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A Study of Ocular Fundus Findings in Hypertension during Pregnancy in a Tertiary Care Hospital

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Abstract

Introduction: Hypertension is one of the most common medical disorders during pregnancy, affecting 6-8% of all pregnancies. Around 16-25% of 1st pregnancy &12-15% of subsequent pregnancies[8]. Ocular fundus changes are found in 40% to 100% of pregnant women with raised blood pressure, whose severity correlates with pre-eclampsia or eclampsia. In hypertensive disorders in pregnancy, ophthalmic manifestations include conjunctival vasculopathy, hypertensive retinopathy, exudative retinal detachment, hypertensive choroidopathy. The retina is involved due to the basic pathology of vasospasm and increased capillary permeability, the consequences of vascular endothelial dysfunction. Rare complications were reversible cortical blindness, and extra-ocular muscle palsy have been documented. **Methodology:** The present study was conducted in the Outpatient Department (OPD) of Ophthalmology at Dr. Vasantrao Pawar Medical College, Hospital and Research Centre, Nashik , Maharashtra. All the 182 cases included in this study underwent indirect ophthalmoscopy during the study period of 2 years (August 2018 to December 2020). Patients were collected from ANC clinic of department of obstetrics and Gynaecology OPD. **Results:** Prevalence of abnormal fundus findings was 10.1% in grade I hypertension while it was 100% in cases with grade II and III hypertension. A significant association was observed between severity of hypertension and abnormal fundus findings ($p<0.01$). Prevalence of abnormal fundus findings was 0% among cases with no proteinuria while it was 85.7% in cases with grade 1+ proteinuria. All the cases with grade 2+ or more proteinuria had abnormal fundus findings. A significant association was observed between severity of proteinuria and abnormal fundus findings ($p<0.01$). No association was observed between laboratory parameters like haemoglobin, uric acid and blood urea nitrogen levels with abnormal fundus findings ($p>0.05$). **Conclusion:** As these vascular changes in the retina usually correlate with the severity of the systemic hypertension, the eyes can truly be considered a mirror to the otherwise elusive vascular changes occurring elsewhere in the body. It thus stands to reason that observing the retinal changes holds the ability to prognosticate and also determine the severity of the disease. Fundoscopy is an essential investigation that needs to be done in all cases of hypertensive disorders of pregnancy with special emphasis in younger and primigravida women.

Keywords: Conjunctival Vasculopathy, Fundus, Hypertension, Ocular, Pregnancy

1. Introduction

Hypertension is one of the significant public health problems due to its high prevalence worldwide[1–4]. Hypertension causes about 7.5 million deaths or around 12.8% of the total of all annual deaths worldwide[5]. It is estimated to be increased to 1.56 billion adults with Hypertension in 2025[6].

Hypertension (HTN) is defined as Systolic Blood Pressure (SBP) values of 130 mmHg or more or Diastolic

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Blood Pressure (DBP) more than 80 mmHg. Hypertension is a chronic medical condition characterized by a persistent rise in arterial pressure[7].

Hypertension is one of the most common medical disorders during pregnancy, affecting 6-8% of all pregnancies. Around 16-25% of 1st pregnancy &12-15% of subsequent pregnancies[8]. Ocular fundus changes are found in 40% to 100% of pregnant women with raised blood pressure, whose severity correlates with pre-eclampsia or eclampsia[9].

For more than 2000 years, Toxaemia of pregnancy is a recognized entity with its known complications and mortality [10–12]. American College of Obstetrics and Gynaecology has given the terminology "Hypertensive Disorders in pregnancy" for Hypertension in pregnancy[11,12].

Hypertensive disorders in pregnancy are divided as -:

1. Gestational Hypertension
2. Pre-eclampsia
3. Eclampsia.

1) **Gestational Hypertension:** New-onset hypertension (when systolic BP>=140mm Hg or diastolic BP >=90mm Hg or both) at two occasions presenting at or after 20 weeks of gestation without proteinuria or other features of pre-eclampsia[11,12].
2) **Pre-eclampsia:** The presence of Hypertension (BP>140/90mmHg) on two occasions with a spacing of four hours and significant proteinuria (>300 mg per 24 hours) or edema[11,12].
3) **Eclampsia:** The occurrence of convulsions or coma unrelated to other cerebral conditions, with signs and symptoms of pre-eclampsia[11,12].

