Uterine and Subendometrial Arteries Doppler in Patients with Recurrent First Trimesteric Abortion

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How to Cite This Article

ORIGINAL ARTICLE

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Abstract

Background: Recurrent pregnancy loss is distressing pregnancy disorder that affects ~2.5% of all females attempting to conceive.

Goal of research: To research the role of uterine and subendometrial arteries Doppler in studied cases with recurrent 1st trimesteric abortion.

Subjects and methods: A prospective study (case-controlled study) was performed during the period from July 2021 to July 2022. We had 100 nonpregnant females presented to Outpatient Clinic AL-Hussein University Hospital, divided into 2 groups: RPL group: fifty cases with a history of unresolved abortions. Fifty cases with no history of abortion and at least 1 full-term child were included in the control group.

Result: Although PI in RPL group was discovered to be greater than in the control group, there was no variation in menstrual cycle length among the 2 groups studied. While a mean number of previous miscarriages is 4.16, and the mean GA at losses is 7.76 weeks.

Conclusion: In cases of recurrent unexplained first trimestric abortion, measuring uterine perfusion with uterine artery Doppler could be useful.

Keywords: Recurrent pregnancy loss, Subendometrial, Uterine

1. Introduction

Abortion is derived from Latin word aboriri, which means to miscarry. Abortion is described as spontaneous or induced termination of pregnancy before foetal viability or if foetus weighs less than 500 g or is shorter than 25 cm in length.[1]

Abortion is divided into 2 types: spontaneous and induced. Isolated and recurrent spontaneous abortions are further characterized. All forms of spontaneous abortion include threatened, unavoidable, complete, incomplete, missed, and septic abortion.[2]

Description of RPL differs, making it more difficult to research the phenomenon and determine which couples to counsel or cure. Various definitions have been provided as examples: 2 or more failed clinical pregnancies as described by ultrasonography or histopathologic test, as well as 3 or more successive spontaneous abortions, are considered recurrent pregnancy loss.[3]

Only about two percent of pregnant females have 2 consecutive miscarriages. Up to fifty percent of RPL studied cases have no clearly described aetiology.[4]

Primary RPL refers to pregnancy loss in females who have never had live birth. Secondary RPL, on other hand, is described as pregnancy loss in females who have previously had a live birth.[4]

Genetics, anatomical, endocrine, and placental anomalies, hormonal complications, infections, and alcohol consumption, exposure to environmental risk factors, psychological trauma, stressful life events, and immunoregulatory protein defects are all reasonable etiologic causes.[5]

The risk of recurrence rises with maternal years old and several previous losses.[6]

It is best to investigate recurrent abortion before another pregnancy happens. Uterine receptivity is influenced by variety of factors, such as uterine perfusion, and is critical to achieving normal pregnancy.[7]

There, the ultrasound with power Doppler makes unique tool to test uterine arteries and sub-endometrial arteries by measuring pulsatility index in mid-luteal stage of spontaneous cycles that could isolate studied cases with recurrent pregnancy loss related to impaired uterine circulation.[8]

The goal of the work was to research the role of uterine and subendometrial arteries Doppler in studied cases with recurrent 1st trimesteric abortion.

2. Studied cases and techniques

The study (case-controlled research) was done during the period from July 2021 to July 2022. We had 100 non-pregnant females presented to Outpatient Clinic AL-Hussein University Hospital. The women were separated into 2 groups: (Group A): fifty members with history of idiopathic recurrent pregnancy loss (cases group) and (Group B): fifty members with no history of abortion and have at least one child born at term (control group).

At recruitment, the purpose of research was described to every member. All of them were subjected to a two-dimensional ultrasound examination and Doppler study for measuring the pulsitility index (PI), of uterine arteries.

Inclusion Criteria for the recurrent pregnancy loss group: Three or more successive unexplained first trimestric abortion, age between 20 and 40 years old, regular menstrual cycles for prior three cycles before research, no hormonal contraception or intrauterine devices, and normal endocrinial status including serum thyroid-stimulating hormone, free thyroxin, glucose tolerance test, and progesterone levels between days nineteen and twenty-one of the menstrual cycle.

