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UTERINE ARTERY DOPPLER AND UTERO PLACENTAL VASCULATURE IN RECURRENT UNEXPLAINED FIRST TRIMESTER PREGNANCY LOSS

By

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ABSTRACT

Background: Recurrent pregnancy loss (RPL) is three or more consecutive pregnancy losses before 20 weeks gestation. After a thorough evaluation, a cause is found in a little more than half of the cases and the rest remain unexplained. Theories suggest that impaired uterine perfusion may be a cause of recurrent unexplained pregnancy loss.

Objective: To investigate the color Doppler sonographic parameters, using transvaginal imaging, of uterine artery and utero placental vasculature (retro chorionic vessels), and comparing them between women with no history of pregnancy loss and women with recurrent first trimester pregnancy loss of unexplained cause.

Patients and Methods: This study was done in outpatient clinic of Om El Masryeen General hospital, from March 2019 to September 2019. One hundred pregnant women were divided equally into two groups: Group I (study group) included women suffering from recurrent unexplained first trimester pregnancy loss, and Group II (control group) included women with no history of pregnancy loss and at least one live birth at term. Age ranged from 18-40 years, and gestational age ranged from 6-13 weeks.

Results: There was a significant increase in mean values of resistance index (RI) and pulsatility index (PI) of both uterine arteries in the study group compared to the control group. In addition, there was a significant increase in mean values of both RI and PI of uterine spiral arteries in the study group compared the control group.

Conclusion: Transvaginal Doppler studies detected increased uterine blood flow resistance in recurrent unexplained first trimester pregnancy loss compared to normal population. Therefore, increased uterine blood flow impedance may serve as a cause for recurrent pregnancy loss.

Keywords: Recurrent pregnancy loss, ultrasonography, Doppler studies, uterine arteries, spiral arteries.

INTRODUCTION

Pregnancy loss is the involuntary loss of a pregnancy before 20 weeks gestation, or the loss of a fetus weighting 500 g or less *(ACOG, 2015)*. Recurrent pregnancy loss, by the traditional definition, is three or more consecutive clinically recognized losses. More recent definitions recommended two or more clinically recognized losses *(ASRM, 2012)*.

Pregnancy loss is common, affecting about 15% of clinically recognized

pregnancies and up to 50% or more, of all conceptions. It is a devastating event for both patients and their caregivers, as it may pose a medical puzzle with a wide array of causes involved *(Kutteh, 2010).*

Recurrent pregnancy loss causes include either genetic, structural, infective, endocrine, immune, thrombophilic disorders or unexplained causes *(Vomstein et al., 2021).* A meticulous evaluation will detect a cause of recurrent loss in over half of the couples seeking treatment only, and the rest will be attributed to unexplained causes *(Lund et al., 2012)*. Many studies suggest that uterine artery perfusion may affect endometrial receptivity, and that poor uterine perfusion could be one of the causes of unexplained pregnancy loss *(ASRM, 2012).*

The introduction of pulsed Doppler ultrasonography provided a noninvasive means for the evaluation of uterine impedance, giving physiologic data, rather than anatomical alone. It has been confirmed that resistance to uterine arterial blood flow is associated with poor obstetrical outcome such as pre-eclampsia and fetal growth restriction *(Bao et al., 2019).*

However, Doppler study of uterine arteries alone doesn't reflect the actual blood flow to the endometrium. As a result, endometrial and sub-endometrial blood flows should be more objectively measured *(Adibi et al., 2015).*

As a result, Pulsed Doppler ultrasonography on the uterine arteries and utero placental vasculature may be useful in distinguishing women with recurrent pregnancy loss caused by vascular dysfunction from women with unexplained recurrent pregnancy loss *(Bao et al., 2019).*

The present work aimed to investigate the color Doppler sonographic parameters, using transvaginal imaging, of uterine artery and utero placental vasculature (retro chorionic vessels), and comparing them between women with no history of pregnancy loss and women with recurrent first trimester pregnancy loss of unexplained cause.

PATIENTS AND METHODS

This study included two groups of pregnant women who attended Obstetrics and Gynecology clinics at Om El Masryeen General hospital:

A. **Group I (study group):** Included 50 women with history of recurrent first trimester pregnancy loss of unexplained cause.

B. **Group II (control group):** Included 50 women with no history of pregnancy loss and at least one live birth at term.

Inclusion criteria:

- Pregnant mother between ages of 18-40 years.
- Gestational age between 6-13 weeks.
- Singleton pregnancy.
- History of recurrent (2 or more) first trimester pregnancy loss with unexplained cause.

Exclusion criteria:

- Cervical incompetence and anatomical abnormalities of the uterus, e.g. bicornuate and septate uterus.
- Chronic medical disorders, e.g. renal, cardiac, connective tissue disorders,

chronic hypertension and diabetes mellitus.

