

Evaluation of Yolk Sac Diameter, gestational sac diameter and Embryonic Heart Rate as Prognostic Factors of First Trimestric Outcome

Mohamed Adel Mohamed Mohamed Soliman ^{1,*} M.B.B.Ch, Mohammad Salah El Din Hassanin ¹ MD
and Bassem Ragab Abdel-Aziz ¹ MD.

*Corresponding Author:

Mohamed Adel Mohamed Mohamed Soliman
Mohamedadel2011@live.com

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¹Obstetrics and Gynecology
Department, Faculty of Medicine,
Al-Azhar University Cairo, Egypt.

ABSTRACT

Background: Ultrasonography is a helpful tool for assessing the state of a pregnancy in its early stages. Sonography in the first trimester is important for determining gestational age, determining location, and even discovering some early malformations. Ultrasonography has a high sensitivity for detecting anomalies of the gestional sac, yolk sac, and embryo that indicate a poor outcome, in addition to documenting normal development.

Aim of the work: To see if the size of the yolk sac, the size of the gestational sac, and the early embryonic heart rate (EHR) may be used to predict pregnancy outcome.

Patients and methods: During the period of January 2021 to June 2021, 200 patients in the outpatient clinic of the obstetrics and gynaecology department of Al-Azhar University hospitals in uncomplicated singleton pregnancy were studied.

Results: The median yolk sac diameter in the ongoing pregnancy group was (2.28+1362 mm) at 6 weeks, compared to (1.76+0.652 mm) in the miscarrying group. Size and shape anomalies of the yolk sac can be utilised as an effective predictor of early gestational loss. The mean gestational sac diameter at 6 weeks in a continuing pregnancy (15.73+1.98 mm) versus (13.86+1.96 mm) in the miscarrying group. The mean embryonic heart rate in the continued pregnancy group was (117.14+8.28) compared to (88.80+15.41) in the miscarrying group at 6 weeks.

Conclusion: The results of a first-trimester vaginal ultrasound can be utilised to evaluate pregnancies that have been complicated by a negative obstetric history. Embryonic heart rate; yolk sac diameter; gestational sac diameter.

Keywords: yolk sac diameter; Gestational sac diameter; Embryonic heart rate.

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INTRODUCTION

Within the first 14 weeks after conception, an obstetrician or healthcare professional will do a first-trimester ultrasonography. It may be utilized as part of a routine prenatal exam or to explain any troubling clinical manifestations (e.g., vaginal bleeding, the suspected passage of fetal tissue, etc.).¹ According to estimates, around 34% of human pregnancies terminate in spontaneous abortion during the first three months of pregnancy after implantation.. Early in pregnancy, a large number of losses occur, but as embryonic heart activity develops, the frequency of spontaneous abortion gradually drops to 2-5 percent.² Sonographically the intrauterine gestational sac is the first to emerge, followed by the yolk sac and the fetal pole with heart activity. Within the gestational sac,

the yolk sac is the earliest apparent embryonic structure. Between the fifth and twelve weeks of gestation, it appears as a circular anechoic region, which thereafter degenerates.³

When the gestational sac diameter is between 5 and 8 mm, trans-vaginal sonography can easily detect a yolk sac. When a gestational sac measures more than 8mm, it is widely agreed that the yolk sac should be examined.⁴ The vitelline duct connects the yolk sac to the embryo. The yolk sac is usually observed as a circular structure with a well-defined echogenic wall and an anechoic core. A yolk sac's inner diameter is typically 3 to 5 mm.⁵ The yolk sac's size, shape, and function, as well as embryonic heart rate, have all been studied in the evaluation and prognosis of first-trimester pregnancy loss. We can reliably demonstrate EHR (Embryonic Heart Rate) and

determine the pregnancy outcome in patients with bradycardia using trans-vaginal sonography.⁶ Prenatal ultrasonography in M-mode can usually detect the embryonic heart rhythm by 6 weeks of pregnancy. A sluggish embryonic heart rate around 6.0-7.0 weeks gestation has been linked to a higher rate of first trimester fetal death, according to several studies, and the death often happens quickly after the slow heart beat is diagnosed.⁷The goal of this study was to see if the size of the yolk sac, the size of the gestational sac and the early embryonic heart rate (EHR) could be used to predict pregnancy outcome.

