

CORRELATION OF ABNORMAL YOLK SAC PARAMETERS IN PREDICTING MISCARRIAGE

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Abstract

Background: Early pregnancy loss affects 10–20% of clinically recognized pregnancies. Ultrasonographic assessment of yolk sac (YS) parameters may predict miscarriage risk.

Objective: To evaluate the association between abnormal yolk sac diameter (YSD) and pregnancy outcomes.

Methods: A prospective observational study of 202 pregnant women (5–10 weeks gestation) was conducted. Transvaginal ultrasound measured YSD and mean sac diameter (MSD). Pregnancy outcomes were categorized as continued beyond 20 weeks or miscarriage. Statistical analysis included sensitivity, specificity, and predictive values.

Results: Of 202 participants, 32 (15.84%) had miscarriages. Abnormal YSD (>6.4 mm or <2.5 mm) had 82.12% sensitivity and 99% specificity for predicting miscarriage. The highest predictive accuracy occurred at 8–10 weeks gestation. MSD showed lower predictive value (sensitivity: 77.56%).

Conclusion: YSD is a reliable early predictor of miscarriage, particularly between 8–10 weeks gestation.

Keywords: Yolk sac diameter, miscarriage, first-trimester ultrasound, pregnancy outcome.

INTRODUCTION

Early pregnancy loss is a significant concern in obstetric practice, defined by the World Health Organization as the spontaneous termination of pregnancy before 20 weeks of gestation or with the expulsion of a fetus weighing less than 500 grams. Clinically recognized early pregnancy loss occurs in about 10% of pregnancies, with approximately 80% of these losses taking place during the first trimester. Age plays a critical role, with miscarriage rates rising from 9–17% in women aged 20–30 years to over 80% in those aged 45 years [1].

Transvaginal ultrasound (TVS) is a vital diagnostic tool in early pregnancy, offering high-resolution visualization of intrauterine structures even in the earliest stages. The yolk sac, the first extraembryonic structure detectable within the gestational sac, plays an essential role in early embryonic development. It functions as a critical conduit for nutrition, hematopoiesis, and metabolic exchange before the establishment of placental circulation [2,3]. Normal yolk sacs typically appear as round, echogenic-ringed structures with an anechoic center and a diameter ranging from 2 to 5 mm, visible by transvaginal sonography around the 5th week of gestation [4].

Abnormalities in yolk sac morphology, such as increased diameter, irregular shape, thickened walls, or calcifications, have been suggested as markers of poor pregnancy prognosis. These changes are hypothesized to reflect underlying embryonic compromise or developmental failure [5]. Prior research has linked yolk sac abnormalities to increased miscarriage risk, yet there remains insufficient consensus to include yolk sac evaluation as a standard predictive parameter in routine obstetric ultrasounds [6,7].

Diagnostic criteria for early pregnancy failure, such as a crown-rump length (CRL) ≥ 7 mm without cardiac activity or a mean sac diameter (MSD) ≥ 25 mm without an embryo, are well-established [8]. However, the utility of yolk sac measurements as early, non-invasive predictors of miscarriage needs further validation. With technological advancements in high-frequency transducers and increased clinical reliance on early ultrasound assessments, yolk sac parameters offer a potentially valuable, yet underexplored, avenue for improving early pregnancy monitoring.

This study was designed to evaluate the association between yolk sac diameter and early pregnancy outcomes. By assessing antenatal women between 5 to 10 weeks gestation using standardized transvaginal ultrasound protocols, we aim to determine whether yolk sac abnormalities correlate significantly with miscarriage, thus providing clinicians with an additional predictive marker to identify at-risk pregnancies during the first trimester.

Aim

The purpose of the study is to assess the size of the yolk sac obtained through transvaginal ultrasound in pregnant women from the 5th to 10th week of gestation and analyze the relationship between the yolk sac and the outcome of pregnancy.

