

# DIAGNOSTIC ACCURACY OF TRANSVAGINAL ULTRASOUND IN EARLY (FIRST TRIMESTER) DETECTION OF ECTOPIC PREGNANCY AND TO EXCLUDE AN ALTERNATIVE DIAGNOSIS

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PJR July - September 2016; 26(3): 212-217

## ABSTRACT

**BACKGROUND:** Ectopic pregnancy is a high risk condition that occurs in 1.9% of reported pregnancies. In the United States, ectopic pregnancy is estimated to occur in 1-2% of all pregnancies and accounts for 3-4% of all pregnancy related deaths. In Pakistan, the reported incidence has been cited as 1:112 to 1:130. This study is a cross sectional prospective study of 469 patients clinically suspected for ectopic pregnancy. **OBJECTIVE:** The objective of this study was to determine Diagnostic accuracy of Transvaginal ultrasound in early (first trimester) detection of ectopic pregnancy and to exclude an alternative diagnosis. **MATERIALS & METHODS:** A total of 469 patients of reproductive age group (14-45 yrs) presenting with complains of amenorrhea with or without vaginal bleeding, lower abdominal pain and Serum Beta (hCG) to a range of 192-10,500 mIU/ml were included in the study. These patients underwent transvaginal ultrasonography followed by surgery. Histopathological correlation was also done. **RESULTS:** The results proved that Transvaginal ultrasound had a sensitivity of 93.98%, specificity of 95.07%, accuracy of 94.45%, PPV of 96.15% and NPV of 92.34% for the diagnosis of ectopic pregnancy. Most patients were between 25-35 yrs of age 53.30% and presented between 7-9 months of amenorrhea. Most common primary feature on ultrasound was complex adnexal mass 43.4% and fluid in pouch of Douglas was the secondary sign 80%. Multiple alternative diagnosis were also made like missed abortion, haemorrhagic/ complex/ endometriotic cyst, ovarian torsion, tubo-ovarian abscess, PID and uterine fibroid. Of these missed abortion was the most commonest 51.8%. **CONCLUSION:** Transvaginal ultrasonography performed in patients with suspected ectopic pregnancy improves patient care by early detection of ectopic pregnancy that will decrease the morbidity and mortality associated with it.

**Key words:** Ectopic pregnancy, transvaginal ultrasonography, Adnexal mass, vaginal bleeding.

## Background

Ectopic pregnancy is a high risk condition that occurs in 1.9% of reported pregnancies.<sup>1</sup> In the United States, ectopic pregnancy is estimated to occur in 1-2% of all pregnancies and accounts for 3-4% of all pregnancy related deaths.<sup>2</sup> Ectopic pregnancy presents a major health problem for women of childbearing age. Without timely diagnosis and treatment, ectopic pregnancy can become a life-threatening situation.<sup>3</sup> The pre-

valence of ectopic pregnancy among women who go to emergency department with first trimester bleeding, pain or both ranges from 6-16%.<sup>4</sup> In Pakistan, the reported incidence has been cited as 1:112 to 1:130.<sup>5</sup> Ectopic pregnancy is a pregnancy in which the fertilized ovum implants in any location other than the endometrial lining of uterus.<sup>6</sup> Pregnancies in the fallopian tube account for 97% of ectopic pregnancies; 55% in the ampulla; 25% in the isthmus; 17% in the fimbria; and 3% in the abdominal cavity, ovary and

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Submitted 11 November 2015, Accepted 15 December 2015

cervix.<sup>7</sup> Moreover, the caesarian scar is recently identified as a nidus for ectopic gestation.<sup>8</sup> The peak age of incidence is 26-30 yrs. Most of the patients have identifiable risk factors, the important risk factors include primigravida, salpingectomy, history of abortion, infertility, pelvic inflammatory disease and history of previous surgery.<sup>9</sup> A classic clinical triad of ectopic pregnancy is pain, amenorrhea and vaginal bleeding. Unfortunately only 50% of patients present typically. Patients may present with other symptoms common to early pregnancy including nausea, breast tenderness, fatigue, lower abdominal pain, heavy cramping, shoulder pain and dyspareunia.<sup>2</sup> Up to 1/3 of patients may die at home despite consultation with the physician or gynaecologist due to a variety of clinical presentation.<sup>10</sup>

The spectrum of ultrasound findings of ectopic pregnancy include live extrauterine embryo, absence of an intrauterine gestational sac, free fluid (particularly hemorrhage) in pelvis or peritoneum, adnexal mass, haematosalpinx and adnexal ring sign.<sup>11</sup> Transvaginal ultrasonography (TVS) has shown great promise in evaluation of patients with suspected ectopic pregnancy. The advantages of sonography are that it is widely available, relatively inexpensive and most importantly, it has no ionizing radiation risk to the patient. This is especially important for pregnant women because of radiation risk to the developing fetus.

