Doppler Sonography of Maternal Opthalmic, Cubital and Uterine Arteries in Hypertensive Disorders of Pregnancy and Normotensive Pregnancy -A Cross Sectional Study

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Abstract

Among the hypertensive disorders that affect pregnancy, preeclampsia is the primary cause of perinatal and maternal morbidity. The identification of women who are at risk of cerebral complications that are associated with adverse pregnancy outcomes must be the goal of preeclampsia management. In this study, doppler sonographic parameters of maternal opthalmic, cubital and uterine arteries of pregnant women with normal blood pressure and preeclampsia were compared.

Methodology: Consecutive patients who came to radiology department who attends to obstetrics and gynecology Outpatient department and are clinically diagnosed to have preeclampsia in the third trimester for routine as well as emergency scans for assessment of fetal well being and Doppler studies. Patients were evaluated with Mindray DC8 USG machine. Ophthalmic artery Doppler and brachial artery Doppler was evaluated using high resolution flat probe12.5 M Hz. Uterine artery Doppler was evaluated using curvilinear probe 6MHz.

Study Design: Cross sectional study

Results: Out of the 140patients included in the study 70 are normotensive , 58 patients diagnosed with mild preeclampsia and 12 patients diagnosed with severe preeclampsia. Ophthalmic artery Doppler studies shows reduced mean resistivity index, pulsatality index among preeclamptic populations compared with normotensive population. Lowest mean resistivity index, and pulsatality index values were observed among the severe preeclamptic patients. Peak ratio of ophthalmic artery showed highest mean value among severe preeclamptic population and lowest value among normotensive population. Uterine artery S/D Ratio was significantly higher among severe PE population compared to normotensive population, which indicating a higher uteroplacental resistance in severe preeclamptic population. No statistically significant evidence of systemic vessel resistance elevation could be demonstrated by studying the brachial artery pulsatality index of preeclamptic patient ,in the present study.

Conclusion: Ophthalmic artery doppler parameters such as resistivity index , pulastality index and peak ratio shows significant reduction in preeclamptic patients compared to normotensive patients and uterine artery S/D ratio is higher in preeclamptic patients.

Keywords: Peak ratio, pulsatality index, resistivity index, S/D ratio.

Background

Hypertension, complicating 5% to 7% of all pregnancies, is a leading cause of maternal and fetal morbidity, particularly when the elevated blood pressure (BP) is due to preeclampsia, either alone (pure) or "superimposed" on chronic vascular disease [1]. Preeclampsia is a major cause of preterm birth and an early marker for future cardiovascular and metabolic diseases, whereas preterm delivery is associated with immediate neonatal morbidity and has been linked to remote cardiovascular and metabolic disease in the newborns [2,3]. Impaired uteroplacental blood flow or placental infarction in pre-eclampsia can affect the fetal–placental unit, causing intrauterine growth restriction, intrauterine fetal demise oligohydramnios, or placental abruption [4,5]. Hypertension in preeclampsia is due primarily to marked vasoconstriction, because both cardiac output and arterial compliance are reduced and loss of the normal pregnancy-associated refractoriness to pressor agents [6]. A possible mechanism of preclampsia is associated with increased cerebral perfusion pressure secondary to peripheral vasoconstriction. Most women with PE, regardless of the severity of the disease, have normal cerebral blood flow, maintained by auto regulation of cerebral blood flow that ensures constant cerebral blood flow despite variations of cerebral perfusion pressure. However, although the flow is normal, the potential harm of high cerebral perfusion pressure is not prevented [7].

Objectives of the Study

To study the Doppler parameters of uterine artery, cubital(brachial) artery and ophthalmic artery in patients with various degree of Preeclampsia, in comparison to normotensive pregnancies and to evaluate the role of Doppler resistance parameters in characterizing the patients with hypertensive disorders of pregnancy

Materials & Methods

A cross sectional study was conducted over a period of two years (June 2013 to April 2015) on patients who attends to obstetrics and gynecology Outpatient department and are clinically diagnosed to have preeclampsia in the third trimester and are referred to department of radiodiagnosis for routine as well as emergency scans for assessment of fetal well being and Doppler studies for further evaluation underwent the study after getting patient consent. Patients were evaluated with Mindray DC8 USG machine.

