International Journal of Enhanced Research in Medicines & Dental Care (IJERMDC),
ISSN: 2349-1590, Vol. 5 Issue 11, November-2018, Impact Factor: 3.015

The Role of Ultra Sound to Diagnosis of Ectopic Pregnancy Confirmed by Histopathology

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ABSTRACT

Objective: To confirm the accuracy of endo-vaginal ultrasound in the diagnosis of ectopic pregnancy compared with transabdominal ultrasound confirmed by the histopathological study. A prospective study was performed at Al- Batool, Gynecological, Obstetrical and infertility Teaching Hospital, Mosul, Iraq from 1st June 2009 to 1st June 2010. 4200 patients in 1st trimester were admitted to Al-Batool hospital with abdominal discomfort and vaginal bleedingwere examined by transabdominal ultrasound.

Results: During the analysis, the incidence of ectopic pregnancy was (1.9%) and the peak incidence of age was (25-29) years. The peak incidence in low parity was (1-2) (44.30%). The common risk factor was the ovulation induction of patients (25.3%). The clinical presentation was the abdominal pain of 75 patients (95%). The ultrasonic findings were fluid in the pouch of Douglas, in transabdominal (60%) and in endo-vaginal (70%). The operative findings were right tubal rupture (36.7%), right tubal pregnancy (27.84%), and the most common type the tubal (97.4%). The most common site was the ampullary (88.61%), and the most common side was the right side (64.54%). The Chi-square test was used in this study, in transabdominal sonography: the sensitivity was (87%), specificity was (99%) and accuracy (99%), while in endo-vaginal , sonography: the sensitivity was (92%), specificity (100%) and accuracy (100%).

Keywords: Ectopic pregnancy- ultrasound- histopathology.

1. INTRODUCTION

Definition: Ectopic pregnancy (hence for the EP) is defined as a conceptus implanting outside the uterine cavity. The most common implantation site is within the fallopian tube, followed by ovarian and abdominal sites, as seen in (Figure 1). The sites of tubal implantation in order of frequency are ampulla, isthmus, fimbrial and interstitial [1].

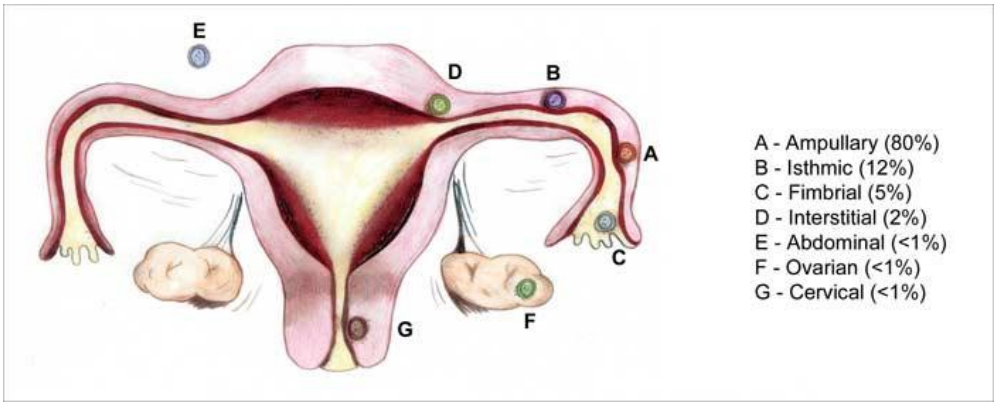


Figure 1: The anatomical sites of ectopic pregnancy

In some forms, ectopic pregnancy accounts for 1.3 to 2 percent of reported pregnancies in the united states. With the advent of a sensitive and specific radioimmuno-assay for the β-subunit of human chorionic gonadotropin (β-hCG), combined with high-resolutionendo-vaginal sonography (TVS), the initial presentation of a woman with an ectopic pregnancy is seldomlife-threatening as it was in the past. Nevertheless, ectopic pregnancies remain an important cause of morbidity and mortality in the United States with an estimated total cost of nearly $295 million in 1998 [2].

The incidence show higher rate during the last 30 years, as a result of the common use of antibiotics therapy reconstructive tubal surgery, and the use of intrauterine loop as contraceptive devices [3]. Ectopic pregnancy is an acute emergency in the first trimester where surgery is the mandatory way of treatment [4].

High- resolution endo-vaginal ultrasonography confirm visualization of normal embryonic development at an earlier stage and with greater details. The reliable diagnosis of ectopic pregnancy depends on the physician's ability to recognize a normal intrauterine pregnancy and the wide spectrum of ultrasonographic appearances of ectopic pregnancies [5].Because none of these previously mentioned anatomic sites can accommodate placental attachment or a growing embryo, the potential for rupture and hemorrhage always exists[6].

PATIENTS AND METHODS

A prospective study of 4200 women first trimester attended to Al-Batool Gynecological and obstetrical teaching hospital in Mosul City. The women were self-referred or referred by a general practitioner or by private clinics from 1st June 2009 till 1st June 2010. The patients summated between 15 and 49 years, presented with abdominal pain accompanied by vaginal bleeding or not. The patients lying down in the supine position and a full bladder and examined trans-abdominally with a transverse and sagittal section by using a device vivid 3, China (the supplying company), vivids the manufacturing company/ 796 MB/sync. Master. C: N/7HVAP 2007- 32J. provided to the unit of ultrasound examination in 2007 with 3 probes and a printer. One vaginal probel of 7.5 MHz and 2 abdominal probes one 3.5MHz and the other 7.5MHz, (Figure. 2).

