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Evaluation of maternal ophthalmic artery Doppler indices and its correlation with fundoscopic changes in normotensive and pre-eclamptic pregnancies: A comparative study

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Abstract

Background: Preeclampsia is a multisystem disease characterized by the development of hypertension after 20 weeks of gestation in a previously normotensive woman with the presence of proteinuria, severity leading to target organ injury, including liver, kidney, heart, lungs, brain and pancreas. We evaluated the ophthalmic artery Doppler indices (PSV, EDV, PI, RI) in normotensive and in pre-eclamptic pregnancies and correlated the Doppler indices changes with fundoscopic findings.

Materials and methods: Orbital Ultrasonography was performed on the pregnant women who developed high blood pressure after 20 weeks of gestation and on the normal pregnant women as control and the Doppler indices of ophthalmic artery were determined. Fundoscopic examination of the patients was done with direct ophthalmoscope. Hypertensive Retinal changes observed in both eyes were taken as positive findings.

Results: The study showed that PSV, RI and PI and S/D ratio were reduced in pre-eclamptic patients when compared with healthy normotensive pregnant women while EDV was increased in pre-eclamptic patients when compared with healthy normotensive pregnant women. Statistically significant relationship among Doppler parameters namely PSV, EDV, PI, RI, S/D values between normotensive and pre-eclamptic patients was noted. Fundoscopic changes were noted among severe pre-eclampsia patients.

Conclusions: Ophthalmic artery Doppler Ultrasonography can detect pre-eclampsia in early stages when compared to fundoscopy and is a cheap, noninvasive, readily available, safe, and reliable tool for evaluation of the central hemodynamic changes in normal pregnancy, and even more so in PE.

Keywords: Ophthalmic artery Doppler, pre-eclampsia, fundoscopy, pregnancy induced hypertension

Introduction

Hypertensive disorders of pregnancy are an important cause of severe morbidity, long term disability and death among both mothers and their babies. Pregnancy-induced hypertension is one of the significant causes of death among women in the reproductive age group. Preeclampsia is a multi-systemic disorder of pregnancy characterized by abnormal vascular response to placentation with increased systemic vascular resistance, a hypercoagulable state and endothelial dysfunction^[1, 2]. Hypertensive disorders of pregnancy occur in about 10% of all pregnant women around the world. Preeclampsia affects 3-5% of pregnancies.³ The incidence of PIH in India is about 7-10% of all antenatal admissions.^[4] Hypertensive disorders of pregnancy include several forms like gestational hypertension, pre eclampsia, eclampsia, and chronic hypertension.

Preeclampsia can present with complications in the eye in 30% to 100% of patients^[5]. Specifically, visual disturbance develops in 25% of women with severe preeclampsia, but blindness is rare. Doppler sonography of the ophthalmic artery is a noninvasive method used to study central territory vascular flow during pregnancy^[6, 7].

With this background, we conducted this study to evaluate the ophthalmic artery Doppler indices in pre-eclamptic pregnancies and compare it with normal pregnancies and also to correlate the Doppler indices changes with fundoscopic findings in pregnant women with pre-eclampsia.

Methodology

Ophthalmic artery Doppler indices of 40 pre-eclamptic women were compared to those of 60

healthy pregnant women in a cross-sectional study. This study was conducted in Department of radio diagnosis, Bangalore Medical College and Research Institute, Bangalore. Based on previous study Oliveria, *et al.* [6] Ophthalmic artery resistive index in normotensive group was 0.70 ± 0.029 and in preeclampsia group was 0.682 ± 0.028 . The sample size was estimated at 40 in each group using the formula for comparison of means between two groups:

$$n = \frac{2(Z_{\alpha} + Z_{1-\beta})^2 \delta^2}{d^2}$$

Consecutive women with preeclampsia were recruited into the study until the sample size was achieved. We included 60 pregnant women with normal blood pressure and 40 pregnant women diagnosed with PIH. We excluded uncooperative and unwilling patients, those with smoking and alcohol consumption history, with history of diabetes. We also excluded patients with Glaucoma and other ocular disorders like cataract, corneal ulcer and those on antihypertensive medication or corticosteroids.

