

## TO EVALUATION OF OF UTERINE ARTERIAL BLOOD FLOW IN EARLY PREGNANCY IN WOMEN WITH RECURRENT PREGNANCY LOSS

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### ABSTRACT

A prospective observational study for evaluation of blood flow resistance in uterine arteries was conducted from March 2012 to April 2013. Around 120 pregnant women at 5 to 9 weeks gestation included and underwent transvaginal pulsed Doppler ultrasound (control group n= 60; and recurrent pregnancy loss group, n= 60). Blood tests for antinuclear and antiphospholipid antibodies were also performed. The uterine arterial pulsatility index in recurrent pregnancy loss group was significantly higher than that in control group. Women with antinuclear or antiphospholipid antibodies had an elevated pulsatility index in the uterine artery, which was prominent in women with recurrent pregnancy loss group. Coagulopathy and vascular dysfunction caused by autoantibodies may impair uterine perfusion. However, the uterine arterial pulsatility index in recurrent pregnancy loss group significantly higher than that in the control group even among women without antinuclear antibodies or antiphospholipid antibodies. This observational study suggests that the uterine artery pulsatility index may be an independent index for recurrent pregnancy loss (which is noninvasive evaluation of uterine impedance).

**KEYWORDS :** Antinuclear Antibodies, Antiphospholipid Antibodies, Pulsed Doppler Ultrasonography, Recurrent Pregnancy Loss

The most beautiful feeling which a women experience in her life to be a mother. Normal pregnancy is the state of carrying a developing embryo with in the womb. An early detection of early pregnancy complications can give us an upper hand to reduce maternal and foetal morbidity. It is also useful to predict the likelihood of success in human reproduction in order to devise strategies for improving the likelihood of live born infant.

The World Health Organization (WHO, 1997) has defined miscarriage as the loss of a foetus weighing  $\leq 500g$ , which would normally be at 20-22 complete weeks of gestation.

Royal College of Obstetrics and Gynecology (RCOG, 2001) defined recurrent spontaneous abortion (habitual abortion or miscarriage) as at least 2 or 3 spontaneous abortions prior to 20 weeks gestational age with the same partner.

Peripheral vascular resistance in normal pregnancy decrease as early as 5 weeks gestation. Resistance in uterine arterial blood flow also decrease progressively after implantation.

These physiological changes are thought to be a major factor for an increase in uterine flow with decreased impedance with advancing gestation in normal pregnancy, which maintains adequate placental perfusion. This impedance to blood flow can be non-invasively studied by

Doppler velocimetry. Placental insufficiency is a major cause of perinatal and maternal morbidity and mortality. Aberrant trophoblastic invasion has been implicated in placental insufficiency (Voigt and Becker et al., 2000). High Uterine Artery PI (Pulsatility Index), RI (Resistance Index), and early diastolic notching have been interpreted as indicators of high impedance (Fleischer, 1996)

The study of blood flow in the uterine arteries may elucidate the vascular changes in patients with recurrent pregnancy loss and may help to identify a portion of patient with recurrent pregnancy loss, which was caused by impaired uterine perfusion.

The introduction of transvaginal sonography has produced a remarkable improvement in recognition of blood vessel indicating the anatomical location plus direction and velocity of blood. Transvaginal pulsed Doppler ultrasonography allow non-invasive evaluation of uterine circulation and gives physiologic data, rather than anatomic information alone (De Carolis S., 1994). It is known that resistance to uterine arterial blood flow is associated with poor obstetrical outcome (DE Carolis S. et al, 1995). Pulsed Doppler ultrasonography in the uterine artery may be useful in distinguishing women with recurrent pregnancy loss (RPL) caused by vascular dysfunction from women with unexplained RPL (DE Carolis S. et al., 1995).

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Antiphospholipid antibody (APLA) emerged as a chief culprit responsible not only for RPL but also for several others adverse pregnancy outcome.

Although ANA (Ante Nuclear Antibody) are not specifically related to pregnancy loss, women with positive ANA may have other autoimmune antibodies predispose to vasculopathy or coagulopathy. These pathological changes are likely to cause elevation of the uterine arterial blood flow resistance and lead to RPL (Bahar et al., 2000).

Impaired uterine perfusion caused by coagulopathy and vascular dysfunction may result in pregnancy loss. In this study, we measured the resistance in uterine arteries of pregnant women with and without RPL in the early first trimester and evaluated the association of autoantibody. The disadvantage of Doppler velocimetry behind that, it is only of prognostic significance but not of much of etiological significance.

**METHODS**

We conducted a prospective observational study for evaluation of association of uterine arterial blood flow in early pregnancy in women with recurrent pregnancy loss at the department of Obstetrics and Gynecology, Mahila Chikitsalya, S.M.S Medical College, Jaipur. During one

year of study period from March 2012 to April 2013 around 120 patient were include and underwent work up.

Women in age group 25 to 29 years included in the study.

