Value of Transvaginal Sonography in Antenatal Management of Ectopic Pregnancy

[1]Saulat Sarfaraz, [1]KhadijaArif, [1]Abdullah Hussain, [1]Shoaib Iftikhar, [2]Muhammad Ikram, [2]Amna Javed
[1]*Department of Radiology, Shaikh Zayed Hospital, Lahore.*
[2]*Department of Obstetrics and Gynecology, Shaikh Zayed Hospital, Lahore.*

ABSTRACT

Introduction: Ectopic pregnancy is a high-risk condition which can lead to mortality and morbidity if not diagnosed and managed promptly. Transvaginal Sonography (TVS) has a major role in diagnosing ectopic pregnancy. Certain signs if identified accurately on TVS examination can help predict or exclude ectopic pregnancy precisely.
Aims & Objectives: To determine the diagnostic accuracy of TVS examination in detecting ectopic pregnancy. It also aims to highlight the need of TVS examination in routine antenatal care during early pregnancy.
Place and duration of study: The study was carried out at Shaikh Zayed Hospital, Lahore with the collaborated effort of Radiology Department and Department of Gynae & Obs. It was conducted over the period of three years from 1-1-2017 to 31-12-2019.
Material & Methods: In this observational study 160 women with suspected ectopic pregnancy were evaluated with β -HCG levels and TVS examinations. Per-operative findings were taken as the gold standard for patients who underwent laparoscopy/laparotomy, and a trend of β-HCG for patients with expectant/medical managements per RCOG guidelines. Statistical analyses were applied to find out diagnostic accuracy of TVS findings. The prospective study pattern with close follow-ups and a managing protocol according to the guidelines were required to reinforce the results.
Results: The sensitivity of TVS in diagnosing Ectopic Pregnancies (EPs) in clinically suspected patients were found to be 92.5%, specificity 84.62%, positive predictive value 94.91%, negative predictive value 78.57% and accuracy rate was calculated as 90.62%. Most frequent signs present were empty uterine cavity, blob sign and embryo with or without cardiac activity.
Conclusion: TVS examination is quite effective in predicting and excluding ectopic pregnancy in early gestation. Majority of patients with ectopic pregnancy had surgery as part of their management.

Keywords: Ectopic pregnancy, transvaginal ultrasound, pregnancy of unknown location, β-HCG

INTRODUCTION

Ectopic pregnancy (EP) is characterized by the implantation of the zygote outside the uterus.[1] it contributes to approximately 10-15% of maternal mortality in the first trimester worldwide.[2] In our country, the reported incidence is 1:129 (0.8%).[3]
Mainly in developing countries, it is a significant cause of maternal morbidity as well as mortality, where the majority of patients present late with rupture leading to hemodynamic compromise.[4] Symptoms such as vaginal bleeding or abdominal pain can occur in 25-30% of viable pregnancies. Recent studies suggest that morbidity and mortality caused by ectopic pregnancy account for 1% to 2% of all pregnancies.[5]
The etiological evidence of ectopic pregnancy is still not clear as multiple risk factors are associated with it.[6] Diagnosing a pregnancy of an unknown location (PUL) necessitates multiple hospital visits for different blood tests, ultrasounds, and possibly needs surgical procedures before a definitive diagnosis can be made.[7]
Transvaginal ultrasonography (TVS) is considered to be the imaging modality of choice for diagnosing ectopic pregnancy.[8] The majority of studies done on the accuracy of TVS shows the sensitivity and specificity of greater than 80% in determining ectopic pregnancy.[9,10] few specific TVS findings like bagel and blob sign show higher positive predictive value.[11]
Another study appraised the accuracy of TVS for detecting ectopic pregnancies (EPs) in women undergoing surgery for suspected ectopic pregnancy and recorded its sensitivity to be 90.9% and specificity of 99.9%.[12] Contrary to the above, a recent study[13] recorded that the sensitivity of TVS in diagnosing ectopic pregnancy was 73.9% and specificity of 99.9%, a positive predictive value

(PPV) of 96.7%, and a negative predictive value (NPV) of 99.4%. These findings significantly differ and need another study to determine the diagnostic accuracy of TVS for the detection of ectopic pregnancy. The rationale of the study is to clarify the ambiguity found in the above studies and records the findings in our local population so that gynecologists and radiologists may have updated knowledge for using this diagnostic modality for the detection of ectopic pregnancy.