PATIENTS AND METHODS

This prospective cohort study was done on 200 patients in outpatient clinics of obstetrics and gynecology department Al-Azhar University hospitals, in uncomplicated singleton pregnancy during period from January 2021 to June 2021. First scan done at 1st antenatal visit (6-9weeks) and repeated every 2 weeks. Inclusion criteria: Patient is sure of her dates, gestational age between (6-9)wks, singleton pregnancies, uncomplicated and patient age from (18-34) years old.

Exclusion criteria: Unsure patient date, any uterine pathology as myomas of malformation, previous pregnancies complicated by blighted ovum, threatened abortion, miscarriages and absent embryonic cardiac activity, patients with any medical disorders as: anemia, hyperthyroidism, diabetes, chronic high blood pressure, and molar pregnancy and an-embryonic sac.

Ethical consideration: Informed written & verbal consents was acquired from all participants in the study. Ethically approved by the department.

All patients were subjected to: On the basis of inclusion/exclusion criteria, all pregnant women who came to clinic in their first trimester of pregnancy were counselled and recruited for the study. A full medical and surgical history was gathered to eliminate any medical or surgical concerns that could distress our study (obstetric and menstrual history), as well as to determine the patient's date of birth. Obstetric history, such as bio-data or personal history, complaints, history of presenting complaints, hospitalization, current pregnancy history, past obstetric history, menstruation history, contraceptive history, past medical & surgical history, drug history and allergies, systemic review, family history, and social history.

The menstrual history is made from of Catamenia or P/C (Period/Cycle) is the first day of the last menstrual period (LMP). Regular? Sure? Is it dependable or not? , Expected delivery date (EDD).

General and physical examination was done.

A general and physical examination were performed on the patient.

Statistical analysis:

Statistical Package for Social Science was used to tabulate and analyse the gathered data (SPSS). To analyse categorical data expressed as a number and a percentage, the "Chi square" or "Z" test was utilised. To analyse continuous variables, the "Student t" test was utilised which were reported as mean and standard deviation. Other appropriate significance tests were performed as required by the situation. In this study, the recognised level of significance was 0.005, (P0.005 was considered significant).

RESULTS

	Frequency	Percent
Miscarriage rate	12	6%
Ongoing pregnancy rate	188	94%

Table 1: Rate of miscarriage as a percent of the study's total population.

Miscarriage rate in relation to the total number of the study was 6%. Patients were classified into 2 groups: Ongoing pregnancy group = group 1 (188 patients), and miscarriage group = group 2 (12 patients) (Table 1).

		Group 1	Group 2	P. value
Age (years)	Median+SD	26.41+4.048	24.17+3.973	<0.063
weight(kg)	Mean+SD	79.81+9.545	75.50+10.596	<0.134
parity	Mean+SD	1.03+1.049	1.17+1.115	<0.668

Table 2: Comparison between group 1 and group 2 regarding age, weight and parity. When comparing age, weight, and parity in groups 1 and 2, the median age in group 1 was 26.41+4.048, whereas the median age in group 2 was 24.17+3.973. In terms of age, between groups 1 and 2, there was no statistically substantial variance (p value 0.063). The mean weight in group 1 was 79.81+9.545, while in group 2 it was 75.50+10.596. Weight differences between groups 1 and 2 were not statistically relevant (p value 0.134). Group 1 had a mean parity of 1.03+1.049, whereas group 2 had a mean parity of 1.17+1.115. There was no statistically substantial variance in parity between groups 1 and 2 (p. value 0.668). (Table 2).

		Group 1	Group 2	P. value
yolk sac at 6 week	Mean±SD	2.28±.362	1.76±.652	< 0.001
yolk sac at 8 week	Mean±SD	3.79±.371	2.86±1.716	< 0.001
yolk sac at 10 week	Mean±SD	5.90±.693	5.18±0.367	< 0.0.01

Table 3: Comparison of groups 1 and 2 in terms of yolk sac at 6, 8, and 10 weeks. When comparing yolk sac at 6 weeks between groups 1 and 2, the median value of yolk sac in Group I was 2.28 +.362 compared to 1.76 +.652 in

Group 2. At 6 weeks, there was important variation between groups 1 and 2 in terms of yolk sac (p value 0.001). At 8 weeks, the mean value of yolk sac in group 1 was 3.79 +.371 against 2.86 + 1.716 in group 2. At 8 weeks, there was a statistically substantial variance between groups 1 and 2 in terms of yolk sac (p value 0.001). At 10 weeks, the mean value of the yolk sac in group 1 was 5.90 +.693 compared to 5.18 + 0.367 in group 2. At 10 weeks, there was a statistically substantial variance between groups 1 and 2 in terms of yolk sac (p value 0.001). (Table 3).

