Yolk sac size and shape, Gestational sac size, and embryonic Heart Rate as prognostic factors of first trimester Pregnancy Outcome.

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CASE SERIES

Yolk Sac Size and Shape, Gestational Sac Size, and Embryonic Heart Rate as Prognostic Factors of First-Trimester Pregnancy Outcome

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Abstract

Background: Approximately 15–20% of pregnancies end in miscarriage. The yolk sac initially forms at around 5 weeks of gestation and may be viewed via ultrasonography. Both the yolk sac and fetal heart rate can be used as predictors of first-trimester gestation result.

Aim and objectives: To determine the relationship between early abortion and each of the ultrasound characteristics measured during the first trimester (gestational sac size, yolk sac size, and fetus heart activity).

Patients and methods: This prospective cohort research was done on 200 pregnant women in their first trimester with a week of gestation of between 5 and 6 weeks at Al-Azhar University’s Department of Obstetrics and Gynecology.

Result: According to the results of ultrasonography in the study group, five (2.5%) of the 34 fetus losses were missed abortions (fetal pole without detectable pulsations), 10 (5%) were blighted ovaries, seven (3.5%) were partial miscarriages, and 12 (6%) were complete miscarriages.

Conclusion: During the first trimester of pregnancy, the monitoring of fetal heart rate, yolk sac diameter and shape, and gestational sac diameter proved to be a great, useful, and noninvasive tool in the evaluation, prognosis, and follow-up of pregnant women. When the gestational sac diameter, crown–rump length, and embryo heart rate were recorded all at the same time, they were able to determine the prognosis of the first trimester better than when each characteristic was used separately.

Keywords: Embryonic heart rate, Gestational sac diameter, Yolk sac diameter

1. Introduction

Ultrasonography is a useful method for determining the status of early pregnancy. First-trimester sonography is useful for dating, assessing a number of gestations, establishing location, and even detecting some early malformations.1

Ultrasonography has great sensitivity for detecting anomalies in the gestational sac, yolk sac, and fetal that indicate a bad result, in addition to documenting normal growth.2

The gestational sac with enlarged deciduas is the earliest sonographic indication of pregnancy. When the mean diameter is 2–3 mm, transvaginal ultrasonography may detect the sac by 4 weeks and 3 days of pregnancy.3

When the embryo is as little as 1–2 mm in length, it may be detected via transvaginal ultrasonography. Both the embryo and the gestational sac should expand 1 mm every day at 5–7 weeks.5

The yolk sac is the first embryonic component seen on sonography inside the gestational sac.5 It

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appears as a circular anechoic region between the 5 and 12 weeks of pregnancy.\(^5\)

The viability of a pregnancy in the first trimester is fairly assured if the yolk sac seems normal and measures between 2 and 5 mm.\(^6\)

In predicting pregnancy loss, the poor quality and early regress of a yolk sac are more unique than their large size. A significantly big yolk sac, even if normal in structure, may be a signal of miscarriage when an embryo is undetected.\(^7\)

Cardiac activity around the yolk sac, suggesting a living fetus, may not be seen until the fetus is 5-mm long, between 5.5 and 6.5 weeks. A heart rate lower than 100 bpm in the embryo is considered typical. Throughout the next 3 weeks, the heart rate rapidly rises to 180 bpm.\(^3\)

The goal of this research was to see whether there was a link between early gestation losses and each of the ultrasound measures measured in the first trimester (gestational sac size, yolk sac size, and fetal heart function).

2. Patients and methods

The research was carried out at Al-Azhar University's Obstetrics and Gynecology Department. This prospective cohort study was conducted on pregnant women, in the first trimester of pregnancy with gestational age between 5 and 6 weeks.

2.1. Inclusion criteria for the study group

Inclusion criteria were those between 5 and 6 weeks of gestational age, had normal menstrual periods, knew when their last menstruation was, were in their first trimester of pregnancy with a single viable embryo at the time of the initial scan, and had no indications of threatening abortion when they were first examined.