MATERIAL AND METHODS

The observational study was conducted over the period of three years dated from 01-01-2017 to 31-12-2019 after approval from the Institutional Review Board at Shaikh Zayed Hospital, Lahore, Pakistan, with the collaborated effort of Radiology Department and Department of Gynae & Obs.
The data was collected prospectively with close follow-ups and a managing protocol according to the guidelines[14] was observed to validate the statistics.
The sample size was estimated using World Health Organisation (WHO) software. By using a formula of estimating a population proportion with expected sensitivity=73.9%[13], expected specificity=99.9%,[13] expected prevalence=33%, and confidence level=95%, with 10% margin of error for sensitivity and 5% margin of error for specificity, the sample size was set at 160. Subjects within the reproductive age group of 18 to 40 years were enrolled in the study using convenient sampling techniques. Females who assured to give a response on follow-ups were included in study. Informed consent was taken from them. Women unwilling to participate and who lost in follow-up were excluded from the study. The gestational age of these patients was from 1 to 12 weeks by LMP.
Females presented to the Accident and Emergency department with the signs and symptoms of suspected ectopic pregnancy were initially evaluated by gynecologist and transabdominal ultrasound examination was performed. Following this, TVS scan was done by a consultant radiologist to detect ectopic pregnancy. Women with positive findings were followed and the data was recorded in a preformed data sheet without including the personal details of patients. Laparotomy findings observed by a consultant gynecologist were kept as gold standard of confirmation for patients having surgery. Patient with medical/expectant management were monitored by falling trend of B-HCG 48 hourly and TVS re-scan to confirm complete resolution of

radiological findings. The management was carried out in concordance with RCOG guidelines.[14]
The sonography findings appreciated in these patients were following grey-scale appearances.[13] Empty endometrial cavity; discordant mass/blob sign in adnexa; bagel sign; a viable or non-viable extra-uterine pregnancy.
Data was analyzed by using SPSS version 10. Descriptive statistics were used to calculate the mean and standard deviation for quantitative variables. Frequencies and percentages were calculated for parity, TVS features and presence/absence of ectopic pregnancy on the final clinical diagnosis made by the consultant gynecologist. A 2x2 table was drawn and the diagnostic accuracy of TVS was recorded by calculating specificity, sensitivity, positive predictive value, and negative predictive value.

RESULTS

Over the period of three years, the total of 160 cases presented in Emergency Department were evaluated to determine the diagnostic accuracy of transvaginal ultrasonography (TVS) for detecting ectopic pregnancies (EPs) in clinically suspected patients. The mean age of patients was 29.6± 4.7 years with 51.8% (n=83) below 30 years while 48.1% (n=77) were between 31-40 years of age. The mean gestational age at presentation was 46 ± 5 days. Majority of patients presented with symptoms related to ectopic pregnancy while few also had non-specific complaints like fever, nausea, vomiting, diarrhea, malaise and anorexia. The frequencies of different symptoms at the time of presentation are mentioned in Table-1.

Clinical Features	Frequency (%)
Amenorrhea	111 (69)
Lower abdominal pain	88 (55)
Abnormal vaginal bleed	101(63)
Syncope	55(34)
Shoulder tip pain	20(12)
Non-specific symptoms	11 (6.8)

Table-1: Frequencies of clinical symptoms at the time of presentation.