The blood pressure was measured using the Korotkoff sounds I and V. Patients were diagnosed as pre-eclampsic when they had a blood pressure of $\geq 140/90$ mm Hg and proteinuria of $\geq 1+$ on using a dipstick. Informed and written consent was taken from selected patients. A detailed history, complete physical examination and fundoscopic examination was done for all patients by the ophthalmologist and Orbital Doppler ultrasound was performed using a PHILIPS A35 ultrasound scanner using

linear probes of frequency ranging from 10-15 MHZ.

The ophthalmic artery is assessed approximately 10mm from the sclera's posterior wall, medial to the optic nerve. After identifying the ophthalmic artery, the incidence angle is verified to ensure that the insonation angle is less than 60° , filter set to 50hz, pulse repetition frequency set to 125hz, and Doppler sample volume adjusted to 2mm. The normal ophthalmic artery flow velocity waveforms have a steep maximum systolic peak with a dicrotic protodiastolic notch and a low diastolic flow wave. After obtaining three consecutive waveforms with similar sizes and shapes, measurements are performed on all three waveforms. Peak systolic velocity, Mean diastolic velocity and Resistive index and Pulsatility index, S/D ratio measured on each of the three waveforms, and average value from the measurements is obtained for each parameter.

The data recorded was analyzed using the Statistical Package for Social Sciences (SPSS), 21 version. The differences in socio-demographics, clinical and ophthalmic parameters between the two groups of women were evaluated with the use of Student's t-test for quantitative variables and χ^2 tests for categorical variables. The level of significance was set at 5% for all significance tests.

Results

A total of 40 pre-eclampsic women and 60 normotensive pregnant women were recruited. The socio-demographic and selected obstetric variables of the study participants in both groups are shown in table 1. There were no significant differences between the two groups in age ($p=0.98$), parity ($p=0.87$) and gestational age ($p=0.82$).

Table 1: Comparison of sociodemographic characteristics of preeclampsia cases and controls

Variables		Pre-eclampsic pregnancy	Normal Pregnancy	Statistical Significance
Age	≤ 20 Years	8 (20)	9 (15)	Yate's chi square - 0.163 p value - 0.98
	21-25 years	15 (37.5)	25 (41.7)	
	26-30 years	14 (35)	23 (38.3)	
	31-35 years	3 (7.5)	3 (5)	
Parity	Multigravida	22 (55)	34 (56.7)	Chi square - 0.027 p value - 0.869
	Primigravida	18 (45)	26 (43.3)	
Age in years (mean \pm SD)		24.7 \pm 3.8	24.6 \pm 3.7	p value - 0.95
Gestational age (mean \pm SD)		31.1 \pm 5.02	31.3 \pm 3.8	p value - 0.82
SBP (mean \pm SD)		155.8 \pm 10.7	111.7 \pm 7.8	p value - <0.001
DBP (mean \pm SD)		104.8 \pm 9.5	74.8 \pm 3.9	p value - <0.001

Slightly over half of the pre-eclampsic women (60%) had mild pre-eclampsia. Forty percent of our study cases were severely pre-eclampsic. The comparisons of the ophthalmic artery Doppler velocimetry parameters are shown in table 2. The mean pulsatility index was significantly lower among cases (1.05, SD=0.3) compared with controls (1.35, SD=0.18) ($p < 0.001$). Similarly, the mean resistivity index

was significantly lower among cases (0.64, SD=0.06) compared with controls (0.78, SD=0.05) ($p < 0.001$). The mean peak systolic velocity ($p < 0.001$), end-diastolic velocity ($p < 0.001$) and the mean peak ratio ($p < 0.001$) were significantly lower among women with preeclampsia compared with the controls.

Table 2: Comparison of ophthalmic artery Doppler velocimetry parameters between preeclampsia cases and controls.

