DIFFERENCE BETWEEN MEAN GESTATIONAL SAC DIAMETER AND CROWN-RUMP LENGTH AS A MARKER OF FIRST TRIMESTER PREGNANCY LOSS IN LOW RISK PREGNANCY

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Abstract

Background: Small CRL (>2 SD below the mean) has been associated with small for gestational age infants and mGSD <50th percentile has been associated with chromosomal abnormalities.
Aim: The present study aimed to find the correlation of the difference between mGSD and CRL and the first trimester pregnancy loss in low risk pregnancy.
Methods: This is a prospective cohort that was carried out in the Outpatient Clinic of the Obstetrics and Gynecology Department, October 6 University Hospital. The study involved 100 pregnant women examined using 2D ultrasonography starting early in the first trimester with a first scan between 6 and 8 weeks. Another follow-up scan was conducted at 12 weeks. Outcome of first trimester was recorded.
Result(s): Mean mGSD was 20.44 mm and mean CRL was 10.8 mm. Fetal loss in first trimester was reported in seven patients (8.8%) and 73 (91.2%) resulted in an ongoing pregnancy and entered the 2nd trimester successfully. There are statistically significant relations for incidence of fetal loss with body mass index, history of vaginal bleeding in current pregnancy, history of fetal loss and difference. Multiple regression analysis demonstrated that independent contributions in explaining the rate of fetal loss were provided by history of vaginal bleeding and overweight/obese which independently increased fetal loss by 123.075 and 10.035 folds respectively.
Conclusion: Difference between mGSD and CRL is correlated with first trimester pregnancy loss in low risk pregnancy and can be used as a marker for it.

Keywords: abortion, first trimester pregnancy loss, ultrasonography, early pregnancy, gestational sac diameter, crown rump length.

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1. INTRODUCTION

Spontaneous pregnancy loss occurs in 25% to 50% of pregnancies prior to 14 weeks of gestation. Transvaginal ultrasound (TVUS) provides high-resolution images, low inter-observer variability with high reliability, and is typically used to make diagnosis of intrauterine pregnancy and to follow up with its development [(1)].
Gestational sac (GS), yolk sac (YS), crown-rump length (CRL), and heart rate (HR) are the parameters measured to evaluate early pregnancy [(2)]. 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 8 mm. The appearance of yolk sac is a marker of successfully growing gestational sac and is identified by transvaginal ultrasound between 4th and 5th week of gestation prior to appearance of fetal pole and embryonic heart [(3)].
Kamel et al. [(4)] evaluated the role of 3D ultrasound measurements of yolk sac volume (YSV) in predicting possibility risks in pregnancy during the first trimester. They concluded that first trimester 3D ultrasound assessment of GSV gives an accurate method for predicting outcome of pregnancy.
Crown-rump length (CRL), measured using ultrasound as early as the first prenatal visit, is generally used to assess gestational age in the first

trimester [5]. **Xu et al.** [6] investigated the association of crown-rump length (CRL) during the first trimester of pregnancy with neonatal outcomes. They concluded that maternal characteristics were independently associated with CRL in the first trimester, which was negatively related to fetal size, SGA, preterm birth, and admission rate to the NICU, but positively related to LGA.

The aim of the present study is to find the correlation of the difference between mGSD and CRL and the first trimester pregnancy loss in low risk pregnancy.

2. PATIENTS AND METHODS

This is a cross sectional analytical study of 100 cases that was carried out in the Obstetrics and gynecology out-patient clinic of 6th of October University hospital.

Inclusion criteria:

- Female patients confirmed to be pregnant by serum B-hCG during the first trimester with a gestational age up to 10 weeks..
- Primigravida and multipara with good past obstetric history.
- Spontaneous pregnancy.

Exclusion criteria:

- Patients with recurrent first trimester abortion.
- History of previous fetal structural or chromosomal anomalies.
- Pregnancies resulting after successful ART.
- Pregnant patients with threatened abortion.
- Fibroid uterus
- Congenital uterine malformations
- Cervical incontinence

Methods:

All participants were subjected to:

- History taking
- General examination including vital signs, cardiac and chest examination, head and neck examination, lower limb examination and lastly abdominal examination.
- U/S to measure CRL and mGSD.

