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Role of Ophthalmic Artery Doppler in Prediction of Preeclampsia

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ABSTRACT

Background: Preeclampsia (PE) is a crucial health issue that complicates roughly 10% of gestations and causes more than 50,000 deaths yearly worldwide. Many studies have appeared in the recent decade attempting to utilize Doppler study of the ophthalmic artery to anticipate the occurrence of preeclampsia and comparing its effectiveness to uterine artery Doppler, which is now considered the most accurate method employed, with promising results of equal sensitivity and specificity.

Objective: This study was designed to demonstrate the ability of changes in ophthalmic artery Doppler indices to predict the progression of preeclampsia.

Patients and methods: This prospective study comprised 120 pregnant women in total. The control group who remained normotensive throughout pregnancy included 96 women and those who developed preeclampsia (preeclampsia group) comprised of 24 women (16 with mild preeclampsia and 8 with severe preeclampsia).Those with severe preeclampsia had considerably higher ophthalmic artery PSV (P1), 2nd systolic peak (P2), peak ratio (p2/p1), and EDV than patients who remained normotensive.

Results: Ophthalmic artery PI had sensitivity of 89.7% and specificity of 75.12% at cutoff value < 1.76 in predicting pre-eclampsia. Also, ophthalmic artery RI had sensitivity of 80.2% and specificity of 74.9% at cutoff value < 0.77 in predicting pre-eclampsia. Peak Ratio (PR) of the ophthalmic artery had sensitivity of 77.3% and specificity of 65.8% at cutoff value > 0.59 in predicting pre-eclampsia. In addition, 2nd systolic peak (P2) ophthalmic artery had sensitivity of 91.7% and specificity of 61.7% at cutoff value > 20.1 in prophesying pre-eclampsia.

Conclusion: Doppler of the ophthalmic artery is an easy, reliable and unbiased technique with a standalone predictive diagnostic value for the development of PE and a promising excellent imaging procedure as the area under the curve for the peak ratio (PR) and the second systolic peak (P2) indices were more than 90%.

Keywords: Ophthalmic artery Doppler, Preeclampsia, Hypertension.

INTRODUCTION

Preeclampsia (PE) is a major morbidity that impacts about 10% of gestations worldwide. The pathophysiology of preeclampsia is still questionable with a unique clinical presentation of newly developed hypertension that usually occurs after 20 weeks of gestation (the systolic and the diastolic blood pressure of ≥ 140- and 90-mm Hg, respectively, on two readings with at least 6 hours in-between) and proteinuria (protein excretion of ≥ 300 mg in a 24-hr. urine collection, or a dipstick of ≥ +2) [(1)]. In absence of proteinuria, the development of any of the following also establishes the diagnosis of preeclampsia; the new onset of low platelet count, renal impairment, disturbed liver functions, pulmonary edema and cerebral and ocular symptoms [(2)].

Despite being challenging with pregnancy, assessment of cerebral circulation is crucial as acute neurological complications of preeclampsia such as eclampsia, brain edema and intracranial hemorrhage cause about 75% of maternal deaths [(3)].

Considering the similarity between ophthalmic artery and intra cranial vessels in embryology, anatomy and function, ophthalmic artery Doppler offers an easily performed and a non-invasive way to assess and monitor changes in cerebral circulation throughout pregnancy [(4)]. Many studies have emerged in the last decade trying to use the ophthalmic artery Doppler to anticipate preeclampsia and compare its efficiency to uterine artery Doppler that is considered the most accurate tool used nowadays with promising results of similar sensitivity and specificity [(5)]. Some problems have been recognized while reviewing these literatures such as the faulty interpretation of the second systolic peak of ophthalmic artery wave as first diastolic peak that has been corrected recently [(6)].

This study was designed to demonstrate the ability of changes in ophthalmic artery Doppler indices to predict the progression of preeclampsia.

PATIENTS AND METHODS

Study Design: This prospective observational cohort study was conducted on 120 normotensive pregnant ladies coming for routine antenatal care in Sers Ellian General Hospital during the period from June 2020 and September 2021.

Ethical consideration:

An approval of the study was obtained from Menoufia University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of participation in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Study population: Normotensive pregnant women who presented for standard ante-natal care before 20 weeks of pregnancy. By the end of the study the cases were divided into normotensive (the control group) and another group who developed preeclampsia (mild & severe): the control group included 96 women and the

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preeclampsia group included 24 women (16 with mild preeclampsia & and 8 with severe preeclampsia).
- After 20 weeks of pregnancy, a previously normotensive woman whose blood pressure elevated to 140/90 and got proteinuria of 0.3 g protein in one day urine sample (equivalent to a urine dipstick reading of 1+) was assigned to the mild preeclampsia subgroup.
- If the case had raised blood pressure of 160/110 on two measures taken at least 6 hours apart with the presence of proteinuria of ≥ 5 g of protein in a 24-hour urine collection (equivalent to a urine dipstick reading of 3+) of two urine samples obtained randomly with 4 hours apart at least, she was assigned to the severe preeclampsia subgroup [(7)].

Inclusion criteria: Normotensive pregnant women less than 20 weeks of gestation with singleton pregnancy.

Exclusion Criteria: Previous history of preeclampsia, pre-existing maternal diseases, any surgical or medical ophthalmic problems that can affect ophthalmic artery, and loss of follow up.