MATERIALS AND METHODS

This prospective observational study was conducted in the Department of Obstetrics and Gynecology at Saveetha Medical College and Hospital, Chennai, from September 2020 to September 2022. The primary aim was to evaluate the predictive value of yolk sac diameter, as assessed by transvaginal ultrasonography, in determining early pregnancy outcomes.

A total of 202 pregnant women, between 5 and 10 weeks of gestation, who visited for routine antenatal care and met the inclusion criteria, were enrolled after obtaining informed written consent. Gestational age was determined based on the last menstrual period or confirmed by early ultrasound. Inclusion was limited to women with singleton pregnancies within the specified gestational age range. Exclusion criteria included multiple gestations, structural uterine or cervical anomalies, anembryonic pregnancies, subchorionic hemorrhage, absence of fetal cardiac activity, pregnancies resulting from assisted reproductive techniques, and those with a history of teratogenic drug use or discordance between crown-rump length (CRL) and mean sac diameter (MSD).

After a detailed clinical history and examination, transvaginal ultrasound scans were performed using a LOGIQ S7 expert ultrasound machine equipped with a 7.7 MHz transducer. Scans were conducted with patients in the dorsal lithotomy position after emptying their bladder. The transducer was inserted with proper aseptic precautions. The yolk sac was identified as a round, echogenic-ringed structure within the gestational sac, and its maximum diameter was measured by placing calipers on the inner margins of the yolk sac.

Yolk sacs were categorized based on morphology and diameter. Those between 2 mm and 5 mm with a regular shape and echogenic rim were considered normal. Any yolk sac with a diameter below 2 mm or above 5 mm, or with irregular margins, was classified as abnormal. Patients were followed up until 20 weeks of gestation to determine pregnancy outcomes. Pregnancies continuing beyond 20 weeks were considered viable, while miscarriages before 20 weeks were classified as nonviable outcomes.

Data were compiled and analyzed using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were presented as mean $\pm$ standard deviation (SD) for continuous variables and as frequencies and percentages for categorical variables. The chi-square test was applied to determine associations between categorical variables, such as yolk sac abnormalities and pregnancy outcome. Independent t-tests were used to compare mean yolk sac diameters between the miscarriage and viable pregnancy groups. Receiver Operating Characteristic (ROC) curve analysis was employed to assess the sensitivity and specificity of yolk sac diameter as a predictive marker for miscarriage. A p-value < 0.05 was considered statistically significant.

RESULTS

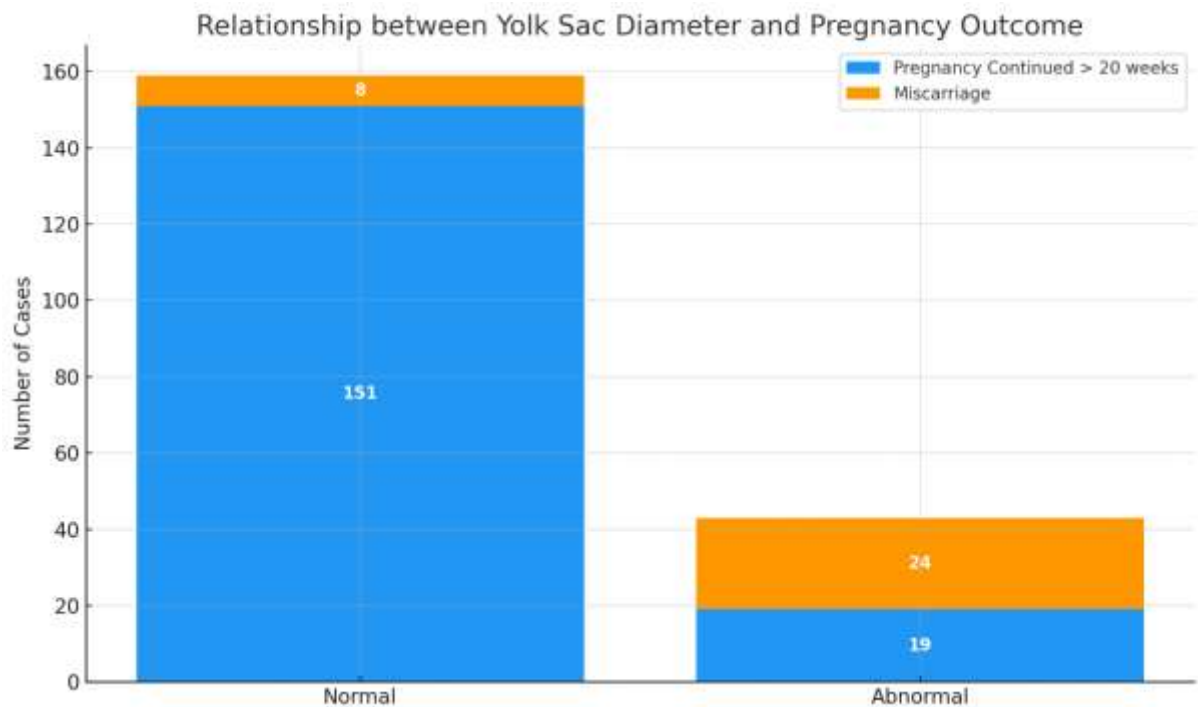
The study enrolled a total of 202 pregnant women between 5 to 10 weeks of gestation. The mean age of participants was predominantly between 21–30 years, representing 82.18% of the cohort. Among the study population, 74.75% were primigravidae and 25.25% were multigravidae.

