Mean Sac Diameter Minus Crown Rump Length as a Predector of Early Pregnancy Outcome

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Original Research Article

ABSTRACT

Background: Mean sac diameter (MSD) is a sonographic measurement of the gestational sac which is usually first seen at around 5 weeks, when it measures about 2-3 mm, It's the average of measurements taken in three dimensions.Crown rump length (CRL) defined as the length of the embryo or fetus from the top of it's head to bottom of torso, it's the most accurate estimation of gestational age in early pregnancy, it's determined by the average of three measurements of the longest fetal length. Aim of the study Determine efficacy of mean sac diameter minus crown rump length (MSD-CRL) in prediction of early pregnancy outcome.

Methods: The study included 80 cases at (6:9) gestational weeks with singletone pregnancy. We examined the case at the initial visit, Mean sac diameter and Crown rump length were calculated for each case. The difference between the MSD and CRL in mm was calculated. Then follow up visit after two weeks later. Pregnancy outcome was then recorded between (11:14w). During transvaginal ultrasound (TVUS) we observed location, size, number and regularity of gestational sac. Cardiac pulsation & Presence or absence of sub-chorionic hematoma.

Results: 73 cases (91, 3%) continued normal pregnancy and 7 cases (8, 8%) had pregnancy failure. It was found that the age, body mass index, gravidity and history of abortion show

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insignificant relation with outcome (p >0.05). Area under a curve was 0.984, p Value was <0.001, 95% CI was (0.961 – 1.000), at the cut off value (MSD-CRL) less than or equal 4, the sensitivity was 71.4%, the specificity was 97.2%, PPV was 71.4% and NPV was 97.3%, while at cut off value less than or equal 5, the sensitivity was 100.0%, specificity was 95.89, PPV was 70.0% and NPV was 100.0%.
Conclusions: (MSD- CRL) is good prediction for early pregnancy outcome but, the optimum threshold for predicting pregnancy outcome needed to be established by further studies, also bigger sample size will provide more advantage.

1. INTRODUCTION

The advantages of ultrasonography have increased in the recent years significantly [1]. In the early stages of a pregnancy, ultrasound is essential in predicting the risk of adverse pregnancy outcomes such as miscarriage, Preeclampsia and the possibility of abnormal cord insertion visualization [2].

It's also used for fetal anatomic surveys during a second-trimester scan to detect fetal malformations, monitoring fetal growth in utero and in pregnancy dating [3]. Mean sac diameter (MSD) is a sonographic measurement of the gestational sac which is usually first seen at around 5 weeks, when it measures about 2-3 mm, It's the average of measurements taken in three dimensions [4].

Crown rump length (CRL) defined as the length of the embryo or fetus from the top of it's head to bottom of torso, it's the most accurate estimation of gestational age in early pregnancy, it's determined by the average of three measurements of the longest fetal length [5].Both two previous parameters routinely measured during early sonograms as a part of well-established criteria for diagnosis of early pregnancy loss [6]. It has previously been thought that the embryo and its associated structures except for the yolk sac grow at a similar consistent velocity [7], with both crown–rump length (CRL) and MSD increasing at a rate of approximately 1 mm per day. However, more recent studies have shown that MSD and CRL grow at variable rates.

A smaller than expected first-trimester embryo has been strongly linked with subsequent miscarriage [8]. For example, in the UK an empty gestational sac, visualized using trans vaginal ultrasound, with a mean sac diameter (MSD) of ≥20 mm may be classified as a miscarriage according to the Royal College of Obstetricians

and Gynecologists' (RCOG) guideline for the management of early pregnancy loss [9].Following a previous public enquiry in the UK, cut-off values for MSD of 20 mm and for CRL of 10 mm were proposed, but never on the basis of a single scan and only after a repeat scan had been carried out at least 7 days later [10] a miscarriage on the basis of an empty gestational sac with a MSD ≥16 mm or, if present, an embryo with a CRL measuring≥5 mm and no heartbeat [11]. Other studies have concluded that an empty gestational sac with a MSD of ≥25 mm or a MSD of ≥20 mm can be used as a safe approach to diagnose miscarriage [12] a CRL cut-off of ≥5 mm and an appropriate cut-off value for MSD of ≥13 mm with or without a yolk sac [13] for diagnosis of miscarriage. MSD> 25mm without an embryo &CRL>7mm without fetal heart beat& absence of fetal heart beat >2weeks after identifying the gestational sac or >11 days after identifying the gestational sac and yolk sac are all considered to be diagnostic of nonviable pregnancy [14]. Other studies have examined the difference between Mean sac diameter& Crown rump length (MSD-CRL) as another predictor of pregnancy loss at the first trimester. For example, Miscarriage rates as high as 94 % were reported with MSD-CRL< 5mm [15,16], the period of viability refers to the period after the twenty-eighth week [17].

