Resistance Index of Uterine and Spiral Arteries as a Predictor of Threatened Miscarriage Outcome

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ABSTRACT

Background: Miscarriage is a common event in the first half of pregnancy. Improvements in Ultrasound and Doppler technology, have led to a better understanding of early pregnancy development. Such a facility may be used in turn to predict pregnancy outcome in threatened miscarriage.

Objective: To assess the ability of the Uterine artery RI and Spiral artery RI to predict outcome in cases of Threatened miscarriage

Patients and methods: Prospective observational study was conducted in the Department of Obstetrics and Gynecology at Menoufia University Hospital. The study included 90 women with gestational age between 5 – 13 w. divided into three groups; Group (A): *involved (30) women diagnosed with threatened miscarriage and was followed up and got aborted before pregnancy completed 24weeks*. Group (B): *(30) women diagnosed with threatened miscarriage and were followed up and the pregnancy continued till 24weeks*. Group (C): 30 women having singleton normal ongoing pregnancy till 24 weeks of gestation as a control group.

Results: In this study, the Doppler study of uterine arteries the subchorionic blood flow revealed that (RI) was significantly higher in the miscarried group than both continued and control groups.

Conclusion: Uterine artery RI and Subchorionic blood flow RI can predict the fate of pregnancy in cases with threatened miscarriage with high accuracy.

Keywords: Threatened miscarriage, Doppler, Uterine artery, Spiral artery.

INTRODUCTION

Threatened miscarriage is extremely common as one fourth or fifth of women experiencing vaginal spotting or bleeding during early pregnancy [1].

Some parameters are considered as prognostic factors such as the morphological characteristics of the yolk sac, adequate visualization of the embryo by transvaginal ultrasound, and changes in fetal heart rate [2]. The introduction of Doppler in obstetrics allowed the evaluation of hemodynamic characteristics at the first trimester of pregnancy [3].

The measures obtained by Doppler ultrasonography that may have prognostic value to the evolution of pregnancy include uteroplacental blood flow also known as trophoblastic flow. **Jaffe *et al.*** reported that abnormal Doppler findings were associated with a significantly higher prevalence of complicated pregnancies [4].

Recently it has been reported that the abnormal resistance of the uterine artery could be useful in the prediction of recurrent fetal loss [5].

Objective: The study aimed to assess the ability of the uterine artery RI and spiral artery RI to predict outcome in cases of Threatened miscarriage.

PATIENTS AND METHODS

This prospective observational study was conducted on 90 women in the Department of Obstetrics and Gynecology at Menoufia University Hospital after obtaining approval from the Ethics

Committee for Human Research of the Faculty of Medicine and obtaining written informed consent from the participating women.

The study was conducted from April 2018 till July 2019. The study included three groups of women (A): involved (30) women diagnosed with threatened miscarriage and was followed up and got aborted before pregnancy completed 24weeks.

Group (B): involved (30) women diagnosed with threatened miscarriage and were followed up their pregnancy completed 24weeks.

Group (C): involved 30 women having a singleton normal ongoing pregnancy till 24 weeks of gestation as a control group. Criteria of selected cases are including women with a singleton pregnancy between the 5th to 13th week of gestation and having normal ongoing pregnancy (Group c) or diagnosed with threatened miscarriage (Group B and A) after documentation of embryonic cardiac pulsation. While patients excluded from the study with any of the following criteria: women with multiple pregnancies, recurrent miscarriage (2 or more) ectopic pregnancy, molar pregnancy, maternal history of systemic diseases (Diabetes Mellitus, Hypertension, vasculopathy) or uterine anatomical abnormalities and women receiving medications such as aspirin and heparin. as well as

uterine malformation and uterine pathologies like myomas, polyps or cervical abnormalities.

After detailed history taking personal history (Name, Age) Present history (Complaint whether it is vaginal bleeding or lower abdominal pain and its analysis. Past history (Medical and surgical). Obstetric history (Parity, outcome of the previous delivery, complication of previous pregnancies).

Then general examination was performed and local examination (P/V was done to assess bleeding and cervical dilatation, speculum examination was done to exclude gynecological causes of vaginal bleeding).