- Multifetal pregnancy or gestational age more than 13 weeks.
- History of pelvic inflammatory disease, endometriosis clinical evidence, smoking, pelvic pathology such as uterine fibroids and ovarian cysts.

All of the experimental procedures of the study as well as its main goal were clearly explained to the participants, and written informed consents were obtained from all the patients.

All women in the study were submitted to complete history taking, general examination, abdominal examination and abdominal U/S investigation.

Transvaginal Ultrasonography was by using GE LOGIC C5 machine equipped with a 7.5-MHz vaginal transducer with pulsed color Doppler.

- Women were asked to empty their bladders and set in the dorsal position.
- Ultrasound assessment included:
  - Uterine size and dimensions: (longitudinal diameter, transverse diameter and anteroposterior diameter).
  - Assessment of ovarian texture and size.
  - Assessment of the Douglas pouch.
  - Women with uterine anomalies, ovarian masses, ovarian cysts or myomas of the uterus were all excluded.
  - Then we proceeded with pulsed color Doppler assessment of the right uterine artery (identified at the lateral border of uterine isthmus) and spectral wave analysis. The process was repeated for the left side.
  - Doppler signal was introduced to assess retro- chorionic blood flow indices.
  - The mean values of sonography were recorded for every subject.

Agreement for this study was obtained from the hospital's ethical committee, and informed consents were obtained from pregnant women after adequate provision of information regarding the study requirements, purpose and risks.

Data were analyzed using SPSS software version 16. Data were represented as range, mean ± standard deviation (SD) and were compared by independent t-test. **The $p \leq 0.05$ was considered statistically significant.**

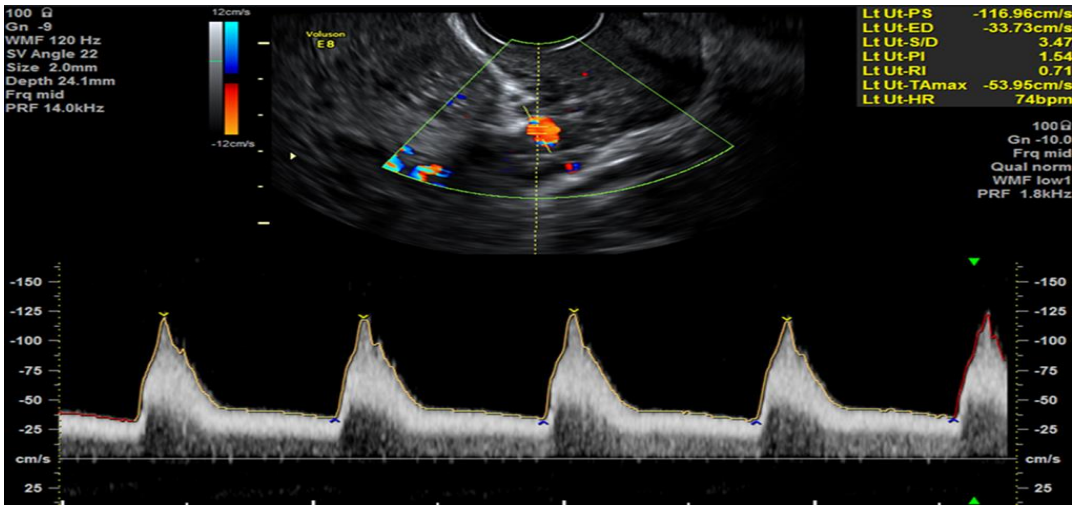

Figure (1): Pulsed color Doppler assessment of uterine artery RI and PI.

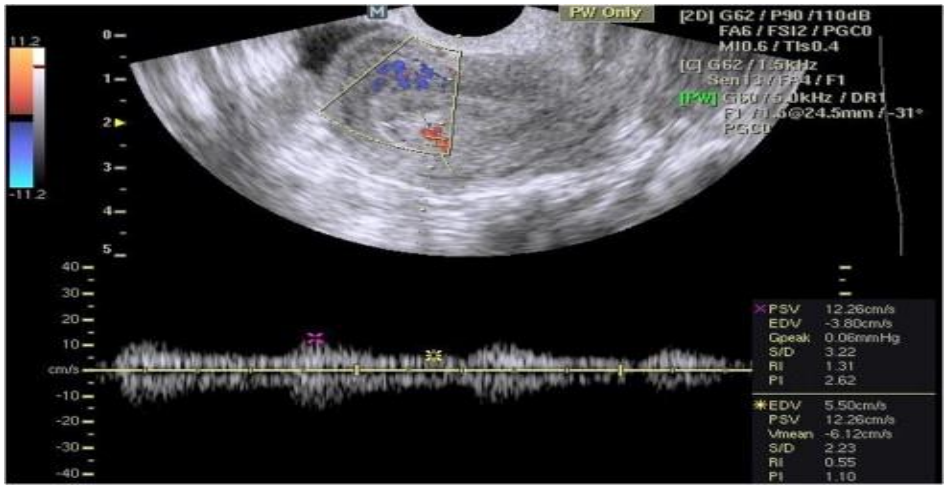

Figure (2): Pulsed color Doppler assessment of spiral artery RI and PI

RESULTS

There were no significant differences between women of both groups regarding the age and gestational age **(Table 1)**.

