Gestational sac size, yolk sac size and embryonic cardiac activity as prognostic factors of first trimester Pregnancy Outcome

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Abstract: Objective: To detect correlation between each of the ultrasound parameters that were assessed in the first trimester (the gestational sac size, yolk sac size and fetal cardiac activity) to early pregnancy loss. **Methods**: 380 pregnant women during the first trimester were entrolled in the study. Each patient was submitted to first ultrasound scan between 5 and 6 weeks of gestation (Gestational sac size, Yolk sac size and Fetal heart rate) and follow up scan of the same parameters every two weeks until 12 weeks of gestation. **Results**: In the pregnancies that resulted in normal 1st trimester, there was a significant association between CRL and FHR ($P < 0.00012$), mean gestational sac diameter ($P < 0.00012$) and mean yolk sac diameter ($P < 0.00012$). In the cases that subsequently resulted in pregnancy loss, FHR for CRL was significantly lower than normal ($P < 0.00012$), the gestation sac diameter was smaller ($P < 0.00012$), but the yolk sac diameter was not significantly different ($P = 0.062$) and no significant association between abnormal yolk sac size and fetal loss was found. **Conclusion**: First trimester ultrasound measurement of these parameters 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 especially those who develop symptoms of threatened abortion.

Keywords: Gestational; sac size; yolk; embryonic cardiac activity; prognostic factor; trimester Pregnancy Outcome

Introudction

Two dimensional ultrasound is commonly performed investigation in first trimester of pregnancy to confirm pregnancy location, viability and gestational age. Measurement of embryonic and fetal crown- rump length (CRL) is conventionally performed to confirm gestational age. Smaller than expected fetal crown- rump length has been associated with subsequent pregnancy lost in studies that involved women with threatened miscarriages. Moreover some chromosomal defect are associated with high intrauterine lethality but associated with fetal growth retardation in first trimester of pregnancy evidenced by smaller than normal fetal crown- rump length [1].

In addition to documenting normal development, ultrasonography has high sensitivity for showing abnormalities of the gestational sac, yolk sac, and embryo that predict poor outcome [2].

The embryo can be identified by transvaginal ultrasound when as small as 1 to 2 mm in length. At 5 to 7 weeks, both the embryo and gestational sac should grow 1 mm daily [3].

The yolk sac is the first sonographically evident embryonic structure within the gestational sac. It is usually visible between the fifth and twelfth week of pregnancy as a round anechoic area [4].

Several ultrasonographic findings early in the first trimester have been reported as abnormal. These include an "empty" amnion, an enlarged yolk sac and a small gestational sac. Criteria for these abnormal findings are presented. Because none of these signs have been extensively studied, they are considered to be suspicious for, though not diagnostic of, failed pregnancy[5].

We suggest that may be a normally appearing yolk sac measuring within the range of 2 mm to 5mm reasonably ensures viability of pregnancy in the first trimester. However variation outside this range does not necessarily mean adverse outcome as in more than 50% of cases, pregnancy still can continue[6].

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. When an embryo is undetectable, a relatively large yolk sac, even of normal shape, may be an indicator of miscarriage [7].

Cardiac activity immediately adjacent to the yolk sac indicating alive embryo may not be seen until the embryo measures 5 mm, from 5.5 to 6.5 weeks, an embryonic heart rate less than 100 beats per minute is normal. During the following 3 weeks there is a rapid increase up to 180 beats per minute[8]. Transvaginalsonography can detect cardiac activity as early as 34 days which corresponds to an embryonic

length of 1.6 mm. Cardiac activity should be detected when the embryo measures between 4 to 5 mm. At this time the MSD should measure between 13 to 18 mm, which corresponds to a GA of 6 to 6.5 weeks. Using transabdominal ultrasound cardiac activity should be seen when the MSD measures 25 mm, which corresponds to a GA of 8 weeks. The embryonic heart rate normally increases between 6 and 9 weeks gestation and then slowly decreases. Prior to 6 weeks, the heart rate is normally between 100 and 115 beats per minute (BPM). The heart rate increases and peaks at 8 weeks at 144 to 159 BPM. By 9 weeks the heart rate plateaus at 137 to 144 BPM. At this early gestational age there is almost no variation in the heart rate, so that a single measurement is acceptable by M mode[9].