The ectopic pregnancy on final clinical diagnosis was recorded in 75.6% (n=121) cases while 24.3% (n=39) had no findings of the morbidity. Ectopic pregnancy was suggested by TVS in 118 (73.7%) patients at presentation. The sonographic examination of all these women confirmed the location of the gestational sac and none of them were labeled as Pregnancy of Unknown Location.

Of these 118 cases, 112 were further confirmed to be true positive. 25 of 33 true negative cases had intra-uterine gestational sac while the remaining 8 cases had no intra/extra-uterine gestational sac.

Among these 121 women with definitive ectopic pregnancy, 36 (29.7%) patients who remained stable were diagnosed as un-ruptured ectopic pregnancy on TVS initially and were successfully managed by expectant/medical treatment as per RCOG guidelines.[14] 60 (49.6%) patients had laparotomy as initial management, out of which 25 patients were diagnosed as ruptured ectopic pregnancy on TVS demonstrating that the diagnostic accuracy of TVS for ruptured ectopic pregnancy was 100%. 25 (20.7%) patients who were stable at presentation and were being managed conservatively initially had laparotomy after developing symptoms of acute abdomen. Table-2 summarizes management protocol of patients with confirm ectopic pregnancy.

Management	Frequency (%)
Expectant/Medical	36(29.7%)
Expectant/Medical followed by surgery	25(20.7%)
Surgery	60(49.6%)

Table-2: Percentage frequency of patient management with confirmed ectopic pregnancy

The sensitivity of TVS diagnosing Ectopic Pregnancies (EPs) in clinically suspected patients were found to be 92.5%, specificity 84.62%, positive predictive value 94.91%, negative predictive value 78.57% and accuracy rate was calculated as 90.62%. (Table-3)

TVS Findings	Ectopic Pregnancy		Total
	Disease (positive)	No Disease (negative)	
Positive	True positive **(a)** 112	False Positive **(b)** 6	118
Negative	False negative **(c)** 9	True negative **(d)** 33	42
Total	121	39	

Table-3: 2×2 table for the findings of the TVS performed to diagnose ectopic pregnancy.

Sensitivity = a / (a + c) x 100 = 92.56%
Specificity = d / (d + b) x 100 = 84.62%
Positive predictive value = a / (a + b) x 100 = 94.91%
Negative predictive value = d / (d + c) x 100 = 78.57%
Accuracy rate = a + d / (a + d + b + c) x 100 = 90.62%

The signs appreciated on TVS for ectopic pregnancy included: empty endometrial cavity, the ring of fire sign, hemoperitoneum in the pouch of Douglas and hepato-renal recess, blob sign or non-homogeneous mass, bagel sign, embryo with cardiac activity, an embryo without cardiac activity, hyperechoic ring around the gestational sac. The frequencies of these features are mentioned in Table-4.

TVS Features	Frequency (%)
Empty endometrial cavity	135 (84%)
Hemoperitoneum	45(28%)
Ring of fire	59(37%)
Blob sign	109 (92%)
Embryo with cardiac activity	35 (22%)
Embryo without cardiac activity	63 (39%)
Heterotopic Pregnancy	00

Table-4: Frequencies of TVS Features seen in ectopic pregnancy.

DISCUSSION

Ectopic pregnancy is considered to be a high-risk condition that contributes to maternal mortality significantly. Some of these cases might be missed on initial evaluation, and it remains the most frequent cause of threatening maternal life. The spontaneous resolution of an ectopic pregnancy might occur, but patients are still at an increased risk of fallopian tube rupture and fatal hemorrhage.[15] Hence, early diagnosis of ectopic pregnancy is imperative to prevent major complications and sequelae as most of the patients present to emergency department with critical symptoms.