The aim of the current study is to determine the accuracy of (mean sac diameter minus crown rump length) as a predictor of early pregnancy outcome.

2. PATIENTS AND METHODS

This study is an observational prospective study. This study was carried at Obstetrics and Gynecology Department of Tanta University Hospital. From August 2019 till August 2020.

Total of eighty pregnant females were included in the study.

- **Inclusion criteria**

Age of Patients (18-35 years old).

- Gestational age (6- 9 weeks).
- Singleton live pregnancy.

- **Exclusion criteria**

- History of recurrent miscarriage due to local causes as patulous internal os, sub mucous fibroid.
- History taking Clinical examination
- Investigations:

A-Laboratory investigations as

1-CBC

2-Thyroid profile.

3-Oral glucose tolerance test.

4-Liver, thyroid and kidney function tests.

B-Transvaginal ultrasound examination

- ➢ **Technique of the transvaginal ultrasound scan:**

  After emptying the urinary bladder, patient lies on an examination bed in lithotomy position. The transvaginal transducer is covered with the conducting gel and a plastic/latex sheath and gel is applied on the plastic sheath for ease of insertion. Then the transvaginal transducer is inserted into the vagina. It is gently moved around the inside of the pelvis and images are taken. Patient might have her lower abdomen pushed with the examiners hand to get some of the pelvic organs closer to the transducer for better pictures. The examination is carried out in "real time". Still photographs are also taken during the examination. At the end of the test, the probe is fully sterilized and clean.

- **Outcome measurement:**

  (MSD-CRL) equal or less than 5mm can predict pregnancy failure

The Mean sac diameter (MSD):

- **Definition:** Mean gestational sac diameter defined as the average of measurements taken in three dimensions (67).

- **Measurement:** The gestational sac is an echo-free space containing the fluid, embryo, and extra embryonic structures. The gestational sac is imaged first in the longitudinal plane, obtaining long axis and anteroposterior measurements perpendicular to each other. Then, in the transverse plane at the level of the anteroposterior measurement, the width measurement is obtained. The Main sac diameter was calculated in mm from the average of three orthogonal dimensions measured from the inner sac wall/chorionic fluid interface.

The Crown rump length (CRL):

- **Definition:** Crown-rump length (CRL) defined as the average of three measurements of the longest fetal length (68). the Crown rump length as taken as the greatest length in mm of the embryo at sagittal plane.

- **Measurement:** technique involves measurement of the fetal length from the tip of the cephalic pole to the tip of the caudal pole. The fetus should be at rest and assuming its natural curvature. When CRL measured ≥7 mm Cardiac activity should be present in an embryo. If it not detected at this size on transvaginal scanning performed by an experienced operator, it is an indicator of failed early pregnancy (missed miscarriage).

2.1 Statistical Analysis

The sample size was calculated using Epi-Info software statistical package created by World Health organization and center for Disease Control and Prevention, Atlanta, Georgia, USA version 2002. The criteria used for sample size calculation (n>33) were 95% confidence limit, 80% power of the study, expected outcome in in treatment group 90% compared to 60% for control groups.

Analysis of data were performed by SPSS v25 (SPSS Inc., Chicago, IL, USA). Quantitative parametric variables (e.g. age) were presented as mean and standard deviation (SD). They were compared between the two groups by unpaired student's t- test and within the same group by paired T test. Quantitative non-parametric variables (e.g. VAS) were presented as median and range and compared between the two groups by Mann Whitney (U) test and within the

same group by Wilcoxon test. P value < 0.05 was considered significant.

