

### **Yolk Sac Size and Shape, Gestational Sac Diameter and Embryonic Heart Rate as Prognostic Factors for First Trimesteric Outcome**

Emad Maarof Abd Ellatif, Abdalla Khalil Ahmad, Mohamed Ali Ali Halawa

Department of Obstetrics and Gynecology, Faculty of Medicine, Al Azhar University

\*Corresponding author: Mohamed Ali Ali Halawa, Mobile: 002001008277407, E-Mail: dr\_halawa\_42 @yahoo.com

#### **ABSTRACT**

**Background:** it is estimated that approximately 30% to 40% of implanted pregnancies resulted in spontaneous abortion during the first trimester, most of which occur in very early stage. 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%. **Aim of the work:** this work aimed to evaluate the correlation between the ultrasound parameters that were assessed in the first trimester (the gestational sac size, yolk sac size and shape and embryonic heart rate) to early pregnancy loss and the correlation between different ultrasound parameter to each other. **Methodology:** this study involved 100 pregnant women attending Al Hussein University Hospital. They were examined by using 2D ultrasonography starting early in the first trimester with a first scan between 6 and 8 weeks. A follow up scan was conducted at 9 and 12 weeks. During follow up, 7 women did not return for follow up and accordingly, the results (gestational sac diameter, embryonic heart rate and yolk sac size and shape) of the remaining 93 women were shown. All patients were evaluated by transvaginal ultrasound using equipped with a real-time, 5-MHz sector electronic array endovaginal probe. The fetal heart rate was measured by M-mode in all cases and the yolk sac diameter (YSD) was determined by placing the calipers on the inner limits of the longer diameter. **Results:** in this study, there was a significant increase in age in fetal loss group more than complete pregnancy group. Regarding the relation between gestational sac diameter at different gestational age period and its relation to the outcome of pregnancy, the gestational sac diameter showed a significant decreasing in the fetal loss group at 6, 9 and 12 weeks, so the GS diameter was a good predictor to fetal loss ( $p < 0.05$ ). **Conclusion:** first trimester ultrasound measurement of these parameters (FHR, YS diameter and shape and GS diameter) 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 gestational sac diameter, CRL and fetal heart rate in combination provided better prediction of the prognosis of the first trimester than when either parameter used alone.

**Keywords:** yolk sac diameter, gestational sac diameter, embryonic heart rate

#### **INTRODUCTION**

It was estimated that approximately 30% to 40% of implanted pregnancies resulted in spontaneous abortion during the first trimester, most of which occurred in very early stage<sup>(1)</sup>.

Significant number of losses predominantly occurred very early in gestation, but once the embryonic heart activity appeared the rate of spontaneous abortion gradually decreases to 2-5 %<sup>(2)</sup>. However intrauterine gestational sac is the first one to appear sonographically, followed by the yolk sac and the foetal pole with cardiac activity<sup>(3)</sup>. Within the gestational sac, yolk sac is the first evident embryonic structure. It is usually visible between the fifth and twelfth week of pregnancy as a round anechoic area; after which it undergoes degeneration<sup>(4)</sup>.

A yolk sac can be detected easily by transvaginal sonography when the mean gestational sac diameter was 5 to 6mm. It is generally accepted that the yolk sac should be observed when a gestational sac measures greater than 8mm<sup>(5)</sup>. The yolk sac is connected to the embryo by the vitelline duct. Normally, the yolk sac appears as a circular structure with an anechoic center surrounded by a uniform well-defined echogenic wall. Usually the

inner diameter of a yolk sac measures 3 to 5 mm<sup>(6)</sup>. In fact, the yolk sac size progressively increases from the beginning of the 5<sup>th</sup> gestational week to the end of the 10<sup>th</sup> gestational week. Afterward, the yolk sac size decreases gradually. When the 10<sup>th</sup> or 11<sup>th</sup> weeks of gestation is completed, the yolk sac begins to shrink rapidly and eventually disappears<sup>(6)</sup>.

A study 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, EHR (Embryonic heart rate) can accurately demonstrate and assess the pregnancy outcome in those with bradycardia<sup>(7)</sup>. The embryonic heart beat can usually be identified at prenatal ultrasonography by 6 weeks gestation in M-mode<sup>(8)</sup>. Another study showed that a slow embryonic heart rate at 6.0–7.0 weeks gestation was associated with a high rate of first trimester fetal demise, and the demise often occurs soon after the slow heart beat is detected<sup>(9)</sup>.

#### **AIM OF THE WORK**

The aim of this work was to evaluate the correlation between each of the ultrasound parameters that were assessed in the first trimester (the gestational sac size, yolk sac size and shape and

embryonic heart rate) to early pregnancy loss and the correlation between different ultrasound parameter to each other.

