Diagnostic Efficacy of Transvaginal Colour Doppler Sonography in Ectopic Pregnancy

Lilyan W. Sersam * , Ra'ad Al-Khayat ** , Ali Mohammed Murad * , Abeer H. Muslt ***

ABSTRACT:

BACKGROUND:

Ectopic pregnancy continues to be a major cause of maternal morbidity and mortality . A dramatic increase in incidence over time has been reported in several countries. The advent and wide application of ultrasound has greately improved the possibility of non- surgical diagnosis of ectopic pregnancy . Images obtained by the higher frequency and better resolution transvaginal ultrasound scan (TVS) probes facilitates the earlier diagnosis of ectopic pregnancy. The addition of Doppler ultrasound have revolutionised the non-invasive diagnosis of ectopic pregnancy.

METHODS:

Patients presenting to Al-Yarmouk Teaching Hospital with clinical suspicion of ectopic pregnancy were evaluated using TVUS. Colour flow imaging was performed and resistance indices (RIs) of the artery blood flow were calculated . The pulsatility indices (PIs) of both uterine arteries were also measured and serum β-hCG was quantitated . The Doppler flow results were correlated with surgical findings at laparoscopy or explorative laparotomy .

RESULTS:

Forty-seven women were enrolled .Six patients with intrauterine gestation were excluded . Tubal pregnancy was diagnosed by TVUS in 28 of 32 patients with ectopic pregnancy, while 30 of 32 patients were diagnosed by colour Doppler sonography. Colour flow in the trophoblastic tissue was detected in 59.3% of the tubal pregnancies, and the mean (±SD) RI of the trophoblastic flow was (0.49 ±0.1) . The RIs tended to decrease at higher β- hCG levels. The average PI of the uterine arteries was (2.29 ± 0.3) . The PIs of the ipsilateral uterine arteries were significantly lower than the contralateral ones. The sensitivity of colour Doppler in the diagnosis of ectopic pregnancy was (93.8%) with accuracy of (85.4%)

CONCLUSION:

Colour imaging is a good supplementary diagnostic tool in modern management of ectopic pregnancy . The addition of colour Doppler flow imaging to transvaginal sonography allows increased sensitivity in the detection of ectopic pregnancy.

KEYWORDS: Pregnancy, Ectopic, Colour Doppler, Transvaginal ultrasound.

INTRODUCTION:

The incidence of ectopic pregnancy has increased dramatically worldwide over the past few decades ,currently accounting for 2% of all pregnancies[(1)]. More than 50 percent of tubal pregnancies are situated in the ampulla [(2)]. The increased incidence of ectopic pregnancy has occurred simultaneously with an increased incidence of pelvic inflammatory diseases, suggesting a causal relationship[(1)].

* Department of Obstetrics and Gynaecology , College of Medicine , Al-Mustansiriya University, Al-Yarmouk Teaching Hospital.

** Department of Radiology , College of Medicine , Al-Mustansiriya University, Al-Yarmouk Teaching Hospital.

*** Department of Obstetrics and Gynaecology , Al-Yarmouk Teaching Hospital.

Several studies have shown that fertility is reduced by one-third for each additional ectopic pregnancy between the first and the third ectopic pregnancies [(3,4)]. Diagnosing ectopic pregnancy continues to be a major problem in gynaecology. Many ectopic pregnancies will follow a relatively chronic course and transvaginal ultrasonography combined with serum hCG measurement permits the confident diagnosis of ectopic pregnancy in many women without resort to laparoscopy [(5-7)]. With the advert of Early Pregnancy Assessment Units (EPUs), treatment options has become less radical as the number of stable ectopic pregnancy diagnosed increases [(8)]. Ectopic pregnancy is one of the conditions changing the normal high-resistance blood flow from the uterine or ovarian artery branches. Colour Doppler is essential to detect such haemodynamic changes in

