ABENHA MEDICAL JOURNAL bmj

Print ISSN 1110-208X.

Online ISSN 2357-0016

Original article

Early Pregnancy Ultrasound Measurements and Prediction of First Trimester Pregnancy Loss

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Received: 18 December 2024

Accepted:25 March 2025

Abstract:

Background: Early pregnancy failure, including conditions such as spontaneous abortion and anembryonic gestation, affects many women. Ultrasound has become a vital tool in assessing early pregnancy, particularly through the measurement of parameters like gestational sac diameter (GSD), yolk sac diameter, and crown-rump length (CRL), which help in predicting pregnancy outcomes. This study aims to evaluate the accuracy of ultrasonographic parameters in predicting early pregnancy failure in women with a history of recurrent first-trimester pregnancy loss. **Methods:** This prospective cohort study included 90 pregnant women with a history of first-trimester recurrent pregnancy loss. Participants were assessed using transvaginal ultrasound to measure mean GSD, yolk sac diameter, CRL, embryonic heart rate, decidua basalis thickness, and the presence of intrauterine hematoma and uterine artery Doppler parameters. **Results:** Significant differences were observed between the ongoing pregnancy and miscarriage groups for CRL, GSD, and yolk sac features. CRL and GS mean sac diameter demonstrated high diagnostic accuracy with area under the receiver operating characteristic curve values of 0.74 and 0.79, respectively. CRL was particularly significant, with a p-value < 0.001. The ongoing pregnancy group exhibited higher gestational age and more favorable ultrasound findings (e.g., regular yolk sac shape, normal embryonic heart rate). Miscarriages were associated with abnormal yolk sac features and higher rates of abnormal GS shapes and locations. **Conclusion:** Ultrasonographic parameters, especially CRL and GS diameter, are reliable indicators for predicting early pregnancy failure in women with a history of recurrent pregnancy loss. These parameters may guide clinical decisions in early pregnancy management.

Keywords: Transvaginal Ultrasound; Mean Gestational Sac Diameter; Crown-Rump Length; Early Pregnancy Failure.

Introduction

Early pregnancy failure encompasses incomplete, complete, or inevitable spontaneous abortion, anembryonic gestation, and missed abortion occurring before 14 weeks, with recurrent first-trimester pregnancy loss defined as three or more consecutive miscarriages [(1)]. Ultrasound has become the primary method for studying early human development, revealing that the celomic cavity and secondary yolk sac are the first anatomical structures to form during early gestation [(2)].

The first ultrasound sign of pregnancy is the gestational sac within the thickened decidua, representing the chorionic cavity and appearing as an anechoic fluid collection surrounded by an echogenic ring of trophoblasts and decidua. The yolk sac, the first identifiable structure within the gestational sac, provides nutrients for embryonic development, enlarging from the 5th to 10th gestational week and disappearing after 14–20 weeks [(3)]. By 6 weeks of gestation, prenatal ultrasonography typically detects the embryonic heartbeat via M-mode, with a slow heart rate at 6–7 weeks associated with a high likelihood of first-trimester pregnancy demise [(4)].

Crown-rump length (CRL) is a key parameter for assessing gestational age in early pregnancy, with mean gestational sac diameter (MGSD): CRL ratios also used to predict pregnancy outcomes, albeit with variable accuracy [(5)]. Sonographic evaluation of the decidua basalis aids in predicting early pregnancy failure, as implantation typically occurs between days 20–24 of the menstrual cycle, followed by trophoblastic invasion into the decidua and myometrium, forming the decidual–placental complex or placenta [(6)].

Doppler studies in threatened abortion yield mixed results, with some showing no predictive value for transvaginal color Doppler ultrasound and others linking a high uterine artery pulsatility index to miscarriage in early viable pregnancies [(7)].

Two-dimensional transvaginal ultrasound (TVUS) remains a reliable tool for assessing embryonic well-being despite advances in three-dimensional imaging, with parameters such as gestational sac, yolk sac, amniotic cavity, and embryonic heartbeat being crucial indicators [(8)].

Discriminatory criteria, including an 8-mm MGSD without a yolk sac or a 16–20-mm MGSD without embryonic heartbeats, aid in predicting pregnancy loss, although exceptions occur. Additionally, a very large yolk sac often predicts poor outcomes, but no universally reliable model exists for distinguishing viable pregnancies from those likely to miscarry [(9)].

