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Research Article

Association between ophthalmoscopic changes and obstetric outcomes in pre-eclampsia and eclampsia

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ABSTRACT

Background: Hypertensive disorder is a major cause of maternal and perinatal mortality and morbidity. The widespread endothelial dysfunction associated with preeclampsia can affect the choroid and the retina leading to characteristic ophthalmoscopic changes. So, we tried to find out the association between ophthalmoscopic changes and obstetric outcomes in women with preeclampsia-eclampsia.

Methods: In a comparative, prospective study carried out from July 2011 to July 2015 in Medical College, Kolkata and KPC Medical College, Kolkata we included antenatal women with pre-eclampsia and eclampsia. Based on the ophthalmoscopic findings they were divided into two groups; group A (no ophthalmoscopic abnormalities) and group B (having ophthalmoscopic abnormalities). The results were analyzed by standard statistical methods.

Results: Out of the total 200 women included, 102 women belonged to group A and 98 to group B. Majority of the patients were ophthalmologically asymptomatic. Most common fundoscopic abnormality in group B was focal arteriolar narrowing. Women in group B had significantly higher level of blood pressure, proteinuria and thrombocytopenia. The need of multiple drugs, incidence of HELLP syndrome and oliguria, rate of Caesarean section and CCU admission were significantly higher in group B compared to group A. There was significantly higher incidence of perinatal complications in group B, viz: IUGR, low birth weight, low Apgar score and NICU admission.

Conclusions: Ophthalmoscopic changes correlate positively with adverse fetomaternal outcomes in preeclampsia. Fundoscopy should be carried out in all preeclamptic mother irrespective of the visual symptoms.

Keywords: Pregnancy, Preeclampsia, Hypertension, Retinopathy, Ophthalmoscopy, Obstetric outcome

INTRODUCTION

Hypertensive disorder in pregnancy is a major concern among the obstetricians. It is a major cause of maternal and perinatal mortality and morbidity world-wide, especially in low and middle income countries where they account for 10-25% of maternal deaths.¹ The Working Group of the National High Blood Pressure Education Program (NHBPEP) defined hypertension as blood pressure $\geq 140/90$ mmHg using Korotkoff V sound for diastolic blood pressure.² The same Working Group classifies hypertensive disorders in pregnancy into four groups- (i) Gestational Hypertension; (ii) Preeclampsia and Eclampsia syndrome; (iii) Superimposed

preeclampsia on chronic hypertension; (iv) Chronic hypertension.² Preeclampsia is defined as presence of hypertension and proteinuria (300 mg or more in 24 hour urine).²

Preeclampsia is a multisystem disorder of vascular function, specific to pregnancy. It arises from placenta, probably as a result of ischemia, and propagates throughout the maternal vascular tree such that virtually all organ systems can be affected. Unfortunately, it continues to be a disease of theories and no one theory, alone, can explain its pathogenesis. Roberts et al proposed that maternal endothelial dysfunction is the key event resulting in diverse clinical manifestation of

preeclampsia.³ So, it is not surprising that this endothelial dysfunction may affect the choroid and the retina leading to characteristic ophthalmoscopic changes.

Ophthalmological examination may provide clinical evidence of vasoconstriction, which otherwise may be difficult to establish. The findings may correlate with severity of preeclampsia. The retinal vascular changes are present in 30-100% of preeclampsia cases, the most frequent being the vasoconstriction of the retinal arterioles.^{4,5} The exudative retinal detachment is a rare cause (under 1%) of visual loss in the preeclampsia-eclampsia syndrome, being produced by the involvement of the choroidal vascularization.⁴ Retinal infarction or ischemia (Purtscher retinopathy) may lead to sudden onset blindness.⁶ Asymptomatic retinal detachment is also common.⁶ In most cases, these changes resolve after delivery.

