Predictors of poor first trimester outcome in asymptomatic women : the value of embryonic heart rate , mid sac diameter / yolk sac ratio & mid sac diameter / crown rump length

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ABSTRACT

Background: Ultrasound provides a powerful tool for assessing early pregnancy and detecting pregnancy failure at first trimester and promoting rapid effective management. Several criteria have been established to predict the pregnancy outcome particularly in symptomatic women .

Aim: To evaluate asymptomatic women at the first trimester of pregnancy , to assess the efficacy of certain ratios as mid sac diameter (MSD) / yolk sac ratio & crown rump length (CRL)/mid sac diameter (as indicator of early first trimester oligohydramnios) in predicting poor 1st trimester outcome

Type of the study: A cross-sectional study.

Patients & Methods: A sixty three asymptomatic women were enrolled in this prospective study . Transvaginal sonography was performed for confirmation of pregnancy viability & exclusion of multiple pregnancies 6-8 weeks of gestation & follow up ultrasound repeated at the beginning of second trimester to confirm the continuation of pregnancy and viability of fetus. Several parameters assessed and tested against each others as embryonic heart rate , the size and morphologic criteria of gestational sac , yolk sac and the crown rump length

Results: The women were classified into two groups: group A are those with successful outcome at the first trimester and group B are those with poor outcome of the 1st trimester . Decrease embryonic heart rate below 100 beat per minute and low mid sac diameter/ yolk sac size ratio of < 1.9 , were found to be significant predictors of poor outcome however mid sac diameter/crown rump length ratio was not found to have a similar significance

Conclusion: In addition to the classical parameters assessed by trans-vaginal ultrasound, other important parameters need to be routinely applied as the embryonic heart rate that predict poor outcome when less than 100 bpm . In addition to the ratio of mid sac diameter to the yolk sac diameter which , if less than 1.9 , may point to abnormal first trimester fate.

Keywords: Transvaginal ultrasound, Gestational sac , poor first trimester outcome .

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Early pregnancy is defined as the first 12 weeks of gestation . The embryonic period is defined as the time from conception to the eight weeks (10 weeks from the LMP),when organs development begins after that , the term fetus is used [1]. Ultrasound provides a powerful tool for assessing early pregnancy and detecting pregnancy failure at first trimester and promoting rapid effective management.Several criteria have been assigned for the normal pregnancy at the first trimester. The earliest of these is significant thickening of the endometrium above 15mm [2].

The next sign is the appearance of the gestational sac (GS) as an anechoic space surrounded by hyperechoic rim of trophoblastic tissue which can be seen by 4.5weeks gestation using transvaginal sonography (TVS) [3]. The normal position of GS is in a mid-position between the uterine walls [4].The GS grows in a linear fashion, from 10mm sac that is equivalent to 5week gestation increasing to 60 mm by 12.2 week with growth rate of 2mm /day.[5] The shape of GS is another valuable predictor of pregnancy healthy status . A normal GS has spherical or fairly rounded shape without angulation , exhibits a double decidual sign (DDS) and a continuous hyerechoic rim at least 2mm in thickness.[6].

Another valuable structure is the yolk sac that appears as a circular structure with an anechoic center surrounded by a uniform well-defined echogenic wall, that is usually seen when mid sac diameter (MSD) reach 8mm at TVS[7]

The embryo is often first seen when the gestation sac has an MSD 12mm, equivalent to the mean gestational age of 6.2 weeks [8], Heart motion should be evident in all embryos with CRL at least 5mm usually by TV ultrasound equivalent to an embryonic age of 6.2 weeks .The heart rates can also evaluated at 5-6 weeks, it should be at least 100 beats per minute rising to between 140-160 beats per minute by eight weeks . There is lower limit of normal for the heart rate less than 90 beats per minute at 5-6 weeks and less than 120 beats per minute by 8 weeks below this range consider a bradycardia of embryo and should be observed closely because a number of these pregnancies are lost. Faster

heart rate are rare and not shown to be pathological significant in the first trimester [9]

The most common complication of pregnancy is miscarriage, which is estimated to affect up to 15% of pregnancies [10]. Several researches have tested the value of demographic criteria and variable sonographic features in suggesting that these pregnancies will end up with abortion [9 , 11-17], with documented association between rising risk for abortion and increased maternal age, previous history of abortion , vaginal bleeding, fetal bradycardia, poor fetal growth rate at early trimester, small gestational sac volume and large yolk sac. However, many of these studies were carried out on highly selected populations,including women presenting with vaginal bleeding or abdominal pain. We aimed at this study to prospectively evaluate asymptomatic women at the first trimester of pregnancy to assess the efficacy of certain ratios as MSD / yolk sac ratio & CRL/MSD (as indicator of early first trimester oligohydramnios) in predicting poor 1st trimester outcome