		Group 1		Group 2		P.value
Yolk sac shape (regularity)	Regular	No.	188	8	< 0.001	
		%	100.0%	66.7%		
	Irregular	No.	0	4		
		%	0%	33.3%		
	Total	No.	188	12		
		%	100.0%	100.0%		

Table 4: In terms of yolk sac morphology, group 1 and group 2 are compared. When comparing the Yolk sac shapes of Group 1 and Group 2, 188 (100%) of Group 1 had regular shapes compared to 8 (66.7%) of Group 2. In terms of yolk sac form, there was a statistically substantial variance between Groups 1 and 2. (p. value 0.001) (Table 4).

		Group 1	Group 2	P. value
Gestational sac at 6 week	Mean±SD	15.73±1.98	13.86±1.96	0.002
Gestational sac at 8 week	Mean±SD	30.99±3.22	22.85±7.49	< .001
Gestational sac at 10 week	Mean±SD	39.26±3.26	26.70±11.30	< .001

Table 5: Comparison of mean gestational sac diameters in groups 1 and 2 at 6.8 and 10 weeks.

When comparing the mean gestational sac diameter at 6 weeks across groups 1 and 2, the mean value for group 1 was 15.73+1.98 mm, while the mean value for group 2 was 13.86+1.96 mm.

In terms of gestational sac at 6 weeks, there was a statistically substantial variance between groups 1 and 2 (p. Value =.002). At 8 weeks, the mean value of gestational sac in group 1 was 30.99 + 3.22, while in group 2 it was 22.85+7.49. In terms of gestational sac at 8 weeks, there was a statistically substantial variance between groups 1 and 2 (p. Value 0.001). At 10 weeks, the mean value of gestational sac in group 1 was 39.26 + 3.26, while in group 2 it was 26.70 +11.30. At 10 weeks, there was a statistically substantial variance between group 1 and group 2 gestational sacs (p. Value 0.001). (Table 5).

	Cut off value	AUC	Sensitivity %	Speci licity%	PPV %	NPV %	Accuracy
Yolk sac	2.48	.69	93%	81.3%	99.1%	86.4%	92%
Gestational sac	15.6	.90	91%	80.5%	85/2%	81.4%	88%
Embryonic heart rate	119.5	.92	99.3%	83.3%	93.1%	88.4%	98%

Table 6: Sensitivity, specificity, PPV and NPV of yolk sac diameter, gestational sac diameter and embryonic heart rate in prediction of miscarriage.

It was 93% in sensitivity, 81.3% in specificity, 99.1% in PPV and 86.4% in NPV of yolk sac diameter. It was 91% in sensitivity, 80.5% in specificity, 85.2% in PPV and 81.4% in NPV of mean gestational sac diameter. It was 99.3% in sensitivity, 83.3% in specificity, 93.1% in PPV and 88.4% in NPV of embryonic heart rate (Table 6).

DISCUSSION

This study showed that Abortion (miscarriage) occurred in 12 cases (6%) compared to ongoing pregnancy 188 cases (94%), regarding comparison between the miscarriage and ongoing pregnancy groups regarding maternal age, weight and parity, mean value of maternal age in ongoing Pregnancy group was 26.41 ± 4.048 years comparing to 24.17 ± 3.973 years in miscarriage group. There was no statistically substantial variance between the miscarriage and ongoing Pregnancy group regarding age (p. value= <.063). Mean value of weight in ongoing pregnancy group was 79.81 ± 9.545 compared to 75.50 ± 10.596 in miscarriage group.