The ophthalmic manifestations of Hypertensive disorders in pregnancy have a particular emphasis on fundus examination. An ophthalmoscope helps detect the pathological changes in the fundus and retinal blood vessels in particular that reflected the effects of Hypertension throughout the vascular system[13].

Common symptoms include -:

1. Blurring of vision
2. Photopsia
3. Scotomas
4. Diplopia

In Hypertensive disorders in pregnancy, ophthalmic manifestations include conjunctival vasculopathy, hypertensive retinopathy, exudative retinal detachment, hypertensive choroidopathy. The retina is involved due to the basic pathology of vasospasm and increased capillary permeability, the consequences of vascular endothelial dysfunction. These changes were mostly reversible and frequently proportional to the grade of severity of Hypertensive disorders in pregnancy[14]. Rare complications were reversible cortical blindness, and extra-ocular muscle palsy have been documented.

As hypertension is one of the most common medical disorders in pregnancy, this study will help us identify fundus changes which are an essential parameter for considering conservative management versus induction or termination of pregnancy[15].

2. Aims and Objectives

To study the ocular Fundus Findings in Hypertension during Pregnancy

3. Materials and Methods

It was a prospective (observational), hospital-based study. The present study was conducted in the Outpatient Department (OPD) of Ophthalmology at Dr. Vasantrao Pawar Medical College, Hospital and Research Centre, Nashik, Maharashtra. Approval for the study protocol had been obtained from the Institutional ethical review committee (IEC). Sample size was 182 patients in this study. All the cases included in this study underwent indirect ophthalmoscopy during the study period of 2 years (August 2018 to December 2020). Patients were recruited from ANC clinic of department of Obstetrics and Gynaecology OPD. All patients were explained about the nature and purpose of the study and written informed consent were taken.

3.1 Inclusion Criteria

All Pregnant women diagnosed with Hypertension in pregnancy (new onset of hypertension after 20th week of gestation) in third trimester of pregnancy (>28 weeks) in a tertiary care hospital.

3.2 Exclusion Criteria

Patients with pre-existing hypertension, patients with diabetes mellitus/Gestational DM, patients with renal disease, patients with SLE and other connective tissue

disorder, Patients with hazy media, patients not willing for participating in study.

3.4 Methodology

A thorough and detailed history was taken of the selected patients with special emphasis on history of drug allergy and systemic illness. Patients underwent a detailed clinical examination that included unaided and best corrected visual acuity using Snellen's chart and near vision. Pupil size and reactions were recorded.

A detailed anterior segment examination was done using Slit lamp Biomicroscopy. Intra Ocular Pressure was measured using a Goldman's Applanation Tonometer. A thorough, careful and detailed examination of the fundus was done first by a direct ophthalmoscope and subsequently with an indirect ophthalmoscope and Slit lamp Biomicroscopy with + 90D lens was performed to look for pathologies and documented.

The collected Data was entered in Microsoft Excel and analysed using SPSS version 24.0th. Mean and SD was calculated for quantitative variables and proportions was calculated for categorical variables. Also, data was represented in form of visual impression like bar-diagram, Pie diagram etc.

4. Results

Mean age of the study cases was pregnancy induced hypertension was 24.48 years with over half of the cases (57.1%) were between the age of 21 to 25 years. Majority of the cases with pregnancy induced hypertension were primi-gravida (63.7%).

No proteinuria was observed in 39.6% cases while grade 1+ and 2+ proteinuria was recorded in 30.8% and 22.5% cases respectively. Grade 3+ or more proteinuria was seen in 7.1% cases.

Based on blood pressure levels, grade I hypertension was seen in 48.9% cases while 44.5% and 6.6% had grade II and III hypertension respectively. Prevalence of abnormal fundus findings among pregnancy induced hypertension cases was 56%.