Figure 2: An Ultrasound device

Ultrasound examination has become the1stchoice in1st-trimester diagnosis without harm or discomfort to the patient. The patients should lie down in supine position with an emptybladder because a full bladder can compress, distort and displace the ectopic gestation.

The endo-vaginal ultrasound probe will be covered with a condom and will have been soaked in disinfectant between uses without the need to use a coupling agent (gel).The endo-vaginal ultrasound probe works in the same way as the abdominal probe dose, but it is long and thin and it is generally a higher frequency probe which means that it generates images of higher resolution that transabdominal because endo-vaginal probe gets closer to the organs being viewed and looks at a smaller area than transabdominal. Those patients who have been diagnosed as having suspected ectopic pregnancy they operated on under general anesthesia by using pentothal (thiopental) 5 ml/kg through the intravenouscannula with monitoring of vital signs, laparotomy done and the specimen sent for histopathological study. The histological assessment was performed by experienced pathologists who already know the clinical, laboratory and imaging characteristics of the patients, by cutting off section with a microtome and staining with hematoxylin and eosin. The early processing of large biopsy is important to avoid autolysis.

Early dissection and sectioning are important to ensure a proper fixation and avoid autolysis. The statistical study done was chi-square test by using the statistical program Minitab version 13, to find the significant by determining Sensitivity, specificity, (+ve) predictive value, (-ve) predictive value.

Define abbreviations and acronyms the first time they are used in the text, even after they have been defined in the abstract. Abbreviations such as IEEE, SI, MKS, CGS, sc, dc, and rms do not have to be defined. Do not use abbreviations in the

THE RESULTS

The patients involved in this prospective study were 4200, the age range of 15 and 49 years. This sample is analyzed according to the results of the endo-vaginal ultrasound and the result was 79 patients (1.9%) has an ectopic pregnancy and those affected by other diseases were 4121 patients (98.1%). The incidence of ectopic pregnancy (the number of ectopic pregnancies per year) was (1.9%), (Table 1.)

Table 1: Percentage of Ectopic pregnancy by total (n=4200)

Total	No. of patients	%
Ectopic pregnancy	79	1.9
Another disease	4121	98.1
Total	4200	100

The incidence of ectopic pregnancy according to the age: the lower limit of age range was 15 years, the upper limit was 49 years and the mean age was 32 years. The higher age incidence was in (25-29) years. 7 patients out of 79 (8.87%) were in (15-19) years age group, 20 patients (25- 32%) were in (20-24) years age group, 24 patients (30-38%) were in (25-29) years age group, 15 patients (18.98%) were in (30-34) years age group, 10 patients (12.66%) were in (35- 39) years age group, 2 patients (2.53%) were in (40-44) years age group and one patient (1.26%) was in (45- 49) years age group as, show in (Table 2 and Figure 3).

Table 2: Relation of age with ectopic pregnancy(n= 4200).

Age	No. of patients	% out of 79 patients
15-19 years	7	8.87
20-24 years	20	25.32
25-29 years	24	30.38
30-34 years	15	18.98
35-39 years	10	12.66
40-44 years	2	2.53
45-49 years	1	1.26
Total	79	100

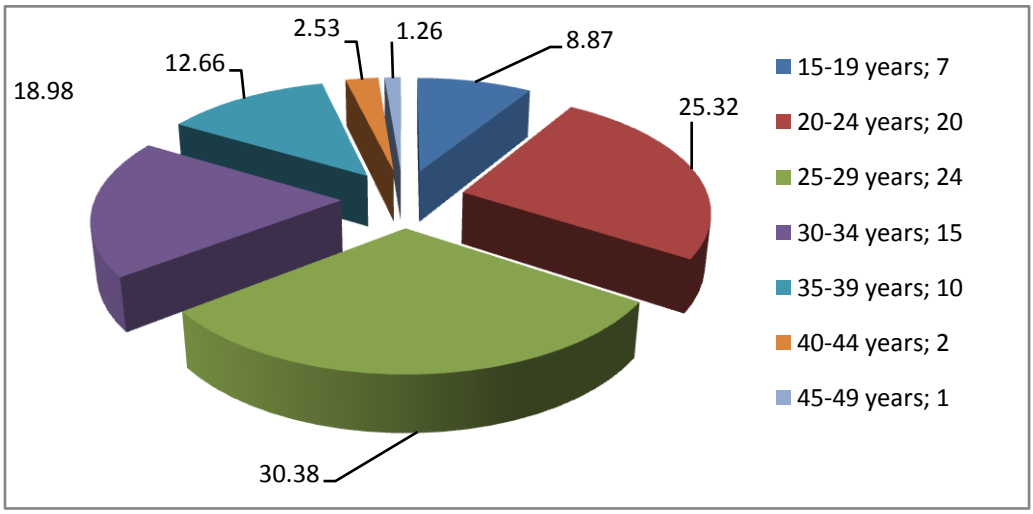


Figure3: Pie chart of shown relation of age with ectopic pregnancy

Concerning the frequency of ectopic pregnancy according to the parity, the ectopic pregnancy was more seen in low parity (1-3), 35 patients out of 79 (44.30%) were of low parity. 5 patients (6032%) were nulliparous, 25 patients (31.64%) were gravida (4-6) and 14 patients (17.72%) were grand multiparous, as shown in(Table 3 and Figure 4).