There was no statistically substantial variance between the miscarriage and ongoing pregnancy groups regarding weight (p. value = < 0.134). Mean value of parity in ongoing pregnancy group was 1.03 ± 1.049 compared to 1.17 ± 1.115 in miscarriage group. There was no statistically substantial variance between the miscarriage and ongoing pregnancy groups regarding parity (p. value = < .668). This agrees with Wie et al.⁸ who found that, In terms of maternal age, maternal weight, and parity, there was no statistically substantial variance between the miscarriage and ongoing pregnancy groups (p. value =.241). Maternal age and a history of recurrent abortion have been associated to miscarriage. 9 In pregnancies with a viable foetus at 6-10

weeks' gestation, the rate of future foetal loss is connected to maternal age, gestation, cigarette smoking, history of vaginal haemorrhage, and ultrasound findings of small gestation sac diameter and foetal bradycardia. 10 Foetal loss risk rises with maternal age, from roughly 4% for those under 20 to around 20% for those over 35; falls with gestation, from around 10% for those having viable foetuses at 6 weeks to around 3% at 10 weeks; and is 2.6 times higher in women than in males. who have had vaginal bleeding during pregnancy than in those who haven't. This study showed that, regarding comparison between the miscarriage and ongoing pregnancy groups regarding abdominal pain, it was present among 4 (2.1%) and absent among 184 (97.9%) in ongoing pregnancy group comparing to present among 4 (33.3%) and absent among 8 (66.7%) in miscarriage group. There was statistically substantial variance between the miscarriage and ongoing pregnancy groups regarding abdominal pain (p. value < .000). This disagrees with Wie et al.⁸ who found that, there was no statistically significant difference between the miscarriage (abdominal pain present in 23.3%) and ongoing pregnancy groups (abdominal pain present in 13.9%) regarding abdominal pain (p. value = < .191). In terms of abdominal discomfort, only period pain has been linked to miscarriage.¹¹

This study showed that, regarding vaginal bleeding, it was present among 6 (3.2%) and absent among 182 (96.8%) in ongoing pregnancy group compared to present among 6 (50.0%) and absent among 6 (50.0%) in miscarriage group. There was statistically substantial variance between, the miscarriage and ongoing pregnancy groups regarding vaginal bleeding (p. value = < .000). This disagrees with Wie et al.⁸ who found that, There was no statistically substantial variance between the miscarriage (vaginal bleeding present in 30%) and ongoing pregnancy groups (vaginal bleeding present in 27.8%) regarding vaginal bleeding (p. value = < .827). Heavy haemorrhage was linked to a higher risk of miscarriage in previous research, while spotting or mild bleeding was not..^{11,12}

This study found that when comparing the yolk sac diameter at 6 weeks in the miscarriage and ongoing pregnancy groups, the mean value of the yolk sac at 6 weeks in the ongoing pregnancy group was 2.28 ± 0.362 mm compared to 1.76 ± 0.652 mm in the miscarriage group. In terms of yolk sac at 6 weeks, There was a statistically substantial variance between the miscarriage and continuous pregnancy groups (p. value = .001). The mean diameter of the yolk sac in the continued pregnancy group was 3.79 ± 0.371 mm at 8 weeks, compared to 2.86 ± 1.716 mm in the miscarriage group. Between the miscarriage and continuing pregnancy groups, there was a statistically substantial variance in yolk sac at 8 weeks (p. value = .000). The yolk sac diameter in the sustained pregnancy group was 5.90 ± 0.693 mm at 10 weeks, compared to 5.18 ± 0.367 in the miscarriage group. Between the miscarriage and continuing

pregnancy groups, there was a statistically substantial variance in yolk sac at 10 weeks (p. value = .000). According to Wie et al.⁸, the enlarged yolk sac was the cause of 77.78 percent of the abortions in his study. Srivastava et al.¹³ found a statistically substantial variance in yolk sac diameter between the miscarriage and extended pregnancy groups. In the case of the yolk sac, the outcomes have been mixed. 5 In some studies, the lack of a yolk sac or a small yolk sac was found to be a major predictor of miscarriage, whereas in others, the existence of a yolk sac or a little yolk sac was found to be a significant predictor of miscarriage. 14 A big yolk sac has been identified as a contributing factor in several studies. 5 The variances appear to be related to a small number of cases or changes in how the yolk sac diameter is measured. Inconsistent measurements can skew results due to the thickness of the yolk sac wall. 15 Our findings suggest that when the yolk sac width is too small for the gestational age, the chance of miscarriage rises, which is in line with prior research involving large numbers of patients. 16,17 Because the yolk sac is the embryo's primary means of communication with the mother before placental circulation develops, it's reasonable to believe that an uneven yolk sac diameter suggests aberrant foetal growth. This study showed that, regarding comparison between the miscarriage and ongoing pregnancy groups regarding mean gestational sac diameter at 6 week, mean value of gestational sac at 6 week in ongoing pregnancy group was 15.73 ± 1.98 mm compared to 13.86 ± 1.96 mm in miscarriage group. There was statistically significant difference between the miscarriage and ongoing pregnancy groups regarding gestational sac at 6 week (p. value = < .002). Mean value of gestational sac diameter at 8 week in ongoing pregnancy group was 30.99 ± 3.22 mm compared to 22.85 ± 7.49 mm in miscarriage group. There was statistically substantial variance between the miscarriage and ongoing pregnancy groups regarding gestational sac at 8 week (p. value = < .000). Mean value of gestational sac diameter at 10 week in ongoing pregnancy group was 39.26 ± 3.26 mm compared to 26.70 ± 11.30 mm in miscarriage group. There was statistically substantial variance between the miscarriage and ongoing pregnancy groups regarding gestational sac at 10 week (p. value = < .000).