## PATIENTS AND METHODS

This study was carried out on 100 pregnant females during the first trimester attended Al-hussein University Hospital. All cases were recruited after fulfilling criteria of inclusion into the study.

### Inclusion criteria:

- Patient is sure of her dates of last menstrual period with regular cycles
- Singelton pregnancy.
- Gestional age from 6 to 8 weeks during the first trimester

### Exclusion criteria:

- Loss to follow-up.
- Any uterine pathology as myomas or malformations.
- Chronic diseases as (SLE, hypertension ,diabetes and cardiac diseases)
- Recurrent fetal loss

### Methods:

After approval of local ethics committee, a written informed consent was taken from each patient and selected patients was subjected to:

- Detailed history taking : age, LMP, obstetric history, medical and surgical history.
- Clinical examination
- All patients between 6 to 8 weeks of gestation were be evaluated by using transvaginal ultrasound equipped with a real-time, 5-MHz sector electronic array endovaginal probe.

The uterus and adnexa were scanned. The intrauterine gestational sac and embryo were identified, the embryo crown rump length was measured to confirm the gestational age and asses the cardiac activity.After embryo viability was confirmed, the embryonic heart rate was measured by M-mode in all cases. The calculation of the heart rate was made by measuring the time interval for at least three waves.The yolk sac diameter (YSD) and geatational sac diameter were determined by placing the callipers on the centre of the yolk sac wall and the gestational sac wall and the measurement of YSD and GSD taken middle-to-middle. Follow up of the selected patients at 9 and 12 weeks of gestation to measure heart rate,yolk sac size,and gestional sac diameter.

### Statistical analysis

Data were analyzed by 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

This study was carried out on 100 pregnant women examined by using 2D ultrasonography starting early in the first trimester with a first scan between 6 and 8 weeks. A follow up scan was conducted at 9 weeks and at 12 weeks. Outcome of first trimester of the 93 pregnancies were recorded. **Table 1** showed demographic data of the studied patients. Females with age <20 was 14(14%), age from 20-35 was 76(76%) and age >35 was 10(10%) and females with BMI <20 was 6(6%), BMI from 20-26 was 41(41%), BMI from 26-29 was 45(45%) and BMI >29 was 8(8%).

**Table 1: demographic data of the studied patients**

	Number	Percent
<b>Age</b>		
<20	14	14.0
20-35	76	76.0
>35	10	10.0
<b>BMI</b>		
<20	6	6.0
20-26	41	41.0
26-29	45	45.0
>29	8	8.0

**Table 2** showed maternal history of the studied group. 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%). Regarding to type of pregnancy, normal cases was higher 97(69%).

**Table 2: maternal history of the studied group**

	Number	Percent
<b>Gravidity</b>		
1	29	29.0
2-3	42	42.0
4-6	26	26.0
6+	3	3.0
<b>Parity</b>		
0	32	32.0
1-2	48	48.0
3+	20	20.0
<b>Abortion</b>		
0	84	84.0
1-2	15	15.0
3+	1	1.0
<b>Type of pregnancy</b>		
Normal	97	97.0
Icsi	3	3.0

**Table 3** showed distribution of the studied patients regarding gestational sac diameter at different period of follow up. At 6 weeks, gestational sac diameter from 2.5-3 was higher 28(28%). At 9 weeks, gestational sac diameter from 2.5-3.5 was higher 41(41.8%) and at 12 weeks gestation sac diameter 6.0+ was higher 43(46.2%).

**Table 3: distribution of the studied patients regarding gestational sac diameter at different period of follow up**

Gestational sac diameter	Number	Percent
<b>At 6 weeks (n=100)</b>		
<2	21	21.0
2.0-2.5	21	21.0
2.5-3.0	28	28.0
3.0-3.5	14	14.0
3.5+	16	16.0
<b>At 9 weeks (n=98)</b>		
<2.5	3	3.1
2.5-3.5	41	41.8
3.5-4.5	26	26.5
4.5+	28	28.6
<b>At 12 weeks (n=93)</b>		
<5	1	1.1
5.0-5.50	14	15.1
5.50-6.0	35	37.6
6.0+	43	46.2

**Table 4** showed distribution of the studied patients regarding yolk sac diameter at different period of follow up. At 6 weeks, yolk sac diameter 6.0+ was higher 40(40%). At 9 weeks, yolk sac diameter 6.0+ was higher 56(57.1%) and at 12 weeks yolk sac diameter <4 was higher 35(37.6%).

