Original Article

YOLK SAC DIAMETER AND EMBRYONIC HEART RATE AS PROGNOSTIC FACTORS OF FIRST TRIMESTER PREGNANCY OUTCOME

NAMRATHA H. R.*, SOWMYA K.

Department of Obstetrics and Gynecology, Kempegowda Institute of Medical Science Hospital, Bangalore, Karnataka, India
*Corresponding author: Namratha H. R.; *Email: namratha.hr91@gmail.com

ABSTRACT

Objective: Yolk sac is the primary source of exchange between the embryo and the mother before placental circulation and during organogenesis. Yolk sac has immunologic, metabolic, nutritive, endocrine, secretory, excretory and hematopoietic functions. Embryonic heart rate is seen after the appearance of foetal node at 7 w by TAS and 6 w by TVS. Studies have been conducted to establish the importance of yolk sac and EHR in pregnancy outcome. The prognostic significance of the yolk sac for the pregnancy outcome has been assessed with TVS. To measure yolk sac diameter and embryonic heart rate in early pregnancy (less than 10 weeks), to correlate yolk sac measurement and embryonic heart rate individually as prognostic factors for first trimester outcome and to evaluate the measurements in combination as a prognostic marker of first trimester pregnancy outcome. In view of this, the present study was undertaken.

Methods: 108 patients attending OPD of Kempe Gowda institute of Medical Sciences Hospital, between 6 to 9 w of gestation, were evaluated with transvaginal sonography and measurements such as CRL, MSD and YSD were taken.

Results: The mean age of the study population was 25 y and 88 % of the study population belonged to 20-30 y. 55.6 % of the study population were primigravida. Incidence of abnormal pregnancy outcome was 18.5%. The probability of abnormal outcome increased with the increase in gravidity of the patient (P= 0.890). There was a significant positive comparison of CRL (P= 0.223), GS (P= 0.251) and YSD (P= 0.016). Yolk sac diameter in the first trimester significantly correlates with the pregnancy outcome. An enlarged yolk sac is associated with an increased risk of preterm delivery. Our study influences the pregnancy outcome by the Embryonic heart rate. Foetal bradycardia is an impending sign of foetal death due to chromosomal abnormalities (Trisomy 18), foetal tachycardia featuring Trisomy 21.

Conclusion: Yolk sac diameter and embryonic heart rate in the first trimester significantly correlates with the first trimester pregnancy outcome. Thus, the present study indicates that the yolk sac size and the embryonic heart rate is a reliable, beneficial and cost-effective in predicting first-trimester pregnancy outcome. The measurement of the secondary yolk sac diameter between 5th to 9th week of gestation can be used as a valuable tool to predict early pregnancy outcome.

Keywords: Yolk sac**,** First trimester**,** Foetal outcome, Amniotic fluid index

INTRODUCTION

Early pregnancy failure or spontaneous abortions in the first trimester is one of the most frequent complications of pregnancy, amounting to 30 % (Williams Gynecology). As the women planning pregnancy is advancing, artificial reproductive technique come into play and with the trend of "One child norm," the couple is anxious about the outcome of pregnancy from the very beginning. Great difficulty is still experienced in reliably anticipating pregnancies which may continue beyond first trimester or which may terminate in abortion [1]. Therefore, there is a need for technique that allow early diagnosis to be made in such patients so that a more active line of management can be performed.

The advent of high-resolution Transvaginal Ultrasound (TVS) has revolutionized our understanding of the pathophysiology and the management of early pregnancy failure. The first extraembryonic structure, the secondary yolk sac can be detected with transvaginal sonography in the chorionic cavity from 5th to 12th w menstrual age [2].

Yolk sac is the primary source of exchange between the embryo and the mother before placental circulation and during organogenesis. Yolk sac has immunologic, metabolic, nutritive, endocrine, secretory, excretory and hematopoietic functions [3]. Embryonic heart rate is seen after the appearance of foetal node at 7 w by TAS and 6 w by TVS [2, 4]. Studies have been conducted to establish the importance of yolk sac and EHR in pregnancy outcome. The prognostic significance of the yolk sac for the pregnancy outcome has been assessed with TVS. In view of this, the present study was undertaken.

MATERIALS AND METHODS

- **Study design:** Prospective study

- **Study duration:** 18 mo (November 2016 to July 2018)

- **Study area:** Kempe Gowda Institute of Medical Sciences Hospital and Research centre Bangalore.

- **Study participants:** Patients attending Obstetric OPD at Kempe Gowda Institute of Medical Sciences Hospital and Research centre Bangalore.

- **Inclusion criteria**

- Pregnant women at menstrual age less than 10 w.

