

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

By

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ABSTRACT

Approximately 30-40% of implanted pregnancies result in spontaneous abortion during the first trimester. Intrauterine gestational sac appears sonographically, followed by the yolk sac and the fetal pole with cardiac activity. Yolk sac and early embryonic heart rate (EHR) are detected easily by transvaginal sonography. Our purpose was to examine whether yolk sac diameter (YSD) and early EHR could serve as prognostic factors in evaluating pregnancy outcome in 200 pregnant women, examined using 2D transvaginal ultrasonography in the first trimester. Fetal heart rate was measured by M-mode and YSD was determined by placing the calipers on the inner limits of the longer diameter. 184(92%) resulted in an ongoing pregnancy and entered the 2nd trimester successfully, while 16 (8%) resulted in miscarriages. Of the 16 fetal losses, 6 were missed abortions, 4 blighted ova, 4 incomplete abortions and 2 complete abortions. The maximal embryonic heart rates presented at 9 weeks of gestation were 159 bpm, and then the fetal heart rates gradually decreased to 136 bpm at 12 weeks of gestation. According to yolk sac out of 194 cases with round and regular yolk sac shape, 184 had normal outcome and 10 had failed pregnancy. 6 cases had irregular shaped yolk sac and were diagnosed as abortion on follow up. Therefore, the important ultrasonographic findings suggestive of a poor outcome for the first trimester were the finding of: a small for date CRL, small gestational sac diameter, irregular shape of yolk sac and fetal bradycardia.

Key Words: Physiology of ovulation, yolk sac, heart development, ultrasound in early pregnancy.

INTRODUCTION

Approximately 30% to 40% of implanted pregnancies result in spontaneous abortion during the first trimester, most of which occur in the very early stage (*Ouyang et al., 2015*).

Significant number of losses predominantly occurs very early in gestation, but once the embryonic heart activity appears the rate of spontaneous abortion gradually decreases to 2-5 % (*Abd Ellatif et al., 2018*).

Within the gestational sac, yolk sac is the first evident embryonic structure. A yolk sac can be detected easily by transvaginal sonography when the mean gestational sac diameter is 5 to 6 mm. It is generally accepted that the yolk sac should be observed when a gestational sac measures greater than 8 mm (*Yoneda et al., 2018*).

In fact, the yolk sac size progressively increases from the beginning of the 5th gestational week to the end of the 10th gestational week. Afterward, the yolk sac size decreases gradually. When the 10th or

11th week of gestation is completed, the yolk sac begins to shrink rapidly and eventually disappears (*Mahjoub, 2019*).

Varelas et al. (2008) 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. By transvaginal sonogram, we can accurately demonstrate EHR (Embryonic Heart Rate) and assess the pregnancy outcome in those with bradycardia. The embryonic heartbeat can usually be identified at prenatal ultrasonography by 6 weeks gestation in M-mode.

The aim of this study was to evaluate yolk sac (diameter and shape) and embryonic heart rate during the first trimester as prognostic markers of first trimester of pregnancy outcome.

PATIENTS AND METHODS

This prospective cross sectional study was carried out on 200 patients in El Hussein University Hospital, Outpatient Clinic and Obstetrics and Gynecology Department in un complicated singleton pregnancy from 20-35 years old, during period from November 2019 to August 2020.

Inclusion criteria:

- Patient is sure of her dates.
- Singleton pregnancies.
- Age from (20-35) years.
- Gestational age starting from 6 weeks.

Exclusion criteria:

- Unwilling for follow up or patient refused transvaginal sonography.

- Any uterine pathology as fibroid or malformation as septum.
- Patients with severe anemia, hyperthyroidism, diabetes mellitus, chronic hypertension and SLE.
- Patient with molar pregnancy.
- Irregular menstrual cycles.
- Ectopic pregnancy.

