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Color Doppler Ultrasound of Spiral Artery Blood Flow in Mid First Trimester (4-8 weeks) in Cases of Threatened Abortion and in Normal Pregnancy

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ABSTRACT

Background: Vaginal bleeding before twenty weeks of pregnancy was designated as a "threatened miscarriage" in medical terminology. Even women who experience this type of threat have a 15% higher chance of losing their pregnancy. Early pregnancy outcome prediction would be a highly advantageous for clinical approach.

Aim: This study aimed to assess spiral artery flow during mid-first trimester (four–eight weeks) in instances of threatening abortion and normal pregnancies.

Subjects and methods: Cohort prospective study was conducted at Obstetrics and Gynecology Emergency Unit Outpatient Clinic of Suez Canal University Hospital on forty expectant women in 1st trimester. Participants were organized into following groups: Group A consisted of twenty pregnant women who presented with threatened miscarriage such as vaginal bleeding or spotting with or without abdominal pain, group B consisted of twenty expectant women who did not have any complaints. In all subjects, spiral artery was sonographically assessed.

Results: There was a notable difference between the 2 groups concerning spiral artery pulsatility index (PI) & resistance index (RI), which were elevated in cases compared to control group, while no significant difference was observed in S/D ratio between groups. In terms of pregnancy outcomes, miscarriage rate was higher in cases (thirty percent) than in control group (zero percent). No significant differences were found between groups regarding other maternal and fetal outcome data.

Conclusion: Female exhibiting vaginal bleeding demonstrated significantly elevated spiral artery pulsatility index (PI), resistance index (RI) compared to normal control group. We determined that dynamics of spiral arterial blood flow in early pregnancy (four–eight weeks gestation) can be evaluated using transvaginal color Doppler sonography.

Keywords: Spiral artery blood flow, Color Doppler ultrasound, Normal pregnancy, Mid first trimester, Threatened abortion.

INTRODUCTION

Vaginal bleeding during 1st twenty weeks of pregnancy, even while it was clinically anticipated that the fetus will survive, is referred to as a "threatened miscarriage" in medical terminology. Abdominal pain may or may not be connected to this bleeding. In the first trimester, around 25% of pregnant women exhibit signs of threatening abortion, and over 50% of these women experience miscarriage [(1)].

Compared to other women, those who have a living embryo and were confronted with abortion had a 15% higher likelihood of miscarrying a child. Given high probability of spontaneous miscarriage in this cases population, it would be a clinically beneficial approach to anticipate outcome of a pregnancy at an early stage of gestation [(2)].

Through implementation of high-frequency transvaginal color Doppler ultrasonography with spectral analysis, it was feasible to evaluate uteroplacental circulation during initial phases of pregnancy. Abnormalities in this circulation have been related with pregnancy complications, such as intrauterine growth restriction (IUGR), fetal distress, early pregnancy failure [(3, 4)].

Studies regarding potential of trans-vaginal Doppler sonography to identify early pregnancy, late pregnancy issues associated with aberrant placentation has been sparked by the technology's ability to evaluate the uteroplacental circulation's even terminal branches' circulation pattern [(5)]. One of the key variables linked to both early and late pregnancy problems is impaired vascular remodeling at the mother-fetal interface [(6)].

Nowadays, majority of individuals concur that irregularities in early invasion of trophoblasts, continuously high spiral artery resistance are the primary causes of the majority of pregnancy-related problems [(7)]. Vascular remodeling at the maternal-fetal interface may result in an increase in uteroplacental blood flow, which may also lower local artery resistance. Placental hematoma and spontaneous miscarriage are two pregnancy complications that are linked to this process's impairment [(8)].

There are no studies on blood flow in spiral artery as seen in a color Doppler ultrasound throughout fourth to eighth week of pregnancy have been conducted, which is not surprising given the state of Egyptian research on instances of imminent abortion. Therefore, our goals are to show if trans-vaginal Doppler sonography can detect potential changes in spiral artery blood flow patterns and

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to explore whether these Doppler results may be used to predict unfavorable pregnancy outcomes.