vessels [9].Transvaginal colour Doppler is a promising innovation, Colour and Pulsed Doppler can help characterize the nature of adnexal mass. Ectopic pregnancy is characterized by ectopic colour flow which is prominent and randomly dispersed within an adrexal mass and separate to the ovary [10]. Colour Doppler helps identify the sometime subtle echogenic ring of an ectopic gestational sac as it lights up with colour. Investigators have found that without the use of Doppler, 2% to 16% of ectopic pregnancies may be overlooked [11]. Pulsed Doppler interrogation reveals a high-velocity, low-resistive blood flow pattern in the trophoblast or peritrophoblast tissue. The use of Doppler technique can increase the sensitivity of ultrasound for detecting ectopic pregnancies [12]. The aim of this study was to assess the efficacy of transvaginal colour Doppler sonography in the diagnosis of ectopic pregnancies and to evaluate its potential benefits in the diagnostic evaluation of tubal pregnancies.

PATIENTS AND METHODS:

In a prospective study, a total of 82 patients presenting to Al-Yarmouk Teaching Hospital with clinical suspicion of ectopic pregnancy, between October 2002 to November 2003. We excluded 35 patients from the study because of profuse haemorrhage or acute abdomen requiring emergency intervention. Finally, 47 patients were included in this study. These patients were in the reproductive age group and had some or all of the following clinical presentation. The patients may or may not have symptoms pointing to pregnancy, with or without a period of amenorrhoea, lower abdominal pain or pelvic pain and irregular vaginal bleeding. Each patient was informed about the method of examination and consent was obtained. A detailed history was taken from each patient and their complaint was registered. A thorough examination was carried out looking for any vaginal bleeding, adnexal or pelvic mass, it's size, consistency, mobility and tenderness, also the presence of an enlarged soft uterus, was looked for. Serum β-hCG was quantitated by Minividas technique. The assay principle combines an enzyme immunoassay sandwich method with a final fluorescent detection (ELFA). The sensitivity of assay was 2mIU/ml. A transvaginal ultrasonographic examinations were carried out on a Kretz-Voluson 350 D apparatus using a 5-8 MHz vaginal probe coupled with pulsed colour Doppler flow facilities. The uterus was first scanned for evidence of an intrauterine pregnancy. Normal intrauterine sacs were not examined with Doppler. Examination of the adnexa were searched to locate a solid or saclike mass separated from the ovary and uterus; we specifically noted the presence of an extrauterine fetal pole, yolk sac, or fetal cardiac pulsation. The diagnosis of ectopic pregnancy was made with transvaginal colour flow imaging when an ectopic fetus or sac was seen or placental flow was identified in an adnexal mass separate from the ovary and uterus. The area of tubal pregnancy was then examined by colour flow imaging; prominent vascularity detected in proximity to the gestational sac was regarded as indicating "trophoblastic flow" and the resistance indexes (RIs) of the artery blood flow patterns were calculated. The pulsatility indexes (PIs) of both uterine arteries were calculated from the flow velocity waveforms obtained from the main branches of both uterine arteries at the level of the inner cervical ring. After exclusion of six patients with intrauterine gestation, 41 patients were referred for laparoscopy and exploratory laparotomy. This was needed for confirmation of the diagnosis and final management. The diagnosis was based on macroscopic finding alone or histopathology examination of the specimens removed during surgery or both. The transvaginal ultrasound and pulsed colour Doppler findings were correlated with surgical findings. **Statistical Analysis:** The results were presented as number, percent, mean ± standard deviation (SD), sensitivity, specificity, positive predictive value, negative predictive value, accuracy, association between variables were measured by using t-test, chi-square test when appropriate. The association was considered to be statistically significant when p value <0.05, simple linear correlation and regression were obtained.