2.2. Exclusion criteria

Pregnant women beyond 12 weeks of gestation, multifetal pregnancies, lost to follow-up, any uterine disease such as myomas or deformity, and patients with signs of imminent abortion were the exclusion criteria.

2.3. Methods

Patients were subjected to the following.

2.3.1. Complete history taking

Personal history, including name, age, marital state, and residence; menstruation history such as age of menarche, menstrual disturbance, dysmenorrhea, and related symptoms; history of parity; present history of chronic diseases and medication; past history of hypertension, diabetes mellitus, family history of similar condition or diabetes, and history of allergy to any medication; and surgical history of operation, laparoscopic interference, and treatment of hirsutism by laser.

Women were asked for early pregnancy symptoms as follows:

Missed period, tender, swollen breasts, nausea with or without vomiting and moodiness, food aversions, and fatigue.

2.4. Examination

General examination included vital signs (temperature, blood pressure, heart rate, and respiration rate) and signs of pallor, cyanosis, jaundice, and lymph node enlargement. Abdominal and local clinical examination included abdominal examination, abdominal palpation, abdominal percussion, and abdominal auscultation. Vulvar examination was done as follows: the vulvar area's basic examination included a basic developmental evaluation, symmetry, hair condition and growing distribution, skin anomalies, swelling, ulcerations, overgrowth such as external genital warts, malignancies, rashes, lacerations, piercings, bruising, and discharge. The labia minora are slightly separated to examine the hymenal ring during vaginal examination. The vaginal walls, especially those toward the rear, relax when little pressure is applied to the bulbocavernous muscle, making speculum entry easier. It is possible to evaluate a cystocele, urethrocele, cystourethrocele, or rectocele, with or without vaginal prolapose or a tumor in the vaginal wall. Bimanual examination is used to determine the size and type of the uterus, as well as the presence or absence of adnexal masses. The uterine mobility and tenderness, as well as the presence of any adnexa discomfort, are assessed. Ovaries are palpable in many premenopausal women with typical habits.

2.5. Investigation

The method used to confirm pregnancy included blood test. Human chorionic gonadotropin hormone is detected in pregnancy testing.

Each patient was subjected to the following.

2.5.1. A first ultrasound scan

According to their first prenatal care appointment, they were between 6 and 8 weeks of gestational age.
at the time. The sizes of gestational sacs were averaged from longitudinal and transverse images. The calipers were placed on the inner boundaries of the larger diameter to calculate the yolk sac diameter (YSD). M-mode sonography was used to get transvaginal measurements of fetal heart rate and crown–rump length (CRL). The adnexa was viewed to exclude extrauterine pregnancy, which is suspected in the presence of an empty uterus; an adenexal mass separates from the ovary. The presence of fluid and blood in Douglas pouch were noted and recorded as well.

2.5.2. Follow up scan

Every 2 weeks, until the pregnancy reached 12 weeks, fetus heart rate, gestational sac diameter, YSD, and CRL were determined. At least two scans were required, including the final one at 12 weeks, unless the patient miscarried before that. The assessments was done using transvaginal ultrasound or/and transabdominal ultrasound.

2.6. Primary outcome measures

The primary outcome measures were to examine the relationship between early pregnancy loss and each of the ultrasound measures measured in the first trimester (fetus heart rate, gestational sac diameter, YSD, CRL) (e.g. silent miscarriage). Different ultrasound parameters have a correlation with each other. Moreover, the correlation between the patient clinical characteristics (patient history and symptoms of the current pregnancy) and early pregnancy loss was assessed.

2.7. Secondary outcome measures

The secondary outcome measures were to evaluate if anatomical anomalies in pregnancies that remain viable at the time of the final scan could be associated with abnormalities in the first-trimester ultrasound parameters.