The study aims to assess accuracy of ultrasonographic parameters (mean gestational sac diameter, yolk sac diameter, crown rump length, embryonic heart rate, decidua basalis thickness, presence of intrauterine hematoma and uterine artery Doppler) in predicting early pregnancy failure in pregnant women with history of first trimester recurrent pregnancy loss.

Patients and methods:

The duration of the study: from October 2023 to October 2024

Design and population

This prospective cohort study included 90 pregnant females with history of first trimester pregnancy loss attending Benha University Maternity Hospital Emergency Room. The study was done after being approved by the Research Ethics Committee of Benha University, Egypt. Informed consent was obtained from all patients or patients' first-degree relatives after discussing the study aim and methods with each patient prior to enrolment.

Inclusion criteria were adult females with a positive pregnancy test, a single intrauterine pregnancy, and a gestational age of 6–10 weeks based on the last menstrual period in patients with regular cycles who are certain of their date. **Exclusion criteria** were women with

uncertain last menstrual period dates, irregular menstrual cycles, or multiple pregnancies.

Assessments

All participants underwent a thorough assessment, including detailed history-taking and clinical examination. History covered personal details (e.g., age, address, consanguinity), menstrual and obstetric history (e.g., cycle regularity, last delivery, complications), past medical conditions (e.g., diabetes, hypertension, autoimmune disorders, chromosomal anomalies), and family history of similar issues. Clinical evaluation included general examination (e.g., weight, height, vital signs), abdominal assessment to exclude organic pathology, and pelvic examination to inspect external genitalia and rule out infections via speculum evaluation.

Transvaginal ultrasound (TVUS)

Transvaginal ultrasound using the Mindray DC30 (50–60 Hz) was performed to assess the MGSD, calculated as the average of three orthogonal diameters (longitudinal, anteroposterior, and transverse) measured from inside the sac, excluding the decidual reaction. The MGSD was typically eccentric in location, embedded in the endometrium, and exhibited a smooth, round, or oval shape [10].

The yolk sac, formed from hypoblast cells after implantation, plays a vital role in early embryonic development. It transitions from a primary to a secondary yolk sac by the second week and becomes visible on ultrasound around the fifth week post-fertilization. Composed of extra-embryonic mesoderm, it contributes to gastrulation, forming the embryonic germ layers: endoderm (visceral organs), ectoderm (outer body tissues), and mesoderm (muscles and cardiovascular system). By the 14th gestational week, the yolk sac typically becomes sonographically undetectable. In this study, its size, shape, echogenicity, and degenerative changes were evaluated, with normal parameters including a 3–7 mm diameter, rounded shape, echogenic rim, and hypoechoic center [11, 12].

CRL is measured as the greatest length from the cranial to caudal end of the embryo or fetus, excluding the yolk sac and extremities, typically in the sagittal plane. This measurement, which is widely used for early pregnancy dating, is recorded as an average of three measurements [13]. A significant association between pregnancy loss and the difference between MGSD and CRL (when the difference is <5mm) has been reported [10]. In this study, the MGSD–CRL ratio was calculated as the difference between the two values. Additionally, the fetal heart rate was assessed using **M-mode**, which provides a real-time representation of the moving fetal heart. The heart rate is measured by calculating the distance between two heartbeat peaks on a frozen M-mode image, with the software displaying the beats per minute [14].

The decidua basalis layer in pregnancies destined to miscarry during the first trimester exhibits distinct sonographic differences, indicating a defective decidual-placental complex due to insufficient trophoblastic invasion [15], thickness is measured perpendicular to the endometrial surface, with three measurements taken to calculate the average. **Intrauterine hematomas** (IUHs), often detected during first-trimester ultrasound, appear as hypoechoic or anechoic crescent-shaped areas between the uterine wall and chorionic membrane. The incidence of IUHs ranges from 1 to 39.5%, influenced by factors like study cohort variability, diagnostic definitions, equipment used, and the timing of diagnosis [16].