Inclusion Criteria for control group: age between 20 and 40 years old, regular menstrual cycles for the prior three cycles before research, no hormonal contraception or intrauterine devices, and normal obstetric history with at least 1 previous term Pregnancy but no abortions.

Exclusion Criteria for both groups: Systemic diseases that may have an impact on hemodynamic indices, such as thrombocytopenia, thyroid disease, autoimmune disease cardiovascular disease, diabetes, and so on Consanguinity history, family history of chromosomal abnormalities, studied case

years old less than 20 years or greater than 40 years, women in the follicular phase or menstrual phase, women having uterine alterations on office hysteroscopy and women having cervical incompetence on transvaginal ultrasonography.

2.1. Steps and methods

All studied cases recruited provided informed consent and were subjected to following:

Complete history containing Personal history: names, years old, addresses, occupations, special habits, and history of consanguinity. **Menstrual history:** asking about the regularity of cycle's frequency, duration and amount of bleeding of every cycle, and date of last menstrual time. **Obstetric history:** asking about parity and technique of prior deliveries, time at which prior abortions had happened and whether they had been followed by surgical evacuation or not, and ask about the date of last delivery or abortion. **History:** a history of systemic diseases like diabetes mellitus, hypertension, renal disease, history of infants with chromosomal abnormalities such as trisomy 21, history of consanguinity, and history of thyroid troubles.

2.2. General examination

Vital signs, Signs of (Pallor, Cyanosis, Jaundice, and Lymph node enlargement), breast examination for swelling or nipple discharge.

2.3. Cardiovascular examination

2.3.1. General inspection
Cyanosis, pallor, and sweatiness in the critically ill studied case. Cachexia was the most essential characteristic to notice on general inspection in nonacute studied cases because it is an important prognostic sign of heart failure. Palpation was required to verify that the girth was caused by excess fluid. There is evidence that certain facial signs are associated with a cardiac condition.

2.3.2. Palpation
Previous to auscultation, examination of precordium was useful sign of prior surgery - for example, midline sternotomy indicates the prior bypass, lateral thoracotomy indicates prior mitral valve, or minimally invasive bypass surgery. Finding apex beat - most lateral and inferior point. There are numerous definitions for abnormal apex beats.

2.3.3. Auscultation

Listening with the diaphragm of the stethoscope over aortic and pulmonary areas and at the left lower sternal edge (better for greater pitches), then using a bell for apex (better for lower pitches).

2.3.4. Chest examination

The environment in which the chest test takes place should be comfortable for both the clinician and studied case. Physical testing began with the taking of history. We greeted them with a handshake, inquired about symptoms that prompted visit, and began a physical examination, noting body position, evaluating the degree of comfort, inspecting and noting grip strength. The format of test was determined by history. Experienced clinicians used history to help 'look' for specific physical results that answered questions raised by previously collected data. Inspection, palpation, percussion, and auscultation are all part of the pulmonary test. The inspection procedure began and was carried out during the studied case encounter. Palpation, when affirmed by percussion, determines tenderness and the degree of chest expansion. Auscultation, sensitive procedure, affirmed prior outcomes and may aid in the identification of previously unknown pathologic processes.

2.4. Abdominal examination

2.4.1. Abdominal inspection

Position studied case flat on the bed, arms by their sides and legs uncrossed, for abdominal examination and palpation.

2.5. Abdominal palpation

2.5.1. Light palpation of abdomen

Lightly palpated every of **9 abdominal regions**, evaluating for clinical marks suggestive of gastrointestinal pathology.

2.5.2. Deep palpation of abdomen

Palpation of every of 9 abdominal regions again was done, by applying **higher pressure** to recognize any **deeper masses** and Monitoring studied case's face for evidence of discomfort.

Pelvic Examination: to assess uterine size and if there were adnexal masses or not.

2.5.3. Type of ultrasound machine

Sonography was performed using an ultrasound machine (mindray dc30) equipped with a vaginal transducer, Transvaginal examination was done in 2nd half of menstrual cycle, between days 18–25 (Due to the endometrium being normally anon

receptive environment for an embryo except during the implantation window). Pulsed wave Doppler gains clear, consistent, flow velocity waveforms of both uterine arteries. Pulsatility index (PI=S-D/mean) is measured bilaterally. PI described was arithmetic mean for last 3 cardiac cycles.