2.8. Ethical consideration

The study protocol was submitted for approval by Institutional Review Board, Al-Azhar University. Each individual who took part in the research gave verbal informed consent.

2.9. Data management and statistical analysis

The data collected during the history, basic clinical examination, laboratory tests, and outcome assessments were coded, entered, and evaluated using Microsoft Excel software. The data were evaluated using the Statistical Package for the Social Sciences (SPSS version 20.0) (Statistical Package for the Social Sciences, IBM Company in Armonk, New York, US) software. Quantitative data were represented as a mean ± SD, whereas qualitative data were expressed as a number and a proportion, depending on the kind of data. The following tests were employed to determine the significant difference: correlation by Pearson’s correlation or Spearman’s correlation. For significant findings, the $P$ value was set at less than 0.05, and for very significant findings, it was set at less than 0.001.

3. Results

This observational study was conducted on 200 pregnant women in the first trimester of pregnancy with gestational age between 5 and 6 weeks (Table 1). There was a significant increase in gestational sac diameter at 12 weeks compared with that at 6, 8, and 10 weeks ($P < 0.001$) (Table 2).

At 6, 8, 10, and 12 weeks, the gestational sac diameter declined substantially in the fetus loss group, indicating that the gestational sac diameter was an excellent predictor of fetal loss ($P < 0.001$; Fig. 1).

Gestational sac diameter (GSD) at 12 weeks with a cutoff value less than 5.2 can detect fetal loss, with sensitivity and specificity of 99.4 and 100%, respectively, as shown in Table 4.

At 6, 8, 10, and 12 weeks, the YSD increased substantially in the fetal loss group, indicating that the YSD was an excellent predictor of fetal loss ($P < 0.05$; Fig. 2).

The most sensitivity detected was at 10 weeks (100%) with cutoff of 6.82, whereas the most specificity detected was at 6 and 12 weeks (100%) with cutoff of 5.47 and 4.49, respectively (Table 5).

Table 1. Distribution of the studied pregnant women as per gestational sac diameter at 6, 8, 10, and 12 weeks.

<table>
<thead>
<tr>
<th>Gestational sac diameter</th>
<th>Test value</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
<td>Median</td>
<td></td>
</tr>
<tr>
<td>At 6 weeks</td>
<td>2.45 ± 0.77</td>
<td>2.30</td>
</tr>
<tr>
<td>At 8 weeks</td>
<td>3.17 ± 0.74</td>
<td>3.11</td>
</tr>
<tr>
<td>At 10 weeks</td>
<td>3.74 ± 0.84</td>
<td>3.82</td>
</tr>
<tr>
<td>At 12 weeks</td>
<td>5.80 ± 0.46</td>
<td>5.76</td>
</tr>
</tbody>
</table>

$P$ value less than or equal to 0.05 statistical significance, $P$ value less than or equal to 0.01 extremely statistical significance.
The CRL showed a substantial decrease in the fetal loss group than ongoing pregnancy at 8 weeks \( (P < 0.05) \), whereas at 6, 10, and 12 weeks, there was no substantial variance between the two groups \( (P > 0.05; \text{Fig. 3}) \).

Table 2 shows the validity of CRL in detection of the outcome of pregnancy. The most sensitivity detected was at 8 weeks (81.4%) with cutoff of 1.15, whereas the most specificity detected was at 10 weeks (95.8%), with a cutoff of 3.23.

Table 6 shows showed the relation between heart rate at different gestational age period and its relation to the outcome of pregnancy. The heart rate showed a substantial increase in the fetal loss group than ongoing pregnancy group at 8 weeks \( (P < 0.05) \), whereas at 6, 10, and 12 weeks, there was no significant difference between the two groups \( (P > 0.05; \text{Fig. 4}) \).

Table 6 shows the validity of heart rate in detection of the outcome of pregnancy. The most sensitivity detected was at 8 weeks (80.8%) with cutoff of 161, whereas the most specificity detected was at 10 weeks (100%) with cutoff of 172.