Methods:

- All pregnant women starting from 6 weeks of gestation were evaluated every three weeks till 12 weeks.
- Detailed history was taken to rule out medical and surgical complication which can affect our study.
- Thorough general and physical examination was done.

Scanning technique:

The machine recruited into our study is GE Healthcare by logic pro5 with TVS probe of 7-12 MHz.

The sonography was done with empty bladder. The endovaginal transducer was covered with a sterile condom lubricated with gel before insertion. The patient was placed in the lithotomy position with a slight reversed Trendelenburg tilt. The transducer was inserted approximately 6-8 cm inside the vagina. Scanning was done in both coronal and sagittal planes.

First, the uterus was scanned then the adnexa, and finally the cul-de sac. The gestational sac and yolk sac was identified. The inner yolk sac diameter was measured by placing calipers at inner margin. The Intra uterine gestational sac and embryo was identified. Later, after

embryo viability will be confirmed, the embryonic heart rate measured.

Primary outcomes:

Pregnancy outcome in relation to first trimester evaluation by u/s parameter (yolk sac diameter, shape and fetal heart rate).

Secondary outcomes:

Detection of abnormality and any pregnancy loss during 1st trimester evaluation by u/s parameter. The abnormal values for yolk sac diameter and embryonic heart rate was > 95 th percentile or < 5 th percentile for gestational age, or ± 2 SD for gestational age.

Statistical analysis:

Data were analyzed using IBM SPSS advanced statistics version (SPSS Inc., Chicago, IL). Numerical data were expressed as mean and standard deviation or median and range as appropriate.

Qualitative data were expressed as frequency and percentage. For quantitative data, comparison between two groups was done using Mann-Whitney test. Spearman-rho method was used to test correlation between numerical variables.

RESULTS

Females with age below 30 was 114 (57%), age more than or equal 30 was 86 (43%) (**Figure 1**).

Females with no abortion before was 128 (64%), females with abortion 1-2 was 60 (30%), females with more than or equal 3 abortions was 12 (6%) (**Figure 2**).

Table (1) found that there was a significant increase in yolk sac diameter in fetal loss group more than ongoing pregnancy at 6 weeks only ($P < 0.05$), while at 12 weeks there was no significance ($P > 0.05$).

Table (2) shows cutoff value of yolk sac diameter at 6 and 9 weeks to predict the outcome of pregnancy. It was 6 at 6 weeks, the sensitivity was 75%, specificity was 60% and the accuracy was 61%. At 9 weeks, the cutoff value was 5, sensitivity was 62%, specificity was 54% and the accuracy was 55%.

Table (3) found that there was significant increase in heart rate in fetal loss group more than ongoing pregnancy at 6 weeks only ($p < 0.05$), while at 9 and 12 weeks there was no significant

difference between the 2 groups ($p > 0.05$) (**Figure 3**).

Table (4) shows cutoff value of heart rate at 6 and 9 weeks to predict the outcome of pregnancy. It was 122 at 6 weeks, the sensitivity was 69%, specificity was 57% and the accuracy was 59%. At 9 weeks, the cutoff value was 170, sensitivity was 56%, specificity was 52% and the accuracy was 52%.

Table (5) shows the distribution of cases according to yolk sac shape and pregnancy outcome, out of 184 (92%) cases with round and regular yolk sac shape. 16 cases (8%) had failed pregnancy, 10 cases (62.5%) had regular shape of yolk sac, 6 cases (37.5%) had irregular shape of yolk sac. It was found that there was significant relation between yolk sac shape and pregnancy outcome ($p < 0.05$) (**Figure 4**).

Table (6) shows the final outcome of ultrasonographic findings in the studied group, of the 16 fetal losses, 6 were missed abortion, 4 blighted ovum, 4 incomplete abortion and 2 complete abortion.