**Table 4: distribution of the studied patients regarding yolk sac diameter at different period of follow up**

Yolk sac diameter in (mm)	Number	Percent
<b>At 6 weeks "n=100"</b>		
<4	10	10.0
4.0-5.0	19	19.0
5.0-6.0	31	31.0
6.0+	40	40.0
<b>At 9 weeks "n=98"</b>		
<5.0	11	11.2
5.0-6.0	31	31.6
6.0+	56	57.1
<b>At 12 weeks "n=93"</b>		
<4	35	37.6
4.0-5.00	34	36.6
5.00+	24	25.8

**Table 5** showed distribution of the studied patients regarding fetal crown-rump length (CRL) at different period of follow up. At 6 weeks, CRL 1+ was higher 52(52%). At 9 weeks, CRL from 1.5-2.5 was higher 41(41.8%) and at 12 weeks CRL <4 was higher 37(39.8%).

**Table 5: distribution of the studied patients regarding fetal crown-rump length (CRL) at different period of follow up**

Fetal crown-rump length (CRL) in (cm)	Number	Percent
<b>At 6 weeks "n=100"</b>		
<0.5	13	13.0
0.5-1	35	35.0
1+	52	52.0
<b>At 9 weeks "n=98"</b>		
<1.5	27	27.6
1.5-2.5	41	41.8
2.5-3.5	30	30.6
<b>At 12 weeks "n=93"</b>		
<4	37	39.8
4.0-5.00	23	24.7
5.00+	33	35.5

**Table 6** showed the final outcome of ultrasonographic findings in the studied group, of the 8 fetal losses, 2 were missed abortions (fetal pole with no visible pulsations), 1 blighted ovum, 2 incomplete abortions and 3 complete abortions.

**Table 6: the final outcome of ultrasonographic findings in the studied group**

Ultrasound finding	Number of cases	Percent (%)
Normal pregnancy	85	91 %
Missed abortion (other than blighted ovum)	2	2.1 %
Blighted ovum	3	1%
Incomplete abortion	2	2.1 %
Complete abortion	1	3.2 %
Total	93	100 %

**Table 7** showed the relation between gestational sac diameter at different gestational age period and its relation to the outcome of pregnancy, the gestational sac diameter show a significant decreasing in the fetal loss group at 6, 9 and 12 weeks, so the GS diameter was a good predictor to fetal loss ( $p < 0.05$ ).

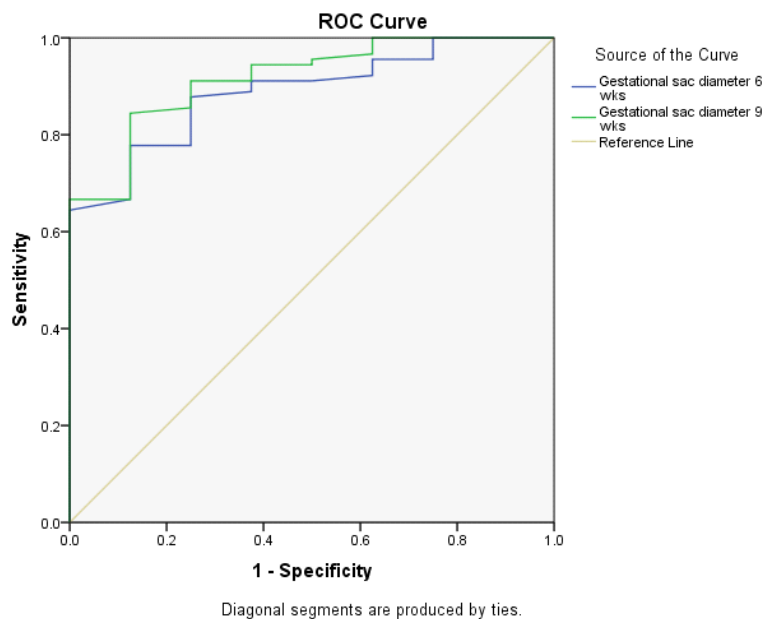
**Table 7: relation between gestational sac diameter at different gestational age period and its relation to the outcome of pregnancy**

Gestational sac diameter	Fetal loss (n= 8)	Ongoing pregnancy (n= 85)	t-test	P
<b>At 6 weeks</b>				
Range	1.22 - 2.47	1.41 - 3.92	16.2	0.001*
Mean	1.81	2.74		
SD.	0.43	0.70		
<b>At 9 weeks</b>				
Range	2.10 - 3.38	2.57 - 5.19	12.6	0.001*
Mean	2.63	3.89		
SD.	0.45	0.79		
<b>At 12 weeks</b>				
Range	4.33 - 5.20	5.33 - 6.51	3.21	0.015*
Mean	4.85	5.95		
SD.	0.46	0.36		

**Table 8** showed the cut off value of gestational sac diameter at 6 and 9 weeks, and the sensitivity, specificity and accuracy to predict the outcome of pregnancy at this cut off value, the cut off value of gestational sac diameter at 6 weeks was 1.92, below this value the loss of pregnancy was 85.0% the more than this value the complete of pregnancy was 78.0%. At 9 weeks, the cut off value was 3.11, the sensitivity was 90.0%, specificity was 93.0% and the accuracy was 91.0%.

