CEOG Clinical and Experimental Obstetrics & Gynecology

The early pregnancy volume measurements in predicting pregnancy outcome

G. Batmaz[1], A. Aksoy[2], S. Aydin[1], P. Ozcan[1], C. Dane[3], B. Dane[1]

[1] Bezmialem University, Faculty of Medicine, Department of Gynecology and Obstetrics, Istanbul
[2] Nenehatun Hospital, Department of Obstetric and Gynecology, Erzurum
[3] Haseki Training and Research Hospital, Department of Gynecology and Obstetrics, Istanbul (Turkey)

Summary

Objective: The authors' aim was to develop a logistic regression model based on the ultrasonographic parameters on maternities which are showing a healthy improvement process during the first trimester of pregnancy. *Material and Methods:* Using 2D transvaginal ultrasound imaging, the crown rump length (CRL), yolk sac (YS), and gestational sac (GS) diameters were recorded in 225 women with gestational age <11 weeks. Simplified V = 0.523 x length x height x width formula was used for the volume calculations. The results which ended in abortion were not included in the study. *Results:* Linear regression analyses between yolk sac volume (YSV), YSV = 0.026 + 0.0018 x CRL (r^2: 0.15; $p < 0.001$), gestational sac volume (GSV), GSV= -9.6 + 1.7 x CRL (r^2: 0.52; $p < 0.001$), and embryo volume (EV), EV = -1.64 + 0.18 x CRL (r^2: 0.4; $p < 0.001$), and CRL was made and a linear relationship was detected. The volume measurements showed a meaningful correlation with the week of pregnancy. The space in the GS (GS volume-embryo volume) increased as the age of pregnancy became older ($r^2 = 0.46$; $p < 0.001$). *Discussion:* The first volume value was made in the first trimester by transvaginal ultrasonography, which showed a correlation with the age of pregnancy.

Key words: Early pregnancy volume measurements; Nomogram.

Introduction

The first trimester is the most critical period in the pregnancy process in which the formation of placenta and embryo occurs. This is the period when many pathological conditions can appear, and the embryo is in its most vulnerable state to external factors. Many researchers have studied various criteria to diagnose gestation prognosis to inform couples who are waiting for a successful pregnancy outcome by examining the ultrasonographic parameters and maternal demographic characteristics acquired before the 12th week of pregnancy [1, 2].

During diagnostic ultrasound in early pregnancy, evaluation of embryo and gestational sac (GS) has significance. For example, the GS and cranium-rump length (CRL) can be determined by measuring the gestational age and the examination of yolk sac (YS) can indicate the current problems at an early stage.

In the early period (six to ten weeks), 7.5% of the fetuses which have been identified as alive may end in abortion. The most important ultrasonographic marker of fetal loss compared to CRL was reported to be the presence of small gestational sacs [3]. According to the result of another study, it has been determined that after the diagnosis of alive gestation process, possibility of fetal loss rate decreases to 3.4 % [4].

Many authors reported that first trimester volume measurements can be able to predict gestations which end in abortion and chromosomal defects [5-7].

In this study, for the events not ending in abortion, the authors aimed at creating and evaluating a linear regression model based on ultrasonographic parameters.

Materials and Methods

This prospective cohort study was performed in Bezmialem University, Faculty of Medicine, Department of Obstetrics and Gynecology, Istanbul, Turkey, between January 2013 and January 2014. Two hundred twenty-five (225) subjects, who consulted at the hospital with a pregnancy doubt, wanted to keep the fetus alive, did not have repetitive abortions, had a healthy singleton pregnancy, between 6^{+6} and 10^{+6} weeks, were included in this study. The mothers who had diabetes mellitus, hypothyroidism, hypertension and autoimmune diseases, multiple pregnancy, and over 40 years of age were excluded from the study. A detailed medical history of all pregnant women included in the study were taken. As maternal age demographic data, previous pregnancy history (gravidity, parity, abortion, curettage), date of last menstrual period (LMP), smoking, and vaginal bleeding data from the current pregnancy was recorded.