Table 3: Relation of parity & ectopic pregnancy (n=4200)

Parity	No. of patients	%
Nullipara	5	6.32
1-3	35	44.30
4-6	25	31.645
> 6	14	17.72
Total	79	100

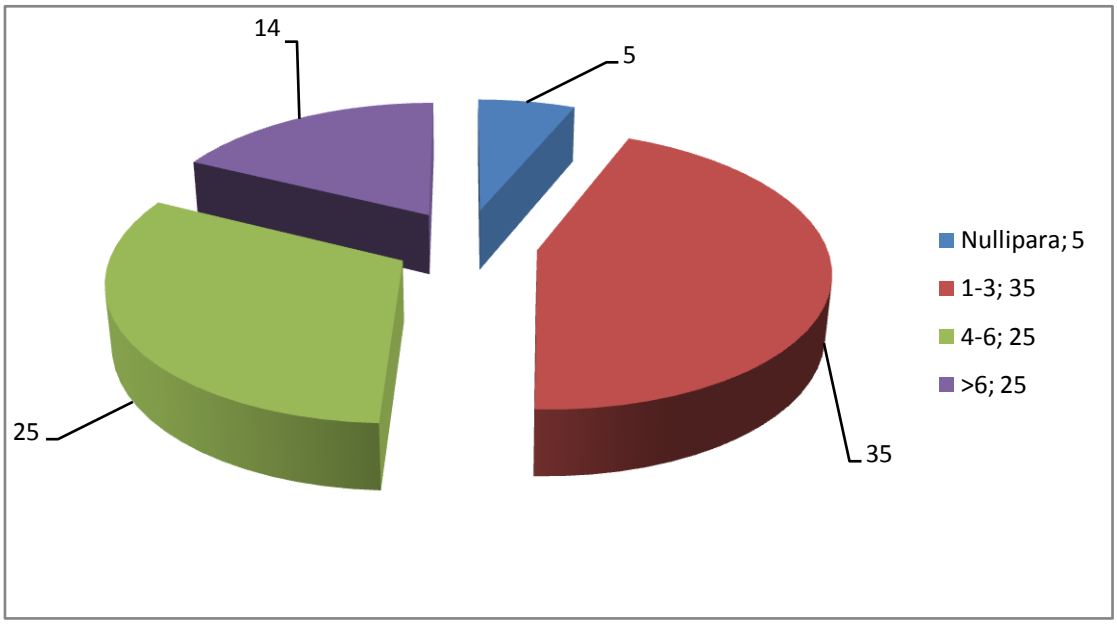


Figure 4: Pie chart of the shown the relationof ectopic pregnancy with parity

As for the common risk factors in ectopic pregnancy, ovulation induction in 20 patients out of 70 (25.3%). The gynecological infection in 18 patients (22.7%), the intrauterine loop device in 16 patients (20.25%, the frequent use of contraceptive pills in 9 patients (11.39%), the history of previous pelvic surgery in 7 patients (8.8%), smoking in one patient (1.2%). No patient had a history of previous ectopic pregnancy and 18 patients (22.78%) had no risk factor, but one patient may score multiple risk factor. The ovulation induction formed a higher percentage (25.30%) and then PID (22.7%), as shown in (table 4 and Figure 5).

Table 4: Risk factors associated with Ectopic Pregnancy

Risk factor	No. of patients	%out of 79 patients
Ovulation induction	20	25.3
Pelvic inflammatory disease	18	22.7
Intrauterine contraceptive device	16	20.25
Oral contraceptive pills	9	11.39
History of previous pelvic surgery	7	8.8
Smoking	1	1.2
History of previous ectopic pregnancy	0	0
No risk factors	18	22.78

***One patient may score more than one risk factor**

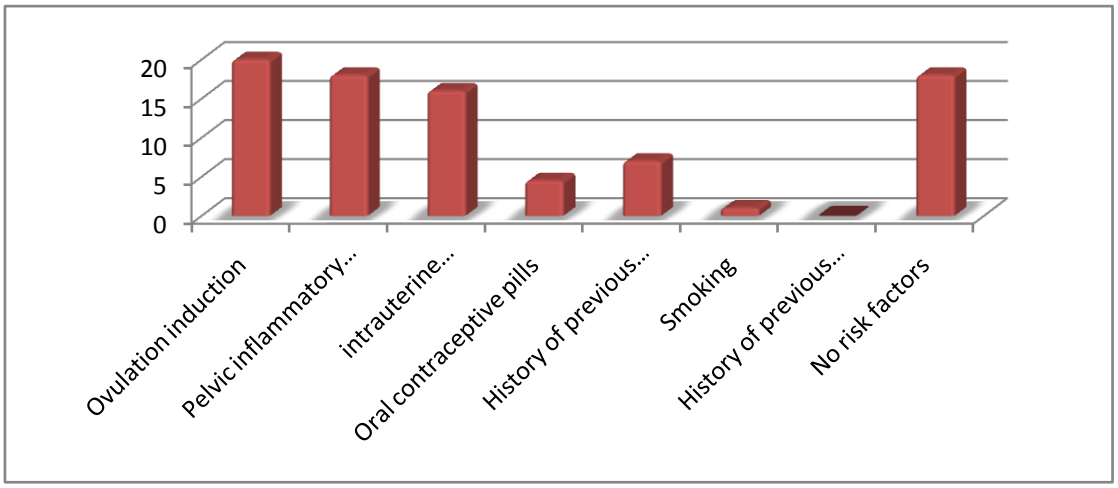


Figure 5: Histogram shows Risk factors associated with ectopicpregnancy

The common presentation was the abdominal pain in 75 patients out of 79 (95%).The abdominal pain in 71 patients was (90%), the vaginal bleeding in 63 patients was (80%), the adnexal tenderness (cervical excitation) in 37 patients was (47%) and the dizziness (syncope attack) in 28 patients was (35%), one patient may have multiple clinicalsymptoms, as shown in(Table 5 Figure 6).