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Patients and Methods: This is a prospective study has been conducted from October 2014 to August 2015 in Department of Radiology at AL- Emamain AL-Kadhmain Medical City. The study included 63 pregnant females , age range from 15-47 years old) who were presented for routine ultrasound examination between 6-8 weeks of gestation for determination & confirmation of pregnancy viability & exclusion of multiple pregnancies. Ultrasound examination was repeated at the beginning of second trimester to confirm the continuation of pregnancy and the fetal viability .

Those patients with a history of habitual miscarriage , history of cervical incompetence, Pre-eclampsia, chronic hypertension, Diabetes mellitus , renal disease, connective tissue disease, patients with vaginal bleeding or significant pelvic pain and patients with no visualization of yolk sac or the embryo were excluded from the study.An informed verbal consent was obtained from the patients to participate in the study

The demographic criteria of the patients were recorded The ultrasound examination was performed using trans vaginal transducer (7.5 MHz) mounted on Philips HD 11-EX and GE Voluson E6 ultrasound machines for confirmation of the presence of intrauterine pregnancy , then assessment of the gestational sac criteria(size , shape & location) , the yolk sac criteria(size , wall & ecchogencity) , the crown rump length (CRL) & fetal heart rate.

The GS diameter is calculated by averaging three diameters in the orthogonal planes , the calibers are placed at the inner aspect of the trophoblastic sac .

The yolk sac is measured in the largest diameter.

The CRL is obtained by measuring the largest diameter between the most caudal & most cephalic point of the embryo The embryonic heart rate was assessed using pulse Doppler .The following variables were assessed against each other: MSD and the yolk sac diameter MSD and the CRL , The yolk sac with CRL, & Fetal heart rate

The collected data were statistically analyzed using statistical package for social science (SPSS)version 22. Chi square test was used to determine the association between different variables & p-value less than 0.05 it was considered to be statistically significant.

Results : Sixty three pregnant females were enrolled in the study and were classified into two groups , those with successful first trimester outcome designated as group A & constituted 52 women & those with unsuccessful first trimester outcome as group B and constituted 11 women .

Age of the patients: Most of pregnant in this study were less than 20 years with age group ranged between (10-49) years with mean age of 29.5 years.The age distribution of the subjects of both groups is shown in Table (1). With increasing age , there Statistically significant increase in the incidence of the unsuccessful outcome.

Table (1):Age groups of the study sample

Age group	No. of patients	%	Group A		Group B		P value
			No.	%	No.	%	
10-19	39	61.92	37	71.15	2	18.18	0.0108
20-29	10	15.86	10	19.23	0	0	
30-39	7	11.11	4	7.69	3	27.27	
40-49	7	11.11	1	1.92	6	54.54	
Total	63	100	52	100	11	100	

EHR (Embryonic Heart Rate): Significant statistical difference was found between group A & B regarding embryonic heart rate with majority of patients with embryonic heart rate <100 BPM ended up with poor outcome (group B)(p=0.0003) (table2)

Table (2): Embryonic Heart Rate in the study groups

EHR, BPM			Outcome results				P value
Type	No.	%	Group A		Group B		
			No.	%	No.	%	
< 100	9	15.79	3	5.77	6	54.55	0.0003
100-109	13	11.84	11	21.15	2	18.18	
110-119	17	25.00	15	28.85	2	18.18	
> 120	24	47.37	23	44.23	1	9.09	
Total	63	100	52	100	11	100	

Ratio of MSD to yolk sac

The MSD:YS ratio was significantly different between group A and group B.The majority of the patients in the group B demonstrated a ratio of 1.9 or less (7 out of 11), while 50 patients in group A demonstrated a ratio of > 2 (table 3)

Table (3): Ratio between MSD & yolk sac

Ratio between MSD & yolk sac			Outcome results				P value
Type	No.	%	Group A		Group B		
			No.	%	No.	%	
=< 1.9	9	14.29	2	5.77	7	63.64	< 0.0001
2-2.5	25	39.68	24	3.85	1	9.09	
2.6-3.1	8	12.70	7	46.15	1	9.09	
3.2-3.7	13	20.64	12	13.46	1	9.09	
>3.7	8	12.69	7	23.08	1	9.09	
Total	63	100	52	100	11	100	