Approval code: MS 13-10-2021

Statistical analysis

The collected data underwent a thorough process of review, coding, and tabulation using the Statistical Package for Social Science (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version

25.0. Armonk, NY: IBM Corp.), with each parameter's data meticulously presented and analyzed according to its inherent characteristics. To assess the normality of data distribution, the Shapiro-Wilk test was applied. Descriptive statistics, including mean, standard deviation (± SD), median, and range for numerical data, and frequency and percentage for non-numerical data, were employed. Analytical statistics were also utilized, with the Student T Test applied to assess the statistical significance of differences between the means of two study groups. Correlation analysis was conducted to examine the strength of associations between quantitative variables, while linear regression analyses, using a 95% confidence interval (CI), estimated the precision of the Odds Ratio (OR). A larger CI indicated lower precision, while a smaller CI indicated higher precision. The p-value was considered significant when <0.05 within a 95% confidence interval, indicating the probability of the results.

Results:

Participants had a mean age of 29.5 years and BMI of 26.42 kg/m², with 56.32% being passive smokers. Common comorbidities included hypertension, diabetes mellitus, thyroid disease, and venous thromboembolism. Placental-related disorders, such as preeclampsia and placental abruption, were noted in previous pregnancies, along with a high rate of miscarriages and D&C procedures. Pregnancy loss was attributed to conditions like antiphospholipid syndrome, thrombophilia, systemic lupus, diabetes, thyroid disorders, and polycystic ovary syndrome. Treatments included aspirin, progesterone, intralipid, heparin, steroids, and antioxidants. Ongoing pregnancies occurred in 54.02%, with a substantial proportion of miscarriages classified as viable pregnancy losses.

There are some significant differences between the ongoing pregnancy and miscarriage groups across various sonographic parameters. Miscarriages were associated with higher rates of CRL and GS measurements below the 5th percentile for GA, irregular GS shapes, and caudally displaced GS locations. Embryonic/fetal heart rates below the 5th percentile and abnormal YS features, including irregular shapes, abnormal diameters, and hypo-echogenic rims, were more common in miscarriages. While some findings, such as degenerative YS changes and intrauterine hematoma, showed trends toward higher abnormalities in miscarriages, they did not reach statistical significance. These parameters may help predict adverse pregnancy outcomes. **Table 1**

The data presents GA measurements for the ongoing pregnancy group (n = 47) and the miscarriage group (n = 40) across different weeks. Significant differences are observed at 6, 7, 8, and 9 weeks, with p-values consistently below 0.05, indicating that the ongoing pregnancy group had higher GA values compared to the miscarriage group. No data is available for the 10-week group. The results suggest a statistically significant difference in GA between the two groups during early pregnancy stages. **Table 2**

The AUROC values for MSD, CRL, and YSD are 0.53, 0.96, and 0.62, respectively, with CRL showing the highest diagnostic accuracy. The 95% confidence intervals (CIs) for these values range from 0.42-0.64 for MSD, 0.89-0.99 for CRL, and 0.50-0.72 for YSD. The p-value for CRL is highly significant (< 0.001), while MSD and YSD have p-values of 0.55 and 0.06, respectively. For the validity analysis, the cut-off value for MSD is ≤ 0.32mm, with a sensitivity of 100%, a positive predictive value (PPV) of 89.3%, and a positive likelihood ratio of 100%, indicating strong accuracy for this threshold. **Table 3**

Table 1: Comparison of ultrasound parameters between ongoing pregnancy and miscarriage groups.