Table 5: Ectopic pregnancy according to clinical symptoms

Clinical presentation	No. of patients	%out of 79 patients
Abdominal pain	75	95%
Vaginal bleeding	63	80%
Abdominal tenderness	71	90%
Adnexal tenderness (Cervical excitation	37	47%
Dizziness (syncope attack	28	35%

* One patient may have more than one clinical presentation of ectopic_pregnancy

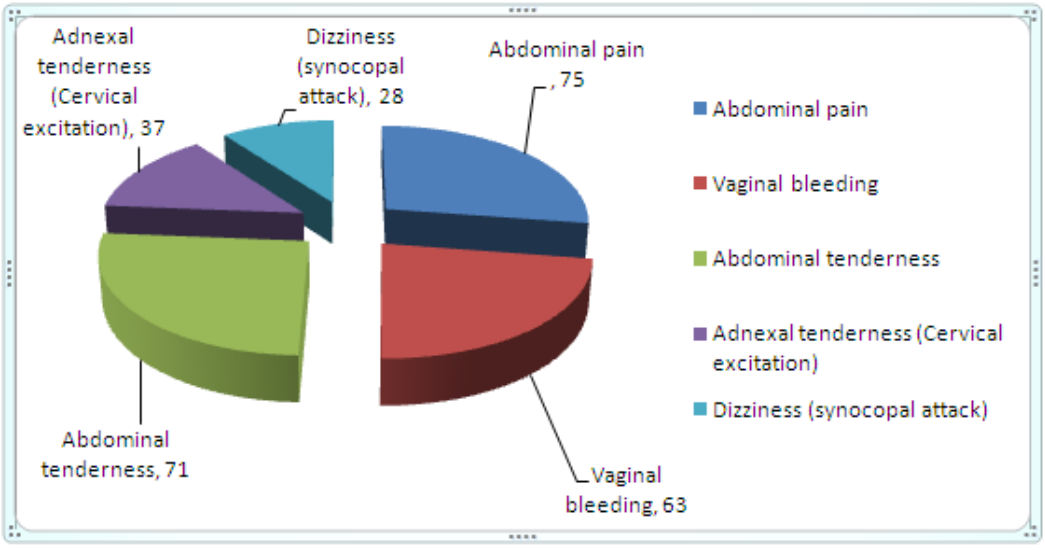


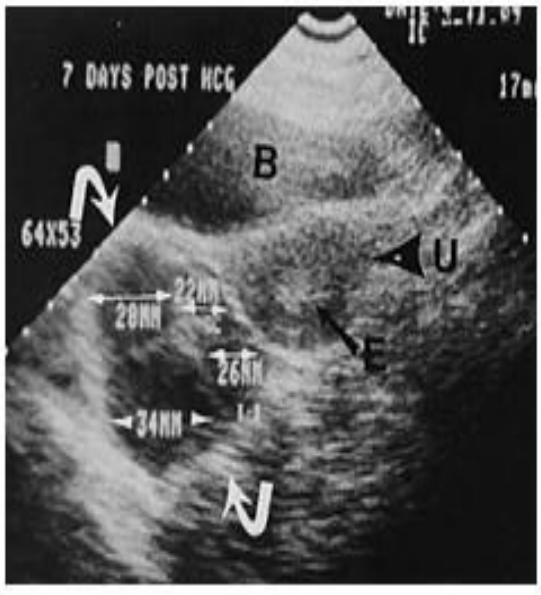
Figure 6: Pie chart of the common clinical symptoms of ectopic pregnancy

The ultra-sonic findings in TAS and TVS, the common finding was a fluid in pouch of Douglas by TAS in 47 patients out of 79(60%) and by TVS in 55 patients (70%), as shown in (Figure 7 Picture 1&2.)The adnexal mass was seen by TAS in 35 patients (45%) and by TVS in 47 patients (60%), as shown in (Figure 7, Picture 3& 4.) The adnexal mass was seen by T. A. S. in 35 patients (45%) and by TVS in 47 patients (60%), as seen in (Figure 7, Picture 3& 4). The pseudo gestational sac was seen by TAS in 12 patients (15%) and by TVS in 16 patients(20%), as shown in(Figure 7, Picture 5), and the less frequent was the live ectopic or gestational sac containing fetal pole which was seen by TAS in 3 patients (4%) and by TVS in 8 patients (10%), as shown in (Figure 7, Picture 6& 7). The total ultrasonic findings in TAS were 97, while in TVS were 126 and this means that the TVS is more accurate than TAS, Chi-square was 0.239. one patient may have more than one ultrasonic finding, as shown in (Table 6 and Figure 8).one patient may have multiple ultrasonic finding, as shown in(Table 6 and Figure 8). The ultrasonic finding of ectopic pregnancy according to the involved side was 64 in the right adnexal side and 33 in the left adnexal side, the number of womenonthe right side was 51 patients (65.82%) and the number of womenon the left side was 26 patients (34.18%), as shown in(Table 7, Figure 9.

