



Ocular Manifestations: Are They Significant in Hypertensive Disorders of Pregnancy?

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Abstract

Background Hypertensive disorders of pregnancy lead to pathological changes in various organ systems of mother and fetus which contributes to maternal and fetal morbidity and mortality. It is a multisystem disorder which can involve end organs like kidneys, liver, eyes, hemopoietic system and placenta. Retinal involvement, though quite common, is rarely investigated. It is a unique site where the blood vessels can be directly observed. Observing retinal vasculature may provide clue to status of similar vessels in other parts of body including placental circulation.

Methods Hospital-based descriptive study which included 150 patients diagnosed as preeclampsia/eclampsia, who were admitted in the intensive care unit. Written consent was obtained from study subjects. Data were collected by history taking and examination of the subjects using pre-structured questionnaire. Ocular examination was carried out by ophthalmologist, which included anterior segment examination, visual acuity and dilated fundus examination. Multiple qualitative and quantitative parameters were studied. Data were analyzed by SPSS 14.0 software.

Results Ocular symptoms were seen in 22% of severe preeclampsia and in 100% of eclampsia patients. Blurred vision was the most common ocular complaint. Fundus changes were seen in 48.7% total study subjects. Arteriolar narrowing was the most common finding on fundus examination. Systolic blood pressure and serum creatinine were found predictive of changes in fundus ($p = .000$). Incidence of fetal growth restriction was found to be significantly associated with fundus involvement (p value .000).

Conclusion Ophthalmic examination including fundus examination should be a routine in the investigational armamentarium of hypertensive disorders of pregnancy.

Keywords Eclampsia · Preeclampsia · Ocular manifestations · Fetal growth restriction

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Introduction

Pregnancy is associated with ocular changes, which most often are transient in nature. Either preexisting conditions exacerbate it or may be associated with development of new conditions. The ocular effects of pregnancy can be either physiological or pathological. A very important pathologic entity, associated with a wide spectrum of ocular changes is hypertensive disorders of pregnancy (HDP) which mainly includes preeclampsia and eclampsia. Preeclampsia and eclampsia are an important cause of maternal and fetal morbidity and mortality. It contributes to 10–15% of maternal mortality [1]. The spectrum of HDP includes gestational hypertension, preeclampsia (non severe/severe), eclampsia, chronic hypertension and preeclampsia super imposed on chronic hypertension [2]. Poorly managed cases of preeclampsia/eclampsia accounts for 75% of all maternal deaths

and can also result in irreversible blindness [3]. Hypertensive disorders of pregnancy account for a great deal of fetal morbidity (acute and long-term), perinatal deaths, preterm birth and fetal growth restriction (FGR). However, the underlying mechanism remains an enigma. The field of preeclampsia research has been enjoying a blossoming of novel ideas and approaches. Let us hope these activities will lead to much earlier diagnostic capacities and newer prophylactic treatments to improve maternal and perinatal outcome.

The intention of our study was to study the ocular manifestations in severe preeclampsia and eclampsia. Ophthalmologic examination should be essentially carried out in every hypertensive patient. Retina is the only site in the body where the small vessels can be visualized and assessed clinically. Fundoscopy of retina is a simple, noninvasive, safe and reliable procedure to interpret the vascular changes. Therefore, there is a need to study if the degree of hypertensive retinopathy in women with preeclampsia is a valid and reliable factor that gives prognostic information on assessment of the severity of preeclampsia.

Hence, the scope of this work is immense in improving the quality of maternal and child health. Visible retinal vascular changes occur in 30–100 percent of preeclamptic patients, and visual symptoms are reported in 25–50 percent. The ocular symptoms include blurred or decreased vision, photopsia, scotomata, diplopia, visual field defects and blindness [4]. Most common findings observed in fundus are constriction/spasm of retinal arterioles, with a decreased retinal artery-to-vein ratio [4, 5]. Other hypertensive retinopathy changes may occur, including exudates, hemorrhages, and cotton-wool spots, arteriovenous crossing changes and macular edema [4, 5]. Possible mechanisms for these changes include hormonal changes, endothelial damage, hypoperfusion ischemia/edema and coexisting systemic vascular disease. Women with HELLP syndrome (hemolysis, elevated liver enzymes and low platelet count) are more likely to develop serious ocular manifestations like exudative retinal detachment than those who do not have the syndrome. Cortical blindness may also occur in women with hypertensive disorders of pregnancy. Literature also mentions a very few cases of extraocular muscle palsy associated with preeclampsia and eclampsia manifesting as diplopia [6]. Retinal venous and arterial occlusion may rarely occur.

