

# CORRELATION BETWEEN ULTRASOUND PARAMETERS AND RECURRENT PREGNANCY LOSS IN FIRST TRIMESTER

By

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## ABSTRACT

**Background:** First trimester recurrent pregnancy loss is three or more consecutive miscarriage which can be due to genetic, anatomical, endocrinological, immunological, microbiological and environmental factors.

**Objective:** To evaluate the correlation between each of the ultrasound parameters that assessed in the first trimester (the gestational sac size, yolk sac size, crown rump length and fetal cardiac activity) to early pregnancy loss.

**Patients and Methods:** This was a prospective study of 100 (1 hundred) pregnant women in their first trimester that were carried out in the outpatient clinic and Emergency Department – Obstetrics and Gynecology Department – Al-Sayed Galal Hospital and Basyoun Hospital during the period from 1st April 2020 till 1st October 2020. They classified into two equal groups:

**Group I:** Pregnant women with history of first trimester recurrent pregnancy loss as cases.

**Group II:** Pregnant women with history of normal obstetric history as controls. Transvaginal ultrasound scan was used to assess mean gestational sac diameter, yolk sac, crown-rump length and fetal heart rate.

**Results:** The gestational sac diameter grew 6.65 mm per week in ongoing pregnancy group, and it was smaller in the pregnancy loss group. However, the difference was not significant until 8 weeks of pregnancy when the median diameter of the gestational sac was 15 mm in pregnancy losses, and 31 mm in ongoing pregnancy ( $p < 0.001$ ). The yolk sac grew 0.38 mm per week in ongoing pregnancy group with  $p$  value  $< 0.001$  at 10th week.

In pregnancy loss group, the yolk sac was either smaller or larger than in ongoing pregnancy group. The crown-rump length grew 7.54 mm per week, and was significantly larger in the ongoing pregnancy than in the pregnancy loss group from 6<sup>th</sup> -10<sup>th</sup> week with  $p$  value  $< 0.001$ . The embryonic heart rate less than 100 b/m was associated with higher risk of pregnancy loss.

**Conclusion:** The diagnosis of miscarriage was made in the presence of fetal pole 10 mm with no fetal heart activity, or the gestational sac diameter was 25 mm but no fetal pole could be demonstrated. In cases of an empty gestational sac 25 mm in diameter, a repeated scan was carried out 1-2 weeks later.

**Key word:** Ultrasound, Gestational sac diameter, Yolk sac, Crown-rump length, fetal heart rate, Recurrent pregnancy loss.

## INTRODUCTION

Early pregnancy loss is also known as pregnancy loss, fetal demise, miscarriage, or spontaneous abortion. It is defined as a

nonviable, intrauterine pregnancy with either an empty gestational sac or a gestational sac containing an embryo or fetus without fetal heart activity prior to

12<sup>th</sup> weeks and 6 days of gestation (ACOG, 2018).

The gestational sac is the first pregnancy structure that can be detected by ultrasound. It is usually visualized from 31 days or 4 weeks and 3 days of gestation using the transvaginal method, when it measures 2-3 mm in diameter. It can be identified about a week later when using the abdominal route (Tan *et al.*, 2014).

Yolk sac is the first recognizable structure inside the gestational sac and should be obtained as regular round extra-amniotic structure when gestational sac reaches 8-10 mm. Normal biometric values of yolk sac diameter during the first trimester are 3-6 mm. Crown rump length is used to estimate growth of the embryo and define the exact gestational age (Jennifer *et al.*, 2013).

Once the embryonic pole is detected, measured of crown rump length of the embryo considered the most accurate ultrasonographic way to date the pregnancy (Napolitano *et al.*, 2014).

Cardiac activity can be identified when the embryo reaches 5 mm in length, equivalent to 6<sup>th</sup> weeks and 3 days gestation and a mean sac diameter of 15-20 mm. All embryo of CRL>7mm in length should demonstrate visible cardiac activity (Yi *et al.*, 2016).

**This work aimed to** evaluate the correlation between each of the ultrasound parameters that assessed in the first trimester (the gestational sac size, yolk sac size, crown rump length and fetal cardiac activity) to early pregnancy loss.