Two- dimensional B-mode scan with Voluson 730 ultrasound machine 5 MHz transvaginal probe was first performed after emptying of the bladder and covering of the probe with a condom to assess: embryonic heart rate. Colour Doppler was used to identifying the Uterine Arteries at the level of the cervicocorporal junction as the transducer was placed in the anterior vaginal fornix and a sagittal section of the cervix was obtained the vaginal probe was then moved laterally until the paracervical vascular plexus was seen. Color flow Doppler was applied and the Uterine Artery was identified at the level of the cervicocorporal junction. Measurements were taken at this point before the Uterine Artery branches into the arcuate arteries till we have three successive characteristic waves.

Then the measurement of different parameters was calculated based on velocities obtained by pulsed-wave Doppler. Flow velocity waveforms were measured and results were analyzed by calculating the resistance (resistive) index (RI) from the following formula RI= S-D/S where RI was the resistance index, S corresponded to the peak systolic velocity and D corresponded to the end-diastolic velocity. The same was repeated with the other uterine artery to obtain its (RI) then mean RI of both uterine arteries was calculated from the formula: mean $(RI) = \frac{(RI)_1 + (RI)_2}{2}$.

The spiral arteries blood flow was then identified, and its RI was then calculated: Spiral arteries are localized just beneath the chorion its flow velocity waveform (FVW) was characterized by low peak systolic velocity (PSV), higher end-diastolic velocity. These arteries are also termed subchorionic, retroplacental, or peritrophoplastic arteries. Then

women were reviewed monthly with u/s to ensure continuity of pregnancy till 24 weeks.

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). The confidence interval was set to 95% the p-value was considered significant as the following: Probability (P-value) P-value ≤0.05 was considered significant.

Ethical approval

The study protocol was approved by the local Ethics and Research Committee at Menoufia University Hospital. Written consent was obtained from all women participating before starting the study. The steps of the study have been cleared to the patients. All data and results of the study have been documented.

Sample Size

Calculation of the sample size was based on the results of the previous observational studies. The STAT CALC feature of Epi Info™ -Version 6 software was used for calculating the sample size guided by Power of the test=80%, Confidence level =95%, Accepted margin of error =5% Total sample accepted according to inclusion criteria =90.

Statistical analysis

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage. Independent-samples t-test of significance was used when comparing two means. Chi-square (x^2) test of significance was used to compare proportions between two qualitative parameters. The confidence interval was set to 95% and the margin of error accepted was set to 5%. The p-value was considered significant as the following: P-value <0.05 was considered significant. P-value <0.001 was considered as highly significant. P-value >0.05 was considered insignificant.

RESULTS

Analysis of the demographic data which included; age, body mass index, parity, and gestational age between the three study groups showed no statistically significant differences as shown in [**Table 1].**

Table (1): Baseline characteristics and demographic data of patients.

	Miscarried (N=30)	Continued (N=30)	Control (N=30)	Kruskal-Wallis test	P-value
Age (years)	25.97±3.85	25.67±4.47	26.40±3.72	0.523	>0.05
Parity	2.24±1.3	2.46±1.66	2.63±1.41	6.28	>0.05
Body mass index (Kg/m²)	26.78±2.38	26.52±2.42	26.62±2.40	0.085	>0.05
Gestational age	7.30±3.10	7.10±2.92	8.13±2.74	1.695	>0.05

Also, the resistance index (RI) of the Uterine and Spiral arteries was higher in the miscarried group (A) than both continued and control groups (B and C) as shown in **[Table 2]**

Table (2): The relation between mean Uterine arteries (RI), Spiral arteries (RI), and the occurrence of miscarriage.

Uterine arteries RI	Miscarried (N=30)	Continued (N=30)	Control (N=30)	ANOVA	p-value
Mean ±SD	0.84±0.07	0.74±0.09[a]	0.72±0.08[a]	3.031	0.011*
Spiral arteries (RI)	**Miscarried (N=30)**	**Continued (N=30)**	**Control (N=30)**	**ANOVA**	**p-value**
Mean±SD	0.58±0.08	0.49±0.07[a]	0.45±0.06[a]	3.709	0.006*

F; ANOVA test; *p-value <0.05 S

(**Table3 and Figure 1**) showed that: Uterine and spiral Artery resistance index (RI) showed statistically significant differences between the three groups under study with a good prediction of threatened miscarriage outcome.