Material and methods

This is a prospective cross sectional study includes 400 pregnant women during the first trimester starts from January 2016 up to 20 August 2016.

Inclusion criteria:

➢ Gestational age between 5-6 weeks.
➢ women with regular menstrual cycles.
➢ Sure of their last menstrual period.
➢ They were in the first trimester of pregnancy with singleton viable fetus at the time of the first scan.
➢ Had no symptoms of threatened abortion when first seen.

Exclusion criteria:

➢ Patient is unsure of her dates.
➢ Multifetal pregnancies.
➢ Loss to follow-up.
➢ Any uterine pathology as myomas or malformations.

All patients between 5 to 6 weeks of gestation were evaluated by using transvaginal ultrasound equipped with a real-time, 5-MHz sector electronic array endovaginalprobe. The uterus and adnexa were scanned.

Each patient was submitted to:

A first ultrasound scan: between 5 and 6 weeks of gestation according to their first antenatal care visit that included the following:

• Gestational sacs,
• The yolk sac diameter (YSD),
• Crow- rump length (CRL) measurement,
• Fetal heart rate measurements.

Follow up scan: was done every two weeks where (gestational sac diameter, yolk sac diameter, crown rump length and fetal heart rate) were measured every time until the pregnancy reached 12 weeks.

Results

The study involved 400 pregnant women examined using 2D ultrasonography starting early in the first trimester with a first scan between 5 and 6

weeks. A follow up scan was conducted every 2 weeks and a final one at 12 weeks. Outcome of first trimester was recorded.

During follow up, 20 women did not return for follow up and accordingly, the results of the remaining 380 women are shown. The mean age of the studied group was 27 years ranged between 17 and 45 years. 38% of women were primigravida (144) and 62% were multiparas (236) of which (11%) females had history of previous fetal loss.

The body mass index was < 20 in 24 patients (17 had normal pregnancy and 7 aborted), between 20-26 in 126 patients (114 had normal pregnancy and 12 aborted), between 26 -29 in 201 of patients (185 had normal pregnancy and 16 aborted), and was >29 in 29 patients (22 had normal pregnancy and 7 aborted).

The study showed that the percentage of fetal loss increased with extremes of body mass index.

Table 1: show clinical characteristics of the previous pregnancies of the studied group. Eleven percent of the patients (11%) reported history of previous miscarriages with a median number of 2 miscarriages and a range between 1 and 5 inevitable or silent (missed) miscarriages. Previous congenital anomalies were rather rare (1.6%), similar to family history of congenital anomalies (1.1%). fifty women were Rh negative representing 13%.

Table 1: **Clinical characteristics of the studied group**

	Number	Percent
Previous miscarriages		
No miscarriages	338	89 %
Inevitable	22	5.8 %
Silent	20	5.2 %
Previous fetal Anomalies	6	1.58 %
Consanguinity	50	13.15 %
Family history of fetal anomalies	6	1.58 %
RH factor		
+ve	330	87 %
-ve	50	13 %

Of the 380 pregnant females in the study group 48 experienced some form of vaginal bleeding during the study period (ranging from mild to severe).

38 of those patients eventually had normal pregnancy while 10 of them aborted.

In the pregnancies resulting in fetal loss compared to those with healthy ongoing pregnancy, the incidence of vaginal bleeding was higher and statistically significant (Table 2), but there was no significant difference in the rate of spontaneous conception (compared to *in vitro* fertilization) or previous obstetric history (percentage of

primigravidae, percentage of those who had only had previous miscarriages and percentage of those who

had previous live births).