## PATIENTS AND METHODS

This was a prospective study of 100 (1 hundred) pregnant women in their first trimester that were carried out in the outpatient clinic and Emergency Department – Obstetrics and Gynecology Department, Al-Sayed Galal Hospital and Basyoun Hospital during the period from 1<sup>st</sup> April 2020 till 1<sup>st</sup> October 2020. They classified into two equal groups:

**Group I:** Pregnant women with history of first trimester recurrent pregnancy loss as cases

**Group II:** Pregnant women with history of normal obstetric history as controls.

### Inclusion criteria:

- Positive pregnancy test.
- Single intrauterine pregnancy.
- Maternal age ranges between 20 and 35 years.
- In the first trimester of pregnancy with no symptoms of threatened miscarriage when first scan.
- History of first trimester recurrent miscarriage.

### Exclusion criteria:

- Multiple pregnancies.
- Maternal age less than 20 or over 35 years
- Symptoms of threatened miscarriage when first scan

**For the scan, we used ultrasound machine:** Logic P5 with 7.5 MHZ Transvaginal probe and 3.5 MHZ Transabdominal probe.

Transabdominal scanning was done with distended bladder. Then, patient was

asked to void urine and transvaginal sonography was done.

**Transvaginal ultrasound scans for assessing:**

- a. Mean gestational sac diameter (MGSD) was determined by measuring the mean of 3 diameters (longitudinal, antero-posterior and transverse) which were measured from inside of the sac excluding the decidual reaction from the measurement. It was normally eccentric in location embedded in endometrium, and had a smooth; round or oval shape.
- b. Yolk sac (YS) was measured by placing the calipers on the inner limits of the longer diameter. It usually appeared at the periphery of the gestational sac and should not be floating within the sac. Size of the sac, shape, Echogenicity of the rim and center of sac, its number and degenerative changes such as calcification were evaluated. YS having diameter between 3-7 mm, rounded shapes, absence of degenerative changes, presence of echogenic rim and hypoechoic center

were considered normal. Any deviation from above parameters was considered abnormal.

- c. Crown-rump length (CRL) was measured as the length of the embryo from the top of its head to bottom of torso excluding the yolk sac and extremities Measured in the sagittal plane of the embryo and recorded as an average of three measurements.
- d. Fetal heart rate by M-mode was calculated as beat per minute using software of ultrasound machine after measuring by electronic calipers of distance between 2 heart waves on frozen M-mode image.

**Statistical method**

Statistical analyses of data carried out using SPSS version 20 data were summarized as mean  $\pm$  standard deviation or median and range.

Both independent and paired t-test or Mann-Whitney U test was used for comparison of means. The P-value was considered significant when  $p \leq 0.05$ .

## RESULTS

The study involved 100 pregnant women examined using 2D ultrasonography starting early in the first trimester. A follow up scan every 2 weeks until the pregnancy reached the end of first trimester unless the patient miscarried before that.

The mean age of the studied group was 26.4 years ranged between 20 and 35 Of the cases group 28 (56%) ongoing pregnancy and entered the 2nd trimester successfully while 22 (44%) resulted in miscarriage (**Table 1**).

**Table(1): The final outcome of the cases group**

Cases group	N	%
Ongoing	28	56.00
Loss	22	44.00
Total	50	100.00

Of the controls group, 46 (92%) were ongoing pregnancy and entered the 2nd

trimester successfully, while 4 (8%) resulted in miscarriage (**Table 2**).

**Table(2): The final outcome of the controls group**

Controls group	N	%
Ongoing	46	92.00
Loss	4	8.00
Total	50	100.00

The gestational sac diameter grew 6.65 mm per week in ongoing pregnancy group, and it was smaller in the pregnancy loss group. However, the difference was not significant until 8 weeks of pregnancy when the median diameter of the gestational sac was 15 mm in pregnancy

losses and 31 mm in ongoing pregnancy ( $p < 0.001$ ).

From 6-10 week gestation a smaller gestational sac was associated with an increased risk of pregnancy loss (**Table 3**).

**Table (3): Comparison of gestational sac diameter in the ongoing pregnancy and pregnancy loss groups**

Groups		Ongoing (N=50)			Loss (N=50)			P-value
Gestational Sac diameter								
5 Weeks	Range	7	-	13	6	-	11	<0.001
	Mean $\pm$ SD	10.12	$\pm$	1.536	8.692	$\pm$	1.70	
6 Weeks	Range	13	-	19	7	-	13	<0.001
	Mean $\pm$ SD	15.46	$\pm$	1.968	9.889	$\pm$	1.83	
7 Weeks	Range	21	-	27	11	-	21	<0.001
	Mean $\pm$ SD	23.29	$\pm$	1.687	15.39	$\pm$	2.69	
8 Weeks	Range	26	-	33	12	-	20	<0.001
	Mean $\pm$ SD	28.73	$\pm$	2.102	16.11	$\pm$	2.47	
9 Weeks	Range	34	-	42	19	-	27	<0.001
	Mean $\pm$ SD	37.12	$\pm$	2.118	20.92	$\pm$	2.36	
10 Weeks	Range	39	-	48	19	-	22	<0.001
	Mean $\pm$ SD	42.70	$\pm$	3.335	20.17	$\pm$	1.47	