2.5.4. Administrative considerations

Official permission was got from University Hospitals. Official permission was obtained from the Institutional Research. Approval was taken from the ethical committee in faculty of medicine.

2.5.5. Ethical consideration

All participants provided informed consent after being informed about the research's goals and procedure, in addition to any applicable objectives. Research processes had no negative impacts on participants or the service provided.

2.6. Statistical analysis

SPSS version 23 was used for data processing and was used to check, enter, and analyze the data. The following statistical techniques were used to analyze the current research's findings. For qualitative variables, data were expressed as numbers and percentages, while quantitative variables were expressed as mean ± standard deviation. Shapiro Walk examination was used to check for the normal distribution of data. Frequencies and relative percentages represent qualitative data. To determine variation among qualitative variables, Chi-square test ($\chi2$) and Fisher exact were used, as indicated. For parametric data, quantitative data were expressed as mean ± SD and for non-parametric data as median and range. For parametric and non-parametric variables, independent T-test and Mann Whitney examination was used to define distinction among quantitative variables in 2 groups.

3. Results

Table 1.

This table shows there is no variation among groups as regard parity. Meanwhile, both groups were comparable in years old and BMI (Table 2).

This table shows that there is no variation among the two tested groups concerning menstrual cycle length. While the mean number of previous miscarriages is 4.16, and the mean GA at losses is 7.76 weeks (Table 3).

This table shows that mean progesterone levels were significantly lower among Group A women compared to Group B (Table 4).

Table 1. Demographic characteristics distribution among 2 groups.

Variables	Group A (RPL) (n = fifty)	Group B (Control) (n = fifty)	t	P
Age (years)				
Mean ± SD	28.52 ± 3.6	29.88 ± 5.35	1.49	0.139
Parity				
Mean ± SD	1.84 ± 0.766	2.7 ± 1.43	MU 848	0.004
BMI (kg/m^2)				
Mean ± SD	27.03 ± 2.68	26.45 ± 2.29	0.543	0.592

Table 2. Clinical features among 2 tested groups.

	Group A (RPL) (n = fifty)	Group B (Control) (n = fifty)	T	P
Menstrual cycle length (days)				
Mean ± SD	27.6 ± 3.12	28.12 ± 2.87	0.162	0.873
Number of previous miscarriages				
Mean ± SD	4.16 ± 0.79	—	—	—
Gestational age at losses (weeks)				
Mean ± SD	7.76 ± 1.95	—	—	—

Table 3. Progesterone levels distribution between the two groups.

Variables	Group A (RPL) (n = fifty)	Group B (Control) (n = fifty)	t	P
Progesterone (ng/mL)				
Mean ± SD	14.16 ± 1.19	14.81 ± 0.971	2.99	0.003

This table shows that endometrial thickness and endometrial volume were lower in RPL group compared to control however without a difference (Table 5).

This table shows that VI, FI and VFI were lower in RPL group compared to control (Table 6).

This table shows that the right left and mean uterine artery PI was greater in RPL group compared to controls.

4. Discussion

Recurrent pregnancy loss (RPL) is distressing pregnancy disorder that affects ~2.5% of females

Table 4. Endometrial characteristics among 2 groups.

Variables	Group A (RPL) (n = fifty)	Group B (Control) (n = fifty)	T	P
Endometrial thickness (mm)				
Mean ± SD	9.55 ± 0.839	9.79 ± 0.949	1.35	0.180
Endometrial volume (ml)				
Mean ± SD	2.23 ± 0.301	2.26 ± 0.312	0.437	0.663

Table 5. PDA indexes distribution between the two groups.

Variables	Group A (RPL) (n = fifty)	Group B (Control) (n = fifty)	T	P
Flow index				
Mean ± SD	10.04 ± 0.642	16.32 ± 2.06	20	0.000
Vascularization index (%)				
Mean ± SD	0.467 ± 0.128	0.988 ± 0.511	MU 451	0.012
Vascularization flow index				
Mean ± SD	0.108 ± 0.056	0.280 ± 0.072	MU 84	0.000

Table 6. Uterine artery doppler among 2 groups.