RESULTS:

Forty-seven women were enrolled. Six patients with intrauterine gestation were excluded. The characteristics of these women are shown in table (1). Lower abdominal pain with vaginal bleeding were the common presenting symptom (31.7%). The commonest risk factor for ectopic pregnancy was pelvic inflammatory disease (PID) (31.2%), while more than one risk factor was disclosed in 20 patients (62.5%), as shown in table (2). Thirty-two patients (78%) had surgically confirmed ectopic pregnancies with nine cases with non ectopic pregnancy (22%), as shown in figure (1). Tubal pregnancy was diagnosed by transvaginal sonography in28 of 32 patients with ectopic pregnancy with a sensitivity of (87.5%). Specificity of (33.3%), positive predictive value

(PPV) (82.4%), negative predictive value (NPV) (42.9%), false positive (66.7%) and false negative (12.5%) with accuracy of (75.6%), while 30 of 32 patients were diagnosed by colour Doppler sonography with a sensitivity of (93.8%), specificity of (55.6%), PPV (88.3%), NPV (71.4%), false positive (44.4%) and false negative (6.2%) with accuracy of (85.4%) as shown in table (3) and figure (2). Figure (3) demonstrate colour flow in the trophoblastic tissue. Colour flow in the trophoblastic tissue was detected in 19 (59.3%) of the 32 tubal pregnancies. The mean RI of these low-resistance flows was (0.49 ±0.1), with range of (0.33-0.81). The distribution of serum β- hCG values and the related trophoblastic flows in 32 patients with tubal pregnancy was shown in table (4). The mean β- hCG levels was significantly higher (P<0.0001) in the cases with trophoblastic flow (984.9 ±154.5mIU/ml) than in those with no colour flow signals (695.2 ±141.3 mIU/ml) as shown in table (5). The RI tended to decrease with increasing β- hCG levels, and there was a negative correlation between them. The correlation between β- hCG and RI was highly significant (P<0.001), as shown in figure (4). The average PI of the uterine arteries was (2.29 ±0.30) range (1.7-3.30);that of the ipsilateraluterine arteries (2.14±0.28)was lower than that of the contralateral ones (2.44±0.32). The difference was highly significant (p<0.0001).In addition, the mean PI of the uterine arteries on the side of tubal pregnancy (ipsilateral) was (1.15±0.31). This was not significantly (p<0.537) lower in the patients with trophoblastic flow than in those without detectable colour flow (2.111+0.22). No correlation was seen between the PIs of the uterine arteries and serum β-hCG levels (R=0.150, P=0.540).

Table 1: The characteristics of patients with ectopic pregnancy.

Characteristics	
Age (years) Mean ± SD	26.7 ± 5.1
Range	18-41
Parity Range	0-8
Duration of gestation (days) Mean ± SD	51.9 ± 10.2
Range	30-76
Clinical symptoms	
Vaginal bleeding – (% , n)	24.3% , 10
Abdominal pain or pelvic pain – (% , n)	21.9% , 9
Vaginal bleeding ± abdominal pain – (% , n)	31.7% , 13

n: number

Table 2: The risk factors of ectopic pregnancy.

Risk factors	Ectopic pregnancy	
	No.	%
Age >35 years	4	12.3
Prior ectopic pregnancy	5	15.6
Pelvic inflammatory disease (PID)	10	31.2
Intra-uterine contraceptive devices (IUCD)	2	6.2
Induction of ovulation	5	15.6
Smoking ≥ 20 cigarettes/day	2	6.2
Previous surgery	9	28.1
More than one risk factor	20	62.5
None	3	9.4

Table 3: The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of TVUS and Doppler in diagnosing ectopic pregnancy.

	TVUS	Doppler
Sensitivity	87.5%	93.8%
Specificity	33.3%	55.6%
Positive predictive value	82.4%	88.3%
Negative predictive value	42.9%	71.4%
Accuracy	75.6%	85.4%

Table 4: The distribution of serum β- hCG and the related trophoblastic flow of the 32 patients with tubal pregnancy.