## Objectives

The objective of this study was to determine diagnostic accuracy of transvaginal ultrasound in early (first trimester) detection of ectopic pregnancy and to exclude an alternative diagnosis.

## Material and Methods

A cross sectional prospective study of 469 patients was conducted. The study included women of reproductive age group (14-45 years) who presented in ER with clinical signs and symptoms of ectopic pregnancy and were referred to Radiology Depart-

ment by the emergency physicians or surgeons for transvaginal ultrasonography. The inclusion criteria was clinical signs and symptoms of amenorrhea with or without vaginal bleeding, lower abdominal pain and serum beta human chorionic gonadotropin in the range of 192-10,500 mIU/ml. Patients showing presence of intrauterine pregnancy on ultrasound, suspected adnexal mass with negative serum Beta hCG levels, suspected ectopic pregnancy but not fit for surgery, already diagnosed case of ectopic pregnancy on conservative treatment or patient not giving consent for TVS were excluded from the study. Initially 500 patients were included. Out of these 31 patients were excluded so the total number of patients was 469.

After taking informed consent, transvaginal ultrasound was performed by a senior radiologist with a minimum of three years of experience using transvaginal high frequency probe 6.0 MHz. Serial longitudinal and transverse images were taken. After performing transvaginal ultrasound of the patients and being diagnosed as having ectopic pregnancy or with negative transvaginal ultrasound, patients went for surgery. After surgical evacuation, specimen were sent to the laboratory for histopathological findings. Final diagnosis depends on histopathological presence or absence of an ectopic pregnancy. All relevant features including patient's name, age, registration number, date of last menstrual period, duration of pregnancy, transvaginal ultrasound and histopathological findings were recorded on performa (Annex-I).

Data compilation and statistical analysis was done on SPSS version 16. Descriptive statistics; frequency and percentage was computed for presentation of qualitative variables including transvaginal ultrasound findings and histopathological findings. Age and duration of pregnancy of the patient were presented by Mean  $\pm$  SD. A 2 x 2 table will be constructed. Sensitivity, Specificity, positive and negative predictive values and diagnostic accuracy of transvaginal ultrasound will be determined by taking histopathology as gold standard. Stratification was done with respect to age, duration of pregnancy and amenorrhea with and without bleeding to control the effect modifier applying chi-square test taken  $P \leq 0.05$  as significant.

## Results

Initially 500 patients were included in the study. Out of these 31 patients were excluded. Ten patients were diagnosed to have intrauterine gestational sac, eleven patients had negative serum beta hCG levels, nine patients did not give consent for transvaginal ultrasound and one patient was already on conservative treatment for ectopic pregnancy. The final number of patients comprising the study was thus 469.

Out of these 469 patients, 100 patients were in the age limit of 14-24yrs (21.32%), 250 were between 25-35yrs (53.30%) and 119 were between 36-45 yrs (25.37%). (Fig. 1) The duration of pregnancy at which the patients presented with sign and symptoms of

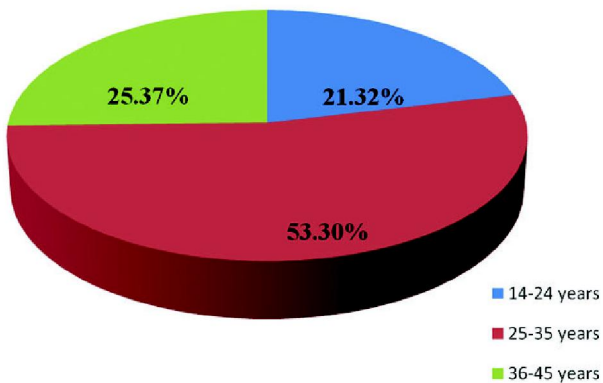


Figure 1: Distribution of age in years

ectopic pregnancy was also assessed according to the last menstrual date. It was found that 200 of the patients presented between 4-5 wks of amenorrhea (42.6%), 230 patients between 6-7 wks of amenorrhea (49%) and only 39 patients presented between 8-9 wks of amenorrhea (8.3%). (Fig. 2)