For Crown- rump length, the baby is measured in centimeters, from the top of their head (crown) to the bottom of their buttocks (rump). The limbs and yolk sac are not included in the measurement. The measurement was then converted to millimeters. The mean sac diameter is measured by summing the gestational sac's height, length, and width and dividing the results by 3. It is expressed in millimeters. The difference between the two measurements were calculated.

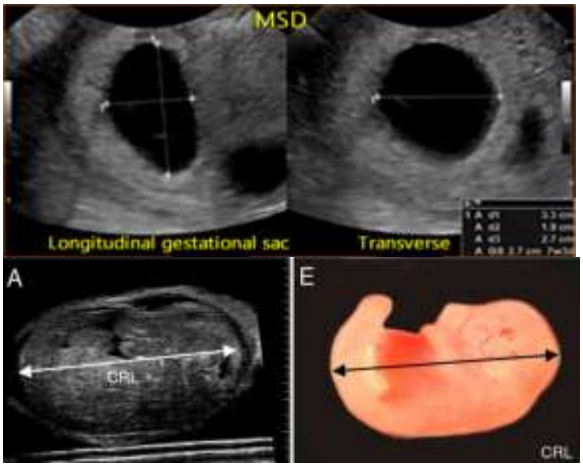

Figure (1): Ultrasonography for measurement of CRL and mGSD

Outcome:

Primary outcome:

Occurrence of first trimester pregnancy loss.

Secondary outcome: (Detection of complications)

- Bleeding.
- Uterine colics.
- Appearance of fetal anomaly.

STATISTICAL ANALYSIS:

Categorical data were analyzed using a two tailed student t-test for independent samples for comparative means of differences of gestational sac diameter and crown rump length in each group. Non parametric results were presented in percentage using fisher test to compare percentages. SPPS 25.0 software was used. $P < 0.05$ was considered to be significant.

3. RESULTS

During follow up, 20 women did not return for follow up and accordingly, the results of the remaining 80 women are shown. The mean age of the studied group was 25.09 years ranged between 19 and 43 years (table 1).

Ultrasonographic features showed that mean mGSD was 20.44 mm and mean CRL was 10.8 mm (tables 2 and 3).

Difference of mGSD and CRL ranged from 2 to 16.29 mm. eleven patients had difference <5 mm (13.8%), 36 patients (45%) had difference from 5 to <10 mm, 19 patients (23.8%) had difference from 10 to <15 mm while 17.5% had difference ≥15 mm (figure 5).

Fetal loss in first trimester was reported in seven patients (8.8%) and 73 (91.2%) resulted in an ongoing pregnancy and entered the 2nd trimester successfully, Of the 7 fetal losses, 3 were missed abortions (fetal pole with no visible pulsations), 1 blighted ovum, 1 incomplete abortions and 2 complete abortions (figure 6).

On finding association between incidence of fetal loss in first trimester and age of patients, the study showed that the percentage of fetal loss significantly increased in overweight (BMI > 25) and obese patients (BMI > 30). Also history of abortion significantly associated with current fetal loss.