- **Exclusion criteria**

- Patients with medical disorders (HTN, DM)

- Genital tract pathology like fibroids

- Congenital structural anomalies of the uterus and cervix.

- First trimester bleeding per vagina at inclusion to the study

- Recurrent abortions

- Multiple pregnancy

Method of data collection

Informed consent was taken from the antenatal women with a gestational age of less than 10 w for inclusion in the study. General

information like Age, parity etc were noted. Consent taken from the patient for the performance of Transvaginal scan, a 7.7MHz transducer used to perform scan. The probe head was cleaned and covered with a condom after applying ultrasonic jelly. The tip of the condom smeared with lignocaine jelly for smooth insertion into the vagina. Patient in dorsal position, the probe was inserted slowly into the vagina. The probe rotated from 12 'o' clock to 9 'o' clock position to obtain transverse section of the uterus. Gestational age by crown-rump length, Gestational sac diameter, foetal cardiac activity, yolk sac diameter was measured. The yolk sac diameter is determined after magnification of the image and by placing out-to-out calipers on the inner limits of the longer diameter. An average of 3 measurements was taken. Embryonic heart rate was measured transvaginally using M-mode sonography. Patients had antenatal checkup, investigations and treatment as per hospital protocol. Patients were followed up till 12 w of gestation when NT scan was performed and healthy pregnancy was confirmed. The outcome at 12 w was considered normal if pregnancy continued beyond 12 w and abnormal outcome if there was spontaneous abortion or blighted ovum or missed abortion.

Estimation of sample size

On the basis of statistics obtained from Department of Medicine, KIMS Medical College and Hospital, an average of 8 cases per month fitting the criteria of the study with study duration of 18 mo, we can expect to have N=144. Based on this population size, using YAMANE equation, for a known population size, sample size (n) equal to

$n = N/1+Ne2$

n=sample size

N=population size

e= margin of error (for 95% of confidence level, margin error =0.05)

n=144/1+144*0.05*0.05 = 144/1.36 = 105.88

Therefore, after approximating, the sample size of the study participants was fixed at 108.

RESULTS

In the present study 108 first-trimester cases, who attended Kempegowda Institute of Medical Sciences Hospital, Bangalore were included as per inclusion criteria and data was collected. The first-trimester pregnancy outcome was evaluated by miscarriage or normal continuation of pregnancy.

The study was conducted in 108 antenatal women between 6 to 10 w of gestational age, after excluding those who met the exclusion criteria previously mentioned.

Mean age was 25.56 y with minimum 18 y and maximum of 40 y.

Table 1: Distribution of the study participants according to their age group

Age	Frequency N	Percentage%
18-20 y	4	3.7
20-30 y	95	88.0
31-40 y	9	8.3
MEAN+SD	25.56±3.81	

88.0% of the study participants belonged to the age group 20-30 years of age. The mean age of the study participants was found to be 25.56±3.81years of age.

Table 2: Gestational Age (weeks) distribution

Gestational Age (weeks)	Frequency N	Percentage %
5-6	14	13.0
6-8	80	74.1
9-10	14	13.0
MEAN+SD	51.91±8.70	

74.1 % of the study population belonged to the gestation of 6-8 w. The mean gestational age of the present study was found to be 51.91±8.70 w.

Table 3: Crown-rump length (cm) distribution

Crown-rump length (cm)	Frequency N	Percentage%
<0.4	22	20.4
0.4-1.8	74	68.5
>1.8	12	11.1
Mean+SD	0.96±0.65	

68.5% of the study population had CRL between 0.4-1.8 cm. The mean CRL of the present study was found to be 0.96±0.65 cm.

Table 4: Gestational SAC (cm) distribution

Gestational SAC (cm)	Frequency N	Percentage %
<1.7	29	26.9
1.7-2.5	37	34.3
>2.5	42	38.9
Mean+SD	2.34±0.89	

38.9% of the study population had gestational sac size>2.5 cm. The mean CRL of the present study was found to be 2.34±0.89 cm.

Table 5: Yolk sac (cm) distribution

Yolk sac (cm)	Frequency N	Percentage %
<0.4	36	33.3
0.4-0.6	68	63.0
>0.6	4	3.7
Mean+SD	0.45±0.17	

63.0% of the study population had yolk sac size in the range of 0.4-0.6 cm. The mean CRL of the present study was found to be 0.45±0.17 cm.

Table 6: Foetal heart rate (bpm) distribution

Foetal heart rate (bpm)	Frequency N	Percentage %
<140	32	29.6
140-160	41	38.0
>160	15	13.9
NA	20	18.5
Mean+SD	146.68±15.30	

The heart rate of the foetus ranged between 140-160, with a mean of 146.68. The heart rate of the foetus predicted the first-trimester pregnancy outcome.