**Table 8: cut off value of gestational sac diameter at 6 and 9 weeks, and the sensitivity, specificity and accuracy to predict the outcome of pregnancy at this cut off value**

Test Result Variable(s)	Area under the curve	p	Cut off value	Sensitivity	Septicity	Accuracy	95% Confidence Interval	
							Lower Bound	Upper Bound
Gestational sac diameter 6 wks	.888	.0001*	<1.92	85.0	78.0	82.0	.799	.976
Gestational sac diameter 9 wks	.917	.0001*	<3.11	90.0	93.0	91.0	.835	.998



**Figure 1: ROC Curve of gestational sac diameter at 6 and 9 weeks, to predict the sensitivity, specificity and accuracy of the outcome of pregnancy**

**Table 9** showed the relation between yolk sac diameter at different gestational age period and its relation to the outcome of pregnancy, it was 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 9 and 12 week there was no significant difference between the two groups ( $P > 0.05$ ).

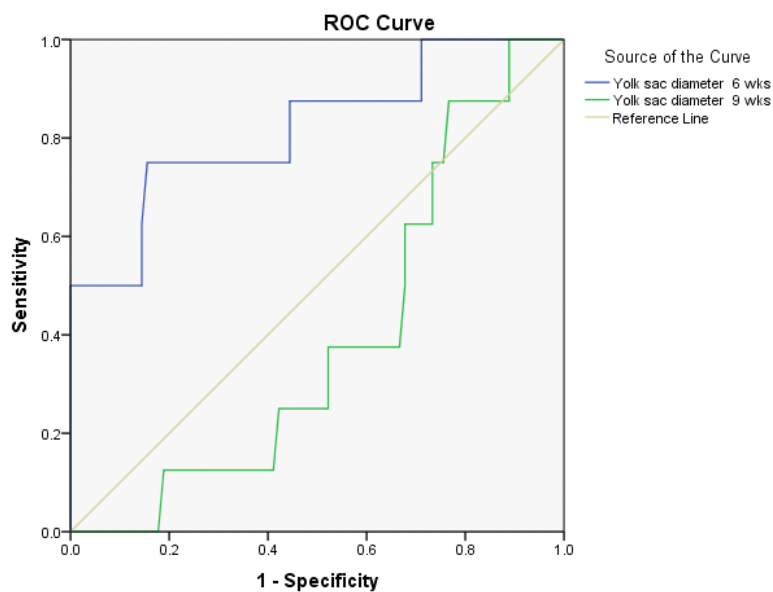
**Table 9: relation between yolk sac diameter at different gestational age period and its relation to the outcome of pregnancy**

Yolk sac diameter	Fetal loss (n= 8)	Ongoing pregnancy (n= 85)	t-test	P
<b>At 6 weeks</b>				
Range	4.95 - 9.20	3.51 - 6.98		
Mean	7.15	5.43	14.25	0.001*
SD.	1.42	0.99		
<b>At 9 weeks “n=98”</b>				
Range	4.74 - 7.30	4.96 - 6.83		
Mean	6.09	5.84	1.01	0.251
SD.	0.74	0.61		
<b>At 12 weeks “n=93”</b>				
Range	3.24 - 4.61	3.24 - 5.52		
Mean	4.04	4.39	0.98	0.378
SD.	0.71	0.68		

**Table 10** showed cut off value of yolk sac diameter at 6 and 9 weeks, and the sensitivity, specificity and accuracy to predict the outcome of pregnancy at this cut off value. The cut off value of yolk sac diameter at 6 weeks was more than 4.6, the sensitivity was 81.0%, specificity was 75% and accuracy was 77%. At 9 weeks, the cut off value was more than 5.3, the sensitivity was 32%, specificity was 28% and the accuracy was 30%.

**Table 10: cut off value of yolk sac diameter at 6 and 9 weeks, and the sensitivity, specificity and accuracy to predict the outcome of pregnancy at this cut off value**

Test Result Variable(s)	Area under the curve	p	Cut off value	Sensitivity	Specificity	Accuracy	95% Confidence Interval	
							Lower Bound	Upper Bound
Yolk sac diameter 6 wks	.819	.003	>6.4	81.0	75.0	77.0	.644	.993
Yolk sac diameter 9 wks	.393	.318	>5.3	32.0	28.0	30.0	.229	.557



Diagonal segments are produced by ties.