Table (1): Difference between Groups regarding Age and Gestational Age

Parameters \ Groups	Group I Study Group (n=50)	Group II Control Group (n=50)	*P*
Age (years) **Range** **Mean ± SD**	 20 – 32 28.68 ± 2.79	 20 – 32 27.76 ± 2.84	 0.106
Gestational Age (weeks) **Range** **Mean ± SD**	 7 – 12 8.74 ± 1.59	 7 – 12 9.14 ± 1.67	 0.222

SD standard deviation

There were statistically significant higher mean values of right and left uterine artery resistance index (RI) and pulsatility index (PI) among women of group I when compared to women of group II **(Table 2)**.

Table (2): Difference between Groups regarding Doppler Indices of Uterine Arteries

Groups / Indices	Group I Study Group (n=50)	Group II Control Group (n=50)	*P*
Right Uterine Artery RI			
Range	0.86-0.97	0.76-0.87	<0.001
Mean ± SD	0.91 ± 0.06	0.82 ± 0.06	
Right Uterine Artery PI			
Range	2.22-3.32	1.74-2.64	<0.001
Mean ± SD	2.65 ± 0.53	2.22 ± 0.43	
Left Uterine Artery RI			
Range	0.81-0.90	0.75-0.86	<0.01
Mean ± SD	0.84 ± 0.05	0.81 ± 0.06	
Left Uterine Artery PI			
Range	2.12-2.73	1.72-2.61	<0.001
Mean ± SD	2.45 ± 0.28	2.18 ± 0.43	

SD standard deviation
RI resistance index
PI pulsatility index

There were statistically significant higher mean values of spiral artery RI and PI among women of group I when compared to women of group II. The differences regarding mean values of arcuate artery RI and PI were statistically insignificant **(Table 3)**.

Table (3): Difference between Groups regarding Doppler Indices of Spiral and Arcuate Arteries

Groups / Indices	Group I Study Group (n=50)	Group II Control Group (n=50)	*P*
Spiral Artery RI			
Range	0.39 – 0.57	0.39 – 0.49	<0.001
Mean ± SD	0.47 ± 0.05	0.44 ± 0.03	
Spiral Artery PI			
Range	0.61 – 1.26	0.51 – 1.17	0.027
Mean ± SD	0.94 ± 0.2	0.85 ± 0.2	
Arcuate Artery RI			
Range	0.5 – 0.7	0.45 – 0.69	0.186
Mean ± SD	0.59 ± 0.08	0.57 ± 0.07	
Arcuate Artery PI			
Range	0.7 – 1.7	0.67 – 1.73	1.000
Mean ± SD	1.19 ± 0.29	1.19 ± 0.33	

SD standard deviation
RI resistance index
PI pulsatility index

DISCUSSION

Women with a history of one pregnancy loss have a 24% risk of miscarriage in next pregnancy, and the risk increases as number of previous pregnancy losses increases, to reach 26% with two previous miscarriages and 32% with three. Therefore, patients with previous two pregnancy losses should be evaluated to detect a cause, which sometimes can be treated *(Ozturk et al., 2012).*

Angiogenesis and uterine blood supply are essential for both endometrial growth and embryo development *(Kutteh, 2010).* As a result, endometrial vascularity has been considered to play a critical role in endometrial receptivity formation and pregnancy maintenance *(El-mashad et al., 2013).*

Doppler ultrasound is a noninvasive method of examining utero placental circulation. Moreover, it has proved to have a high predictive value for several obstetric events throughout pregnancy *(Kwak-Kim et al., 2011).*

This study aimed to investigate the color Doppler sonographic parameters, using transvaginal imaging, of uterine artery and utero placental vasculature (retro chorionic vessels), and comparing them between women with no history of pregnancy loss and women with recurrent first trimester pregnancy loss of unexplained cause.

In the present work, age ranged from 20 to 32 years, and there were no statistically significant differences between both groups regarding age. Gestational age ranged from 7 to 12 weeks, and there were no statistically significant differences between women in both groups regarding gestational age.

