Ultrasonographic Prediction of Early Miscarriages

Rajib Pal[1], Anwshka Kumari[2], Suman Das[3], Prabir Kumar Sengupta[4], Mrinal Kanti Ghosh[5]

[1]*Associate Professor, Department of Obstetrics & Gynecology, Deben Mahata Government Medical College, Purulia*
[2,4]*Junoir Resident, Professor & Head Department of Obstetrics & Gynecology, Burdwan Medical College, Burdwan.*
[3]*Senior Resident, Department of Community Medicine, Malda Medical College, Malda*
[5]*Professor & Head, Department of Radiodiagnosis, Burdwan Medical College, Burdwan.*
Corresponding Author: Dr. Rajib Pal

Abstract*:*
Background: *Spontaneous miscarriage is defined as an involuntary termination of pregnancy before 20th week of gestation or spontaneous expulsion of fetus below a fetal weight of 500 gm. Antenatal ultrasonography has been extremely useful in providing better understanding the etiology of first trimester spontaneous abortion and a basis for its clinical classification and management The aims and objective of this study is to identify abnormal ultrasound parameters and correlate the ultrasonic findings with the clinical outcomes.*
Materials and Methods: *The study included 100 pregnant women attending outpatient department or also admitted in inpatient at 5-12 weeks of gestation fulfilling inclusion and exclusion criteria.*
Results: *The abortion rate in our study was 34%. Out of that 18% abortion occurred at< 8 weeks and 16% occurred at 8-12 weeks of gestation. In this study, 30 patients had threatened abortion out of which 23(76 %) had abnormal TVS parameters. In our study 44 patients had abnormal findings in TVS, of which 32 (72.7%) had EPF.*
Conclusion: *This study emphasizes the role of ultrasound in prediction of early pregnancy failure in first trimester. It can also help in taking decision whether to continue, abort or follow conservative management in early pregnancy.*
Key Word: *Early pregnancy failure, Spontaneous abortion, First trimester ultrasonography.*

I. Introduction

Antenatal ultrasonography (USG) has revolutionized the management of early pregnancy failure[1].Spontaneous miscarriage is involuntary termination of pregnancy before 20th week of gestation or spontaneous expulsion of fetus below fetal weight of 500 grams[2]. Approximately 12-24% of all pregnancies suffer miscarriages and 80% of all cases of pregnancy loss occur within the first trimester and most of the early miscarriages are caused by chromosomal abnormalities, and the risk of which increases with maternal age[3]. Overall, autosomal trisomies are the most common abnormality (usually involving chromosomes 13-16, 21, or 22), followed by monosomy X (45, X) and polyploidies[3]. Common symptoms of early pregnancy loss like vaginal bleeding and abdominal cramping are also common in normal gestation, ectopic pregnancy, and molar pregnancy[4].Before initiating treatment, it is important to distinguish early pregnancy loss from other early pregnancy complications. Treatment of an early pregnancy loss before confirmed diagnosis can have detrimental consequences, including interruption of a normal pregnancy, pregnancy complications or birth defects. Successful blastocyst implantation requires precise synchronization between the embryo and the uterine environment. New evidence which indicates that failure of placentation is associated with an imbalance in reactive oxygen species which affects placental development and function and may therefore have an influence on both the fetus and the mother.

The advent of high-resolution transvaginal ultrasound (TVS) has revolutionized our understanding of the pathophysiology and the management of early pregnancy failure[5].Being non-invasive, safe and without hazards of radiation, it has gained wide acceptability, as an integral part of basic investigative procedures. In particular, Transvaginal ultrasonography (TVS), with its ability to provide accurate images of the early gestational sac, has provided important clues to the epidemiology and pathophysiology of early pregnancy failure[5].Improved imaging is achieved with higher frequency transducers that provide better resolution but with less penetration. TVS allows the probe to be placed closer to the uterus and therefore higher frequency probes

