EFFICACY OF FIRST TRIMESTER SONOGRAPHIC PARAMETERS - YOLK SAC DIAMETER AND EMBRYONIC HEART RATE IN PREDICTING PREGNANCY OUTCOME TILL MID PREGNANCY

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ABSTRACT

Introduction: Yolk sac is the first ultrasonic evidence of embryonic structure, visible as early as 5 weeks period of gestation and heart rate is an important marker for fetal viability, visible by 5 weeks 5 days period of gestation by transvaginal ultrasound. TVS is highly sensitive for picking up abnormalities of yolk sac and embryonic heart rate which can predict the outcome of pregnancy. Patients with abnormal parameters were followed up 2 weeks later and all patients were further followed up with NT scan and anomaly scan. Outcome was noted at the end of each scan. Analysis was done using SPSS version 22. Proportions and means were calculated. Chi square tests and independent t tests were applied. ROC curve analysis was done. Methods: Study was conducted in 70 low risk antenatal women, among them 64 progressed normally beyond 20 weeks and 6 had poor outcome either due to abnormal yolk sac diameter or embryonic heart rate. Results: Sensitivity and specificity of yolk sac in predicting outcome of pregnancy was found to be 66.7% and 98.7% respectively. Conclusion: Normal yolk sac and normal embryonic heart rate were both good predictors for successful pregnancy outcome. Among the two parameters embryonic heart rate is more specific in predicting adverse outcome of pregnancy.

KEY WORDS: yolk sac, pregnancy, gestational sac
INTRODUCTION

Diagnostic ultrasound is a sophisticated electronic technology, which utilises pulses of high frequency sound to produce an image which may be employed in a variety of specific circumstances during pregnancy such as in detecting complications, or where there are concerns about fetal growth. Because adverse outcomes may also occur in pregnancies without clear risk factors, assumptions have been made that routine ultrasound in all pregnancies will prove beneficial by enabling earlier detection and improved management of pregnancy complications. Routine screening may be planned for early pregnancy.\(^1\)

Ultrasoundography is an integral part for determining the status of early pregnancy. Sonography helps to assess the normal development of gestational sac and embryo. It is highly sensitive for picking up abnormalities of yolk sac and embryonic cardiac activity which can predict the outcome of pregnancy. Ultrasound plays a vital role to characterize miscarriages.

Improvements in ultrasound technology especially transvaginal sonography has led to a better understanding of early pregnancy development which helps antenatal women to have an earlier and accurate assessment of their pregnancy. First trimester sonographic features help to reassure them that their pregnancy is progressing normally or counsel them that their pregnancy will fail. It also helps to identify the type of twinning in multiple gestations allowing for appropriate counseling and management.\(^1, 2\)

The first trimester of pregnancy starts with the first day of the last menstrual period (LMP) and continues until the end of the twelfth week. Although, conception normally occurs two weeks after the LMP, the LMP is chosen as the start of the first trimester because it is a recognizable sign for most women.

Accurate assessment of gestational age is an important part of any obstetric examination and presently the most effective way to date pregnancy is by the use of ultrasound. Several sonographically derived fetal parameters are used to date pregnancy. They are fetal crown-rump length (CRL), biparietal diameter (BPD), head circumference (HC), femur length (FL), abdominal circumference (AC) and placental thickness measurement.\(^2, 3\)
The single most useful piece of information that obstetric sonography provides is the accurate determination of menstrual age. Knowledge of menstrual age is important to obstetricians because it affects clinical management in a number of important ways, which are as follows:

- Knowledge of menstrual age is used in early pregnancy for the scheduling of invasive procedures such as chorionic villous sampling, amniocentesis and in the interpretation of biochemical tests such as expanded maternal serum alpha-fetoprotein screening in which the normal range of values changes over time.
- Knowledge of menstrual age allows the obstetrician to anticipate normal spontaneous delivery or to plan elective delivery at term.
- Gestational age is important in evaluating fetal growth.
- Virtually all important clinical decisions require knowledge of menstrual age.
- Menstrual history could be misleading for a number of reasons, such as:
  - Many women may not accurately recall the first day of last menstrual period, particularly if they are not trying to conceive.
  - LMP may be unreliable or misleading because of oligomenorrhea, abnormal bleeding events, use of oral contraceptives and becoming pregnant in the first ovulatory cycle after a recent delivery.
  - Ovulating very early (< day 11) or very late (> day 21) in the menstrual cycle.

Majority of the obstetric sonograms are performed due to uncertainty regarding the gestational age. Objective knowledge of the expected date of delivery is essential in the management of all pregnancies particularly with regard to the method of termination of pregnancy, management of high-risk pregnancies, elective planned induction of labour and elective caesarean for previous caesarean section deliveries.

