, ectopic pregnancies, known uterine abnormalities, assisted reproductive pregnancies and women with chronic medical conditions, such as diabetes mellitus, hypertension, thyroid conditions or autoimmune diseases, were done to prevent any confounding factors that might affect pregnancy outcome.

Methodology

The participants were all clinically assessed in detail, and the following data were obtained: demographic data, obstetric history, and presenting symptoms. An experienced radiologist used a high-frequency probe under standard conditions to perform a transvaginal ultrasonography in order to reduce inter-observer variability. In each case, the gestational sac, yolk sac, embryo, crown-rump length and embryonic cardiac activity were measured. The yolk sac diameter was determined by measuring the inner diameter to the inner diameter of the yolk sac in the plane where it seemed largest and the average of the two measurements was taken to enhance accuracy. Normal and abnormal classification of the yolk sac was done using the predetermined gestational age-specific reference ranges. A yolk sac diameter of less than 3 mm or more than 6 mm was taken to be abnormal. Morphologic characteristics like shape and echogenicity were also recorded.

The subjects were tracked on a prospective trimester basis. Outcome of pregnancy was classified as viable and non-viability. A viable pregnancy continued after 12 weeks and few non viable outcomes including spontaneous abortion or missed abortion. Regular follow-up ultrasonography was done or sooner in case it was clinically indicated. To record the ultimate outcome, clinical records were reviewed.

Statistical Analysis: The information was entered into a structured proforma and analyzed with the help of Statistical Package for the Social Sciences software (SPSS version 25). Continuous variables were contained in terms of mean and standard deviation, whereas the categorical variables were contained in terms of frequencies and percentages. The relationship between the yolk sac diameter and the pregnancy outcome was evaluated with the help of the chi-square test or Fisher's exact test depending on the suitability. The p value of 0.05 was taken to be statistically significant. The predictability of abnormal yolk sac diameter in relation to adverse pregnancy outcome was assessed in regards to sensitivity, specificity, positive predictive value and negative predictive value.

Observation and Results

The study involved a total of 105 pregnant women whose intrauterine singleton pregnancies were confirmed to be between 5-10 weeks of gestation and were followed-up prospectively until the first trimester was completed. Baseline transvaginal ultrasonography was performed on all participants

and the yolk sac diameter (YSD) was effectively measured at the baseline at the time of enrolment. All pregnancies reported embryonic cardiac activity in the course of initial examination. The first-trimester scans did not show any gross fetal structural abnormalities.

Table 1: Baseline Demographic and Obstetric Characteristics of the Study Population

Variable	Number of Patients	Percentage (%)
Age (years)		
≤ 20 Years	12	11.4
21–30 Years	66	62.9
31–40 Years	27	25.7
Gravidity		
Primigravida	49	46.7
Multigravida	56	53.3
History of previous abortion		
Present	18	17.1
Absent	87	82.9
Associated medical conditions		
Anemia	10	9.5
Hypothyroidism	7	6.7
None	88	83.8

The average age of the population under study was 25.6, SD=4.8 (18-37). The majority of the participants (62.9) were aged between 21 and 30 years. Primigravida was 46.7 percent and multigravida was 53.3 percent. There were 18 patients with a history of prior pregnancy loss (17.1%). Less serious medical conditions like anemia (9.5%) and hypothyroidism (6.7) were observed but were equally divided between the groups of outcomes and were not statistically significant in their ability to relate with pregnancy outcome.

Table 2: Distribution of Yolk Sac Diameter in Relation to First Trimester Pregnancy Outcome (n = 105)

Yolk Sac Diameter	Viable Outcome (n = 90)	Non-viable Outcome (n = 15)	Total	p value
Normal (3–6 mm)	78 (86.7%)	4 (26.7%)	82	<0.001
Abnormal (<3 mm or >6 mm)	12 (13.3%)	11 (73.3%)	23	
Total	**90 (100%)**	**15 (100%)**	**105**	

Chi-square test was applied and observed statistically significant

Among the 105 pregnancies, 90 (85.7%) had viable outcomes where they were continued after 12 weeks of gestation, and 15 pregnancies (14.3) had non-viable outcomes, including the following: missed abortion (9 cases) and spontaneous abortion (6 cases). The percentage of abnormal results was seen to be greater in women who had abnormal yolk sac diameter than in women with normal YSD.

