Using Ultrasound for Pregnancy Failure in Patients with 1st Trimester Recurrent Pregnancy Loss

Abdelhaseib salah Saad¹, **Zakaria Fouad Sanad¹**, **Ahmed Hammouda Hossameldin²**, **Dalia Ibrahim¹** ¹Obstetrics and Gynecology Department, Faculty of Medicine, Menoufia University, Menoufia, Egypt

²Obstetrics and Gynecology Department, Rashid General Hospital, Al Behera, Egypt

*Corresponding author: Ahmed H. Hossameldin, Mobile: +201005440517, E-mail: docahmedhamoda@gmail.com

ABSTRACT

Background: Pregnancy loss is the interruption and/or termination of pregnancy, either spontaneously or intentionally, before the fetus develops sufficiently to survive. About 80% of abortions occur in the first 12 weeks of pregnancy. **Objective:** To determine the accuracy of U/S parameters in predicting early pregnancy failure in pregnant with history of 1st trimesteric recurrent pregnancy loss.

Patients and methods: This was a prospective study that included 120 pregnant females with history of first trimesteric recurrent pregnancy loss. It was conducted in Obstetrics and Gynecology Department, Menoufia University Hospitals, and Rashid General Hospital, Al-Bahira, Egypt during the period from April 2019 until August 2020.

Results: There is no significant difference between miscarriage group and ongoing pregnancy group regarding risk factors and demographic data (p > 0.05). In addition, crown-rump length (CRL) below 5th percentile for gestational age (GA) category more significantly prevalent in the miscarriage group compared to the ongoing pregnancy group. While, mean gestational sac diameter (MGSD) below 5th percentile for GA, caudal displacement of gestational sac (GS) or irregular GS could predict subsequent miscarriage. Embryonic heart rate/Fetal heart rate (EHR/FHR) below 5th percentile for GA was statistically significantly more prevalent in the miscarriage group than in ongoing pregnancy group. Abnormally large YSD (> 95th percentile for GA), absent yolk sac (YS), floating YS, deformed, irregular or hypo-echoic YS could predict subsequent miscarriage. Uterine artery resistance index (RI), pulsatile index (PI) and systolic/diastolic (S/D) ratio did not differ significantly between the miscarriage group compared to the ongoing pregnancy group across the various gestational ages.

Conclusion: 1st trimester U/S parameters are useful diagnostic tool to prognosis pregnancy outcome among patients with history of recurrent 1st trimester pregnancy loss.

Keywords: aborted cases, miscarriage, ongoing pregnancy, pregnancy outcome, ultrasonographic predictor, 1st trimesteric pregnancy.

INTRODUCTION

Recurrent pregnancy loss (RPL) also known as recurrent miscarriage or habitual abortion is defined as three or more consecutive pregnancy losses prior to 24 weeks gestational age from the last menstrual period ⁽¹⁾. American Society of Reproductive Medicine and European Society for Human Reproduction and Embryology defined RPL as two or more clinical and consecutive pregnancy losses, ectopic and molar pregnancies being excluded. However, RPL is to be considered after two or more failed pregnancies, which have a radiological or histopathological documentation. Some investigation must be done after each pregnancy loss with a comprehensive evaluation to be done after three or more losses. 80.0% of miscarriages occurs early in pregnancy (in the first trimester) and the rate decreases with advancement of gestational age ⁽²⁾.

Fetal chromosomal aberrations are the most frequent cause of first trimester abortion, but possibility of abortion due to fetal aneuploidy decreases with subsequent pregnancy losses. A structural chromosomal defect, usually a balanced translocation is found in either of the spouse in 2–5% couples with RPL ⁽³⁾. American College of Obstetrics and Gynecology recommends karyotyping of products of conception in

woman with 2 consecutive or 3 non-consecutive miscarriages. For an aneuploidy fetus, no further

evaluation of couple is required and pre-implantation genetic diagnosis may be attempted in future pregnancies ⁽⁴⁾. Empirical treatment in women with unexplained recurrent miscarriage is superfluous and should be avoided. Rather, there is a need of focus on pre-conceptional prophylactic folic acid, correction of hormonal imbalance, any preexisting genital infection and correctable structural defect in the reproductive tract ⁽⁵⁾. Stress reduction and lifestyle modification like curtailing use of tobacco, alcohol, and illicit drugs must be emphasized as these factors may also contribute and hamper a successful pregnancy outcome ⁽⁶⁾.