Out of 202 pregnancies, 170 (84.16%) continued beyond 20 weeks while 32 (15.84%) resulted in miscarriage. When yolk sac diameter (YSD) was categorized, 159 participants had a normal YSD (2–5 mm), of which 151 continued pregnancy and 8 miscarried. Meanwhile, 43 had an abnormal YSD (< 2 mm or > 5 mm), among whom only 19 continued pregnancy while 24 resulted in miscarriage (Table 1). This association was statistically significant ($p < 0.001$).

Table 1: Relationship between Yolk Sac Diameter and Pregnancy Outcome

Yolk Sac Diameter	Pregnancy Continued > 20 weeks	Miscarriage	Total
Normal	151	8	159
Abnormal	19	24	43

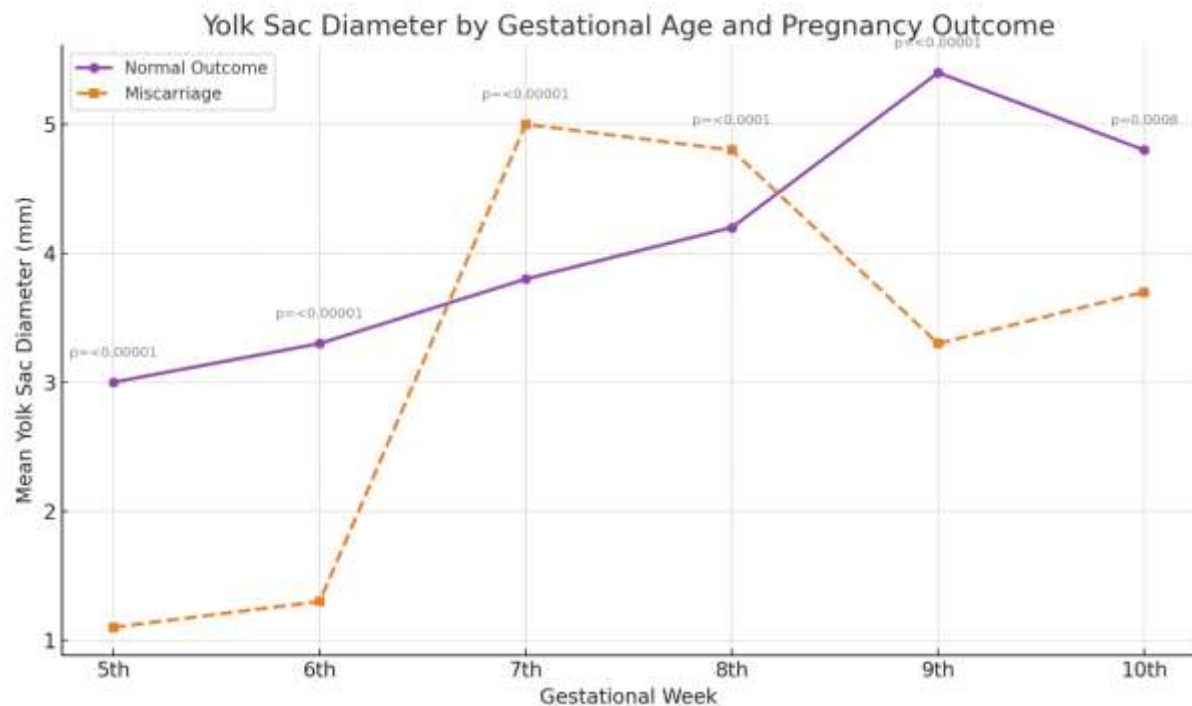
Total	170	32	202
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The mean yolk sac diameters for each gestational week were calculated and compared between outcomes. For instance, at 8 weeks, normal pregnancies had a mean YSD of 4.2 mm (SD $\pm$ 0.826), while those ending in miscarriage had a mean of 4.1 mm (SD $\pm$ 0.839). Statistically significant differences ($p < 0.05$) were found across all weeks between normal and abnormal outcome groups (Table 2).

