The Role of Transvaginal Duplex Doppler Ultra Sonography in Early Detection of Tubal Pregnancy

TAREK R. ABBAS, M.D.*; HESHAM F.A. ABOU SENNA, M.D.* and HOSAM EI-DIN G. MOHAMMAD, M.D.**

The Department of Obstetrics & Gynecology*, Faculty of Medicine, Al-Azhar University and Radiology** Department, Faculty of Medicine, Assiut University.

Abstract

Introduction: Ectopic pregnancy is not recognized in 5-23% of all cases using state-of-the-art diagnostic procedures.

Aim of the Work: To evaluate the role of transvaginal duplex Doppler ultra-sonography in early detection of tubal pregnancy.

Material and Methods: Blood flow in tubal arteries was measured using a trans-vaginal duplex Doppler ultra-sonography system. A 3.5 MHz Doppler transducer coupled to a 5 MHz imaging transvaginal sector probe was used to detect flow characteristics in the tubal branch of the uterine artery. This was performed in 3400 patients.

Results: There was a significant increase in the blood flow on the tubal gestation side (p<0.0001, z =-4.08). This between-side difference was determined using qualitative frequency shift analysis. The mean reduction in the resistance index on the side with the ectopic pregnancy as compared to the contralateral side was 15.6%. These changes appear to be due to trophoblast invasion. Between-side differences showed no dependence on gestational age (between gestational weeks 4 and 12 post menstruation). We compared these data with those from the control group (early viable intrauterine pregnancy and early intrauterine pregnancy failure).

In the control group, the impedance to flow, expressed as 'resistance index', showed no significant between-side difference. All control groups had significantly higher mean resistance index values than the ectopic pregnancy side, but did not differ from the contralateral side of the ectopic pregnancy group. The advantages of this new method in diagnosing ectopic pregnancy are early detection, non-invasively and immediate results.

Conclusion: With this non-invasive method, the experienced investigator can identify within minutes patients at enormous risk of ectopic pregnancy out of a group of unselected women. The examination can be performed under almost any circumstances and has good patient compliance.

Key Words: Transvaginal duplex doppler – Early detection – Tubal pregnancy.

Introduction

WHEN a patient presents with suspected ectopic pregnancy [1,2], history, clinical examination and analysis of gestational hormones (human chronic gonadotropin (hCG) in urine and quantitative concentration in serum) are the first routine diagnostic steps [3-8]. For the past 20 years, transabdominal sonography has been used as a diagnostic tool with varied results. Adnexal and cul-de-sac masses, thick (progesterone-stimulated) endometrium and cul-de-sac fluid were all described [19,20] because of inherent physical and clinical limitations.

Ectopic pregnancies are usually only diagnosed by transabdominal at a relatively advanced stage. In 1983, transvaginal ultrasonography was introduced to replace transabdominal imaging [21-29]. In many cases, invasive diagnostic steps, such as culdocentesis and pelviscopy, are needed to confirm the diagnosis of ectopic pregnancy'. Organ-saving treatment is only possible when an 'ectopic pregnancy' is accurately and quickly diagnosed. The earlier the diagnosis, the better on the literature, chances of retaining functional tubes [30-32].

In the literature, we find false-negative diagnoses of ectopic pregnancy in 5-23% of patients diagnosed by abdominal & transvaginal Ultrasound [33,34]. Reviewing our own data, we found an incidence of 5.7% false-negative results. In our service, conventional transvaginal scanning predicts an ectopic pregnancy with a sensitivity of 92%, a specificity of 52% and a predictive value of 0.87 [35].

Searching for a new, independent diagnostic step to improve the detection of ectopic pregnancy,
we hypothesized that a change in tubal blood flow might be caused by trophoblast invasion [36]. We used transvaginal pulsed wave color Doppler ultrasonography to evaluate flow characteristics [37-52].

**Material and Methods**

This prospective study was carried out from March 1st 2007 – April 30th 2009, in Al-Rafie Hospital (Mekkah Al-Mukarramah, Saudi Arabia and Sayed Galal University Hospital, Cairo Egypt). During this period 3400 women screened at an early stage of pregnancy (mean age, 26.5 years; range, 15-41 years). All patients were unselected and each patient volunteered for the examination. The Doppler flow investigation was performed at the time of their first visit. All of them had a positive result in the semi-quantitative hCG test of blood, most were suffering from pelvic pain or had vaginal bleeding. All qualitative Doppler blood flow measurements were performed prospectively without knowledge of final diagnosis or routine diagnostic results. At the end of the study, we divided all pregnant women into three groups according to definite diagnostic findings.

**Group definitions:**

Altogether 3400 patients were included in this study, 34 in the ectopic pregnancy group, and 408 in early intrauterine pregnancy failure group, 2958 in the early viable intrauterine gestation group. These groups were defined according to the following findings:

1- Ectopic pregnancy was confirmed by laparoscopy and histopathology. The mean duration of secondary amenorrhea was 5.8 weeks (4-12 weeks post-menstruation) at the time of Doppler flow investigation. Twenty one patients were managed by laparoscopic salpingostomy, nine patients by laparotomy with salpingotomy & four patients treated by methotrexate (50ml/m² of body surface area).