The confirmed ectopic pregnancies were managed according to the guidelines: (i) Expectant /Medical management included close follow-up and monitoring of the patient initially after admission, on daily basis, with monitoring of worsening signs and symptoms and then followed up until serum B-HCG levels became less than 20IU/l according to guidelines. The need for surgical treatment were also kept under consideration (n=36); (ii) Expectant/Medical followed by surgical management (n=25); (iii) Surgical – the gestational sac was surgically removed along with the affected fallopian tube where needed (n=60).[14]

The patients presented usually with typical symptoms. In our study, the most common presenting complaint was secondary amenorrhea (69%) followed by abnormal vaginal bleeding (63%). Shoulder tip pain (12%) was found most infrequently in the patients along with some non-specific symptoms. On imaging, most ectopic pregnancies are found in the fallopian tube.[15] Other sites include ovarian and abdominal ectopic pregnancies. The absence of intra- or extra-uterine

pregnancy on TVS is labeled as pregnancy of an unknown location (PUL).[16]

Empty uterus with adnexal mass on TAS with a positive UPT or raised β-HCG level are strongly predictive of ectopic pregnancy. Trans-abdominal ultrasound (TAS) gave indeterminate findings like thickened endometrium with cystic area in adnexa as shown in Fig-1.

Fig-1: Transverse transabdominal ultrasound image showing a cystic area in right adnexa (arrow) in patient with lower back pain suspicious for ectopic pregnancy.

The patients with inconclusive pelvic findings on TAS mandated a subsequent TVS for confirmation of ectopic pregnancy. The most frequent TVS features were empty endometrial cavity, blob sign and ring of fire sign. These findings are shown in Fig-2 and Fig-3.
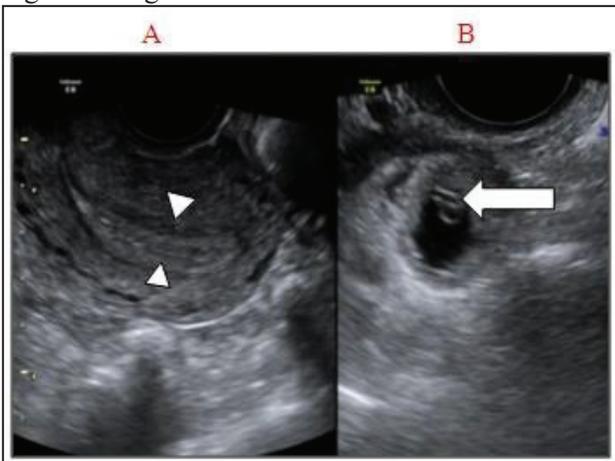

Fig-2: Sagittal transvaginal ultrasound image of the same patient showing thickened endometrium (between the arrowheads), however no intrauterine gestational sac was seen (A). Axial image of the right adnexa showed gestational sac with fetal pole (arrow), confirming the ectopic pregnancy (B).
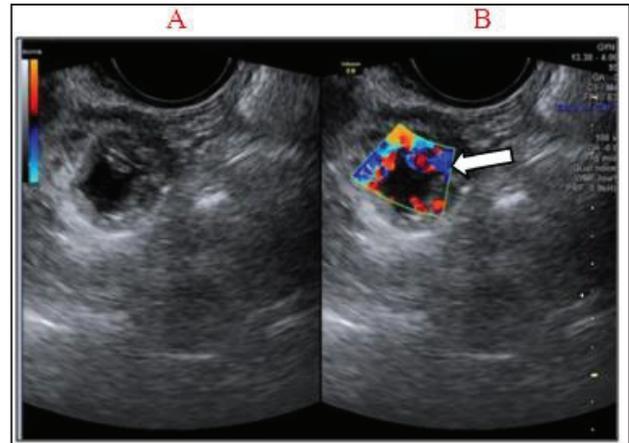

Fig-3: Axial transvaginal ultrasound images of right adnexa on grey scale (A) and color doppler (B). Cystic area in the adnexa was suspicious for ectopic pregnancy, color doppler showed a peripheral rim of blood flow (arrow), suggestive of ectopic pregnancy. This peripheral rim is also known as "ring of fire" sign.