All included ladies were subjected to the following:
On first visit for routine antenatal care before 20 weeks of gestation:

Full history was taken, blood pressure measures were recorded and the body mass index (BMI) was calculated. Routine pelvic ultrasound examination (using either transabdominal (2-6 MHz) convex probe or transvaginal (4-9 MHz) endoluminal probe) was performed (using Siemens Acuson X 300 ultrasound system, premium edition, Germany). Right ophthalmic artery Doppler was only done (previous studies did not find any statistically significant hemodynamic differences between both eyes) [(8)].

Each case rested in the supine position, and they were asked to close eyelids. Gel was applied and the linear array (5-10 MHz) transducer was used horizontally over the superior aspect overlying the eye globe. By color Doppler, the right ophthalmic artery was identified about 1.5 cm posterior and medially to the optic disc. The sample gate of the pulsed wave Doppler was 2 mm with insonation angle less than 15º. After getting at least 5 consecutive waves, the following indices were measured: Peak systolic velocity (P1), end diastolic velocity (EDV), resistive index (RI) and pulsatility index (PI) were automatically traced by the machine. 2nd systolic peak (P2) was the only index to be traced manually. Peak ratio (PR) was calculated manually using the formula (PR = 2nd systolic peak (P2) / peak systolic velocity (P1).

On follow up:

For all the enrolled women coming for routine visits after 20 weeks of gestation, blood pressure measurement and the presence or absence of proteinuria were recorded. All subjects were followed up till termination of pregnancy to document the development of preeclampsia and complications.

Statistical analysis:

Descriptive statistics contain data descriptions in the form of mean ± SD for the quantitative data and the frequency, the percentage for qualitative data, where the mean is the sum of all observations divided by the number of observations. While the standard deviation is a measure of the degree of scatter of individual varieties around their mean. Analytical statistics included standard student-t test (t), Chi-Squared (χ^2), one way ANOVA (F test), Spearman's correlation (r) and the ROC (receiver operating characteristic) curves. $P \leq 0.05$ was deemed to be statistically significant.

RESULTS

The age of the included cases ranged from 19 to 38 years with a mean of 24.77 ± 4.27 years. The mean BMI of them was 27.23 ± 3.16 kg/m^2 and they gave birth twice in 33.33% of cases as shown in table (1).

Table (1): Demographic data of the studied patients (N=120)

Variable	All studied Patients N= 120	
Age (years)		
Mean ± SD	24.77 ± 4.27	
Range	19.00-38.00	
BMI (kg/m^2)		
Mean ± SD	27.23 ± 3.16	
Range	21.00-33.00	
Parity	**N**	**%**
P1	34	28.33
P2	40	33.33
P3	6	5.00
P4	8	6.67
PG	32	26.67

BMI: Body mass index.

BMI was significantly increased among patients who developed severe preeclampsia (30.75 ± 1.66 kg/m^2) than normotensive and patients who developed mild form of preeclampsia (27.19 ± 3.07 and 25.69 ± 3.10 kg/m^2 respectively). In addition, there was a significant difference in parity and proteinuria by urinary dipstick between the studied groups ($P < 0.05$). In contrast, there was no significant variation between the analyzed groups in terms of age or delivery mode ($P > 0.05$) (Table 2). Out of the included cases, 4 women who were assigned as severe preeclampsia had developed complications in the form of eclampsia and placental abruption (2 cases in each category) (Table 2).

Table (2): Comparison between the studied groups regarding demographic data and development of complications

Variable	Degree of PE of all studied patients						F	P value
	Normal (Control) N=96		Mild preeclampsia N=16		Severe preeclampsia N=8			
Age (year)								
Mean ± SD	24.63 ± 4.32		24.63 ± 4.84		26.75 ± 2.36		0.454	0.637
Range	19.00-38.00		19.00-32.00		25.00-30.00			
BMI (kg/m^2)								
Mean ± SD	27.19 ± 3.07		25.69 ± 3.10		30.75 ± 1.66		3.771	**0.029***
Range	21.00-32.00		23.00-31.00		29.00-33.00			
	N	%	N	%	N	%	X^2	
Parity								
P1	26	27.08	8	50	0	0	23.214	**0.003***
p2	34	35.42	2	12.5	4	50		
P3	2	2.08	0	0	4	50		
P4	6	6.25	2	12.5	0	0		
PG	28	29.17	4	25	0	0		
Proteinuria by urinary dipstick								
Negative	96	100	0	0	0	0	120.000	**< 0.001***
Positive +1	0	0	10	62.5	0	0		
Positive +2	0	0	6	37.5	0	0		
Positive +3	0	0	0	0	2	25		
Positive +4	0	0	0	0	6	75		
Mode of delivery								
CS	74	77.08	10	62.50	8	100	2.120	0.347
SVD	22	22.92	6	37.50	0	0		
Complications								
No	94	97.92	16	100	4	50	44.397	**< 0.001***
Eclampsia	0	0.00	0	0	2	25		
Placental abruption.	0	0.00	0	0	2	25		
postpartum HGE	2	2.08	0	0	0	0		

The enrolled cases in the severe preeclampsia subgroup had systolic blood pressure (SBP) at the time of the scan that was higher (110.00 ± 11.55 mmHg) than mild and normal groups (110.00 ± 9.26 and 101.88 ± 8.16 mmHg respectively). Furthermore, there were extremely significant variations in SBP and diastolic blood pressure (DBP) after 20 weeks and termination of pregnancy ($P < 0.05$). However, there was no significant variability between the analyzed groups in terms of DBP at the time of the scan or gestational age ($P > 0.05$) (Table 3).