SUBJECTS AND METHOD

This prospective cohort study involved forty 1st - trimester pregnant female at Obstetrics, Gynecology Emergency Unit & Out Clinic at Suez Canal University Hospital through the period from January 2021 to May 2023. Participants were split into two groups: Twenty pregnant women in group A (spotting or bleeding vaginally, with or without abdominal pain) expressed concern about miscarriage, and twenty pregnant women in group B (no complaints).

Inclusion criteria: Individuals who are pregnant (positive pregnancy test) or who have a potentially dangerous spontaneous abortion between age range 18 to 35 years who presented in the mid-first trimester, or 4 to 8 weeks. Also, a single intrauterine gestational sac could be seen on a real-time abdominal/transvaginal ultrasound.

Exclusion criteria: Cases with uterine pathology, such as malformations or fibroids, those whose tests exceeded ten minutes, individuals whose spiral arteries should not be adequately assessed, cases with a history of molar pregnancy or 2 or more consecutive pregnancy losses and cases who experienced irregular menstrual cycles within past 3 months. Chronic diseases, patients receiving progesterone during pregnancy, and patients whose medications affect their vascular system such as antihypertensive or antihypotensive drugs.

Based on how long the amenorrhea lasted (in weeks or days), the gestational age was determined. Pregnant women in the control group had no concerns. A complete medical history, a physical examination, and laboratory testing for BHCG, CBC, ABO, and RH were done for every patient.

Ultrasound/Doppler evaluation:

The women were advised to empty their bladders prior to the assessment. Following a gentle insertion of the transvaginal probe into the posterior fornix of the vagina, scans were performed on the uterus, adnexa, and cervical region to detect any cervical lesions and confirm existence of an intrauterine gestational sac and heart pulse. Uterine spiral arteries were assessed once utilizing MINDRAY DC-60 device in triplex mode, which at 5 weeks of gestation integrates a grayscale image with color Doppler and a spectral flow waveform. Power Doppler imaging was employed to evaluate spiral arteries situated beneath chorion frondosum. Flow velocity waveforms were generated by utilizing Doppler gate on colored areas and engaging pulsed-wave Doppler function. Width of pulsed Doppler sample volume was established at 2 mm. High-pass filter was configured at fifty Hz. For soft tissues, mechanical index (MI) was 0.82, thermal index (TI) was 0.7. Machine's software automatically calculated pulsatile indices (PI), resistance index (RI) and systolic/diastolic (S/D) ratio for the spiral arteries. Two consecutive flow velocity waveforms were compared, and the average of their respective values was calculated. To prevent inter-observer differences, a single experiment investigator carried out all sonographic procedures.

Outcome measures: The subjects were monitored for pregnancy difficulties up to delivery, such as miscarriage, abortion in the second trimester, hypertensive disorders during pregnancy, preterm labor, and intrauterine fetal death, using examination, ultrasound, Doppler, and lab tests as needed. The delivery method and additional neonatal metrics, such as the Apgar score, the requirement for NICU admission, and the existence of congenital abnormalities were noted.

Ethical consideration: The study was conducted in accordance with Helsinki Standards. The whole study design was approved by The Research Ethics Committee, Obstetrics and Gynecology Department, Faculty of Medicine, Suez Canal University, Egypt. Confidentiality and personal privacy were respected in all levels of the study. Signed informed consents were obtained from all participants.

Statistical Analysis

Data were analyzed using IBM SPSS software version 20.0 (Armonk, NY: IBM Corp). Qualitative data were expressed as numbers and percentages, while quantitative data were described using means and standard deviations. The Kolmogorov-Smirnov and Shapiro-Wilk tests were used to assess the normality of distribution. The significance of results was determined at the 5% level. The following statistical tests were used: the Chi-square test for categorical variables to compare groups, Fisher's Exact Test for correction when more than 20% of cells had expected counts less than 5, the Student t-test for comparing normally distributed quantitative variables between two groups, and the F-test (ANOVA) for comparing more than two groups. P-values were interpreted as follows: $P>0.05$ indicated non-significance (NS), $P<0.05$ indicated significance (S), and $P<0.001$ indicated high significance (HS).