Table (2): relationship between demographic data and fetal loss rate:

Variable	Ongoing pregnancy (n=338)	Fetal loss (n=42)	Statistical analysis
Assisted reproduction	34(9%)	8 (19%)	P = 0.29
Primiparous	132 (39 %)	12(28.5 %)	P = 0.68
Previous fetal loss	35 (10.4 %)	7 (16 %)	P = 0.27
Previous live birth	215 (63.6 %)	25(59.5 %)	P = 0.95
Vaginal bleeding	38 (11.2 %)	10 (23.8 %)	P = 0.43

In the total 380 pregnancies, 338(88.9%) resulted in an ongoing pregnancy and entered the 2nd trimester successfully, while 42 (11.1%) resulted in miscarriages.

Of the 42 fetal losses, 18 were missed abortions (fetal pole with no visible pulsations), 8 blighted ovum, 10 incomplete abortions and 4 complete abortions and two cases of partial hydatiform mole (table3).

Table (3): the final outcome of ultrasonographic findings in the studied group:

Ultrasound finding	Number of cases	Percent (%)
Normal pregnancy	338	88.9 %
Missed abortion (other than blighted ovum)	18	4.7 %
Blighted ovum	8	2.1%
Incomplete abortion	10	2.6 %
Complete abortion	4	1.05 %
Hydatidiform mole	2	0.5 %
Total	380	100 %

The mean embryonic heart rates at $5 - 6^{+6}$ week of gestation were 122 ± 12 bpm. After the 5th week of gestation, the embryonic heart rates gradually increased to 156 ± 17 bpm at $7 - 7^{+6}$ week of gestation. The maximal embryonic heart rates presented at $8 - 8^{+6}$ week of gestation were 175 ± 9 bpm. Then the fetal heart rates gradually decreased to 150 ± 12 bpm at $11 - 11^{+6}$ week of gestation (table 4).

Of the 42 cases with fetal loss, 36 cases had fetal heart rate less than 100 bpm. These cases were seen after a week of the last scan. 25 cases have already aborted at the time of the next scan and 12 cases were

found to have a missed abortion at the follow up scan, 5 cases aborted about 2 weeks later.

Table (4): embryonic and fetal heart rates at different gestational ages.

Gestational age	Fetal heart rate (bpm) mean ± SD
$6 - 6^{+6}$	122 ± 12
$7 - 7^{+6}$	156 ± 17
$8 - 8^{+6}$	175 ± 9
$11 - 11^{+6}$	150 ± 12

Table (5): Distribution of cases according to yolk sac shape and pregnancy outcome

Yolk sac shape	Pregnancy outcome		Total
	Normal outcome	Failed pregnancy	
Regular	335	25	360
Irregular	0	20	20

Table (5) shows that out of 360 cases with round and regular yolk sac shape, 335 (94.39 %) had normal outcome & 25 (5.6 %) had failed pregnancy. 20 cases had irregular shaped yolk sac and all of them were diagnosed as missed abortion on follow up.

Discussion

The study of the first 12 weeks of intrauterine development is more interesting than the last 12

weeks. It is surely the most crucial period in any being's existence [10].

The findings of this study demonstrate that the incidence of fetal loss increases with maternal age, from about 4% for those aged less than 20 years to about 24% for those aged more than 35 years, is 2.6 times higher in women with a history of vaginal bleeding in pregnancy compared to those with no bleeding and increase with increase body mass index.

Finally we found an increase in the number of miscarrage with loss of early follow up which has an extreame importance in completing pregnancy or not.

The exponential increase in the rate of fetal loss with maternal age is compatible with the findings of previous reports. Thus, in a study of 2139 women presenting before 10 weeks of gestation, the miscarriage rate after confirmation of fetal viability was about 2% those aged less than 40 years and about 14% in those who were 40 years or older [11].

Similarly, a study of 201 pregnancies achieved after ovulation induction and demonstration of fetal cardiac activity at 7–9 weeks of gestation reported that the rate of subsequent fetal loss increased from 2.1% for women aged 35 years or less, to 14.9% for those aged 36–39 years and 20% for those over 40 years [12].

The majority of pregnancies resulting in early fetal loss are chromosomally abnormal, and the well-reported exponential increase in risk for fetal trisomy with increasing maternal age is the most likely explanation for the association [13].

The study also showed that vaginal bleeding is an early feature of miscarriage and inevitably the rate of fetal loss was higher in those women with bleeding compared to those without.