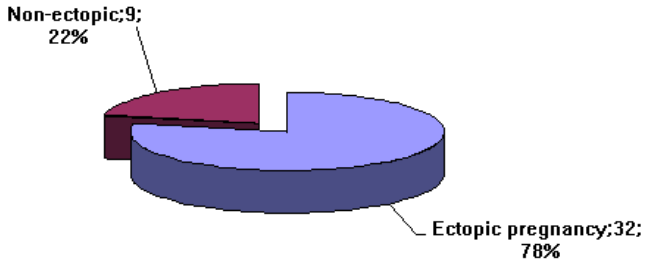
β -hCG level (mIU/ml)	Detectable flow	Undetectable flow
450-900	9	12
901-1500 & above	10	1
Total	19	13

χ^2=6.91, d.f. =1, P=0.009 (Highly significant)

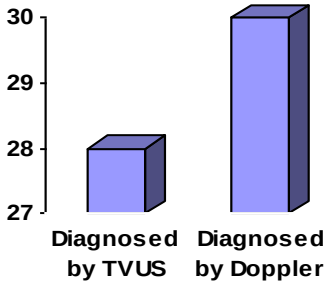
Table5: The mean β-hCG in relation to trophoblastic flow of tubal pregnancy.

	Trophoblastic flow		P value
	Detectable (n=19) Mean±SD (Range)	Undetectable (n=13) Mean±SD (Range)	
β-hCG (mIU/ml)	984.9 ±154.5 (800-1500)	695.2±141.3 (450-920)	0.0001*

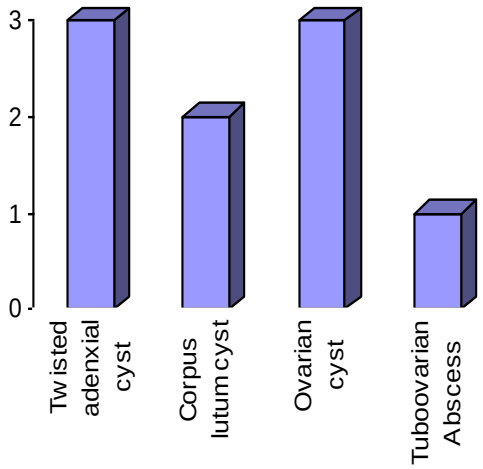
* Significant difference



(A)



(B)



(C)

Figure 1: Demonstrate number and percentage of ectopic and non ectopic pregnancy cases found at surgery (A). The No. of diagnosed ectopic cases detected by TVUS and color Doppler (B). The No. of diagnosis found at surgery for non ectopic cases (C).

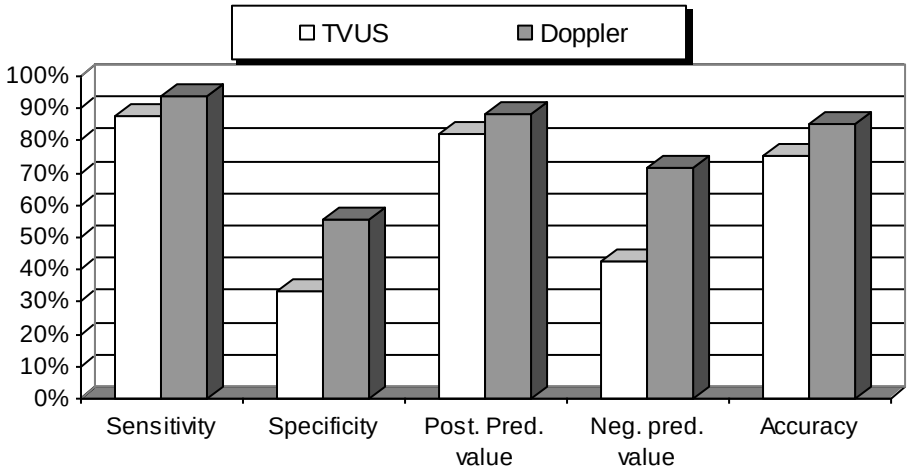


Figure 2: The sensitivity, specificity, PPV, NPV and accuracy of TVUS and Doppler in diagnosing ectopic pregnancy.