The yolk sac grew 0.38 mm per week in ongoing pregnancy group with p wave <0.001 at 10 week. In pregnancy loss

group, the yolk sac was either smaller or larger than in ongoing pregnancy group (**Table 4**).

**Table (4): Comparison of yolk sac diameter in the ongoing pregnancy and pregnancy loss groups.**

Groups		Ongoing (N=50)			Loss (N=50)			P-value
Yolk sac Diameter								
5 Weeks	Range	2	-	2.8	1.6	-	2.6	<0.001
	Mean $\pm$ SD	2.288	$\pm$	0.190	2.046	$\pm$	0.399	
6 Weeks	Range	2.3	-	2.9	1.6	-	3.7	<0.001
	Mean $\pm$ SD	2.564	$\pm$	0.201	2.844	$\pm$	0.725	
7 Weeks	Range	2.7	-	3.3	3	-	4.9	<0.001
	Mean $\pm$ SD	3.044	$\pm$	0.186	3.638	$\pm$	0.727	
8 Weeks	Range	2.7	-	3.7	2.9	-	5.2	<0.001
	Mean $\pm$ SD	3.250	$\pm$	0.294	4.022	$\pm$	0.879	
9 Weeks	Range	3	-	4.1	2.1	-	4.3	<0.002
	Mean $\pm$ SD	3.813	$\pm$	0.263	3.485	$\pm$	0.653	
10 Weeks	Range	3.6	-	4.5	1.8	-	3.2	<0.001
	Mean $\pm$ SD	4.150	$\pm$	0.303	2.856	$\pm$	0.475	

The crown-rump length grew 7.54 mm per week, and was significantly larger in the ongoing pregnancy than in the

pregnancy loss group from 6-10 week with p value <0.001 (Table 5).

**Table (5): Comparison of crown-rump length diameter in the ongoing pregnancy and pregnancy loss groups**

Crown-rump length diameter		Ongoing (N=50)			Loss (N=50)			P-value
5 Weeks	Range	1.9	-	4.3	1.5	-	3.1	0.004#
	Mean ±SD	2.529	±	0.761	2.131	±	0.509	
6 Weeks	Range	4.3	-	6.4	2.5	-	4.4	<0.001
	Mean ±SD	4.964	±	0.610	3.356	±	0.760	
7 Weeks	Range	10.8	-	13.4	4.5	-	6.1	<0.001
	Mean ±SD	11.775	±	0.772	5.038	±	0.472	
8 Weeks	Range	17.8	-	19.7	4.2	-	5.9	<0.001
	Mean ±SD	18.563	±	0.585	5.178	±	0.710	
9 Weeks	Range	24.7	-	28.3	6.2	-	16.9	<0.001#
	Mean ±SD	25.924	±	0.983	10.942	±	3.780	
10 Weeks	Range	35.3	-	37.3	5.8	-	13.1	<0.001#
	Mean ±SD	36.110	±	0.547	7.333	±	2.224	

# Mann-Whitney U test was used.

The embryonic heart rate can be visualized as early as 5th-6th week of gestation and the mean heart rate progressively increases from 6<sup>th</sup> week (120 – 140 bpm) to 9<sup>th</sup> week (145 – 170 bpm), then the heart rate gradually decreased to 150 bpm at 12th week of gestation. Bradycardia at initial scan was not an absolute indicator for an unhealthy

pregnancy as there was significant bradycardia in some patient at initial scan which turned out to have a normal pregnancy and demonstrated increased heart rate at subsequent scans. It has been observed that the embryonic heart rate less than 100 bpm is associated with higher risk of pregnancy loss (Table 6).