2- Early viable intrauterine gestation was verified in 2958 women. The course of pregnancy was uneventful and all patients were cared for in our department until birth.

3- Early intrauterine pregnancy failure’ was determined by histopathology of curettage or spontaneous abortion material.

**Management:**

We used the Acuson 128 computed sonography system. Our equipment included a 3.5 MHz pulsed color Doppler transducer to a 5 MHz imaging transvaginal sector probe. During examination, the patient layed in a supine position on a two-level foam mattress, so that the upper part of the body was on a higher level. With her knees bent and slightly elevated, the patient’s feet rested on the mattress. In this special position, the examiner was able to manipulate the transvaginal probe at different angles, rotate and slide it. A coupling gel was applied to the probe, which was then inserted into a lubricated digit of a sterile rubber glove. The probe was introduced into the vagina. Scanning in a median longitudinal section through the uterus, we searched for the right and left cornual region of the endometrium. Continuing from there, we detected the hypoechoic strip in the myometrium. Adjacent to this, we saw the tubal branch of the ascending arch of the uterine artery color Doppler imaging enabled the investigator to be sure of achieving the right position with ease. Switching to the Doppler mode, time-velocity waveforms of the arterial flow were displayed (Figs. 1,2).

![Fig. (1):](A) Duplex color Doppler sonogram of the Fallopian tube and the tubal artery of the extragynecologic tubal pregnancy side. The picture shows the transvaginal B-mode sector the Doppler flow waveforms and qualitative frequency shift analysis of the tubal artery. (B) Duplex color Doppler sonogram of the Fallopian tube and the tubal artery of the same patient: Contralateral side.
We used the resistance index (RI) to characterize the Doppler frequency shift \[53\]. This form of qualitative analysis is independent of the insonation angle. The resistance index was calculated on the basis of at least six waveform singles of good quality. A high-pass filter was used to eliminate Doppler shifts of less than 100 Hz. The resistance index as a numerical value is easy to measure. Qualitative blood flow was analyzed in the right and left tubal arteries. Adequate measurements were obtained in all cases. The time of investigation was less than 15 min. in each case.

**Statistical analysis:**

Apart from descriptive statistical methods, we used the two-tailed Wilcoxon signed-rank test for statistical analysis to compare between-side differences of the resistance index, the student's \(t\)-test, 95% confidence intervals and one-way ANOVA to evaluate mean resistance indices and the percentage of the between-side difference of the resistance index of blood flow in the tubal arteries (PSDTBF). Simple regression analysis and Pearson coefficients were computed to investigate the correlation between gestational age, hCG and PSDTBF.

**Results**

Analyzing our qualitative Doppler flow examination of the tubal blood circulation, we found a significant decrease in the resistance index for blood flow in the tubal arch of the uterine artery on the extra uterine pregnancy side (RI mean, 0.72, SD, 9.91, range, 0.50-0.91), depicting a decreasing diastolic resistance. The mean resistance index on the contralateral side of the tubal blood circulation in the same patients was 0.85 (range, 0.71-1.00). We evaluated the percentage of between-side difference of blood flow in the tubal arteries (PSDTBF) in each patient. To compute the PSDTBF in patients presenting with ectopic pregnancy, we subtracted the RI of the tubal blood flow in the ectopic gestation side from the RI of the contralateral side. The mean PSDTBF was 15.6% in the ectopic pregnancy group. Flow rates analyzed by resistance index showed no between-side difference in all other groups. In all of them, using the most conservative approach, we obtained the PSDTBF by subtracting the lower value of RI from the higher one, regardless of the side location. Due to the fact that the corpus luteum occurs with an equal probability on each side, this method shows the maximal possible influence of the corpus luteum on the PSDTBF. In our study, we analyzed the mean PSDTBF as 3.9% in the control groups. These results suggest that the high PSDTBF is caused by the invasion of the trophoblast. The mean RI values of the 'early viable pregnancy' group were 0.87 on the right side (range, 0.68-1.00) versus 0.87 (range, 0.71-1.00) on the left side, which is not significant.

In the 'early intrauterine pregnancy failure' control group, the mean RI values were 0.82 (range, 0.62-1.00) on the right side, and 0.82 (range 0.60-1.00) on the left (Fig. 3).

The analysis of the percentage of the between-side difference in the resistance index in tubal blood flow shows a mean difference of 15.6% (95% confidence limits (CL), 11.2-20.0%) in the ectopic pregnancy group, 4.9% (SD, 4.0% 95% CL, 3.5-6.3%) in the early viable intrauterine gestation group and 3.6% (SD, 3.4%, 95% CL, 1.6-4.9%) in the 'early intrauterine pregnancy failure' group.
The Role of Transvaginal Duplex Doppler Ultra Sonography

Ectopic pregnancy

Contralateral side

Viable pregnant left

Viable pregnant right

Abortus left

Abortus Right

* Indicates the significant difference of ectopic pregnancy side to all other groups.