**Figure 2: ROC curve of yolk sac diameter at 6 and 9 weeks, to predict the sensitivity, specificity and accuracy of the outcome of pregnancy**

**Table 11** showed relation between fetal crown–rump length (CRL) at different gestational age period and its relation to the outcome of pregnancy. It was found that there was a significant decrease in CRL in fetal loss group less than ongoing pregnancy at 6 weeks only ( $P < 0.05$ ), while at 9 and 12 week there was no significant difference between the two groups ( $P > 0.05$ ).

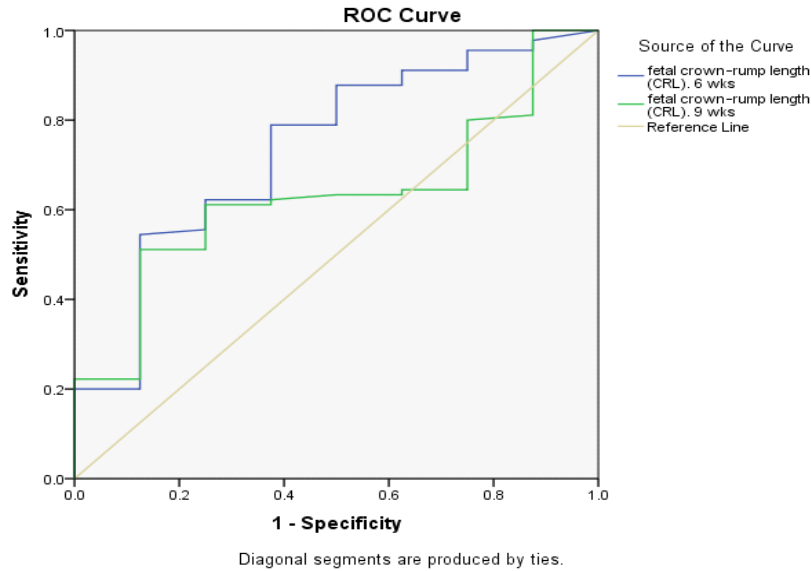
**Table 11: relation between fetal crown–rump length (CRL) at different gestational age period and its relation to the outcome of pregnancy**

Fetal crown–rump length (CRL).	Fetal loss (n= 8)	Ongoing pregnancy (n= 85)	t-test	P
<b>At 6 weeks</b>				
Range	0.28 - 1.52	0.28 - 1.85		
Mean	0.73	1.07	5.91	0.001*
SD.	0.37	0.43		
<b>At 9 weeks “n=98”</b>				
Range	1.03 - 2.86	1.04 - 3.47		
Mean	1.76	2.13	1.89	0.172
SD.	0.53	0.73		
<b>At 12 weeks “n=93”</b>				
Range	3.66 - 5.26	3.12 - 5.85		
Mean	4.20	4.44	0.219	0.64
SD.	0.92	0.89		

**Table 12** showed cut off value of CRL at 6 and 9 weeks, and the sensitivity, specificity and accuracy to predict the outcome of pregnancy at this cut off value. The cut off value of CRL at 6 weeks was less than 0.8, the sensitivity was 70%, specificity was 65% and accuracy was 76%. At 9 weeks, the cut off value was less than 1.9, the sensitivity was 48%, specificity was 50% and the accuracy was 49%.

**Table 12: cut off value of CRL at 6 and 9 weeks, and the sensitivity, specificity and accuracy to predict the outcome of pregnancy at this cut off value**

Test Result Variable(s)	Area under the curve	P	Cut off value	Sensitivity	Specificity	Accuracy	95% Confidence Interval	
							Lower Bound	Upper Bound
Fetal crown–rump length (CRL). 6 wks	.737	.027	<0.8	70.0	65.0	67.0	.555	.919
Fetal crown–rump length (CRL). 9 wks	.632	.218	<1.9	48.0	50.0	49.0	.469	.795



**Figure 3: ROC Curve of CRL at 6 and 9 weeks, to predict the sensitivity, specificity and accuracy of the outcome of pregnancy**

Table 13 showed relation between Heart rate at different gestational age period and its relation to the outcome of pregnancy. It was found that there was a 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 week there was no significant difference between the two groups ( $P > 0.05$ ).

