

Role of First Trimester Ultrasonographic Parameters for Prediction of Early Pregnancy Failure - A Prospective Observational Study from Punjab, India

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ABSTRACT

BACKGROUND

Early pregnancy failure is stated as noncompatible, intrauterine pregnancy with either an empty gestational sac or a gestational sac that contains an embryo or fetus which does not have any fetal cardiac activity in the initial 12 weeks of the pregnancy. In the assessment of early pregnancy, ultrasound plays a significant role.

METHODS

A prospective observational study was conducted in a tertiary care hospital between May 2019 and April 2020 among 500 pregnant females fulfilling the inclusion and exclusion criteria. Patient follow up was done by weekly telephonic calls until completing 12 weeks gestation or reporting miscarriage. Also, all patients were followed by the recommended routine ultrasound (US) scanning with or without emergency visits.

RESULTS

In our study period, 500 women fulfilling the inclusion criteria were included in our study. Out of whom, 85 (17.5 %) women had an early pregnancy failure (before 12 weeks). There was significantly lower mean gestational sac diameter (GSD), crown to rump length (CRL), fetal heart rate (FHR), and P-value < 0.001 in women who experienced early pregnancy failure. In pregnancies where the GSD, CRL, and FHR were below the 5th percentile, early pregnancy failure was a more prone outcome. All pregnancies with FHR below 75 beats per minute ended in failure in the present study. When FHR was less than 128 beats per minute, there was enormous rise in the frequency of pregnancy failure. By comparison, yolk sac diameter (YSD) was a less significant predictor of early pregnancy failure.

CONCLUSIONS

First-trimester ultrasonographic estimations help in predicting early abortion. Risk appraisal tables dependent on combinations of abnormal parameters could significantly help in identifying abnormal pregnancy from normal pregnancy and could improve prediction rates.

KEYWORDS

Early Pregnancy Failure, Prediction, Transvaginal Ultrasonography, Ultrasonography

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BACKGROUND

Early pregnancy failure is stated as non-compatible, intrauterine pregnancy with either an empty gestational sac or a gestational sac that contains an embryo or fetus which does not have any fetal cardiac activity in the initial 12 weeks of the pregnancy. In the first trimester, the term miscarriage, spontaneous abortion and early pregnancy loss are utilised reciprocally and there is no agreement on wording in the literature.¹ Approximately 12 – 24 % of all pregnancies endure failure and the greater part of the early failures are brought by chromosomal abnormalities and the danger of which increments with maternal age.²

Regular symptoms of early pregnancy loss are vaginal bleeding, uterine cramping, decline in the symptoms of pregnancy (breast tenderness, nausea).¹ It causes tension and mental injury for pregnant women.³ These ladies ought to be consoled about the risk of miscarriage by the care giver. Early pregnancy units have been developed in countries like UK with goal of providing a one stop outpatient service to women with stomach torment, vaginal bleeding or tension, as to the location and viability of their pregnancy.⁴

Different investigations have demonstrated that sonographic findings in early pregnancy have prognostic incentives in anticipating pregnancy outcome.³ Ultrasound additionally helps in determination any untoward occasion in early pregnancy and also help in suitable management. It is an easily accessible device to separate usual from unusual pregnancy. It is likewise imperative to figure out what establishes an abnormal early pregnancy measurement because this will assist clinicians to guide the pregnant ladies in their care.⁴

METHODS

A prospective observational study was directed in a tertiary care hospital between May 2019 and April 2020 on 500 females full filling the inclusion and exclusion criteria who came for well-being scan and female were followed for 13 weeks or prior appropriately. Inclusion criteria for our study was spontaneous conception, singleton fetus and females knowing the exact date of last menstrual period. Females not willing to participate in study and females with multiple pregnancy and females with chronic diseases in pregnant women like; heart disease, diabetes, chronic hypertension, renal diseases, bronchial asthma were excluded from study. Every single antenatal patient (6 - 12 weeks) went through transabdominal or transvaginal ultrasonography examination on VolusonE8 Expert BT 12 (Wipro GE) ultrasound machine. Ultrasound parameters including gestational sac diameter, crown to rump length, yolk sac diameter, fetal heart rate and trophoblastic reaction (TR) were recorded.