Table (3): Comparison between the studied groups regarding clinical data at time of scan and after 20 weeks of gestation

Variable	Degree of PE of all studied patients			F	P value	95 %CI	
	Normal (Control) N=96	Mild preeclampsia N=16	Severe preeclampsia N=8			Lower	Upper
SBP at time of scan (mmHg) Mean ± SD	101.88 ± 8.16	110.00 ± 9.26	110.00 ± 11.55	4.37	**0.017***	101.18	105.82
P1=0.015, P2=0.072, P3=1.000							
DBP at time of scan (mmHg) Mean ± SD	65.42 ± 8.49	68.75 ± 8.35	72.50 ± 9.57	1.64	0.203	64.10	68.56
GA (weeks) Mean ± SD	10.13 ± 2.65	9.88 ± 1.81	11.00 ± 2.31	0.27	0.762	9.50	10.80
SBP after 20 weeks (mmHg) Mean ± SD	104.17 ± 8.95	145.00 ± 5.35	172.50±9.57	174.80	**<0.001***	108.32	120.02
P1=0.000, P2=0.000, P3=0.000							
DBP after 20 weeks (mm Hg) Mean ± SD	69.79 ± 7.29	105.00 ± 5.35	117.50 ± 5.00	157.26	**<0.001***	2.26	73.15
P1=0.000, P2=0.000, P3=0.005							
Termination (weeks) Mean ± SD	38.69 ± 1.09	38.38 ± 0.92	36.50 ± 0.58	8.03	**<0.001***	0.15	38.20
P1=0.440, P2=0.000, P3=0.005							

GA: Gestational age, DBP: Diastolic blood pressure, SBP: Systolic blood pressure

The ophthalmic artery parameters (PSV (P1), 2nd systolic peak (P2), peak ratio (p2/p1), and EDV were considerably greater in the severe group compared to the non-preeclampsia group. The PI and RI of the ophthalmic artery were substantially greater in women without preeclampsia than in the severe group (Table 4).

Table (4): Comparison between the studied groups regarding ophthalmic artery Doppler indices

Variable	Degree of PE of all studied patients			F	P value	95 %CI	
	Normal (Control) N =96	Mild preeclampsia N=16	Severe preeclampsia N=8			Lower	Upper
PSV (P1) of Ophthalmic artery							
Mean ± SD	35.55 ± 8.24	36.06 ± 8.85	54.25 ± 20.74	7.354	**<0.001***	34.19	39.54
Range	23.30-65.50	28.60-51.70	31.90-71.90				
P1=0.886, P2=0.000, P3=0.003							
2nd systolic peak (P2) of Ophthalmic artery							
Mean ± SD	17.82 ± 4.35	24.55 ± 5.12	37.05 ± 13.11	27.895	**<0.001***	18.12	21.89
Range	9.70-25.20	20.00-35.30	23.60-48.30				
P1=0.002, P2=0.000, P3=0.000							
Peak ratio (p2/p1) of Ophthalmic artery							
Mean ± SD	0.50 ± 0.09	0.69 ± 0.07	0.69 ± 0.03	23.357	**<0.001***	0.51	0.57
Range	0.28-0.65	0.56-0.75	0.67-0.73				
P1=0.000, P2=0.000, P3=1.000							
EDV of Ophthalmic artery							
Mean ± SD	7.20 ± 1.38	9.81 ± 3.56	14.15 ± 4.34	25.237	**<0.001***	7.31	8.72
Range	3.60-10.00	7.20-17.80	8.60-17.60				
P1=0.001, P2=0.000, P3=0.001							
PI of Ophthalmic artery							
Mean ± SD	2.07 ± 0.36	1.62 ± 0.18	1.48 ± 0.13	10.793	**<0.001***	1.87	2.07
Range	1.45-3.54	1.23-1.75	1.29-1.55				
P1=0.001, P2=0.001, P3=0.493							
RI of Ophthalmic artery							
Mean ± SD	0.79 ± 0.04	0.73 ± 0.03	0.74 ± 0.03	10.221	**<0.001***	0.77	0.79
Range	0.69-0.90	0.66-0.76	0.69-0.76				
P1=0.000, P2=0.009, P3=0.920							

PSV: peak systolic velocity, EDV: End-diastolic volume, PI: pulsatility index, RI: resistive index

Ophthalmic artery PI had sensitivity of 89.7% and specificity of 75.12% at cutoff value < 1.76 in predicting pre-eclampsia. Also, ophthalmic artery RI had sensitivity of 80.2% and specificity of 74.9% at cutoff value < 0.77 in predicting pre-eclampsia. Peak Ratio (PR) of the ophthalmic artery had sensitivity of 77.3% and specificity of 65.8% at cutoff value > 0.59 in predicting pre-eclampsia. In addition, ophthalmic artery 2nd systolic peak (P2) had sensitivity of 91.7% and specificity of 61.7% at cutoff value > 20.1 in prediction of pre-eclampsia (Table 5 and Figures 1, 2, 3 and 4).