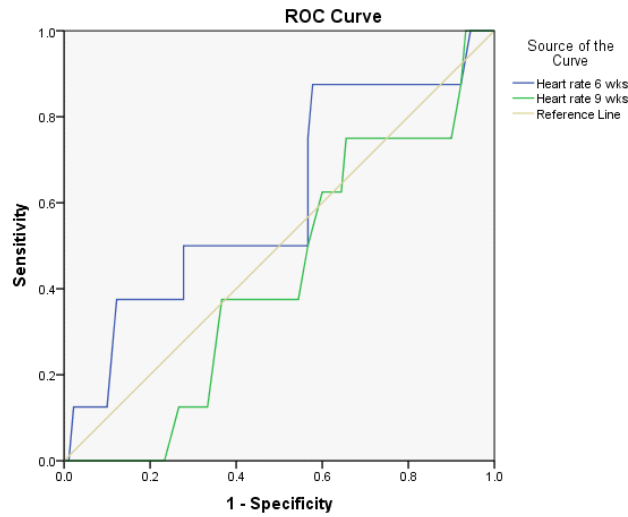
**Table 13: relation between Heart rate at different gestational age period and its relation to the outcome of pregnancy**

Heart rate	Fetal loss (n= 8)	Ongoing pregnancy (n= 85)	t-test	P
<b>At 6 weeks</b>				
Range	98.0 - 180.0	95.0 - 181.0	2.32	0.028*
Mean	140.40	133.86		
SD.	28.84	25.64		
<b>At 9 weeks “n=98”</b>				
Range	144.0 - 173.0	140.0 - 190.0	1.75	0.165
Mean	159.50	163.26		
SD.	11.17	13.70		
<b>At 12 weeks “n=93”</b>				
Range	124.0 - 160.0	122.0 - 162.0	0.69	0.46
Mean	136.33	142.04		
SD.	20.50	11.92		

Table 14 showed cut off value of heart rate at 6 and 9 weeks, and the sensitivity, specificity and accuracy to predict the outcome of pregnancy at this cut off value. The cut off value of heart rate at 6 weeks was more than 135, the sensitivity was 55%, specificity was 60% and accuracy was 56.8%. At 9 weeks, the cut off value was more than 157, the sensitivity was 32%, specificity was 25% and the accuracy was 28%.

**Table 14: cut off value of heart rate at 6 and 9 weeks, and the sensitivity, specificity and accuracy to predict the outcome of pregnancy at this cut off value**

Test Result Variable(s)	Area under the curve	p	Cut off value	Sensitivity	Septicity	Accuracy	95% Confidence Interval	
							Lower Bound	Upper Bound
Heart rate 6 wks	.606	.0424	>135	55.0	60.0	56.8	.392	.819
Heart rate 9 wks	.428	.500	>157	32.0	25.0	28.0	.248	.607



Diagonal segments are produced by ties.

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

Table 15 showed the distribution of cases according to yolk sac shape and pregnancy outcome, out of 85 cases with round and regular yolk sac shape, 85 (91.3%) had normal outcome and 5 (6.3 %) had failed pregnancy. 3 cases had irregular shaped yolk sac and all 3 were diagnosed as missed abortion on follow up, it was found that there was a significant relation between yolk sac shape and pregnancy outcome ( $p < 0.05$ ).

**Table 15: distribution of cases according to yolk sac shape and pregnancy outcome**

Yolk sac shape	Pregnancy outcome				Total
	Normal outcome		Failed pregnancy		
	No.	%	No.	%	
Regular	85	93.7	5	5.3	90
Irregular	0	0.0	3	4.2	3
Total	85		8		93
X <sup>2</sup>	31.9				
P	0.0001*				

Table 16 showed the correlations between the different studied parameters, it was found that there was a positive significant correlation between CRL at (6 and 9) weeks, and gestational sac at 6 and 9 weeks, also, there was a positive significant correlation between CRL and yolk sac at 6 and 9 months.

**Table 16: correlations between the different studied parameters**

		Gestational sac 6 wks	Gestational sac 9 wks	Yolk sac 6 wks	Yolk sac 9 wks	(CRL). 6 wks	(CRL). 9 wks	Heart rate 6 wks	Heart rate 9 wks
Age	R	-.130-	-.176-	.149	-.077-	-.005-	.020	.052	-.151-
	P	.196	.084	.138	.452	.962	.843	.606	.136
BMI	R	-.083-	-.159-	.087	-.194-	-.080-	-.021-	.003	-.075-
	P	.413	.117	.391	.056	.427	.835	.977	.464
Gestational sac 6 wks	R	1	.116	-.130-	-.067-	<b>.32**</b>	<b>.313**</b>	-.036-	-.172-
	P		.255	.197	.513	<b>.001</b>	<b>.001</b>	.719	.091
Gestational sac 9 wks	R	.116	1	-.093-	.135	<b>.471**</b>	<b>.248**</b>	-.133-	.109
	P	.255		.362	.184	<b>.0001</b>	<b>.003</b>	.191	.284
Yolk sac 6 wks	R	-.130-	-.093-	1	.005	<b>.354**</b>	<b>.428**</b>	.049	-.115-
	P	.197	.362		.960	<b>.001</b>	<b>.001</b>	.625	.261
Yolk sac 9 wks	R	-.067-	.135	.005	1	<b>.294**</b>	<b>.394**</b>	-.079-	.041
	P	.513	.184	.960		<b>.007</b>	<b>.001</b>	.440	.690
(CRL). 6 wks	R	<b>.32**</b>	<b>.471**</b>	<b>.354**</b>	<b>.294**</b>	1	<b>.288**</b>	-.063-	.001
	P	<b>.001</b>	<b>.0001</b>	<b>.001</b>	<b>.007</b>		<b>.004</b>	.536	.991
(CRL). 9 wks	R	<b>.313**</b>	<b>.248**</b>	<b>.428**</b>	<b>.394**</b>	<b>.188**</b>	1	.177	.048
	P	<b>.001</b>	<b>.003</b>	<b>.001</b>	<b>.001</b>	<b>.004</b>		.081	.636