Preeclamptic women may have visual complaints. The most common symptoms are scotoma, a transient perception of bright or black spots. There may be sudden inability to focus blurred vision and in severe cases, complete blindness. The visual symptom is considered as of the criteria for defining severe preeclampsia.² The NICE clinical guidelines consider visual disturbance or papilloedema in the background of hypertension and proteinuria as severe preeclampsia and recommend consideration of prophylactic magnesium sulphate therapy in such conditions.⁷

Keeping all these in mind, our study was done to find out the association between ophthalmological changes and obstetric outcomes in women with preeclampsia and eclampsia.

The aims of our study are (1) to find out the factors associated with retinopathy in preeclampsia-eclampsia; and 2) to detect the correlation between ophthalmoscopic changes and maternal and fetal outcomes in preeclampsia-eclampsia.

METHODS

A comparative prospective study was carried out simultaneously in pregnant women attending the Emergency and the Out Patient Department of the Department of Obstetrics and Gynecology, Medical College and Hospital, Kolkata and KPC Medical College and Hospital, Kolkata from July 2011 to July 2015. Hypertension was defined according to NHBPEP criteria, i.e., women having BP \geq 140/90 mm Hg in at least two occasions, six hours apart were included in the study. Antenatal women with preeclampsia and eclampsia-were all included. Excluded were women having gestational hypertension, chronic hypertension, preeclampsia superimposed on chronic hypertension, pre-existing diabetes, known myopia or other known retinopathy, thyrotoxicosis, anaemia or other haematological disorders, renal disorders and women presenting in

postpartum period. Total 200 women were studied in the study period.

After getting the clearance from the Institutional Ethical Committee (IEC), informed consent was obtained from all the participants. Detailed history taking and systemic and obstetric examination were done. Proteinuria was provisionally diagnosed by dipstick urine test method (\geq 1+ or \geq 300 mg/ litre) and confirmed by presence of \geq 300 mg protein in 24 hour urine collection. Laboratory investigations were done with special reference to haemoglobin and platelet count, lactate dehydrogenase (LDH), liver enzymes (SGOT- Serum glutamate oxaloacetate transferase and SGPT- Serum glutamate pyruvate transferase) and creatinine, obstetric ultrasound to detect fetal growth and liquor volume and colour Doppler studies whenever indicated.

Detailed ophthalmological check-up was done including detailed history (especially blurred vision, scotoma, diplopia, blindness), examination of visual acuity followed by detailed choroidoretinal check up with the help of direct ophthalmoscope using tropicamide as mydriatic, soon after the diagnosis of hypertension.

Treatment was started as indicated, using antihypertensive drugs, antenatal corticosteroids and magnesium sulphate when indicated. All the women were followed up regularly to note control of BP, worsening of clinical and/or laboratory parameters, development of eclampsia and fetal growth and well-being. The labour events, mode of delivery, gestational age at delivery and birth weight, Apgar score, admission to NICU (Neonatal Intensive Care Units) were also studied. The maternal conditions particularly noted were eclampsia, pulmonary oedema, HELLP syndrome (Haemolysis, Elevated Liver enzymes and Low Platelet counts), oliguria, haemorrhage, caesarean section rate, admission to CCU (Critical care unit) and maternal mortality.

The women were divided into two groups based on the findings of ophthalmological examination. Those without ophthalmoscopic changes were included into the "Group A" and those with such changes, into the "Group B".

Both the groups were compared in terms of demographic variables, clinical and laboratory parameters and maternal and fetal outcomes. The results were analysed by standard statistical methods like two sample 't' test (both tailed or one tailed accordingly) and Fisher's exact test (using 2 x 2 contingency table) and p value <0.05 was considered to be significant.

RESULTS

Total 200 women were studied. Out of these 200 women, 102 women did not have any abnormalities in ophthalmoscopic examination. They were included in group A. The rest 98 women had ophthalmoscopic changes. They were included in group B. Thus 48%

women with hypertension had retinal changes at ophthalmoscopy (Figure 1).

Table 1: Distribution of the women according to the visual symptoms.