1st trimester oligohydramnios Ratio of CRL to MSD

Majority of patients in group A had normal amniotic fluid as judged by the difference between the MSD & CRL of more than 5 mm (47 out of 52) while 4 out of 11 patients in group B showed evidence of oligohydramnios

In those patients with oligohydramnios , the MSD : CRL ratio was found to be < 1.2 . Most of the patients with successful 1st trimester outcome had a ratio of 1.3-3.2 as demonstrated at table 4 , however the difference was not found to be statistically significant (p value =0.0628) figure 1

Table (4): The MSD : CRL ratio in the study groups

Ratio between MSD & CRL			Outcome results				P value
Type	No.	%	Group A		Group B		
			No.	%	No.	%	
<1.2	9	14.29	5	9.62	4	36.36	
1.3 - 2.2	29	46.03	27	51.92	2	18.18	0.0628
2.3- 3.2	13	20.63	11	21.15	2	18.18	
>3.2	21	19.05	9	17.31	3	27.27	
Total	63	100	52	100	11	100	

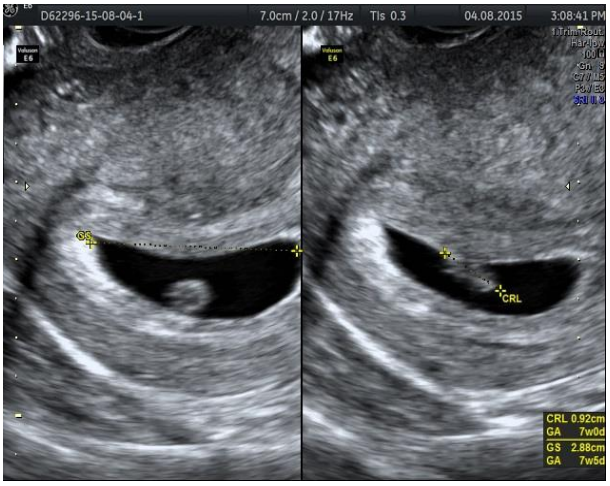

Figure (1): Ratio between MSD & CRL

Regularity of the gestational sac (G.S)

Majority of the patients in group A had regular gestational sac walls (49 out of 53) , while 7 out of 11 patients in group B had irregular GS wall (P < 0.0001)

Double decidual sign(DDs)

The presence of DDs was seen in 48 cases , most of these were in group A (47 patients) while only 1 patient demonstrated this sign in group B . The majority of patients with group B showed single decidual reaction (10 out of 11).

Appearance of the yolk sac

Abnormal yolk sac was seen in 8 out of 11 patients in group B while only 4 patients in group A demonstrated an abnormal yolk sac

Position of the GS

Twenty five patients had the gestational sac at fundal part of the uterus, 19 in the mid part either in posterior or anterior wall, 15 in the lower part either in the anterior or posterior wall , in all mentioned above locations of GS , the majority of the patients were in group A ,while significant numbers of patients (3 out of 4) with GS in the most lower part just above the cervical canal were in group B. (table 5)

Size of the yolk sac

Forty three cases showed yolk sac size < 6mm , 42 of cases (the bulk) go with group A while , 13 cases show size ranged(7-10mm) also the majority of them (8)go with group A , 7 cases with yolk sac diameters > 10mm , 5 of them go with group B. table 6

Table (5): Position of GS

Position of GS			Outcome results				P value
Type	No.	%	Group A		Group B		
			No.	%	No.	%	
Fundal	25	39.68	24	46.15	1	9.09	0.0041
Mid part	19	30.16	16	30.77	3	27.27	
Lower part	15	23.81	11	21.15	4	36.36	
Most lower part	4	6.35	1	1.92	3	27.27	
Total	63	100	52	100	11	100	

Table (6):size of the yolk sac

Appearance of the yolk sac			Outcome results				P value
Type	No.	%	Group A		Group B		
			No.	%	No.	%	
< 6 mm	43	68.25	42	80.77	1	9.09	< 0.0001
7-10 mm	13	20.64	8	15.38	5	45.45	
> 10 mm	7	11.11	2	3.85	5	45.45	
Total	63	100	52	100	11	100	

Discussion

Trans-vaginal ultrasonography is one of the most important and useful diagnostic tool in the field of modern obstetric medicine as it is safe and free of biological hazards to the growing embryo .It is considered as the standard technique in the assessment of the early pregnancy & predicting its complication .We aimed at this study to assess some

of sonographic signs that may predict poor outcome at the 1st trimester

Several studies have considered that that advanced maternal age is one of risk factor of early pregnancy loss[8,10]. In the current study , the impact of the increased maternal age was further confirmed , as significant number of patient in group B were above 40 years of age