Ultrasound has its profound influence on the practice of medicine, either in obstetrics or in gynecology. The invention of transvaginal ultrasound (TVUS) has markedly enhanced the assessment of early pregnancy in cases of threatened abortion. The rate of fetal loss is about 15% in females with threatened abortion and a living baby in first trimester. The use of color Doppler is beneficial in assessing abnormalities. Ultrasound checkup has become the "gold standard" in assessment and follow-up of pregnancy and the development of complications in early pregnancy. Ultrasonographic findings such as irregular wall of



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gestational sac, low fetal heart rate (intrauterine bradycardia), pregestational hematoma etc. are indicative of threatened abortion. It has helped in managing the patients ⁽⁷⁾. Therefore, the aim of this study was to assess accuracy of ultrasonographic parameters in predicting early pregnancy failure in pregnant women with history of first trimesteric recurrent pregnancy loss.

SUBJECTS AND METHODS

This was a prospective study included 120 pregnant females with history of first trimesteric recurrent pregnancy loss. It was conducted at Obstetrics and Gynecology Department, Menoufia University Hospitals, and Rashid General Hospital, Al-Bahira, Egypt during the period from April 2019 till August 2020.

Inclusion criteria: single intrauterine pregnancy, gestational age by last menstrual period of 6-10 weeks in patients with regular cycles and sure of their last menstrual period date, history of first trimestric recurrent pregnancy loss.

Exclusion criteria: women who were uncertain of their last menstrual period date, women with irregular menstrual cycles and multiple pregnancies.

Patient were subjected to the following:

History taking: personal and family history, detailed obstetric history including parity, method and place of previous deliveries, time at which previous abortions had occurred, past history with special interest directed towards past history of systemic diseases such as diabetes mellitus, hypertension, past history of infants with chromosomal abnormalities.

Clinical examination: general, abdominal, pelvic examination and TVUS were done. Mean gestational sac diameter (MGSD) was determined by measuring mean of 3 diameters, which is measured from inside of the sac excluding the decidual reaction from the measurement. Yolk sac was measured by placing calipers on the inner limits of the longer diameter. Size

Table	(1):	Demogra	phics	of	studied	grouns
Table	(1)•	Demogra	pines	01	stuuteu	groups

of the sac, shape, echogenicity of the rim and center of sac, its number and degenerative changes was evaluated. CRL was measured as the length of the embryo from the top of its head to bottom of torso excluding the yolk sac and the extremities, measured in the sagittal plane of the embryo and recorded as an average of three measurements. Embryonic/Fetal heart rate was calculated as beat per minute using software of ultrasound machine after measuring by electronic calibers of distance between 2 heart waves on frozen M-mode image. Uterine artery Doppler with measurement of S/D ratio, resistance index (RI) and pulsatility index (PI) of uterine arteries.

Ethical consent:

An approval of the study was obtained from Menoufia University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of the study after explanation of the trial benefits and hazards. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical Analysis

Our data were tabulated and analyzed statistically using Microsoft Excel 2019 and SPSS v. 21 (SPSS Inc., Chicago, IL, USA). Statistical analysis was done using descriptive and analytical tests. Descriptive included percentage (%), mean and standard deviation. Analytical included Chi-square (χ^2) test, Fischer exact test, student t test and Mann-Whitney test. Considering P-value ≤ 0.05 statistically significant.

RESULTS

In our study, mean for age in aborted and ongoing pregnant cases was 30.5 ± 2.8 year and 31.1 ± 3.6 year, (P=0.436). The mean for BMI of them was 29.8 ± 2.75 kg/m² and 29.1 ± 2.84 kg/m² respectively. There was no statistically significant difference between the two groups regarding age or BMI. Regarding GA at 1st visit was 6.97 ± 0.73 and 6.8 ± 0.79 weeks in aborted and ongoing pregnant cases (Table 1).

Variable	Overall Cases (n=120)	Aborted Cases (n=50)	Ongoing Pregnancy (n=70)	P value
Age (years)	30.8 ± 3.55	30.5 ± 2.8	31.1 ± 3.6	0.436
BMI (kg/m^2)	29.4 ± 2.9	29.8 ± 2.75	29.1 ± 2.84	0.280
GA at 1 st visit (wks.)	6.8 ± 0.82	6.97 ± 0.73	6.8 ± 0.79	0.330

GA: gestational age BMI: body mass index

Regarding risk factors, SLE cases were 4 cases among aborted cases (10.3%) and 6 cases in ongoing pregnant cases (11.8%). APL cases were 6 cases among aborted cases (15.4%) and 9 cases in ongoing pregnant (15.4%). Cases with thrombophilia were 4 cases among aborted cases (10.3%) and 8 cases in ongoing pregnant cases (15.7%). Cases of hypo or hyper thyroids were 4 cases among aborted cases (10.3%) and 12 cases among ongoing pregnant cases (23.5%). Aborted cases with consanguinity were 7 cases (18%) while ongoing pregnant cases with positive consanguinity were 3 cases (5.9%) as shown in table (2).