This agrees with Wie et al.⁸ who found that, There was statistically substantial variance between the miscarriage and ongoing pregnancy groups regarding gestational sac (p. value = < .001). A tiny gestational sac diameter is highly linked to eventual miscarriage, according to this study. Impaired placentation is likely the cause of a tiny gestational sac for gestational age. Previous studies have discovered a relationship between abnormal yolk sac size and early foetal loss.

For example, Kucuk et al.¹⁸ investigated the potential utility of yolk sac diameter in the

prediction of unfavourable pregnancy outcomes in a sample of 250 first-trimester pregnancies using trans-vaginal ultrasound. In comparison to 20/31 losses, only 8/219 fetuses with a normal outcome showed an abnormal yolk sac size. Another study of 486 pregnancies found that in 27 percent of the 159 women who miscarried, the yolk sac diameter was more than 2 SDs above or below the usual mean for gestation, compared to only 7% of those who had a normal result.. This study showed that, regarding comparison between the miscarriage and ongoing pregnancy groups regarding embryonic heart rate at 6 week, mean value of embryonic heart rate at 6 week in ongoing pregnancy group was 117.14 ± 8.28 compared to 88.80 ± 15.41 in miscarriage group. There was statistically substantial variance between the miscarriage and ongoing Pregnancy groups regarding embryonic heart rate at 6 week (p. value = $< .000$). Mean value of embryonic heart rate at 8 week in ongoing pregnancy group was 149.75 ± 8.66 compared to 111.25 ± 41.44 in miscarriage group. There was statistically substantial variance between the miscarriage and ongoing pregnancy groups regarding embryonic heart rate at 8 week (p. value = $< .000$). Mean value of embryonic heart rate at 10 week in ongoing pregnancy group was 143.02 ± 6.16 compared to 132.02 ± 2.02 in miscarriage group. There was no statistically substantial variance between the miscarriage and ongoing pregnancy groups regarding embryonic heart rate at 10 week (p. value = $< .049$).

According to Wie et al.⁸, there was a statistically substantial variance in embryonic heart rate between the miscarriage and continuous pregnancy groups (p. value = $.007$). Foetal bradycardia has been connected to miscarriage. ^{16,19} Given that the foetal heart rate rapidly increases until the eighth or ninth week of pregnancy, defining a cutoff value for foetal bradycardia without taking gestational age into account is unreasonable, though several studies have reported a reference value of 110 to 120 beats per minute for predicting miscarriage. The ^{7,19} FHR gene has been extensively researched, and multiple studies have found a clear link between abnormal FHR and foetal loss. Foetal bradycardia is a sign of impending foetal mortality since it means the circulatory system is likely to fail. A recent study showed the validity of absent yolk sac and fetal bradycardia for prediction of fetal demise in the first trimester of pregnancy. Clinicians should be alert that there is a clear increased chance of spontaneous abortion if any of these two signs is detected but when both signs are observed; the chance of abortion is markedly increased.²¹

CONCLUSION

Embryos with a healthy yolk sac, gestational sac, and heart rate have a decent chance of surviving. The results of a first-trimester vaginal ultrasound can be utilised to evaluate pregnancies that have been complicated by a negative obstetric history.