Fig. (3): Means and standard deviations of the resistance indices of all investigated study groups. Bars and numbers represent means.

The test for equality of the means of the PSDT-BF in all four groups was highly significant: $F = 23.00, p < 0.0001$.

As a further important result of the study, no correlation was seen between the blood flow in the tubal artery, measured by the resistance index, and the gestational age in the ectopic and early viable intrauterine pregnancy study groups. The observation time was between the 4th and 12th weeks of gestation post-menstruation. The Pearson coefficients for correlation between PSDTBF and gestational age were 0.071. The measures between-side differences are independent of the time of gestation in the ectopic pregnancy group. This side difference can even be detected in the 4th week of gestation post-menstruation. Also, there was no correlation between hCG levels and qualitative Doppler blood flow analysis in ectopic pregnancy (Pearson correlation coefficient, 0.081). Nevertheless, the well-known increasing levels of hCG levels were seen in continuing pregnancy.

Analyzing the results of the extra uterine pregnancy group, three patients presented with contrary between-side difference compared to all other women in this group.

As an explanation, a large ruptured bleeding corpus luteum cyst was found on the contralateral side in two patients, (case 1: corpus luteum cyst diameter 48mm, case 2: diameter 50mm). In our view, the normal corpus luteum does not significantly affect tubal blood flow, whereas a large ruptured bleeding corpus luteum cyst may confuse the diagnosis of ectopic pregnancy by mean of Doppler blood flow analysis. In the third patient with no between-side deference in the analysis of tubal blood flow, the diagnosis of tubal abortion in the 4th week of gestation post-menstruation was verified morphologically and histophthologically.

In 15 patients presenting with ectopic pregnancy, there were no direct or indirect sono-morphological signs of ectopic pregnancy.

Five women had para-ovarian masses, three of them also showed free fluid in the pouch of Douglas. Only four out of the 'ectopic pregnancy' group complained of vaginal bleeding.

A cut-off point of 9% between-side difference in tubal blood flow was established for diagnosing ectopic pregnancy. The sensitivity of this Doppler technique for the detection of an ectopic tubal pregnancy was 83% and specificity 87%. Characteristic between-side differences for the resistance index are shown in Fig. (4), for all four study groups.

![Fig (4): Median and percentiles of resistance index between-side differences of all study groups. Boxes represent 25%, 75% and 50% centiles, bars the 10% and 90% centiles.](image)

**Discussion**

Time is of the essence of every physician faced with the question of ectopic pregnancy. Routine diagnostic procedures in many cases take more time than the investigator likes not only in asymptomatic women, but even in patients presenting with the whole range of clinical symptoms, such as pelvic pain, spotting and secondary amenorrhea. Therapy may therefore, come too late to prevent secondary damage of reproductive function.

Consider a female patient presenting with short-term secondary amenorrhea, positive hCG levels confirming pregnancy. The woman insists on an ultrasound examination, but the investigator finds nothing to indicate an intrauterine or ectopic pregnancy, because typical sonographic signs of pregnancy cannot be detected earlier than the 4th or 5th week of gestation. Even on transvaginal sonography, a chorionic sac, the yolk sac, fetal heart action or the fetus cannot be seen earlier than the 4th week post-menstruation. Therefore, a thick
progesterone-stimulated endometrium has no diagnostic value for distinguishing intrauterine from ectopic gestation. Even adnexal tumours have multiple etiologies. In this early stage of gestation, is there any means of answering the all-important question: Viable intrauterine or ectopic pregnancy?

Observation of the course of gestation as well as serial hCG and ultrasound examinations will ultimately provide a clear diagnosis within weeks. If there is a suggestion of ectopic pregnancy, invasive diagnostic methods such as pelviscopy or culdocentesis follow.

There is not a lack of a diagnostic method to differentiate early intrauterine from ectopic pregnancy. Our result with qualitative Doppler frequency shift analysis in tubal arteries offer a completely new direction for the diagnosis of ectopic gestation. For the first time, it is possible to make a correct diagnosis of ectopic gestation as early as the 4th week of pregnancy. Commonly used Doppler techniques to evaluate ectopic pregnancy require the detection of an adnexal mass for the visualization of a peri-trophoblastic circulation. However this does not permit earlier recognition than when customary sonographic procedures are used. Measuring the blood flow in the tubal arteries does not call for the typical sonographic signs characterizing ectopic pregnancy and therefore permits earlier diagnosis. Although lacking many clear morphological signs, we found both tubal arteries in each case.

Conclusion:
With this non-invasive method, the experienced investigator can identify within minutes patients at enormous risk of ectopic pregnancy out of a group of unselected women. The examination can be performed under almost any circumstances and has good patient compliance.

This method demands highly sophisticated technical equipment and a certain amount of experience on the part of the investigator. The use of this method to screen all pregnant women is therefore unlikely, although if instituted it might reduce morbidity and secondary damage.

References
The Role of Transvaginal Duplex Doppler Ultra Sonography