Risk factor	Overall cases	Aborted cases	Ongoing pregnancy
	(N=120)	(N=50)	(N=70)
SLE	20(16.67%)	8(16%)	12 (17.14%)
APL	30(25%)	12(24%)	16(22.86%)
Thrombophilia	24(20%)	8(16%)	14(20%)
Thyroid disorder	26(21.66%)	8(16%)	24(34.29%)
Consanguinity	20(16.67%)	14(28%)	4(5.71%)

Table (2): Risk factors for abortion in pregnant women of the study

SLE: Systemic lupus erythematosus. APL: Anti phospholipid

In the current study, CRL was < 5th percentile for GA was 20 cases among miscarriage group (60.6%) while 8 cases in ongoing pregnancy group (16.3%), CRL between 5th and 95th percentile for GA was 13 cases among miscarriage group (39.3%), while it was 41 cases in ongoing pregnancy group (83.6%). A statistically significant difference between both groups, with the MGSD below 5th percentile for GA category, more prevalent in the miscarriage group compared to the ongoing pregnancy group. Moreover, embryonic HR/fetal heart rate < 5th percentile for GA was 17 cases among miscarriage group (70.8%) and 5 cases in ongoing pregnancy group (10.2%), EHR/FHR between 5th and 95th percentile for GA was 7 cases among miscarriage group (29.1%) while 44 cases in ongoing pregnancy (89.7%), (P < 0.001). Regarding, YS diameter > 95th percentile for GA was 27 cases among miscarriage group (10.2%). YS diameter between (5th and 95th) percentile for GA was 6 cases among miscarriage group (18.1%) while 44 cases in ongoing pregnancy group (89.7%) as shown in table (3).

Table (3): CRL, MGSD, EHR/FHR and yolk sac diameter percentile categories in the ongoing pregnancy and miscarriage groups

CRL percentile	Ongoing pregnancy	Miscarriage group	P-value
for GA	(N=70)	(N=39)	
• $<5^{\text{th}}$	16 (22.86%)	25 (64.10%)	< 0.001*
• 5^{th} -95 th	54 (77.14%)	14 (35.90%)	
• >95 th	0 (0%)	0 (0%)	
MGSD	Ongoing pregnancy (n=70)	Miscarriage group (n=44)	P-value
• $<5^{th}$	14 (20%)	30 (68.18%)	< 0.001*
• $5^{th} -95^{th}$	56 (80%)	14 (31.82%)	
• $>95^{th}$	0 (0%)	0 (0%)	
Embryonic/Fetal heart rate	Ongoing pregnancy (n=70)	Miscarriage group (n=30)	P-value
• $<5^{th}$	15 (21.43%)	20 (66.67%)	< 0.001*
• $5^{th} -95^{th}$	55 (78.57%)	10 (33.33%)	
• $>95^{th}$	0 (0)	0 (0%)	
Yolk sac diameter	Ongoing pregnancy (N=70)	Miscarriage group (N=39)	P-value
• $<5^{th}$	0 (0%)	0 (0%)	< 0.001*
• $5^{th} - 95^{th}$	55 (78.57%)	9 (23.08%)	
• $>95^{th}$	15 (21.43%)	30 (76.92%)	

GA: gestational age CRL: Crown rump length GS-MSD: Gestational sac mid sac diameter *significant

In addition, in the current study, absent YS was statistically significantly more prevalent in miscarriage group compared to ongoing pregnancy group. Floating YS could predict subsequent miscarriage. Deformed or irregular YS could predict subsequent miscarriage. Uterine artery S/D ratio did not differ significantly between the miscarriage group compared to the ongoing pregnancy group across the various gestational ages (Tables 4, 5 & 6).

Table (4): Changes of degenerative YS for prediction of subsequent miscarriage.

Changes of	Ongoing	Miscarriage
dogonorativo VS	pregnancy	group
degenerative 15	(N=70)	(N=39)

Absent	62 (88.57%)	29 (74.36%)	
Present	8 (11.43%)	10(14.29%)	
AUC	0.67		
P value	0.28		
Sensitivity	43.21%		

Specificity	85.74%
Positive likelihood ratio	1.55(0.722 - 4.965)
Negative likelihood ratio	0.360 (0.115 - 2.843)
PPV	83.01%
NPV	59.86%

AUC: area under curve PPV: positive predictive value NPV: negative predictive value

Table (5): YS prediction and uterine artery S/D in the ongoing pregnancy and miscarriage groups

	Ongoing	Miscarriage	P value
	pregnancy (N=70)	group (N=39)	
Absent YS	0(0.0%)	6(12%)	0.0169
Round regular YS	65(92.8%)	33(66%)	0.028
Irregular YS	4(5.7%)	11(22%)	0.042
Adherent YS to GYS	64(91.4%)	34(68%)	0.009
Floating YS	5(7.1%)	11(22%)	0.016
Uterine artery S/D ratio	5.71±3.04	5.41±3.07	0.280

Table (6):	Uterine artery	/ S/D in the	ongoing pregna	ncy
and miscar	riage groups a	across the va	arious GA.	