There is a scarcity in the literature of studies which clearly state the importance of ocular changes in HDP and fetal outcomes of the same. Improved understanding of pathophysiology of these will offer opportunity for meaningful counseling and management of pregnant women who present with such changes.

This study was done to determine the ocular manifestations in women affected by preeclampsia and eclampsia and to know if there is any association between them and various parameters like age, parity, blood pressure, proteinuria and

other factors that determine severity of the disease and fetal growth restriction.

Materials and Methods

This study was conducted in the Department of Obstetrics and Gynecology, Institute of Maternal and Child Health, Calicut. This was a descriptive cross-sectional study conducted over a period of 12 months in 2018. Patients admitted to the high dependency unit (HDU) for severe preeclampsia and eclampsia were included in the study.

For the purpose of analysis, the various parameters studied were divided into quantitative and qualitative variables.

The quantitative data studied included age, gestational age at development of preeclampsia/eclampsia, blood pressure and laboratory parameters {hemoglobin, platelet count, alanine transaminase (ALT) and serum creatinine levels—which indicated functional status of related organs}. The qualitative parameters studied were parity, symptoms, ocular and fundus changes, presence of IUGR and its relation to ocular manifestations.

Patients with history of chronic hypertension/convulsions, renal diseases and systemic disorders such as diabetes mellitus, hematological disorders, infectious diseases and ocular diseases prior to pregnancy were excluded from the study.

A written consent was obtained from the study subjects. Data were collected by taking history and conducting examination of subjects on a daily basis using a pre-structured questionnaire. Ocular examination included visual acuity recording, anterior segment examination and fundus examination. Bedside visual acuity was recorded with unilluminated Snellen's chart. Anterior segment examination was carried out under torch light. Pupils were dilated with tropicamide and examination of dilated fundus was carried out with ophthalmoscope.

Data analysis was done using SPSS version 14.0. Qualitative variables were analyzed with the Chi-square test and quantitative tests with t test and ANOVA tests.

Results

A total of 150 patients with ocular manifestations were included in the study. There were 141 cases of severe preeclampsia and nine cases of eclampsia. The majority of patients were in the 26–35 years age group: youngest and oldest being 18 years and 38 years, respectively. Mean age of the study subjects was 27.20 ± 4.38 years. The majority of patients were multigravida (66%). Most patients were in their third trimester during detection of preeclampsia/eclampsia which corresponds with the normal physiological

rise in BP. Around 40% study population belonged to gestational age between 28 and 34 weeks. The lowest gestational age included in the study was 26 weeks and the highest was 39 weeks.

Highest systolic BP (SBP) was 190 and diastolic BP (DBP) was 140 mmHg. The mean SBP was 155.40 mm Hg, while the mean DBP was 97.62 mm Hg. Mean values of systolic and diastolic BP were higher in eclampsia. Mean platelet count values were lower in eclampsia whereas mean ALT levels, and serum creatinine were higher in the same.

Most common impending symptoms noted were headache (52%), followed by blurring of vision (26.7%), nausea/vomiting and epigastric pain.

FGR was seen in 33.3% of eclampsia patients and 29.1% of preeclampsia patients. Its incidence was noted to be higher and statistically significant in eclampsia (p value = .001).

Ocular symptoms were seen in 22% of preeclampsia and in 100% of eclampsia patients. The majority complained of defective vision. Other symptoms included flashes, diplopia and colored halos.

Visual acuity was worse in a few with a range of 6/12–6/60. A total of ten patients had anterior segment (AS) findings (two eclampsia patients and eight preeclampsia patients). There were two cases of lid edema, six cases of chemosis, one case of squint due to lateral rectus palsy and one case with relative afferent pupillary disorder due to central retinal artery occlusion (CRAO). All subjects with AS findings had associated posterior segment findings.

Fundus changes were seen in 48.7% of the study population. This included all patients who had eclampsia and 45% of preeclampsia cases (p value = .001). Fundus assessment is significant in a case of preeclampsia/eclampsia because retina is a unique site where vasculature of body is directly visualized, and the changes in these arteries indicate a similar state in other parts of body, including placental circulation. Fundus changes were significantly associated with FGR. Its involvement was higher for multigravida than primigravida. Even asymptomatic patients had fundus changes. Out of 73 cases with fundus changes, 87% had no anterior segment changes. However, all those with anterior segment findings had fundus changes and this was found to be statistically significant. Those with fundus changes had a higher mean SBP, DBP and serum creatinine values, and this was statistically significant (p value < .05). Regression analysis was done, and it was found that SBP and serum creatinine were predictive of fundus changes ($r=0.49$, $p=.000$).