**Table (6): Comparison of fetal heart rates in the ongoing pregnancy and pregnancy loss groups**

Fetal heart Rates		Ongoing (n=50)			Loss (n=50)			P-value
5 Weeks	Range	90	-	120	95	-	115	<0.003
	Mean ±SD	105.412	±	9.931	110.615	±	6.225	
6 Weeks	Range	110	-	120	98	-	126	0.086
	Mean ±SD	115.909	±	3.300	113.111	±	10.937	
7 Weeks	Range	130	-	150	100	-	150	<0.001
	Mean ±SD	137.294	±	4.753	111.769	±	18.948	
8 Weeks	Range	150	-	171	84	-	162	0.001#
	Mean ±SD	164.727	±	6.084	126.778	±	32.155	
9 Weeks	Range	160	-	170	80	-	178	<0.001#
	Mean ±SD	167.118	±	2.619	111.077	±	37.279	
10 Weeks	Range	160	-	174	84	-	178	0.002#
	Mean ±SD	167.727	±	4.735	123.143	±	40.806	

# Mann-Whitney U test was used.

## DISCUSSION

In this study, we aimed to predict the risk of spontaneous miscarriage in patients with first trimesteric recurrent pregnancy loss by using the first trimesteric ultrasonographic markers. The case that subsequently resulted in pregnancy loss had a smaller gestational sac for gestation than in those who continued to have normal pregnancy. The study of *Mukri et al. (2013)*, where women with history of recurrent pregnancy loss, revealed that gestational sac was smaller in pregnancies that subsequently ended in miscarriage than in those that remained viable. The study of *Datta et al. (2017)*, reported that gestational sac below the 5th percentile would predict early pregnancy loss.

The finding of this study demonstrated that the large yolk sac was a good indication that the probability of pregnancy loss will be significantly high. In the study of *Tan et al. (2014)*, they had shown that pregnant women between 6- 9 weeks of gestation has revealed that enlarged yolk sac visualization before the 7th weeks of gestation is strongly associated with a significantly increased risk for spontaneous miscarriage. In the study of *Ashoush et al. (2015)*, they had shown that a large yolk sac at any gestational age was associated with early pregnancy loss.

The current study showed that the crown-rump length was statistically significantly different between both groups, whereas the cases that subsequently resulted in pregnancy loss had a smaller mean crown-rump length for gestation than in those who continued to have a normal pregnancy. *Altay et al. (2010)* found that the risk of fetal loss was

higher when crown-rump length was below the 50th percentile for gestational age. *Papioannou et al. (2011)* reported that about 85% of miscarriage the embryonic crown-rump length at the time of early scan was 12 mm (below the 5th percentile for gestational age). This reflects the inverse relationship between the rate of miscarriage and gestational age because the majority of embryonic death, either resulting from lethal abnormalities or placental failure occurs before the 8th week of pregnancy. *Bottomley et al. (2012)* demonstrated the association between the smaller than expected embryonic crown-rump length and the increase probability of subsequent miscarriage.

In the current study, the embryonic heart rate can be visualized as early as 5<sup>th</sup>-6<sup>th</sup> week of gestation, and the mean heart rate progressively increases from 6<sup>th</sup> week (120 – 140 bpm) to 9<sup>th</sup> week ( 145 – 170 bpm) then, the heart rate gradually decreased to 150 b/m at 12th week of gestation. The embryonic heart rate less than 100 b/m was associated with higher risk of pregnancy loss. *Pillai et al. (2018)* reported that HR  $\leq$  110 beats per minute (BPM) was the most reliable model to predict a subsequent pregnancy loss, with a sensitivity of 68.4%, a specificity of 97.8%, a positive likelihood ratio of 31.7 (95% confidence interval 12.8–78.8), and a negative likelihood ratio of 0.32 (95% confidence interval 0.16–0.65). In pregnancies with vaginal bleeding, in addition to an HR  $\leq$  110 BPM, prediction of an early loss was higher. *Shenker et al. (2010)* reported that embryonic heart rates before the 7th week of pregnancy showed an increase in rates between 7<sup>th</sup> and 9<sup>th</sup>

gestational weeks. The rates gradually declined thereafter until the 15<sup>th</sup> week.

### CONCLUSION

The ultrasound is intended to be primarily used to diagnosis of early pregnancy loss.

The diagnosis of miscarriage was made if in the presence of fetal pole 10 mm there was no fetal heart activity, or if the gestational sac diameter was 25 mm but no fetal pole could be demonstrated.

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## العلاقة بين الموجات فوق الصوتية وفقد الحمل المتكرر فى الثلث الأول

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**خلفية البحث:** فقدان الحمل المبكر أو فقدان الحمل أو وفاة الجنين أو الإجهاض أو الإجهاض التلقائي - يعرف بأنه "حمل داخل الرحم غير قابل للحياة مع كيس حمل فارغ أو كيس حمل يحتوي على جنين أو جنين بدون نشاط قلب الجنين قبل 12 أسبوع و 6 أيام من الحمل.