RESULTS

No significant difference in demographic information, blood pressure was observed between the 2 groups (Table 1).

Table (1): Demographic data and blood pressure of both studied groups

Variables	Threatened cases (N=20)	Normal control (N=20)	T/X^2	P
Age (years)	26.3 ± 4.4	26.05± 4.2	0.18	0.85
Gestational age (weeks)	6.2 ±1.1	6.4 ± 1.3	0.52	0.6
Weight (Kg)	67.5 ± 8.5	71.1 ± 9.05	-1.3	0.20
Height (m)	1.65 ± 0.3	1.72 ± 0.4	0.62	0.53
BMI (kg/m^2)	24.4 ± 2.09	25.1 ± 2.82	-0.78	0.43
Residence Urban Rural	 13 (65%) 7(35%)	 14 (70%) 6 (30%)	X^2=0.11	0.73
SBP (mm Hg)	100.1 ± 9.8	105.5 ± 10.4	1.7	0.09
DBP (mm Hg)	61.5 ± 8.8	64.1 ± 6.6	1.05	0.29

Concerning parity, no significant difference was seen between the 2 groups (Table 2).

Table (2): Parity of both studied groups

Variables	Threatened cases (N=20)	Normal control (N=20)	X^2	P
Parity **PG** **1** **2** **3**	 4 (20%) 5 (25%) 8 (40%) 3 (15%)	 5 (25%) 2 (10%) 7 (35%) 6 (30%)	2.4	0.48

While statistically negligible, the likelihood of previous pregnancy loss was greater in threatening cases compared to normal controls (Table 3).

Table (3): Previous pregnancy loss of both studied groups

Variables	Threatened cases (N=20)	Normal control (N=20)	X^2	P
Previous pregnancy loss	4 (20%)	1 (5%)	2.05	0.15

A notable disparity existed between the 2 groups concerning PI & RI, which were elevated in cases compared to control group, but no significant difference was observed in S/D ratio (Table 4).

Table (4): Spiral artery Doppler indices (RI, PI, S/D ratio) of both studied groups

Variables	Threatened cases (N=20)	Normal control (N=20)	T	P
PI	0.81 ± 0.14	0.51 ± 0.06	8.35	<0.0001*
RI	0.52 ± 0.1	0.31 ± 0.06	7.25	<0.0001*
S/D ratio	1.92 ± 0.24	1.81 ± 0.18	1.55	0.12

Miscarriage rate in case group was 30% all in first trimester while no first or second trimester miscarriage in control group (Table 5).

Table (5): Early outcome of both studied groups

Variables	Threatened cases (N=20)	Normal control (N=20)	F	P
Miscarriage	6 (30%)	0 (0%)	F	**0.04**

Additional outcome data did not reveal a substantial disparity between the 2 groups (Table 6).

Table (6): late outcome data of both studied groups.

Variables	Threatened cases (N=14)	Normal control (N=20)	F/X^2	P
Intrauterine fetal death	1 (7.1%)	0(0%)	F	0.49
Pregnancy hypertensive disorders	2 (14.3%)	1 (5%)	X^2=0.88	0.34
Preterm labor	3 (21.4%)	1 (5%)	X^2=2.14	0.14
Mode of delivery **CS** **VD**	 11 (78.6%) 3 (21.4%)	 14 (70%) 6 (30%)	X^2=0.31	0.57

No significant difference was seen between the 2 groups for fetal outcomes (Table 7).

Table (7): Fetal outcome data of both studied groups

Variables	Threatened cases (N=14)	Normal control (N=20)	F/X^2	P
Presence of congenital anomaly	0 (0%)	0 (0%)	**F**	**0.99**
Apgar score < 7	2 (14.3%)	0 (0%)	F	0.16
NICU admission	4 (28.6%)	2 (10%)	X^2=1.95	0.16

Pulsatility index (PI) & resistance index (RI) were markedly elevated in cases with poor outcomes compared to those with favorable outcomes & normal control group, although no significant difference was observed in systolic/diastolic (S/D) ratio (Table 8).