Table (1): Distribution of The Studied Patients According to Age

	Mean ± SD	***Range***
Age (year)	25.09 ± 4.77	19 - 34

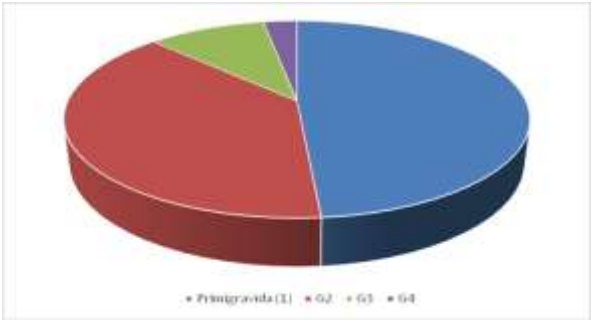

Figure (2): Pie Chart Showing Distribution of Patients According to Gravidity

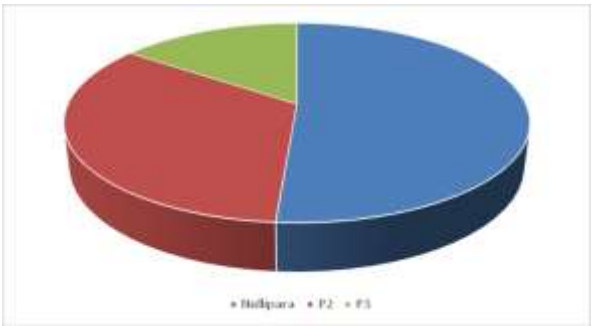

Figure (3): Pie Chart Showing Distribution of Patients According to Parity

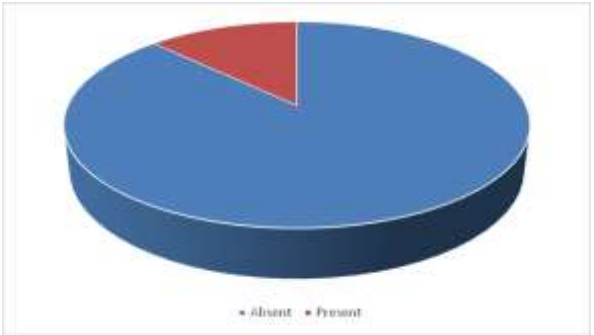

Figure (4): Pie Chart Showing Distribution of Patients According to Vaginal Bleedin

Table (2): Distribution of The Studied Patients According to 2D Ultrasonographic Findings (mGSD)

	Mean ± SD	***Range***
mGSD	20.44 ± 5.82	9.2 – 28.4

Table (3): Distribution of The Studied Patients According to 2D Ultrasonographic Findings (CRL)

	Mean ± SD	***Range***
CRL	10.8 ± 4.65	2.7 – 20.2

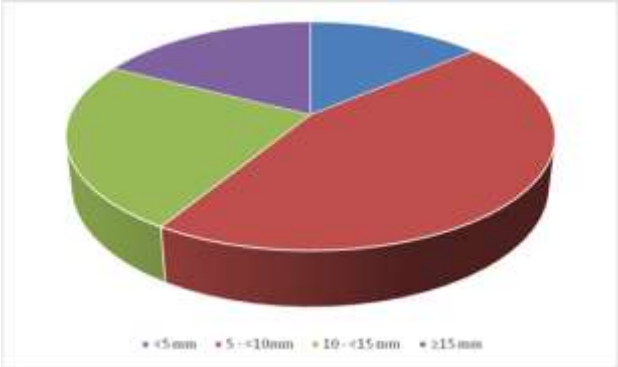

Figure (5): Pie Chart Showing Distribution of Patients According to Difference Between mGSD and CRL

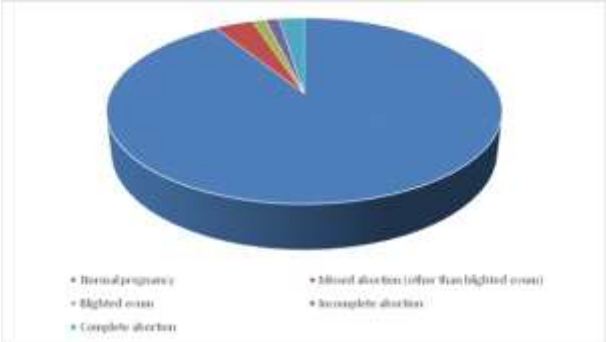

Figure (6): Pie Chart Showing Distribution of Patients According to Ultrasonographic Findings

Table (4): Relation Between Incidence of Fetal Loss and Body Mass Index of Studied Women

Parameter	**Fetal loss** N=7(%)	**Ongoing pregnancy** N=73(%)	χ^2	**p**
BMI				
Average	2 (28.6%)	55 (75.3%)	Fisher	0.019*
Overweight/obese	5 (71.4%)	18 (24.7%)		

χ2Chi square test, t independent sample t test, *p<0.05 is statistically significant

Table (5): Relation Between Incidence of Fetal Loss and History of Vaginal Bleeding of Studied Women

Parameter	**Fetal loss N=7(%)** **Mean ± SD**	**Ongoing pregnancy N=73 (%) Mean ± SD**	χ^2	**p**
Vaginal bleeding:				
Absent	1 (14.3%)	69 (94.5%)	Fisher	<0.001*
Present	6 (86.7%)	4 (5.5%)		

χ^2: Chi square test, *p<0.05 is statistically significant.

