



The role of Doppler indices of uterine arteries to predict the fate of threatened miscarriage in 1st trimester

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Abstract

Background: The possibility to identify uteroplacental vascular alterations from the first trimester of pregnancy could provide a diagnostic tool for the clinical management of early pregnancies complicated by uterine bleeding. In patients with normal pregnancies, when embryo vitality is confirmed, the rate of pregnancy loss is low (3.2%). **Objective:** To assess the role of Doppler indices of uterine arteries to predict the fate of threatened miscarriage in 1st trimester. **Conclusion:** Uterine artery Doppler analysis has the potential to predict pregnancy complications associated with uteroplacental insufficiency before the onset of clinical features.

Keywords: Uterine artery Doppler, Threatened Miscarriage.

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Introduction

Miscarriage is defined as interruption of pregnancy before viability, it may occur early before 12 week or late from 12 to 20 week^[1].

Threatened abortion defined by the world health organization (WHO) as pregnancy-related bloody vaginal discharge or frank bleeding during the first half of pregnancy without cervical dilatation^[2].

Incidence:

The incidence of threatened miscarriage is as high as 31%, though that incidence decreases to approximately 10% when considering only losses occurring in clinically recognized pregnancies^[3].

Clinical Manifestations

The clinical features of threatened abortion are vaginal bleeding before 20 weeks of gestation, accompanied by cramping pain, without changes of the cervix and without evidence of embryonic demise^[4].

The bleeding during a threatened abortion is typically mild to moderate. The abdominal pain may present as intermittent cramps, suprapubic pain, pelvic pressure, or lower back pain^[5].

Diagnostic Evaluation of Miscariage

The prediction of miscarriage is made by history, physical exam, measurement of beta-human chorionic gonadotropin (beta-hCG), and an ultrasound.

History — A history of vaginal bleeding and/or crampy pelvic pain in a woman with known



pregnancy is suggestive of miscarriage but is not diagnostic. The pregnant women may also note a reduction in pregnancy-related symptoms that were previously present. Occasionally, can be diagnosed by history alone in a patient who reports heavy vaginal bleeding with a known intrauterine pregnancy whose subsequent human chorionic gonadotropin (hCG) testing is negative. However, in most cases, further evaluation with ultrasound or serial hCG testing is required for definitive diagnosis^[6].

Imaging :

In prediction of threatened miscarriage the sonographic data have an important role that interacts with other clinical and chemical factors. Some parameters considered as prognostic factors that include irregular wall of gestational sac, peri-gestational hemorrhage and embryonic bradycardia. Color Doppler is used to get information about the presence, direction and velocity of blood flow by assessment of uterine artery indices^[7].

Prognostic Feature of Miscarriage

Bleeding in the first trimester can originate from the uterus, cervix, or vagina, or it can be extra-genital. Thorough physical examination is essential to differentiate between genital and extra-genital causes. After exclusion of extra-genital causes, several parameters have been associated with prognosis

1. History

Older women are at increased risk of miscarriage in the general population. And the rate of fetal loss declines with advancing gestational age^[8]

2. Sonographic evaluation

Sonography can usually differentiate between an intrauterine pregnancy (viable or non-viable), a molar pregnancy, or an inevitable abortion.

Furthermore, sonographic features of pregnancy have been proposed as predictors.

Gestational sac diameter

An empty gestational sac with a diameter of at least 15 mm at seven weeks and 21 mm at eight weeks has diagnostic accuracy of 90.8% in threatened miscarriage^[9].

A mean sac diameter of at least 17 mm without an embryo or 13 mm without a yolk sac can predict non-viable gestation with a specificity and a positive predictive value of 100%^[10]

Fetal heart activity

The average fetal heart rate is between 110 and 160 beats per minute. It can vary by 5 to 25 beats per minute. The fetal heart rate may change as the baby responds to conditions in the uterus. An abnormal fetal heart rate may mean that baby is not getting enough oxygen or that there are other problems^[11].

Fetal heart activity should be visible with trans-vaginal sonography once the fetal pole is at least 5 mm long at fifth week. The introduction of trans-vaginal ultrasound has greatly improved the assessment of threatened abortion, clarifying the differential diagnosis of missed abortion, ectopic pregnancy, blighted ovum, and threatened abortion with a live embryo^[12].

Most prospective series found a loss rate of 3.4-5.5% if bleeding occurs after fetal heart activity starts^[13].

Identification of fetal heart activity by ultrasound predict pregnancy continuing beyond 20 weeks in 97% on cases. Previous studies have suggested a substantially higher spontaneous loss rate for early pregnancies with embryonic heart rates of 90 bpm or less^[14].

Patients with slow fetal heart rate (<120 bpm) in first-trimester threatened abortion may eventually be at risk for pregnancy loss. If it

survives the first trimester, the likelihood of subsequent death is low^[15].