	Group A (n = 102)	Group B (n = 98)
Blurred Vision, Scotoma	21 (20.59%)	49 (50.00%)
Diplopia	0 (0.00%)	2 (2.04%)
Blindness	0 (0.00%)	1 (1.02%)
Asymptomatic	81 (79.41%)	46 (46.94%)

In group A, i.e., women without any ophthalmoscopic abnormalities, majority (79.41%) were ophthalmologically asymptomatic and only few women (20.59%) had mild symptoms like blurred vision or scotoma. In contrast half (50.00%) of the women in group B, i.e., women with ophthalmoscopic changes, had complaints of visual blurring and/ or scotoma. One woman (1.02%) developed sudden onset blindness (due to central serous retinopathy) that resolved after delivery. Two (2.04%) complained of diplopia. It is important to note that 46 women with ophthalmoscopic abnormalities (46.94%) did not have any visual complaints (Table 1).

Table 2: Ophthalmoscopic findings in women in group B.

	Number of women (n = 98)	Percentage (%)
Arteriolar narrowing	68	(69.39%)
Cotton wool exudates	7	(7.14%)
Retinal oedema	8	(8.16%)
Retinal haemorrhage	2	(2.04%)
Macular changes	5	(5.01%)
Retinal detachment	4	(4.08%)
CSR	1	(1.02%)
Papilloedema	0	(0.00%)

In group B, the most common ophthalmoscopic finding (in 69.39% cases) was focal arteriolar narrowing leading to decreased arterio-venous (A:V) ratio (from 2:3 to 1:3). Retinal oedema, cotton wool exudates, retinal haemorrhage and macular oedema and macular stars were also common findings. Central Serous Retinopathy (CSR) was noted in one woman. However, not a single case of papilloedema was reported (Table 2).

Both the groups were comparable in terms of demographic variables like maternal age, gravida, Body mass index (BMI) and gestational age at diagnosis of hypertension. Women with group B had significantly higher levels of both systolic blood pressure (SBP) and diastolic blood pressure (DBP) compared to those in group A. Also, in group B, the severity of proteinuria and

thrombocytopenia were significantly higher than in group A. However, there was no significant statistical correlation between ophthalmoscopic findings (group B) and laboratory parameters like serum LDH, liver enzymes and serum creatinine (Table 3).

Table 3: Factors associated with ophthalmoscopic changes.

	Group A (n = 102) Mean ± SD	Group B (n = 98) Mean ± SD	p-value
Maternal Age (years)	24.52±2.98	24.06±3.31	0.3025
Gravida	1.23±1.05	1.08±0.98	0.2980
BMI (Kg/m ²)	22.89±1.53	23.09±1.78	0.3946
Gestational age at diagnosis (weeks)	28.82±8.32	29.50±6.25	0.5155
SBP (mm Hg)	150.00±10.7	158.80±11.3	<0.0001*
DBP (mm Hg)	112.56±10.2	116.95±10.8	0.0036*
Proteinuria ^a	1.69±0.32	2.10±0.21	<0.0001*
Platelet count (lacs/cmm)	1.56±0.32	1.34±0.21	<0.0001*
Serum LDH (IU/L)	675.45±94.8	672.93±82.9	0.8419
SGPT (IU/L)	48.76±10.75	51.85±12.79	0.0655
SGOT (IU/L)	57.92±7.74	59.75±6.38	0.0702
Serum creatinine (mg/dl)	0.94±0.12	0.91±0.23	0.2463

BMI- body mass index; SBP- systolic blood pressure; DBP- diastolic blood pressure; LDH – lactate dehydrogenase; SGOT- Serum glutamate oxaloacetate transferase; SGPT- Serum glutamate pyruvate transferase;

^aMeasured by dipstick, confirmed by 24 hours urinary protein excretion; *Significant p-value

While carefully analysing the maternal outcomes we found that requirement of multiple drugs to control BP, incidence of oliguria, Caesarean section rate, rate of admission to CCU and maternal mortality were higher in group B compared to group A and this difference was statistically significant (p value <0.05 was considered significant). In contrast, there was no significant difference between these two groups in terms of development of eclampsia, placental abruption and pulmonary oedema. Regarding perinatal outcomes, the incidence of intrauterine growth restriction (IUGR), low Apgar score at birth, low birth weight and NICU admission rate were significantly higher in the babies of women in group B than those in group A. However, incidence of oligohydramnios and perinatal mortality were similar in both the groups (Table 4).