Grade I retinopathy was seen in 26.9% cases while grade 2, 3 and 4 retinopathy among cases with pregnancy induced hypertension was seen in 22%, 3.8% and 3.3% cases respectively. Visual acuity of 6/6 among pregnancy induced hypertension cases was seen in 75.8% cases while it was 6/9 and 6/12 in 18.7% and 5.5% cases respectively.

Raised blood urea nitrogen and uric acid levels were seen in 30.8% and 7.7% cases of pregnancy induced hypertension. Prevalence of anaemia was 12.1% in present study (Table 1).

Mean age of cases with abnormal fundus findings was lower than cases with normal findings showing an association between young age and abnormal fundus findings in cases with pregnancy induced hypertension

Table 1. Distribution of study cases as per various factors

Age group	**Age group (yrs)**	**N**	**%**
	< 20	20	11.0%
	21- 25	104	57.1%
	26- 30	44	24.2%
	31- 35	12	6.6%
	>35	2	1.1%
	Total	182	100.0%
	Mean age - 24.48 +/- 3.8 years		
Gravidity	**Multi**	66	36.3%
	Primi	116	63.7%
Proteinuria	**NIL**	72	39.6%
	1+	56	30.8%
	2+	41	22.5%
	3+	7	3.8%
	4+	6	3.3%
Grades of Hypertension	**I**	89	48.9%
	II	81	44.5%
	III	12	6.6%
Fundus findings	**Normal**	80	44.0%
	Abnormal	102	56.0%
Retinopathy	**No**	80	44.0%
	Grade 1	49	26.9%
	Grade 2	40	22.0%
	Grade 3	7	3.8%
	Grade 4	6	3.3%
Visual acuity	**6/6**	138	75.8%
	6/9	34	18.7%
	6/12	10	5.5%
	Raised BUN (> 21 mg %)	56	30.8%
	Raised S. Uric Acid (> 6 mg %)	14	7.7%
	Anemia (Hb<10 gm %)	22	12.1%

(p-0.041) (Table 2). No association was observed between gravidity of cases with pregnancy induced hypertension and abnormal fundus findings (p-0.54) (Table 3). No association was observed between visual acuity of cases with pregnancy induced hypertension and abnormal fundus findings (p-0.50) (Table 4).

Prevalence of abnormal fundus findings was 10.1% in grade I hypertension while it was 100% in cases with grade II and III hypertension. A significant association was observed between severity of hypertension and abnormal fundus findings (p<0.01) (Table 5). Mean systolic and diastolic blood pressure was significantly higher among cases with abnormal fundus findings (p<0.01) (Table 6).

Prevalence of abnormal fundus findings was 0% among cases with no proteinuria while it was 85.7% in cases with grade 1+ proteinuria. All the cases with grade 2+ or more proteinuria had abnormal fundus findings. A significant association was observed between severity of proteinuria and abnormal fundus findings (p<0.01) (Table 7). No association was observed between laboratory parameters like haemoglobin, uric acid and blood urea nitrogen levels with abnormal fundus findings (p>0.05) (Table 8).

Table 2. Mean age comparison among cases with normal and abnormal fundus findings

Variables	Fundus	N	Mean	SD	p-value
Age (years)	Abnormal	102	23.28	3.42	0.041
	Normal	80	25.75	4.26	

Table 3. Association of gravidity with fundus findings

Gravida	Fundus		Total
	Abnormal	Normal	
Multi	35	31	66
	53.0%	47.0%	100.0%
Primi	67	49	116
	57.8%	42.2%	100.0%
Total	102	80	182
	56.0%	44.0%	100.0%
p-value - 0.54			

Table 4. Association of visual acuity with fundus findings

Vision	Fundus		Total
	Abnormal	Normal	
6/6	80	58	138
	58.0%	42.0%	100.0%
6/9	16	18	34
	47.1%	52.9%	100.0%
6/12	6	4	10
	60.0%	40.0%	100.0%
Total	102	80	182
	56.0%	44.0%	100.0%
p-value - 0.50			

5. Discussion

Pregnancy Induced Hypertension (PIH) is a multisystem hypertensive disorder which is a clinical syndrome that afflicts 3-5% of pregnancies and is a leading cause of maternal mortality, especially in developing countries[10].