Arteriolar narrowing, macular edema, serous retinal detachment, localized and diffuse choroidal changes were analyzed. Arteriolar narrowing (p value = .001) and macular edema (p value = .000) had a higher occurrence rate in eclampsia patients which was found to be statistically significant.

Fundus changes were as follows (Fig. 1):

- (1) *Arteriolar Narrowing* This was the most common finding on fundus examination. It was seen in 44% of the patients. Generalized arteriolar narrowing was seen among 60, and focal constriction was seen among six patients. Arteriolar changes were significantly associated with anterior segment changes. The mean SBP, DBP and serum creatinine values were higher in those with arteriolar narrowing than those with no arteriolar narrowing (p value < .05). It was also observed that mean values were higher with cases of generalized narrowing than that of focal narrowing.
- (2) *Macular Edema* The second most common finding was macular edema (12.7%). All women with macular edema had higher SBP and DBP. Patients with macular edema had a higher incidence of FGR ($p < .05$).
- (3) *Serous Retinal Detachment (SRD)* was seen in four patients (2.7%). Mean ALT and serum creatinine levels were significantly higher, while platelet levels were lower in these patients. Retinal detachment was significantly associated with HELLP (p value = .009). Elschnig's spots (black spots surrounded by bright yellow or red halos finding on fundoscopy) were seen in two patients.
- (4) *Arteriovenous Crossing Changes* There were six cases and of these, three cases with retinal superficial hemorrhage and two cases with cotton-wool spots (fluffy white patches on the retina caused by damage to nerve fibers).

Incidence of FGR was found to be significantly associated with fundus involvement (p value .000). Fifty-four percent cases with fundus changes had FGR compared to 6% with no FGR. Fifty-two percent cases of macular edema were associated with FGR, whereas only 25% without macular edema had FGR ($p < .05$). The majority of the cases with arteriolar narrowing had FGR. Statistical significance was

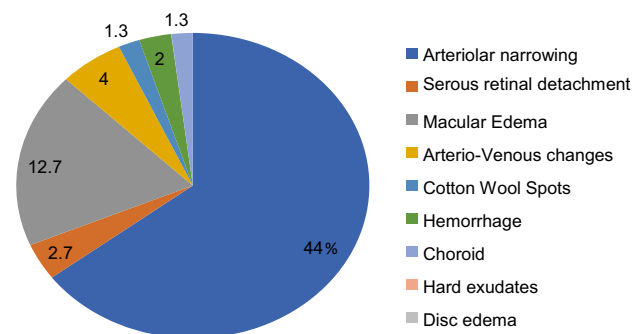


Fig. 1 Distribution of fundus findings in study population

Table 1 Fundus changes and FGR (fetal growth restriction)

Variable	Fundus changes		p value
	Yes (n=73)	No (n=77)	
FGR Present	39	5	.000

*p value significant at the level of .05

Table 2 Arteriolar narrowing and FGR

Variable	Arteriolar narrowing			p value
	Nil (n=84)	Generalized (n=60)	Focal (n=6)	
FGR Present (n=44)	7	35	2	.00

*p value significant at the level of .05

obtained with fundus involvement, arteriolar narrowing and macular edema (Tables 1 and 2; Fig. 2).

Discussion

Progression of retinal vascular changes is a sign of increasing severity of preeclampsia/eclampsia [7, 8]. A positive correlation has been established between the degree of retinopathy, the severity of preeclampsia and fetal mortality. Over a period of the last three decades, there has been a paradigm shift in the indications for termination of pregnancy based on maternal ophthalmic conditions [9]. Chawla et al. mention severe retinopathy and rapidly progressing arteriospasm in maternal circulation as a harbinger of poor fetal prognosis. Alizadeh Ghavidel et al. also advocate for using retinal findings as a guideline for prompt intervention as these findings may reflect similar ischemic vascular changes in placenta. In our study, fundus findings correlated well with FGR.

There was a predominance of multigravida over primigravida. Shah et al. noted a similar observation in their study [10]. As reported in the literature, more cases were seen in the third trimester and higher range of blood pressure was associated with eclampsia. Eclamptic patients were noted to have worse laboratory parameters including thrombocytopenia, abnormal liver and renal function tests.

In our study, all women with eclampsia had symptoms whereas only 22% preeclampsia patients complained of symptoms. Samra et al. found that symptoms occur in about 25% preeclampsia and 50% eclampsia patients [11].