Ultrasound examination was conducted using Mindray DC8 machine. Ophthalmic artery Doppler and brachial artery Doppler was evaluated using high resolution flat probe 12.5 M Hz. Uterine artery. Doppler was evaluated using curvilinear probe 6MHz.

Statistical Analysis

The data were managed in Microsoft Excel and descriptive statistics on the population of interest were generated from the data obtained. Statistical analysis done using Epi info 7.Significance of difference in means was found by calculating the p value value using ANOVA test. This is followed by post hoc test. This was done using software SPSS.

Results

Sample distribution

In 140 patients studied 70 are normotensives and 70 are preeclamptic. out of

the 70 preeclamptic patients 58 (41%) had mild preeclampsia ,and 12 (8%) had severe preeclampsia. Regarding the age group of the normal population, maximum population constituted by 27 to 29 age group.(27%). In hypertensive population max percentage of population constituted by 21 to 23 age group. In our study, in the normotensive group, 54.23% were primigravidae. 45.71% were multigravidae. In the hypertensive group,61.43%were primigravidae, 38.57% were multigravidae. Although a wide range of 32 to 38 weeks of mean gestational age was included in sample size in order to avoid gestational age as a confounding factor in the group of normotensive pregnant women and hypertensive patients were selected confined to that of similar gestational age.32 to 33 weeks.

Using Doppler sonography ophthalmic artery was evaluated and resistivity index,

pulsatality index, and peak ratio were determined. Mean ± 2SD resistivity index of ophthalmic artery Doppler in normal pregnant patients was found to be 0.7619±.12 .and in mild PE patient was found to be lower 0.6438±.1. In patients with severe PE the value was found to be still lower with a mean of .5517±.1.this difference in means was found to be significant since we calculated the p value value using ANOVA test P-value = 0.0001. Which indicates that there is significant difference in means among either of these groups. This is followed by post hoc test to provide specific information on which means are significantly different from each other. Since the significance level between all the groups is <.05, there is statistically significant difference in means between either of these groups separately.ie between severe P E ,mild PE ,and NORMOTENSIVE groups.
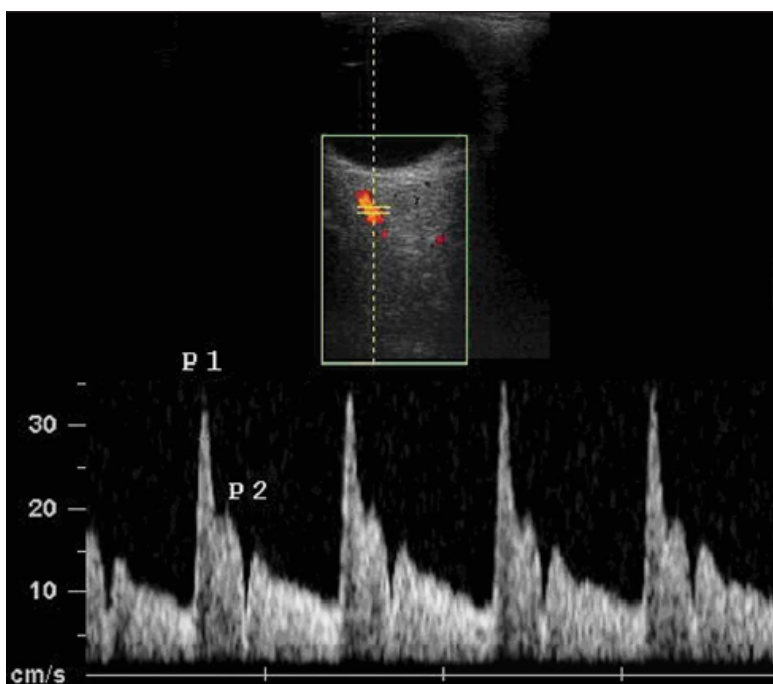
Figure 1: showing first (p1) and second peak(p2) of normal ophthalmic artery wave form. peak ratio = peak 2/peak
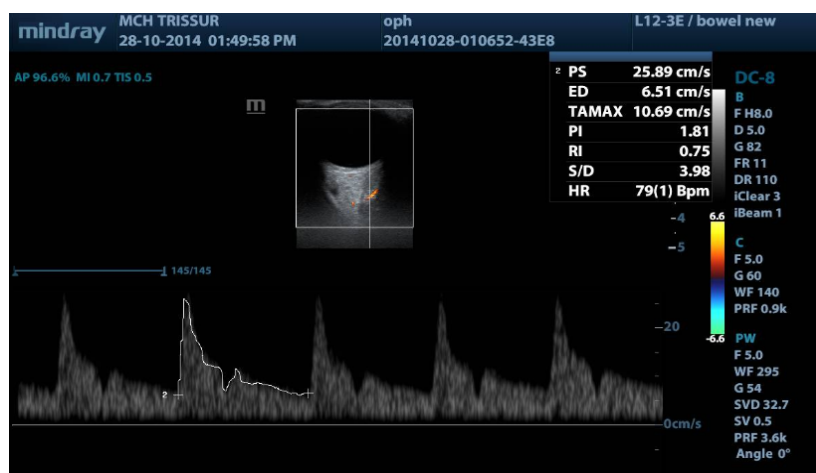
Figure 2: showing ophthalmic artery Doppler in a patient of normotensive patient