4. Discussion

Any obstetric checkup should include an accurate evaluation of gestational age, and ultrasonography is currently the most effective tool to date a gestation period. To date a gestation period, many sonographically determined fetal markers are employed. The measurements to pay attention to include the fetus CRL, biparietal diameter, head circumference, femur length, abdominal circumference, and placental thickness.  

The mean maternal age in our studied cases was 30.72 ± 6.61 years and ranged from 19 to 42 years. Regarding anthropometric measurements, the mean weight, height, and BMI were 77.39 ± 8.31 kg, 173.23 ± 8.89 cm, and 25.99 ± 3.82 kg/m², respectively. The mean gestational age in our studied cases was 5.50 ± 0.50 weeks and ranged from 5 to 6 weeks. Regarding gravidity, 40% cases were gravida 3. Regarding parity, 28% cases were para 2, and 47.5% of cases had no history of previous abortion.

Our findings were supported by the study of Nilgün et al., as they included 88 patients. The average age of the mothers was 31.3 ± 4.5 years (range, 20–43 years). The average gestational age was 1.76 ± 0.4 (range, 1–5), the average parity was 0.35 ± 0.5 (range, 0–4), and the average abortion number was 0.1 ± 0.4. (range, 0–4).

However, in the study by Bhattarai and Baral, the participants’ average age was 24.0 ± 14.76 years.
The current research revealed that in terms of the distribution of the examined patients' gestational sac diameter at various follow-up periods, during the follow-up at 6, 8, 10, and 12 weeks, the gestational sac diameter increased significantly. Regarding the distribution of the examined patients' YSD at various follow-up periods, YSD was significantly reduced at 12 weeks compared with 6, 8, and 10 weeks \((P < 0.001)\).

In accordance with our results, the study of Poornima et al.\(^8\) showed that progressively increasing mean YSD was found with advancing gestational age between 6th and 9th week of gestation, from 4.4143 to 6.2818 mm following, which starts decreasing in size by 10th week.

In accordance with our results, the study by Abd Ellatif et al.\(^10\) reported that in terms of the distribution of the examined patients' gestational sac diameter during various follow-up periods, the gestational sac diameter from 2.5 to 3 was the highest at 6 weeks, as seen in 28 (28\%) patients; at 9 weeks, the gestational sac diameter from 2.5 to 3.5 was the highest, as seen in 41 (41.8\%) patients; and at 12 weeks, the gestational sac diameter of 6.0\(\pm\) was the highest, as seen in 43 (46.2\%) patients. Regarding the distribution of the examined patients' YSD at various follow-up periods, at 6 weeks, the YSD of 6.0\(\pm\) was the highest, as seen in 40 (40\%) patients, at 9 weeks, the YSD of 6.0\(\pm\) was the highest, as seen in 56 (57.1\%) patients, and at 12 weeks, the YSD of less than 4 was the highest, as seen in 35 (37.6\%).

Moreover, Cepni et al.\(^11\) reported the constant rise in YSD from 5 to 11 weeks of pregnancy in normal pregnancies, following which, it diminishes by 12 weeks. Chama et al.\(^12\) reported a linear increase in mean YSD from 2.27 mm at 5 weeks to 5.61 mm at 11 weeks of pregnancy. Lindsay et al.\(^22\) found that although the mean gestational sac diameter (MSD) is smaller than 15 mm, the yolk sac increases at a pace of around 0.1 mm/mm growth of the MSD, and then slows to 0.03 mm/mm development of the MSD.

The current study showed that regarding the distribution of the studied patients regarding fetal CRL at different period of follow-up, there was a significant increase in fetal CRL at 12 weeks compared with that at 6, 8, and 10 weeks \((P < 0.001)\).