Table 2: Yolk Sac Diameter by Gestational Age and Pregnancy Outcome

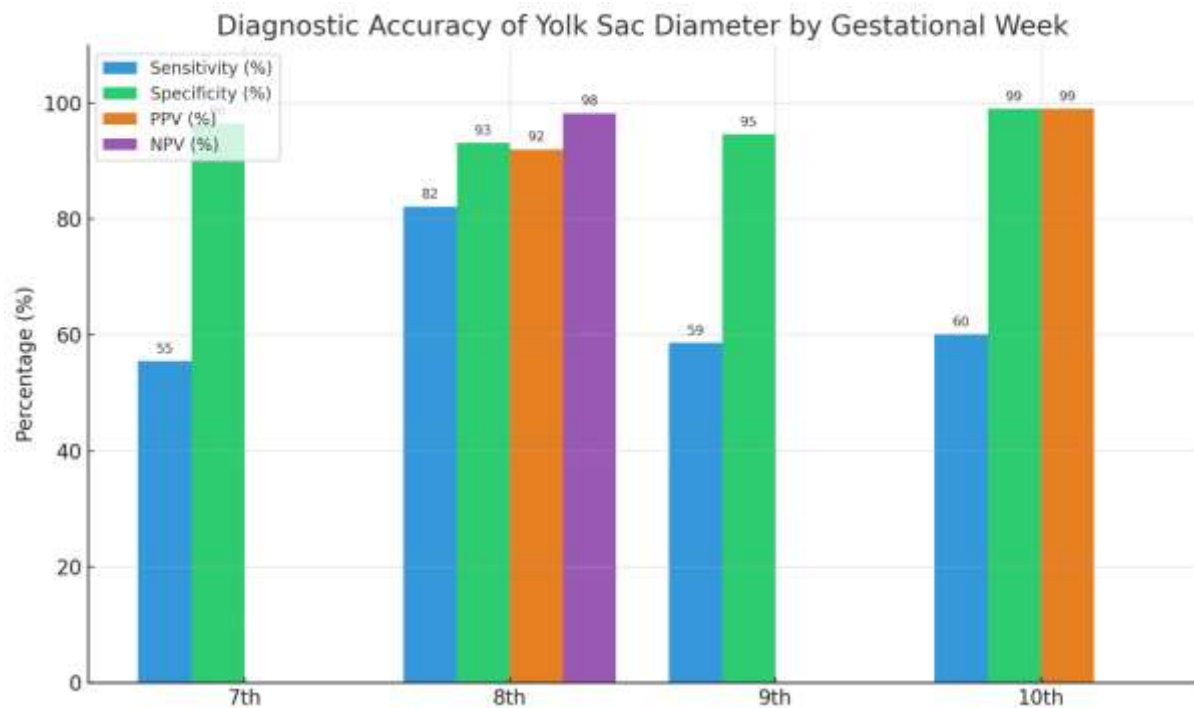
Gestational Week	Normal Outcome (Mean YSD mm)	Miscarriage (Mean YSD mm)	P-value
5th (35–41 days)	3.0	1.1	<0.00001
6th (42–48 days)	3.3	1.3	<0.00001
7th (49–55 days)	3.8	5.0	<0.00001
8th (56–62 days)	4.2	4.8	<0.0001
9th (63–69 days)	5.4	3.3	<0.00001
10th (70–76 days)	4.8	3.7	0.0008