Variables	Group A (RPL) (n = fifty)	Group B (Control) (n = fifty)	T	P
Right uterine PI (mm)				
Mean ± SD	2.45 ± 0.322	2.23 ± 0.22	3.94	0.000
Left uterine PI (ml)				
Mean ± SD	2.54 ± 0.281	2.33 ± 0.215	4.21	0.000
Mean uterine PI				
Mean ± SD	2.48 ± 0.295	2.27 ± 0.217	4.23	0.000

attempting to conceive. RPL is characterized by the failure of 2 or more clinically recognized pregnancies before twenty-four weeks of gestation and contains embryonic and foetal losses.[9]

Color Doppler ultrasonography, an impactful, repeatable, and noninvasive technique of evaluating endometrial, was widely used in the field of RPL in recent decades.[10]

The goal of the work is to research the role of uterine and sub endometrial arteries doppler in studied cases with recurrent 1st trimesteric abortion.

A case-controlled study was performed throughout time from July 2021 to the end of the research. We had 100 nonpregnant females presented to Outpatient Clinic AL-Hussein University Hospital.

At recruitment, the purpose of the research was explained to every participant. All of them were subjected to a two-dimensional ultrasound examination and a Doppler study for measuring the pulsitility index (PI), of uterine arteries and subendometrial arteries.

Informed consent was got from all females joining research after giving them full information about the study.

Full history was taken; Body mass index (BMI), Laboratory investigations, and statistical analysis of data were prepared.

In our study regarding the demographic characteristics of tested groups, there was a variation among groups as regard parity. Meanwhile, both groups were comparable in years old and BMI. The mean Parity was 1.84 ± 0.766 in RPL group and 2.7 ± 1.43 in control group ($P = 0.004$), mean age were 28.52 ± 3.6 years in RPL group and 29.88 ± 5.35 years in control group ($P = 0.139$), mean BMI were 27.03 ± 2.68 kg/m^2 in RPL group and 26.45 ± 2.29 kg/m^2 in control group ($P = 0.592$).

In recent research by Yang et al.,[10] years old-matched comparisons were made between 870 studied cases in the RPL group and 237 females in control group ($P > 0.05$). There were no variations in BMI, parity, termination technique, or gestation weeks among the 2 groups ($P > 0.05$).

In agreement was another research by Garhy et al.,[11] purpose of this research was to see if there was any variation in uterine artery pulsitility index among females with a history of recurrent unexplained 1st trimestric abortion and females without this history. Of the 100 cases contained in this research, fifty were with history of recurrent unexplained abortion. There were no variations in mean years old among the RPL group and control group, which was 28.036 ± 4.83 years and 28.04 ± 5.771.

Control group's mean parity was greater than RPL group's, at 1.12 ± 1.023 and 2.62 ± 1.338 ($P = 0.001$).

Also, El-Mazny et al.,[12] in females with unexplained infertility, use pulsed Doppler to assess uterine artery blood flow and (3D) power Doppler to assess endometrial and sub endometrial micro vascularization.

In another study by Abdel Wahab et al.,[13] uterine artery blood flow and sub endometrial blood flow were compared in females with unexplained RPL to normal fertile females. mean $\pm$ SD years old of studied cases in study group (RM group) was 28.6 ± 4.6 years compared to 26.2 ± 4.7 years in control group ($P = 0.02$).

In the current research progesterone levels distribution among 2 groups showed that mean progesterone levels were lower among RPL Group women compared to the control Group. On another hand, endometrial characteristics among the 2 groups showed that endometrial thickness and endometrial volume were lower in RPL group compared to control however without a statistical significance difference ($P > 0.05$).

In previous research by El-Mazny et al.,[12] aimed to Pulsed Doppler is used to assess uterine artery blood flow, and (3D) power is used to assess endometrial and sub endometrial micro vascularization. Endometrial thickness and volume, as well as serum estradiol and progesterone levels, were not changed among 2 groups, according to Doppler. They concluded that in females with unexplained infertility, peri-implantation endometrial perfusion is impaired. As a result, Doppler's research on uterine hemodynamics must be regarded in infertility workups.