In accordance with our results, the study by Abd Ellatif et al.\(^10\) reported that regarding the distribution of the studied patients regarding fetal CRL at different period of follow-up, CRL 1\(\pm\) was greatest at 6 weeks, as seen in 52 (52\%) patients; CRL from 1.5 to 2.5 was greatest at 9 weeks, as seen 41 (41.8\%) patients, whereas CRL 4 was greatest at 12 weeks, as seen in 37 (39.8\%) patients.

In terms of the end result of ultrasonographic findings in our research group, five (2.5\%) of the 34 fetus losses were missed abortions (fetal pole with no apparent pulsations), 10 (5\%), blighted ovum, seven (3.5\%) incomplete miscarriages, and 12 (6\%) complete abortions.

Our results were in line with the study by Abd Ellatif et al.\(^10\) as they revealed that two of the eight fetal losses in the study group were missed abortions (fetal pole with no visible pulsations), one blighted ovum, two incomplete abortions, and three complete abortions, according to the final outcome of ultrasonographic findings.
In the study by Doubilet et al., with a viable fetus at or beyond 14 weeks of pregnancy, 245 (41.5%) of the 590 research cases had a favorable first-trimester outcome. The remaining 345 (58.5%) pregnancies ended in miscarriage in the first trimester.

In this study, at 6, 8, 10, and 12 weeks, the gestational sac diameter decreased significantly in the fetal loss group, indicating that the gestational sac diameter was an excellent predictor of fetal loss ($P < 0.001$). GSD at 12 weeks with a cutoff of less than 5.2 can detect fetal loss, with sensitivity and specificity of 99.4 and 100%, respectively.

Our findings matched with those of Abd Ellatif et al., as they reported that in terms of the relationship between gestational sac diameter at various gestational ages and pregnancy outcome, the gestational sac diameter decreased significantly in the fetal loss group at 6, 9, and 12 weeks, indicating that the gestational sac diameter was a reliable predictor of fetal loss ($P < 0.05$).

Previous published data have demonstrated that pregnancies that lack YS or have a YSD that is less than the gestational age are more likely to end in spontaneous abortion. Very big YS pregnancies are almost invariably connected with bad outcomes.

The current investigation revealed that there is a link between YSD and gestation results at various gestational ages. At 6, 8, 10, and 12 weeks, the YSD increased substantially in the fetal loss group, indicating that the YSD was an excellent predictor of fetal loss ($P < 0.05$). The most sensitivity detected was at 12 weeks (100%) with a cutoff of 6.82, whereas the most specificity detected was at 6 and 12 weeks (100%) with cutoff values of 5.47 and 4.49, respectively.

In accordance with our results, the study of Lebda et al. found that the presence of an enlarged YS (four instances), as well as an irregular or nonexistent YS (one case each), was strongly linked to fetal loss. This shows that measuring the YSD was a good predictor of the first trimester’s outcome. Their research shows that visualizing YS is essential for a healthy pregnancy result. Only one (2.5%) case of 41 of normal YSD aborted, which agrees with Moradan and Forouzeshfar.

Furthermore, Sheikh and Anjana found with a sensitivity of 65%, a specificity of 97%, and a positive predictive value of 71%, the YSD of 2 SD of the mean for the menstrual age permitted prediction of an undesirable pregnancy outcome.

Manchanda et al. found that pregnancies with a YSD more than 6 mm had a sensitivity and specificity of 100 and 96%, respectively, for predicting bad outcomes. In a different retrospective research conducted by Bae and Karnitis, the rates of continued pregnancy for YSD of 2, 2–6, and more than 6 mm was 20, 89.2, and 20%, respectively, indicating that the YSD of 2–6 mm is the most compatible.

The present research found that there is a link between CRL and pregnancy outcome at various gestational ages. At 8 weeks, the fetal death group had a considerably shorter CRL than the continued pregnancy group ($P < 0.05$), whereas there was no substantial variance between the two groups at 6, 10, or 12 weeks ($P > 0.05$). The most sensitivity detected was at 8 weeks (81.4%) with a cutoff of 1.15, whereas the most specificity detected was at 10 weeks (95.8%) with a cutoff of 3.23.