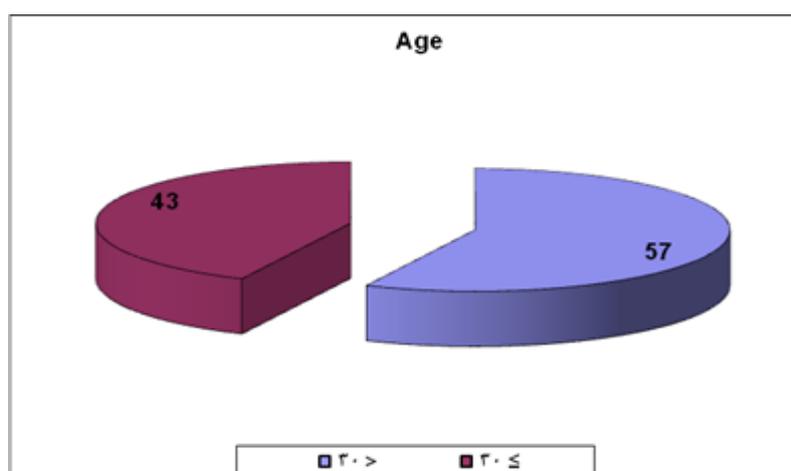


Figure (1): Demographic data of the studied patient

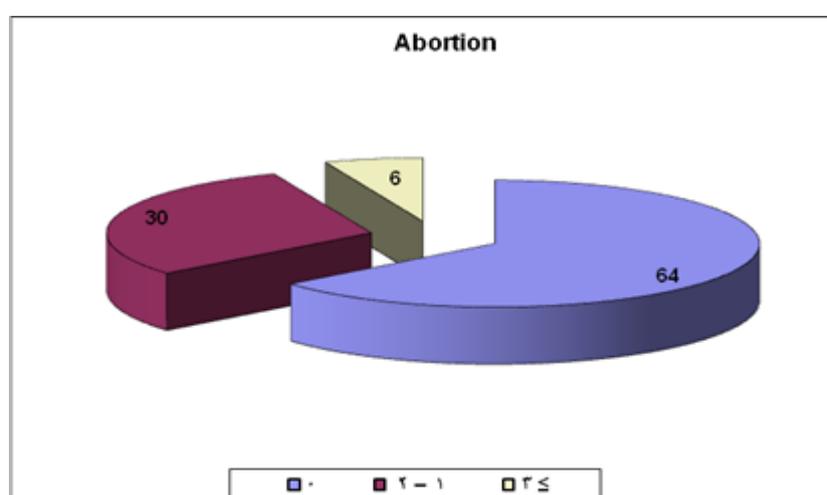


Figure (2): Number of abortions that females previously had

Table (1): Relation between yolk sac diameter at different gestational age period and its relation to the outcome of pregnancy

		Fetal Loss (n=16)	Ongoing pregnancy (n=184)		
6 w.	Range	5.8 – 9.1	3.6 – 6.3	13.821	0.001*
	Mean \pm SD	7.33 \pm 1.09	4.90 \pm 0.63		
9 w.	Range	3.7 – 7	3.5 – 6	2.168	0.031*
	Mean \pm SD	4.97 \pm 1.06	4.65 \pm 0.50		
12 w.	Range	3.5 – 6	3.4 – 6	0.269	0.788
	Mean \pm SD	4.88 \pm 0.79	4.94 \pm 0.87		

Table (2): Cutoff value of yolk sac diameter at 6 and 9 weeks, the sensitivity, specificity and accuracy to predict the outcome of pregnancy at this cut off value

Yolk Sac	Cutoff	AUC	Sensitivity	Specificity	Accuracy
6 w.	6.0	0.858	75	60	61
9 w.	5	0.536	62	54	55