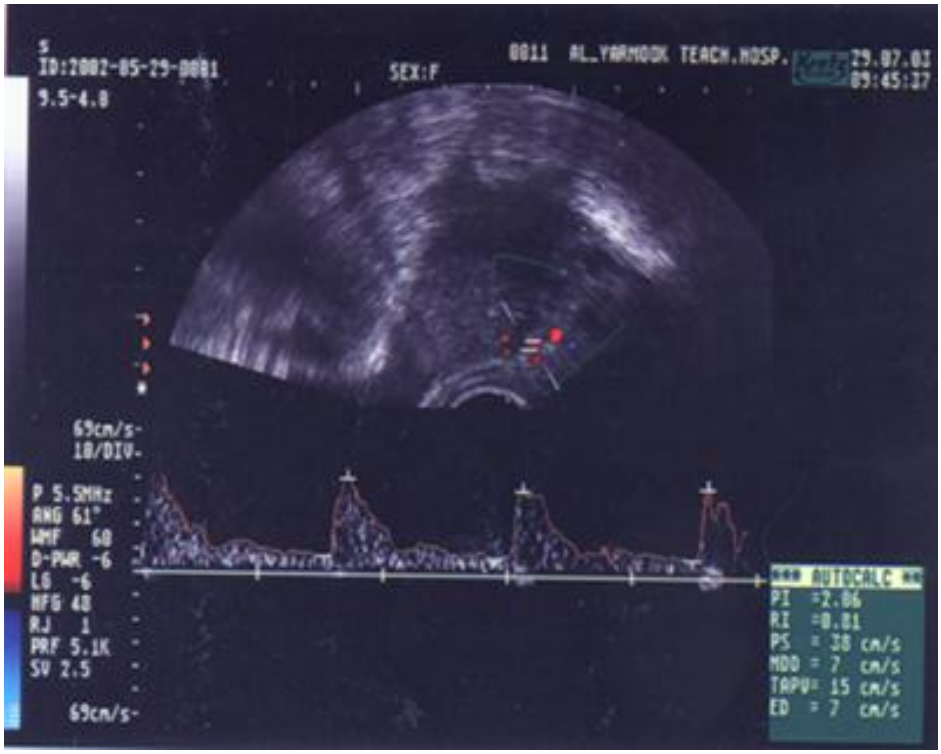


Figure (3): Trans-vaginal color flow demonstrates trophoblastic flow in an ectopic pregnancy.

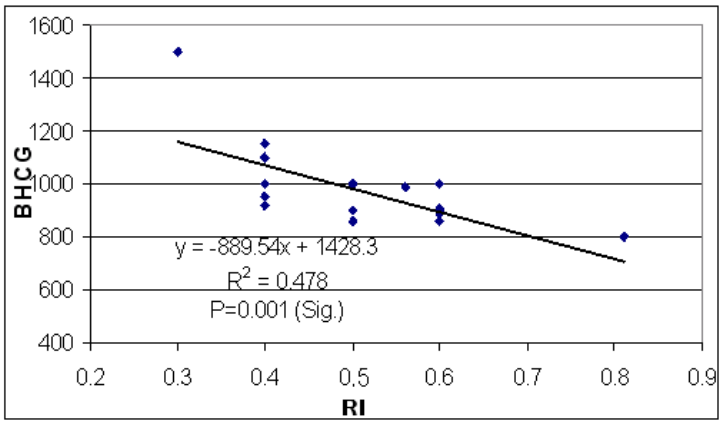


Figure 4: The correlation between β-hCG and RI in ectopic pregnancy.

DISCUSSION:

The incidence of ectopic pregnancy has increased over the last 20 years and has become a major public health problem [13]. Despite improvement in diagnosis and treatment, in industrialised countries ectopic pregnancy remains the leading cause of maternal mortality during the first trimester, where it is responsible for 10% of all maternal deaths[14,15]. This increase in incidence result, inpart, from an increase in pelvic inflammatory disease (PID). The largest risk factors are upper genital tract infection due to sexuality transmitted infections (STIs). Of the serious long term sequelae of PID are post-infection scarring, adhesion formation leading to infertility and ectopic pregnancy (16). Numerous case-control studies provide evidence for an associaton between salpingitis; and ectopic pregnancy: they show that the risk of ectopic pregnancy is two to seven times higher following this infection [17,18] and 50% of patients with an ectopic pregnancy had a history of salpingitis [17,18]. In our study, the highest risk factor for ectopic pregnancy was PID, this was evident in (31.2%) of cases. This was in concordance with previous studies as PID & STIs being the major risk factor [17,18] . Accurate diagnosis of ectopic pregnancy rests on a combination of clinical history, serum β-hCG and sonographic appearance. Transvaginal colour Doppler sonography has increased the reliability of the early normotopic and ectopic pregnancy and allowed the study of blood flow in the embryonal and early placental vessels [19,20] . In our study transvaginal sonography disclosed the diagnosis correctly with sensitivity of (87.5%) and specificity (33.3%), while colour Doppler sonography disclosed the diagnosis with sensitivity of (93.8%), the accuracy of ectopic pregnancy diagnosis was (75.6%) by transvaginal sonography while it was (85.4%) with colour Doppler. This finding was in agreement with Taylor et al who identified in this study an increased sensitivity of diagnosis in (95%) with endovaginal colour flow imaging while the sensitivity eas only (53%) with endovaginal imaging alone. Colour Doppler imaging was able to detect trophoblastic flow in only (59.3%) of cases in our stuffy. In the study of Tekay et al[21], trophoblastic flow was demonstrated in (50%) o cases which was in concordance with our results where as the figure in previous transvaginal series was (87.6%) [22]. The difference is probably due to rather low serum β-hCG levels measured here. Taylor et al [19] hypothesized that absence of a detectable Doppler signal in an ectopic pregnancy may indicate a non-viable gestation. In our study a highly significantdifference was found between the distribution of serum β-hCG and the related trophoblastic flow, ten out of eleven cases with β-hCG range (901-1500 mIU/ml & above) were found to have detectable flow.While only nine out of twenty-one cases with low β-hCG values (a range of 450-900 mIU/ml_)showed detectable flow as in table (4). The range of the RI (0.33-0.81) of the trophoblastic flow patterns in our study was broader and the mean value was (0.49±0.1). This was somewhat higher than the previous figures of (0.38±0.2) reported by Taylor et al [19] and (0.36±0.02) reported by Kurjak et al [22] and slightly lower than Tekay et al [21] (0.51±0.12). Because of inter-observer and technical variability in the hardware and software among different devices,

comparisons between results from different centers may not be relevant. The broad range of RIs presented here does not support the use ofan absolute discriminatory index index value of differential diagnsis of tubal pregnancy. The lack of a detectablecolour trophoblastic flow in the majority of patients with low β-hCG measurement in our series is supported by Taylor et al [19,20] Hypothesis. Moreover the RIs tended to decrease with increasing β-hCG values, and comparison of the mean β-hCG level showed a significant difference between the patients with trophoblastic flow and those without. Because β-hCG is a sensitive marker of an active trophoblast, it is logical to suspect an early pregnancy or its death in these cases with low serum β-hCG values. There isa negative correlation between the RIs of trophoblastic flows and β-hCG levels which is highly significant (P=0.001) as shown in figure (4). These results where in comparison with other studies [21,22]. A viable ectopic trophoblast, represented by a low impedence flow, seems to alter the pulsatility of the waveform of the ipsilateral uterine artery. In our study, we found lower PI of ipsilateral than that of the contralateral uterine artery which was highly significant (P<0.0001) while Tekay et al found that the average PI of ipsilateral uterine artery was slightly lower than that of the contralateral uterine arteries but the difference was not statistically significant, therefore our results demonstrated that there is a significant relation between the location of the tubal pregnancy to PIs of the uterine arteries. Therefore monitoring uterine artery PIs does aid in identifying the side of tubal pregnancy.

CONCLUSION:

Colour imaging is a good supplementary diagnostic tool in modern managemet of ectopic pregnancy. The addition of colour Doppler flow imaging to transvaginal sonography allows increase sensitivity in the detection of ectopic pregnancy.