Table 7: Outcome distribution of patients

Outcome	Frequency N	Percentage %
Normal	88	81.5
Abnormal	20	18.5
Missed abortion	16	14.8
Spontaneous abortion	4	3.7

18.5% of patients had abnormal outcome in study population.

Table 8: Association of CRL/GS/YS with the outcome of patients

Variables	Outcome			Total	P value
	Normal	Missed abortion	Spontaneous abortion		
CRL	0.98±0.65	0.99±0.70	0.41±0.17	0.96±0.65	0.223
GS	2.39±0.85	2.28±1.12	1.64±0.51	2.34±0.89	0.251
YS	0.43±0.08	0.56±0.40	0.41±0.05	0.45±0.17	0.016*

There is a significant correlation between CRL and gestational sac diameter. The yolk sac diameter increases as the CRL, gestational sac diameter and gestational age increases

DISCUSSION

Miscarriage occurs in approximately 30-40% of implanted pregnancies, which is the commonest complication of pregnancy [5]. Numerous studies have examined the potential value of demographic characteristics and various ultrasonographic parameters in the prediction of those pregnancies that will miscarry. These studies have reported an association between increased risk for miscarriage and advanced maternal age, previous history of miscarriage, foetal bradycardia, vaginal bleeding, early-onset foetal growth restriction.

In our prospective study, 108 antenatal women were included belonging to first trimester who attended Kempegowda Institute of Medical Sciences Hospital during November 2016 to July 2018. Our study supports the fact that as the maternal age increases, chances of spontaneous abortion also increase. Studies have also shown that the rate of spontaneous abortion following cardiac activity is influenced by maternal age [6]. So, a cardiac activity is not necessarily a reassuring sign in the older patient.

The mean age of the study population was 25.56 y and 88% of the study population belonged to the age group of 20-30 y. In this study, 55.6 % of the study population were primigravida.

In our study, abnormal outcome was defined as spontaneous abortion, or missed abortion before 24 w of gestation or demonstrable foetal anomalies. Lindsay *et al.* considered abnormal outcome as first-trimester embryonic or foetal death or demonstrable foetal anomaly. In an Indian study Nawal Rajani *et al.* [7], the incidence of abnormal outcome was 20% which included missed abortion and blighted ova before 12 w of gestation.

In our study, the probability of abnormal pregnancy outcome did not vary with maternal age. This is contradictory to the results of previous studies, which show an increase of miscarriage with an increase in maternal age. According to these studies, until age 30, the incidence of miscarriage is around 12%, then increases rapidly, exceeding to 50% in women older than 45 y.

The present study shows that a history of previous abortion increases the risk of abnormal outcome in subsequent pregnancies.

Previous abortions have significantly influenced the present pregnancy. Among 39 cases with previous abortions, 6 of them aborted in the present pregnancy. According to Soyoung Bae *et al.* [8], for women with a history of recurrent pregnancy loss, if embryonic cardiac activity, yolk sac and gestational sac markers were present, the rate of accurate positive prediction was 94%, but any change in these parameters may affect current pregnancy as per the study. Makrydimas *et al.* [9] seem to agree with the negative impact of advanced age and history of miscarriages to subsequent pregnancy outcome. During the first trimester, the increase in yolk sac diameter and its correlation with gestational age lie in agreement with most of the previous studies [10]. Cepni *et al.* [10] demonstrated the steady increase in YSD from 5 to 11 w of gestation in normal pregnancies after which it disappears by 12 w.

Lindsay *et al.* [11] 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 the slows to 0.03 mm per mm growth of MSD.

Embryonic heart rate has a significant correlation with the first trimester outcome in our study. FHR studies have demonstrated a strong association between pathological FHR and foetal loss. Foetal bradycardia is a sign of impending foetal death, reflecting the forthcoming collapse of the cardiovascular system. Abnormal FHR is another miscarriage that may be an underlying chromosomal abnormality as in trisomy 18, which is associated with foetal bradycardia and trisomy 21 (Down Syndrome) with foetal tachycardia [12].

The Ultrasonographic estimation of gestational age in our study has significant correlation with pregnancy outcome (p<0.001**). In previous studies of 6337 pregnancies reported an inverse correlation between gestation and rate of subsequent foetal loss, which decreased by 1% per week from 9.6% at 7 w to 2.3 at 14 w.

Lindsay *et al.* [11] reported that no pregnancy with normal outcome had a yolk sac diameter of greater than 5.6 mm at less than 10 w of maternal age. In 6 patients, the yolk sac diameter was more than 5.6 mm. All 6 had abnormal outcome. In our study, no pregnancy with a normal outcome had yolk sac diameter more than 6.4 mm, between

5 to 9 w GA and 3 cases had yolk sac diameter more than 6.4 mm, all had missed abortion.