Parameters	Pre-eclampsic pregnancy	Normal Pregnancy	p value
Peak systolic velocity (cm/s)	26.3 \pm 3.4	38 \pm 5.02	<0.001
End-diastolic velocity (cm/s)	9.6 \pm 0.93	7.9 \pm 1.3	<0.001
Pulsatility index	1.05 \pm 0.3	1.35 \pm 0.18	<0.001
Resistivity index	0.64 \pm 0.06	0.78 \pm 0.05	<0.001
S/D	2.8 \pm 0.44	4.9 \pm 0.96	<0.001

Among 40 pre-eclampsic women, the funduscopy findings revealed that the most common finding was generalized arteriolar attenuation which was present in 35% of cases.

The other funduscopy findings are described in table 3. In the study group majority (27.5%) showed grade I changes, followed by grade II changes (10%), followed by grade IV

(2.5%) changes.

Table 3: Distribution of study subjects according to funduscopy findings and retinopathy

		Frequency (%)
Funduscopy findings	Generalized arteriolar attenuation	14 (35)
	Focal arteriolar attenuation	5 (12.5)
	AV Nicking	3 (7.5)
	Hemorrhages/exudates	-
	Serous retinal detachment	1 (2.5)
Grades of retinopathy	Grade I	11 (27.5)
	Grade II	4 (10)
	Grade III	0
	Grade IV	1 (2.5)

The values used as the cutoff points of the pulsatility index, resistive index and peak ratio for identifying severe preeclampsia are shown in Table 4.

Table 4: Analysis of the Doppler Index Cutoff Points for Identifying Severe Preeclampsia

Doppler findings	Cutoff Point	AUC (95% CI)
Peak systolic velocity	32.3	0.039 (0.006-0.072)
End-diastolic velocity	8.66	0.869 (0.797-0.94)
Pulsatility index	1.101	0.159 (0.062-0.256)
Resistive index	0.71	0.049 (0.013-0.085)
Peak ratio	3.333	0.005 (0.000-0.014)

In the study ROC curves was made for OAD parameters to predict pre-eclampsia and severity. End-diastolic velocity was the better predictor compared to others (Figure 1)

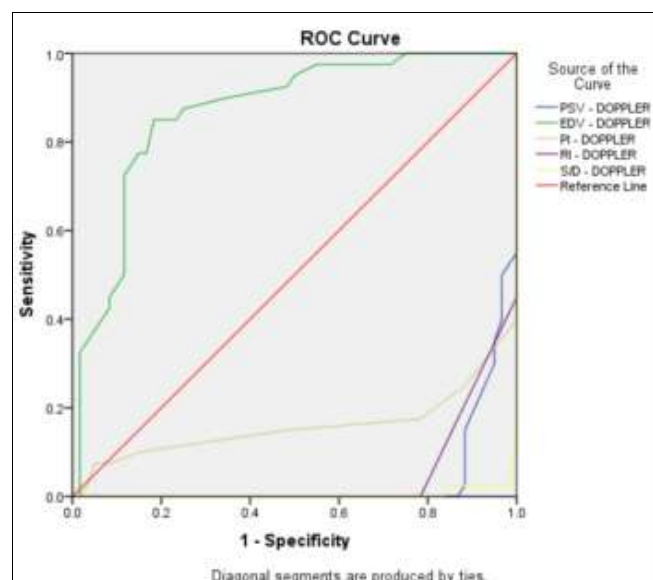


Fig 1: ROC showing comparison of S/D with grading in funduscopy

Discussion

This study compared the ocular and ophthalmic velocimetric features among pre-eclamptic women with normotensive pregnant women. There were significant differences in the intraocular pressure and the velocimetric indices between women with preeclampsia compared with normotensive women.