3. RESULTS

Observations were made on a total of 80 live singleton pregnancies during the course of this study. 73 cases (91, 3%) continued normal pregnancy and 7 cases (8, 8%) had pregnancy failure, the mean age of failure was 69.71±4.72 days (Table 2)

Regarding the basic demographic and clinical data, the mean age of the studied group was 25.08±4.86 years, the body mass index was 26.61±4.29 kg/m2. The mean gravidity was 2.54±1.28, 20 cases were primigravida and 57 cases were multipara and 3 cases were nullipara. 22 cases (27.5%) have history of abortion (Table 1). According to the relation between demographic data and the outcome of pregnancy, It was found that the age, body mass index, gravidity and history of abortion show insignificant relation with outcome (p >0.05) (Table 3).

MSD, CRL, (MSD-CRL) were measured for every case in the initial visit and also after two weeks. The mean CRL at 1st visit was 11.71±6.20 mm, and increased after 2 weeks to be 27.51±9.17mm. MSD in the 1st visit was 25.42±7.68 and increased after 2 weeks to be 38.97±8.35, the difference between MSD and CRL at 1st visit was 14.06±3.68 and after 2 weeks was 11.68±4.30 mm (Table 4).

At the first visit, it was found that there was a significant decrease in the difference of MSD and CRL in failed pregnancy cases less than normal pregnancy, the mean difference in normal pregnancy was 14.63±2.82, while in failed pregnancy cases was 3.86±1.07, (p <0.001) (Table 5), (Fig. 1). After two weeks, it was found that there was a highly significant decrease in MSD-CRL in failed cases less than normal pregnancy the main difference in normal pregnancy was12.54 ± 3.23 while in failed pregnancy was 1.50 ± 0.55   (p <0.001) (Table 6), (Fig. 2).

At the first visit, Area under a curve was 0.984, p Value was <0.001, 95% CI was (0.961 – 1.000), at the cut off value(MSD-CRL) less than or equal 4, the sensitivity was 71.4%, the specificity was 97.2%, PPV was 71.4% and NPV was 97.3%, while at cut off value less than or equal 5, the sensitivity was 100.0%, specificity was 95.89,

PPV was 70.0% and NPV was 100.0% (Table 7), (Fig. 3).

At the second visit (after two weeks), Area under curve was 0.996, P value was<0.001, 95% C.I was (0.987 – 1.000), at the cut off value less than or equal 2, the sensitivity was 100%, the specificity was 98.59%, PPV was 85.7% and NPV was 100.0% (Table 8), (Fig. 4).

4. DISCUSSION

Therefore they suggested that MSD and MSD–CRL nomograms should be done for each gestational week [18].

Previous study to detect sensitivity of Small sac size in the first trimester as a predictor of poor fetal outcome, study included (68 patients) which divided into study group and control group. The study group: 16 patients with gestational age (5.5-9 weeks), small sac size, and fetuses with normal cardiac activity.   Small sac was diagnosed when (MSD-CRL) was less than 5 mm. the control group: 52 patients with gestational age (5.5 -9 weeks), normal sac size, and fetuses with normal cardiac activity. In the study group, 15 cases (94%) had pregnancy failure. In the control group, 4 cases (8%) had pregnancy failure, this is matched with our study [19], however this study was small.

In previous study for prediction of spontaneous miscarriage in 149 viable early pregnancies with bleeding. In this prospective study a significant association was found between the occurrence of miscarriage and fetal bradycardia, an abnormal MSD-CRL (< 0.5 SD from the mean) and discordant menstrual and sonographic age (> 1 week). The probability of miscarriage was highest when all three risk factors were present (84%). embryonic bradycardia had the most powerful independent association with pregnancy outcome in women with threatened miscarriage [21]. Our study did not include embryonic bradycardia as a parameter but, we had advantage that, the sample population was not selected on the basis of bleeding symptoms.

Previous study to determine the incidence of small gestational sac syndrome and its association with abortion, karyotype of the abortus, and known abortion factors, the study included 539 patients , Rate of pregnancy failure was 80.0% when (MSD -CRL) was less than 5 mm & 26.5% when (MSD-CRL) was 5-7.9 mm , and 10.6% when (MSD-CRL) was 8 mm. When

(MSD-CRL) was 5-7.9 mm (P less than0 .002 compared with less than 5 mm), and when (MSD-CRL) was 8 mm or more (P less than .0001 compared with less than 5 mm)) [22].