Picture 1: Sagittal.

Picture 2: transverse

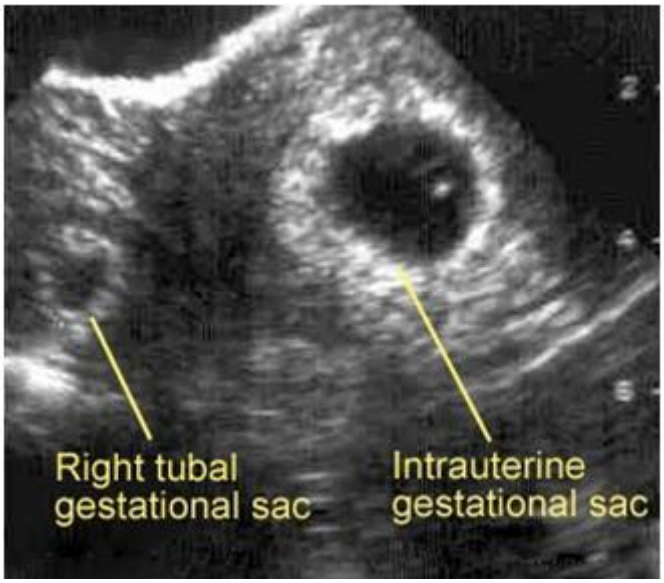
Endo-vaginal ultrasound images demonstrating echogenic fluid in the cul-de-sac posterior the uterus



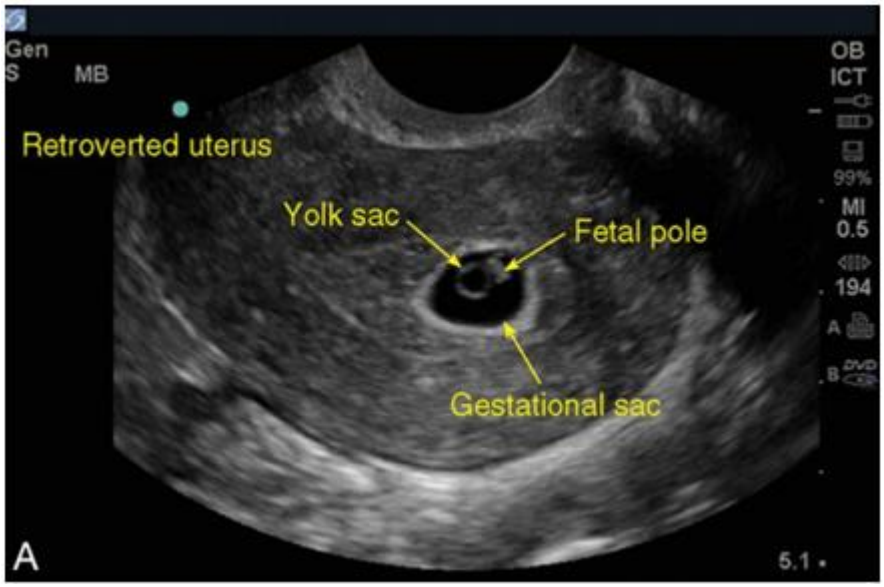
Picture 3

picture 4

Picture 3& Picture 4: Complex left adnexal mass is oriented medial to left ovary and lateral to the uterus(white arrow).



Picture 5: Pseudo gestational sac in the uterine cavity (yellow arrow) and right tubal ectopic pregnancy (yellow arrow).



Picture 6 & Picture 7: Ectopic pregnancy. Endo-vaginal ultrasound demonstrating a right adnexal mass with a fetal pole and yolk sac.

Figure 7: The ultrasonic findings in TVS

Table 6: The ultrasonic findings in Transabdominal sonography (TAS) and Endo-vaginal sonography (TVS)

Findings	Transabdominal sonography		Endo-vaginal sonography	
	No. of Patients	%	No. of patients	%
Fluid in the pouch of Douglas	47	60	55	70
Adnexal mass	35	45	47	60
Pseudo gest. Sac	12	15	16	20
Live ectopic or gest. Sac Containing yolk sac or fetal pole	3	4	8	10
Total	97	124	126	160

One patient may harbor more than one finding, which is found better in the endo-vaginal examination.
Chi-square = 0,239 mean TVS is more sensitive than TAS