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can be used[6]. These advantages result in improved spatial resolution and near field focussing compared with transabdominal ultrasonography (TAS) [6]. Consequently, the findings of an intrauterine pregnancy can be seen at an earlier gestational age and a lower level of human chorionic gonadotropin (HCG) using TVS[6]. Ultrasonography in first trimester should include a thorough evaluation of the uterus and adnexa for the presence of gestational sac[7]. If a gestational sac is seen, the presence of yolk sac or embryo should be noted[7]. The gestational age should be confirmed by the length of the embryo[7]. If an embryo is not visualized, then the mean sac diameter should be used as a measure of gestational age[7]. The presence or absence of cardiac activity should be reported[7]. TVS findings can be conclusive of early pregnancy failure (EPF) or can be suggestive. If the findings are suggestive of EPF, then the patient should be followed up after 11-14 days and meanwhile rest and symptomatic management is to be done. Based on further findings and proper counselling of couple, further management should be planned. This study is aimed to assess the accuracy of first trimester USG markers as mean gestational sac diameter MGSD), Yolk sac diameter (YS), crown rump length (CRL), MGSD-CRL, embryonic heart rate (EHR), retro placental or perisac collections predict the risk of early pregnancy failure (EPF). This study also aims to identify abnormal ultrasound parameters and correlate the ultrasound findings with the clinical outcomes.

II.   Material And Methods
This observational study was conducted in the Department of Obstetrics and Gynecology, Burdwan Medical College and Hospital, Burdwan, West Bengal for a period of one year from June 2018 to May 2019.
Study design: Prospective observational study
Study Location: This was a tertiary care teaching hospital based study done in Department of Obstetrics and Gynecology, Burdwan Medical College and Hospital, Burdwan, West Bengal.
Study Duration: June 2018 to May 2019
Sample Size: 100 patients
Sample size calculation: The sample size was estimated on the basis of a single proportion design. We assumed that the confidence interval of 10% and confidence level of 95%.
Subjects and selection methods: 100 Pregnant women attending antenatal clinic of Burdwan Medical College & Hospital at 5-12 weeks of gestation fulfilling inclusion and exclusion criteria were subjected to transvaginal ultrasound examination after proper informed consent and normal embryonic development and signs of early pregnancy failure was identified. All the patients were followed up to 20 weeks to see the outcome.
Inclusion criteria: All age, any parity, single intrauterine pregnancy, pregnant women with estimated gestational age of 5-12 weeks, subjects with accurate last menstrual period (LMP) with previous history of regular cycle and any subject of threatened abortion.
Exclusion criteria: Patient refusal, multiple pregnancies, known fetal or uterine abnormalities, chronic diseases in pregnant women like heart disease, diabetes, chronic hypertension, renal diseases, renal diseases, bronchial asthma etc.

Procedure Methodology:
Selected patients were subjected to transvaginal ultrasound examination using USG Machine (Philips HD7) with transvaginal probe of frequency 5-7.5 MHz. Their normal embryonic development and signs of early pregnancy failure were identified. All the cases were subjected to detailed history, general, physical, and systemic as well as obstetrical examination at the time of their antenatal visit and at the time of admission. Patient was asked to void her urine before the procedure and one female attendant was allowed with patient. The patient was placed in lithotomy position. The disinfected endovaginal probe was covered with a sterile condom lubricated with gel before insertion. The transducer was inserted approximately 6-8 cm into the vagina.

Gestational age was calculated by modified Naegele's rule. LMP derived gestational age was compared with ultrasound derived gestational age using CRL and marked discrepancy of one or more weeks led to exclusion of participants from the study. MGSD was assessed by averaging three dimensions (longitudinal, anteroposterior and transverse). Sac was measured from inside of the sac to the inside of the decidual reaction; excluding the latter in the measurement. Yolk Sac was determined by placing calipers on the inner limits of the longer diameter. Size of the sac, shape, echogenicity of the rim and centre of sac, its number and degenerative changes such as calcification was evaluated. YS having diameter between 3-6 mm, rounded shapes, absence of degenerative changes, presence of echogenic rim and hypoechoic centre was considered normal. Any deviation from above parameters was considered abnormal. CRL was measured in sagittal plane of the embryo avoiding inclusion of YS. CRL >4 mm in TVS who fail to demonstrate heart beat were judged as non-viable and CRL <4 mm without a visible heart beat were asked to return for repeat USG after 7 days. EHR of less than 100 beats per minute at 8 weeks or earlier was classified as slow. Presences of any perisac collection or hemorrhages in or around sac or placenta were noted.

