

ORIGINAL ARTICLE

Prediction of Pregnancy Outcome by using Three-Dimensional Ultrasound in the First Trimester

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ABSTRACT

<p>Keywords: Pregnancy Outcome, Three-Dimensional Ultrasound, First Trimester</p> <p>*Corresponding author: Weam Mohamed Khairy; Email: omarorosona@gmail.com; Phone: 01142548718</p>	<p>Background: Ultrasound is a useful tool for important measurements in pregnancy progress and outcome monitoring. Objective: Aims of this study was to prediction of pregnancy outcome in the first trimester by using Three-dimensional ultrasound. This study was carried out at the Obstetrics & Gynecology Department in Aswan University Hospitals. Methods: The study included 60 pregnant women during first trimester of their pregnancy (from 6 to 11 weeks of gestation). Results: 2D US CRL showed a significance difference between the cases developed miscarriage and non- miscarriage cases (continued pregnancy till 24 weeks) with P value <0.001. The GSV via the 30° VOCAL method using 3D-TV US showed also difference between both groups. The single predictor of miscarriages cases according to results was MGSD, FHR and CRL via 2D transvaginal ultrasound. Conclusion: Measurement of gestational sac diameter, CRL and fetal heart rate in combination provides better prediction of the prognosis of the first trimester than when either parameter used alone</p>
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INTRODUCTION

with the development of 3-dimensional sonography, including the ability to measure exact volumes, ⁽¹⁾ Several authors have reported GSV measurements in relation to prediction of abortion in the first trimester ⁽²⁾ chromosomal defects and prediction of successful expectant management in missed miscarriage ⁽³⁾. 3D assessment of gestational sac volume in the first trimester has been found to be a sensitive indicator of pregnancy outcome, with a smaller than expected gestational sac volume being predictive of failing early pregnancy ^(4, 5). Nowadays, 3D ultrasound using VOCAL imaging program are widely distributed in obstetrics and gynecology field as in measurement of the endometrial volume for diagnosis of endometrial polyps in Premenopausal women with abnormal uterine bleeding ⁽⁸⁾. The aim of this study was to Prediction of pregnancy outcome in the first trimester by using Three-dimensional ultrasound.

PATIENT AND METHODS:

The Type of the study; Prospective cohort observational study. It was calculated at antenatal care clinic of obstetrics and gynecology department in Aswan University (Aswan, Egypt). from October 2017 to July 2018. The protocol of the study had been approved by the ethical committee of faculty of medicine Aswan University. Women attending to antenatal care clinic in Aswan University, 60 women were selected from ANC clinic and were eligible for the study. Inclusion criteria: 1) Age: 20 – 35 years, 2) Single fetus pregnancy, 3) Gestational age from 6 to 12 weeks. Exclusion criteria: 1) Patients with congenital malformations in uterus (e.g. bicornate uterus, septate uterus), 2) ART pregnancy, 3) Patients with recurrent pregnancy loss, 4) Patients with submucous fibroid, 5) Multiple pregnancies Thrombophilia, 6) Patients with medical disorders: diabetes mellitus and thyroid diseases. All women were counselled and offered to join study after obtaining a written consent, the consent was signed after explanation of the study purpose. These cases allocated into two groups. The first group: included 30 women who had the all inclusion criteria and did not have any of the exclusion criteria with gestational age 6-8 weeks. Included 30 women with the same inclusion and exclusion criteria except a history of one miscarriage with gestational age 9-12 weeks. All patients who were eligible to the study subjected to: A detailed history taking: the data were collected from women included in this study by history to detect; age, parit, gestational age (calculated from the 1st day of LMP) and past history of early pregnancy miscarriages. Women included in the study were sure of dates, conceived spontaneously with no history of infertility and had a positive serum pregnancy test. General examination: blood pressure, pulse and abdominal examination to exclude chronic illness. Ultrasound scanning was done using (General Electric Company) GE health-care, Voluson 730 pro V ultrasound machine, Austria, year launched 2008. We used the 6.5 MHz for trans-vaginal ultrasound prop. By single investigator. Ultrasound scans between 6 and 11 weeks of gestation done by the transvaginal prop of two-dimension ultrasound. The following were measured crown- rump length (CRL) measurement using 2D ultrasound Proper measurement of the CRL was done according to obtaining a true, unflexed, longitudinal section of the embryo or fetus, with the end-points of the crown (the top of the head) and rump (the end of the trunk) clearly defined, and then placing the calipers correctly on these defined end-points. Yolk sac diameter (largest outer to outer measure), shape, size characters. Mean gestational sac diameter (arithmetic mean of 3 diameters: length, width, and height). Embryonic heart rate. the heart rate was determined from M- mode tracings using electronic calipers. The heart rate was calculated as beats per minute using the software of the ultrasound machine after measurement by electronic calipers of the distance between two heart waves on a frozen M –mode image. The next table shows the 50% and 95% of the embryonic CRL, embryonic HR, mean GSD and YSD according to the nomograms of. For GSV calculation, the VOCAL method was used. After switching to the 3D mode, the region of interest box was positioned over the entire gestational sac. After scanning, the gestational sac was displayed automatically on the monitor as three simultaneous orthogonal perpendicular planes (axial, sagittal, and coronal). The VOCAL switch was activated using a 30° rotation angle and the manual setting. Calipers were positioned on the superior and inferior extremities of the structure, and, after obtaining six sequential planes, the equipment automatically displayed the reconstructed image and its volume. For YSV measurement, the yolk sac moves to the center of the plane. Calipers were positioned on the superior and inferior extremities of the structure and after obtaining six sequential planes, the equipment automatically displayed the yolk sac as a 3D image with its volume in cm.