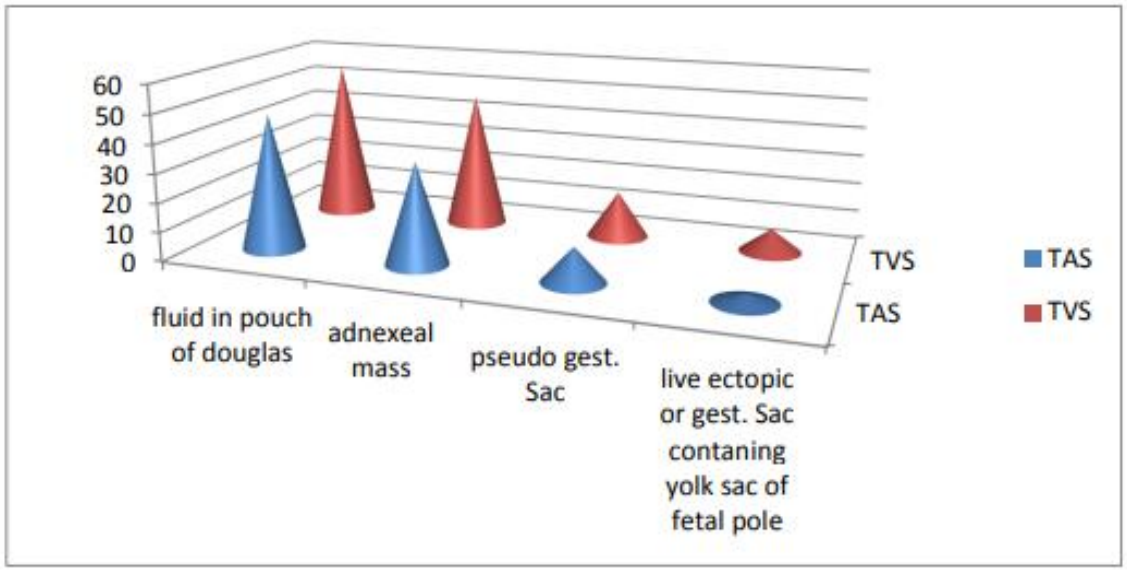


Figure 8: Histogram of the ultrasonic findings in Transabdominal sonography (TAS) and Endo-vaginal sonography (TVS).

Table 7: The Transabdominal findings according to theinvolved side

Findings	Right side		Left side	
	No. of Patients	%	No. of patients	%
Fluid in the pouch of Douglas	29	36.70	18	22.78
Adnexeal mass	25	31.64	10	12.66
Pseudo gest. Sac	8	10.12	4	5.06
Live ectopic or gest. Sac Containing yolk sac or fetal pole	2	2.53	1	1.26
Total	64	80.99	33	41.76
No. of the patients out of 79	51	65.82	26	34.18

*** One patient may harbor more than one finding**

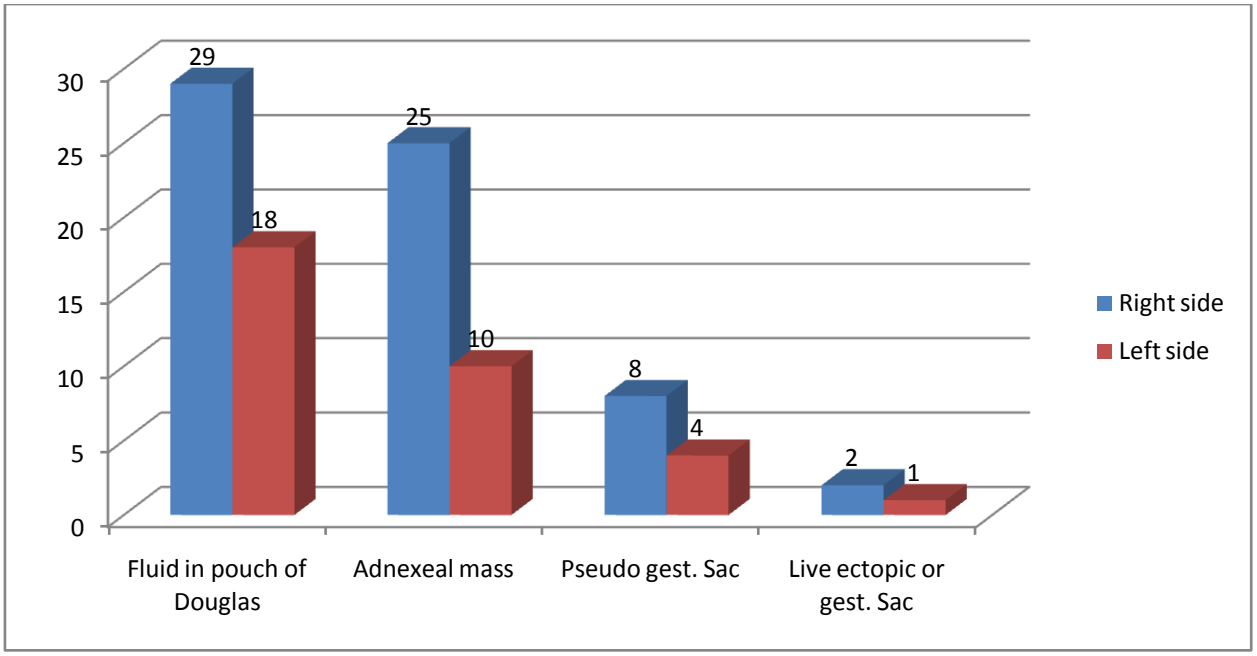


Figure 9: Histogram of the transabdominal findings according to the involved sides

The operation had been done for 120 patients 21 patients out of 120 patients (17.5%) had ovarian cysts, 16 patients (13.3%) had pelvic inflammatory diseases, two patients (2.4%) had no pathology, one patient (0.83%) had twisted fallopian tube and one patient (0.83%) had appendicitis. 79 patients (65%) had ectopic pregnancies proved by histopathology. The right tubal rupture was common. operative finding in 29 patients out of 79 (39.7%).

The right tubal pregnancy was in 22 patients (27.84%). The left tubal rupture was in 14 patients (17.72%). The left tubal pregnancy was in 12 patients (15.18%) and abdominal ectopic pregnancy was in 2 patients (2.53%), the right tubal pregnancy is seen more than the left tubal pregnancy, as shown in(Table 8 and Figure 10). As for the incidence of ectopic pregnancy according to the type and side of the fallopian tube, the higher incidence tubal ectopic was in 77 patients out of 79 (97.47%), the abdominal ectopic was in 2 patients (2.53%). 70 patients (88.61%) had the ampullary location of ectopic pregnancy which was the more frequent tubal ectopic pregnancy, as shown in (Table 8 and Figure 10).