Table (3): Diagnostic performance of uterine arteries, subchorionic blood flow in discrimination of miscarriage.

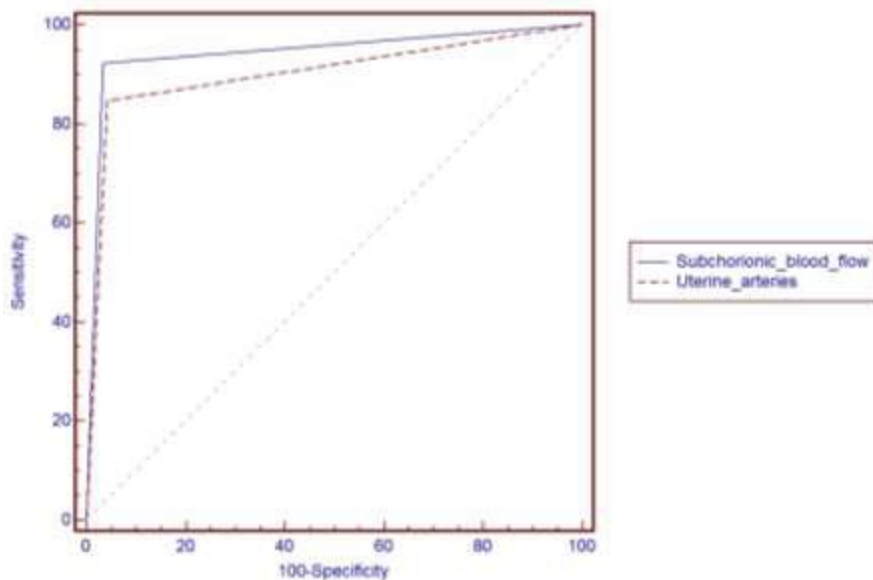| Parameters	Cut-off	Sensitivity	Specificity	PPV	NPV	Accuracy
Mean of Uterine arteries RI	**<0.82**	84.6%	95.7%	68.8%	98.2%	94.6%
Mean of Spiral arteries RI	**<0.53**	92.3%	97.4%	80.0%	99.1%	96.9%

Fig. (1): ROC curve, the diagnostic performance of uterine and spiral arteries in discrimination of threatened miscarriage outcome.

DISCUSSION

Normal implantation is very important to achieve a normal pregnancy through the trophoblastic invasion into the myometrium and migration through the entire length of maternal spiral arteries. resulting in low resistance and high flow state in the intervillous space and an increase in uterine blood flow that regulates uterine receptivity and is important for normal placentation. Invasion occurs through 2 waves. The first wave at the 4th-5th weeks of gestation, the second wave at the 14th week. These changes lead to a progressive reduction in the uterine arterial blood flow resistance. Uterine artery Doppler ultrasound helps assess uteroplacental perfusion. The study aimed to assess the ability of the uterine artery RI and spiral artery RI to predict outcome in cases of Threatened miscarriage [6].

In this study, the three study groups did not show any statistically significant differences regarding maternal age, BMI, parity, gestational age and this comes in agreement with **Dadkhah et al.** [7] but this disagrees with the findings of **Makrydimas et al.** [8] this contrast in the results may be due to methodological differences.

According to this study, the mean Uterine Arteries resistance index (RI) showed statistically significant differences between the three groups under study. the mean Uterine arteries RI was a good predictor of pregnancy outcome in cases of threatened miscarriage at a cutoff point **<0.82** with a sensitivity of 84.6% specificity of 95.7% positive predictive value of 68.8%, the negative predictive value of 98.2% with a diagnostic accuracy of 94.6%. And this agrees with a study done by **Cooley et al.** [9] the measurement of RI of uterine artery was found mostly higher in patients who suffered abortion.