The patients were studied once with transabdominal sonography using an endocavitary 5- to 9-MHz transducer by a single sonographer (G.B.) experienced in performing these examinations. The presence of intrauterine pregnancy and YS, fetal pole

Revised manuscript accepted for publication January 12, 2015

Table 1. — *EV, GA, GSV, and YSV according to gestation weeks.*

		YSV (cm³)				GSV (cm³)				EV (cm³)			
GA	n	5th	50th	95th	Median	5th	50th	95th	Median	5th	50th	95th	Median
6 w	9	0.01	0.027	0.05	0.03	1.87	5.65	14.00	5.65	0.05	0.08	0.50	0.125
7 w	60	0.02	0.04	0.095	0.04	3.35	9.7	22.5	8	0.095	0.66	1.03	0.3
8 w	68	0.02	0.058	0.10	0.06	8.4	18.3	37.2	17	0.35	1.11	2.06	0.99
9 w	46	0.02	0.069	0.11	0.07	9.0	27.1	57.4	23.5	1.37	2.42	3.97	2.18
10 w	12	0.01	0.075	0.195	0.05	14.85	51.7	92.7	44	3.19	5.22	8.77	4.77

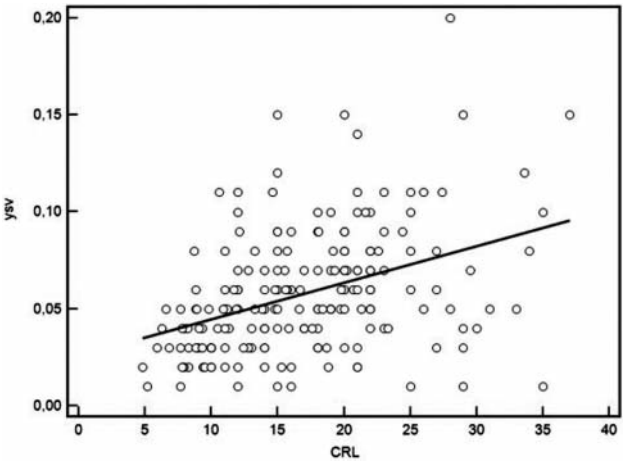

Figure 1. — Relation between CRL and YSV.

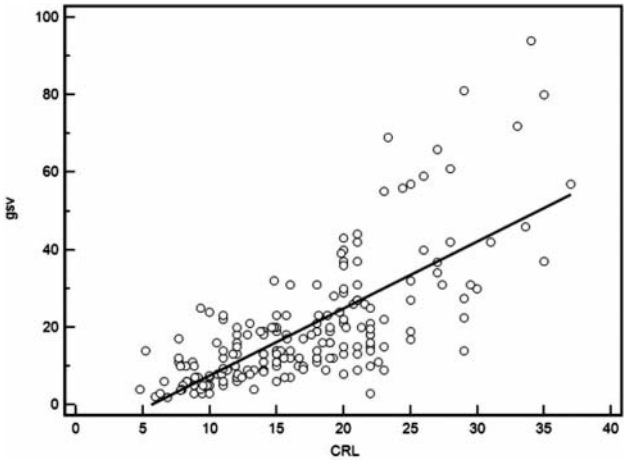

Figure 2. — Relation between CRL and GSV.

presence in gestational sac detected by the help of detailed ultrasonography reviews of each patient. In order to measure average GS, inner wall sac diameter-length of the chorionic liquid surface level, width, and height (three orthogonal diameters) were measured in millimeters (mm) and then an average was made. Gestational week was determined by measuring CRL by its longest distance in mm. In order to calculate, average YS diameter, the length of the outer surface, width, and height (three orthogonal diameters) were measured and an average was made in mm. Volume measurements were done by using a simplified formula for the volume of a prolate ellipsoid: V = 0.523 × length × height × width [8]

Data were collected on an Excel spreadsheet and analyzed using the software SPSS, version 15.0. Scatter graphs were generated to evaluate the correlation between yolk sac volume (YSV), gestational sac volume (GSV), embryo volume (EV), and CRL. Regression models were constructed using YSV, GSV, and EV as the dependent and CRL as the independent variables. A p value < 0.05 was considered significant.

Approval for this study was obtained from the Local Institutional Review Board of the Faculty of Medicine, Bezmialem University. Informed consent was obtained from all participants.

Results

Twenty-four (24) patients out of the 225, who were included in the study, could not be reached and 11 pregnancies were excluded from the study because of abortion. One hundred and ninety (190) women between six and ten weeks' gestation, who met the eligibility criteria, were enrolled in the study. The median maternal age (±SD) was 28 ± 5.2 years (range 19–40). One hundred twenty-one (121) women (63.7%) were parous and 69 women (36.3 %) were nulliparous.