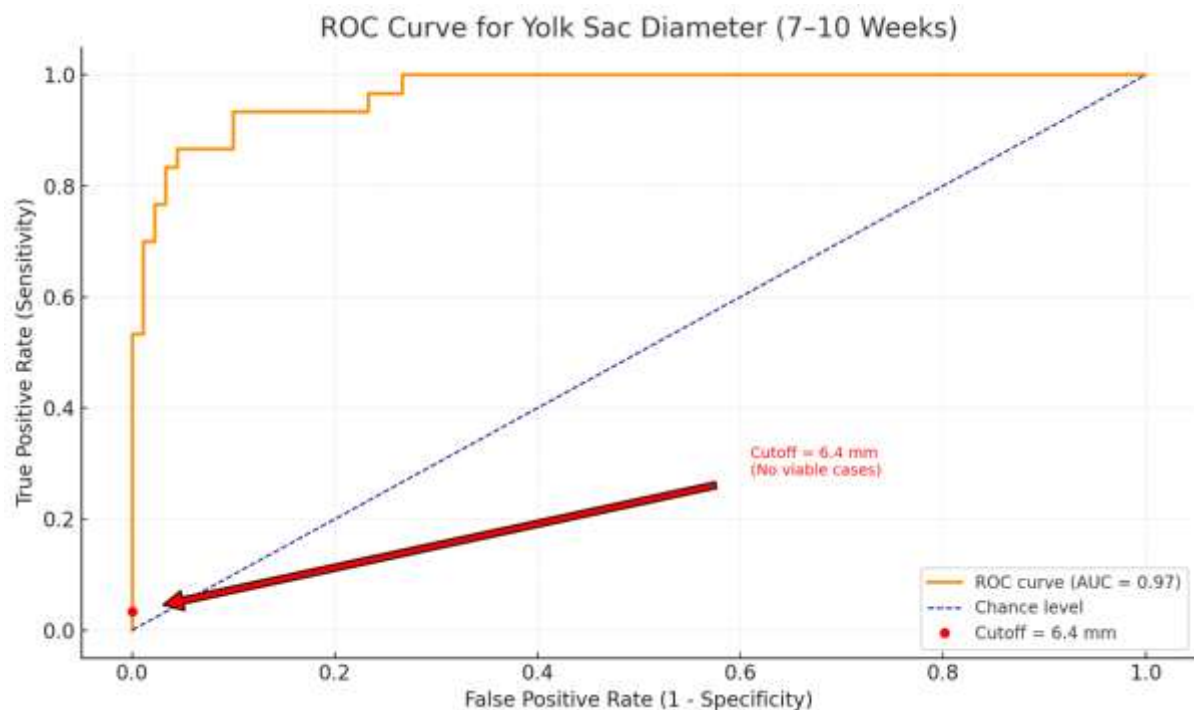
To further determine diagnostic performance, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for different gestational weeks. The 8th week demonstrated the highest sensitivity (82.12%) and NPV (98.24%), indicating strong predictive power for miscarriage risk. The highest specificity (99%) and PPV (99%) were recorded during the 10th week of gestation, suggesting it is the most reliable period for confirming ongoing viable pregnancies (Table 3).