All the participants were followed up to 20 weeks to see whether there was any spontaneous loss or any other early pregnancy complication or if the pregnancy is continued normally as suggested by previous TVS findings. All USG was done and reviewed by a single radiologist to reduce the observational bias. Outcome of pregnancy was defined as adverse if there was spontaneous abortion at 20 weeks of gestation. EPF is said when abortion occurred at ≤12 weeks and late when abortion occurred after 12 weeks of gestation.

Statistical analysis: Statistical significance of the result was evaluated by
➢ Percentage
➢ Predictive value
➢ Comparison of groups was done by using Pearson's Chi Square test for Independence of Attributes/ Fisher's Exact Test as appropriate.
The statistical software SPSS version 20 has been used for the analysis. A value of $p<0.05$ was considered statistically significant.

III. Result

Results of studies are depicted in following tables. Categorical variables are expressed as number
Distribution of pregnant women by age, parity and outcome of pregnancy is depicted in Table 1. Table 2 and 3 shows the distribution of each parameter and their predictive value. Table 4 and 5 shows same parameters and their predictive value in women with threatened abortion. Chi-square test was applied to find out any association between pregnancy outcome and early pregnancy parameters.

Table 1: Distribution of study subjects according to certain characteristics

Certain characteristics	Frequency	Percent
Age in years among all pregnant women (n=100)		
≤ 20	15	15.0
21-25	23	23.0
26-30	39	39.0
> 30	23	23.0
Parity among all pregnant women (n=100)		
P_{0+0}	49	49.0
P_{0+1} to P_{0+5}	22	22.0
P_{1+0} to P_{2+0}	21	21.0
P_{3+0}	8	8.0
Age among pregnant women with outcome as abortion (n=34)		
≤ 20	4	11.7
21-25	8	23.5
26-30	11	32.4
> 30	11	32.4
Parity among pregnant women with outcome as abortion (n=34)		
P_{0+0}	14	41.2
P_{0+1} to P_{0+5}	11	32.4
P_{1+0} to P_{2+0}	8	23.5
P_{3+0}	1	2.9
Period of gestation in weeks among pregnant women with outcome as abortion (n=34)		
< 8	18	52.9
8 to 12	16	47.1

Table 2: Distribution of abnormal parameters in TVS among all pregnant women (n=100)

Abnormal parameters	Frequency	Percent
MSD >25 with No Embryo	14	14.0
YSD >6 mm	4	4.0
Abnormal Morphology of YS	3	3.0
CRL >4 mm with No Cardiac Activity	8	8.0
SCH or PGH	4	4.0
EHR <100 bpm	3	3.0

Table 3: Inter-relationship of different TVS parameters and prediction value (n=34)

TVS Parameters	TP	TN	FP	FN	PPV	NPV	Diagnostic accuracy
MSD >25 mm and Embryo Absent	14	50	0	13	100.00	79.37	83.12
CRL >4 mm and Cardiac Activity Absent	6	60	2	13	75.00	82.19	81.48
YSD >6 mm	4	66	0	30	100.00	68.75	70.00
EHR ≤100 min	2	57	1	11	66.67	83.82	83.10

SCH or PGH presence	2	64	2	32	50.00	66.67	66.00
Abnormal USG : Threatened Abortion	19	7	4	0	82.61	100.00	86.67
Predictive	13	12	0	19	100.00	38.71	56.82
Abnormal USG	32	54	12	2	72.73	96.43	86.00