Distribution of Values Resistivity Index Ophthalmic Artery

TABLE 1: Post Hoc Test; Resistivity Index ophthalmic artery

Descriptive Statistics for Each Value of Crosstab Variable						
	Obs	Mean	Variance	Std Dev		P-Value
Severe P E	12.0000	0.5517	0.0032	0.0569		< 0.05
Mild PE	58.0000	0.6438	0.0042	0.0650		
Normotensives	70.0000	0.7619	0.0037	0.0611		
Bonferroni groups		**Mean Difference (I-J)**	**Std. Error**	**Sig.**	**95% Confidence Interval**	**P-Value**
					Lower Bound / Upper Bound	
Severe PEvs	MildPE	-.09213*	0.01981	.000	-0.1401 / -0.0441	< 0.05
Mild PE vs	Normal	-.11806*	0.01109	.000	-0.1449 / -0.0912	
Normal vs	Severe PE	.21019*	0.01951	.000	0.1629 / 0.2575	

The Mean ± 2SD peak ratio of ophthalmic artery in patients with severe PE was found to highest with mean of .89± .1. .still lower with mild preeclamptics (mean .73 ± .1) .lowest value was among normotensive population(mean.56± .2). we calculated the p value using ANOVA test. P-value = 0.00001.

Which indicates that there is significant difference in means among either of these groups. This is followed by post hoc test, to provide specific information on which means are significantly different from each other.

Distribution of Values Peak Ratio - Ophthalmic Artery

Table 2: Post Hoc Tests: Peak Ratio Ophtalmic Artery

	Obs	Mean	Variance	Std Dev	P-Value
severe PE	12.0000	0.8900	0.0047	0.0688	< 0.05
Mild PE	58.0000	0.7328	0.0044	0.0666	
Normotensive	70.0000	0.5677	0.0102	0.1008	
Bonferroni GROUP		**Mean Difference (I-J)**	**Std. Error**	**Sig.**	**95% Confidence Interval**	**P-Value**

					Lower Bound	Upper Bound	
Severe VS	Mild PE	.15724*	.02718	.000	.0914	.2231	< 0.05
Mild PE VS	Normal	.16504*	.01522	.000	.1282	.2019	
Normal	Severe PE	-.32229*	.02677	.000	-.3872	-.2574	
*. The mean difference is significant at the 0.05 level.							