Table 3: Diagnostic Accuracy of Yolk Sac Diameter by Gestational Week

Week	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
7th	55.48	96.49	—	—
8th	82.12	93.1	92	98.24
9th	58.67	94.58	—	—
10th	60.11	99	99	—



ROC curve analysis and statistical testing confirmed that the difference in yolk sac measurements between viable and nonviable pregnancies was significant particularly between 7th and 10th gestational weeks ($p < 0.00001$). Notably, no viable pregnancy had a yolk sac diameter greater than 6.4 mm, and all such cases ended in miscarriage.



These findings suggest that yolk sac measurements between 7 and 10 weeks serve as a reliable predictor for early pregnancy outcome, supporting their integration into routine ultrasound protocols for first-trimester screening.

DISCUSSION

This study investigated the prognostic significance of yolk sac diameter (YSD), assessed through transvaginal ultrasonography (TVS), in predicting early pregnancy outcomes. We observed a significant association between abnormal yolk sac parameters and increased risk of miscarriage. Of the 202 pregnancies studied, 43 exhibited abnormal yolk sacs, and more than half of these (24 cases) resulted in miscarriage, supporting the premise that yolk sac anomalies serve as early markers for pregnancy failure.

Our findings are consistent with previous research by Lindsay et al. [2], who reported that abnormal yolk sac diameters, particularly those exceeding 5.6 mm, were closely linked to early pregnancy loss. Similarly, Kucuk et al. [5] demonstrated that yolk sac measurements outside the 2–5 mm range were associated with an elevated risk of miscarriage, with a specificity of 97% and a positive predictive value of 60%. These conclusions are mirrored in our own results, where the specificity reached 99%, and sensitivity peaked at 82.12% during the 8th gestational week.

Stampone et al. [4] emphasized that not only the size but also the shape and wall characteristics of the yolk sac were crucial indicators of gestational viability. Yolk sacs with irregular shapes or thickened walls were more frequently associated with adverse outcomes. This supports our classification approach, which considered both size and morphological features to categorize yolk sacs as normal or abnormal.

The high miscarriage rate observed in pregnancies with abnormal YSD can be attributed to compromised embryonic development. The yolk sac plays an essential role during early pregnancy, functioning as the site of primary hematopoiesis, nutritional exchange, and metabolic activity until placental circulation is established [3]. Deviations in yolk sac morphology may reflect underlying embryonic or placental insufficiencies, predisposing to fetal demise.

Wilcox et al. [1] noted that approximately 31% of pregnancies are lost post-implantation, and nearly 80% of these losses occur in the first trimester. Early sonographic detection of abnormalities, such as yolk sac enlargement or absence, therefore offers an invaluable opportunity for early risk stratification and counseling.

Despite this, studies such as those by Acharya et al. [7] and Cepni et al. [6] have highlighted the limitations of YSD as a standalone marker. While it provides valuable insight, the integration of YSD with other parameters like crown-rump length (CRL), mean sac diameter (MSD), and embryonic cardiac activity enhances diagnostic precision. Doubilet et al. [8] proposed guidelines using CRL and MSD thresholds for definitive diagnosis of pregnancy failure; however, our data suggest that incorporating YSD can improve early detection before these thresholds are crossed.

Emerging literature also suggests a link between yolk sac anomalies and chromosomal abnormalities. Angiolucci et al. [9] observed that trisomy 22 and other genetic anomalies frequently present with yolk sac enlargement, reinforcing its potential as a non-invasive marker for underlying cytogenetic disorders. Similarly, Berdahl et al. [10] found that abnormally large yolk sacs, even in pregnancies that progressed beyond the first trimester, were associated with increased risk of complications such as preterm labor.

In our study, the most predictive YSDs were recorded between 7 and 10 weeks of gestation, aligning with Babinski et al. [3], who described this period as the peak of yolk sac functionality. After this window, the yolk sac typically regresses as placental development becomes established, further emphasizing the importance of timing in yolk sac evaluation.