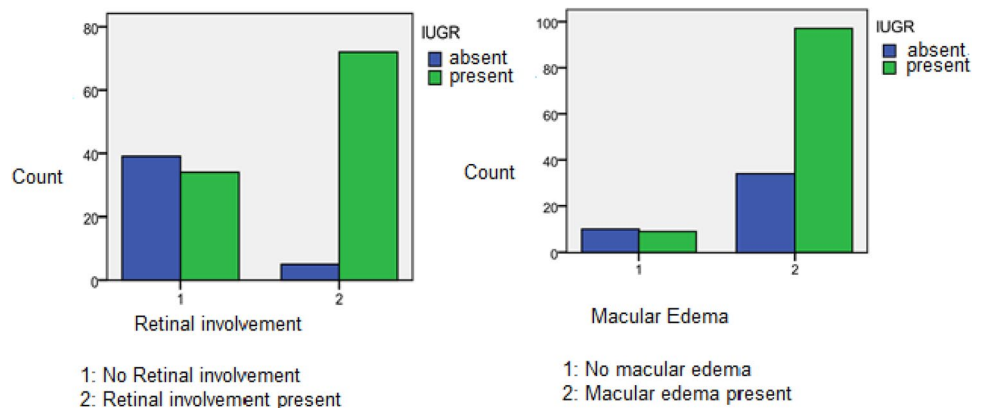
Out of 73 cases with fundus changes, 87% had no anterior segment changes. However, all those with anterior segment findings had fundus changes and this was found to be statistically significant. Hence, similar to ocular symptoms, anterior segment changes may not be as prevalent as fundus changes.

Fundus changes were seen in 48.7% of the study population. Some studies report the incidence of retinopathy may be as high as 85% in cases of pregnancy hypertension. Dasgupta et al. found this incidence to be 49%, and Sudha et al. found the same to be 53.29%. A few studies showed lower prevalence as in Manpreet Kour et al. where the fundus changes were seen in only 31.11% patients [12]. Abu Samara K mentioned that 25% of women with preeclampsia may have visual symptom and in ophthalmoscopy 50% of the women may have abnormalities. This demonstrates the importance of retinal examination as the patients can have fundus changes even without ocular symptoms. Therefore, in all women with preeclampsia, fundoscopic examination should be considered irrespective of the symptoms.

Those with fundus changes had mean gestational age of 33 weeks, whereas those without fundus changes had mean gestational age of 34 weeks (p value = .01). This shows that fundus involvement is associated with a severe spectrum and early onset of disease.

In our study, changes in fundal examination were seen in all eclampsia subjects and 45.4% of preeclampsia subjects. This observation was statistically significant (p = .001)

Fig. 2 Occurrence of FGR with fundus findings



which reinforces that fundus involvement is seen more with higher grades of the disease. It was noted that those with fundus changes had higher BP and higher creatinine levels than those without fundus changes (p value = .00). This observation was obtained for all the subjects and for preeclampsia subjects separately as well. However, this association was not found statistically significant for eclampsia subjects, probably because of lesser number of eclampsia subjects. Since eclampsia is a severe disease, with increased morbidity and mortality, this observation is clinically relevant.

It was found that by using regression analysis, SBP and serum creatinine were predictive of fundus changes ($r = .49$, $p = .000$). The association between BP and fundus changes in the present study does not go along with the study of Gupta et al., who said that severity of retinopathy does not correlate with degree of SBP and DBP [13]. But similar results were observed by Bhandari et al. and Varija et al. who quoted that severe grades of retinopathy are seen with increase in BP and increasing grades of proteinuria [14].

Our study showed that the presence of fundus changes in a patient of preeclampsia/eclampsia was significantly associated with FGR (p value .00). Statistically significant relationship of FGR was found with fundus findings in the forms of macular edema and arteriolar narrowing (p value < .05). Li et al. reported significant association between retinal vascular caliber and fetal growth restriction [15]. Dasgupta et al. also demonstrated that retinal microvasculature changes are closely associated with FGR. Bakhda et al. reported higher incidences of preterm births, still births and low birth weight babies in preeclampsia/eclampsia patients with fundus changes [16].