The diagnosis of ectopic pregnancy was made on the basis of transvaginal ultrasonographic findings. (Tab.1) Ectopic gestational sac with yolk sac and fetal pole was found in 104 out of 260 positive cases (40%). The fetal pole did not show any cardiac activity in these patients. 32 out of 260 patients presented with ectopic gestational sac without the presence of yolk sac and fetal pole (12.3%). 11 out of the 260 positive cases, live ectopic pregnancy was diagnosed (4.2%). In these patients, fetal cardiac activity was

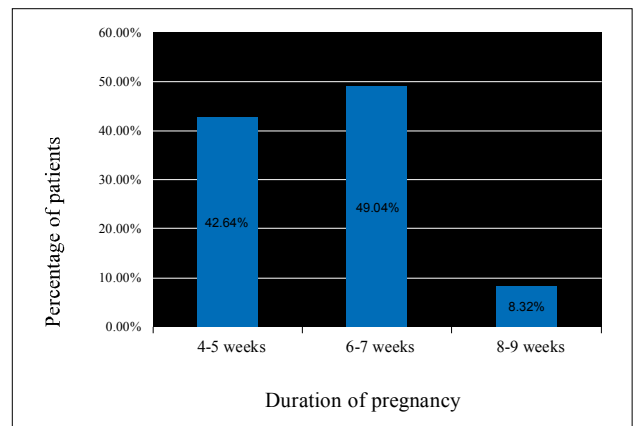


Figure 2: Duration of pregnancy during which patient's presented with sign and symptoms of ectopic pregnancy

Criteria	Number of Occurrence (%)
<b>Primary signs</b>	
Ectopic gestational sac with yolk sac and fetal pole	40%
Ectopic gestational sac without yolk sac	12.3%
Fetal pole with cardiac activity	4.2%
Complex adnexal mass	43.4%
<b>Secondary signs</b>	
Decidual reaction/ pseudosac	18%
Fluid in pouch of douglas/pelvis/peritoneum	80%
Ring of fire sign	60%
Organized collection	24%

Table 1: Diagnostic criteria for ectopic pregnancy in 260 positive cases, and occurrence rates

detected using transvaginal ultrasound. A complex adnexal mass was found in 113 out of 260 cases. It was found that most of the patients presented with a complex adnexal mass with a very high suspicion of ectopic pregnancy. These complex adnexal masses were most often associated with free fluid or organized collection representing ruptured ectopic pregnancy. Fluid in pouch of douglas/pelvis/peritoneum was present in about 200 out of 260 cases (80%). It is the most important and sensitive sign in making the diagnosis of ectopic pregnancy. Most of the patients presented with variable amounts of fluid. Presence of fluid in the morrison's pouch is highly suspicious of ruptured ectopic pregnancy. Ring of fire sign was present in 120 out of 260 patients (60%). In 60 out

of 260 patients, organized collection was found (24%). On the basis of transvaginal ultrasonographic findings, ectopic pregnancy was diagnosed in 260 of the patients and 209 of the patients were labelled as not having ectopic pregnancy. Of the 260 patients diagnosed with ectopic pregnancy, 250 were positive and 10 were negative for ectopic pregnancy on histopathological examination. Of the 209 patients not having ectopic pregnancy, 193 were also negative on histopathological examination. In 16 patients, ectopic pregnancy was misinterpreted as negative. Correct assessment for ectopic pregnancy was made in 443 out of 469 patients (94.45%). Incorrect assessment was made in 26 out of 469 patients (5.54%). (Tab. 2)

	Histopathology +ve	Histopathology -ve	Total #
US diagnosis +ve	250 (TP)*	10 (FP)**	260
US diagnosis -ve	16 (FN)***	193 (TN)****	209

\*TP: True-positive, n = 250  
 \*\*FP: False-positive, n = 10  
 \*\*\*FN: False-negative, n = 16  
 \*\*\*\*TN: True-negative, n = 193

**Table 2:** Summary of Results

Ectopic pregnancy was correctly diagnosed prospectively in 250 of 266 patients using US (sensitivity, 93.98%). Ectopic pregnancy was correctly excluded prospectively in 193 of 203 patients (specificity, 95.07%). The overall accuracy was 94.45% for diagnosing ectopic pregnancy. The positive and negative predictive values were 96.15% and 92.34% respectively (Tab. 3).