Table 4: Association between TVS report and pregnancy outcome in threatened abortion (n=30)*

USG report	Live [No(%)]	Dead [No(%)]	p value#
Abnormal	4 (17.4)	19 (82.6)	**<0.001**
Normal	7 (100.0)	0 (0.0)	

Note: * Fisher's Exact Test# p value <0.05 has been considered significant

Table 5: Inter-relationship between different abnormal parameters in threatened abortion and prediction value

TVS Parameters	TP	TN	FP	FN	PPV	NPV	Diagnostic accuracy
MSD >25 mm and Embryo Absent	8	4	0	11	100.00	26.67	52.17
CRL >4 mm and Cardiac Activity Absent	4	3	1	15	80.00	16.67	30.43
Abnormal Yolk Sac	5	4	0	14	100.00	22.22	39.13
SCH or PGH presence	2	2	2	17	50.00	10.53	17.39
Other Anomaly	0	3	1	19	0.00	13.64	13.04

Table 6: Pregnancy Outcome in the study population

Outcome	Frequency	Percent
N	66	66.0
EPF/LPF	34	34.0
Total	100	100.0

Table 7: Relationship of pregnancy outcome with symptoms (n=100)*

		Symptoms			
		Absent [No (%)]	Present [No (%)]	p Value	Significance
Outcome	N	55(83.3)	11(16.7)	**<0.001**	Significant
	EPF/LPF	15(44.1)	19(55.9)		
Total		70(70.0)	30(30.0)		

Note: * Chi-square test

IV.   Discussion

Spontaneous abortion accounts for approximately 17-22% of pregnancies and approximately 12-15% of recognized pregnancies undergo miscarriage[8, 9]. In our study majority of the individuals were in age group of 26-30 years whereas 23% of the individuals were found to be above 30 years of age. Forty-nine percent of patients were primigravida and rests were parous. 34% of pregnancies suffered spontaneous abortion, out of which 11% were more than 30 years of age. There is an increasing tendency of early miscarriage in nullipara (41.17%) also among those who had previous history of one or more miscarriage (32.35%).

In our study majority of abortion occurred less than 8 weeks of gestation. Increasing maternal age was found to be a risk factor for miscarriage[10]. Majority of abortions (39%) occurred among mothers who were aged between 26 -30 years. Incidence of Abnormal Parameters in TVS and inter-relationship of different TVS parameters were showed in Table 2 and Table 3. The findings of our study demonstrate that prediction of subsequent miscarriage in singleton pregnancies presenting with a live embryo is provided by a combination of maternal factors, including age, parity, history of vaginal bleeding and ultrasound measurements of MGSD, YS, CRL, EHR, SCH or PGH. The first reliable gray-scale evidence of an IUP is visualization of a small (1-2 mm fluid collection surrounded by an echogenic rim) gestational sac within the thickened decidua. Gestational sac (GS) is the first definitive landmark of pregnancy which is consistently visible by 5 weeks of gestation, even with TAS, GS should be at least 10 mm larger than the CRL[11].The embryo can first be visualized when the

