

Ultrasound golden roles in early pregnancy failure and miscarriage diagnosis

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ABSTRACT

To identify the ultrasonic role and its parameters in diagnosing early pregnancy failure and miscarriage. It is a retrospective surveyed study comprising 1750 pregnant ladies in their 1st trimester period, who were classified into three group: first group comprised 453 women with CRL 6.9 mm and above which expected to end in abortion early beside other gestational failure criteria, second group comprised 507 ladies who had threatened abortion sign and bleeding, they complete pregnancy period till 13 week of gestation then followed by pregnancy failure. third control group comprised 790 women with normal pregnancy. Ultra sonographic parameters comprised fetal heart rate (FHR), Gestational sac diameter (GSD), Crown-rump length (CRL), Yolk sac diameter, and GSD-CRL ratio Comparison between these parameters was conducted through sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). Significant statistical difference were present among these two miscarriage groups and third control group, regarding Fetal heart rate (its mean value estimation among these groups were 99 +/- 15, 162.0, 159 in first, second and third group respectively while CRL mean value 6.95 mm, 7.30 mm, 8.7 mm in the first, second and third group respectively GSD and YSD were higher significantly in actual miscarriage (threatened abortion ending in actual abortion) as the mean 51.42 mm and 6.74 mm for the (first and second group), 38.6 mm and 4.68 +/- 0.35 mm GSD and YSD respectively for ladies who completed their pregnancy (third group) ladies with a mean GSD-CRL ratio < 5mm, comparing to the reference value mean GSD-CRL of 5-9.9 mm (42.9 % for the ratio < 5 mm vs. 15.6 % p <.0001 reference value for the mean ratio of 5 -9.9), actually miscarriage ladies was high among threatened abortion group ending with abortion with percentage (37%), sensitivity, specificity, PPV and NPV for ultrasonic indicators proved that ultrasonic can detect 89% of early pregnancy failure cases. Using ultrasonic techniques and devices to investigate and diagnosis early pregnancy failure have a golden role in management and reduce miscarriage cases , as it can also predict actual miscarriage which contributes in avoid occurrence of it.



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1. INTRODUCTION

Naturally, the pregnancy period is completed and end by delivery of the full term fetus, but sometimes it doesn't complete for one reason or another, in which many of pregnant women suffer from problems in their first trimester, thus early pregnancy problems are the most known reasons that urge pregnant women to get medical care [1]. The diagnosis of threatened miscarriage is assumed in the presence a vaginal bloody discharge or bleeding occurs during the first trimester of pregnancy. These could be occurred among women by ratio 20-25% during early pregnancy period and may continue for days or even weeks as well as, almost 50% of these pregnancies exposed to abortion [2]. The investigation of these women in fact needs a reliable and easy technique, Ultrasonic is a reliable golden technique which suitable to examine such ladies at any time, and become a standard routine investigation, trans vaginal ultrasound scans (TUS) introduce a good investigation [3]. Ultrasound was from the oldest method which had been used , it was used in the assessment and Diagnosis of early intrauterine pregnancy loss [4], [21- 28] Presence of ultrasound and its high-resolution images have enabled the demonstration of normal anatomy findings , development of the early fetal node part , asses yolk sac diameter which is being the earliest sign of conception .Many factors seen in ultrasound pointing toward early pregnancy loss and miscarriage to be of high reliability such as the difference between gestational sac and fetal node size i.e., gestation sac diameter (GSD) with fetal node ratio , yolk sac diameter , and the embryonic cardiac speed and pulsation [7], [27- 38].

Beside the ability of TVS in providing accurate images (in vivo) for the early gestational sac, it also gives a significant indicator to the epidemiology and path- physiology for miscarriage and early pregnancy failure (2). using ultrasound, plus serum gestational enzyme levels (such as progesterone and human chorionic gonadotropin) [HCG] aids in early pregnancy loss diagnosis, control and management; however any mistakes in usage and wrong interpretation of these examinations can make significant damage [3]. However, in most of pregnancy cases, ladies have a normal pregnancy inside uterus. if there are viable embryos, a number of measurements must be performed, comprising embryo crown-rump length (CRL), fetus heart rate (FHR), gestational sac diameter (GSD) and yolk sac diameter (YSD) [8].

2. Patients, Materials and Methods

2.1 Study community

This is a retrospective surveyed study for 1950 pregnant ladies who had been scanned by trans vaginal and trans abdominal ultrasound between (January 2015 to November 2019) in CMC private hospital in Erbil city and radiology private clinic in Mosul city, the sono graphic cut off value for examinations of early pregnancy failure and miscarriage assessed and performed accurately.