DISCUSSION

Ophthalmological changes are common in hypertensive disorders in pregnancy. The fundoscopic changes may reflect the global endothelial dysfunction that characterizes preeclampsia. More than fifty years ago, Pollak VE and Nettles JB reported that retinal vascular

changes correlate with renal biopsy findings in preeclampsia.⁸

Some studies reported the incidence of retinopathy may be as high as 85% in cases of pregnancy-hypertension.⁸ A recent study of Uto M et al showed incidence of choroidoretinal changes in pregnancy-hypertension was 43.2%. In our study we found this incidence 49%.⁹

Abu Samara K mentioned that 25% of women with preeclampsia may have visual symptom and in

ophthalmoscopy 50% of the women may have abnormalities.⁵ Similarly, in our study, out of the 200 cases 127 women had no visual symptoms whereas 98 women had fundoscopic abnormalities. Thus, it is worthy to note that even without any visual symptoms, retinal changes may be present, which may carry adverse prognosis from obstetric point of view. So, in all women with preeclampsia, fundoscopic examination should be considered irrespective of the symptoms.

Table 4: Maternofetal complications associated with ophthalmological changes.

	Group A (n = 102)		Group B (n = 98)		p-value
Requirement of multiple drugs to control BP	34	33.33%	60	61.22%	<0.0001*
Eclampsia or CVA	2	01.96%	6	06.12%	0.1637
Placental abruption	2	01.96%	8	08.16%	0.548
HELLP syndrome ^a	0	00.00%	2	02.04%	0.2388
Oliguria ²	6	05.88%	18	18.37%	0.0084*
Pulmonary oedema	4	03.92%	10	10.20%	0.1000
Caesarean section	30	29.41%	44	44.90%	0.0281*
Admission to CCU	10	09.80%	24	24.49%	0.0078*
Maternal Mortality ^c	1	0.98%	2	2.04%	0.6157
IUGR ^d	29	28.43%	46	46.94%	0.0085*
Oligohydramnios ^e	32	31.37%	40	40.82%	0.1861
Preterm delivery ^f	44	43.14%	54	52.94%	0.1194
Apgar score <7 at 5 min after birth	10	9.80%	22	22.45%	0.0199*
Birth weight <2.5 kg	48	47.06%	64	65.31%	0.0106*
NICU admission	10	09.80%	24	24.49%	0.0078*
Perinatal mortality ^g	2	01.96%	6	06.12%	0.1637

BP- Blood Pressure; CVA- Cerebro-Vascular Accident; HELLP- Haemolysis; Elevated Liver enzymes; Low Platelet count; CCU- Critical care unit; IUGR- Intrauterine Growth Restriction; NICU- Neonatal Intensive Care Unit; ^aDefined as per NICE guidelines; ^bas urine output <30 ml/hour or <100 ml/ 4 hour; ^cOne mother died of coagulopathy, one of renal failure, one of embolism; ^d Defined as estimated fetal weight less than 10th percentile with respect to gestational age; ^eDefined as single largest vertical pocket <2 cm or Amniotic Fluid Index (AFI) <5 cm; ^fBirth before 37 completed weeks, spontaneous or iatrogenic; ^gInclude still birth (>28 weeks of gestation and early neonatal (<7 days) death; *Significant p-value

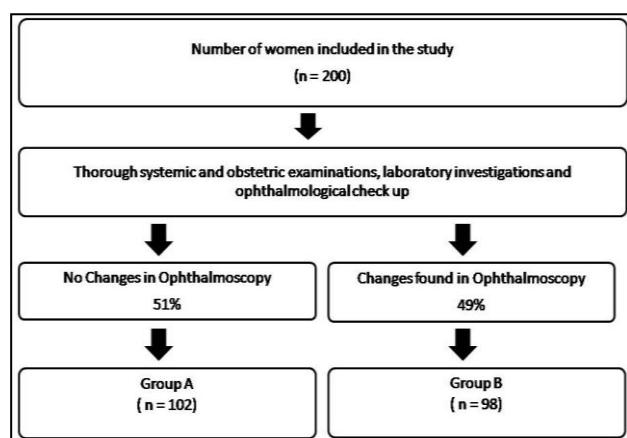


Figure 1: Distribution of the women according to the ophthalmoscopic findings.