Routine Antenatal Monitoring: Weight, BP, Haemoglobin, ABORh, urine complete examination, fasting blood sugar, HbsAg, VDRL, HIV testing, Thyroid profile, Liver function test, renal function test, complete hormonal profile was done. All 120 patients were subjected to duplex Doppler examination by Transvaginal route. Blood sample collected from these patient and sample evaluate for Autoantibody include Antiphospholipid antibody (anti B2 glycoprotein antibody and anticardiolipin antibody) and antinuclear antibody.

**RESULTS**

The mean gestational age of case group and control group which was  $6.60 \pm 1.13$  and  $6.43 \pm 0.98$  respectively (p value >0.05) (Table 1).

The mean pulsatility index of case and control group subjects was  $2.66 \pm 1.16$  and  $1.53 \pm 0.48$  respectively. The mean Pulsatility index of case group subjects was found to be higher as compared to control group subjects and statistically highly significant (p < 0.001) (Table 2).

**Table 1 : Mean Value of Gestational Age of Cases & Control**

	Case	Control	P- value	Significance
Mean + SD	6.60 + 1.13	6.43 + 0.98	> .05	Not Significant

**Table 2 : Mean Value of PI of Case & Control Groups**

	Case	Control	P- value	Significance
PI (Pulsatility Index)	2.66 + 1.16	1.53 + 0.48	< .001	Highly Significant

**Table 3 : Mean value of Anti β2 glycoprotein IgM level in Case & Control Groups**

	Case	Control	P- value	Significance
Ig M	8.67 + 2.20	7.92 + 1.44	< .01	Significant

**Table 4 : Mean Value of Anticardiolipin Antibody of Cases & Controls Group**

	Case	Control	P- value	Significance
Anticardiolipin antibody	0.80 + 0.22	0.74 + 0.10	> .05	Not Significant

**Table 5: Distribution According to Antinuclear Antibody in Case & Control**

Antinuclear antibody	Case		Control	
	No.	%	No.	%
Negative	36	60.00	57	95.00
Positive	24	40.00	3	5.00
Total	60	100.00	60	100.00

$\chi^2 = 19.116$     d. f.=1    P < .001    HS

Anti  $\beta$  2 glycoprotein IgM positivity in case and control group subject was 11 (18.33%) and 3 (5%) respectively. Anti  $\beta$  2 glycoprotein IgM positivity was found to be higher in the case group than control group and statistically significant (Table 3).

Anticardiolipin antibody negativity of case and control group subjects was 54 (90%) and 58 (96.67 %) respectively. Anticardiolipin antibody positivity of case group subjects was 6(10%) and 2(3.33%) in control group but the difference was statistically not significant (Table 4).

Antinuclear antibody negativity in case and control group subjects was 36 (60%) and 57 (95.00 %) respectively. Antinuclear antibody of case group subjects was 24(40%) and 3(5.00%) in control group but the difference in Antinuclear antibody in case and control group subjects was statistically found highly significant (Table 5).

## DISCUSSION

Trophoblastic invasion during first trimester coincide with a decrease in uterovascular resistance at beginning of the second trimester. Antiphospholipid antibodies are known to interfere with syncytium formation in trophoblast in early pregnancy and cause decidual vasculopathy, thrombosis and placental infarction later in pregnancy.

Dysfunction of trophoblasts caused by APAs may involved in elevation of uterine arterial PI that observed more likely to be associated with vascular dysfunction rather than impaired trophoblastic invasion. Trophoblastic invasion has little effect on uterine arterial blood flow at 4 to 5 weeks gestation, because the decrease in blood flow resistance in uterine artery is very slow until 8 weeks of gestation.

Although ANAs are not specific etiologic factor for pregnancy loss, some women with ANAs may have

other autoimmune or coagulopathy such as APAs. These pathologic changes are likely to cause elevation of uterine arterial blood flow resistance and lead to RPL, early onset of preeclampsia or foetal growth restriction.

A portion of the group of women with both RPL and elevated PI in uterine artery did not have abnormal blood test results. Although the apparent underlying pathophysiological mechanisms of these cases were not elucidated, there may have subclinical vasculopathy, which was not diagnosed on basis of routine screening tests for RPL, even those with negative APA test results, had elevated PI in uterine artery. These observation suggest that the PI in uterine artery may be an independent index for RPL. However, analysis of this index combined with blood tests may help in evaluating the risk of pregnant women. The introduction of Pulsed Doppler ultrasonography has provided the means for the noninvasive evaluation of uterine impedance, thus providing physiologic data on hemodynamic abnormalities in early pregnancy failures.

## CONCLUSION

Early detection of uterine artery perfusion by pulse Doppler ultrasonography in pregnant women with history of recurrent pregnancy loss suggest an association between impaired uterine blood flow with recurrent pregnancy loss and early intervention helps in improving the fetomaternal outcome.

Some patients in case group with abnormal Doppler study did not have abnormal blood test results. These observation suggest that abnormal Doppler study might an independent index for RPL.

Doppler study is primary tool for evaluation of uterine arterial impedance as non-invasive, cost effective and easily approvable in comparison to the blood tests.

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