The median CRL was 16 ± 6.7 mm (range, 4.8–37). The mean YSV varied from 0.027 to 0.075 cm³ between six and ten weeks, respectively. Medians and 5th and 95th centiles for each measurement by weeks of gestational age are shown in Table 1. The YSV positively correlated with the CRL, and the linear regression of its values also yielded better a correlation. The following equation describes this relation: YSV= 0.026 + 0.0018 x CRL (r^2: 0.15; $p < 0.001$) (Figure 1). The mean YS diameter positively correlated with the CRL, and the following equation describes this relation: YS = 3.8 + 0.05 x CRL (r^2: 0.15; $p < 0.001$).

Mean GSV ranged from 5.65 cm³ at six weeks to 51.7 cm³ at ten weeks. Medians and 5th and 95th percentiles for each measurement by weeks of gestational age are shown in Table 1. There was a moderate positive correlation between GSV and CRL. The following equation describes this relation: GSV = -9.6 + 1.7 x CRL (r^2: 0.52; $p < 0.001$) (Figure 2). The mean GS diameter (MSD) positively correlated with the CRL, and the following equation describes this relation: MSD = 16.6 + 0.91 x CRL (r^2: 0.56; $p <$ 0.001).

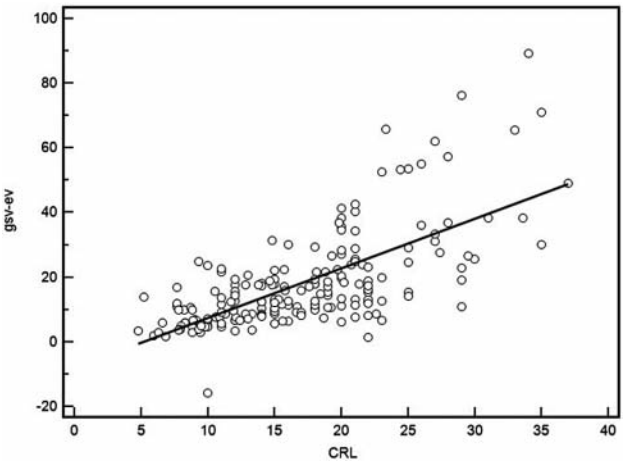

Figure 3. — Relation between CRL and GSV-EV.

Mean EV ranged from 0.08 cm^3 at six weeks to 5.2 cm^3 at ten weeks. Medians and 5th and 95th centiles for each measurement by weeks of gestational age are shown in Table 1. There was a moderate positive correlation between EV and CRL. The following equation describes this relation: EV = -1.64 + 0.18 x CRL (r^2: 0.4; $p < 0.001$)

As the gestational age became higher, the area outside (GSV - EV) of the embryo in the GS increased ($r^2 = 0.46$; $p < 0.001$) (Figure 3).

Discussion

Due to socio-cultural reasons, advanced maternal age has been increasing in recent years and how pregnancy will continue or what the results will be the in continuing pregnancies is unknown. Therefore, predicting pregnancy outcome studies in recent years shifted to the much earlier stages of the pregnancy. For this reason, various sonographic parameters are used in the early weeks of pregnancy, such as localization and size of the GS [8], the relationship between GS and the average size of the CRL [9-12] and, the size and shape of the YS [13, 14]. GS, YS, and ability to set EV allow the formulation of age-related pregnancy percentile. There are several published analyses which examine the relationship between first trimester ultrasonographic volume parameters and pregnancy outcome [5, 6, 15]. Earlier studies showed that YS size began to decrease and disappeared towards to the end of first trimester, besides seeing the YS before monitoring fetal pole indicated no valuable prediction on pregnancy outcomes [16, 17]. YS diameter is two to five mm in the 7th and 10th weeks in two-dimensional US and the average value is 2.0 ± 2.0 mm [18]. In the present study, the average YS diameter was 4.7 mm; maximum value 7.9 mm, and minimum value 2.7 mm.

A study conducted that the YS diameter was correlated with gestational age and it was found to increase progressively with gestational week [19]. In the present study, YS diameter increased with gestational week and was found to be positively associated with the CRL. Bagratee *et al.* conducted a study that showed that first trimester YSV reference intervals increased in a linear fashion for up to ten weeks, then up to 11 weeks it plateaued and decreased afterwards. They suggested that it was caused by decreased vascularization [20]. The present study were similar to these studies. However, when evaluating the results, it was seen that the YS size increased with gestational age, while the two-dimensional measurements correlated more significantly. In the first trimester, the GS consists of amniotic and celomic cavity and it reflects the embryonic development environment. GSV measurements can help to distinguish between normal and abnormal pregnancies.