Statistical Measure	Results	
	%	Numbers
Sensitivity	93.98%	250/266
Specificity	95.07%	193/203
Accuracy	94.45%	443/469
*PPV	96.15%	250/260
**NPV	92.34%	193/209

\*PPV = positive predictive value, \*\*NPV = negative predictive value.

**Table 3:** Sensitivity, specificity, accuracy, ppv and npv of sonography in assessing ectopic pregnancy

Alternative diagnosis was suggested in 193 patients. These were missed abortion 51.8%, haemorrhagic cyst 12.9%, endometriotic cyst 11.3%, complex ovarian cyst 6.2%, tubo ovarian abscess 7.7%, ovarian torsion 2.6%, pelvic inflammatory disease 3.1% and uterine fibroid 4.1% of the patients. (Tab. 4)

Diagnosis	Occurrences (%)
Missed abortion	51.8%
Haemorrhagic cyst	12.9%
Endometriotic cyst	11.3%
Complex ovarian cyst	6.2%
Tubo- ovarian abscess	7.7%
Ovarian torsion	2.6%
Pelvic inflammatory disease	3.1%
Uterine fibroid	4.1%

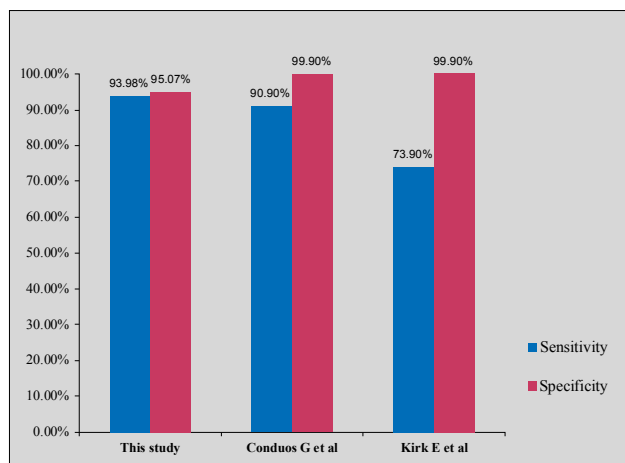
**Table 4:** Alternative diagnosis suggested by tvs in 193 patients without ectopic pregnancy

## Discussion

This study was a prospective study of 469 patients clinically suspected for ectopic pregnancy. After a detailed history, clinical examination and consent, the patients were subjected to ultrasound examination of the pelvis using transvaginal technique. The study included women of reproductive age group (14-45 years) who presented in ER with clinical signs and symptoms of ectopic pregnancy and were referred to Radiology Department by the emergency physicians or surgeons.

Most of the women who came with sign and symptoms of ectopic pregnancy were between 25-35 years of age group. In a study conducted in Guinea, amenorrhoea and abdomino-pelvic pain were found to be the main symptoms in ectopic pregnancy.<sup>12</sup> In this study, abdominal pain with vaginal bleeding were the main symptoms recognized. It also concluded that most of the patients present with symptoms of ectopic pregnancy during 6-7 weeks of amenorrhoea (49%). Apart from visualization of an ectopic gestational sac with yolk sac and fetal pole and adnexal mass, fluid in the pouch of Douglas/pelvis/peritoneum and ring of fire sign were the two most frequent ultrasound