In agreement Garhy et al.,[11] described that there were no variations among RPL group and control group regarding endometrial thickness, it was 9.7 ± 2.9 mm and 11.2 ± 2.5 mm respectively ($P = 0.43$). mean serum progesterone level of women in control group was greater than that in RPL group, it was 14.0 ± 2.7 ng/ml and 14.3 ± 2.4 ng/ml ($P = 0.002$). Endometrial volume was 2.20 ml ± 0.52 ml in the study group and 2.30 ml ± 0.50 ml in the control group however changes were not significant (P value 0.69).

Abdel Wahab et al.,[13] showed that Endometrial thickness in study group was 9.7 mm ± 1.8 mm and 9.7 mm ± 1.4 mm in control group, however, variation was not significant ($P = 0.9$). Likewise, there was no big variation in endometrial volume between the 2 groups ($P = 0.6$), and no relationship was shown among endometrial thickness and endometrial volume among 2 studied groups.

According to PDA indexes distribution among 2 groups, outcomes presented that VI, FI and VFI were lower in RPL group compared to control. *P* values were 0.012, 0.000, and 0.000.

Abdel Wahab et al.,[13] reported that, VI ($P = 0.000$), FI ($P = 0.000$), and VFI ($P = 0.000$) were lower in study group than in control group, and significant negative relationship was shown among VI (r = −0.56, $P = 0.00$) and recurrent miscarriage in study group (r = −0.79, $P = 0.00$).

As regards vascularity index (VI), **Garhy et al.,**[11] showed that it was significantly greater in control group (2.278 ± 0.325) than in the case group (2.513 ± 0.415). (*P* value 0.002). Furthermore, the flow index (FI) was greater in the control group (16.87 ± 3.4) than in the case group (10.2 ± 1.03), which was significant (*P* value 0.000), and the vascular flow index was greater in the control group (0.27 ± 0.11) than in case group (0.12 ± 0.08), which was significant (*P* value 0.048).

Also, **El-Mazny et al.,**[12] reported that, Endometrial VI ($P = 0.029$), FI ($P = 0.031$), and VFI ($P = 0.001$) were lower in unexplained infertility group, as were subendometrial VI ($P = 0.032$), FI ($P = 0.040$), and VFI ($P = 0.005$).

Wu et al.,[14] found that sub-endometrial VFI on day of HCG was greater in pregnant group and outperformed endometrial volume, sub-endometrial VI, and FI in predicting the result in fifty-four studied cases.

In terms of uterine artery doppler among the 2 groups, the current research found that the RPL group's right left, and mean uterine artery PI was higher than controls, with all *P* values being 0.000.

This result is consistent with several earlier types of research on studied cases who have recurrent pregnancy loss **El-Mazny et al.,**[12] in a previous study showed that uterine artery PI ($P = 0.003$) and RI ($P = 0.007$) were raised in unexplained infertility group.

In a study conducted by **Lazzarin et al.,**[15] They discovered that uterine arteries PI values in RPL studied cases (2.42 ± 0.79) were greater than those shown in control group (2.08 ± 0.47), and when studied cases were grouped according to different reasons for RPL, greatest PI values were shown between studied cases with uterine abnormalities (2.82 ± 1.0), antiphospholipid antibodies syndrome (2.70 ± 1.1), and unexplained RPL (2.6 ± 0.7).

In another previous study **Abdel Wahab et al.,**[13] In luteal stage of spontaneous cycles, uterine artery PI was shown to be greater in recurrent miscarriage group (2.7 ± 0.38) compared to control group (1.8 ± 0.29) ($P = 0.000$).

4.2. Conclusion

Based on our outcomes, the mean uterine artery (PI) value in RPL group was greater than in control group, indicating increased impedance to blood flow in uterine arteries in females with a history of RPL. In females with unexplained infertility, peri-implantation endometrial perfusion is impaired; consequently, Doppler research of uterine hemo-dynamics must be regarded in infertility workups.

Consent for publication

I verify that all authors have agreed to submit the manuscript.

Availability of data and material

Available.

Funding

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article.

Conflicts of interest

Authors affirm that they have no conflicts of interest concerning publication of paper.

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