Follow up of the cases and outcomes all pregnancies were followed for their pregnancy outcomes after completion of 12 week by either subsequent scan or telephone interview. Adverse outcome was miscarriage occurring before or at 12 weeks of gestation. The sample size calculation required sample size was estimated using the Power Analysis and Sample Size software (PASS, NCSS statistical software, LLC, Kaysville, Utah, USA). A sample size of 60 patients was calculated to

achieve a power of 80% and confidence level of 95% for detection of a statistically significant difference. All the 60 patients met the inclusion criteria during the period of the study and were attended to our hospital outpatient clinic. Statistical analysis of results was collected tabulated and statistically analyzed by an IBM compatible personal computer with SPSS statistical package version 20 (SPSS Inc. Released 2011. IBM SPSS statistics for windows, version 20.0, Armonk, NY: IBM Corp). P-value of < 0.05 was considered statistically significant. Ethical consideration of the confidentiality of all patients admitted to the study was protected. The study participants will not be identified by name in any report or publication.

RESULTS

The study involved 60 pregnant women examined using 2D and 3D vaginal ultrasonography between 6 and 12-weeks gestational age and the included women were allocated into two groups. The first group I: included 40 women who had continued the pregnancy. The second group II: included 20 women who had miscarriage. The 20 miscarriage cases which represented 33% of the 60 cases and they ended by the following 9 cases (45%) had taken induction and followed by evacuation and curettage, 4 of cases took induction of miscarriage (40%) and did not need any surgical interference and 3 (15%) of cases spontaneous miscarriage occurred but need evacuation and curettage, 2cases (10%) spontaneous miscarriage developed before 13 weeks while 2 cases happened at 16 weeks and 17weeks. In table (1) Demographic features shown (gravidity, parity, GA, age, weight, residence and occupation) there were no statistically significant difference between both groups except in the (P value 0.001). In table (2) the ultrasound parameters of the participants in group A &B. All these parameters were insignificant statistically except in FHR which was higher in group B than A (P value 0.005). According to ultrasound parameters. The 2D US gestational sac diameter, 2D.CRL, 3D.US gestational sac volume all of them show statistically significant differences between both groups. absent yolk sac was seen only in the miscarriage group (30%) while did not present in non-miscarriage group (p value 0.01).