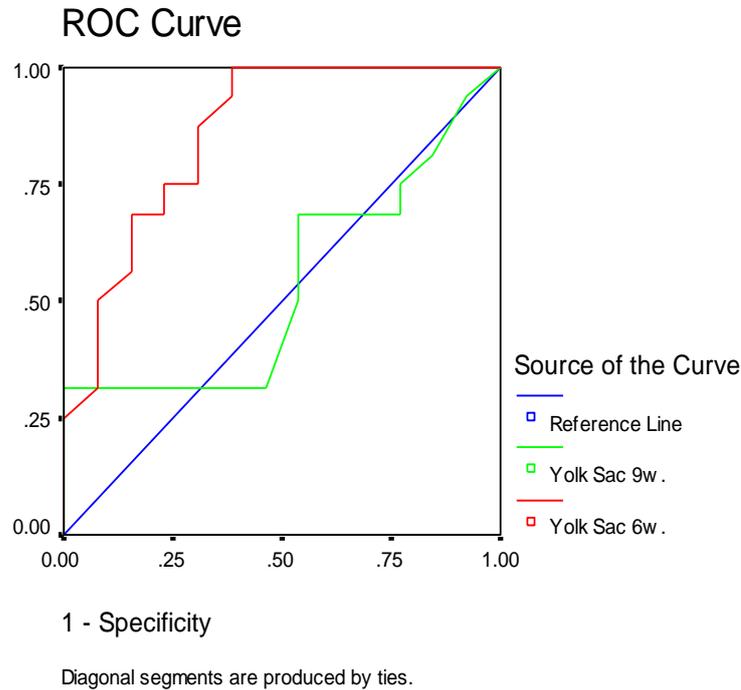


Figure (3): ROC curve of yolk sac diameter at 6 and 9 weeks, the sensitivity, specificity and accuracy to predict the outcome of pregnancy

Table (3): Relation between heart rate at different gestational age period and its relation to the outcome of pregnancy

		Fetal Loss (n=16)	Ongoing pregnancy (n=184)		
6 w.	Range	110 – 145	103 – 130	2.911	0.004*
	Mean ± SD	121.50 ± 11.07	115.98 ± 6.87		
9 w.	Range	156 – 195	155 – 195	0.787	0.432
	Mean ± SD	170.56 ± 12.71	168.32 ± 10.80		
12 w.	Range	120 – 180	120 – 180	1.056	0.292
	Mean ± SD	160.56 ± 14.05	156.32 ± 15.53		

Table (4): Cutoff value of heart rate at 6 and 9 weeks, the sensitivity, specificity and the accuracy to predict the outcome of pregnancy at this cut off value

Heart rate	Cutoff	AUC	Sensitivity	Specificity	Accuracy
6 w.	122	0.757	69	57	58
9 w.	170	0.524	56	52	52