Collections like retroplacental collection were likewise considered. (Figure 1). Patients follow up was done by weekly telephonic calls until completing 12 weeks' gestation or reporting miscarriage. Also, all patients were followed by the recommended routine US scanning with or without emergency visits. Continuation of pregnancy beyond 12

weeks which was ultrasound confirmed was end point of study.

Strategy of Estimation of Different Parameters

A composed informed consent of the patient was taken before the procedure. Following parameters were measured by transabdominal sonography (TAS) / transvaginal sonography (TVS) at 6 - 12 weeks of gestation.

1. MSD (Mean gestational Sac Diameter).
2. Yolk sac diameter.
3. Crown-rump length.
4. Embryonic heart rate.
5. Trophoblastic reaction.

Modified Nagele's rule was used to calculate the gestational age. This gestational age was compared with gestational age derived by ultrasound parameters.

Mean gestational sac diameter was surveyed by averaging three measurements (longitudinal, antero-posterior and transverse). Gestational sac's measurement was taken from inside of the sac to the inside of the decidual reaction, baring the last in the estimation.

Yolk sac measurement was done by positioning the caliper on the inner limits of the larger diameter. Size of the sac, shape, echogenicity of the rim and centre of sac, its number and degenerative changes such as calcification was assessed. Yolk sac having diameter between 3 - 6 mm, rounded shape, absence of degenerative changes, presence of echogenic rim and hypoechoic centre was considered normal. Any deviation from above parameters was viewed as abnormal. Crown rump length was estimated in sagittal plane of embryo neglecting the inclusion of yolk sac. Fetal heart rate was measured on frozen M-mode and was calculated as beats per minute (bpm).

Statistical Analysis

Proper descriptive and inferential analysis was completed by SPSS 24.0. Fischer exact test was used to compare nominal categorical data. $P < 0.05$ was considered to be statistically significant. Student t-test was used to compare normally distributed continuous variable among two group. The data collected was also subjected to multiple logistic regression analysis and coefficient of determination (R²) analysis.

RESULTS

In the present study period, 500 ladies satisfying the inclusion criteria were taken. Out of whom, 85 (17.5 %) ladies had an early pregnancy failure (before 12 weeks). There was significantly lower mean GSD, CRL, and FHR with P value of less than 0.001 in females who experienced early pregnancy failure. However, mean yolk sac diameter among women who experienced early pregnancy failure was significantly greater with P value of 0.031 (Table 1).

There was a much greater chance of early pregnancy failure in those pregnancies where GSD, CRL, and FHR were

underneath the 5th percentile (Table 2). Pregnant females having yolk sac diameter above the 95th percentile was also more prone to have failure of pregnancy, however, the failure was less expected in the pregnancies where YSD was lower than 5th percentile or between the 5th and 95th percentile. All the pregnancies with fetal heart rate less than 75 beats per minute had failure of pregnancy in the present study. When the heart rate of fetus was below 128 bpm, there was a very sharp increase in the frequency of pregnancy failure. The value of coefficient of determination (R²) for heart rate of fetus less than 128 bpm was 0.29. The results of our study showed that with reduction of each 10 beats per minute in fetal heart rate below 128, the chances of abortion were increased by 26.9 %. The ideal cut-off value of fetal heart rate for the extension of pregnancy was 128 beats per minute. (Table 3). The pregnancies that ended in abortion had a significantly lower mean GSD–CRL difference with P value of less than 0.001. However, this difference was not very significant at 6 - 7 weeks or 10 - 11 weeks of pregnancy. There was a significantly increased chance of pregnancy getting aborted where the GSD–CRL difference was lower than 5 mm. A difference of 11 mm or more in the GSD–CRL was the ideal cut off value for the continuance of pregnancy. (Table 4)

It was found that the chances of pregnancy resulting in failure were the highest (OR 66.61) when both the crown rump length and heart rate of fetus were below the 5th percentile and the rest of the two parameters were normal as shown by the analysis of abnormal variable combinations. It was also found that if crown rump length, gestational sac diameter and heart rate of fetus were less than the 5th percentile with a normal yolk sac diameter, the chances of pregnancy getting aborted were very likely (OR 34.27). This risk was very identical to the risk of abortion in pregnancies where all the parameters were abnormal.