Mean maternal age among the study group was 24.65 ± 3.82 , and the control group was 24.6 ± 3.66 . Few Nigerian studies also reported the mean age between 25 to 30 years. [10, 12]

However, in the studies conducted by Olatunji *et al.* [8], and Onwudiegwu *et al.* [9] reported the mean maternal age was 32 among the study group. Onwudiegwu *et al.* [9] In our study, in both the study and control group majority were multigravida. Similar results were published by Onwudiegwu *et al.* [9] However, in the study conducted by Olatunji *et al.* [8], most of the women in the control and study group were primigravida. Following the criteria of WHO to classify Pre-eclampsia, in our study, 60% were having mild pre-eclampsia, and 40% were having severe pre-eclampsia. Onwudiegwu *et al.* [9] reported 48% mild/moderate PE and 52% severe PE and the study conducted by Olantunji *et al.* [8], showed similar findings, 42.9% of the pre-eclamptic patients were diagnosed with severe PE, and 57.1% had mild PE.

Generally, there were significantly lower values of the velocimetry parameters among the cases compared with the control group. Various other studies have also reported similar results [8, 9, 13, 14].

In our study, the majority (27.5%) showed grade I change, followed by grade II changes (10%), followed by grade IV (2.5%) changes. 35% had generalized arteriolar attenuation, 12.5% had focal arteriolar attenuation, 7.5% had AV nicking, 2.5% had Serous retinal detachment.

These findings were supported by Jayashree MP *et al.* [15]

Conclusion

This study has shown that PSV, RI and PI and S/D ratio were reduced in pre-eclamptic patients when compared with healthy Normotensive pregnant women. The funduscopy changes were observed only in severe pre-eclamptic patients and majority of them showed grade I followed by grade II hypertensive retinopathy changes. No significant funduscopy findings were noted among mild pre-eclampsia patients. Overall, this study has shown that ophthalmic artery Doppler Ultrasonography can identify central hemodynamic changes even in mild pre-eclampsia compared to funduscopy. Ophthalmic artery Doppler parameters also can differentiate mild from severe pre-eclampsia.

Image Gallery

Case -1

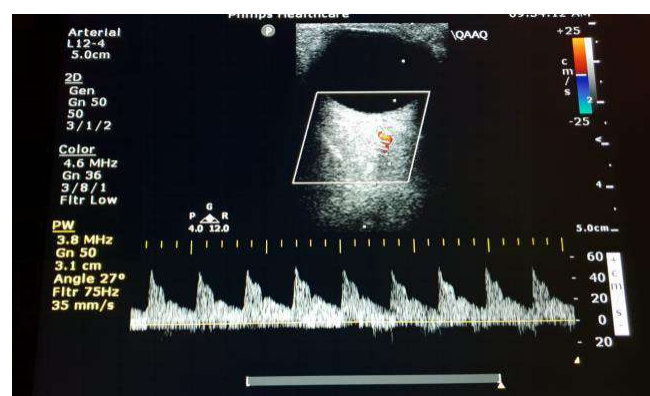


Fig 2: The waveform of Ophthalmic artery in normotensive pregnant women is typical for relatively high resistance artery. There is a sharp initial peak followed by an incisura and relatively little flow during diastole

Case -2

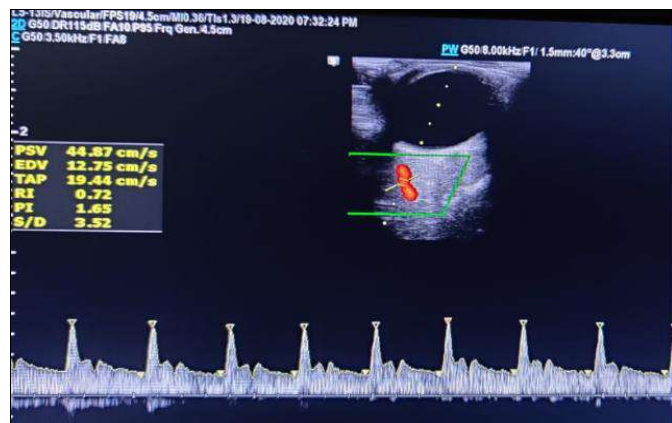


Fig 3: Ophthalmic artery doppler in normotensive pregnant women with high resistance flow.