	Ongoing Pregnancy Group [n = 47]	Miscarriage Group [n = 33]	P value
Crown-Rump Length			<0.001
<5th percentile for GA.	7(14.89%)	21 (63.63%)	
5th – 95th percentile for GA.	40 (85.10%)	12 (36.36%)	
>95th percentile for GA.	0 (0%)	0 (0%)	
GS – Mean sac diameter			<0.001
<5th percentile for GA	6 (12.76%)	28 (70.0%)	
5th – 95th percentile for GA	41 (87.23%)	12 (30.0%)	
>95th percentile for GA	0 (0%)	0 (0%)	
GS location Eccentric	45 (95.74%)	24 (60.0%)	<0.001a
fundal Displaced caudally	2 (4.25%)	16 (40.0%)	
GS shape			<0.001
Regular, rounded	44 (93.61%)	14 (35.0%)	
Irregular	3 (6.38%)	26 (65.0%)	
MSD-CRL difference			<0.001
≤ 5mm	5 (10.6%)	20 (60.6%)	
> 5 mm	42 (89.3%)	13 (39.3%)	
Embryonic/Fetal heart rate			<0.001
<5th percentile for GA	5 (10.63%)	17 (73.9%)	
5th – 95th percentile for GA	42 (89.36%)	6 (26.0%)	
>95th percentile for GA	0 (0%)	0 (0%)	
Yolk sac diameter			<0.001[a]
<5th percentile for GA	5 (10.6%)	0 (0%)	
5th – 95th percentile for GA	42 (89.3%)	7 (21.2%)	
>95th percentile for GA	0 (0%)	26 (78.7%)	
Number of yolk sac(s)			0.02
Absent	0 (0%)	4 (12.1%)	
Equal to number of embryos	47 (100.0%)	29 (87.8%)	
> Number of embryos	0 (0%)	0 (0%)	
Yolk sac site			0.04
Adherent to GS wall	44 (93.6%)	25 (75.7%)	
Free floating	3 (6.3%)	8 (24.2%)	
Yolk sac shape			0.002
Rounded, regular	45 (95.7%)	23 (69.6%)	
Deformed, irregular	2 (4.2%)	10 (30.3%)	
U/S appearance of YS rim			0.006
Echogenic	45 (95.7%)	24 (72.7%)	
Hypo-echoic	2 (4.2%)	9 (27.2%)	
Hyper-echoic	0 (0%)	0 (0%)	
U/S appearance of YS centre			0.07
Sonolucent	46 (97.8%)	28 (84.8%)	
Echogenic	1 (2.1%)	5 (15.1%)	
Degenerative YS changes			0.15
Absent	44 (93.6%)	27 (81.8%)	
Present	3 (6.3%)	6 (18.1%)	
Intrauterine hematoma			0.09
Absent	46 (97.8%)	35 (87.5%)	
Present	1 (2.1%)	5 (12.5%)	

CRL: Crown-Rump Length, GA: Gestational Age, GS: Gestational Sac, MSD: Mean Sac Diameter, CRL: Crown-Rump Length, EHR: Embryonic Heart Rate, FHR: Fetal Heart Rate, YS: Yolk Sac, U/S: Ultrasound

Table 2: Comparison of the mean decidua basalis thickness in the ongoing pregnancy and miscarriage groups.

GA	Ongoing Pregnancy Group [n = 47]	Miscarriage Group [n = 40]	P
6 wks	4.3 ± 1.4	2.4 ± 1.8	**<0.001**
7 wks	3.7 ± 2.1	1.9 ± 1.1	<0.001
8 wks	0.7 ± 1.1	0.1 ± 0.03	**<0.001**
9 wks	0.4 ± 0.9	0.1 ± 0.01	**0.03**
10 wks	-	-	-

GA: gestational age

Table 3: ROC curve analysis for prediction of first trimester miscarriage using daily MSD, CRL and YSD growth velocity

	MSD	CRL	YSD
AUROC	0.53	0.96	0.62
95% CI	0.42-0.64	0.89-0.99	0.50-0.72
P-value (AUCE=0.5)	0.55	< **0.001**	0.06
Validity	Cut-off value	≤ 0.32mm	
	Sensitivity (%)	100.0%	
	PPV	89.3%	
	+ve likelihood ratio	100.0%	
	-ve likelihood ratio	0.0	

MSD: Mean Sac Diameter, CRL: Crown-Rump Length, YSD: Yolk Sac Diameter, AUROC: Area under the Receiver Operating Characteristic Curve, CI: Confidence Interval, P-value: Probability value, AUCE: Area Under the Curve Estimation, PPV: Positive Predictive Value.

The findings suggest different characteristics for each parameter based on the GA percentile. For CRL percentile, measurements greater than the 5th percentile indicate normal development, while those below suggest potential concerns. GS location is typically eccentric and fundal when above the 5th percentile and displaced caudally when below. A regular, rounded shape is seen in larger sacs, while smaller ones are more likely to be irregular. For MSD-CRL difference, a difference greater than 5mm is indicative of potential issues. YS features, such as shape, echogenicity, and degeneration, vary considerably, with abnormal findings often associated with smaller yolk sacs or adverse conditions like intrauterine hematomas. The evaluation of the EHR/FHR and YSD percentiles also shows a clear distinction in the developmental status of pregnancy based on measurements above or below the 5th percentile for GA. **Table 4**

Table 4: Proposed composite score for prediction of first trimesteric miscarriage.