DISCUSSION:

The results of this study represented the statistically differences of 3D ultrasound between the group developed miscarriage and non-miscarriage group. 2D US gestational sac diameter and 3D US gestational sac volume showed the highest P value (0.001, 0.006, 0.009). Since, 3D US allowed tracing of the external surface. It was more accurate than 2D US in evaluating the volume of irregularly shaped objects and it has been previously used to assess several first trimester structures, such as the gestational sac and yolk sac^(9,10). According to *Aviram et al.*⁽¹¹⁾, they reported a strong relation between the gestational sac volume, embryonic volume and the CRL. They found that, volume may be a better parameter than a single longitudinal measure to evaluate embryonic growth during the first trimester. Many studies were done to examine both measurement of GSV and YSV using 3D ultrasound throughout the application of VOCAL method and using the nomograms of GSV and YSV as a reference and predictors for pregnancy loss^(2,10,12). In the present study, the mean of GSV measured by 3D ultrasound using VOCAL method was statistically lower in the patient who developed miscarriage than patients continued pregnancy with P value 0.009. But the GSV had lower screening parameters in this study for the prediction of miscarriage with sensitivity 87.5%, specificity 65% and diagnostic accuracy 80% at a cutoff point of 13.75 cm³. However, YSV had lower screening parameters than previous marker. The YSV show no significant difference between the women who developed miscarriage and those who continued pregnancy with P value 0.08. In the current study the cutoff value of YSV was 0.56 cm³ with sensitivity 77.5%, specificity 37.5% and diagnostic accuracy 66%. So YSV could not be a good independent screening tool in prediction of miscarriage between gestational age (6-11 weeks). This concept was similarly found among other investigators like^(2,4,12). These present results agreed with *Babinszki and colleagues*⁽⁴⁾ who reported that GSV was a good predictor of adverse pregnancy outcomes, while YSV was not a good

predictor. *Figueras and colleagues* ⁽²⁾ did not find 3DUS to be more useful than 2DUS in the prediction of first trimester pregnancy loss *Cosmi and colleagues* ⁽¹²⁾, who used the VOCAL method to compare the YSV of type 1 diabetics and non-diabetic women. Since, the yolk sac is a relatively regular structure. They concluded that, the main advantage of the VOCAL method in their results was the shorter time required to obtain the YSV. for YSV assessed by the VOCAL method can be used as a reference to evaluate cases at high risk for early pregnancy loss. Various first trimester ultrasound parameters such as yolk sac, embryonic heart rate and mean gestational sac growth have been linked with adverse pregnancy outcome ⁽¹³⁾. Other ultrasound parameters were included in the current study. It was found that, using the two-dimensional MGSD measurement as a predictive parameter for miscarriage showed significant difference which was lower in the women who developed miscarriage with p value 0.006. MGSD showed Sensitivity 95.0%, Specificity 55.0% and diagnostic Accuracy 82% at a cutoff value of 29.0 mm. This implies that when MGSD is ≤ 29 mm, pregnancies are more likely to turn nonviable pregnancy among gestational age between 6-11 weeks. Comparing of our results with previous studies have shown a strong connection between small gestation sac and subsequent fetal loss ^(14, 15, 16, 17). Instance, *Cunningham et al.* ⁽¹⁴⁾ who performed ultrasound scans every week from 5 to 12 weeks in 40 high-risk pregnancies and reported that the 20 which subsequently miscarried had a smaller gestational sac from as early as the fifth week and the rate of increase in gestational sac was also significantly lower than in those with a normal outcome. A small gestation sac diameter in early pregnancy may be the consequence of small amniotic cavity or celomic cavity or both. YSD was another ultrasound parameter studied in the current study. Pregnancies that have a mean yolk sac diameter equal or larger than 5 mm as visualized in early ultrasound are associated with a three folds increased risk of first trimester loss. Visualization of a large size yolk sac is a predictor of poor pregnancy outcome ⁽¹⁸⁾. This result showed that, comparison between the group developed miscarriage and the non-miscarriage group depending on the yolk sac diameter showed no statistically difference between the both groups according to gestational age from the 6-11 weeks with P value 0.21. The cutoff point was ≤ 4.4 mm with sensitivity 50% and specificity reached 50%. According to current results, YSD considered poor screening parameters as ultrasound parameters for prediction of developing miscarriage. This differ with *Ivanisević et al.* ⁽¹⁹⁾, *Rolo and colleagues* ⁽¹⁰⁾ also *Cepni and associates* ⁽²⁰⁾. Also *Rolo and colleagues* ⁽¹⁰⁾ studied the yolk sac diameter as predictors of pregnancy outcome using 2D-US. YSD ranged from 2 to 5 mm, with a mean value of 2.09 mm between the seventh and tenth week. They measured the yolk sac diameter from inner to inner border. While in a study involving 67 normal pregnancies, *Cepni and associates* ⁽²⁰⁾ reported that the mean YS diameter between 5 and 10 weeks was 5.2 mm (range 3.8 - 7 mm) and concluded that YSD could be screening parameters for prediction of miscarriage. The discrepancies in the results from different studies may be a consequence of the small number of cases examined and also may be related to methodological differences in the measurement of YSD. The current study showed three cases with yolk sac diameter above the (95% centile according to nomograms of *George et al.* ⁽²¹⁾ the yolk sac diameter in one case pregnant 6-7 weeks was 5.6mm and the 95% was till 5mm the two other cases the yolk sac diameter was 7mm 6.9mm were above 95% (6.2mm- 6-4mm). and the three cases continue the pregnancy and gave birth to normal infant. The only evidence in this study was that, an absent yolk sac was the most characteristic features of cases developed miscarriage while the round yolk sac was the most characteristic features of cases continued till 24 weeks and this agree with several studies using 2DUS. These studies suggested a relation between abnormal yolk sac diameter or shape and adverse pregnancy outcome.