Table (5): ROC Curve analysis of ophthalmic artery indices for prediction of pre-eclampsia

	Area	Std. Error	Asymptotic Sig.	Cutoff	Sensitivity	Specificity	PPV	NPV	95% Confidence Interval	
									Lower Bound	Upper Bound
PI	0.066	0.031	**<0.001***	<1.76	89.7%	75.12%	12%	48%	0.005	0.127
RI	0.088	0.037	**<0.001***	<0.77	80.2%	74.9%	12%	48%	0.016	0.16
PR (P2/P1)	0.968	0.027	**<0.001***	>0.59	77.3%	65.8%	12%	48%	0.916	1.00
2nd systolic peak (P2)	0.906	0.042	**<0.001***	>20.1	91.7%	61.7%	12%	48%	0.824	0.989

PPV: Positive predictive value, NPV: Negative predictive value

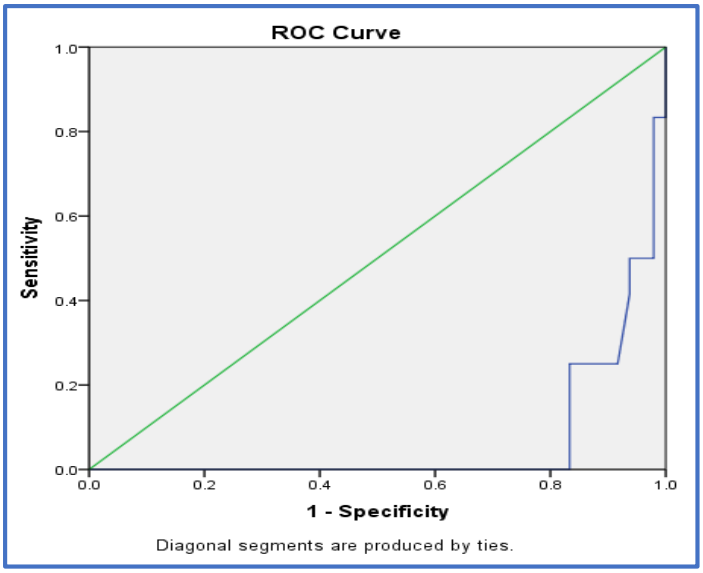

Fig. (1): ROC Curve analysis of PI Ophthalmic artery for predicting of pre-eclampsia

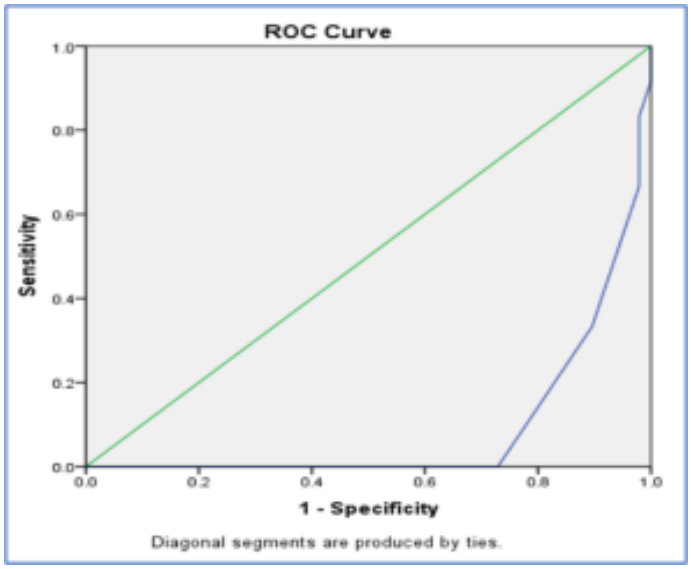

Fig. (2): ROC Curve analysis of RI Ophthalmic artery for predicting of pre-eclampsia

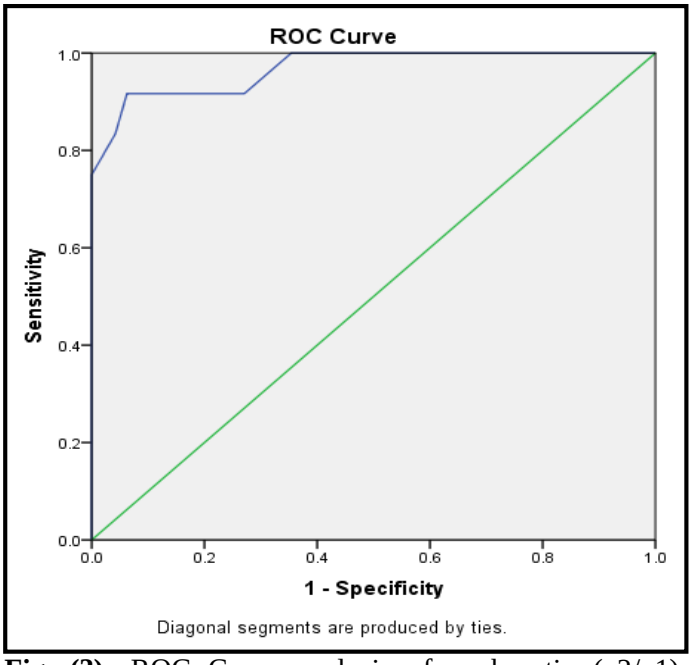

Fig. (3): ROC Curve analysis of peak ratio (p2/p1) Ophthalmic artery for predicting of pre-eclampsia