Maternal characteristics recorded are age, conception method (whether it was spontaneous or assisted one which requiring IVF), taking any medicines (yes or no) and parity. We recorded the last menstrual period (LMP) date and classified it as a regular cycle (26–30 days) with definite LMP, regular-indefinite, irregular-unknown and conception within three cycles after last pregnancy or stop taking the contraceptive pill indicators of assessment in ultrasound hospital unit were Classified into: vaginal bleeding / brownish discharge, pain in the lower aspect of the abdomen, anxiety which due to previous occurring of miscarriages or ectopic pregnancies and finally, pregnancy date.

Ladies who were subjected to the current study had gestational age ranging between 5th -13th week which was calculated depending on the last menstrual period, then the pregnancy has been confirmed using ultrasound diagnosis. In our study, we excluded the cases with multiple gestation that have abortion secondary to cervical incompetence, or who had abortion whether it was inevitable or incomplete abortion, and also we excluded the cases with ectopic pregnancy or GTD (Molar pregnancy).

These 1950 pregnant ladies included in this study, 200 ladies were excluded according to exclusion standards of the study, so the sample were 1750 pregnant women, 960 lady were assisted due to presentation as threatened abortion, little vaginal bleeding had moderate abdominal pain or even no pain, the rest cases (790) were healthy women who had normal pregnancy. All women had been exposed to examine full history, abdominal, and trans vaginal ultrasound (3-5 MHZ), measure fetal heart rate (FHR), gestational sac diameter (GSD), Crown-rump length (CRL), Yolk sac diameter and GSD-CRL ratio.

In the beginning, these (1750) women had been subjected to the examination of serum level of beta human chorionic Gonadotropin distributed into three groups:

First group comprised 453 women assisted with routine ultrasound examination which expected to end in abortion early,

Second group comprised 507 ladies have history of threatened abortion in which their pregnancy completed till 13 weeks.

Third group comprised 790 ladies that have normal pregnancy.

2.2 Ultrasonic study

For these three group of the participated pregnant women, the ultrasound was conducted regarding the following indicators as follows:

- 1- Mean gestational sac diameter (MSD): MSD had been measured according to the mean diameters, which is The diameter of the sac was measured longitudinally, transversally, obliquely ignoring the decidual reaction. It is usually inside endometrium, and has a round or oval shape and it is smooth [9].
- 2- Yolk sac (YS), it is estimated by putting calipers on the internal walls of the longer diameter. It often exists at peripheral of GS and should not be free from the sac., sac dimension, its morphology, echogenicity of the edge, the sac's center, the number of it, and retrograde modifications, (calcification as example) are observed thoroughly, the diameter of normal Yolk sac ranges between 3-5 mm, it shape is spherical, with no retrograde changes, existence of echogenic edge and hypo echoic center are considered as normal [10]. Any aberration from mention parameters refereed to abnormal signs.
- 3- Crown-rump length (CRL) it represents the embryo length from the crown (top of the head) to the rump bottom Without the yolk sac or extremities [11], to be estimated in sagittal part of the embryo then it is recorded as three measurements ' mean.
- 4- The ratio of GSD, to crown-rump length (MGSD-CRL) was calculated for any difference between them, if this difference was less than 5 mm are expected to be miscarriage within first trimester [12].
- 5- Embryonic heart rate (FHR) was also calculated at M-mode depending on beat / minute using ultrasound device ' software,

A scan was conducted to demonstrate measurements of a viable embryo in a singleton pregnancy Regarding the mentioned indicators CRL, HR, GSD and YSD (Fig. 1)