The yolk sac diameter showed progressive and significant increase with the increasing gestational age in normal pregnancies. The viable pregnancy group had a mean YSD of 5.21 0.47mm with a range of values 3.9mm to 6.1mm. However, the mean YSD in the pregnancies that had abnormal outcomes was also significantly higher with 5.96 (0.58 mm) mean (range: 4.2 mm-6.8 mm) and this difference was statistically significant ($p < 0.001$). Abnormal values of YSD were strongly linked to the poor outcomes of pregnancy when examined regardless of gestational age.

Using preset criteria, yolk sac diameter was classified as normal (3 -6 mm) and abnormal (less than 3 mm or more than 6 mm). Out of 90 viable pregnancy, 78 (86.7%) were found to be normal and 12 (13.3) were found to be abnormal. On the contrary, the 15 non-viable pregnancies all (11 of the 15) contained abnormal YSD with only 4 of the 15 having normal YSD. The statistical significance of the relationship between abnormal YSD and pregnancy loss was significant ($p < 0.001$).

Table 3: Diagnostic Performance of Abnormal Yolk Sac Diameter in Predicting Adverse Pregnancy Outcome

Parameter	Value (%)
Sensitivity	73.3
Specificity	86.7
Positive Predictive Value (PPV)	47.8
Negative Predictive Value (NPV)	95.1
Diagnostic Accuracy	84.8

The predictive diagnostic score of abnormal yolk sac diameter in the poor first-trimester pregnancy outcome was tested. Abnormal YSD had a sensitivity of 73.3, specificity of 86.7, positive predictive value of 47.8 and negative predictive value of 95.1. These results show that a normal yolk sac size is a strong predictor of pregnancy survival, although abnormal YSD is a significant risk factor of first-trimester loss.

Analysis of correlation showed that there was a significant positive correlation between yolk As diameter and gestational age ($r = 0.34$, $p < 0.01$), crown -rump length ($r = 0.41$, $p < 0.01$) and gestational sac diameter ($r = 0.29$, $p < 0.05$). The same correlations were in agreement with the physiological pattern of growth of the yolk sac during early pregnancy. Nevertheless, it was observed that pregnancies with negative outcomes had unequal expansion of YSD as compared to gestational age and embryonic growth parameters.

Discussion

Prevention of pregnancy outcome at the first trimester is one of the critical goals in obstetric practice because a large percentage of pregnancy losses are done at this stage. The earliest extra-embryonic organ that is visualized on ultrasonography is the yolk sac, which is essential in the nutrition of the embryo, in hematopoiesis and metabolic exchange until the embryo has a placental circulation. This may be a compromise of the embryo at the onset of its form or size. The current research examined the yolk sac diameter (YSD) as a predictive variable of first-trimester pregnancy outcome and proved that abnormal YSD is strongly correlated with poor pregnancy outcomes.

In the present study, it was found that abnormal pregnancy outcome occurred in 14.3 percent of cases which is comparable to the ones mentioned in earlier studies with the range of 8-20 percent in cohort pregnancy cases [9, 14, 18]. The average yolk sac diameter of living pregnancies was steadily growing with gestation age, and it is indicative of normal embryological growth. This result is in line with previous accounts that explain a linear and predictable rise in YSD throughout the course of 6-10 gestation weeks [9,12,17]. On the contrary, adverse pregnancy outcomes showed disproportionately high or abnormal YSD values which corroborate the hypothesis that abnormalities of the yolk sac are precursors of embryonic death.