In the current study, the mean values of the resistance index (RI) of the right and left uterine arteries were significantly higher in women of group I when compared to women of group II. In their work, *Chen et al. (2010)* reported that there was no statistically significant difference between cases with recurrent abortion and normal control subjects as regard uterine resistance index. Although these results agree with our study in increased (RI) in study group, it does not reach the statistical significance observed in the present study.

Our mean values of the pulsatility index (PI) of the right and left uterine arteries were significantly higher in women of group I when compared to women of group II. These results were in context with several other authors as *Ferreira et al. (2011)* and *El-mashad et al. (2013)* who reported that there was statistically significant increase in uterine artery pulsatility index in cases with recurrent abortion in comparison to control cases.

On the other hand, *Chen et al. (2010)* reported that there was statistically insignificant difference between study and control groups as regard uterine artery blood flow indices. These differences may be attributed to the fact that they used a different scanner and different Doppler type and settings.

In our study, there were statistically significant higher mean values of spiral artery RI and PI among women of group I when compared to women of group II. However, the differences regarding mean values of arcuate artery RI and PI were

statistically insignificant. These results were consistent with the results reported by *Wang et al. (2010), Abdel Wahab et al. (2011)* and *Mercé et al. (2012).*

On the other hand, *Özkan et al. (2015)* reported that no significant differences in Doppler parameters were detected between patients with first-trimester threatened abortion that ended in abortion, and control patients. This can be attributed to different inclusion criteria.

In our study, we found a significant positive correlation between uterine arteries (PI), (RI) and spiral arteries (PI), (RI) in the unexplained RPL group.

No cut off values for prediction of miscarriage in the current study may be attributed to small sample size and short period of follow up so larger prospective studies are needed aiming to confirm such results and reaching values that can accurately predict such cases.

CONCLUSION

Impaired uterine circulation, as indicated by increased uterine blood flow impedance, may serve as a pathogenic background in cases of unexplained RPL.

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أشعة الدوبلر علي الشريان الرحمي و الأوعية الدموية المغذية للرحم و المشيمة في الأجهاض المتكرر غير معلوم السبب في الثلث الأول من الحمل

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خلفية البحث: الأجهاض المتكرر يعرف بفقدان الحمل 3 مرات متتابعة قبل اتمام 20 أسبوع من تاريخ بداية أخر دورة شهرية. و أسباب الأجهاض المتكرر متعددة. و يؤدي تعدد الأسباب إلي تعدد الفحوصات لمعرفة سبب الأجهاض و أختلاف وسائل العلاج، و علي الرغم من ذلك لا يتم التوصل لسبب محدد في نسبة قد تصل من 50% إلي 75% من الحالات. كانت الكثير من الأبحاث قد أقترحت نظرية تأثير نضح الرحم ،عن طريق الشريان الرحمي و الأوعية الدموية المغذية للرحم و المشيمة، علي سلامة الحمل و أعتبرت وجود أي ضعف فيه قد يكون سببا للأجهاض المتكرر.

الهدف من البحث: قياس المقاومة في الشريان الرحمي و الأوعية الدموية المغذية للرحم و المشيمة عن طريق أشعة الدوبلر و مقارنتها بين السيدات اللاتي تعاني من الأجهاض المبكر المتكرر غير معلوم السبب ، و السيدات اللاتي لم يجهضن من قبل و سبق لهن الأنجاب.

المريضات وطرق البحث: أجريت هذه الدراسة في العيادات الخارجية في مستشفى أم المصريين العام، وقد شملت 50 سيدة حامل في الثلث الأول من الحمل ممن تعرضن للأجهاض المبكر المتكرر غير معلوم السبب، بالأضافة إلي 50 سيدة حامل في الثلث الأول من الحمل ممن لم يجهضن من قبل و سبق لهن الأنجاب كمجموعة ضابطة.

نتـــائج البحـــث: أظهــرت الدراســة الحاليــة وجــود مقاومــة أعلــى لتــدفق الــدم لــدى الحـــالات التـــى ســـبق وأن تعرضـــت لفقـــد الحمـــل المتكـــرر مقارنـــة بالمجموعـــة الضابطة.

الاســـتنتاج: فشـــل الـــدورة الدمويـــة داخـــل الـــرحم، المســـتدل عليـــه بزيـــادة إعاقـــة تـــدفق الـــدم داخـــل الـــرحم، قـــد يعمـــل كخلفيـــة مرضـــية فـــى حـــالات فقـــد الحمـــل المتكـــرر. وتوصـــى الدراســـة بضـــرورة إجـــراء المزيـــد مـــن الدراســـات علـــى مجموعة أكبر لتأييد هذه النتائج.

الكلمـــات الدالـــة: الأجهـــاض المتكـــرر، الأشـــعة التلفزيونيـــة، أشـــعة الـــدوبلر، الشريان الرحمي، الشريان الحلزوني الرحمي.