It was also found that crown-rump length under the fifth percentile, heart rate of fetus under the 130 bpm and 5th percentile were independent risk factors affecting the completion of pregnancy. By correlation, it was found that yolk sac diameter was an insignificant indicator of early pregnancy failure.

Duration of Pregnancy (in Weeks)	No. of Cases		Gestational Sac (mm)		P Value
	SA	OP	SA	OP	
6 - 7	15	79	15.14 ± 3.25	18.06 ± 3.46	< 0.001
7 - 8	18	83	18.0 ± 6.59	25.79 ± 5.00	< 0.001
8 - 9	24	92	19.72 ± 8.29	33.27 ± 4.53	< 0.001
9 - 10	17	95	28.19 ± 7.17	39.49 ± 4.42	< 0.001
10 - 11	11	66	34.77 ± 8.48	45.80 ± 3.77	< 0.001
Overall	85	415	21.87 ± 9.18	32.06 ± 10.34	< 0.001

Table 1. Gestational Sac Diameter in the Study Women with Spontaneous Abortion (SA) and Those with Ongoing Pregnancy (OP) by Duration of Pregnancy

Duration of Pregnancy (in Weeks)	No. of Cases		Yolk Sac Diameter (mm)		P Value
	SA	OP	SA	OP	
6 - 7	15	79	4.47 ± 0.96	4.01 ± 0.62	0.009
7 - 8	18	83	4.66 ± 1.23	4.34 ± 0.63	< 0.001
8 - 9	24	92	5.23 ± 0.93	4.71 ± 0.61	< 0.001
9 - 10	17	95	5.09 ± 0.70	4.85 ± 0.61	< 0.001
10 - 11	11	66	4.8 ± 0.76	5.50 ± 0.51	< 0.001
Overall	85	415	4.89 ± 0.97	4.66 ± 0.76	< 0.001

Table 2. Yolk Sac Diameter in the Study Women with Spontaneous Abortion (SA) and Those with Ongoing Pregnancy (OP) by Duration of Pregnancy

Duration of Pregnancy (in weeks)	No. of Cases		Fetal Heart Rate (beats per minute)		P Value
	SA	OP	SA	OP	
6 - 7	15	79	105.00 ± 18.85	128.11 ± 11.6	0.031
7 - 8	18	83	113.33 ± 23.39	147.48 ± 9.20	< 0.001
8 - 9	24	92	127.90 ± 21.27	161.86 ± 7.62	< 0.001
9 - 10	17	95	123.21 ± 29.90	164.90 ± 7.10	< 0.001
10 - 11	11	66	111.25 ± 17.92	157.30 ± 7.36	< 0.001
Overall	85	415	117.68 ± 23.96	152.52 ± 15.90	< 0.001

Table 3. Fetal Heart Rate in the Study Women with Spontaneous Abortion (SA) and Those with Ongoing Pregnancy (OP) by Duration of Pregnancy

Duration of Pregnancy (in weeks)	No. of Cases		Crown to Rump Length (mm)		P Value
	SA	OP	SA	OP	
6 - 7	15	79	4.39 ± 1.34	5.711 ± 1.86	0.031
7 - 8	18	83	6.59 ± 3.25	10.63 ± 2.69	< 0.001
8 - 9	24	92	9.28 ± 3.69	18.54 ± 3.74	< 0.001
9 - 10	17	95	17.29 ± 7.80	26.64 ± 4.45	< 0.001
10 - 11	11	66	24.50 ± 6.39	33.09 ± 3.91	< 0.001
Overall	85	415	11.18 ± 8.02	18.67 ± 10.34	< 0.001

Table 4. Crown to Rump Length in the Study Women with Spontaneous Abortion (SA) and Those with Ongoing Pregnancy (OP) by Duration of Pregnancy