It was shown that the current study has statistically significant results concerning abnormal YSD and first-trimester pregnancy loss ($p < 0.001$). In line with these, Abdelrahman et al and El-Kady et al also reported that enlarged yolk sac diameters that were greater than gestational age-specific reference ranges were strongly related with miscarriage [1,7]. The Sharma et al. as well as Patel et al. also indicated that abnormal YSD especially in association with other ultrasound indicators, like a heartbeat of the embryo, were strong predictors of non-viable outcomes [2,3]. All these findings support the role of YSD as a prognostic variable of early pregnancy.

The sensitivity and specificity of abnormal YSD in this investigation were 73.3 and 86.7 respectively and the negative predictive value was very high (95.1). The large NPV is very encouraging that a standard yolk sac diameter is a good indicator of pregnancy survivability. Similar diagnostic sensitivity has been found in a number of previous studies. Chama et al. found sensitivity and specificity of 91.4% and 66, respectively, to predict abnormal outcomes with the use of YSD (12). Similar claims were made by Stampone et al and Kucuk et al with high specificity and negative predictive value and the authors highlight that YSD is useful in eliminating poor outcome where measurements fall within normal limits [13,14].

Even though the sensitivity in the current research is a bit less, compared to some previous reports, this disparity could be caused by the differences in sample size, gestational age at the time of assessment, and cutoff values that are used in definition of abnormal YSD.

The present research indicated that the correlation analysis of YSD and gestational age, the length of the crown–rump, and the diameter of the gestational sac exhibited significant positive correlation. This has been consistent with other past reports which had shown that physiological correlation existed between yolk sac development and embryonic development [9,16]. Papaioannou et al. developed normative reference ranges of YSD and validated it to be linearly related to gestational age during normal pregnancies [9]. Nonetheless, the pregnancies which later ended up with miscarriage would have values of YSD that were above these

normative ranges, indicating an indicator of abnormal yolk sac enlargement that portrays distress in the embryo.

Disagreement on definition of abnormal YSD is an issue in studies. Although some authors have employed gestational age specific mean +2 standard deviations to establish abnormality [4,12,14], others have suggested fixed cutoff levels of 5 mm- 6.6 mm to make it easy to apply clinically [10,15]. A pragmatic limit of less than 3 mm or more than 6 mm was applied in the current study, which was in line with the commonly mentioned thresholds in recent literature [2,8,15]. Nevertheless, the consistentity in the relation of abnormal YSD and negative outcome between studies indicates that the relative deviation compared to the expected growth, and not absolute value, may be of greater clinical significance.

The data of the current research confirm the previous findings that the anomalies of yolk sac can be preceding problems with embryonic heart rate or crown-rump length, and YSD can be an early and sensitive sign of pregnancy viability [11,17]. It has significant clinical consequences because with the early detection of high-risk pregnancies, it is possible to monitor them more closely, provide timely follow-up ultrasound and properly advise pregnant women. The non-invasiveness, simplicity, and reproducibility of the yolk sac diameter measurement are also an added advantage to its applicability in the first-trimester routine ultrasound assessment.

The paper has some weaknesses. The sample used was quite small and based on one tertiary care facility and its findings are not likely to be generalized. The inter-observer variability in the measurement of yolk sac though reduced, cannot be completely neglected. The morphology of the yolk sac including the shape and echogenicity was not determined in a detailed manner. Also, the first trimester was the only period of follow-up and there were no measurements of long-term pregnancy consequences. To further prove the prognostic role of yolk sac diameter, larger multicentric studies with standard cutoff values and more follow-up are suggested.

Conclusion

Yolk sac diameter is a non-invasive, simple and reliable ultrasonographic parameter which is a prognostic outcome of first-trimester pregnancy. The current research shows that there is a strong relationship between an abnormal yolk sac diameter and poor pregnancy outcomes where normal yolk sac diameter has got a high negative predictive value of pregnancy survival. An early method to measure the yolk sac diameter during pregnancy would help in early stratification of risks, follow-up strategies, and proper counselling of people who are pregnant. Attempts to incorporate yolk sac diameter measurement in regular first-trimester ultrasound examination could help to improve earlier identification of at-risk pregnancy.

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