Presently, the most effective way to date pregnancy is by use of ultrasound. Ultrasonography helps in evaluating the duration of pregnancy based on measurement of the fetus, using size as an indirect indicator of menstrual age. The yolk sac is a round structure with an anechoic center and an echogenic rim, and is the first structure that can be identified within a true gestational sac. The yolk sac grows in size to reach its maximum diameter of 5 to 6 mm at 10 weeks gestation, and then gradually decreases. Its presence is diagnostic of a true gestational sac, with a positive predictive value of 100%.
Using transvaginal ultrasound, the yolk sac may first be visualized at a MSD of 5 mm, which corresponds to a gestational age of 5 weeks, and should be seen when the MSD measures 8 mm, which corresponds to 5.5 weeks. In early pregnancy, a small embryo at the threshold of detection can often be identified by its close approximation to the more obvious yolk sac. Yolk sac is the first ultrasonographic evidence of embryonic structure lying within the gestational sac seen as a round anechoic area, visible as early as fifth week. A large yolk sac with an undetectable embryo is an indicator of poor outcome of pregnancy. A regressing yolk sac is more specific than a large yolk sac in predicting the outcome of pregnancy. A normal yolk sac has a maximum diameter of 6 mm at 10 weeks gestation. Some studies have found that an abnormal yolk sac diameter is associated with subsequent pregnancy failure. An abnormal appearance of the yolk sac, such as an irregular shape, calcifications, increased echogenicity, or a duplicated yolk sac are all associated with early pregnancy failure.

It is estimated that approximately 10-15% of human pregnancies result in spontaneous abortion after implantation. The intrauterine gestational sac is the first one to appear sonographically, followed by the yolk sac and the fetal pole with cardiac activity. Significant number of losses occurs very early in gestation, but once the embryonic heart activity appears the rate of spontaneous abortion gradually decreases to 2.5%.

Trans-vaginal sonography can accurately demonstrate EHR (Embryonic Heart Rate) and assess the pregnancy outcome in those with bradycardia. The embryonic heart beat can usually be identified by ultrasonography at 6 weeks gestation in M-mode. Several studies have documented that a slow embryonic heart rate at 6.0–7.0 weeks gestation is associated with a high rate of fetal demise. High frequency transvaginal ultrasound can detect cardiac activity as early as 34 days of gestation. During the first trimester, cardiac rates vary with gestational age. Prior to 6 weeks, the heart rate is relatively slow and averages between 100 and 115 beats per minute (BPM). However, heart rates of 82 BPM at 5 weeks gestation and 96 BPM at 6 weeks gestation are associated with normal outcomes. Between 34 to 56 days of gestation, the embryonic heart rate increases by approximately 4 beats / min / day. The embryonic heart-rate peaks at 8 weeks gestation between 144 and 159 BPM, and after 9 weeks the rate plateaus at 137 to 144 BPM. Unlike the fetal heart-rate, there is minimal variation in the embryonic heart rate, so that a reliable heart rate can be obtained from a single measurement.
It is known that a slow heart rate is a risk factor for miscarriage. Specifically, a heart rate less than 100 BPM before 6.2 weeks, and less than 120 BPM between 6.3 and 7.0 weeks, has been associated with an increased rate of pregnancy loss. Embryonic heart-rates less than 80 BPM before 6.3 weeks gestation and below 100 BPM between 6.3 to 7 weeks have loss rates approaching 100%\(^{15}\). An embryo with a slow heart-rate that survives the first trimester has a relatively good prognosis. However, these pregnancies may be at increased risk for congenital anomalies and aneuploidy\(^ {16}\). Recent studies have investigated the size, structure and function of the yolk sac in addition to embryonic heart rate in evaluation and prognosis of first trimester pregnancy loss.

The purpose of the present study is to examine whether yolk sac diameter and early embryonic heart rate (EHR) could serve as prognostic factors in evaluating pregnancy outcome.

**MATERIALS AND METHODS**

**STUDY DESIGN** Cross sectional study

**STUDY POPULATION**

Patients attending obstetric OPD at CHRI with pregnancy in first trimester between 6 weeks to 10 weeks. Sixty eight cases with pregnancy in first trimester between 6 weeks to 10 weeks.

**STATISTICAL ANALYSIS:**

Analysis was done with SPSS version 22.0 software

Proportions and means were calculated.

Chi square tests and independent t test were applied

ROC curve analysis was done along with Sensitivity, specificity, PPV and NPV.