Pulsatality index of ophthalmic arteries Mean ± 2SD value among normotensive population is 1.7 ±.2,and among mild PE group 1.4 ± .3,and among severe PE group 1.1 ± .2 . Statistical significance of difference in means of each of the group is determined by ANOVA TEST which shows p value<<.05.Which indicates that there is significant difference in means among either of these groups.

Distribution of Values Ophthalmic Artery-Pulsatality Index

Table 3: Post Hoc Tests Ophthalmic Artery -Pulsatality Index

|		Obs	Mean	Variance	Std Dev	P-Value	
	severe PE	12.0000	1.1425	0.0124	0.1114	< 0.05	
	Mild PE	58.0000	1.3776	0.0329	0.1814		
	Normotensives	70.0000	1.7426	0.0186	0.1365		
Bonferroni GROUP		**Mean Difference (I-J)**	**Std. Error**	**Sig.**	**95% Confidence Interval**		**P-Value**
					Lower Bound	**Upper Bound**	
SeverePE VS	Mild PE	-.23509*	.04920	.000	-.3543	-.1158	< 0.05
MildPE VS	Normal	-.36499*	.02755	.000	-.4317	-.2982	
Normal VS	Severe PE	.60007*	.04847	.000	.4826	.7176	
*. The mean difference is significant at the 0.05 level.							
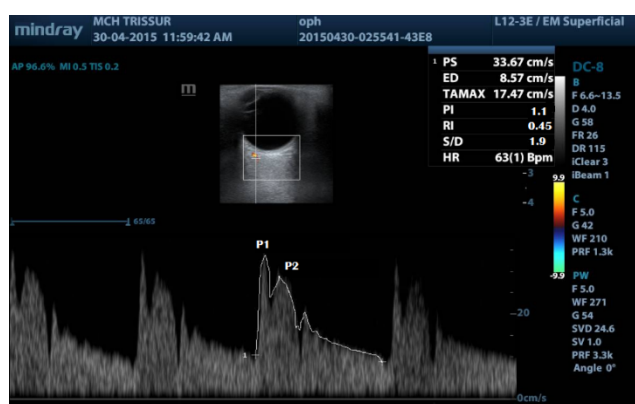
Figure 3: showing ophthalmic artery Doppler in severe PE patient. The increased diastolic perfusion and a higher second peak(p2) can be seen

Placental uterine arteries studied in cases of lateral placenta and mean of right and left uterine arteries were taken in cases of central placenta. Mean ± 2SD value among normotensive population is 1.9±.6,and among mild PE group 2.05 ± .8,and among severe PE group 2.7 ±.4.Statistical significance of difference in means of each of the group is

determined by ANOVA TEST which shows p value <0.05.Which indicates that there is significant difference in means among either of these groups. This is followed by post hoc test The post hoc test shows the significance level 0.951 between normotensives and mild PE, which indicates, the is no significant difference in means between mild PE and Normotensive groups. But there is significant difference in means between group mild PE and severe PE.