Table 8: The post-operative findings out of 79 patients

Findings	No. of patients		%out of 79 patients	
Right tubal rupture	29	43	36.71	54.43
Left tubal rupture	14		17.72	
Right tubal pregnancy	22	34	27.85	43.04
Left tubal pregnancy	12		15.19	
Abdominal ectopic pregnancy	2		2.53	
Total	79		100%	

As for the incidence of ectopic pregnancy according to the type and side of the fallopian tube, the higher incidence tubal ectopic was in 77 patients out of 79 (97.47%), the abdominal ectopic was in 2 patients (2.53%). 70 patients (88.61%) had ampullary tubal ectopic pregnancy which was the most common tubal ectopic pregnancy. 3 patients (3.79%) had a fimbrial ectopic pregnancy. 2 patients (2. 53%) had isthemic ectopic pregnancy as shown in (Table 9 Figure 10).

Table 9: The frequency of ectopic pregnancy according totype, part of the fallopian tube out of 79 patients

Findings	No. of patients	%out of 79 patients
Abdominal	2	2.53
Ampullary part of the fallopian tube	70	88.61
Fimbrial part	3	3.80
Isthmic part	2	2.53

Cornual (interstitial)	2	2.53
Total	79	100%

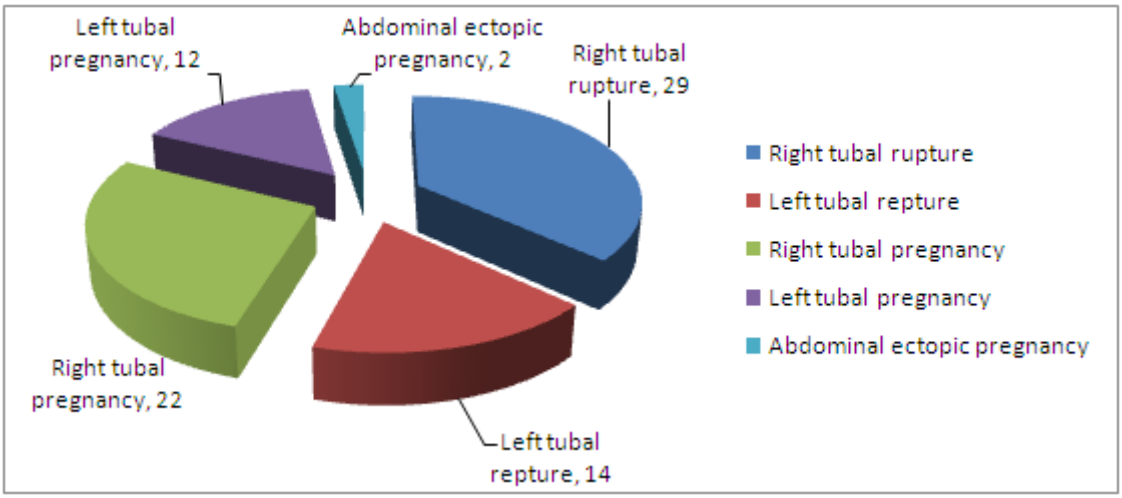


Figure 10: Pie chart of the operative findings out of 79

With regard to the ultrasonic (abdominal) analysis of the 4200 patients, 2888 patients (68.76%) had threatened abortions, 546 patients (13%) were missed abortions, 252 patients (6%) were complete abortions, 210 patients (5%) were incomplete abortions, 126 patients were blighted ova, 120 patients (2.9%) were ectopic pregnancies, and 58 patients (1.38%) were hydatidiform moles, as shown in(Table 10).

Table 10: The analysis of random specimen (4200) by Transabdominalsonography (TAS)

Findings	No. of patients TAS	%out of 4200 patients
Threatened abortion	2888	68.76
Missed abortion	546	13
Complete abortion	252	6
Incomplete abortion	210	5
Blighted ovum	126	3
Ectopic pregnancy	120	2.9
Hydatidiform mole	58	1.38
Total	4200	100

Concerning finding of screening tests of trans abdominal sonography versus histopathology and trans vaginal sonography versus histopathology, in TAS 69 true (+ve) (present in histopathology), 51 false (+ ve) (absent in histopathology), sensitivity: 87%, specificity: 99%, accuracy: 99%, predictive value of (+ ve) result: 57%, predictive value of (- ve)result: 100%, as show in(Table 11).

Table 11: Results of a screening test of trans abdominal versus histopathology

Screening test	Gold stander Histopathology		Total
	Present in Histopathology (+ ve)	Absent in Histopathology (- ve)	
Present in transabdomenal songraphy	69 A (True + ve)	51 B (False + ve)	120 Total test + ve
Absent in transabdomenal songraphy	10 C (False- ve)	4070 D (True- ve)	4080 Total test -ve
Total	89 Total disease + ve	4121 Total disease- ve	4200 Grand total

Sensitivity: 87%, Specificity: 99%, Accuracy: 99% Predictive value of + ve result: 57%, Predictive value of- ve result: 100%.

The results of screening tests of endo-vaginal sonography versus histopathology in TAS 73 true (+ ve) (present in histopathology), 10 false (+ ve) (absent in histopathology), Sensitivity: 92%, Specificity: 100%, Accuracy: 100%, Predictive value of + ve result: 88%, Predictive value of- ve result: 100%, as show in (Table 12).