When the fetal pole is seen without fetal cardiac activity in late pregnancy, the diagnosis of missed abortion cannot be questioned. However, in early pregnancy, it can be difficult to diagnose. The fetal pole is not very clear in this period, and GSV measurements may facilitate the diagnosis of failed pregnancy. In a study comparing missed miscarriage and ongoing pregnancy, larger mean gestational diameter and GSV were identified compared to CRL and embryo volume. Furthermore, it showed that volumetric measurements can have diagnostic value [15]. The first volumetric assessment of first trimester using three-dimensional US was a small pilot study made by Steiner *et al.* They described a linear relationship between gestational age and GSV by using three-dimensional US measurements [21].

In the present study, the results were similar to earlier studies; the authors found that GSV increased in a correlated manner with CRL with gestational age [18, 22]. Some studies showed that GSV has predictive value for failed pregnancy outcomes [5, 6, 23]. Falcon *et al.* conducted a study showing that GS measurements according to gestational week, seem to be normal size in early pregnancy of fetuses with trisomy 18, trisomy 21, and Turner syndrome, while fetuses with triploidy and trisomy 13 GS were demonstrated significantly smaller [7]. Also, Papaioannou *et al.* conducted another study which showed one in four of the abortion cases, median GSD was below the 5th percentile [1]. This reveals the importance of early ultrasonography. Average GS diameter is associated with gestational age and fetal growth. Bromley *et al.* reported that when MSD - CRL is less than five mm, it corresponds to a 94% abortion rate; when it is more than five mm, abortion rate is 8% [10]. However, in this study growth parameters and the linear relationship between them were examined in healthy pregnancies but were not compared to miscarriages and healthy pregnancies.

A combination of several variables in determining the value of a failed pregnancy outcome is better than a single variable, although this may not be always practical or clinically appropriate. In subsequent studies, easily formalized methods which can be applied to clinical practice should be developed.

The limitation of this study is the small number of patients. However, the power of the study is that all patients were examined by the same researcher in the same center.

In conclusion, assessing the early pregnancy volumetric parameters using linear regression models can assist in predicting failed pregnancy outcomes and to determine appropriate management. However, much more extensive studies are needed with larger groups of patients.

References

[1] Papaioannou G., Syngelaki A., Maiz N., Ross J.A., Nicolaides K.H.: ''Ultrasonographic prediction of early miscarriage''. *Hum Reprod.*, 2011, *26*, 1685.

[2] Oates J., Casikar I., Campain A., Müller S., Yang J., Reid S., Condous G.: "A prediction model for viability at the end of the first trimester after a single early pregnancy evaluation". *Aust. N. Z. J. Obstet. Gynaecol.*, 2013, *53*, 51-7.

[3] Makrydimas G., Sebire N.J., Lolis D., Vlassis N., Nicolaides K.H.: "Fetal loss following ultrasound diagnosis of a live fetus at 6-10 weeks of gestation". *Ultrasound Obstet. Gynecol.*, 2003, *22*, 368.

[4] Tannirandorn Y., Sangsawanq S., Manotaya S., Uerpairojkit B., Samritpradit P., Charoenvidhya D.: "Fetal loss in threatened abortion after embryonic/fetal heart activity". *Int. J. Gynaecol. Obstet.*, 2003, *81*, 263.

[5] Figueras F., Torrents M., Muñoz A., Comas C., Antolin E., Echevarria M., *et.al.*: ''Three-dimensional yolk and gestational sac volume. A prospective study of prognostic value''. *J. Reprod. Med.*, 2003, *48*, 252.

[6] Babinszki A., Nyari T., Jordan S., Nasseri A., Mukherjee T., Copperman A.B.: ''Three-dimensional measurement of gestational and yolk sac volumes as predictors of pregnancy outcome in the first trimester''. *Am. J. Perinatol.*, 2001, *18*, 203.

[7] Falcon O., Wegrzyn P., Faro C., Peralta C.F.A., Nicolaides K.H.: "Gestational sac volume measured by three-dimensional ultrasound at 11 to 13+6 weeks' gestation: relation to chromosomal defects". *Ultrasound Obstet Gynecol.*, 2005, *25*, 546.