In contrast, **Pellizzari et al.** [10] found no statistical significance of this variable by comparing the values in patients with normal pregnancies and those complicated by uterine bleeding.

In this study, Spiral artery RI showed a statistically significant difference between the study groups, and it was another good predictor for threatened miscarriage outcome, with a sensitivity of 92.3% specificity of 97.4% positive predictive value of 80%, the negative predictive value of 99.1% with a diagnostic accuracy of 96.9%. at a cutoff point **<0.53** this is in agreement with **Jauniaux et al.** [11] they stated that the resistive index of trophoblastic and uteroplacental flow was statistically significant as a consistent Doppler variable that might be a predictor of adverse pregnancy outcome.

Although **Alcázar et al.** [12] didn't find a significant difference in the uteroplacental circulation between patients with threatened abortion and control group patients. Also, in **Manal et al.** [13] study, Uterine Artery RI was 0.82 ±0.18 0.79 ±0.1 0.78± 0.11 in the 3 groups with P-value 0.17 there was no significant difference between the 3 studied groups regarding RI.

CONCLUSION

The Uterine and Spiral arteries RI can predict the fate of pregnancy in cases with threatened miscarriage with high accuracy.

REFERENCES

1. **Bae S, Karnitis J (2011):** Triple ultrasound markers including fetal cardiac activity are related to miscarriage risk. Fertility and Sterility, 96(5): 1145-48.
2. **Papaioannou G, Syngelaki A, Maiz N et al. (2011):** Ultrasonographic prediction of early miscarriage. Human Reproduction, 26(7): 1685-92.
3. **Kurjak A, Crvenkovic G, Salihagic A et al. (1993):** The assessment of normal early pregnancy by transvaginal color Doppler ultrasonography. Journal of Clinical Ultrasound, 21(1): 3-8.
4. **Jaffe R, Dorgan A, Abramowicz J (1995):** Color Doppler imaging of the uteroplacental circulation in the first trimester: value in predicting pregnancy failure or complication. American Journal of Roentgenology, 164(5): 1255-58.
5. **El-mashad A, Mohamed M, Farag M et al. (2010):** Role of uterine artery Doppler velocimetry indices and plasma adrenomedullin level in women with unexplained recurrent pregnancy loss. Journal of Obstetrics and Gynaecology Research, 37(1): 51-57.
6. **Aseel G (2020):** Doppler Ultrasound Screening of the Uterine Arteries as a Predictor for Early Miscarriage. International Journal of Women's Health and Reproduction Sciences, 8 (1): 79–84.
7. **Dadkhah, F, Kashanian M, Eliasi G (2010):** A comparison between the pregnancy outcome in women both with or without threatened abortion. Early Human Development, 86(3): 193-96.
8. **Makrydimas G, Sebire N, Lolis D et al. (2003):** Fetal loss following ultrasound diagnosis of a live fetus at 6-10 weeks of gestation. Ultrasound in Obstetrics and Gynecology, 22(4): 368-72.
9. **Cooley S, Donnelly J, Walsh T et al. (2011):** The impact of umbilical and uterine artery Doppler indices on the antenatal course, labor, and delivery in a low risk primigravid population. Journal of Perinatal Medicine, 39(2): 135-38.
10. **Pellizzari P, Pozzan C, Marchiori S et al. (2002):** Assessment of uterine artery blood flow in normal first-trimester pregnancies and those complicated by uterine bleeding. Ultrasound in Obstetrics and Gynecology, 19(4)366-70.
11. **Alcázar J, Ruiz M (2000):** Uteroplacental circulation in patients with first-trimester threatened abortion. Fertility and Sterility, 73(1)130-35.
12. **Jauniaux E, Johns J, Burton G (2005):** The role of ultrasound imaging in diagnosing and investigating early pregnancy failure. Ultrasound in Obstetrics and Gynecology, 25(6): 613-24.
13. **Manal M, Soha S, Mahmoud A et al. (2013):** Uterine artery Doppler and urinary hyperglycosylated HCG as predictors of threatened abortion outcome. Middle East Fertility Society Journal, 18: 42–46.