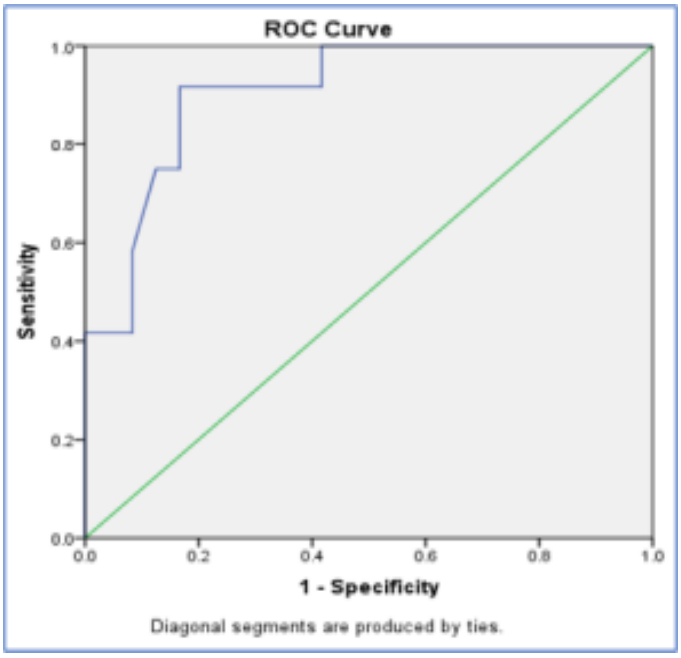

Fig. (4): ROC Curve analysis of 2nd systolic peak (P2) Ophthalmic artery for predicting of pre-eclampsia

Illustrative cases are shown in figures 5, 6, and 7 representing the three groups of the enrolled study.

CASE (1)

A P1, 28 years old, pregnant patient, 10 weeks of gestation, with BMI= 27 presented at the antenatal care clinic. Ophthalmic artery Doppler study revealed: normal ophthalmic artery Doppler indices were as follow: PSV (P1) = 26.9 cm/sec, second systolic peak (P2) =14.1 cm/sec, peak ratio (PR) = 0.52, end diastolic velocity (EDV) = 5.5 cm/sec, pulsatility index (PI) = 1.97 and resistive index (RI) = 0.79. The patient did not develop preeclampsia on follow up.

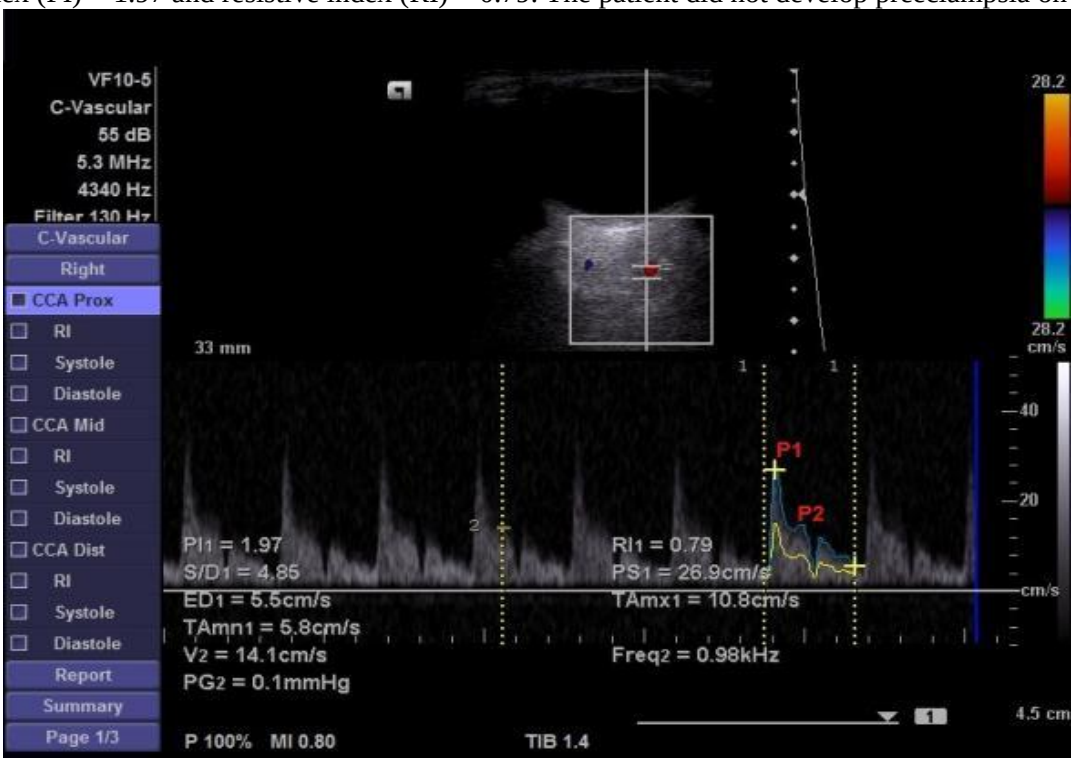

Fig. (5): Right ophthalmic artery Doppler study at 10 weeks of gestation of case (1). The patient did not develop preeclampsia on follow up