After obtaining informed consent

- Patients attending obstetric OPD at CHRI with pregnancy in first trimester between 6 weeks to 10 weeks.
- History, examination and routine investigations
- Ultrasound examination using transvaginal probe 7-11MHz with SEIMENS ACUSON 300X machine.
- Parameters collected are – yolk sac diameter and embryonic heart rate
- A scan is considered normal if all sonographic parameters are within normal limits for gestational age and considered abnormal if there are any deviations.
• Patients with abnormal parameters will be followed up with subsequent scan 2 weeks later. All patients are further followed up with a NT scan between 11 weeks -13.6 weeks.

• All patients will be further followed up with an anomaly scan between 18-20 weeks and pregnancy outcome will be noted.

RESULTS

Study was conducted in 70 antenatal low risk women after applying the exclusion and inclusion criteria. Current study evaluates the role of yolk sac and heart rate in predicting the outcome till 20 weeks. After taking informed consent, patient was subjected to a transvaginal scan and parameters such as yolk sac diameter, heart rate and CRL were evaluated. Among 70 women 64 progressed normally beyond 20 weeks of gestation. Six women had poor outcome either due to heart rate or yolk sac abnormality.

DISCUSSION

Before placenta is fully formed, the developing embryo derives its nutrition from yolk sac. The yolk sac reaches its highest level of functional activity between 4th and 7th week of gestation and meets metabolic, endocrine, immunologic and haemopoietic needs of embryo in early stages of its development. The appearance of yolk sac is a marker of successfully growing gestational sac and is identified by transvaginal ultrasound between 4th and 5th week of gestation prior to appearance of foetal pole and embryonic heart. It is a circular structure and identified by its thin echogenic rim and central hallow. The initial diameter is around 3-4 mm and gradually it increases at the rate of 0.1 mm per day and finally undergoes atresia by 10th to 11th week of pregnancy. Once the placental circulation is established, the blood supply to yolk sac gradually decreases and finally disappears. If a large yolk sac persists, it indicates aberrant embryonic development and high chance of miscarriage. Other variations in appearance of yolk sac include calcification, very small yolk sac (<2mm) and irregular yolk sac. The calcified yolk sac almost indicates impending pregnancy loss and on the other hand irregular rim of yolk sac can be still associated with successful pregnancy outcome. Our study focused on the diagnostic value of first trimester ultrasonography between 6-10 weeks of gestation. The development in the obstetric ultrasound 50 years ago mainly focussed on documentation of embryonic heart rate in the first trimester scan to confirm viability. Subsequently it was realized that slow embryonic heart rate was
associated with increased rate of spontaneous abortions \(^{25}\). Now it is universally known that embryonic heart rate serves as one of the important predictors of imminent fetal demise \(^{26, 27}\). Transvaginal ultrasonography has higher resolution and hence it can be used for visualization the embryonic heart beat in M mode. The embryonic heart rate can be visualized as early as 5 – 6 weeks of gestation and it is known that the mean heart rate progressively increases from 6 weeks (120 to 140 bpm) to 9 weeks (145 to 170 bpm) after which it slowly stabilizes to lesser heart rate for rest of the pregnancy \(^{28}\). It has been observed that embryonic heart rate less than 100 bpm (beats per minute) is associated with higher risk of miscarriage and the risk of embryonic demise almost touches 100 % when the rate is less than 80 bpm \(^{25, 29}\). The rate of chromosomal abnormalities and structural abnormalities are significantly higher in surviving foetuses when they have slow heart beat s \(^{30}\).

In this study 70 pregnancies in the 1st trimester (6-10 weeks) were analysed to determine the role of yolk sac and heart rate as a predictor of pregnancy outcome.

Our study reported maximum of population belongs to 25-29 age group (45.71%), and mean age group of the study population was 25.97. In this study 64.3% of study group was primigravidae.

**PREGNANCY OUTCOME IN THE STUDY POPULATION:**

In the present study we had 8.57 % incidence of abnormal pregnancy outcome. This is close with the study by Roth \(^{31}\) who estimated the frequency of spontaneous abortion to be 15% of recognizable pregnancies. In the study conducted by Lindsay \(^{32}\) to evaluate the role of yolk sac size and shape as predictor of pregnancy outcome, the incidence of abnormal pregnancy outcome was 32.7% (159/486).

But the criteria for defining an abnormal outcome varies in different studies, for example in our study, abnormal outcome was defined as spontaneous abortion, or missed abortion before 20 weeks of gestation whereas, Lindsay et al considered abnormal outcome as first trimester embryonic or fetal death or demonstrable fetal anomaly.

The study indicates that the probability of abnormal outcome decreases with the increase in gravidity of the patient with \(P = 0.049\). The result was found to be statistically significant.