The routine use of TVS in the investigation and diagnosis of early pregnancy problems has been led to improving in the management of early pregnancy loss [13]. Increase in awareness among women and improved access to early pregnancy units led to choices in the management of early pregnancy problems and led to increasing demand for more conservative management of early miscarriage. Nearly 70% of women will choose expectant management of miscarriage when given choice. Hence, for this purpose, the predictors of early foetal demise and monitoring is essential. Therefore, follow up scans for all patients were followed.

CONCLUSION

The conclusion drawn from the present study that the measurement of the secondary yolk sac diameter between 5th to 9th week of gestation can be used as a valuable tool to predict early pregnancy outcome. Finally, the data available from the literature and results based on the study is certain that abnormal yolk sac diameter is associated with poor pregnancy outcome. Thus, the present study indicates that the yolk sac size and the embryonic heart rate is are reliable, beneficial and cost-effective in predicting first-trimester pregnancy outcome.

FUNDING

Nil

AUTHORS CONTRIBUTIONS

All authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

REFERENCES

1. Cunningham FG, Bloom SL, Hauth JC, Rouse DJ, Spong CY. Implantation, embryogenesis and placental development. In: Williams obstetrics. 23rd ed. McGraw-Hill; 2010.
2. Kaur A, Kaur A. Transvaginal ultrasonography in first trimester of pregnancy and its comparison with transabdominal ultrasonography. J Pharm Bioallied Sci. 2011;3(3):329-38. doi: 10.4103/0975-7406.84432, PMID 21966152. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3178938.
3. Ross C, Boroviak TE. Origin and function of the yolk sac in primate embryogenesis. Nat Commun. 2020 Jul 28;11(1):3760. doi: 10.1038/s41467-020-17575-w, PMID 32724077.
4. Murugan VA, Murphy BO, Dupuis C, Goldstein A, Kim YH. Role of ultrasound in the evaluation of first-trimester pregnancies in the acute setting. Ultrasonography. 2020 Apr;39(2):178-89. doi: 10.14366/usg.19043, PMID 32036643.
5. Knudsen UB, Hansen V, Juul S, Secher NJ. Prognosis of a new pregnancy following previous spontaneous abortions. Eur J Obstet Gynecol Reprod Biol. 1991 Mar 21;39(1):31-6. doi: 10.1016/0028-2243(91)90138-b, PMID 2029953.
6. Smith KE, Buyalos RP. The profound impact of patient age on pregnancy outcome after early detection of fetal cardiac activity. Fertil Steril. 1996 Jan;65(1):35-40. doi: 10.1016/s0015-0282(16)58024-8, PMID 8557152.
7. Rajani N, Sushila K, Deepika J, Rakesh P, Vinay M. To assess value of yolk sac in predicting pregnancy outcome during first trimester: observational study. Natl J Med Res. 2012 Sep;2(3):343-7.
8. Bae S, Karnitis J. Triple ultrasound markers, including fetal cardiac activity, are related to miscarriage risk. Fertil Steril. 2011 Nov 1;96(5):1145-8. doi: 10.1016/j.fertnstert.2011.08.009, PMID 21890130.
9. Makrydimas G, Sebire NJ, Lolis D, Vlassis N, Nicolaides KH. Fetal loss following ultrasound diagnosis of a live fetus at 6-10 w of gestation. Ultrasound Obstet Gynecol. 2003 Oct;22(4):368-72. doi: 10.1002/uog.204, PMID 14528471.
10. Cepni I, Bese T, Ocal P, Budak E, Idil M, Aksu MF. Significance of yolk sac measurements with vaginal sonography in the first trimester in the prediction of pregnancy outcome. Acta Obstet Gynecol Scand. 1997 Nov;76(10):969-72. doi: 10.3109/00016349709034911, PMID 9435738.
11. Moradan S, Forouzeshfar M. Are abnormal yolk sac characteristics important factors in abortion rates? Int J Fertil Steril. 2012;6(2):127-30. PMID 25493170.
12. Liao AW, Snijders R, Geerts L, Spencer K, Nicolaides KH. Fetal heart rate in chromosomally abnormal fetuses. Ultrasound Obstet Gynecol. 2000 Dec;16(7):610-3. doi: 10.1046/j.1469-0705.2000.00292.x, PMID 11169365.
13. Papaioannou GI, Syngelaki A, Maiz N, Ross JA, Nicolaides KH. Ultrasonographic prediction of early miscarriage. Hum Reprod. 2011 Jul;26(7):1685-92. doi: 10.1093/humrep/der130, PMID 21531997.