In agreement with our results, Abd Ellatif et al. found that there was a substantial decrease in CRL in fetal loss group less than ongoing pregnancy at 6

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### Table 5. The relationship between crown–rump length at various gestational ages and the pregnancy outcome.

<table>
<thead>
<tr>
<th></th>
<th>Normal pregnancy ($N = 166$)</th>
<th>Fetal loss ($N = 34$)</th>
<th>Test value</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Median</td>
<td>Mean ± SD</td>
<td>Median</td>
</tr>
<tr>
<td>Crown–rump length</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At 6 weeks</td>
<td>1.05 ± 0.44</td>
<td>1.01</td>
<td>0.94 ± 0.35</td>
<td>0.97</td>
</tr>
<tr>
<td>At 8 weeks</td>
<td>1.61 ± 0.53</td>
<td>1.61</td>
<td>1.37 ± 0.54</td>
<td>1.42</td>
</tr>
<tr>
<td>At 10 weeks</td>
<td>2.36 ± 0.66</td>
<td>2.35</td>
<td>2.09 ± 0.45</td>
<td>2.11</td>
</tr>
<tr>
<td>At 12 weeks</td>
<td>4.57 ± 0.78</td>
<td>4.60</td>
<td>4.45 ± 0.49</td>
<td>4.24</td>
</tr>
</tbody>
</table>

$P$ value less than or equal to 0.05 statistical substantial, $P$ value less than or equal to 0.01 extremely statistical substantial.

* Mann–Whitney U test.

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![Fig. 3. ROC curve of crown–rump length in detection of the outcome of pregnancy. ROC, receiver operating characteristic.](image-url)
weeks only \((P < 0.05)\), whereas at 9 and 12 weeks, there was no substantial variance between the two groups \((P > 0.05)\). The cutoff value of CRL at 6 weeks was less than 0.8, with sensitivity of 70\%, specificity of 65\% and accuracy of 76\%. At 9 weeks, the cutoff value was less than 1.9, with sensitivity of 48\%, specificity of 50\%, and accuracy of 49\%.

Poornima et al.,\(^8\) found that first-trimester newborns with typical sized and seeming yolk sacs and embryo heart rates exceeding 100 bpm had 66.7\% sensitivity, 100\% specificity, 33.3\% positive prediction value, and 0\% negative predictive value when predicting outcome. Heart rate was shown to have a diagnosis accuracy of 92.8\%.

Similarly, Abdulkadhim\(^{19}\) reported that a fetal heart rate of less than 120 bpm was linked to a greater risk of miscarriage, with sensitivity, specificity, positive and negative predictive value, and accuracy of 54.2, 94.8, 72.2, 89.2, and 86.7\%, respectively. This was the most accurate cutoff point for predicting the outcome of a pregnancy. The results of this research show that fetal death usually happens before the conclusion of the first trimester.

Furthermore, Aseri,\(^{20}\) demonstrated that the fetal heart rate strongly influenced the pregnancy outcome in the first trimester \((t\)-test, \(P = 0.048)\).

In the study by Abdulkadhim,\(^{19}\) there was substantial statistical variance between groups A and B in terms of embryonic heart rate, with the majority of individuals with an embryonic heart rate of less than 100 bpm having a bad prognosis \((P = 0.0003)\).

### 4.1. Conclusion

The ultrasound assessment of fetal heart rate, YSD and shape, and gestational sac diameter during the first trimester of pregnancy proved to be an essential, useful, and noninvasive tool in the evaluation, prognosis, and follow-up of pregnant women in their early gestation period. When the gestational sac diameter, CRL, and fetal heart rate were measured together, they were able to predict the prognosis of the first trimester better than when each characteristic was measured separately.

### Conflict of interest

There are no conflicts of interest.

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