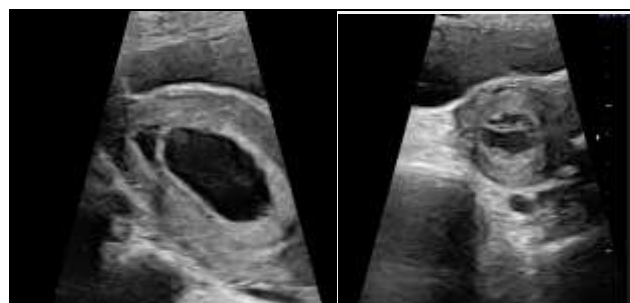


Figure 1. Ultrasonography Images Depicting Focal Sub-Chorionic Collection in an Ongoing Pregnancy with Gestational Age of 8 Weeks

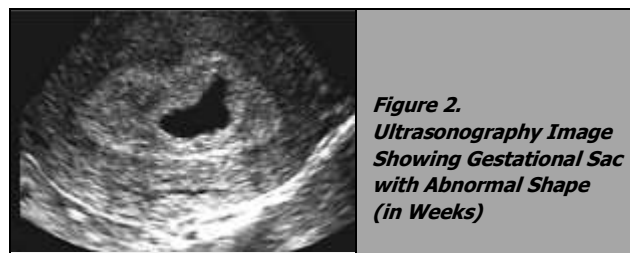


Figure 2. Ultrasonography Image Showing Gestational Sac with Abnormal Shape (in Weeks)

DISCUSSION

In our study in prediction of early pregnancy failure using various ultrasound parameters we found that, CRL and FHR underneath the fifth percentile and FHR under 128 beats per minute developed as autonomous indicator of pregnancy ending in failure. A difference of 11 mm or more in the GSD–CRL and fetal heart rate of 129 beats per minute or lower were considered as the ideal cut off value for the pregnancy to move towards completion. An unusual sized yolk sac within the sight of normal GSD, CRL, and FHR measurements was the weakest indicator of early pregnancy failure (Figure 2).

Different studies have indicated that diverse sonographic parameters measured in early pregnancy can foresee result of pregnancy. In a study directed on 556 pregnant females, Frates et al. unconstrained that the spontaneous abortion rate was greater among ladies with abnormal sonography

findings than among those with normal findings (15.2 % versus 8.2 %).⁵

Oh et al. reported that in pregnancies finishing in failure the mean GSD was significantly smaller (4.5 mm vs. 8.2 mm; $P < 0.001$),⁶ whereas Wie et al. discovered that GSD beneath the 5th percentile had an odds ratio of 4.87 ($P = 0.018$) for first and second-trimester abortion.⁷ Papaioannou et al. detailed that GSD below the 5th percentile had a sensitivity of 23.6 % for prediction of abortion,⁴ while Makrydimas et al. detailed a sensitivity of 24.4 % for the same parameter.⁸ In our study we found that there was altogether lower mean GSD ($P < 0.001$) and GSD below the 5th percentile in ladies who experienced early pregnancy failure.

Abuelghar et al.⁹ detailed that 56.6 % of ladies who experienced abortion had CRL beneath the 5th percentile, and this variable anticipated early abortion with a sensitivity of 56.6 %, specificity of 81.9 %, positive predictive value (PPV) of 36.6 %, negative predictive value (NPV) of 91.1 %, and likelihood ratio positive of 3.15. D'Antonio et al.¹⁰ found that CRL below the 5th percentile was related with abortion with an odds ratio of 2.21 ($P = 0.023$). Similarly, Mukri et al. reported that 61 % of ladies who experienced pregnancy failure had CRL below the 5th percentile.¹¹ In our study we found that there was significantly lower mean CRL ($P < 0.001$) and CRL beneath the 5th percentile in women who experienced early pregnancy failure.