Table 1. Demographic characters of the studied cases (n = 80)

	No.	%
Age (years)		
Mean ± SD.	25.08 ± 4.86	
Body mass index (kg/m^2)		
Mean ± SD.	26.61 ± 4.29	
Gravidity		
Mean ± SD.	2.54 ±1.28	
Parity (n = 80)		
Primigravida	20	25
Multipara	57	71.25
nullipara	3	3.75
History of abortion		
No abortion	58	72.5
Abortion	22	27.5

Table 2. Distribution of the studied cases according to outcome and age of failure (n = 80)

	No.	%
Outcome		
Normal pregnancy	73	91.3
Failed pregnancy	7	8.8
Age of failure (days) (n = 7)		
Mean ± SD.	69.71 ±4.72	

Table 3. Relation between outcome and demographic data (n = 80)

	Outcome				Test of Sig.	p
	Normal pregnancy (n = 73)		**Failed pregnancy (n = 7)**			
	No.	%	No.	%		
Age (years)	25.05 ± 4.97		25.29 ± 3.73		t=0.119	0.905
Body mass index (kg/m^2)	26.64 ± 4.34		26.29 ± 4.07		t=0.210	0.835
Gravidity	2.56 ±1.31		2.29 ±0.95		U=232.50	0.687
Parity						
Primi	20	25	3	42.86	χ^2= 0.351	[FE]p= 0.660
Multipara	57	71.25	2	28.57		
Nullipara	3	3.75	2	28.57		
History of abortion						
No abortion	52	71.2	6	85.7	χ^2= 0.672	[FE]p= 0.667
Abortion	21	28.8	1	14.3		

t: Student t-test; U: Mann Whitney test

χ^2: Chi square test; FE: Fisher Exact

p: p value for comparing between Normal pregnancy and Failed pregnancy

Table 4. Comparison between 1st visit and After 2 weeks according to different measures (n = 80)

	1st visit	After 2 weeks
CRL (mm)		
Min. – Max.	3.0 –34.0	11.0 – 48.0
Mean ± SD.	11.71 ±6.20	27.51 ± 9.17
Median (IQR)	10.0 (7.0 –16.0)	26.0 (21.0 – 35.0)
MSD (mm)		
Min. – Max.	10.0 –39.0	12.0 – 52.0
Mean ± SD.	25.42 ±7.68	38.97 ± 8.35
Median (IQR)	25.0 (19.0 –31.0)	40.0 (34.0 – 45.0)
MSD-CRL (mm)		
Min. – Max.	2.0 –19.0	1.0 – 18.0
Mean ± SD.	14.06 ±3.68	11.68 ± 4.30
Median (IQR)	15.0 (13.0 –17.0)	12.0 (9.0 – 15.0)

Table 5. Relation between outcome and MSD-CRL (mm) 1st visit (n = 80)

MSD-CRL (mm) 1st visit	Outcome		U	p
	Normal pregnancy (n = 73)	**Failed pregnancy (n = 7)**		
Min. – Max.	4.0 – 19.0	2.0 – 5.0	8.0[*]	<0.001[*]
Mean ± SD.	14.63 ± 2.82	3.86 ± 1.07		
Median	15.0	4.0		

U: Mann Whitney test
p: p value for comparing between Normal pregnancy and Failed pregnancy
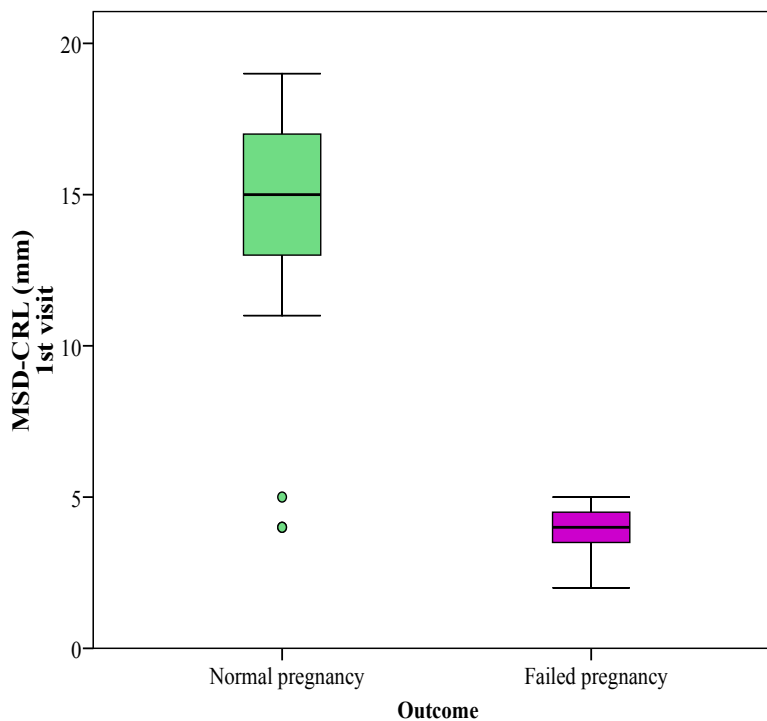**: Statistically significant at p ≤ 0.05*