Crown rump length (CRL)

Crown rump length is the length of the embryo or fetus from the top of its head to bottom of torso. It is the most accurate estimation of gestational age in early pregnancy. CRL is measured as the largest dimension of embryo, excluding the yolk sac. It is used as a primary measure of gestational age between 6-13 weeks. After 13 weeks, head circumference, biparietal diameter, and femur length measurements become more useful measurements for assessing fetal growth. If the original CRL measurement was adequate, the measurement is considered the baseline for all subsequent age measurements. The earlier in pregnancy a scan is performed, the more accurate the age assignment from crown rump length^[16].

Overall, the accuracy of sonographic dating in the first trimester is +/-5 days (95% confidence range). With a CRL ≥ 7 mm the Cardiac activity should be present in the embryo. If it not detected at this size on transvaginal scanning performed by an experienced operator, it is an indicator of failed early pregnancy (missed miscarriage)^[17].

It has been reported that patients in whom (mean sac diameter) is less than 5 mm greater than crown rump length (i.e. MSD - CRL = < 5 mm) are prone to first trimester miscarriage, despite a normal heart rate. Chromosomal anomalies, particularly trisomy 18 and triploidy are markedly associated with growth restriction, i.e. decreased crown rump length^[16].

Fetal bradycardia and discrepancy between gestational age and crown to rump length are adverse prognostic factors^[18]. The presence of any of three risk factors (fetal bradycardia, discrepancy between gestational sac and crown to rump length, and discrepancy between menstrual and sonographic age by more than one week) increases the rate of abortion from

6% when none are present to 84% when all three are present^[9].

Subchorionic haematoma

The prognostic value of a subchorionic haematoma in ultrasound has been disputed. Although a large separation has been associated with about a threefold increase of risk of miscarriage (19% vs 71%) in women with bleeding^[19].

The presence of an intrauterine haematoma in the first trimester of pregnancy increases the risk of severe obstetric complications, irrespective of the presence of symptoms of threatened miscarriage^[20].

3. Biochemical evaluation:

Serum β hCG

Women with threatened miscarriage in their first trimester have lower serum hCG values compared with women continuing the pregnancy and asymptomatic pregnant women^[21].

If the pregnancy fails to develop a placenta, then the levels may be normal initially but fail to rise. No single level of Beta hCG is diagnostic of early pregnancy loss and serial levels can demonstrate atypical trends in some cases. Hence, interpretation of these results should be done in conjunction with clinical and sonographic findings to arrive at a correct diagnosis^[22].

Beta-hCG is important to confirm the pregnancy and distinguish it from dysfunctional uterine bleeding or bleeding from another etiology. It helps to distinguish complete abortion from threatened abortion or ectopic pregnancy^[23].

If hCG levels don't come close to doubling after 48 to 72 hours, we have concern that the pregnancy is at risk. Medically, this may be called a possible "nonviable pregnancy, indicates the embryo is no longer developing and the body

isn't producing more hormones to support its growth^[24].

If the hCG level is above 1500-2000 mIU/mL, then transvaginal ultrasonography should detect a viable intrauterine pregnancy. A level over 3000 mIU/mL should enable one to visualize a viable intrauterine pregnancy by transabdominal ultrasonography^[25].

Progesterone concentrations

Progesterone concentrations show a narrow variation in the first trimester. The lowest serum progesterone concentration associated with a viable first trimester pregnancy is 5.1 ng/ml and a single serum progesterone measurement of at least 25 ng/ml carries a 97% likelihood for viable intrauterine pregnancy, being more sensitive than two serial hCG measurements. A single progesterone value of less than (14 ng/ml) is able to differentiate between abnormal and normal (ongoing) pregnancies with high sensitivity and specificity^[26].

In a recent series, women with threatened abortion and fetal heart activity at presentation, serum inhibin A, activin A, and hCG concentrations were much lower in cases in which the women eventually miscarried^[27].

Ovarian carcinoma antigen

Women with threatened abortion who eventually miscarried had constant or increasing concentrations of ovarian carcinoma antigen CA125 over 5-7 days, whereas those who continued with pregnancy had a constantly low or steeply declining CA125 concentration^[28].

Also, a single CA125 concentration of at least 43.1 IU/ml was associated with a greater risk of miscarriage^[29].

Uterine Artery Doppler

◆Technique:

Doppler assessment of uterine artery impedance can be performed between 11 + 0 and 13 + 6 weeks' gestation via a trans-abdominal or trans-vaginal approach. The trans-abdominal approach is the preferred method as it is less invasive with good inter observer reproducibility^[30].