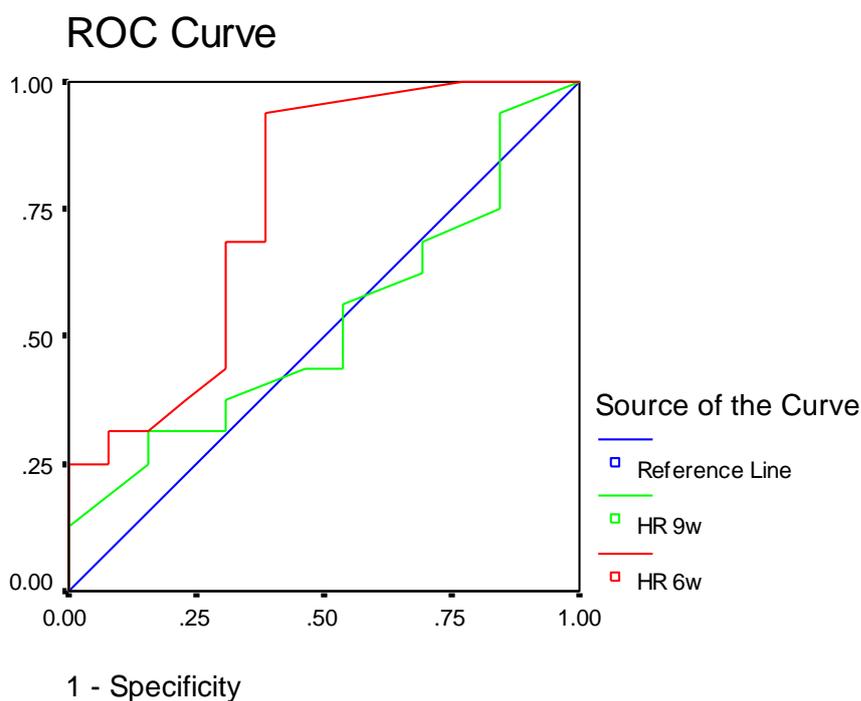


Figure (4): ROC curve of heart rate at 6 and 9 weeks, the sensitivity, specificity and the accuracy to predict the outcome of pregnancy

Table (5): Distribution of cases according to yolk sac shape and pregnancy outcome

Yolk sac shape	Fetal Loss (N=16)		Ongoing pregnancy (N=184)		X ²	P-value
	N	%	N	%		
Regular	10	62.5	184	100	17.132	0.001*
Irregular	6	37.5	0	0		
Total	16	100	184	100		

Table (6): The final outcome of ultrasonographic findings in the studied group

Ultrasound findings	N	%
Normal pregnancy	184	92 %
Missed abortion (other than blighted ovum)	6	3 %
Blighted ovum	4	2 %
Incomplete abortion	4	2 %
Complete abortion	2	1 %
Total	200	100 %

DISCUSSION

Approximately 15-20% of the pregnancies are terminated by miscarriage (*Cunningham et al., 2010*). The pregnancies with a yolk sac diameter >5

mm had a significantly higher risk of miscarriage. As pregnancy with normal yolk sac advances in the first trimester, the frequency of complications reduces. The sensitivity of predicting normal outcome

with regular yolk sac is as high as 94.2% (*Shetty et al., 2015*).

The embryonic heart beat can usually be identified, with improved visual resolution as early as 5 weeks. Both Doppler studies and motion mode (M-mode) are useful in this regard. Fetal heart rate increased significantly from 118 BPM to 167 BPM between 6 and 10 weeks of gestation (*Wong et al., 2014*).

The aim of this study was to evaluate yolk sac (diameter and shape) and embryonic heart rate during the first trimester as prognostic markers of first trimester of pregnancy outcome.

A prospective cross-sectional study was carried out on 200 patients using 2D ultrasonography starting early in the first trimester with a first scan between 6 and 8 weeks.

In our study, females with age from 20-26 years was 130 (65%), age from 26-29 years was 57 (28.5%), age >29 years was 13 (6.5%). BMI <20 was 12(6%), BMI from 20 -26 was 82 (41%), BMI from 26-29 was 90 (45%), BMI >29 was 16(8%).

Our results were supported by study of *Sheikh and Anjana (2020)* who revealed that 49 cases were from age group of 20 years or less than 20 years (19.29%), 184 cases belong to 21 to 30 years' age group (72.44%) and 21 cases (8.27%) were from 31 years or more than 31 years' age group. The mean age of the study group was 23.94±3 years.

In our study, females with gravidity ranged from 2-3 was 96 (48%), gravidity ranged from 4-5 was 52 (26%), gravidity more than or equal 6 was 20 (10%). Females with parity 0 was 52 (26%),

females with parity from 1-2 was 104 (52%), parity more than or equal 3 was 44 (22%). Females with no abortion before was 128 (64%), females with abortion 1-2 was 60 (30%), females with more than or equal 3 abortions were 12 (6%). Normal spontaneous pregnancies were 196 (98%), pregnancies via ICSI were 0 (0%), and pregnancies via intrauterine insemination (IUI) were 4 (2%).

Our results were supported by study of *Abd Ellatif et al. (2018)* as they reported females with gravidity ranged from 2-3 were higher 42 (42%). Parity from 1-2 was higher 48(48%). Non-abortion cases were higher 84 (84%). Normal cases were higher 97 (69%).