Distribution Of Values-Uterine Artery S/D Ratio

Table 4: Post HOC tests :S/D ratio uterine artery

| UTERINE ARTERY S/D RATIO							
Descriptive Statistics for Each Value of Crosstab Variable							
	Obs	**Mean**	**Variance**	**Std Dev**	**P-Value**		
severe PE	12.0000	2.7917	0.0827	0.2875	< 0.05		
Mild PE	58.0000	2.0586	0.1937	0.4401			
Normotensives	70.0000	1.9900	0.1209	0.3477			
Multiple Comparisons							
Bonferroni GROUP		**Mean Difference (I-J)**	**Std. Error**	**Sig.**	**95% Confidence Interval**		**P-Value**
					Lower Bound	**Upper Bound**	
SevereE VS	Mild PE	.7330*	.1221	.000	.437	1.029	< 0.05
MildPE VS	Normal	.0686	.0683	.951	-.097	.234	
Normal VS	Severe	-.8017*	.1202	.000	-1.093	-.510	
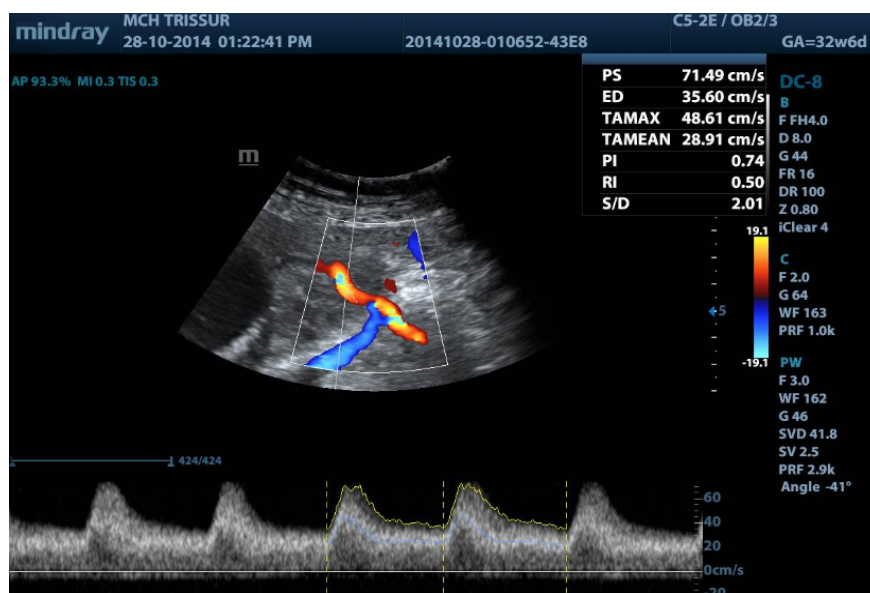
Figure 4: showing normal low resistant flow in uterine artery of normotensive patient
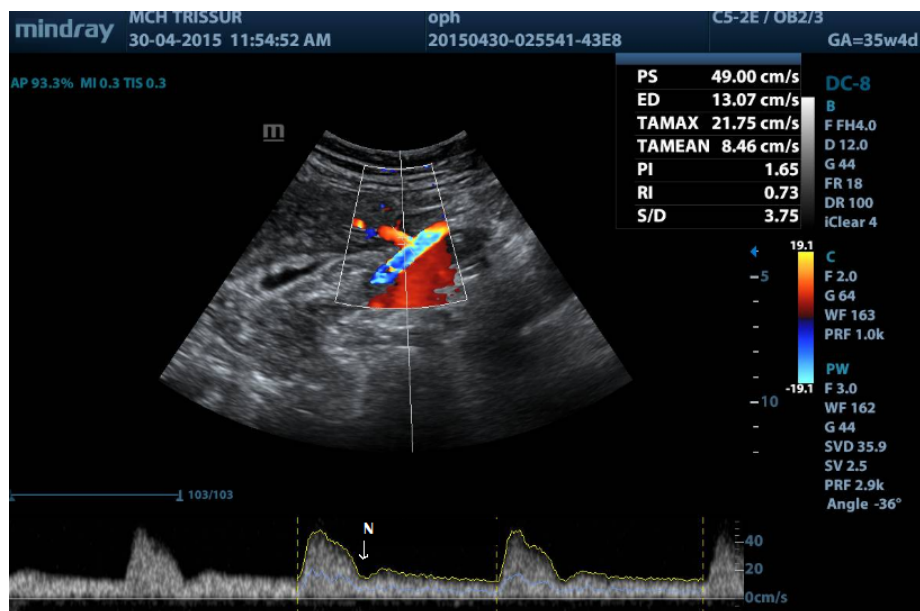
Figure 5: showing uterine artey Doppler in severe PE patient.early diastolic notching(N) can be seen

Brachial artery Doppler was done Pulsatality index was calculated. Means and standard deviation calculated. Level of significance of these indices in three groups were estimated using p value.p value was found <<.0001. Mean ± 2SD value among normotensive population is 3.2±..6, and among mild PE group 3.4± .8, and among severe PE group 3.5 ±.5.

Statistical significance of difference in means of each of the group is determined by ANOVA TEST which shows p value P-value =0.08946 which indicates that there is no significant difference in means among either of these groups.