		0	1
CRL percentile		> 5th percentile for GA	< 5th percentile for GA
	MSD percentile	> 5th percentile for GA	< 5th percentile for GA
Gestational Sac			
	Location	Eccentric, fundal	Displaced caudally
	Shape	Regular, rounded	Irregular
MSD-CRL difference		> 5mm	≤ 5mm
EHR/FHR percentile		> 5th percentile for GA	< 5th percentile for GA
	YSD percentile	< 95th percentile for GA	> 95th percentile for GA
	Number	Equal to number of embryos	Absent
	Site	Adherent to GS wall	Free floating
Yolk Sac	**Shape**	Rounded, regular	Deformed, irregular
	YS rim	Echogenic	Hypo-echogenic
	YS center	Sonolucent	Echogenic
	Degeneration	Absent	Present
Intrauterine hematoma		Absent	Present

CRL: Crown-Rump Length, GA: Gestational Age, MSD: Mean Sac Diameter, EHR: Embryonic Heart Rate, FHR: Fetal Heart Rate, YSD: Yolk Sac Diameter, GS: Gestational Sac, YS: Yolk Sac.

Discussion:

Early pregnancy failure, including conditions such as spontaneous abortion and anembryonic gestation [(1)], affects many women. Ultrasound has become a vital tool in assessing early pregnancy [(3)], particularly through the measurement of parameters like GSD, YSD, and CRL, [(5)] which help in predicting pregnancy outcomes. This study aims to evaluate the accuracy of ultrasonographic parameters in predicting early pregnancy failure in women with a history of recurrent first-trimester pregnancy loss.

This study found no statistically significant differences in age or BMI between the miscarriage and ongoing pregnancy groups. Most pregnancies were spontaneous, with a minority resulting from intracytoplasmic sperm injection (ICSI). Passive smoking was common among participants but showed no significant association with miscarriage. These findings align with some authors who reported no significant demographic differences between pregnancy outcomes [(17)]. Similarly, it was highlighted that increased miscarriage risks in older women [(18)], it was noted that there is a higher odds of miscarriage in obese or underweight individuals [(19)], and a study reported no significant link between passive smoking and miscarriage, consistent with our study [(20)].

In terms of obstetric history, patients in the study had various complications, including preeclampsia, fetal growth restriction, fetal demise, placental abruption, and preterm deliveries due to placental insufficiency. These findings are consistent with the results of a study which confirmed that a history of placenta-related pregnancy complications increases the risk of miscarriage [(21)].

In this study, the most common cause of miscarriage was endocrine disorders, followed by antiphospholipid antibody syndrome, hereditary thrombophilia, secondary antiphospholipid antibody syndrome, and one case of abnormal karyotyping. A significant portion of cases

had unexplained etiologies. Treatments included low-dose aspirin, progesterone, and various other interventions such as LMWH, steroids, antioxidants, thyroid disease treatment, insulin sensitizing agents, insulin therapy, and intralipid. These findings align with some authors who found that acquired thrombophilia increases the risk of fetal loss, particularly in the first trimester [(22)].

In this study, CRL percentile categories showed significant differences between the miscarriage and ongoing pregnancy groups, with CRL below the 5th percentile more common in the miscarriage group. ROC analysis suggested that CRL below the 5th percentile could predict miscarriage. These findings a study that reported significant CRL differences between the two groups [(17)], and other study which found a significant CRL difference between early pregnancy loss and non-loss groups [(23)]. Additionally, some authors highlighted an inverse relationship between miscarriage rates and gestational age, with most embryonic deaths occurring before the eighth week [(24)].

This study found that the GSD below the 5th percentile for gestational age was significantly more prevalent in the miscarriage group compared to the ongoing pregnancy group. ROC analysis showed that GSD below the 5th percentile could predict miscarriage. These results align with findings from a study which also reported a significant difference in GSD between the two groups [(17)], and another study whcih noted that the median GSD was reduced in miscarriage cases [(24)].

This study found significant differences in the distribution of GS locations between pregnancy outcome groups, with caudal displacement of GS predicting miscarriage with high specificity. It also identified that irregular GS shape was more common in the miscarriage group. These findings align with some authors who reported that both caudal displacement of GS and irregular GS shape are associated with an increased risk of miscarriage [(25)].