**الهدف من البحث:** تقييم العلاقة بين كل من المحددات بالموجات فوق الصوتية التي سيتم تقييمها في الأشهر الثلاثة الأولى (حجم كيس الحمل، حجم كيس المح، طول التاجى المقعدى ونشاط القلب الجنيني) لفقدان الحمل المبكر.

**المريضات وطرق البحث:** هذه دراسة مستقبلية لـ مائة (100) امرأة من الحوامل في الأشهر الثلث الأولى من الحمل أجريت في العيادة الخارجية وقسم الطوارئ، قسم أمراض النساء والولادة، مستشفى السيد جلال الجامعى ومستشفى بسيون المركزى خلال الفترة من الأول من أبريل 2020 حتى الأول من أكتوبر 2020

وقد تم عمل فحص بالموجات فوق الصوتية عبر المهبل واشتمل على:

قطر كيس الحمل، قطر كيس المح، طول التاجى المقعدى، ومعدل ضربات قلب الجنين.

**نتائج البحث:** من بين 50 امرأة حامل في مجموعة الدراسة لديهن تاريخ من فقدان الحمل المتكرر فى الثلث الأول من الحمل، 28 (56%) نتج عنه حمل مستمر ودخلن الثلث الثانى بنجاح بينما أدت 22 (44%) إلى إجهاض ومن بين 50 امرأة حامل فى مجموعة الدراسة مع تاريخ الولادة الطبيعى 46 (92%) نتج عنها حمل مستمر ودخلن الثلث الثانى بنجاح بينما أدت 4 (8%) إلى إجهاض.

**كيس الحمل:** ينمو قطر كيس الحمل 6.65 ملم في الأسبوع في مجموعة الحمل المستمرة وكان أصغر في مجموعة فقدان الحمل. ومع ذلك لم يكن الاختلاف كبيراً حتى 8 أسابيع عندما كان متوسط كيس الحمل 15 ملم في فقدان الحمل و 31 ملم في الحمل المستمر. من 6 إلى 8 أسابيع من الحمل ارتبط كيس الحمل الأصغر بزيادة خطر فقدان الحمل.

**كيس المخ:** ينمو كيس الصفار 0.38 ملم في الأسبوع في مجموعة الحمل المستمرة وكان أصغر أو أكبر من ذلك في مجموعة فقدان الحمل.

**طول التاجي المقعدى:** ينمو طول التاجي المقعدى 7.54 ملم في الأسبوع وكان أكبر بشكل ملحوظ في الحمل المستمر عنه في مجموعة فقدان الحمل من 6-10 أسابيع.

**معدل ضربات القلب الجنيني:** يمكن تصور معدل ضربات القلب الجنيني في وقت مبكر من الأسبوع الخامس إلى السادس من الحمل ويزداد متوسط معدل ضربات القلب تدريجياً من 6 أسابيع (120-140 نبضة في الدقيقة) إلى 9 أسابيع (145-170 نبضة في الدقيقة) ثم ينخفض معدل ضربات القلب تدريجياً إلى 150 نبضة في الدقيقة في الأسبوع 12 من الحمل. لم يكن بطء ضربات القلب في الفحص الأولى مؤشراً مطلقاً على وجود حمل غير صحي حيث كان هناك بطء قلب كبير لدى بعض المرضى في الفحص الأولى والذي تبين أنهن تتمتع بحمل طبيعي وأظهر زيادة في معدل ضربات القلب في عمليات المسح اللاحقة. وقد لوحظ أن معدل ضربات القلب الجنيني الأقل من 100 نبضة في الدقيقة يرتبط بارتفاع مخاطر فقدان الحمل.

**الاستنتاج:** الموجات فوق الصوتية يمكن استخدامها بشكل أساسي لتشخيص فقدان الحمل المبكر. ويتم تشخيص الإجهاض إذا لم يكن هناك نشاط لقلب الجنين في وجود عمود الجنين 10 مم أو إذا كان قطر كيس الحمل 25 مم ولكن لا يمكن إثبات وجود عمود جنيني.

**الكلمات الدالة:** الموجات فوق الصوتية، فقدان الحمل المتكرر، كيس الحمل، كيس المخ، طول التاجي المقعدى، معدل ضربات القلب الجنيني.