Pregnancies that have a mean yolk sac diameter equal or larger than 5 mm on early ultrasound are also associated with a threefold increased risk for first trimester loss, independent of maternal risk factors such as age, body mass index, polycystic ovary syndrome, smoking, and diabetes. The lack of a yolk sac or a smaller than gestational age yolk sac diameter is indicative of pregnancies that may result in spontaneous abortion. Pregnancies with a very large yolk sac are generally always associated with poor outcomes (*Berdahl et al., 2010*).

The present study showed that there was a significant increase in yolk sac diameter in fetal loss group more than ongoing pregnancy at 6 weeks only ($P < 0.05$), while at 12 weeks there was no significance ($P > 0.05$).

Our results were supported by study of *Lebda et al. (2019)* as they found that enlarged YS (4 cases), irregular or absent YS (one case each) were highly significant associated with fetal loss. This

study demonstrated the fact that visualization of YS is crucial for a normal pregnancy outcome. One case only out of 41 cases of normal YSD aborted 2.5%. This in agreement with *Moradan and Forouzeshejfar (2012)*.

Another study from Turkey conducted by *Tan et al. (2011)* prospectively evaluated sonographic characteristics of yolk sac in 305 viable singleton pregnancies with gestational age between 6 to 9 weeks and found abnormal yolk sacs in 66 patients. An irregular yolk sac was observed in 78.8% (52/66), an enlarged yolk sac in 12.1% (8/66) and echogenic yolk sac in 9.1% (6/66). Abortion occurred in 37.5% (3/8) of patients with enlarged yolk sacs and interestingly abortion rates were similar to normal population in patients with irregular yolk sacs and echogenic yolk sacs.

Papaoannou et al. (2010) revealed that at 6–10 weeks there were significant quadratic associations between CRL (crown-rump length), GSD (gestational sac diameter), YSD (yolk sac diameter) and gestation.

Furthermore, *Aseri (2019)* demonstrated that the yolk sac size varied between 2.5 to 7.0 with a mean of 4.892 mm. The Yolk sac size has significant correlation with the 1st trimester pregnancy outcome.

The current study showed that the cutoff value of yolk sac diameter at 6 weeks was 6, the sensitivity was 75%, specificity was 60% and the accuracy was 61%. At 9 weeks, the cutoff value was 5, sensitivity was 62%, specificity was 54% and the accuracy was 55%.

Our results were supported by study of *Sheikh and Anjana (2020)* who revealed that the sensitivity was more i.e. 66.67% for 8 weeks – 8 weeks 6 days group and 10 weeks - 10 weeks 6 days group. The sensitivity and PPV was not good for 7 weeks- 7 weeks 6 days group. The specificity was high in 9 weeks - 9 weeks 6 days group which was 95.08%. Among all gestational age groups, the sensitivity, specificity, PPV and NPV was high for 8 weeks – 8 weeks 6 days group which shows that YSD is more valuable tool in predicting pregnancy outcome in this particular gestational age group.

In our study, there was significant increase in heart rate in fetal loss group more than ongoing pregnancy at 6 weeks only ($p < 0.05$), while at 9 and 12 weeks there was no significant difference between the 2 groups ($p > 0.05$).

Our results were supported by study of *Abdulkadhim (2017)* as they reported that Regarding the embryonic heart rate (EHR), Most of the patients who had poor first trimester outcome (group B) had EHR below 100 BPM (6 out of 9).

The present study showed that the cut off value of heart rate at 6 weeks was 122, the sensitivity was 69%, specificity was 57% and the accuracy was 59%. At 9 weeks, the cutoff value was 170, Sensitivity was 56%, specificity was 52% and the accuracy was 52%.

In the study of *Adiga et al. (2015)*, the sensitivity, specificity and accuracy for embryonic heart rate (≥ 100 bpm) were 99.3%, 83.3% and 98.5%.