GA	Ongoing pregnancy (n=70)	Miscarriage group (n=44)	P value
6 weeks 7 weeks 8 weeks 9 weeks 10 weeks	$5.71 \pm 3.04 \\ 5.63 \pm 2.99 \\ 5.53 \pm 2.79 \\ 5.48 \pm 2.65 \\ 5.31 \pm 2.82$	$5.41 \pm 3.07 \\ 5.35 \pm 3.01 \\ 5.24 \pm 2.85 \\ 5.19 \pm 2.63 \\ 5.17 \pm 2.77$	0.64 0.66 0.63 0.61 0.81

GA: gestational age/week

DISCUSSION

Our study results agree with **Detti** *et al.* ⁽⁸⁾ who demonstrated that there was no statistical difference regarding maternal age and BMI that signify miscarriage. Also, **Radwan** *et al.* ⁽⁹⁾ found that there was no statistical difference regarding maternal age and BMI that signify miscarriage. On the other hand, our results stand against **Kanmaz** *et al.* ⁽¹⁰⁾ who found in his study that there was a significant increase in the maternal age for cases with miscarriage.

In our study, there was no statistically difference between the two groups regarding SLE, APL, thrombophilia, thyroid disorders and consanguinity of couples. These agree with Skeith et al. (11) and Bradley et al. (12) who found no significant relation between thrombophilia and recurrent miscarriage, which runs in line with our results. The results disagree with Burkui et al. ⁽¹²⁾ who found a significant correlation between SLE and recurrent miscarriage either due to SLE itself or due to increase APL in their sera. Skeith et al. (11) documented in their guidelines that hyperthyroidism increases the risk of pregnancy complications. All women were subjected to ultrasonographic examination to analyze its value in the prediction of the pregnancy outcome at the end of the first trimester. However, it should be noted that some patients were excluded from analysis in some U/S parameters due to arrest of embryonic development prior to its visualization by U/S. CRL percentile categories were statistically significantly different between both groups; with the CRL below 5th percentile for GA category more prevalent in the miscarriage group compared to the ongoing pregnancy group. For this reason, the presence of CRL < 5th percentile for GA could predict subsequent miscarriage. Also, Detti et al. (8) reported that the deterioration in progressive increase in the CRL signify miscarriage of pregnancies in their group of women, which runs in line with our results. Radwan et al. (9) found that there was no significant difference between miscarriage group and ongoing pregnancy group regarding CRL, which is conflicting with our results.

In our study, mean GS diameter $< 5^{\text{th}}$ percentile for GA was significantly more prevalent in the miscarriage group. Yi et al. (13) found that the increase in the GSD was associated with increased incidence of completion of pregnancy while reduction in GSD was highly associated with miscarriage which runs in line with our results. Radwan et al.⁽⁹⁾ found no significant difference between miscarriage group and ongoing pregnancy group regarding GSD, which is conflicting with our results. Our study revealed the presence of GS caudally or irregular GS commonly denoted that the pregnancy will be miscarriage. Lebda et al. (14) found a significant correlation between irregularity in the GS and the miscarriage, which is in agreement with our results. Our study revealed reduction of FHR below 5th percentile for GA was statistically signifies miscarriage of the pregnancy. Datta and Raut (15) found that the decrease in the FHR below 5th percentile was significantly associated with increased incidence of miscarriage which runs in line with our results.

In our study enlarged YSD > 95th percentile for GA, absent YS or irregular deformed YS usually signify miscarriage of the present pregnancy. **Lebda** *et al.* ⁽¹⁴⁾ found that the increase in YSD above 95th percentile, absent YS or irregular deformed YS was significantly associated with increased incidence of miscarriage, which runs in line with our result. Our study found that uterine artery RI, PI and S/D ratio did not significantly

differe among miscarriage group compared to ongoing pregnancy group. **El-Behery** *et al.* ⁽¹⁶⁾ found a relation between the unilateral elevation of uterine arteries PI in the first trimester and the subsequent occurrence of miscarriage, which disagree with our results.

CONCLUSION

We concluded that, 1st trimester U/S parameters are useful diagnostic tool for prognosis of pregnancy outcome among patients with history of recurrent 1st trimester pregnancy loss.

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