Table (8): Spiral artery Doppler indices (RI, PI & S/D ratio) of good and bad outcome of threatened cases compared to control group.

Variables	Bad outcome threatened cases (N=10)	Good outcome threatened cases (N=10)	Normal control (N=20)	P
PI	0.88 ± 0.2	0.73 ± 0.07	0.51 ± 0.06	<0.0001*
RI	0.55 ± 0.12	0.47 ± 0.06	0.31 ± 0.06	<0.0001*
S/D ratio	1.97 ± 0.2	1.85 ± 0.16	1.81 ± 0.18	0.347

DISCUSSION

15% of clinically diagnosed pregnancies result in miscarriage, a common pregnancy complication [9]. Once an ultrasound confirms the pregnancy, this rate typically drops to 1.6–6.7%. It is crucial for women's and families' psychological well-being to know that patients who have threatened miscarriage have a 2.5 times increased risk of miscarriage [10]. Approximately twenty five percent of expecting moms display indications of threatened abortion in 1st trimester, with over fifty percent of these female ultimately experiencing miscarriages. When compared to general population, women who face threats of abortion have a 15% higher likelihood of losing their pregnancy [11].

Uterine artery Doppler ultrasonography has been well validated as advantageous for evaluating uteroplacental perfusion, forecasting onset of pre-eclampsia, fetal growth restriction, placental abruption, and stillbirth during 2nd trimester [12].

This study was conducted to evaluate spiral artery flow during 1st trimester (four-eight weeks) in both normal pregnancies and cases of threatening abortion. Patients in both groups were chosen at random, matching according to certain demographic information. According to **OKïU *et al.*** [9] the rate of threatening abortion rises as mothers' age advances. Numerous studies have suggested that the rising incidence of threatening miscarriages could be caused by insufficient or incorrect progesterone secretion as a result of ovarian aging [13, 14].

Every case in both study groups in the current investigation was less than 35 years old, in accordance with earlier findings. Furthermore, the mean and range of ages in both groups are equal. According to **Ghimire *et al.*** [15], women in reproductive age have a higher chance of miscarriage when their Body Mass Index (BMI) rises. Based on these results, all cases in both groups were matched in the current investigation with regard to body mass index. Cases in both groups were matched for gestational age. Research indicates that as gestational age advances, frequency of miscarriage diminishes [16].

Power of the current study is increased by the random selection of cases that are matched in both investigated groups with respect to body mass index, mother age, previous pregnancy loss, gestational age, and parity.

Our study's findings validate the transvaginal spiral artery Doppler examination as a non-invasive technique for identifying anomalies related to trophoblastic invasion in the first 8 weeks of pregnancy. The results suggested that compared to patients with uncomplicated pregnancies, patients presenting with indicators of imminent miscarriage have significantly higher pulsatility indexes (PI) and resistance indices (RI). **Bhoil *et al.*** [11] mean values of RI & PI for threatened abortion group were 0.48 & 0.72 respectively, while mean values for normal control group were 0.25 & 0.41. RI & PI values of both groups differed in a statistically significant way. Furthermore, **Nagy and Gardo** [17] investigated the Doppler features of the spiral arteries in two groups of thirty patients each. The one with problematic pregnancies that were 8–12 weeks gestation and the other with straightforward pregnancies. Difficult pregnancy group had markedly elevated peak systolic velocity, resistance index and pulsatile index relative to normal control group. They advocated for utilization of spiral artery Doppler imaging for noninvasive evaluation of disturbances in trophoblast invasion during initial phases of pregnancy. Our results correspond to conclusions presented **by Mercé *et al.*** [20], **Wang *et al.*** [18] and **Abdel Wahab *et al.*** [19]. **Al Halaby *et al.*** [21] showed in a different study that the miscarried group had greater RIs in the uterine and spiral arteries compared to the control groups. Additionally, **Waeely *et al.*** [23] and **Aktham *et al.*** [22] found that during 1st trimester, PI of spiral arteries was significantly higher in women who faced the threat of abortion than it would be in a typical pregnancy. Also, **Rifat** [24] mean values of indices in threatened group were considerably greater than those in control group. A significant disparity was seen in average PI & RI values. He discovered that although there was a notable disparity in S/D ratio between the 2 groups in our investigation, while the difference was not statistically significant.