The current study showed that out of 184 (92%) cases with round and regular yolk sac shape, 16 cases (8%) had failed

pregnancy, 10 cases (62.5%) had regular shape of yolk sac, 6 cases (37.5 %) had irregular shape of yolk sac. There was significant relation between yolk sac shape and pregnancy outcome ($p < 0.05$). Of the 16 fetal losses, 6 were missed abortion (fetal pole with no visible pulsation), 4 blighted ovum, 4 incomplete abortion and 2 complete abortion.

In the study of *Ghali et al. (2020)*, regarding normal YSD with the abnormal outcome, three cases with a normal YSD and regular morphology aborted after the 8th week of gestation. Regarding large-sized YSD, it was found in three cases; two cases ended in a missed miscarriage at 8th week with YSD 8.4 mm and 8.2mm respectively. In contrast, the third one with YSD 6.8 mm finally continued beyond 20 weeks with no demonstrable fetal anomalies. *Salah et al. (2016)* reported that 25 out of 400 cases with normal YS size and shape had failed pregnancy.

Burton and Jauniaux (2018) reported an abnormal outcome with normal YS size and shape. These findings support that not usually YSD of normal range will eventually have a good outcome. Changes in YS morphology may reflect an abnormal embryonic development or death, rather than being a primary cause of pregnancy loss. Another explanation, Between 8th and 10th weeks of gestation; the disappearance of arterial signals in the yolk sac circulation and simultaneously an increase in the umbilical placental blood flow indicates that the transition from the yolk sac to the placenta occurs as an important source of blood supply to the embryo and may be a defect in the switch to umbilical placental blood flow occur at

this time. This may be considered an etiology for miscarriage, and further studies are required at this particular gestational age.

According to *Prabhjot et al. (2016)*, when the association between outcomes in pregnancies with normal and abnormal YSD was studied, the p value was highly significant ($p < 0.0001$) which was in accordance with the study by *Srivastava et al. (2016)* where p value was < 0.001 .

CONCLUSION

First trimester ultrasound measurement of FHR, YS diameter and shape proved to be an important, helpful and noninvasive tool in the investigation, diagnosis as well as the follow up of pregnant females in their early pregnancy.

Measurement of yolk sac diameter and fetal heart rate in combination provides better prediction of the prognosis of the first trimester than when either parameter used alone.

The important ultrasonographic findings of a large yolk sac diameter and fetal bradycardia suggest poor prognosis for the outcome of the first trimester.

Irregular shaped yolk sac proved to be an important prognostic factor in pregnancy outcome in our study.

In the pregnancies that resulted in normal 1st trimester, there was a significant association between gestational age and mean yolk sac diameter.

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تقييم قطر وشكل كيس المح ومعدل ضربات القلب الجنينية كعوامل تنبؤية في ناتج الثلاثة شهور الأولى من الحمل

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**قسم التوليد وأمراض النساء، كلية الطب، جامعة الأزهر

تشير التقديرات الى ان ما يقرب من 30% - 40% من حالات الحمل ينتج عنها الاجهاض التلقائى خلال الاشهر الثلاثة الاولى، ومعظمها يحدث في مرحله مبكرة للغاية. كيس الحمل داخل الرحم هو اول ما يظهر بالموجات فوق الصوتية، يليه كيس المح والقطب الجنيني مع نشاط القلب. يمكن الكشف عن كيس المح بسهولة عن طريق الكشف بالموجات فوق الصوتية المهبلية وذلك عندما يكون متوسط قطر كيس الحمل (5-6 مم) ومن المتوقع عليه عموما انه يجب ملاحظه كيس المح عندما يكون قطر كيس الحمل اكثر من 8 مم.