CASE (2)

A P1, 11 weeks gestation 28 years old, BMI= 26 presented at the antenatal care clinic. Ophthalmic artery Doppler study revealed **increased P2 (white arrow) and PR but decreased PI and RI values** as follow: Peak Systolic Velocity (P1) = 30.2 cm/sec, second systolic peak (P2) = 22.5 cm/sec, peak ratio (PR) = 0.74, end diastolic velocity (EDV) = 8.3 cm/sec, pulsatility index (PI) = 1.68 and resistive index (RI) = 0.72. The patient developed mild pre-eclampsia on follow up.

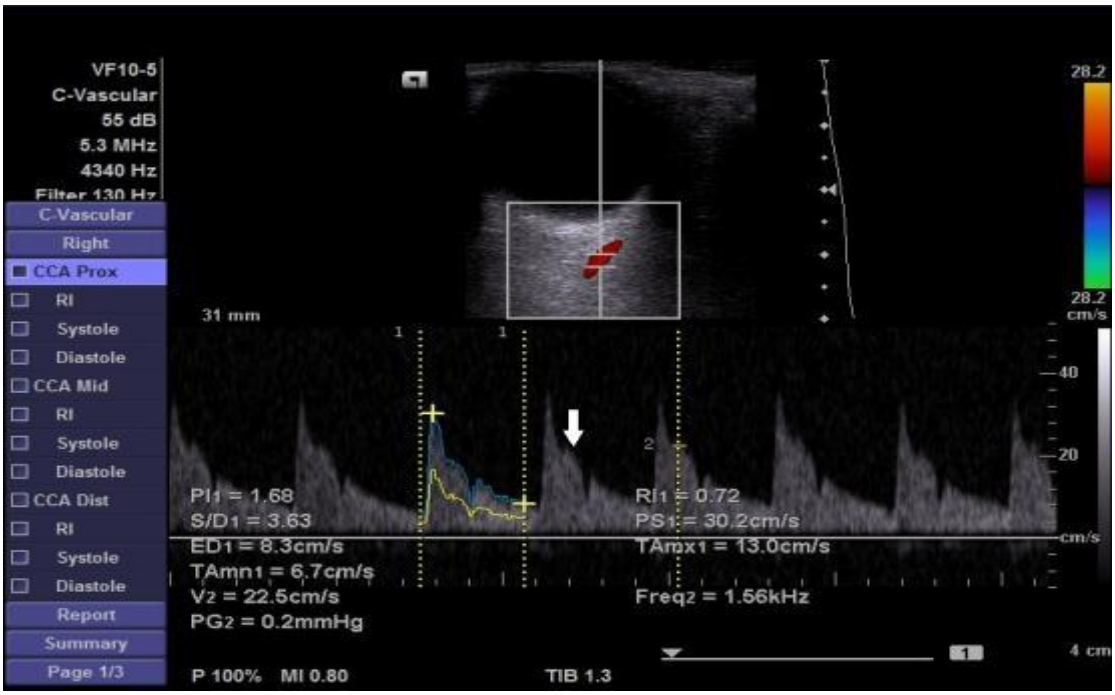

Fig. (6): Right ophthalmic artery Doppler study at 11 weeks of gestation of case (2). The patient developed mild preeclampsia on follow up

CASE (3)

A P2, 10 weeks gestation 30 years old, BMI = 33 presented at the antenatal care clinic. Ophthalmic artery Doppler study revealed **increased P2 and PR but decreased PI and RI values** as follow: Peak systolic velocity (P1) = 31.9 cm/sec, second systolic peak (P2) = 23.6 cm/sec, peak ratio (PR) = 0.73, end diastolic velocity (EDV) = 8.6 cm/sec, pulsatility index (PI) = 1.53 and resistive index (RI) = 0.73. The patient developed severe pre-eclampsia that was complicated by placental abruption at the 3rd trimester.