Table (6): Relation Between Incidence of Fetal Loss and History of Abortion of Studied Women

Parameter	**Fetal loss N=7(%)** **Mean ± SD**	**Ongoing pregnancy N=73 (%) Mean ± SD**	χ^2	**p**
Abortion:				
No	3 (42.9%)	66 (90.4%)	Fisher	0.011*
Yes	4 (57.1%)	7 (9.6%)		

χ^2: Chi square test, t independent sample t test, *p<0.05 is statistically significant

Table (7): Multivariate Regression Analysis of Factors Associated with Fetal Loss Among the Studied Patients

Parameter	β	p	AOR	95% C.I.	
				Lower	Upper
Vaginal bleeding in current pregnancy	4.813	<0.001*	123.075	8.478	1786.8
Overweight and obese	2.306	0.077	10.035	0.782	128.79

AOR: Adjusted Odds Ratio, CI: Confidence Interval, *P≤0.001 is Statistically Highly Significant

4. DISCUSSION

Threatened miscarriage is defined as any bleeding in the first half of pregnancy and is seen in about 20–25% of pregnancies, therefore is a fairly common complication during pregnancy. First trimester ultrasonography is routinely performed after infertility treatment to confirm pregnancy location and assess viability. Mean gestational sac diameter (mGSD; defined as average of measurements taken in three dimensions) and crown-rump length (CRL; defined as the average of three measurements of the longest fetal length) are two parameters routinely measured during early sonograms that are part of well-established criteria for diagnosing early pregnancy loss. Specifically, mGSD ≥25mm without an embryo, CRL ≥7mm without a fetal heartbeat ≥2 weeks after identifying a gestational sac or ≥11 days after identifying a gestational sac and yolk sac are all considered to be diagnostic of a nonviable gestation [(7)]. These values were confirmed by **Preisler et al.** [(8)]. Although these criteria are useful to diagnose a nonviable gestation, clinicians often seek to predict pregnancy loss by identifying at-risk patients in advance of the pregnancy failure.

Salomon et al. [(9)] investigated the role of CRL in the assessment of fetal size such as birth weight, small for gestational age (SGA) and large for gestational age (LGA), which has a close relationship with fetal, neonatal, and adult health. **Culliney et al.** [(10)] found that SGA is a risk factor for cerebral palsy, psychological disorders, and poor intellectual performance in term and moderate to late preterm infants. For LGA, infants are exposed to long-term metabolic complications credibly, including childhood obesity, and the metabolic syndrome in their adulthood.

Yi et al. [(11)] explored associations between mGSD, CRL, and future pregnancy outcome. Small CRL (>2 SD below the mean) has been associated with small for gestational age infants and mGSD <50th percentile has been associated with chromosomal abnormalities such as triploidy and trisomy 16. Both small CRL and small mGSD have also been independently associated with first trimester pregnancy loss.

The present study aimed to find the correlation of the difference between mGSD and CRL and the first trimester pregnancy loss in low risk pregnancy. This is a prospective cohort that was carried out in the Outpatient Clinic of the Obstetrics and Gynecology Department, October 6 University Hospital. The study involved 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 at 12 weeks. Outcome of first trimester was recorded. Eighty women completed the study. During follow up, 20 women did not return for follow up and accordingly, the results of the remaining 80 women are shown.

About 44% of women were primigravida and 56.2% were multiparas. **Xu et al.** [(6)] found that 63.7% were primiparous.

IAbd Ellatif et al. [(13)] evaluated 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 Yolk Sac Size and Shape and embryonic heart rate) to early pregnancy loss and the correlation between different ultrasound parameter to each other. They found that parity from 1-2 was higher 48(48%). Non-abortion cases were higher 84(84%).

In the current study, ultrasonographic features showed that mean mGSD was 20.44 mm and mean CRL was 10.8 mm. Another results were obtained by **Gordon et al.** [(14)], with CRL average of 12wk5d ± 3 d (p = 0.482). While **Rolo et al.** [(15)] reported mean CRL of 23.4 mm ± 7.9 SD ranging from 9 to 40 mm.

In the current study, difference of mGSD and CRL ranged from 2 to 16.29 mm. eleven patients had difference <5 mm (13.8%), 36 patients (45%) had difference from 5 to <10 mm, 19 patients (23.8%) had difference from 10 to <15 mm while 17.5% had difference ≥15 mm.

Fetal loss in first trimester was reported in seven patients (8.8%) and 73 (91.2%) resulted in an ongoing pregnancy and entered the 2nd trimester successfully. Also, **Abd Ellatif et al.** [(13)] found that normal cases were higher [97(69%)].

In our study, of the 7 fetal losses, 3 were missed abortions (fetal pole with no visible pulsations), 1 blighted ovum, 1 incomplete abortions and 2 complete abortions. Also, **Abd Ellatif et al.** [(13)] found

that 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.