REFERENCES

1. Bangsgaard N, Lund C, Ottesen B, Nilas L. Improved fertility following conservative surgical treatment of ectopic pregnancy.Br J Obstet Gynaecol 2003;110:765-70.
2. Monga A. Disorders of early pregnancy. In Gynaecology By Ten Teachers,18th edn. Edward Arnold, 2006; 89-102.
3. Skjeldestad FE, Hadgn A, Eriksson N. Epidemiology of repeat ectopic pregnancy: a population-based prospective cohort study. Obstet gynaecol 1998; 91:129-135.
4. Ego A, Subtil D, Cosson M, Legoueff F, Houfflin-Debarge V, Querleu D.Survival analysis of fertility after ectopic pregnancy.Fertil Steril 2001;75:560-566.
5. Ankum W. Laparoscopy in the diagnosis of ectopic pregnancy. In: Grudzinskas JG, O'Brien PMS, editors. Problems In early pregnancy:Advances in diagnosis and treatment. London:BJOG press;1997;154-9.
6. Mol B, Van der Veen F. Role of transvaginal ultrasonography in the diagnosis of ectopic pregnancy. Fertil Steril 1998;70: 594-5.
7. Ankum W, Hajenius P, Schrevel L, Van der Veen F. Management of suspected ectopic pregnancy:impact of new diagnostic tools in 686 conservative cases. J Reprod Med 1996;41:724-8.
8. Candous G, Okaro E, Bourne T.Complimentary role of ultrasound and serum hormone measurements in the management of early pregnancy complications. In:Studd J, editor. Progress in Obstetrics and Gynaecology, vol 16. Edinburgh: Churchill Livingstone; 2005;1-21.
9. Kurjak A, Kupesic S. Ectopic pregnancy. In:Textbook on Color Doppler in Gynaecology, Infertility and Obstetrics; 1999.p.54-58.
10. Tsakos E,Amso N. Ultrasound diagnosis of ectopic pregnancy:common pitfalls. Gynaecology Forum 1997;2:12-15.
11. Pellerito Js,Taylor KJW,Quedens-Case C, Hammers LW, Scott LM, Ramos IM. Meyer WR.Ectopic pregnancy: evaluation with endovaginal color flow imaging. Radiology 1992; 183:407-411.
12. Sohaey R, Branch DW.Ultrasound in Obstetrics. In:Scott JR, Di Saia PJ, Hammond CB, Spellacy WN, editors.Danforth's Obstetrics & Gynaecology .8th edn. Lippincott Williams & Wilkins;1999.213-242.
13. Job-Spira N, Coste J, Bouyer J. Minimising the risk of ectopic pregnancy. Gynaecology forum 1997;2:7-11.
14. Ory ST.New Options for diagnosis and treatment of ectopic pregnancy. J Am Med Assoc 1992;267:534-7.
15. Centers for Disease Control. Ectopic pregnancy-United States,1988-1989. Morbid Mortal Week Rep 1992;41:591-4.
16. Mann MC.Infection and sexual health. In:Louesley DM,Baker PN,editors. Obstetrics and gynaecology An evidence-based text for MRCOG 1st edn. Arnold;2004;p.671-674.

17. Coste J, Job-spira N, Fernandez H, Papiernik E, Spira A. Risk factors of ectopic pregnancy: a case-control study in france, with special focus on infectious factors.Am J Epidemiol 1991;133:839-49.

18. Coste J, Laumon B, Bremond A, et al. Seually transmited diseases as majo causes of ectopic pregnancy:results from a large case-control study in France. Fert Steril 1994;62:289-95.

19. Taylor KJW, Ramos IM, Feyock AL, Snower DP, Carter D, Shapiro BS, Meyer WR, Cherney AH.Ectopic pregnancy:Duplex Doppler evaluation. Radiology 1989;173:93-97.

20. Taylor KJW, Meyer WR. New techniques in the diagnosis of ectopic pregnancy.Obstet Gynaecol Clin North Am 1991;18:39-54.

21. Tekay A,Jouppila P.Color Doppler flow as an indicator of trophoblastic activity in tubal pregnancies detected by transvaginal ultrasound. Obstet Gynaecol 1992;80:995-9.

22. Kurjak A,Zalud I, Schulman H. Ectopic pregnancy: Transvaginal color Doppler of trophoblastic flow in gestionable adnexa. J Ultrasound Med 1991; 10:685-9.