Multiple organs may be involved in PIH. Cardiovascular effects include vasospasm, increased cardiac output and haemoconcentration. Renal function abnormalities include decreased GFR and sodium retention. Hepatic dysfunction and platelet abnormalities

Table 5. Association of grade of hypertension with fundus findings

Grade of Hypertension	Fundus		Total
	Abnormal	Normal	
I	9	80	89
	10.1%	89.9%	100.0%
II	81	0	81
	100.0%	0.0%	100.0%
III	12	0	12
	100.0%	0.0%	100.0%
Total	102	80	182
	56.0%	44.0%	100.0%
p-value <0.01			

Table 6. Mean systolic and diastolic blood pressure in cases with normal and abnormal fundus findings

Variables	Fundus	N	Mean	SD	p- value
SBP	Abnormal	102	142.12	11.21	<0.01
	Normal	80	136.05	12.03	
DBP	Abnormal	102	98.78	6.27	<0.01
	Normal	80	93.77	5.12	

Table 7. Association of proteinuria with fundus findings

Proteinuria	Fundus		Total
	Abnormal	Normal	
1+	48	8	56
	85.7%	14.3%	100.0%
2+	41	0	41
	100.0%	0.0%	100.0%
3+	7	0	7
	100.0%	0.0%	100.0%
4+	6	0	6
	100.0%	0.0%	100.0%
Nil	0	72	72
	0.0%	100.0%	100.0%
Total	102	80	182
	56.0%	44.0%	100.0%
p-value <0.01			

Table 8. Mean blood urea nitrogen, uric acid and haemoglobin comparison among cases with normal and abnormal fundus findings

Investigations	Fundus	N	Mean	SD	p- value
BUN	Abnormal	102	18.74	4.55	0.87
	Normal	80	18.63	4.34	
UA	Abnormal	102	4.98	0.67	0.61
	Normal	80	4.79	0.70	
Hb	Abnormal	102	11.73	1.44	0.80
	Normal	80	11.78	1.53	

may occur. Neurological involvement may vary from headache and drowsiness to seizures, hemiplegia and coma[10].

The visual system may be involved in PIH. Visual system involvement is due to the severe toxaemia. The most common abnormality seen is a spasm and narrowing of the retinal vessels. The arteriolar constriction may take some days to develop and may last for weeks to months. It is believed to be due to a toxin that irritates the vessels and indicates state of vessels of similar size in the brain and in the kidneys. This may persist for sometimes or may be permanent after the termination of the pregnancy. The choroid is also frequently affected in the disease. There occurs choroidal ischemia and infarction. Ischemia of the optic nerve and of the occipital lobe may also occur and recovery usually occurs unless there is significant infarction[13].

In pregnancy induced hypertension, the various pathological changes in different organs of the body can be studied directly visualizing the ocular fundus and may give a true index of changes in vascular system of brain and retina[13].

The present hospital based cross sectional study aimed at estimating the prevalence and associated factors of retinal changes in hypertension in pregnancy. Study included 182 females diagnosed with pregnancy induced hypertension fulfilling the eligibility criteria.

5.1 Socio-demographic Factors

Mean age of the study cases was pregnancy induced hypertension was 24.48 years with overt half of the cases (57.1%) were between the age of 21 to 25 years.

In a similar study by Bharathi RN *et al.*[16], a total of 150 patients was studied. The age ranged from 18-32 with a mean of 23.06 + 3.03 years. Mean age in the study by Sharma JC *et al.*[17] was 22.33 years with most of the cases were between 20-25 years. Mean age in the study by Varija T *et al.*[18] was 22.77 years while in the study Reddy SC *et al.*[19], Shah AP *et al.*[20] and Sudha R *et al.*[21] was 30.2±6.2 years (range 21-45 years), 25.1 years and 24.12 years respectively.