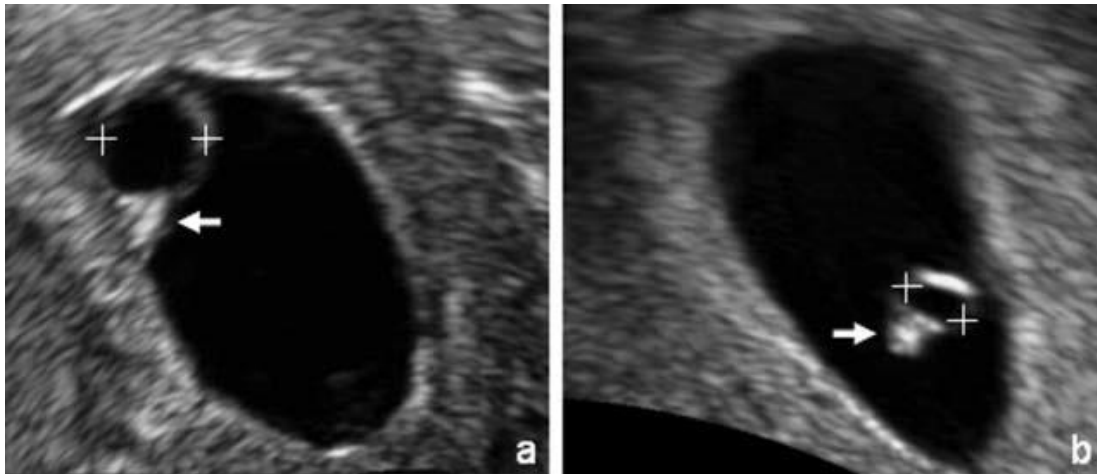


Figure 1a: illustrates abnormal yolk sac measure 7 mm **Figure 1 b:** illustrates normal yolk sac 2mm

2.3 Statistical analysis

The Collected data had been analyzed depending on the statistical package for social sciences program, (SPSS Inc, U.S.A, version 20.0). Where Quantitative data had been represented as mean ± standard deviation (SD), but Qualitative one had been represented as percentage and frequencies. As well as, sensitivity, positive predictive values (PPV), negative predictive values (NPV), specificity, odds ratios have been assessed, probability value was < 0.05 which means as statistically significant difference.

3. Results

Among these 1750 ladies that participated in this study which distributed into three categories, There wasn't significant statistical difference between the three study groups regarding age, parity, Body mass index, GA, or the number of previous abortions, these data were illustrated in table 1

Table (1): demographic data of pregnant ladies in study

Demographic Data	1st group		Sec group		Third group		Probability (p value)
	Mean	standard deviation	Mean	standard deviation	mean	standard deviation	
Age	28.1	4.5	29.1	6.2	31.0	6.6	>0.05
Parity	1.3	0.82	1.3	1.2	1.2	1.4	NS
Body mass Indicator	27.99	2.8	26.2	3.01	26.2	2.5	
Gestational age	6.7	2.3	7.31	2.1	7.6	2.2	
Pervious abortion	1.1	0.67	0.68	0.42	0.82	0.54	

The ultrasonic examination showed a statistically difference among control group (third group, n= 790) and first group who aborted before 13 weeks of gestational age (n=453) and second group who suffered from threatened miscarriage but they completed their pregnancy till 13 weeks (n=507) regarding FHR (fetal heart rate) and crown rump length CRL (table 2).

Table (2): ultrasonic parameters (FHR, CRL) for three groups

Ultrasonic Parameters	1 st group Aborted		2 nd group Incomplete miscarriage till 13 w		3 rd group Control		P value
	average	SD	average	SD	average	SD	
FHR	99.01	±15	162.8	±20.1	159.1	±24.9	<0.05
CRL	6.95	±0.13	7.3	±0.5	8.7	±1.9	

The current study showed that GSD and YSD were higher significantly in (first & second group), for women end with actual abortion as the mean were 51.42 ± 17.99 mm and 6.74 ± 0.7 mm respectively. If compared to the third group in which GSD and YSD were 38.6 ± 14.01 mm and 4.68 ± 0.35 mm respectively for women who completed their pregnancy, as shown in table (3)

Table (3): Ultrasonic parameters (GSD, YSD, CRL) between 1st, 2nd and 3rd group

Ultrasonic indicators	First & second group (n= 960)		Third group (n= 507)		P value
	Mean	SD+/-	Mean	SD +/-	
CRL	7.12	± 0.31	8.7	±1.9	0.10
GSD	51.42	±17.99	38.60	±14.01	0.03
YSD	6.74	±0.7	6.08	±0.24	0.04

The sensitivity, specificity, PPV and NPV have been calculated for significant predictors for the fetal heart rate (FHR) at 109 bpm, and crown –rump length at 7 mm +/- 0.2 mm these value shown in table (4) as follows:

Table (4): The sensitivity, specificity, PPV and NPV for miscarriage

predictors	Sensitivity	Specificity	positive predictive values (PPV),	Negative predictive values (NPV)
FHR (109) +/- 15 beat/minute	98.2	99	89	91
CRL (7 mm +/- 0.2)	45.0	39.98	35.60	34.01