Conflict of interest : none

REFERENCES

1. Choong S, Rombauts L, Ugoni A, and Meagher S. Ultrasound prediction of risk of spontaneous miscarriage in live embryos from assisted conceptions. *Ultrasound Obstet Gynecol.* 2003; 22: 571-7.
2. Prashant A, Selvi C, Lavanya R et al. Evaluation of yolk sac diameter and embryonic heart rate as prognostic factors of gestational outcome in early singleton pregnancies. *Sch J App Med Sci.* 2015; 3(2A):543- 50.
3. Kucuk T, Duru NK, Yenen MC, Bede M, Ergiin A, et al. Yolk sac size and shape as predictors of poor pregnancy outcome. *J Perinat Med.* 1999; 27: 316-20.
4. Levi CS, Lyons EA, Lindsay DJ. Early diagnosis of nonviable pregnancy with transvaginal US. *Radiology.* 2005; 167:383.
5. Berdahl DM, Blaine J, Van Voorhis B, Bokras A. Detection of enlarged yolk sac on early ultrasound is associated with adverse pregnancy outcomes. *Fertil Steril.* 2010; 94:1535-7.
6. Varelas FK, Prapas NM, Liang RI, Prapas IM, Makedos GA. Yolk sac size and embryonic heart rate as prognostic factors of first trimester pregnancy outcome. *Eur J Obstet Gynecol Reprod Biol.* 2008 May; 138(1): 10-3. Epub 2007 Aug 10.
7. Chittacharoen A, Herabutya Y. Slow fetal heart rate may predict pregnancy outcome in firsttrimester threatened abortion. *Fertil Steril.* 2004; 82(1): 227-9.
8. Wie JII, Choe S, Kim SJ, Shin JC, Kwon JY, et al. Sonographic parameters for prediction of miscarriage: role of 3-dimensional volume measurement. *J Ultrasound Med.* 2015; 34 (10): 1777-84.
9. Stephenson M, Kutteh W. Evaluation and management of recurrent early pregnancy loss. *Clin Obstet Gynecol.* 2007; 50:132-45.
10. Makrydimas G, Sebire NJ, Lolis D Vlassias N, Nicolaides KH. Fetal loss following ultrasound diagnosis of a live fetus at 6-10 weeks of gestation. *Ultrasound Obstet Gynecol.* 2003; 22: 368-72.
11. Hasan R, Baird DD, Herring AH, Olslian AF, Jonsson Funk ML, et al. Association between first-trimester vaginal bleeding and miscarriage. *Obstet Gynecol.* 2009; 114:860-7.
12. Bottomley C, Van Belle V, Kirk E, Van Huffel S, et al. Accurate prediction of pregnancy viability by means of a simple scoring system. *Hum Reprod.* 2013; 28:68-76.
13. Srivastava G, Nagwani M, Pasricha N, Tewari V. Size of yolk sac by ultrasonography and its correlation with pregnancy outcome int *J Anat Res.* 2016; 4(1):2052-57.
14. Stampone C, Nicotra M, Muttinelli C, Cosmi EV. Transvaginal sonography of the yolk sac in normal and abnormal pregnancy. *J Clin Ultrasound.* 1996; 24:3-9.

15. Papaioannou GI, Syngelaki A, Poon LC, Ross JA, Nicolaides KH. Normal ranges of embryonic length, embryonic heart rate, gestational sac diameter and yolk sac diameter at 6-10 weeks. *Fetal Diagn Ther.* 2010; 28:207-19.
16. Papaioannou GI, Syngelaki A, Maiz N, Ross JA, Nicolaides KH. Ultrasonographic prediction of early miscarriage. *Hum Reprod.* 2011; 26:1685-92.
17. Bae S, Karnitis J. Triple ultrasound markers including fetal cardiac activity are related to miscarriage risk. *Fertil Steril.* 2011; 96:1145-8.
18. Kaur A, Kaur A. Transvaginal ultrasonography in first trimester of pregnancy and its comparison with transabdominal ultrasonography. *J Pharm Bioallied Sci.* 2011; 3(3): 329-8.
19. Rauch ER, Schattman GL, Christos PJ, Chicketano T, Rosenwaks Z. Embryonic heart rate as a predictor of first-trimester pregnancy loss in infertility patients after in vitro fertilization. *Fertil Steril.* 2009; 91:2451-4.
20. Liao AW, Snijders R and Geerts L. Fetal heart rate in chromosomally abnormal fetuses. *Ultrasound Obstet Gynecol.* 2000; 16:610-15.
21. Abdallah Y, Daemen A, Guha S, Syed S, et al: Gestational sac and embryonic growth are not useful as criteria to define miscarriage:a multicenter observational study. *Ultrasound Obstet Gynecol.* 2011; 38: 503-9