This study found that a difference of ≤ 5mm between MGSD and CRL was significantly more common in the miscarriage group, and that this measurement could predict subsequent miscarriage with high specificity. These results are consistent with some authors who also identified a threshold of ≤ 5mm for predicting miscarriage, with a high probability of pregnancy continuation [(26)]. However a study found that the MGSD-CRL difference was not an effective predictor of miscarriage, contrasting with the findings of this study [(27)].

This study found that EHR/FHR below the 5th percentile for gestational age was more prevalent in the miscarriage group and could predict subsequent miscarriage with high specificity. These findings align with some authors who reported significantly lower embryonic heart rates in pregnancies that ended in miscarriage compared to those that continued [(28)], as well as it was identified that there is a significant differences in fetal heart rates between continuing pregnancies and those resulting in miscarriage during the first trimester [(17)].

The current study found that an abnormally large YSD was more prevalent in the miscarriage group, and ROC analysis indicated that an enlarged YSD could predict subsequent miscarriage. These findings are consistent with some authors who noted that the yolk sac plays a critical role in early pregnancy exchange [(29)], and with others who reported significant differences in YSD between early pregnancy loss and continuing pregnancies [(23)]. However, the results contrast with those of some authors who found that the yolk sac was smaller in the pregnancy loss group after the first trimester [(17)].

The current study found that absent YS was more common in the miscarriage group, though ROC analysis revealed poor accuracy in predicting miscarriage based on the number of YS. These results align

with a study that observed a higher absence of YS in miscarriage cases [28], and with other study which noted significant differences in YS size between the two groups [17]. However, the findings contrast with some authors who concluded that the presence or absence of the yolk sac is not a predictive indicator of miscarriage [30].

The current study found significant differences in YS site and shape between the miscarriage and ongoing pregnancy groups, with floating YS identified as a predictor of miscarriage. The hypo-echoic YS rim was more prevalent in the miscarriage group, while the echogenic YS center was also more common, though not significantly different between groups. YS degenerative changes did not differ significantly between the two groups. These findings align with some authors who linked large YS to miscarriage risk but found no relationship with irregular or echogenic YS appearance [31], and others who observed similar abnormalities in missed miscarriage cases [32].

The current study found no significant difference in the presence of IUH between the miscarriage and ongoing pregnancy groups, with a poor predictive accuracy for subsequent miscarriage. These findings align a study which reported no difference in miscarriage rates between women with and without IUH [32], but contrast with another study found that IUH adversely affected pregnancy outcomes, leading to missed miscarriage in a higher percentage of women with IUH [33].

The current study found that the mean decidua basalis thickness for gestational ages between 6 and 10 weeks was significantly lower in the miscarriage group compared to the ongoing pregnancy group. This finding is consistent some authors who observed thinning of the decidua basalis in early pregnancy loss cases from 5-6 weeks onwards when compared with normal pregnancies [15].

The current study found that in embryonic pregnancies that subsequently miscarried, the decidua basalis did not exhibit the typical increase in thickness seen in normal pregnancies, and appeared more echogenic near embryonic demise, with the placenta showing areas of hypo echogenicity. Additionally, daily CRL growth velocity was a significant predictor of first-trimester miscarriage, with a cut-off of ≤0.32mm showing strong predictive power. However, daily MSD and YSD growth velocities did not demonstrate significant predictive ability. These findings align with some authors who noted an overlap in MSD growth rates between viable and non-viable pregnancies and identified a CRL growth cut-off of 0.2 mm/day as associated with miscarriage [5].

Our study has some limitations, such as no cut off values for prediction of miscarriage in the current study may be attributed to small sample size and short period of follow up.

Conclusion:

Ultrasonographic parameters, especially CRL and GS diameter, are reliable indicators for predicting early pregnancy failure in women with a history of recurrent pregnancy loss. These parameters may guide clinical decisions in early pregnancy management.

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To cite this article: Ashraf I. El. Mashad , Yehia M. Edris, Heba A. El Sayed, Mai S. Hagag. Early Pregnancy Ultrasound Measurements and Prediction of First Trimester Pregnancy Loss. BMFJ 2025;42(5):186-196.