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A clinical study of fundus changes in pregnancy induced hypertension in tertiary health care Centre in Sevagram, Wardha, India

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Abstract

Introduction: The most common abnormalities seen in pregnancy induced hypertension (PIH) are fundus spasm, focal/generalized narrowing of retinal arterioles, haemorrhages, exudates, peripapillary or focal retinal oedema, serous retinal detachment, bilateral retinal detachment, exudative retinal detachment and severe macular oedema. There is a paucity of data available in the published literature on the prevalence of retinal changes in PIH from India.

Aim: The purpose of the present study was to find the prevalence of retinal changes in PIH and the association between the retinal changes and severity of PIH.

Materials and Methods: 350 women with gestational ages between 20 and 40 weeks admitted in the maternity ward in the Department of Obstetrics and Gynaecology of Mahatma Gandhi Institute of Medical Sciences, Sevagram, Wardha between November 2017 and November 2019 with features of PIH both asymptomatic and symptomatic were included in this cross-sectional study. Age, parity, gestational period, blood pressure and proteinuria of the patients were documented. Fundus examination was done to find the retinal changes (hypertensive retinopathy) according to Keith Wagener classification. Comparison of the distribution of categorical variables was done using Fisher's exact test.

Results: Of 350 patients, 218 (62.3%), 92 (26.3%), 34 (9.7%), 5 (1.4%) and 1 (0.3%) had normal, Grade I, Grade II, Grade III and Grade IV fundus changes respectively. The prevalence of Grade III/IV hypertensive retinopathy was significantly higher in eclampsia 4/34 (11.8%) as compared to gestational hypertension 0/210 (0.0%) and preeclampsia 2/106 (1.9%) (p-value < 0.0001). The prevalence of Grade III/IV hypertensive retinopathy was significantly higher in patients who had systolic blood pressure > 180 mm of Hg 1/4 (25.0%), diastolic blood pressure > 110 mm of Hg 1/9 (11.1%).

Conclusion: The occurrence of hypertensive retinopathy is associated with pregnancy-induced hypertension. Fundus examination is very important in patients having PIH.

Keywords: pregnancy-induced hypertension, hypertensive retinopathy, proteinuria

Introduction

Pregnancy-induced hypertension (PIH) is a multisystem disorder affecting 6.0% to 8.0% of all pregnancies and is a major cause of maternal and fetal morbidity and mortality. PIH affects the retinal as well as choroidal vasculature with clinical findings resembling hypertensive retinopathy [1]. Hypertensive disorders complicating pregnancy are one of the common and significant causes of maternal morbidity and mortality, especially in developing countries. They are responsible for 8% - 9% of maternal deaths in India and 15.0% - 20.0% of maternal deaths in western world. Overall, they complicate 5.0% to 10.0% of pregnancies in India [2]. The incidence of PIH is 15.2% in India and it is four times higher in primipara women than in multipara [3-4]. Hypertensive disorders occur in about 8.0% - 10.0% of all pregnant women all over the world. The incidence of preeclampsia in nulliparous population ranges from 3.0% to 10.0% worldwide [5]. The incidence of eclampsia in the developed countries is about 1 in 2000 deliveries [6]. Sudden diminution of vision associated with progressive spasm of retinal arterioles, retinal oedema, the onset of macular oedema, papilledema, or detachment of the retina, are the warning signs for the termination of pregnancy to save the vision and also to prevent further pathological changes in the arterioles of the other organs in the body [7]. It is reported that there is a close correlation between blood pressure elevation and retinal arteriolar spasm [8]. The retina is a unique site where the vasculature in the human body is visualized directly with the help of an ophthalmoscope. The eye serves as a window through which the vessels of the body can be studied [9].

The retinal vascular changes generally, but not always, correlate with the severity of systemic hypertension.¹⁰⁻¹¹ Fundoscopy is a simple, non-invasive and cost-effective investigative procedure that can be performed in the outpatient department or at the bedside. The data in the published literature on the prevalence of retinal changes in PIH from India is modest. The aim of the present study was to determine the prevalence of retinal changes in PIH and the association between the retinal changes and severity of PIH.