5.2 Obstetric History

Majority of the cases with pregnancy induced hypertension were primi-gravida (63.7%) in present study.

In the study by Bharathi RN *et al.*[16] also, most of the cases, 105 (70%) were primigravidae and 45 (30%) were multigravidae. In the study by Sharma JC *et al.*[17] 61.8% cases of primigravida while 38.2% cases of multi-gravida. About 66.7% cases were primi-gravida in the study by Varija T *et al.*[18]. Prevalence of primi-gravida among PIH cases in the study by Reddy SC *et al.*[19], Shah AP *et al.*[20] and Sudha R *et al.*[21] was 43.6%, 50.7% and 51.4% respectively.

5.3 Prevalence of Retinal Changes

In present study, prevalence of abnormal fundus findings among pregnancy induced hypertension cases was 56%. Grade I retinopathy was seen in 26.9% cases while grade 2, 3 and 4 retinopathy among cases with pregnancy

induced hypertension was seen in 22%, 3.8% and 3.3% cases respectively.

Varija T *et al.*[16] in their study observed that 115 out of 150 cases had no change (76.66%). Abnormal fundus findings were seen in 35 cases (23.33%). Of these, 17.33% were grade I retinopathy while 0.67% and 4% were grade II and III respectively. Sharma JC *et al.*[17] observed that 68% patients had retinal changes on fundoscopic examination. Of those patients with retinal changes, most patients (54.9%) had KW grade 1. Only 4.5% had grade 4 changes on fundoscopy. 32% of cases in this study had history of visual disturbances. Out of the 423 patients with PIH studied by Varija T *et al.*[18], the prevalence of retinal changes (hypertensive retinopathy changes) was noted in 181 (42.7%) patients. Grade I retinal changes were the commonest among all the groups of PIH. Retinal changes (hypertensive retinopathy) were noted in 46 (59%) out of 78 patients. Of these, 52.6% were grade I retinopathy while 6.4% were grade II respectively. Shah P *et al.*[20] observed retinal changes (hypertensive retinopathy) in 12% patients - Grade 1 in 8% and Grade 2 in4%. Sudha R*et al.* [(21)] in their study of 70 cases, observed that changes related to the retina were observed in 37 PIHs i.e., 53.29% of patients. Grade 1 retinal changes were seen in 33(47.14%) and grade 2 in 4 (6.15%) patients. The observations made by various authors are tabulated below (Table 9).

Table 9. Prevalence of Fundal changes

Authors	Prevalence of Fundal changes
Bharathi RN *et al.*[16]	23.33%
Sharma JC *et al.*[17]	68%
Varija T *et al.*[18]	42.8%
Reddy SC *et al.*[19]	59.0%
Shah AP *et al.*[20]	18%
Sudha R *et al.*[21]	53.3%
Tadin I *et al.*[22]	45%
Kurdoğlu Z *et al.*[24]	48%
Present Study	56%

5.4 Association of Retinal Changes with Various Factors

5.4.1 Age

Mean age of cases with abnormal fundus findings was lower than cases with normal findings showing an association between young age and abnormal fundus findings in cases with pregnancy induced hypertension (p-0.041).

In the study by Varija T *et al.*[18], all grades of retinopathic changes were observed more among women in the younger age group between 20-25 years compared to other age groups and this difference was found to be statistically significant.

Bharathi RN *et al.*[16] however observed no significant effect of extremes of age (<20 or > 30) on the degree of changes (p=0.24). Sharma JC *et al.*[17] and Varija T *et al.*[18] also observed that age was not associated with occurrence of retinopathy.

5.4.2 Blood Pressure

Prevalence of abnormal fundus findings was 10.1% in grade I hypertension while it was 100% in cases with grade II and III hypertension. A significant association was observed between severity of hypertension and abnormal fundus findings (p<0.01). Mean systolic and diastolic blood pressure was significantly higher among cases with abnormal fundus findings (p<0.01).