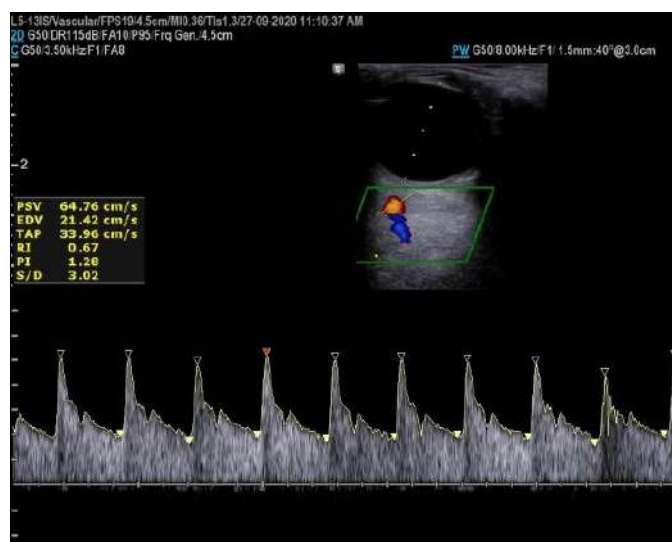


Fig 4: Ophthalmic artery doppler image in mild pre-eclampsia patient showing mildly reduced PI and RI values.



Fig 5: Fundoscopy image in the same patient shows no hypertensive retinopathy changes

Case 4

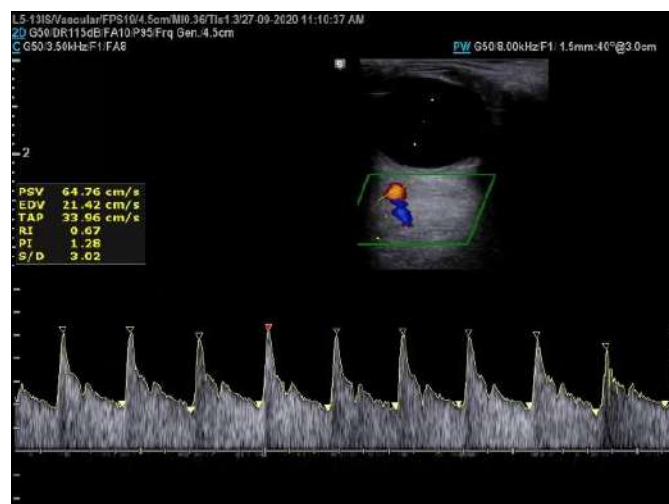


Fig 6: Ophthalmic artery doppler image in mild pre-eclampsia patient showing mildly reduced PI and RI values.

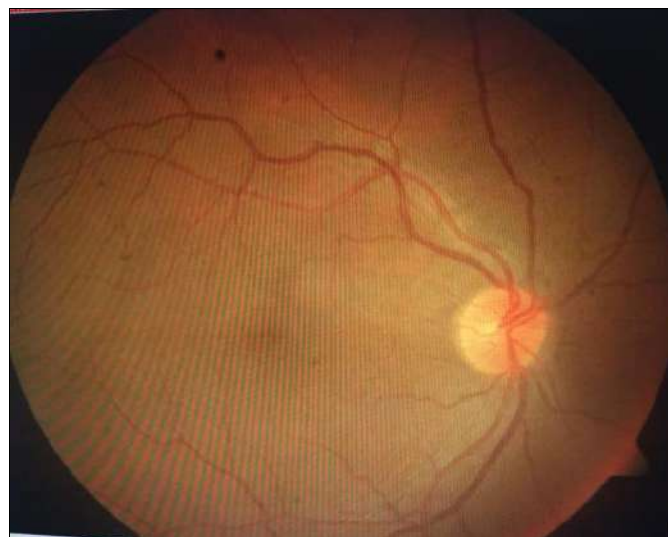


Fig 7: Fundoscopy image in the same case shows no hypertensive retinopathy change



Fig 8: Ophthalmic artery doppler image in mild pre-eclampsia patient showing mildly reduced PI and RI values.