بواسطه الموجات فوق الصوتية المهبلية يمكن وبدقه قياس معدل ضربات القلب الجنينية والتنبؤ بنتائج الثلاثة اشهر الاولى من الحمل وخاصة بالاجنه التى يكون بها معدل ضربات القلب اقل من الطبيعى حيث انه يمكن قياس معدل ضربات القلب الجنينية فى الاسبوع السادس من الحمل باستخدام (M-mode) وقد وجد ان بطئ ضربات القلب الجنينية فيما بين الاسبوع السادس والسابع يعتبر مؤشرا لحدوث الاجهاض.

تهدف الدراسة الحالية الى تقييمالعلاقة بين (معدل ضربات القلب الجنينية، حجم وشكل كيس المح) وناتج الثلاثة اشهر الاولى من الحمل.

اشتملن الدراسة على 200 امراه حامل والتى ترددت على مستشفى الحسين الجامعى حيث تم فحصهما باستخدام الموجات الصوتية ثنائيه الابعاد بدا من المرحلة الاولى من الحمل مع اجراء فحص اولى من 6 اسابيع ثم عند الاسبوع التاسع والاسبوع 12.

وتم قياس قطر كيس الحمل، ومعدل ضربات القلب الجنينية وحجم وشكل كيس المح. وقد تبين ان 196 حاله من حالات الحمل كان حمل تلقائي اى بمعدل (98%)، وتلقيح صناعي 4 حالات بنسبه 2%.

ومن اجمالى 200 حاله كان هناك 184 حاله استمر الحمل بنجاح خلال الثلاثة أشهر الاولى أي بنسبه 92%، بينما كان عدد حالات الاجهاض 16 حاله بنسبه 8% مقسمه الى 6 حالات اجهاض متروك، 4 حالات بويضه غير مخصبه، 4 حالات اجهاض غير مكتمل، حالتين اجهاض كامل.

كان متوسط معدل ضربات القلب الجنينية فى الاسبوع 6-8 من الحمل 140 (98-180) ن/د، وفى الاسبوع التاسع من الحمل 159 (144-173) ن/د، ثم انخفض معدل ضربات قلب الجنين تدريجيا الى 136 ن/د (124-160) عند الاسبوع الثانى عشر.

وفقا لكيس المح فمن ضمن 194 حاله كان كيس المح شكله منتظم حدث الاجهاض فى 10 حالات منهم، وقد نجح الحمل فى عدد 184 حاله. وكان شكل كيس المح غير منتظم فى 6 حالات وتم تشخيصهم كاجهاض مفقود عند المتابعه.

زياده قطر كيس المح عن المعدل الطبيعى يكون دلالة على حدوث الاجهاض ولكن فى غالبية الحالات التى حدث بها اجهاض كان قطر كيس المح فى المعدل الطبيعى اى انه ليس هناك علاقه وطيده بين حجم كيس المح وحدث الاجهاض.

يعتبر حجم كيس الحمل عامل تنبؤى لحدوث الاجهاض فى الحالات الآتية:

- عدم ايجاد كيس المح عندما يكون قطر كيس الحمل 8 مم او أكثر.
- عدم ظهور نبضات القلب الجنينية عندما يكون كيس الحمل 16 مم او أكثر.

وبناء على ذلك يمكن الاستنتاج من هذه الدراسة ان نتائج الموجات فوق الصوتيه الهامة التى توحى بحدوث الاجهاض خلال الثلاث اشهر الاولى من الحمل هي:

- قياس طول الجنين من الراس حتى المؤخره صغير بالنسبة لعمر الجنين (مقارنه بتاريخ اخر دوره).

- قطر كيس الحمل الصغير بالنسبه لعمر الجنين (مقارنه بتاريخ اخر دوره).

- شكل كيس المح غير المنتظم وبطيء معدل ضربات القلب الجنينه.

هذا وقد اثبتت الموجات فوق الصوتيه انها اجراء هام ومفيد لمتابع الحمل والتنبؤ بالعوامل التى تؤدى الى حدوث اجهاض خلال الاشهر الثلاثه الاولى من الحمل.