This finding agreed with other studies for example: it was previously reported that in about 20% of pregnancies complicated by early vaginal bleeding. In these women with early bleeding ultrasound examination demonstrates a nonviable pregnancy in 40% of cases and in those with a live fetus subsequent fetal loss occurs in about 10% [14].

Our study demonstrated that the cases that subsequently resulted in pregnancy loss had a smaller mean CRL for gestation than in those who continued to have a normal pregnancy (p<0.0001). They suggested that early first trimester growth restriction was associated with subsequent intrauterine death.

Also the relation of CRL to gestational sac diameter was proved also significant as a predictor for subsequent pregnancy failure (P <0.0001).

Our findings agreed with many other studies which demonstrated also that crown–rump length (CRL) measurement, had a prognostic value. On the basis of CRL measurements it was possible to predict spontaneous miscarriage for example:

Choong et al, (2003) [15] carried a prospective cross-sectional survey that involved 301 live singleton embryos in women from an assisted reproductive technology program. Spontaneous miscarriage occurred in 13.6% of the cases at mean GA of 10 weeks. In their study smaller than expected CRL was associated with early pregnancy loss on subsequent scans. (Odds ratio 0.069 and confidence interval 95% 0.57 to 0.83).

Reljic, (2001)[16] had conducted a study where fetal CRL was measured in 310 singleton pregnancies with live fetuses, presented with threatened miscarriage before 13 weeks of gestation. The relationship between fetal CRL and pregnancy outcome was investigated. In those cases with CRL deficit more than 2 standard deviations (SDs) the incidence of miscarriage was 13.7%, whereas if the CRL was between the mean and−2 SDs the incidence of miscarriage was 8.3%.

Goldstein (1994)[17] found that the risk of early pregnancy decreased as the CRL increased. If an embryo developed up to 5 mm in length, subsequent loss of viability occurred in 7.2% of cases. Loss rates dropped to 3.3% for embryos of 6–10 mm and to 0.5% for embryos over 10 mm.

In the present study we did not find a significant association between abnormal yolk sac size and fetal loss suggesting that measurement of the yolk sac diameter was not a reliable prognostic factor for first trimester outcome.

This finding agreed with the findings of *Jauniaux et al., (1991)*[18], who concluded that most pregnancies which miscarry during the third month of pregnancy have normal secondary yolk sac measurements at their initial scan before 8 weeks of gestation. It is usually the yolk sac that is found to persist inside the gestational sac after embryonic demise.

In this study the pattern of change of fetal heart rate with advancing gestational age showed that the mean embryonic heart rates at $6 - 6^{+6}$ weeks of gestation were 122 ± 12 bpm. After the 6th week of gestation, the embryonic heart rates gradually increased with gestationl age till a maximal embryonic heart rates presented at $8 - 8^{+6}$ weeks of gestation then decreased thereafter to be range between 150 ± 12 bpm at 12 weeks gestation.

This pattern of change in heart rate with gestational age coincided with many studies as for example the study by **Lazarus E (2003)**[19] which concluded that the heart rate varies with gestational age, ranging from 100 bpm at six weeks to 170 bpm at eight weeks.

New early first-trimester diagnostic criteria for nonviable pregnancy recommended by the Society of Radiologists in Ultrasound via a multispecialty consensus panel extended the diagnostic size criteria of crown-rump length from 5 to 7 mm for embryos without a heartbeat and mean sac diameter from 16 to 25 mm for "empty sacs[20].

In women who present with a viable intrauterine pregnancy at the primary scan, advancing maternal age in the presence of clots per vagina increases the probability of subsequent miscarriage. Whereas, in women with a higher embryonic heart rate in the

presence of an increased GS volume/CRL ratio, the likelihood of subsequent miscarriage is reduced[21]**.**

Conclusion

First trimester ultrasound measurement of these parameters 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 especially those who develop symptoms of threatened abortion.

It can provide reassurance for many patients anxious about the health of their pregnancy and allows the physician to provide appropriate care and adequate close follow up for those with indicators of a possible unhealthy pregnancy.

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