## DISCUSSION

It is estimated that approximately 30-40 % of human pregnancies result in spontaneous abortion during the first trimester after implantation. 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 % <sup>(2)</sup>.

However intrauterine gestational sac is the first one to appear sonographically, followed by the yolk sac and the foetal pole with cardiac activity <sup>(3)</sup>. Within the gestational sac, yolk sac is the first evident embryonic structure. It is usually visible between the fifth and twelfth week of pregnancy as a round anechoic area; after which it undergoes degeneration <sup>(4)</sup>.

A study 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 <sup>(7)</sup>. The embryonic heart beat can usually be identified at prenatal ultrasonography by 6 weeks gestation in M-mode <sup>(8)</sup>. A study showed that a slow embryonic heart rate at 6.0–7.0 weeks gestation was associated with a high rate of first trimester fetal demise, and the demise often occurs soon after the slow heart beat was detected <sup>(9)</sup>.

This work aimed to evaluate the correlation between each of the ultrasound parameters that were assessed in the first trimester (the gestational sac size, yolk sac size & shape and embryonic heart rate) to (early pregnancy loss) and the correlation between different ultrasound parameter to each other. Our study was carried out on 100 pregnant women examined using 2D ultrasonography starting early in the first trimester with a first scan between 6 and 8 weeks. A follow up scan was conducted every 2 weeks and a final one at 12 weeks. Outcome of first trimester was recorded. In this study, there was a significant increase in age in fetal loss group more than complete pregnancy group. Regarding the relation between gestational sac diameter at different gestational age period and its relation to the outcome of pregnancy, the gestational sac diameter show a significant decreasing in the fetal loss group at 6, 9 and 12 weeks, so the GS diameter was a good predictor to fetal loss ( $p < 0.05$ ). **Prashant *et al.***<sup>(10)</sup> demonstrated that before placenta is fully formed, the developing embryo derives its nutrition from yolk sac. The yolk sac reaches its highest level of functional activity between 4<sup>th</sup> and 7<sup>th</sup> week of gestation and meets metabolic, endocrine, immunologic and haemopoietic needs of embryo in early stages of its development <sup>(11)</sup>. The appearance of yolk sac is a marker of successfully

growing gestational sac and is identified by transvaginal ultrasound between 4<sup>th</sup> and 5<sup>th</sup> week of gestation prior to appearance of fetal pole and embryonic heart <sup>(10,12)</sup>.

It is a circular structure and identified by its thin echogenic rim and central hallow. The initial diameter is around 3 - 4 mm and gradually it increases at the rate of 0.1 mm per day and finally undergoes atresia by 10th to 11th week of pregnancy. Once the placental circulation is established, the blood supply to yolk sac gradually decreases and finally disappears. If a large yolk sac persists, it indicates aberrant embryonic development and high chance of miscarriage <sup>(6)</sup>. Other variations in appearance of yolk sac include calcification, very small yolk sac (<2mm) and irregular yolk sac.

The calcified yolk sac almost indicates impending pregnancy loss and on the other hand irregular rim of yolk sac can be still associated with successful pregnancy outcome <sup>(13)</sup>. **Figueras *et al.*** <sup>(14)</sup> conducted a study to find the relation between yolk sac volume and risk of spontaneous abortion. They found that yolk sac volume outside the 5th to 95th percentile were associated with significant occurrence of retrochorial haematoma and subsequent pregnancy loss. In a prospective cohort study, abnormal yolk sac characteristics (yolk sac diameter outside the range of 2-5 mm, irregular shape, presence of degenerative changes, unequal number with embryo and presence of calcifications) were found in 22 first trimester ultrasound scans <sup>(15)</sup>. Abortion occurred in 14 (63.63 %) compared to 3.55 % (6/169) signifying the fact that normally functioning yolk sac is vital for the survival of the embryo. Also, our study confirms the same findings. Another study from Turkey 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 <sup>(14)</sup>. 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). It was found that 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 (3.8% and 1.5% respectively).