In a study of 188 pregnancies, Wie et al. inferred that YSD below the 2.5th percentile or above the 97.5th percentile had an odds ratio of 15.86 ($P < 0.001$) for abortion.⁷ Tan et al. reported that YSD more than 1 standard deviation above the mean had a sensitivity of 37.5 % for predicting abortion.¹² Papaioannou et al. reported that if YSD was below the 5th percentile, the chance of abortion would be 8.5 % with a false-positive rate of 5 %, whereas if it was above the 95th percentile, the chance would be 22.4 % with a false-positive rate of 5 %.⁴ Similarly, Makrydimas et al. reported that YSD underneath the 5th percentile had 7.4 % sensitivity with a false-positive rate of 5 % for predicting early abortion, whereas YSD above the 95th percentile had 9.8 % sensitivity with a false-positive rate of 5 %.⁸ In the current study, yolk sac diameter under the 5th percentile had a sensitivity of 2.9 % and NPV 83 % for prediction of early pregnancy failure. Furthermore, yolk sac diameter above the 95th percentile immensely linked with abortion; however, it was not a reliable indicator. In our study we found that in pregnancies where yolk sac diameter was above the 95th percentile, they were likely to result in pregnancy failure. But pregnant females having yolk sac diameter under the 5th percentile or between the 5th and 95th percentile had lower chances of pregnancy ending in failure.

Wie et al. likewise inferred that FHR beneath the 5th percentile had a significant correlation with spontaneous abortion (OR 6.43' $P = 0.018$).⁷ Papaioannou et al. demonstrated the sensitivity of predicting pregnancy failure was 23.9 % with a false-positive rate of 5 % for FHR values below the 5th percentile.⁴ Altay et al. inferred that FHR underneath the 5th percentile had a sensitivity of 50 %, specificity of 94.9 %, PPV of 50 %, NPV of 98.9 %, and P value 0.01 for prediction of abortion. Likewise, Makrydimas

et al. reported a sensitivity of 26.5 % with a false-positive rate of 5 % for FHR values.

In our study, it was found that fetal heart rate lower than the 5th percentile had a sensitivity of 71.1 %, positive predictive value of 86.2 %, and NPV of 94.2 % for estimation of early failure of pregnancy.

Dede et al. discovered that an FHR value lower than 130 bpm had 81.4 % sensitivity and 85.1 % specificity for predicting abortion.¹³ Chittacharoen and Herabutya reported that FHR values below 120 bpm predicted early abortion with a sensitivity of 54.2 % and false-positive rate of 5 %. In the present study, the ideal cut off for fetal heart rate in the prediction of abortion was 128 bpm.¹⁴ In our study we found that all pregnancies having FHR below 75 bpm had pregnancy failure as outcome. There was sudden increment in the frequency of pregnancy failure when FHR was below 128 bpm. The coefficient of determination (R^2) for heart rate of fetus under the 128 bpm was 0.29. Therefore, the risk of abortion increased by 26.9 % for every 10 bpm decrease in FHR. The ideal cut off value of FHR for pregnancy to continue was 128 bpm.

Jakal et al. studied 87 pregnancies and found that females in continued pregnancy group had the GSD–CRL difference more than 5 mm, whereas only two women had a GSD–CRL difference of more than 5 mm in the abortion group ($P = 0.002$). They reported an abortion rate among pregnancies with a GSD–CRL difference of less than 5 mm and among those with a GSD–CRL difference of 6 – 10 mm was 21 % and 28 % respectively.¹⁵ In the current study, a GSD–CRL difference under the 5 mm had an odd's ratio of 4.0 for pregnancy resulting in failure; additionally, a 12-mm difference was the ideal cut off for assessing the risk of early pregnancy failure. In our study we found that there was significantly less mean gestational sac diameter–crown to rump length difference among the pregnancies that aborted ($P < 0.001$), but the difference was insignificant at 6 - 7 weeks and at 10 - 11 weeks of pregnancy. A GSD – CRL difference of below 5 mm had an extremely high chances of abortion. It was also found that for the pregnancy to continue; pregnancy optimum cut off value for gestational sac diameter – Crown to rump length difference was 11 mm or more.

CONCLUSIONS

First-trimester ultrasound parameters are predictors of early pregnancy failure. Tables estimating the chances of early pregnancy failure based on mixture of unusual measurements might bring improvement in the prediction rates. To our knowledge, very few studies in the past have analysed the prediction of early pregnancy failure by using various combinations of abnormal parameters. In conclusion, early ultrasound measures of crown to rump length, gestational sac diameter, heart rate of fetus and yolk sac diameter have a great role in the assessing the chances of pregnancy ending in failure and these measurement should be routinely documented in each and every scan performed in the early gestation. Tables and charts made using different data collected by the early pregnancy

ultrasonographic scanning will guide us in predicting the risk of early abortion.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.

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