In the current study, there is statistically significant relation between incidence of fetal loss and body mass index. Among women with fetal loss, 71.4% were overweight/obsess versus 24.7% of those with normal pregnancy. But, **Kamel et al.** [4] found no statistically significant difference between both groups according to BMI.

As regard the history of vaginal bleeding in the current study there is statistically significant relation between incidence of fetal loss and history of vaginal bleeding in current pregnancy. Out of 10 patients with history of vaginal bleeding, 6 had fetal loss while remaining four had normal ongoing pregnancy. Also, there is statistically significant relation between incidence of fetal loss and history of fetal loss. Four patients (57.1%) of those with fetal loss had positive history of abortion versus 9.6% among those with normal pregnancy.

In the current study, there was statistically significant relation between incidence of fetal loss and difference between mGSD and CRL. Three patients out of seven patients (42.9%) had difference <5mm, two patients (28.6%) had difference from 5 to <10 mm, one patient (14.3%) had difference 10 - <15 mm and one patient (14.3%) had difference≥15 mm with statistically difference in distribution between or within the same group. **Rashid et al.** [16] found that a mean z-score of CRL was significantly lower in the miscarriage group of women compared with continued viable pregnancy group (-1.43 vs. -0.80, P = 0.030).

Multiple regression analysis demonstrated that independent contributions in explaining the rate of fetal loss were provided by history of vaginal bleeding and overweight/obese which independently increased fetal loss by 123.075 and 10.035 folds respectively. **Kapfhamer et al.** [12] revealed a fourfold higher odd of first-trimester loss in pregnancies with mGSD-CRL <5 mm and a decreased odd of loss with mGSD-CRL of 10–14.99.

The presence of an early ultrasound prior to 6 weeks 3 days was predictive of early pregnancy loss in the current study population. This likely represents confounding by indication, because early signs of miscarriage, such as vaginal bleeding or abnormal rise in serum levels of hCG, would typically prompt an early ultrasound. The decreased pregnancy loss associated with subchorionic hemorrhage appears to be counterintuitive. It is possible that a subchorionic hemorrhage impinging on the gestational sac might distort measurements of the GSD, making the mGSD-CRL appear lower than it actually is.

Models considering mGSD and CRL alone were both better at predicting pregnancy loss than the difference (mGSD-CRL). This is likely due to the fact that mGSD-CRL describes the difference in these variables, but not how the difference was achieved. For example, both increasing CRL and decreasing mGSD would decrease the mGSD-CRL.

It seems unlikely that changes in these two variables have equivalent effects on pregnancy loss. In other words, a change in one of these variables might lead to a more significant effect than the other. In addition, these measurements are constantly changing with early fetal growth, and normative values have been established for different gestational ages (17).

Kapfhamer et al. [12] found a strong inverse relationship between mGSD-CRL and first-trimester pregnancy loss in IVF patients, although the incidence of pregnancy loss with a mGSD-CRL <5mm was significantly lower than previously reported. Small mGSD-CRL was not associated with an increased risk of complications in pregnancies that continued beyond 20 weeks. The association between mGSD, CRL, and miscarriage is complex.

Abd Ellatif et al. [13] concluded that first trimester ultrasound measurement of 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 and CRL in combination provided better prediction of the prognosis of the first trimester than when either parameter used alone.

Xu et al. (2022) found that maternal characteristics were independently associated with CRL in the first trimester, which was negatively related to fetal size, SGA, preterm birth, and admission rate to the NICU, but positively related to LGA.

The current study is one of the first studies examining the difference between mGSD and CRL in low-risk pregnant patients, to investigate the relationship between mGSD-CRL and multiple pregnancy outcomes, and to compare multiple models using CRL, mGSD, and mGSD-CRL.

Finally, we were able to demonstrate that a complex relationship exists between mGSD and CRL and that miscarriage rates with mGSD-CRL <5mm in low-risk pregnant patients are significantly lower than previously reported in unassisted pregnancies.

5. CONCLUSION

A relationship exists between mGSD-CRL and miscarriage in the first trimester. Although the mGSD-CRL difference is important, the relationship between these variables is complex and the individual contribution of mGSD and CRL to the difference appears to be more important in predicting miscarriage than the difference itself. Therefore, the difference between mGSD and CRL is correlated with first trimester pregnancy loss in low risk pregnancy and can be used as a marker for it.

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