The current study was planned to clarify the ambiguity found in studies regarding the diagnostic accuracy of TVS and record the findings in our population so that gynecologists and radiologists may have updated knowledge for using this diagnostic modality for the detection of ectopic pregnancy. Diagnostic accuracy of Transvaginal Ultrasonography (TVS) for the detection of Ectopic Pregnancies (EPs) as 92.56% sensitivity, 84.62% specificity, 94.91% positive predictive value, 78.57% negative predictive value, and accuracy rate was calculated as 90.62%. The significant accuracy rate is primarily attributed to adequate availability of better ultrasound machines and enormous experience of radiology consultants.

The results of our study are congruent with a previous study[12] that evaluated the accuracy of transvaginal ultrasonography (TVS) for detecting ectopic pregnancies (EPs) in women undergoing surgery for suspected ectopic pregnancy and recorded its sensitivity to be 90.9% and specificity of 99.9%.

Contrary to the above, a recent study[13] recorded that the sensitivity of the TVS in diagnosing ectopic pregnancy was 73.9% with a specificity of 99.9%, a positive predictive value (PPV) of 96.7%, and a negative predictive value (NPV) of 99.4%. These findings significantly differed from our study and the above study as well.

Condous Get. Al, reported most frequent TVS signs present in their data for ectopic pregnancy are blob sign (57%), embryo cardiac activity (13.2%), hyperechoic ring in adnexa (20.4%) with two heterotopic pregnancies. While the most common signs in our study were empty endometrial cavity

(84%), blob sign (92%), and absent embryo cardiac activity (39%). No heterotopic pregnancy was found in our study.

The statistic in our data shows the higher number of patients (70.3%) presenting to emergency department with ectopic pregnancy ultimately had surgery as part of their management in our setting. This was mainly due to either late presentation of patient with increased sac size or features of ruptured ectopic pregnancy. The diagnostic accuracy of TVS is higher so it is recommended that scan should be considered as a part of routine antenatal care in early pregnancy for timely diagnosis to prevent from comorbidities of surgery and ruptured ectopic pregnancy. TVS as a screening tool is considered in some studies[17] for high-risk patients only but it has not been suggested for each pregnancy before.

The strengths of our study lie in prospective pattern with regular follow-ups. The patients were followed with B-HCG levels and transvaginal rescan after achieving stable levels, until the resolution of ectopic pregnancy. We reviewed all identical cases with similar managing protocols according to the guidelines.[14] Limitations included lack of data collections for normal pregnancies to calculate incidence rates of ectopic pregnancies. We also did not discuss the risk factors and ectopic gestations in future pregnancies in affected females.

CONCLUSION

We conclude that the results of single transvaginal ultrasonography (TVS) for detecting ectopic pregnancies (EPs) in clinically suspected patients are significantly effective. Not only it is reasonably accurate in diagnosing ectopic pregnancy, but also it can assure that the pregnancy is intra-uterine. Due to this quality of TVS, it can become a part of antenatal care as a screening test for ectopic pregnancy in early gestation.