Various retinal changes have been described in relation to preeclampsia. Abu Samara K concluded that the most common finding was severe arteriolar vasospasm.⁵ In our study also, we found that the most common ophthalmoscopic finding was segmental narrowing of retinal arterioles (69.39%). In the literature, many cases of retinal detachments were described, most of which subsided after delivery of the baby and control of blood pressure.^{5,10,11} Bos A M et al concluded that the management of retinal detachment as a complication in obstetrics should be conservative and retinal detachment in (pre) eclampsia may be an indication for termination of pregnancy.¹⁰ In our study, there were 4 cases of retinal detachments, which subsided after delivery. We also encountered a case of central serous retinopathy presenting with blindness which recovered completely after delivery with control of blood pressure. So, the mainstay of management of women presenting with such

severe forms of retinopathy should be immediate termination of pregnancy along with conservative measures like control of blood pressure to prevent permanent visual damage.

Hong J et al showed that the degree of retinopathy correlated positively with the degree of gestosis and the degree of hypertension and they concluded that fundus examination in gestosis patients is an significant guideline for clinical treatment.¹² In their retrospective study on hypertensive women who delivered at term, Gupta A et al found that the severity of retinopathy might be independent of systemic BP.¹³ In contrast, Kalliaperumal S et al reported that the severity of retinopathy was more closely related with diastolic BP rather than systolic BP and the significance of this correlation increased in severe preeclampsia.¹⁴ In our study, however, we found that both SBP and DBP were significantly higher in women having ophthalmoscopic abnormalities, compared to women having normal fundus. Again, we found that severity of both proteinuria and thrombocytopenia was significantly higher in women having retinopathy than women without retinopathy. This can be explained by the fact that retinopathy represents the widespread multi-system vasospasm occurring in preeclampsia.

Retinopathy may serve as an independent indicator of severe preeclampsia. Araújo J et al reported a case of a woman with malignant hypertensive retinopathy who was discovered to bear a dead fetus.¹⁵ Our study found that obstetric complications were common in women having retinal changes compared to those without the changes. Some of these complications might be life threatening, viz: HELLP syndrome and oliguria. The rate of Caesarean section, admission to CCU and the need of more than one drugs to control BP were significantly higher in women having retinal abnormalities. So, we can easily argue that the ocular changes can predict the severity of preeclampsia.

Both Gupta A et al. and Kalliaperumal S et al. suggested that retinopathy in preeclampsia may indirectly indicate the level of placental insufficiency and thus can predict IUGR.^{13,14} In our study also, we found that the women having retinopathy had significantly higher incidence of IUGR than women having no retinopathy.

Karki P et al performed a prospective cohort study in 153 subjects and found that ophthalmoscopic changes were associated with low birth weight and low Apgar score.¹⁶ In our study also, the incidence of low birth weight, low Apgar score and NICU admission rate were significantly higher in the mothers having fundoscopic changes compared to those without changes.

Garg A, et al, demonstrated subclinical retinal and choroidal thickening in the setting of severe preeclampsia, which may reflect rising levels of vascular endothelial growth factor.¹⁷ Therefore; retinal and

choroidal markers could serve as novel predictive markers of severe preeclampsia. This further establishes the need of routine ophthalmoscopic examinations in all preeclamptic mothers irrespective of visual complaints.

CONCLUSIONS

Ophthalmoscopic examination should be done in all cases of hypertensive disorders of pregnancy, even if the patient is asymptomatic. The choroidoretinal changes may indicate ongoing vascular damages and correlate with obstetric complications and poor perinatal outcomes. They may be the first warning sign of impending fetomaternal complications. DIPSI criteria was also found to be effective and comparable method of screening with respect to GCT/WHO GTT with 75 gm glucose, but larger studies are required to further validate its importance.

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