However, while an abnormal YSD correlates with poor outcomes in many cases, not all enlarged yolk sacs result in miscarriage. Cho et al. [11] highlighted that qualitative features—such as echogenicity, wall thickness, and the rate of yolk sac regression—may be more reliable predictors than diameter alone. These nuances suggest that sonographers should perform a composite assessment rather than relying on size in isolation.

Our study also reinforces the importance of standardized imaging protocols. Measurement accuracy is influenced by operator experience, machine resolution, and patient factors. Inconsistent measurement techniques may contribute to conflicting findings in the literature. Therefore, clear guidelines on YSD measurement, including when and how to measure, are essential for its incorporation into clinical protocols.

Although the present study did not evaluate maternal metabolic or immunological conditions, previous research indicates that conditions such as diabetes mellitus and autoimmune disorders may also impact yolk sac morphology [12]. In particular, Cosmi et al. [12] demonstrated that diabetic pregnancies exhibited yolk sac

structural abnormalities more frequently, suggesting that maternal factors must also be accounted for in comprehensive risk assessment.

Our study was limited by the absence of genetic testing and maternal biomarker evaluation, which could have clarified the underlying etiology of yolk sac anomalies. Additionally, longitudinal follow-up beyond 20 weeks would have allowed us to explore late gestational outcomes in pregnancies initially classified as viable.

Nonetheless, the strength of this study lies in its prospective design, robust sample size, and standardized ultrasound methodology. The high specificity and negative predictive value observed confirm the clinical relevance of YSD as a tool for early pregnancy assessment. Yolk sac diameter is a valuable ultrasonographic marker that offers predictive insight into pregnancy viability, particularly in the early gestational weeks. When integrated with other sonographic parameters and clinical findings, it enhances the ability to identify high-risk pregnancies. Further multicentric studies incorporating genetic, biochemical, and immunologic analyses are warranted to establish comprehensive predictive models for early pregnancy outcomes.

Conclusion and Recommendations

This study underscores the diagnostic and prognostic value of yolk sac diameter (YSD) assessment via transvaginal ultrasonography (TVS) during the first trimester of pregnancy. Our findings confirm that abnormal yolk sac parameters—defined by diameters less than 2 mm or greater than 5 mm, or those displaying irregular morphology—are significantly associated with early pregnancy loss. With a sensitivity of 82.12% and specificity of 99% observed particularly during the 8th to 10th gestational weeks, YSD emerges as a reliable early marker for miscarriage prediction. Yolk sac assessment offers a non-invasive, accessible, and cost-effective tool for risk stratification in early pregnancy, especially in resource-limited settings where advanced genetic or hormonal profiling may not be readily available. Incorporating yolk sac evaluation into routine first-trimester ultrasound protocols could enhance early detection of potentially nonviable pregnancies, allowing clinicians to plan timely interventions and provide appropriate counseling. Given that yolk sac anomalies may also reflect underlying chromosomal abnormalities, future studies should explore integrating sonographic findings with genetic and biochemical markers. Longitudinal studies extending beyond 20 weeks of gestation could offer insights into the role of YSD in predicting later complications such as intrauterine growth restriction, preterm labor, or stillbirth.

We recommend the following:

1. **Routine Measurement:** Yolk sac diameter should be routinely measured in all first-trimester ultrasounds between 5–10 weeks of gestation.
2. **Composite Evaluation:** Yolk sac parameters should be evaluated alongside crown-rump length (CRL), mean sac diameter (MSD), and embryonic cardiac activity to enhance predictive accuracy.
3. **Standardization:** Training and standardization in yolk sac measurement techniques across sonographers is essential for consistent interpretation and clinical utility.
4. **Further Research:** Multicenter, prospective studies combining YSD with maternal risk factors, biochemical markers, and cytogenetic evaluations will help establish comprehensive guidelines.

In conclusion, the yolk sac, long considered a passive embryological remnant, should be reappraised as an active clinical marker. Its size and morphology provide early, crucial insights into pregnancy viability and should be utilized more comprehensively in obstetric practice.

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