REFERENCES

1. Shabab U, Hashmi HA. Different Pattern of Presentation of Ectopic Pregnancy and its Management.J Surg Pak (Int) 2013; 18:37:40.
2. Karadağ C, Çalışkan E. Ectopic Pregnancy Risk with Assisted Reproductive Technology. Current Obstetrics and Gynecology Reports. 2020 Sep; 9(3):153-7.
3. Islam A, Fawad A, Shah AA, Jadoon H, Sarwar I. Analysis of two years cases of ectopic pregnancy. Journal of Ayub Medical College Abbottabad. 2017 Jan 25; 29(1):65-7.
4. PantiA, I kechukwu N E, Lukman O O, Yakubu A, Egondu S C, TankoBA.Ectopic pregnancy at UsmanuDanfodiyo University Teaching Hospital Sokoto:a ten year review.Ann Niger Med.2012;6(2):87-91
5. Brady, Paula C.MD New Evidence to Guide Ectopic Pregnancy Diagnosis and Management, Obsterical and Gynaecological Survey; October 2017-Volume 72-Isuue 10:618-625
6. Lawani O L, Anozie O B, Ezeonu P O. Ectopicpregnancy: a life-threat ening gynaecological emergency. IntJ Women Health. 2013; 5:515-21
7. Senapati S, Barnhart KT. Biomarkers for Ectopic Pregnancy and Pregnancy of Unknown Location. FertilSteril. 2013; 99(4):1107–16.
8. Berry J, Davey M, Hon MS, Behrens R. Optimising the diagnosis of ectopic pregnancy. Journal of Obstetrics and Gynaecology. 2016 May 18; 36(4):437-9.
9. Richardson A, Gallos I, Dobson S, Campbell BK. Accuracy of first-trimester ultrasound in diagnosis of tubal ectopic pregnancy in the absence of an obvious extrauterine embryo: systematic review and meta-analysis. Ultrasound Obstet Gynecol 2015; 47:28–37.
10. Nadim B, Infante F, Lu C, Sathasivam N, Condous G. Morphological ultrasound types known as 'blob' and 'bagel' signs should be reclassified from suggesting probable to indicating definite tubal ectopic pregnancy. Ultrasound Obstet Gynecol 2018; 51:543–9.
11. Shetty VH, Gowda S, Muralidhar L. Role of Ultrasonography in Diagnosis of Ectopic Pregnancy with Clinical Analysis and Management in Tertiary Care Hospital. J Obstet Gynecol India 2014;64:354–7
12. Phatak S, Shrivastav D, Marfani G, Daga S, Madurwar K, Samad S. Transvaginal sonography and elastography evaluation of ectopic pregnancy. Journal of Datta Meghe Institute of Medical Sciences University. 2019 Apr 1; 14(2):86.
13. Emma Kirk, Aris T. Papageorghiou, The diagnostic effectiveness of an initial transvaginal scan in detecting ectopic pregnancy, Human Reproduction, Volume 22, Issue 11, November 2007, Pages 2824–2828
14. Diagnosis and Management of Ectopic Pregnancy [Internet]. Obgyn.onlinelibrary.wiley.com. 2016 [cited 17 June 2021]. Available from: https://obgyn.onlinelibrary.wiley.com/doi/epdf/10. 1111/1471-0528.14189
15. Murray H, Baakdah H, Bardell T, Tulandi T. Diagnosis and treatment of ectopic pregnancy. Canadian Medical Association Journal. 2005; 173(8):905-912.
16. Carusi D. Pregnancy of unknown location: Evaluation and management. InSeminars in Perinatology 2019 Mar 1 (Vol. 43, No. 2, pp. 95-100). WB Saunders.

17. Cacciatore B. Early screening for ectopic pregnancy in high-risk symptom-free women. The Lancet. 1994; 343(8896):517-518.

The Authors:

Dr. Saulat Sarfraz
Head of Department,
Department of Radiology,
Shaikh Zayed Hospital, Lahore.

Dr. Khadija Arif
Trainee Resident,
Department of Radiology,
Shaikh Zayed Hospital, Lahore.

Dr. Abdullah Hussain
Trainee Resident,
Department of Radiology,
Shaikh Zayed Hospital, Lahore.

Dr. Shoaib Iftikhar
Trainee Resident,
Department of Radiology,
Shaikh Zayed Hospital, Lahore.

Dr. Muhammad Ikram
Head of Department,
Department of Obstetrics and Gynecology,
Shaikh Zayed Hospital, Lahore.

Dr. Amna Javed
Assistant Professor,
Department of Obstetrics and Gynecology,
Shaikh Zayed Hospital, Lahore.

Corresponding Author:

Dr. Saulat Sarfraz
Head of Department,
Department of Radiology,
Shaikh Zayed Hospital, Lahore,
Email: saulatsarfraz@gmail.com