1. Transabdominal Ultrasound Technique. A 5 or 3.5-MHz curvilinear trans-abdominal transducer is used. A mid-sagittal section of the uterus and cervical canal is obtained and the transducer is moved laterally until the para-cervical vessels are visualized. Color flow Doppler is applied. The uterine arteries are seen as aliasing vessels along the side of the cervix. Using pulsed wave Doppler, flow velocity wave forms from the ascending branch of the uterine artery at the point closest to the internal os are obtained, with the Doppler sampling gate set at 2mm. Care is taken to use the smallest angle of insonation (<30°) in order to achieve the highest systolic and end-diastolic velocities. When three similar consecutive waveforms are obtained, the PI can be measured. The mean PI is calculated as the average reading from each side combined. Another site for Doppler insonation of the uterine artery is at the level of its apparent cross over with the external iliac artery. Using this method, the probe is positioned approximately 2-3 cm inside the iliac crests and then directed toward the pelvis and the lateral side of the uterus. Color flow Doppler is used to identify each uterine artery. Pulsed wave Doppler is applied approximately 1 cm above the point at which the uterine artery crosses over the external iliac artery. This ensures that Doppler velocities are obtained from the main uterine artery trunk^[31].

This is similar to the technique commonly adopted for measurement of the uterine artery Doppler waveform in the second trimester^[32].

Lefebvre et al.^[32] Compared the two different trans-abdominal sites of measurement in the first trimester and correlated the findings with impedance indices obtained in the second



trimester at 21-22 weeks' gestation. Uterine artery PI values taken from the ascending branch at the level of internal os were higher than at the level of the apparent cross over with the external iliac artery. In addition, the former correlated better with mid trimester values. Measurements of uterine artery Doppler were easier to obtain at the level of the internal cervical os from its ascending branch, as the site of uterine artery cross over with the external iliac artery can be harder to locate with a smaller uterus in the first trimester. (Figure 1) provides an example of the transabdominal uterine artery flow velocity waveform.

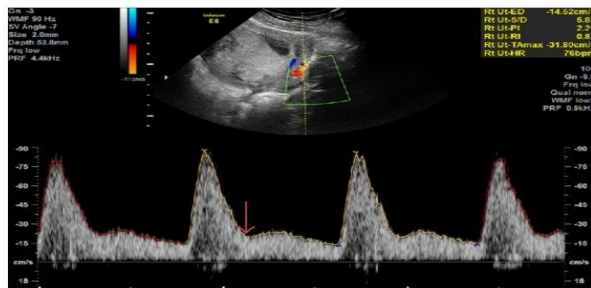


Figure (1):Trans-abdominal Doppler Interrogation of the uterine artery at the level of the internal cervical os. Uterine artery waveform demonstrating raised PI with an early diastolic notch(arrow).Reproduced with permission from Associate Professor F. da Silva Costa.

2. Transvaginal Ultrasound Technique. A 4.6–8MHz trans-vaginal transducer is used. The transducer is placed in the anterior vaginal fornix and a sagittal section of the cervix is obtained. The vaginal probe is then moved laterally until the paracervical vascular plexus is seen. Color flow Doppler is applied and the uterine artery is identified at the level of the cervico-corporeal junction. Measurements are taken at this point before the uterine artery branches into the arcuate arteries^[33].

A prospective study by **Plasencia et al**^[34], found that the mean uterine artery PI at 11–13 + 6 weeks' gestation measured trans-abdominally was lower than that measured trans-vaginally: 1.83 (95% CI: 1.78–1.89) as against 1.98 (95% CI 1.93– 2.08) ($p < 0.05$). Appropriate reference charts should thus be used.(figure 2) provides an

example of the trans-vaginal uterine artery flow velocity waveform .



Figure(2):Trans-vaginal Doppler interrogation of the uterine artery at the cervico-corporeal junction. Normal uterine artery waveforms. Reproduced with permission from Associate Professor F. da Silva Costa.

In the non pregnant state and in early pregnancy, Doppler of the uterine artery typically demonstrates low end-diastolic velocities and an early diastolic notch^[35].

Indications

Uterine artery Doppler analysis has the potential to predict pregnancy complications associated with uteroplacental insufficiency before the onset of clinical features. For almost 30 years, uterine artery Doppler studies have been utilized as a screening tool for uteroplacental insufficiency, mostly in the second trimester (from 18–23 + 6 weeks' gestation) ^[36].

Factors affecting

Uterine artery impedance can be affected by various factors such as maternal heart rate, anti hypertensive use, hormonal changes in the menstrual cycle, and chronic hyperandrogenism in the polycystic ovarian syndrome. Resistance to blood flow within the uteroplacental circulation is transmitted up stream to the uterine arteries and can be measured as an increased pulsatility index (PI) or resistance index (RI) ^[37].



Uterine artery PI values are affected by ethnicity and are lower in women with a high body mass index (BMI) [38].

Uterine artery PI and RI values decrease with increasing gestational age, a change that is thought to be secondary to a fall in impedance in uterine vessels following trophoblastic invasion. In a prospective cross-sectional study by Gómez et al., the mean uterine artery PI continued to fall in the third trimester until week 34[39].

Conclusion:

Uterine artery Doppler analysis has the potential to predict pregnancy complications associated with uteroplacental insufficiency before the onset of clinical features. In such cases, information regarding the uteroplacental circulation obtained with the use of color Doppler ultrasound could provide prognostic information. Another larger well controlled studies and systematic reviews are still needed to elucidate these conflicts.

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