Fig. 1. Relation between outcome and MSD-CRL (mm) 1st visit (n = 80)

Table 6. Relation between outcome and MSD-CRL (mm) After 2 weeks
(n = 80)

MSD-CRL (mm) after 2 week	Outcome		U	p
	Normal pregnancy (n = 73)	**Failed pregnancy (n = 7)**		
Min. – Max.	2.0 −18.0	1.0 −2.0	1.500[*]	<0.001[*]
Mean ± SD.	12.54 ±3.23	1.50 ±0.55		
Median	13.0	1.50		

U: Mann Whitney test
p: p value for comparing between Normal pregnancy and Failed pregnancy
*: Statistically significant at p ≤ 0.05

Table 7. Validity (AUC, sensitivity, specificity) for MSD-CRL (mm) 1st visit to prognoses failed pregnancy patients (n = 7) from normal pregnancy (n = 73)

	AUC	p	95% C.I	Cut off	Sensitivity	Specificity	PPV	NPV
MSD-CRL (mm) 1st visit	0.984	<0.001[*]	0.961 −1.000	≤4	71.43	97.26	71.4	97.3
				≤5	100.0	95.89	70.0	100.0

*AUC: Area Under a Curve ; **p value:** Probability value*
CI: Confidence Intervals
*NPV: Negative predictive value; **PPV:** Positive predictive value*
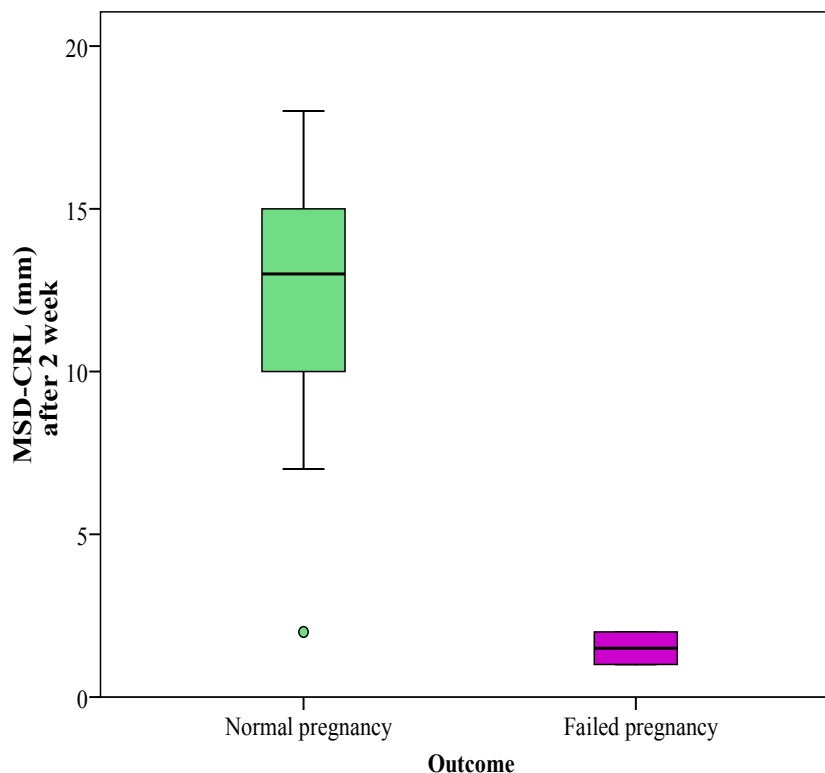**: Statistically significant at p ≤ 0.05*