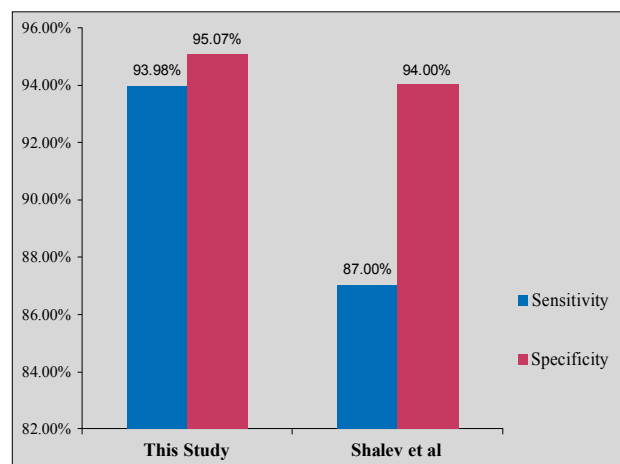
findings observed in this study. Perriera L proposed that suspicion of an ectopic pregnancy increases if free fluid (representing blood) is visualised, either surrounding the uterus or in the Pouch of Douglas, although a small amount of free fluid in the Pouch of Douglas, a transudate due to increased vascular permeability, is common in early pregnancy.<sup>13</sup> It was also observed that presence of fluid in pouch of douglas/pelvis/peritoneum is a highly sensitive secondary sign which was found in 80% of the patients. However, this sign is not specific for diagnosis of ectopic pregnancy because other pathological conditions related to pelvis can also cause this. Ring of fire sign was also an important secondary sign detected in 60% of the patients. In this study, transvaginalultrasund was able to detect a live ectopic pregnancy in 4% of cases out of true positive cases. This study concluded that transvaginal ultrasonography has a sensitivity of 93.98%, specificity of 95.07%, and accuracy of 94.45% to detect ectopic pregnancy. In one study, conducted by Condous G et al, the sensitivity and specificity of transvaginal ultrasonography to detect ectopic pregnancy is 90.9% and 99.9% respectively.<sup>14</sup> In another study conducted by Kirk E et al, sensitivity and specificity of transvaginal ultrasonography in the diagnosis of ectopic pregnancy is 73.9% and 99.9% respectively.<sup>15</sup> These two studies show marked variation in sensitivity of transvaginal ultrasonography in the diagnosis of ectopic pregnancy. Results of my study show better sensitivity and accuracy than these two studies. (Fig. 3)



This study : 93.98% and 95.07%  
 Condous G et al. : 90.90% and 99.90%  
 Kirk E et al. : 73.90% and 99.90%

**Figure 3:** Comparison of sensitivity and specificity with studies of Condous G et al & Kirk E et al.

In another large prospective study of 6621 patients, ectopic pregnancy was correctly diagnosed by TVS with a sensitivity of 90.9% and specificity of 99.9%.<sup>16</sup> Shalev and colleagues found that the use of TVS in the diagnosis of an ectopic pregnancy has a sensitivity of 87%, specificity of 94%, and positive predictive value of 92.5%. The sensitivity of my study is also greater than these two studies. (Fig. 4)



This study : 93.98% and 95.07%  
 Shalev et al : 90.90% and 99.90%

**Figure 4:** Comparison of sensitivity and specificity with study of Shalev et al.

There were 10 false positive cases in this study. False positives can, however, occur if other structures such as the corpus luteum, bowel, a paratubal cyst, a hydrosalpinx or an endometrioma are mistaken for an ectopic pregnancy. One false positive case was of a 28 year old female who was diagnosed with ovarian torsion on histopathological examination. In one of the false negative cases, decidual reaction of ectopic pregnancy was falsely interpreted as retained products of conception of missed abortion. Another case that turned out to be false positive was of a 30 years old female who was diagnosed as tubo-ovarian abscess secondary to tuberculosis on histopathological examination.

There were 16 false negative cases. False negatives can occur if the ectopic is small or if it is concealed by bowel or uterine anomalies such as fibroids. It is therefore possible for an ectopic pregnancy to go unnoticed on an ultrasound scan, especially if the patient is asymptomatic. It has been established that ectopic pregnancies have lower mean serum beta hCG levels than healthy pregnancies. False negativity

also decreases as the operator gains experience. Gynecologic disorders were the most common set of conditions that mimicked ectopic pregnancy in our study. Ovarian pathologies commonly mimic ectopic pregnancy clinically, and women of child bearing age with lower abdominal pain have the greatest risk of misdiagnosis.

## Conclusion

In conclusion, the overall accuracy of transvaginal ultrasonography in the diagnosis of ectopic pregnancy in patients with clinical signs and symptoms of ectopic pregnancy is statistically very high.

Transvaginal ultrasonography performed in patients with suspected ectopic pregnancy improves patient care by early detection of ectopic pregnancy that will decrease the morbidity and mortality associated with it.

Experience, commitment with work and better quality of ultrasound equipment can improve the sensitivity and specificity of this traditionally believed to be operator dependent examination.

Taking into account the above benefits and high sensitivity, transvaginal ultrasonography should be highly recommended as a routine screening method in patients with clinical suspicion of ectopic pregnancy.

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