The study also indicated that the number of actually miscarriage ladies was high among threatened abortion group ending with abortion with percentage (37%) it means 674 women from 1750 lost their fetus before 13 weeks of gestational age , followed by second group who were expected to complete their pregnancy till 13 weeks of GA, where it was (6%) of women lost their fetus after 13 weeks (means 105 /1750), while among the third group (healthy pregnancy cases) there was only two cases who lost their fetus (2/1750), these results showing in the following graph (figure 1)

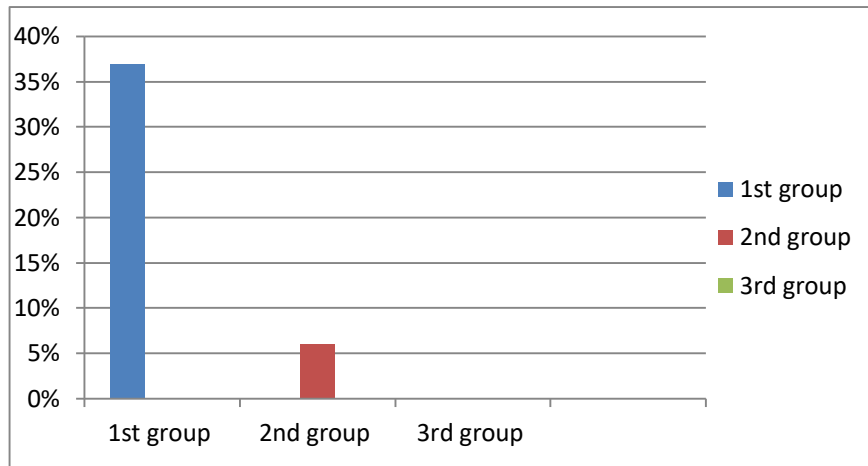


Figure (1) Graph shows the percentage of actual miscarriage for the groups of the study

Regarding to the ratio of GSD mean to crown-rump length (MGSD-CRL), results illustrated that during first – trimester gestational age Uni variants analyses showed that higher rates of early pregnancy failure among pregnant ladies with a m GSD-CRL < 5mm, comparing to the reference value m GSD-CRL of 5–9.9 mm (42.9 % vs. 15.6 %, $p < .0001$), as shown in Figure 2.

Oppositely, miscarriage cases were less prevalent in pregnant ladies with mGSD-CRL 10–14.9 mm (10% vs. 16%; $p < .007$) or ≥ 14.9 mm (7 % versus 16%; $p < .018$) comparing to the reference value of mGSD- CRL of 5–9.99mm

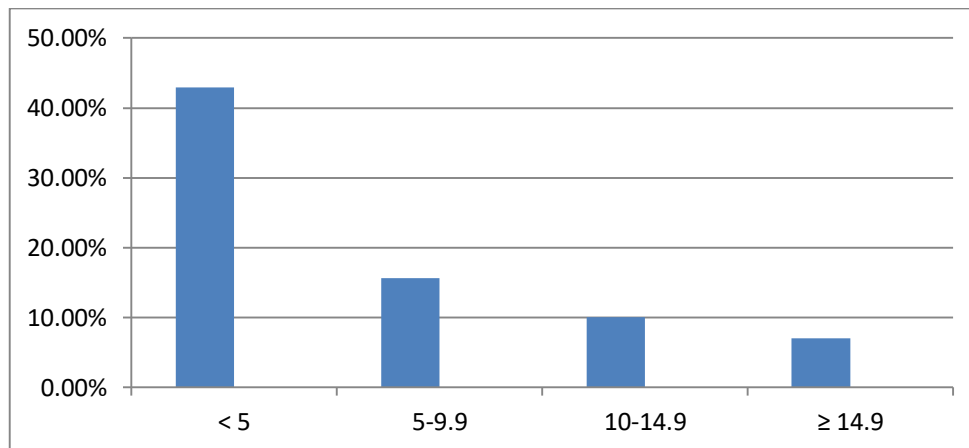


Figure (2) the percentage of number of miscarriage according to Measure of MGSD-CRL

Regarding the gestational sac diameter, there were a significant statistical difference between miscarriage and control groups, in which among the first group the no. of pregnant ladies that have mean gestational sac diameter of 24 +/- 16 mm with no embryo about 220 out of 453 (48.5 %), while in the second group that have gestational sac diameter of 24 +/- 16 mm with no embryo 276 out of 507 (54.4 %), while in the third group is (0 %). So that in this current study the use of mean gestational sac diameter with a lowest cutoff value of 16 mm among the first and second group with no fetal node give the false positive rate of about 4.8 %, while the mean gestational sac diameter more than 24 mm with no fetal node give 100 % specificity of the early pregnancy failure and miscarriage.