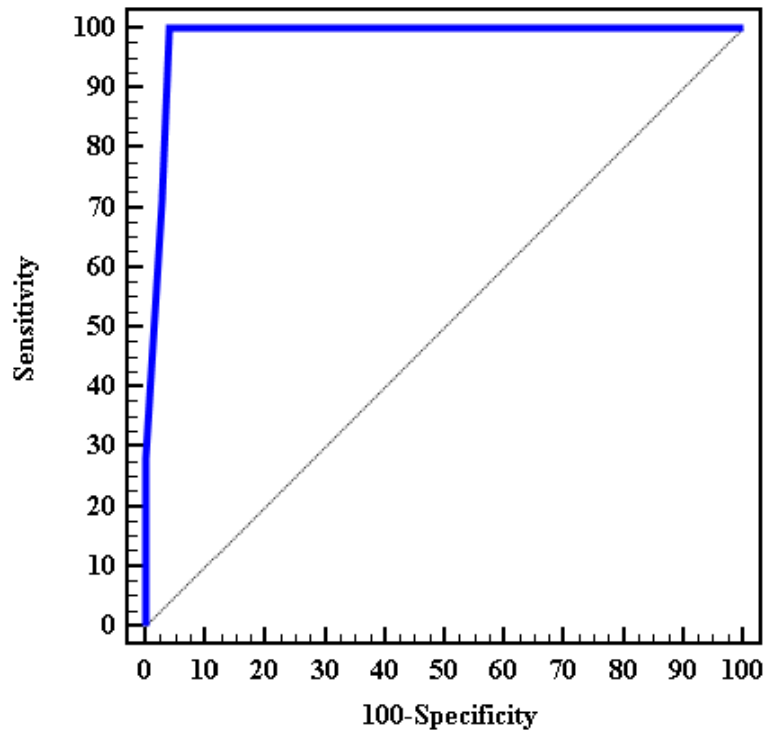**Fig. 2. Relation between outcome and MSD-CRL (mm) after 2 week**

Fig. 3. ROC curve for MSD-CRL (mm) 1ˢᵗ visit to prognoses failed pregnancy patients (n = 7) from normal pregnancy (n = 73)
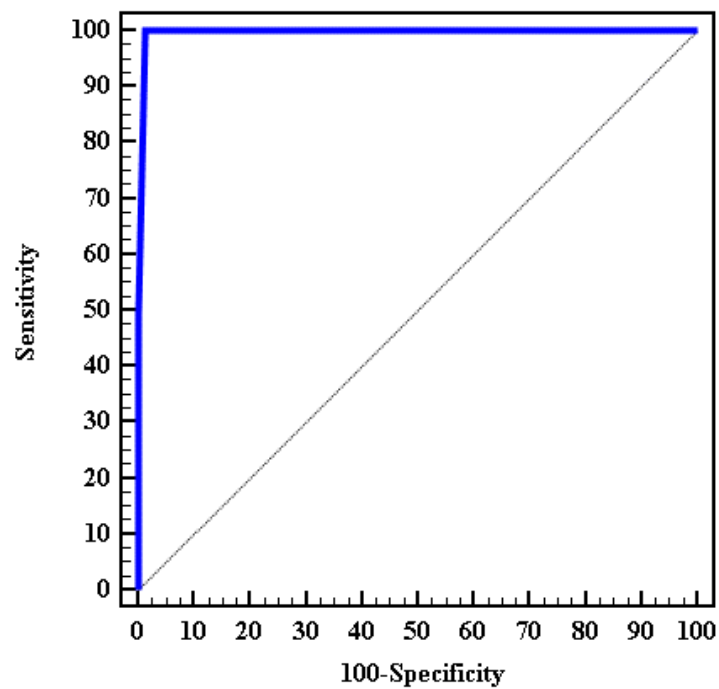

Fig. 4. ROC curve for MSD-CRL (mm) after 2 week to prognoses failed pregnancy patients (n = 7) from normal pregnancy (n = 73)

Table 8. Validity (AUC, sensitivity, specificity) for MSD-CRL (mm) after 2 week to prognoses failed pregnancy patients (n = 7) from normal pregnancy (n = 73)