Bharathi RN *et al.* [16] in a similar study also observed a significant association between the fundus changes and the levels of hypertension (p<0.001). Fundal changes were seen in 45.7% cases with BP reading over 160/110 mm Hg as compared to only 13.6% in cases with BP values below 160/110 mm Hg. Sharma JC *et al.*[17] in their study showed the there was a significant rise in the mean systolic and diastolic blood pressure with increased grades of retinopathy. Mean BP in patients with no retinal change was 143.54/92.15 mmHg (±SD 4.84/8.56) and it was 207.14/112.86 mmHg (±SD 4.21/7.55) in patients with grade 4 changes. This difference in the mean systolic blood pressure and diastolic blood pressure was statistically significant (P-value 0.001). Varija T *et al.*[18] also observed that as the severity of the PIH increased the Odds of women developing retinopathy also increased substantially from OR: 17.6; 95% CI: 3.1 - 136.3 in severe PIH to OR: 253; 95% CI: 47.2 - 1935 in Imminent eclampsia and this association between the severity of PIH and the development of retinopathy changes was found to be statistically significant. Varija T *et al.*[18] and Shah P *et al.*[20] in their studies observed a statistically significant positive association between the presence of retinal changes and blood pressure (p<0.01). Our observations were also similar to that of S.C. Reddy *et al.* study[19], Sudha R*et al.*[21] and Tadin I *et al.* study[22].

5.4.3 Proteinuria

Prevalence of abnormal fundus findings was 0% among cases with no proteinuria while it was 85.7% in cases with grade 1+ proteinuria. All the cases with grade 2+ or more proteinuria had abnormal fundus findings. A significant association was observed between severity of proteinuria and abnormal fundus findings ($p<0.01$).

Sharma JC *et al.*[17] observed that 46% of patients with plus 1 proteinuria had no retinopathy and 29% had grade 1 only. Compared to this, in patients with proteinuria of 4 plus, 50% had grade 3 and 50% had grade 4 changes showing a significant correlation between the degree of proteinuria and retinopathy. Varija T *et al.*[18] and Shah P *et al.*[20] in their studies also observed a statistically significant positive association between the presence of retinal changes and proteinuria ($p<0.01$). Sudha R *et al.*[21] observed that retinal vascular changes observed in 27%, 44%, 71% and 100% of cases with proteinuria 1+, 2+, 3+ and 4+ respectively. This will show that retinal vascular changes were observed in more cases with high degree of proteinuria.

Thus, to summarize, retinal changes occur in over half of the patients with hypertensive disorders of pregnancy. As described in the literature, the wellbeing of the foetus depends on the placental circulation and it is believed that the vascular changes in the placenta can be indicated by the presence of changes in the retinal arterioles and retinal haemorrhages and therefore ophthalmoscopic examination of mother's fundus may give a clue to similar micro-circulation changes in the placenta and indirectly to the foetal wellbeing. Fundus examination in patients with PIH is an important clinical evaluation to predict adverse foetal outcomes[23]. Fundoscopy is thus an essential investigation that needs to be done in all cases of hypertensive disorders of pregnancy with special emphasis in younger and primi-gravida women.

6. Conclusion

Retinal changes occur in over half of the patients with hypertensive disorders of pregnancy. The retina offers a unique opportunity to directly observe the pathological changes occurring in the vasculature. As these vascular changes in the retina usually correlate with the severity of the systemic hypertension, the eyes can truly be considered a mirror to the otherwise elusive vascular changes occurring elsewhere in the body. It thus stands to reason that observing the retinal changes holds the ability to prognosticate and also determine the severity of the disease. Fundoscopy is an essential investigation that needs to be done in all cases of hypertensive disorders of pregnancy with special emphasis in younger and primigravida women.

Limitations of this study were that review of retinal changes at 6 weeks also should be done to assess the effect of treatment on fundal changes. A prospective multi-centric study with a larger sample size is likely to provide better results by removing the effect of confounding variables and determining effect of treatment.

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