4. Discussion

In this study, there wasn't significant statistically differences among groups of the study regarding characteristics of pregnant women (maternal age, BMI, gestational age and parity). These results agrees with some another studies such as [13]. [14]. The mean age of pregnant ladies in the current study was 29.4 years (standard deviation SD = 5.76). In this current study illustrates that actual miscarriage was high among threatened abortion group ending with complete abortion in a percentage of 37% it means that 674 women from 1750 lost their fetus before 13 weeks of gestational age. Followed by second group who were expected to complete their pregnancy till 13 weeks of gestational age where it was (6%) i.e. till 13 weeks (105 women from 1750), while among the third group (healthy pregnancy cases) there was only two cases who loss their fetus (2/1750), thus these percentages insure the importance of ultrasound roles for the assessment and follow up of pregnancy & detects early failure.

Measurements of some indicators such as FHR, GSD, YSD, CRL, and MGSD-CRL could detect 89% of women that subsequently have positive miscarriage which ensure that US being a golden role in the detection of early miscarriage. Univariate analyses showed that higher rates of early pregnancy failure among pregnant ladies with a mean GSD-CRL ratio $< 5\text{mm}$ (42.9%) in the first group and the rate was less in the second group that had mean GSD-CRL ratio ≤ 14.9 (7%), thus these results in this current study Consistent with other studies [12], [15].

In this study there is important association between mean sac diameter, CRL and Fetal heart Rate. Among first group the no. of patient that have equal and $> 24\text{ mm}$ cut off sac diameter with fetal node of about CRL 6.95 ± 0.13 with no fetal heart rate 175 out of 453 (38.63 %). In the second group mean sac diameter above 24 mm with CRL $> 8\text{ mm}$ with no cardiac pulsation an about 175 out of 507 (34.51%)

The current study also indicated that abnormal GSD related to the fetal node and abnormal YSD were higher in actual miscarriage groups i.e. Women who aborted in (first and second group) than women who completed their pregnancy (third group), this result agrees with studies [18], [19] iation The cutoff value of FHR (109 bpm) can contributes in determining the cases ends with missed abortion specially for those that have history of bleeding and abdominal pain , , this can help to modify therapy given to both groups Because there is increase in FHR value that was between 109 -120 at 5th week of gestation by TVUS to 170 bpm at the 9th week of gestational age , copes with normal morphological advancement and growth of the fetal heart (20). Study cutoff value points to the occurrence of miscarriage with high degree among cases that showed low FHR value at 9th week of gestation and no any significant increase that reflects the weak cardiac development and eventual miscarriage. In about 3% of miscarriages the CRL measure assessment scan at early pregnancy was smaller than its measure among healthy cases. This indicated that the presence of an inverse relationship measure of CRL, GSD, and FHR implies the high definite possibility of early pregnancy failure.

5. Conclusion

Briefly early pregnancy failure and miscarge cutoff value can be defined as presence of pregnancy sac within the thickened decidual reaction and endometrial cavity with the absence of yolk sac , when the sac diameter measure an about $8\text{-}10\text{ mm}$ trans vaginally = 5 w and 20 mm and above = 7 w trans abdominally with absent visible fetal node , with mean sac diameter of $24\text{ mm} \pm 16\text{ mm}$ with absent fetal heart in an embryo that have CRL 6.95 ± 0.13 or the appearance of an empty sac sign with thickened chorionic reflections Using ultrasound machine to investigate and diagnosis early pregnancy failure in combination with quantitative beta human chorionic gonadotropin hormone level assessment and progression give definite powerful entity in diagnosis and management for the normal and abnormal pregnancy outcome, thus improve management and reduce miscarriage cases, as it can also predict actual miscarriage which

contributes to avoid their occurrence, also important in assessing the predisposing factor and searching for the cause, it is give the issues for the definite accurate pregnancy follow up interval of the patient suspected to have pregnancy failure. In such current study we depend on the following measures and parameters that are FHR, CRL, GSD, YAS, GSD-CRL RATIO and they get Specific and reliable results that consistent with many other studies, generally being good job to investigate using trans abdominal probe 3-5 MHZ as a valid and sensitive device to determine residual minute tissues and retained pieces of product of conception after actual miscarriage.

Manage miscarriage by using ultrasound indicators and parameters, could significantly decrease the number of early pregnancy failure, and improve pregnancy outcome based on the standards and measurements used.

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