	AUC	p	95% C.I	Cut off	Sensitivity	Specificity	PPV	NPV
MSD-CRL (mm) after 2 week	0.996	<0.001[*]	0.987 −1.000	≤2	100.0	98.59	85.7	100.0

AUC: Area Under a Curve ; p value: Probability value
CI: Confidence Intervals
NPV: Negative predictive value; PPV: Positive predictive value
*: Statistically significant at p ≤ 0.05

In previous study for assessment of the gestational sac diameter, crown–rump length, progesterone and fetal heart rate measurements at the 10th gestational week to predict the rate of spontaneous abortion, the Study included ninety nine patients. Gestational age was (6:9weeks), Rate of pregnancy failure was 8cases (8.08%), at cutoff value (MSD–CRL) <10 mm, four of 15 (26.7%) resulted in abortion. At cutoff value (MSD–CRL) ≥ 10 mm four of 84 (4.8%) pregnancies resulted in abortion, in this study (P = 0.004). Area under curve was 0, 16. Sensitivity was66.67% and specificity was 89.21% positive predictive value was 42.10%, and negative predictive value was95.78% [23]. In our study, We did not find a significant difference between the groups when we took 10 mm as threshold level, When we took 5 mm as threshold level, however, there was a significant difference .

In previous study for prediction of risk of abortion before 13weeks of gestation by comparison of gestational sac size, crown rump length and fetal heart rate. The study included 603 patients, Twenty three pregnancies ended in first trimester miscarriage after viability has be detected by ultrasound. The authors did not use the traditional MSD − CRL parameter; instead, nomograms were generated for the ratio of gestational sac size (GSS) /CRL against embryonic heart rate (EHR), gestational age and CRL. They found that, plotting the GSS/CRL ratios of the aborted cases on the GSS/CRL versus LMP monogram had higher sensitivity for miscarriage (78.3%) specificity (97.8%) and a false-positive rate of (2.2%) than embryonic heart rate. Their two dimensional sac size/CRL ratio is not however an established parameter of embryonic growth and it was unfortunate that the authors did not use the conventional three dimensional MSD which is a more widely accepted parameter of sac size [24].

Previous study to detect Sensitivity and specificity of using serial measurements of embryonic growth for the prediction of early pregnancy loss, study included 1078 cases, 773 (71.7%) remained viable at12 w and 305 (28.3%) miscarried. By Using CRL, sensitivity was 60.7% and specificity was 93.1%, PPV was 33.3%, &NPV was 97.7%. Using MSD gave sensitivity of 67.6% and specificity of 84.5% , PPV 50% & NPV 91.9%. Using MSD/CRL ratio gave sensitivity of 44.4% and specificity of 96.6% PPV 70.6% & NPV 90.3%. (MSD-CRL) predicted early pregnancy loss very poorly) [25].

In our study, it was found that there was no significant relation between the outcome and demographic data which include age, body mass index, gravidity and history of abortion, this is matched with previous studies [26-29]. On the other hand, In previous study increasing maternal age is associated with increased risk of abortion, Older women had a slightly smaller fetus at the beginning of pregnancy (P = 0.0279) (SE = 0.065) but, there was a positive relation between maternal age and CRL along the first trimester, older women had a greater increase in CRL (P = 0.0046) (SE = 0.0015). About 0.0042 mm in CRL per day of gestation for each 1 year increase in maternal age. The AIC of the model was 5038.6 .The difference in CRL at 12 weeks gestation between a woman of 20 years and a woman of 40 years was 4.18 mm (equivalent to approximately 2 days gestation) [30]. Also, maternal age was significantly different (P = .011) in patients with small sac syndrome [31]. In the multivariate model, increasing maternal age had greater risk of early pregnancy failure (OR, 1.14; 95% CI, 1.03–1.27). In older mothers, meiotic non disjunction during oogenesis is more frequent. The incidence of chromosomal abnormalities in the first trimester Abortion was 61.5% [32].

5. CONCLUSIONS

(MSD-CRL) was a good predictor for early pregnancy outcome . at cut off value equal or less than 5 mm , the sensitivity was 100.0%, specificity was 95.89, PPV was 70.0% and NPV was 100.0%.

CONSENT

As per international standard or university standard, Participants' written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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