The development in the obstetric ultrasound 50 years ago mainly focussed on documentation of embryonic heart rate in the first trimester scan to confirm viability <sup>(10)</sup>.

Subsequently it was realized that slow embryonic heart rate was associated with increased rate of spontaneous abortions <sup>(9, 10)</sup>. Now it is universally known that embryonic heart rate serves as one of the important predictors of imminent fetal

demis. Transvaginal ultrasonography has higher resolution and hence it can be used for visualization the embryonic heart beat in M mode.

The embryonic heart rate can be visualized as early as 5 - 6 weeks of gestation and it is known that the mean heart rate progressively increases from 6 weeks (120 to 140 bpm) to 9 weeks (145 to 170 bpm) after which it slowly stabilizes to lesser heart rate for rest of the pregnancy. It has been observed that embryonic heart rate less than 100 bpm (beats per minute) is associated with higher risk of miscarriage and the risk of embryonic demise almost touches 100 % when the rate is less than 80 bpm<sup>(10)</sup>. The rate of chromosomal abnormalities and structural abnormalities are significantly higher in surviving fetuses when they have slow heart beats<sup>(15)</sup>. In one study, genetic amniocentesis was performed in 6 women with slow embryonic heart rates [25]. After karyotype analysis it was found that 2 fetuses had trisomy21, which represented significantly higher incidence (33%) of aneuploidy.

In our study too, we found higher rate of abortions with reduced heart rate, however we did not perform any karyotype analysis of the abortus or genetic amniocentesis. The results of the present study indicates that first trimester fetuses with correctly sized and normally appearing yolk sacs and embryonic heart rate above 100 bpm are associated with very good chance of ongoing successful pregnancies. In this study, the cut off value of gestational sac diameter at 6 and 9 weeks, and the sensitivity, specificity and accuracy to predict the outcome of pregnancy at this cut off value, the cut off value of gestational sac diameter at 6 weeks was less than 1.92, low this value the loss of pregnancy was 85.0% the more than this value the complete of pregnancy was 78.0%. At 9 weeks, the cut off value was less than 3.11, the sensitivity was 90.0%, specificity was 93.0% and the accuracy was 91.0%.

Regarding the relation between yolk sac diameter at different gestational age period and its relation to the outcome of pregnancy, it was found that there was a significant increase in yolk sac diameter in fetal loss group more than ongoing pregnancy at 6 weeks only, while at 9 and 12 week there was no significant difference between the two groups. There was a significant relation between yolk sac shape and pregnancy out come.

The correlations between different studied parameters showed that there was a positive significant correlation between CRL at (6 and 9) weeks and gestational sac at 6 and 9 weeks, also, there was a positive significant correlation between CRL and yolk sac at 6 and 9 months. **Varelas et al.**<sup>(1)</sup> investigate embryonic heart rate (EHR) and yolk sac diameter (YSD) during the first trimester

and their role as prognostic markers of first trimester pregnancy outcome. Prospective cohort study involved 219 women. They found that the EHR and YSD were significantly correlated to advancing gestational age in pregnancies continuing beyond 12 weeks. Pregnancies that resulted in spontaneous abortion exhibited a statistically significant lower EHR, smaller YSD or absent yolk sac.

ROC curve analysis demonstrated the predictive value of the combination of GA with EHR (area under the ROC curve: 0.971,  $p < 0.001$ ) and GA with YSD (area under the ROC curve: 0.858,  $p < 0.001$ ) for first trimester pregnancy outcome. EHR and YSD progressively increase in healthy pregnancies during the first trimester. Embryonic bradycardia and absence of yolk sac or even a smaller yolk sac diameter than expected for any gestational age are predictors of poor pregnancy outcome during the first 12 weeks.

## CONCLUSION

First trimester ultrasound measurement of these parameters (FHR, YS diameter and shape and GS diameter) 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 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. It was found in this study that the important the ultrasonographic finding of a small for date CRL, small gestational 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 1<sup>st</sup> trimester, there was a significant association between CRL and mean gestational sac diameter ( $P < 0.001$ ) and mean yolk sac diameter ( $P < 0.001$ ).

## RECOMMENDATION

As shown in the present study, in cases with poor ultrasonographic prognostic factors as small GS diameter, fetal bradycardia, invisible yolk sac and irregular yolk sac we should take certain precautions and managements to guard against fetal loss and to reassure the couples. If demise occurs, it is advantageous to make the diagnosis quickly to avoid occurrence of vaginal bleeding at an inconvenient time and place and to minimize the period of concern and uncertainty for the parent. Our study was restricted by the small number of patients with pregnancy loss. Further prospectively

large-scale studies are warranted to define the new criteria fit for new high-resolution ultrasound equipment.

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