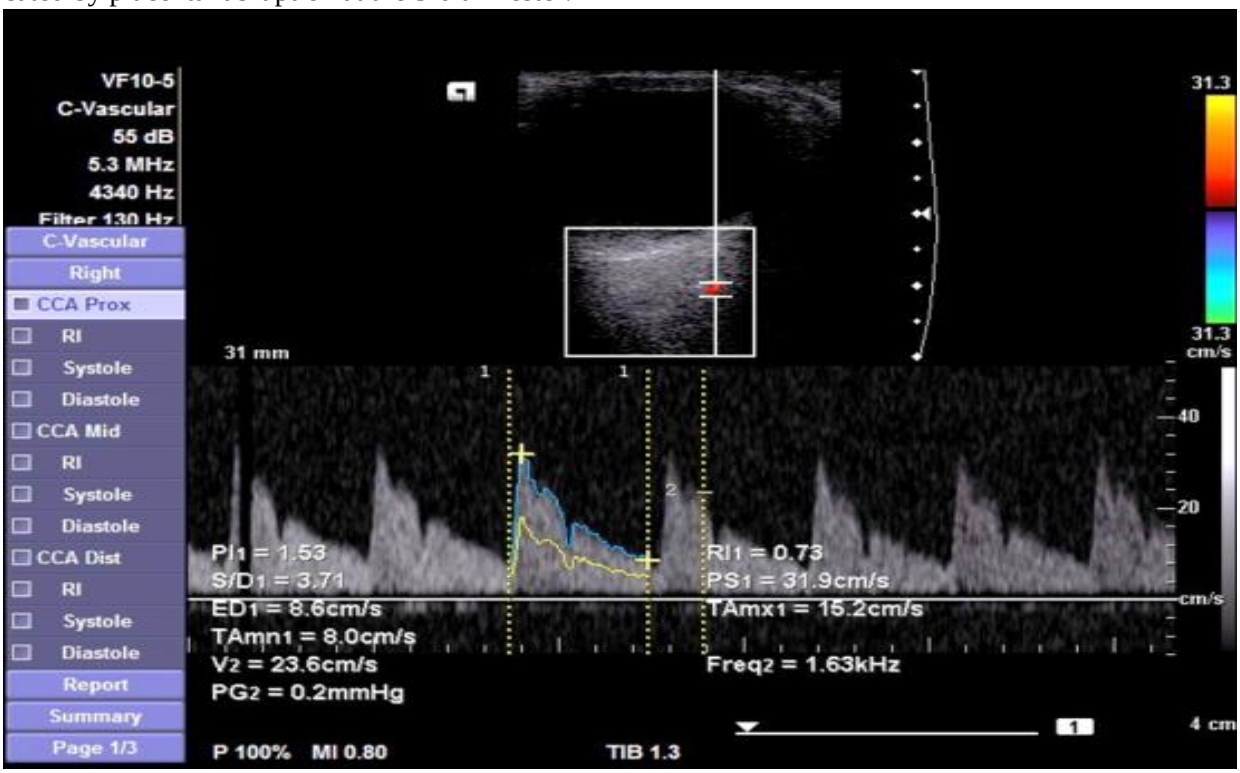

Fig. (7): Right ophthalmic artery Doppler study at 10 weeks of gestation of case (3). The patient developed severe preeclampsia on follow up

DISCUSSION

PE is a serious cause of maternal death. Effective prohibition of its associated morbidity and mortality is dependent on the tripod of the precise anticipation of its onset, its progression, and its prohibition. As a result, research should be converged to increase the capacity to forecast its development and consequences. Doppler sonography is the most often used transorbital noninvasive approach for measuring ophthalmic artery perfusion in pregnant women [(9)].

In terms of age, the current study found no significant variability between the analyzed groups. The mean age in the non-pre-eclampsia group was 24.63 ± 4.32 years, while in the mild group was 24.63 ± 4.84 years and in the severe group was 26.75 ± 2.36 years. These findings are congruent with those of **Diniz *et al.*** [(10)], who found that the mean age of the mild and severe pre-eclampsia patients in the study group was 26.1 ± 6.1 years compared to 26.7 ± 4.1 for the non-pre-eclampsia women. The current study's mean age was lower than that reported by **Olatunji *et al.*** [(9)], which was 32.5 ± 3.9 years among the PE group and 32.4 ± 4.7 years among the normotensive group.

The present study found that patients with severe PE had a substantially higher BMI (30.75 ± 1.66 kg/m^2) than those with no or moderate PE (27.19 ± 3.07 and 25.69 ± 3.10 kg/m^2 respectively). This is consistent with the findings of **Alves *et al.*** [(11)], who found that having a higher BMI was related with a greater risk of PE. Also, **Akolekar *et al.*** [(12)], **Plasencia *et al.*** [(13)] and **Llurba *et al.*** [(14)] all agree.

This study found that the SBP at the time of scanning and after 20 weeks, as well as the DBP after 20 weeks, were significantly much more in the severe group than in the mild and normal groups. The DBP at the time of scanning revealed no significant differences between the examined groups.

The current study revealed that the mean SBP after 20 weeks of gestation for the normal group, mild PE group, and the severe PE group were 104.17 ± 8.95, 145.00 ± 5.35, and 172.50 ± 9.57 mmHg respectively. The mean DBP after 20 weeks of gestation for the same groups were 69.79 ± 7.29, 105.00 ± 5.35, and 117.50 ± 5.00 respectively. In line with this, **Olatunji *et al.*** [(9)] discovered that the mean SBP and DBP were considerably greater in individuals with severe PE. Their mean SBP and DBP in participants with severe PE were 182.78 ± 23.21 and 118.89 ± 14.10 mmHg respectively, and 159.58 ± 7.51 and 99.17 ± 4.08 mmHg in those with mild PE (P <0.001). Similarly, **Diniz *et al.*** [(10)] found that the mean SBP for mild and severe pre-eclamptic women was 148 ± 7.6 and 163.6 ± 15.9 mm Hg respectively, while the mean DBP was 95.5 ± 7.4 and 104.5 ± 8.8 mm Hg. The healthy pregnant women's mean SBP was 105 ± 15 mm Hg and their mean DBP was 73 ± 14 mm Hg.