MSD measures between 5-12mm which corresponds to a gestational age of 5-6 weeks. Embryo should be present where MSD is >25 mm. Approximately 94% of EPF occur in MSD >25 mm without an embryo[12].In our study 14%miscarriageshad MSD>25 mm without an embryo. Hence there was a positive correlation with early pregnancy failure with MSD>25 mm with no embryo. Yolk sac should be seen by 7 weeks of gestation and it disappears by 10 weeks. Abnormal size and calcification of YS leads to spontaneous miscarriage[13]. Our study showed relationship between yolk sac diameter (YSD) and pregnancy outcome. Larger yolk sac is associated with poor pregnancy outcome. Our study showed 4% of EPF occurred with yolk sac> 6 mm. Fetal cardiac activity is the earliest proof of a viable pregnancy[14].The single most important feature for confirmation of embryonic and fetal life is identification of cardiac activity. Using TVS, cardiac activity is typically seen by the time an embryo is 2 mm in size, and is almost always seen by 5-mm CRL. The cut-off CRL for detecting cardiac activity by TVS is 4 mm and by TAS is 9 mm[12, 15]. Different studies documented that a slow EHR at 7-9 weeks gestation is associated with high rate of first trimester pregnancy demise[16]. In our study we found out of 3 who had EHR < 100, 2 were aborted. So, we firmly consider evaluation of EHR as soon as possible in all pregnancies because regardless of the presence of symptoms, it is a consistent parameter in the outcome of pregnancy. Any collection or hemorrhage around gestational sac has been associated with poor pregnancy outcome and same findings were seen in our study. The association of subchorionic hematomas with early pregnancy failure is variable, but most studies support that worse outcomes are seen in "large" hematomas extending 50% or more of the circumference of the gestational sac and in hematomas diagnosed earlier in the first trimester. SCH or PGH were found in 4 women in our study out of which 2 miscarried giving a positive predictive value of 50% but diagnostic accuracy is only 17.39 in our study because mere presence of SCH or PGH doesn't correlate with pregnancy outcome but its size, location, history of vaginal bleeding, maternal age and underlying disorders[17]. In cases of threatened abortions, abnormal USG parameters have a good correlation with adverse pregnancy outcome. In this study, 30 patients had threatened abortion out of which 23(76 %) had abnormal TVS parameters of which 19 (82.6%) patients suffer miscarriage. In cases of threatened abortion in our study as shown in table 5, 8 out of 30 threatened pregnancies had MGSD>25mm with no embryo and all suffered EPF[18].4 out 5 pregnancies with CRL>4mm without cardiac activity miscarried[19]. All 5 pregnancies with abnormal yolk sac in TVS had abortion[20]. Out of total 4 patients with SGH 2 had EPF and 2 progress normally further[21]. Abnormal TVS parameters can be used as a good predictor for EPF. In our study 44 patients had abnormal findings in TVS, of which 32 (72.7%) had EPF. Our study also shows positive impact of conservative management. Out of 31 abnormal worrisome/suspicious findings, 12 pregnancies were found to be normal in subsequent TVS after 1 week and absolutely normal till 20 weeks. Table 6 showed Pregnancy Outcome in the study population. In our study out of hundred 34 had pregnancy failure. In Table 7 there was relationship between symptoms presented by patient and pregnancy outcome. Here also p value is <0.001 which is statistically significant. It is therefore clear that there are increased chances of poor pregnancy outcome in symptomatic patients. Hence, we recommend proper evaluation of pregnancy by ultrasonography and conservative management followed by a USG after 7-14 days instead of terminating the pregnancy only based on symptoms.

V.   Conclusion

Pregnancy is a dynamic state which requires continuous monitoring and particularly first trimester is very important as 80% pregnancy loss occurs during this period. Only clinical examination is not sufficient and need regular sonological assessment. First trimester ultrasonography before 12 weeks of gestation can differentiate between viable pregnancy and ongoing abnormal pregnancy. Its use in first trimester can enable to study normal development of embryo. Transvaginal Sonography (TVS) with high resolution is superior to Transabdominal Sonography (TAS) in first trimester and any abnormal parameters can be diagnosed approximately 1 week before TAS. The transducer probe of TVS being placed close to pelvic organs gives superior information. TVS can help in early diagnosis of EPF in asymptomatic patients. Timely appearance of parameters like Gestational Sac, CRL, EHR, Yolk Sac and evaluation of retroplacental and perisac area can be used to predict pregnancy outcome. It can also help in taking decision whether to continue, abort or follow conservative management. In addition it also helps clinician to give assurance to mother confidently when every parameters is normal. It can avoid continuation of abnormal pregnancy and reduce the number of unnecessary termination of pregnancy in patients with symptoms of EPF and can diagnose EPF in asymptomatic patients.

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