CONCLUSION

Measurement of gestational sac diameter, CRL and fetal heart rate in combination provides better prediction of the prognosis of the first trimester than when either parameter used alone. Ultrasonography finding of a small for date CRL, small gestational sac diameter and fetal

bradycardia suggest poor prognosis for the outcome of the first trimester. YSV was not a good predictor of pregnancy outcome but GSV may have a little role in the prediction of pregnancy outcome.

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Table (1): Demographic data of both groups (A&B):-

	Group A (n=30) Mean ±SD	Group B (n=30) Mean ±SD	Mann Whitney test	P value
Gravidity	2.43 ± 1.25	3.63 ± 1.32	3.21	0.001
Parity	1.43 ± 1.25	1.36 ± 1.27	0.29	0.76
GA (weeks)	8.06 ± 1.33	8.16 ± 1.28	0.29	0.76
Age	27.70 ± 5.63	28.43 ± 4.36	T. test 0.56	0.57
Weight	77.23 ± 11.72	79.70 ± 9.25	T. test 0.90	0.36
	No. (%)	No. %	X²	P value
Residence Rural	17 (56.7)	15 (50.0)	0.07	0.79
Urban	13 (43.3)	15 (50.0)		
Occupation:			1.07	0.30
House wife:	18 (66.7)	13 (36.7)		
Working:	12 (43.3)	17 (63.3)		

SD: standard deviation

Table (2): Different ultrasonic parameters in group A&B :-

	Group A (n=30) Mean ±SD	Group B (n=30) Mean ±SD	Test of sig	P value
2D.US mean gestational sac diameter(mm)	41.88 ± 13.61	38.79 ± 11.88	t=0.90	0.36
2D.US yolk sac diameter(mm)	5.21 ± 1.33	5.10 ± 1.21	t=0.32	0.74
2D.US CRL (mm)	26.72 ± 8.40	24.01 ± 9.61	U=1.16	0.24
FHR(b/m)	133.90 ± 21.97	153.31 ± 20.97	t=2.99	0.005
3D.US gestational sac vol. (cm ³)	22.40 ± 10.71	21.53 ± 14.15	U=0.74	0.45
3D.US yolk sac vol. (cm ³)	0.12 ± 0.10	0.11 ± 0.09	U=0.53	0.59