Contrary to our findings an investigation revealed no significant difference in Doppler indices of spiral arteries between cohorts of early pregnant female without complications and those at risk of abortion. In individuals who had an abortion threatened, they did not show any discernible changes in early uteroplacental circulation. They came to conclusion that under these situations, predicting outcome of a pregnancy is not possible with color Doppler ultrasonography [25]. Furthermore, no discernible variation in the uteroplacental circulation was seen by **Alcázar and Ruiz-Perez** [1] between the group of patients who were threatened with abortion and the control group. Similarly, **OKïU *et al.*** [9] reported that uterine, spiral artery PI, RI, & S/D values exhibited no significant differences ($P > 0.05$) across groups. This could be because their investigation had a large number of cases and a different type of machine.

It is noteworthy that pulsed Doppler ultrasonography poses significant technological challenges, particularly when dealing with tiny channels such as spiral arteries, and is an operator-dependent procedure [26]. This could function as a deterrent to its widespread application in conventional clinical practice. Every sonographic examination was conducted by same

investigator to mitigate inter-observer variability in our study.

The current study's findings showed a significant difference in miscarriage rates between the 2 groups, which was higher in cases (30%) than in the control group (0%), and with regard to mode of delivery, which was 70% and 30% of cases and 78.6% and 21.4% of control delivered by CS and VD respectively. Regarding the other outcome data, there was no discernible difference. Furthermore, there was no discernible difference in fetal fate between the 2 groups. In line with our research, **Rifat** [(24)] demonstrated that all of the expectant mothers in the normal control group experienced a normal pregnancy and that no unfavorable outcomes were reported. On the other hand, the Doppler indices increased in all five of the 28 pregnancies that ended in a poor outcome for the endangered group. The bad outcomes within the threatened group rose in tandem with the mean values of PI rising from the normal control group to the threatened group. The researchers used logistic regression to determine which Doppler measurement was strongly correlated with the desired outcome since the results suggest that the Doppler measurements can likely anticipate unfavorable outcomes. Along the same lines, **Bhoil *et al*.** [(11)] came to the conclusion that a spiral artery color Doppler could be a helpful tool for determining the prognosis of patients who have been warned about a miscarriage. Additionally, **Ozkaya *et al*.** [(27)] showed that in a small number of cases, spiral artery resistance index increase increased risk of IUGR, preterm labor, placental abruption and miscarriage. Furthermore, spiral arteries displayed distinct modifications in the early stages of pregnancy, according to **Özkan *et al*.** [(28)], especially in the fifth and sixth weeks of pregnancy, there can be a greater chance of spontaneous abortion in pregnancies with high spiral artery RI.

A spiral artery color Doppler study could provide important details about the pregnancy at hand and provide useful insight into the prognosis and course of events. It may take longer for research to establish utero placental Doppler as a primary inquiry in cases of impending miscarriage.

CONCLUSION

Our investigation demonstrated that, despite comparable demographic characteristics in both groups, spiral artery PI & RI values of female experiencing vaginal bleeding were significantly elevated compared to those of normal control group. We determined that transvaginal color Doppler sonography may assess spiral arterial blood flow dynamics during early pregnancy (four-eight weeks gestation). Despite sonography being a treatment primarily reliant on operator, facing technological limitations in identifying small vessels like spiral arteries, it remains a viable method for evaluating hemodynamic alterations in spiral arteries during early pregnancy, particularly in high-risk populations. To enhance sensitivity of these minute arteries to diminished blood flow, a power Doppler might be more advantageous.

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- **Competing interests:** None.

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