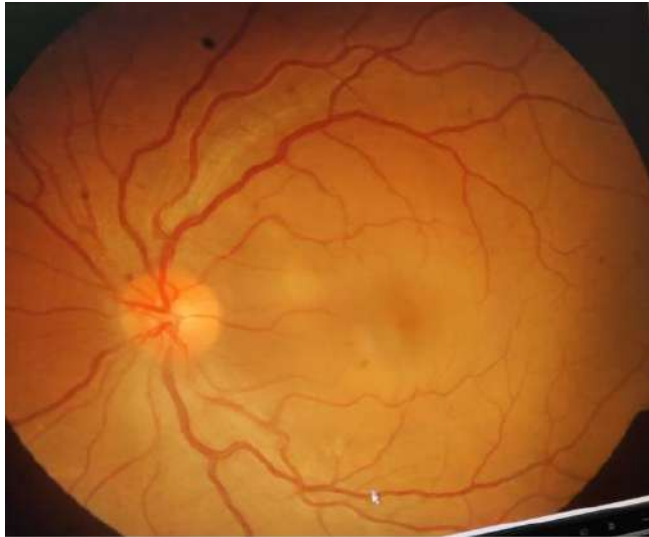


Fig 9: Fundoscopy image in the same patient shows no hypertensive retinopathy changes.

Case -6

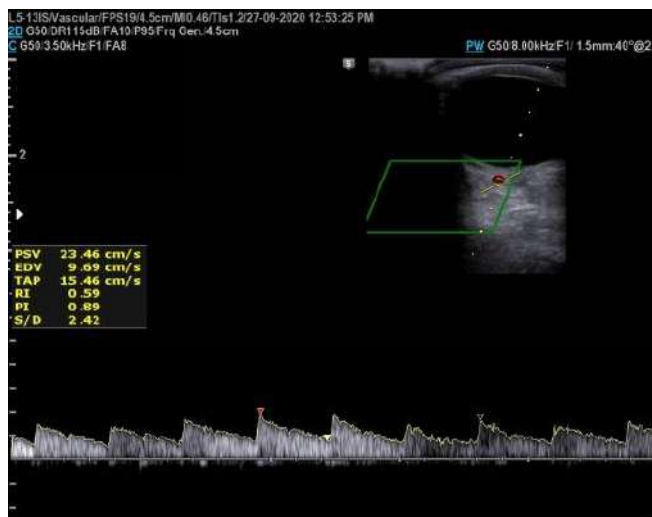


Fig 10: Ophthalmic artery doppler in severe pre-eclampsia shows increased diastolic flow with reduced PI and RI value.



Fig 11: Fundoscopy in same patient shows generalized arteriolar narrowing.

Case 7



Fig 12: Ophthalmic artery doppler in severe pre-eclampsia showing decrease in RI.

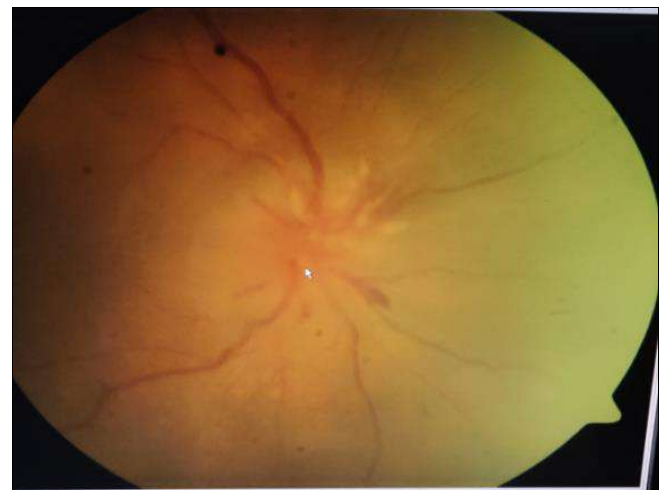


Fig 13: Fundoscopy image in the same patient shows focal arteriolar attenuation and exudates.

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