**CORRELATION OF YOLK SAC WITH NORMAL AND ABNORMAL OUTCOME**
In this study, a highly significant positive correlation was found between normal yolk sac (n=65) and normal pregnancy outcome (n=63), and also between abnormal yolk sac (n=5) and abnormal pregnancy outcome (n=4). Our study showed that 80% cases with abnormal yolk sac ended in abnormal pregnancy outcome. In a study by Moradan et al., 63% of cases with abnormal yolk sac ended in spontaneous abortion. P value in our study was less than 0.05, hence statistically significant. The result showed that the probability of abnormal outcome increases with the abnormal yolk sac 66.7%.

**BIOMETRY OR GROWTH OF YOLK SAC WITH GESTATIONAL AGE IN PREGNANCIES WITH NORMAL OUTCOME:**

In our study, progressively increasing mean YSD was found with advancing gestational age between 6th and 9th week of gestation, from 4.4143 mm to 6.2818 mm following which it starts decreasing in size by 10th week.

Cepni et al. demonstrated the steady increase in YSD from 5 to 11 weeks of gestation in normal pregnancies after which it disappears by 12 weeks. Chama et al. [14] reported a linear increment in mean YSD from 2.27 mm at 5 weeks of gestation to 5.61 mm at 11 weeks of gestation. Lindsay et al. reported that yolk sac grows at a rate of approximately 0.1 mm per mm growth of the MSD when the MSD is less than 15 mm and then slows to 0.03 mm per mm growth of MSD.

In the present study Chi square test was applied to test the significance of difference between the means of YSD of normal and abnormal pregnancy outcome. The difference between the mean yolk sac diameters between normal and abnormal outcomes was significant with P value less than 0.05.

**VALUE OF ABNORMAL YOLK SAC DIAMETER AS A PREDICTOR FOR ABNORMAL PREGNANCY OUTCOME**

In this study a range of yolk sac diameter with 95% confidence limits was established based on the pregnancies with normal outcomes for each gestational week. With respect to this range, there were 5 pregnancies with abnormal yolk sac diameter; all of them measuring lesser than 2SD below the mean and 4 of those pregnancies subsequently had an abnormal outcome.

For a yolk sac diameter which is lesser than the 2SD below the mean, the sensitivity of predicting an abnormal outcome was 66.7%, the specificity was 98.7% and PPV was 33.7% (P < than 0.05) in comparison to 15.6%, 95.3% and 44.4% respectively, reported by Lindsay et al. The results of our study are more likely comparable to the...
results of the study by Kucuk et al. They found a yolk sac diameter of 2 standard deviations of the mean for the menstrual age allowed prediction of an abnormal pregnancy outcome with a sensitivity of 65%, a specificity of 97%, and PPV of 71% which were comparable to our study group sensitivity-66.7 %, specificity-98.7 %, PPV of 33.7 % respectively found in our study.

**DISTRIBUTION OF OUTCOME WITH RESPECT TO HEART RATE:**
In this study Embryonic heart rate with 95% confidence limits was established based on the pregnancies with normal outcomes for each gestational week. Our study reported progressively increasing mean embryonic heart rate was found with advancing gestational age between 6th and 9th week of gestation, from 127.79 to 153.00 BPM. Similarly Shenker L, et al. carried out a study on embryonic heart rates before the seventh week of pregnancy which showed an increase in the rates between the 7th and 9th gestational weeks; the rates gradually declined thereafter until the 15th week.

The results of the present study indicate that first trimester fetuses with normal sized and normally appearing yolk sacs and embryonic heart rate above 100 bpm are associated with 66.7% sensitivity, 100% specificity, 33.3% positive predictive value and 0% of negative predictive value in predicting outcome. The diagnostic accuracy of heart rate was found to be 92.8%. Similarly, Chittacharoen et al. reported that a fetal heart rate <120 bpm was associated with a high likelihood of pregnancy loss. The sensitivity, specificity, positive and negative predictive value, and accuracy were 54.2%, 94.8%, 72.2%, 89.2%, and 86.7%, respectively. This was the best cutoff point for prediction of pregnancy outcome. The results of this study confirm that fetal demise tends to occur well before the end of the first trimester.

**CONCLUSION**
Normal yolk sac and normal embryonic heart rate are both good predictors for successful pregnancy outcome. Amongst the two parameters EHR is more specific in predicting an adverse outcome of pregnancy.

As our study was performed on a low risk population, identification of either abnormal yolk sac diameter or EHR allows us to closely monitor the index pregnancy and predict occurrence of complications. This will help us to counsel the patient appropriately.

**REFERENCES**