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). This result came in agreement with those of Doubilet et al [18] who found that an HER below 90 beats per minute at 6 to 8 weeks of gestation have been shown to be associated with a high likelihood of subsequent first trimester demise. Another similar study by Benson et al [9] determine the survival rate according to the fetal heart rate in 6.3-7 gestational weeks to be approximately 52% when the HER between 100-119 bpm and this drop to 0% when the heart rate drop to less than 100 bpm

Concerning the yolk sac , a study by Cho FN et al [19] found that the largest acceptable size of yolk sac was 8.1mm , these results are in agreement with the results of this study that showed that most of the patients in group B had yolk sac size more than 10mm (5 out of 7) while the majority of the patients in group A had yolk sac size of less than 6mm . In addition to the size , the quality of the yolk sac is also an important predictor of the outcome of pregnancy . The poor quality and early regression of a yolk sac are more specific than the large size of a yolk sac in predicting pregnancy loss. According to SinanTan et al [20] , assessment of yolk sac should be part of a complete first trimester sonographic examination as an abnormality in the sonographic appearance of a yolk sac can predict subsequent embryonic death .Another study made by Donald et al [21], gave the criteria of subsequent first trimester demise depending on the quality of the yolk sac as :1-Absenceof the yolk sac , 2-Too large yolk sac more than 6mm (sensitivity 16%, specificity 97 %) ,and 3-Too small yolk sac less than 3mm (sensitivity 15%, specificity 95%). In the Current study those patients with non visualization of the yolk sac were not included.

We tested the value of combination of the MSD & YS diameter as a predictor of pregnancy well being . It has been found that a significant numbers of patients in group B had ratio of < 1.9 which could be either due to small size of the GS or large size of the yolk sac . The difference between the study groups was statistically significant (p value <0.0001). To our knowledge there is no similar study that have dealt with ratio of MSD & yolk sac

On the other , assessment of the ratio between the MSD and the CRL did not show significant variation between the study groups with a p value of > 0.06. This finding was not surprising as this ratio may be an indicator of the first trimester oligohydramnios which is not considered as a frequently encountered findings and is frequently associated with cardiac or extensive renal anomalies or following chorionic villous sampling [22]

Regarding the regularity of the gestational sac (GS), in this study most of pregnant with regular gestational sac (N=49) were in group A (p value <0.0001).Chaitaliet al [23] stated that several features of abnormal GS were determined including large diameter of the sac, irregular or distorted shape, low position of the sac in the endometrial canal, thin decidual reaction of < 2 mm & absent double-decidual reaction

It is well known fact that the presence of the DDs confirms the normal intrauterine pregnancy however its absence dose not rule out the presence of early pregnancy but in the presence of single decidual reaction , it is more likely that either the intrauterine pregnancy is abnormal as in embryo demise or it represent a psudodecidual reaction of ectopic gestation [1] . In the present study , double decidual reaction (DDs) was found in most of the group A patients (N=47) while most of patients in group B had a single decidual layer (p value < 0.0001)

Regarding to the normal appearance of the yolk sac , 51 out of 63 patients show normal appearance of the yolk sac , the majority of these (N=48) were in group A . In a study by Varela et al [24], absence of yolk sac in presence of an embryo is always abnormal. Moreover 2/3 of patients with abnormal yolk sacs ended up with abortion

The position of the gestational sac was another criteria that has been assessed in this study .Most of the patients (4 out of 7) in group B had gestational sac in the lower most part of the uterus (just above the cervical canal) while majority of the patients in group A had their GS in other location of the uterus , in the fundal part (24 out of 25) and mid uterine part (16 out of 19). Comparing these result with study done by illy et al [25], gestational sac situated completely or partially in the lower uterine segment is seen in 20% of abnormal pregnancies and predicts an abnormal outcome in 94% of cases

Conclusion : In addition to the classical parameters assessed by trans-vaginal ultrasound (gestational sac regularity & position , the presence & criteria of the yolk sac , the double decidual reaction sign) , other important parameters need to be routinely applied as the embryonic heart rate that predict poor outcome when less than 100 bpm . In addition to the ratio of mid sac diameter to the yolk sac diameter which , if less than 1.9 , may point to abnormal first trimester fate . The validity of the mid sac diameter : crown rump length ratio was not verified at this study probably due to limited sample size .

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