Figure 6: showing triphasic flow pattern in cubital artery

Distribution of Values, Brachial Artery Pulsatality Index

Table 7: Descriptive Statistics for Each Value of Crosstab Variable

	Obs	Mean	Variance	Std Dev	P-Value
Severe PE	12.0000	3.5333	0.2642	0.5140	< 0.05
Mild PE	58.0000	3.4007	0.2096	0.4578	
Normotensive	70.0000	3.2911	0.1029	0.3208	

Discussion

In our study, significant differences observed in the ophthalmic Doppler indices of patients with mild and severe preeclampsia (lower resistive and pulsatility indices and a higher peak ratio) compared to those observed in pregnant women with normal blood pressure.

Ophtalmic Artery Resistive Index

In our study the mean resistive index of ophthalmic artery was lowest among severe preeclamptic group with a mean of .55 ± .1. The mean resistive index of mild preeclamptic patients were found to be still higher (.64 ± .1) and among normotensive patients were found to be highest (.76±.12).This show a lower impedance to ocular blood flow (central over perfusion) in the group with severe preeclampsia. The same results (orbital hyper perfusion) in patients with preeclampsia were also described by Cristiane Alves de Oliveira et al, Ohno et al, Ayaz et al, and Diniz et al. Cristiane Alves de Oliveira [8] compared the ophthalmic artery Doppler indices observed in women with singleton pregnancies complicated by hypertension and to correlate the indices observed in hypertensive pregnant women with those observed in healthy pregnant women. The mean resistive index among normotensive were 0.75 + 0.05 were, among mild preeclamptic group 0.73 + 0.06 and among severe preeclamptics were 0.63+ 0.09. The peak ratio among normotensive, mild preeclamptic and severe preeclamptics were 0.52 +0.10   0.65 + 0.10   0.89+ 0.12 respectively. The results of our study matches with the above study. Similar study done by Diniz et al [9] reported lower impedance to flow in the ophthalmic artery in women with preeclampsia (not classified) compared to women with chronic hypertension (resistive index, 0.63 + 0.17 and 0.74 + 0.06, respectively).

Peak Ratio

The peak ratio, which is a ratio of the values for the peak diastolic velocity (after the protodiastolic notch) and the initial peak (peak systolic velocity), was first described in 2002 in studies by Nakatsuka et al [10]. The increased values of this index in patients with severe preeclampsia suggest that there is a reduction in the impedance to flow in the ophthalmic artery. Although the mechanism of elevation of this index remains unclear, the peak ratio has been proposed to be the most sensitive indicator of vascular changes associated with the orbital over perfusion [11].

In our study Severe preeclamptic patients showed a higher peak ratio (.89 ± .1) compared to mild PE group(.73 ± .1). The peak ratio was lowest among normotensive group(.56 ± .2).The difference in means of peak ratio among either of these groups were statistically significant. Cristiane Alves de Oliveira [8] compared the ophthalmic artery Doppler indices observed in women with singleton pregnancies complicated by hypertension and to correlate the indices observed in hypertensive pregnant women with those observed in healthy pregnant women The peak ratio among normotensive, mild preeclamptic and severe preeclamptics

were 0.52 ±0.10, 0.65 ± 0.10, 0.89±0.12 respectively .The results of our study matches with the above study.

Similar study done by Diniz et al [9] reported lower impedance to flow in the ophthalmic artery in women with preeclampsia (not classified) compared to women with chronic hypertension peak ratio, 0.82 ± 0.09 and 0.64 ± 0.13, respectively, i.e., highest among severe PE group. P= .0001 for all indices.

Ophthalmic Artery Pulsatality Index

In our study pulsatality index of ophthalmic artery was calculated. Normotensives showed a mean value of 1.7±.2. The mean value obtained in mild PE group was lower 1.3±.3 and mean value among severe PE group was lowest 1.1±.2 .These values also indicates there is orbital over perfusion among preeclamptic patients

Cristiane Alves de Oliveira [8] compared the ophthalmic artery Doppler indices observed in women with singleton pregnancies complicated by hypertension and to correlate the indices observed in hypertensive pregnant women with those observed in healthy pregnant women the pulsatality index among normotensive 1.88 + 0.43, mild preeclamptic 1. 63 +0.35 and severe preeclamptics were 1.13 + 0.31 respectively.