The majority of those with fundus involvement had FGR (p value .00). We also noted that there was higher incidence of FGR in those with arteriolar narrowing (p value = .00) and macular edema (p value = .02). This reinforces the fact that retinal vasospasm relates to placental perfusion. Li et al. had similar observation which said that retinopathy possibly reflects placental insufficiency. Gupta and colleagues also observed the same. In a study done by Taj et al., 42 women out of 86 (48.8%) with fundus changes and 33 women out of 216 (15.27%) without fundus changes had FGR babies. They concluded that there is a statistically significant association between fundus changes and FGR. Hence, hypertensive disorders with FGR should undergo routine fundus examination.

Conclusions

Retinal vascular changes are hallmark of hypertensive disorders of pregnancy with increasing severity in severe preeclampsia/eclampsia. Even asymptomatic patients can have changes on fundus examination reiterating the importance of

routine retinal examination. We suggest fundus examination be used as a screening tool for all patients with preeclampsia and eclampsia as routine screening. This will help in detecting even those patients who do not have symptoms and thus help in early detection of fetal growth restriction which will eventually make the management more efficient and help in achieving better outcomes. Fundus changes were seen in 48.7% of the study population. Retinal microvasculature changes are closely associated with FGR.

Authors' Contribution All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by [Dr JRC], [Dr. IBN] and [Dr JR]. The first draft of the manuscript was written by [Dr IBN] and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethics Approval All procedures performed in this study involving human participants were in accordance with the ethical standards of the Institutional Ethics Committee of Government Medical College Kozhikode, Kerala, Reference number GMCKKD/RP/2016/IEC/05/21-01 and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

Informed Consent Informed consent was obtained from all individual participants included in the study.

References

1. Shekhawat SK, Choudhary V, Shekhawat U. Co-relation of fundus changes & pregnancy induced hypertension: a prospective observational study. *IOSR J Dent Med Sci (IOSR-JDMS)*. 2019;18(04):46–54.
2. Cunningham F, Leveno K, Bloom S, et al. *Williams obstetrics*, 25th edition 2018; chapter 40. London: Mcgraw-Hill; 2018.
3. World Health Organization. *Maternal mortality: Factsheet 2015*.
4. Krishnakumar S, Chatterjee P. Fundus changes in preeclampsia. *J Evol Med Dent Sci*. 2016;5(36):2159–62.
5. Mobeen Taj SV, et al. Fundoscopic changes in pre-eclampsia and fetal outcome. *IOSR J Dent Med Sci (IOSR-JDMS)*. 2020;19(1):14–24.
6. Yevale A, Vasudeva A, Mundkur A, et al. Isolated sixth cranial nerve palsy in a case of severe pre-eclampsia presenting as postpartum diplopia. *J Clin Diagn Res JCDR*. 2017;11(8):QD01.
7. Sudha R, Moizuddin Kavya SSK, et al. Study of prevalence of fundus changes in pregnancy induced hypertension in a teaching hospital. *Indian J Clin Exp Ophthalmol*. 2019;5(2):215–8.
8. Marcos-Figueiredo P, Marcos-Figueiredo A, Menéres P, et al. Ocular changes during pregnancy. *Revista Brasileira de Ginecologia e Obstetrícia*. 2018;40(1):32–42.
9. Chawla S, Chaudhary T, Aggarwal S, et al. Ophthalmic considerations in pregnancy. *Med J Armed Forces India*. 2013;69(3):278–84.

10. Shah AP, Lune AA, Magdum RM, et al. Retinal changes in pregnancy-induced hypertension. *Med J DY Patil Univ.* 2015;8:304–7.
11. Samra KA. The eye and visual system in the preeclampsia/eclampsia syndrome: what to expect? *Saudi J Ophthalmol.* 2013;27(1):51–3.
12. Kour M, Gupta V. Prevalence of fundus changes in pregnancy induced hypertension: a clinical study. *Int J Med Biomed Stud.* 2019. <https://doi.org/10.32553/ijmbs.v3i5.278>.
13. Gupta A, Kaliaperumal S, Setia S, Suchi ST, Rao VA. Retinopathy in preeclampsia: association with birth weight and uric acid level. *Retina.* 2008;28(8):1104–10.
14. Bhandari AJ, Bangal SV, Gogri PY. Ocular fundus changes in pre-eclampsia and eclampsia in a rural set-up. *J Clin Ophthalmol Res.* 2015;3:139–42.
15. Varija T, Vanaja D, Sindhura RB. A study of prevalence and association of fundus changes in pregnancy induced hypertension. *Int J Reprod Contracept Obstet Gynecol.* 2016;5:1375–9.
16. Li L-J, Aris I, Su LL, et al. Associations of maternal retinal vasculature with subsequent fetal growth and birth size. *PLoS ONE.* 2015;10(4):e0118250.

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