The TVS is more sensitive, specific and accurate than TAS.***Equations***

Table 12: Results of a screening test of endo-vaginal versus histopathology

Screening test	Gold stander Histopathology		Total
	Present in Histopathology (+ ve)	Absent in Histopathology (- ve)	
Present in endo-vaginal sonography	73 A (True + ve)	10 B (False + ve)	83 Total test + ve
Absent in endo-vaginal sonography	6 C (False- ve)	4111 D (True- ve)	4117 Total test -ve
Total	79 Total disease + ve	4121 Total disease- ve	4200 Grand total

Sensitivity: 92%, Specificity: 100%, Accuracy: 100%, Predictive value of + ve result: 88%, Predictive value of - ve result: 100%.

THE DISCUSSION

1. In this series, the incidence is (1.9%). So it is parallel with the above studies, Table 1.

2. The age incidence, Udigqwe, G. et al., in Nigeria (2010) pointed that the peak age group in ectopic pregnancy was 26-30 years and the lower age incidence was below 20 years and the upper age group was above 40 years old [7]. Malik, S. et al., (2009) stated that the most common age group with pelvic mass was between (26-30) years, the mean age was 30 y..33392ears [8].

3. In this series, the peak age incidence was (25-29) years, the lower age incidence was (15-19) years (8.87%) and the upper age incidence was (45- 49) years (1.26%), the mean age was 32 years. So it is consistent with the above studies, (Table 2, Figure 4)(Pie chart).

4. According to the parity incidence, the authors Udiqwe, G. et al., (2010) mentioned that the prevalence is equal in both primigravida and secundigravida (low parity) was (36.1%) of their patients [9]. Malik, S. et al., (2009) stated that (45%) of their patients were of low parity [8]. Thia, E. et al., (2009) pointed out that (51.8%) of the patients were primigravidae [4].

5. The smoking, the author Damotta, G. et al., in a study done in Brazil in (2010) found that (19.1%) of their patients were a smoker (37). In this series (1.2%) of patients were a smoker, which is lower than Damotta's study because most of the women in our community are not a smoker, Table 4, Figure 6(Histogram).

6. Transabdominal ultrasonic findings, Malik, S. et al., in Pakistan (2009) found that adnexal mass in (91%) of their patients, fluid in the Cul-de-sac was present in (97%) of their patients and pseudogestational sac was present in (35%) of their patients [8]. Vajnar, J. (2007) found that pseudo gestational sac was present in (20%) of the patients [10]. Schurz, B. et al., study in India (2007) stated that pseudo gestational sac was present in (6.9%) of the patients [11]. Nassem, I et al., a study in Karachi (2007) stated that adnexal mass and pelvic fluid was present in (76%) of the patients and the live ectopic was present in (4%) of their patients [12]. In this series, the fluid in pouch of Douglas was present in (60%) of the patients, adnexal mass was present in (45%) of the patients, pseudo gestational sac was present in (15%) of the patients, and live ectopic was present in (4%) of the patients. The difference between this study and the above studies due to differences in the skillsof physicians in interpretationandqualityof the equipment and the time of presentation of the patients, Table 6, Figure 9 (Histogram).

7. Endo-vaginal ultrasonic findings Periera, P.et al., in a study done in Brazil (2009) found that adnexal mass was present in (24.75%) of their patients (31). Adhikari, S. et al., in study in USA (2006) stated that complex adnexal mass in (61%) of their patients, echogenic fluid in the Cul-de-sac in (21%), and (13%) of the patients presented with live ectopic pregnancy [13], Condous, G. et al., in study done in London (2005) found that (57.9%) of the patients had adnexal mass and (13.2%) of the patients had live ectopic pregnancy [14Sutton, D. (2003) stated that complex adnexal mass in (90%) of the patients, pseudo gestational sac in (20%) of the patients and live ectopic in (25%) of the patients [15]. In this series the fluid in pouch of Douglas was in (70%) of the patients, adnexal mass was in (60%) of the patients, pseudo gestational sac was in (20%) and live ectopic pregnancy in (10%) of the patients, Table 6, Figure 9 (Histogram). These results were more or less near the above studies.

The transabdominal sonography (TAS) showed 97 ultrasonic findings in 79 patients, while endo-vaginal sonography showed 126 ultrasonic findings in the same patients, that the TVS is more sensitive than TAS.

CONCLUSIONS

The ultrasound is the basic imaging modality used to evaluate ectopic pregnancy, transabdominal u/s should be the initial technique employed for this purpose whereas T. V. S is better used in resolution as compared to T. A.S, todiagnosis of the ectopic pregnancy can be made with T.V.S, alone but T. A.S should always be in conjunction with T. V. S., although endo-vaginal sonography was superior to transabdominal sonography, the former may miss an ectopic pregnancy that is located in a high location beyond the field of view of endo-vaginal sonography transducer so the extrauterine gestation may be located above the uterus so endo-vaginal sonography frequently shows a small amount of fluid that had not been seen on transabdominal sonography in the pelvic cavity in all groups of patients.

SUGGESTIONS

We suggest to open a new unit for early pregnancy women " early pregnancy unit" (EUP) like other countries, to make endo-vaginal sonography as routine examination for early diagnosis of ectopic pregnancy and subsequently more appropriates treatment like medical by methotrexate or surgical by laparoscopy, so better prognosis and less complications and more preservation for future fertility.

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