Similar study done by Diniz et al [9] reported lower impedance to flow in the ophthalmic artery pulsatality index in women with preeclampsia (not classified)(1.12 ± 0.28) compared to women with chronic hypertension, (1.68 ± 0.41).

Uterine Artery Dopplr

In our study the patients with severe preeclampsia the uterine artery showed higher mean S/D ratio, this was statistically s significantly high as compared to normotensive population. Though mean S/D ratio was slightly higher in patients with mild preeclampsia, compared to normotensive

patients, no statistically significant difference were obtained between the mean S/D of normotensive and patients with mild preeclampsia. Mean S/D±2SD of SYSTOLIC /DIASTOLIC ratio of uterine arteries in normotensive population is 1.99±.6, Mean S/D±2SD of uterine arteries in mild PE population is 2.05±.8, and severe PE group is 2.7±.4 .Uterine artery notching was also found in two patients with severe preeclampsia.

The results of this study indicating a higher uterine artery Doppler resistance among severe PE group, matches with the results obtained in following study. Gupta, A Qureshi [12] did a study on uterine artery s/d ratio in third trimester uterine artery and had a similar result. The mean S/D ratio values higher (6.15) among PE patients at 32-34, with mean 2.04 among normotensive patients at 32-34 weeks. Adiel Fleischer, M.D. et al [13] did similar study on third trimester uterine artery s/d ratio and found that Doppler velocimetry of the uterine arteries shows that normal pregnancy occurs when the systolic/diastolic ratio is ≤2.6. When the ratio exceeds this level and there is a notch in the waveform, the pregnancy is complicated by maternal preeclampsia. This study matches with our present study that ,among the severe preeclamptic group, the mean S/D ratio is more than 2.6

Cubital artery

In our study the mean pulsatality index of cubital artery among the normal population was 3.2±.6. The mean pulsatality index of mild preeclampsia patients were 3.4±.8 and in severe preeclamptic patients were 3.5±.1. Anova test was performed, but could not demonstrate any statistically significant difference in the means among the three study groups, i.e., normal, mild and severe preeclampsia. Barbara Schiessl et al [14] did study on Sixty-seven women with normal pregnancies, 17 with PE, 12 with IUGR

underwent Doppler sonographic investigation of the cubital arteries. The Pulsatility Index (PI) was calculated The mean PI at the cubital artery is 3.005 in the normal group and 4.652 in the IUGR group (P-0.05) and 3.365 in the PE group (P-0.05). [15] Hence they concluded that Pregnancies with IUGR are associated with elevated peripheral resistance in the maternal arterial system as seen in pregnancies with preeclampsia, reflecting the pathogenesis of preeclampsia, defined as a high resistance vasospastic condition. But this relationship could not be demonstrated in our study. Though some difference were obtained among the means of normotensive, mild PE, and severe PE patients, ANOVA test failed to demonstrate any statistically significance among the difference in means (p value>.05).

Conclusion

Ophthalmic artery Doppler studies shows reduced mean resistivity index, pulsatality index among preeclamptic populations compared with normotensive population. Lowest mean resistivity index, and pulsatality index values were observed among the severe preeclamptic patients. Peak ratio of ophthalmic artery showed highest mean value among severe preeclamptic population, and lowest value among normotensive population. All these change in ophthalmic artery parameters among preeclamptic population indicates orbital over perfusion, compared to normotensive population.

Uterine artery S/D Ratio was significantly higher among severe PE population compared to normotensive population, which indicating a higher uteroplacental resistance in severe preeclamptic population.

No statistically significant evidence of systemic vessel resistance elevation could be demonstrated by studying the brachial artery pulsatality index of preeclamptic patient, in the present study.

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