Table (3): Ultrasound parameters in group developed miscarriage and non- miscarriage group (continued till 24 weeks):

	Non miscarriage group (n=40) Mean \pm SD	Miscarriage group (n=20) Mean \pm SD	Test of sig	P value
2D.US gestational sac diameter(mm)	42.86 \pm 8.50	35.44 \pm 17.85	U=2.77	0.006
2D.US yolk sac diameter (mm)	5.25 \pm 1.16	4.82 \pm 1.46	t=1.24	0.21
2D.US CRL (mm)	26.74 \pm 7.06	21.92 \pm 12.37	U=2.25	0.02
FHR	144.74 \pm 22.72	134.80 \pm 29.43	U=0.68	0.49
3D.US gestational sac vol. (cm ³)	24.31 \pm 11.05	17.27 \pm 13.99	U=2.6	0.009
3D.US yolk sac vol. (cm ³)	0.13 \pm 0.10	0.08 \pm 0.07	U=1.74	0.08

Table (4): Yolk sac characters in the miscarriage and the non- miscarriage group:

2D yolk sac shape	Non miscarriage group (n=40) No %	Miscarriage group (n=20) No %	Z test	P value
Absent:	0 (0.0)	6(30.0)	2.54	0.01
Calcified:	0 (2.5)	2 (10.0)	1.18	0.23
Oval:	0 (0.0)	2 (10.0)	1.18	0.23
Round:	39 (97.5)	10 (50.0)	3.89	<0.001

Table (5): 3D.US parameters in non- miscarriage cases between 6—11 weeks of pregnancy:-

	GA	N	Mean	S.D	95% C I	
3D US gestational sac volume (cm ³)	6-<7	2	17.1500	6.29325	2.153	32.147
	7-<8	10	26.4680	16.10503	19.761	33.175
	8-<9	12	19.2542	7.60638	13.132	25.377
	9-<10	10	24.2500	8.25486	17.543	30.957
	10-11	6	33.3667	6.26440	24.708	42.025
3D US	6-<7	2	.0850	.02121	.068	.238

Yolk sac volume (cm ³)	7-<8	10	.1200	.10111	.052	.188
	8-<9	12	.1383	.08632	.076	.201
	9-<10	10	.1370	.11480	.069	.205
	10-11	6	.1700	.14353	.082	.258

*C I: confidence interval

Table (6): 3D.US parameters in cases developed miscarriage between 6—11 weeks of pregnancy:-

	GA	N	Mean	S.D	95% C I	
3D US Gestational sac volume (cm ³)	6-<7	3	3.6700	4.46396	7.240	14.580
	7-<8	8	11.6875	6.74779	5.006	18.369
	8-<9	2	10.3000	.70711	3.062	23.662
	9-<10	3	38.1000	11.20536	27.190	49.010
	10-11	4	26.5000	13.77026	17.051	35.949
3D US Yolk sac volume (cm ³)	6-<7	3	.0267	.04619	.063	.116
	7-<8	8	.0425	.04027	.012	.097
	8-<9	2	.1500	.21213	.040	.260
	9-<10	3	.1067	.08622	.017	.196
	10-11	4	.0525	.03775	.025	.130

Table (7): Screening parameters of gestational US measurements for the study participants between 6-11 weeks

	*AUC	Cut off point	Sensitivity	Specificity	*PPV	*NPV	Accuracy
3D US Gestational sac volume (cm ³)	0.70	≤ 13.75	87.5%	65.0%	83%	72%	80%
3 D US Yolk sac volume (cm ³)	0.56	≥ 0.05	77.5%	37.5%	76%	40%	66%

*AUC: area under curve * PPV: positive predictor value

* NPV: negative predictor value