The current data demonstrated that the severe group had significantly greater ophthalmic artery PSV (P1), 2nd systolic peak (P2), peak ratio (p2/p1), and EDV than those who did not exhibit any signs of preeclampsia. While PI and RI of the ophthalmic artery were considerably greater in individuals who remained normotensive throughout pregnancy than in those who developed severe preeclampsia. This is in agreement with **Takata *et al.* [16] and de Souze *et al.* [17]** where the PR was considerably higher among the severe PE ladies during the third trimester. Furthermore, **Ayaz *et al.* [18]** discovered that the RI and PI of the ophthalmic arteries had recorded lower values in 30 females with mild PE compared to 30 normotensive women after 32 weeks of gestation.

In the current study, there was a highly significant variability in the complications among the analyzed groups. Most of the studied patients had no complications, while 4 out of the 8 patients developed severe PE had eclampsia and placental abruption, 2 cases for each representing (25% for eclampsia & 25% for placental abruption). This is consistent with **Gad *et al.* [19]** who reported that preeclampsia can lead to eclampsia if it presents as hemolysis, elevated levels of liver enzymes and a decreased platelet count (HELLP) syndrome.

Currently, elicited significant correlation between the degree of PE and the ophthalmic artery PI, RI, PSV (P1), 2nd systolic peak (P2) & peak ratio (p2/p1) and EDV, SBP and DBP after 20 weeks was declared. Otherwise, there was no significant correlation between the degree of PE and the age, parity, gestational age, the DBP at time of scanning and the mode of delivery. Concerning the mode of delivery, **Sarno *et al.* [20]** showed that, the effects of peak systolic velocity ratio can predict the subsequent delivery at 35-37 weeks gestation. **Alves *et al.* [11]** discovered that the ophthalmic artery Doppler examination of a gravid female was more effective in diagnosing late-onset PE. In contrast, **North *et al.* [21]** discovered that nulliparous pregnant women had a 9.0% risk of PE.

This study stated that the ophthalmic artery PI had sensitivity of 89.7% and specificity of 75.12% at cutoff value < 1.76 in predicting pre-eclampsia. Also, RI Ophthalmic artery had sensitivity of 80.2% and specificity of 74.9% at cutoff value < 0.77 in predicting pre-eclampsia. **Olatunji *et al.* [9]** also calculated the cutoff values of certain OAD characteristics to anticipate the existence of PE in their study. Peak ratio (PR) value of ≥ 0.72 can indicate PE with excellent sensitivity equals 90.5 % and specificity reaches 81.3%. A threshold value of 0.61 for RI may similarly distinguish mild degree from severe degree PE with a sensitivity equals 75% and a specificity of 78% (P = 0.02). In another meaning, RI values < 0.61 indicated an advancement to severe degree PE. Another study by **Oliveira *et al.* [22]** revealed a cutoff value of 0.657, which is slightly higher than the current study, with a sensitivity of 73.3 % and a specificity of 88.8 %.

PI and peak ratio, on the other hand, were not beneficial for discriminating the mild degree from the severe degree PE using receiver operating characteristic curves according to **Olatunji *et al.* [9]**. **Velauthar *et al.* [23]** found that the Doppler study of the uterine artery during the first trimester had sensitivity of 47.8% (95% CI: 39.0-56.8) and specificity of 92.1% (95% CI: 88.6-94.6), for the development of preeclampsia. The ophthalmic artery Doppler demonstrated sensitivity of 61.0 % (95% CI 44.2-76.1) and specificity of 73.2% (95% CI 66.9-78.7) using the first diastolic peak velocity, suggesting that in screening for preeclampsia, ophthalmic artery Doppler examination may be equally efficient as uterine artery Doppler assessment.

Limitation of the study: Most of the researchers in this topic recruited women with gestational age more than 20 weeks and almost all of them were exclusively done in South America, thus lack of comparison with studies on the same race.

CONCLUSION

Doppler study of the maternal ophthalmic artery is a straightforward, reliable, and objective approach with a predictive diagnostic value for the development of PE that is comparable to Doppler examination of the uterine artery. The association between ophthalmic artery Doppler indices and PE cannot be explained by trophoblast invasion theory and may be due to maternal hemodynamic tailoring to pregnancy. Ophthalmic artery RI, PI, peak ratio (p2/p1) and 2nd systolic peak (P2) had sensitivity of 80.2%, 89.7%, 77.3% and 91.7% and specificity of 74.9%, 75.12%, 65.8% and 61.7% at cutoff value <0.77, < 1.76, > 0.59 and > 20.1 respectively in predicting pre-eclampsia.

RECOMMENDATIONS

Future large-scale studies to demonstrate the capacity of changes in ophthalmic artery Doppler indices to anticipate the onset of preeclampsia are advised. More research will be needed in diverse populations to determine how effectively ophthalmic artery Doppler (OAD) ultrasonography measurements can predict PE consequences and pregnancy outcomes. The establishment of defined cutoff values in ophthalmic artery Doppler different indices in pre-eclampsia screening is an ongoing concern.

Abbreviations: OAD= ophthalmic artery Doppler, PE= Preeclampsia, BMI= body mass index, RI= Resistance index, PI= Perfusion index, PSV= Peak systolic velocity, EDV= End diastolic velocity, PR= Peak ratio, GA= gestational age, SBP= systolic blood pressure, DBP= diastolic blood pressure, HELLP= (H =hemolysis, EL=elevated liver enzymes, LP=Low platelets (thrombocytopenia)).

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