[8] Verwoerd-Dikkeboom C.M., Koning A.H., Hop W.C., Rousian M., Van Der Spek P.J., Exalto N., *et. al.*: ''Reliability of three dimensional sonographic measurements in early pregnancy using virtual reality''. *Ultrasound Obstet. Gynecol.*, 2008, *32*, 910.

[9] Nyberg D.A., Laing F.G., Filly R.A.: ''Threatened abortion: sonographic detection of normal and abnormal gestational sac''. *Radiology*, 1986, *158*, 379.

[10] Bromley B., Hatlow B.L., Laboda L.A., Benacerraf B.R.: "Small sac size in the first trimester: a predictor of poor fetal outcome''. *Radiology*, 1991, *178*, 375.

[11] Dickey R.P., Olar T.T., Taylor S.N., Curole D.N., Matulich E.M.: "Relationship of small gestational sac-crown-rump length differences to abortion and abortus karyotypes''. *Obstet. Gynecol.*, 1992, *79*, 554.

[12] Nazari A., Check J.M., Epstein R.M., Dietterich C., Farazner S.: "Relationship of small-for-dates sac size to crown-rump length and spontaneous abortion in patients with a known date of ovulation''. *Obstet. Gynecol.*, 1991, *78*, 369.

[13] Reece E.A., Scioscia A.L., Pinter E., Hobbins J.C., Green J., Mahoney M.J., *et al.*: '"Prognostic significance of the human yolk sac assessed by ultrasonography''. *Am. J. Obstet. Gynecol.*, 1988, *159*, 1191.

[14] Lindsay D.J., Lovett I.S., Lyons E.A., Levi C.S., Zheng X.H., Holt S.C., Dashefsky S.M.: ''Yolk sac diameter and shape at endovaginal US: predictors of pregnancy outcome in the first trimester''. *Radiology*, 1992, *183*, 115.

[15] Acharya G., Morgan H.: ''First-trimester, three-dimensional transvaginal ultrasound volumetry in normal pregnancies and spontaneous miscarriages''. *Ultrasound Obstet. Gynecol.*, 2002, *19*, 575.

[16] Gulbis B., Jauniaux E., Cotton F., Stordeur P.: ''Protein and enzyme patterns in the fluid cavities of the first trimester gestational sac: relevance to the absorptive role of secondary yolk sac''. *Mol. Hum. Reprod.*, 1998, *4*, 857.

[17] Hessert M.J., Juliano M.: ''Fetal loss in symptomatic first-trimester pregnancy with documented yolk sac intrauterine pregnancy''. *Am. J. Emerg. Med.*, 2012, *30*, 399.

[18] Rôlo L.C., Nardozza L.M., Araujo Júnior E., Nowak P.M., Moron A.F.: ''Yolk sac volume assessed by three-dimensional ultrasonography using the VOCAL method''. *Acta Obstet. Gynecol. Scand.*, 2008, *87*, 499.

[19] Tan S., Gülden Tangal N., Kanat-Pektas M., Sirin Özcan A., Levent Keskin H., Akgündüz G., *et al.*:"Abnormal sonographic appearances of the yolk sac: which can be associated with adverse perinatal outcome?''. *Med. Ultrason.*, 2014, *16*, 15.

[20] Bagratee J.S., Regan L., Khullar V., Connolly C., Moodley J.: ''Reference intervals of gestational sac, yolk sac and embryo volumes using three-dimensional ultrasound''. *Ultrasound Obstet. Gynecol.*, 2009, *34*, 503.

[21] Steiner H., Gregg A.R., Bogner G., Graf A.H., Weiner C.P., Staudach A.: ''First trimester three-dimensional ultrasound volumetry of the gestational sac''. *Arch. Gynecol. Obstet.*, 1994, *255*, 165.

[22] Müller T., Sütterlin M., Pöhls U., Dietl J., ''Transvaginal volumetry of first trimester gestational sac: a comparison of conventional with three dimensional ultrasound''. *J. Perinat. Med.*, 2000, *28*, 214.

[23] Goldstein S.R., Kerenyi T., Scher J., Papp C.: ''Correlation between karyotype and ultrasound findings in patients with failed early pregnancy''. *Ultrasound Obstet. Gynecol.*, 1996, *8*, 314.

Address reprint requests to:
G. BATMAZ, M.D.
Orhan Veli Kanık Cad. Gün Sk
Mihrabata Sitesi B Blok, No: 5-7 Daire: 20
Kavacık- Beykoz, Istanbul (Turkey)
e-mail: drgoncabatmaz@yahoo.com