Materials and Methods

This cross-sectional observational study was conducted between November 2017 and November 2019 in the Department of Ophthalmology of Mahatma Gandhi Institute of Medical Sciences, Sevagram, Wardha, India with the active collaboration of the Department of Obstetrics and Gynecology. After approval from the institutional ethics committee written informed consent was obtained from all the patients prior to enrolment explaining the risks and benefits of the study. Patients between 20 and 40 years of age with gestational age between 20 and 40 weeks admitted in the maternity ward in the Department of Obstetrics and Gynecology with features of PIH both asymptomatic and symptomatic such as headache, blurring of vision, loss of vision were included. Patients who had pre-existing hypertension, diabetes mellitus, renal disease, connective tissue disorders and ocular diseases like high myopia, cataract, corneal opacities, hazy media which will not permit fundus visualization were excluded.

Shah AP *et al.* reported the prevalence of hypertensive retinopathy in 18/150 (12.0%) patients^[9]. The sample size was calculated by formula $N = (Z_{\alpha})^2 p(1-p)/d^2$. We took $Z_{\alpha} = 2.58$ a standard normal variate at 1% type I error. A total sample size of 280 was calculated by the above method^[12]. A total of 350 patients were included to validate the results. Age, parity, gestational period, ocular complaints, blood pressure, proteinuria, liver function tests and kidney function tests of the patients were documented.

PIH was defined as systolic blood pressure (SBP) >140 mm Hg and diastolic blood pressure (DBP) >90 mm Hg^[13]. The severity of PIH was classified into preeclampsia (mild and severe) and eclampsia, based on the following findings: Mild preeclampsia as SBP >140/90 mm Hg, proteinuria +, and/or mild edema of legs; Severe preeclampsia as SBP >160/110 mm Hg, proteinuria ++ or +++, headache, cerebral or visual disturbances, epigastric pain, impaired liver function tests, and increased serum creatinine; Eclampsia as severe preeclampsia+ convulsions. Proteinuria was tested using dipstick method and was graded as + = 0.3gm/L, ++ = 1gm/L, and +++ = 3gm/L.¹¹ Fundus examination was done under tropicamide mydriasis. A 0.5% tropicamide eye drops were instilled. After instillation of

eye drops, patients were advised punctal obstruction for 3 min after closing their eyes to avoid systemic absorption. Both slit-lamp biomicroscopy and direct ophthalmoscopy were done. The retinal changes (hypertensive retinopathy) were graded according to Keith-Wagener-Barker classification.¹⁴ Grade I: Mild generalized arterial attenuation, particularly of small branches. Grade II: Grade I plus definite focal arteriolar attenuation of arterioles and arteriovenous crossings. Grade III: Grade II plus retinal hemorrhages, hard exudates and cotton wool spots. Grade IV: Grade III plus optic disc swelling (Papilledema). Statistical analysis was done using SPSS Version 20.0 from IBM Corporation Armonk, NY, USA. The data on categorical variables are shown as n (% of cases), and the data on continuous variables were presented as mean and standard deviation (SD). Comparison of the distribution of categorical variables was done using Fisher’s exact test. The confidence limit for significance was fixed at a 95% level with a p-value < 0.05.

Results

Table 1 shows the association between various parameters and severity of hypertensive retinopathy. Of 350 patients, 156 (44.6%), 132 (37.7%), 54 (15.4%) and 8 (2.3%) were between 20 and 24, 25 and 29, 30 and 34 and 35 and 40 years respectively. The mean ± SD of age of patients was 25.8 ± 3.9 years. 58.0% were primigravidae and 54.0% were primipara. Of 350 patients, 210 (60.0%), 106 (30.3%), and 34 (9.7%) had gestational hypertension, preeclampsia and eclampsia respectively. Of 350 patients, 218 (62.3%), 92 (26.3%), 34 (9.7%), 5 (1.4%) and 1 (0.3%) had normal, Grade I, Grade II, Grade III and Grade IV fundus changes respectively. Of 350 patients, 210 (60.0%), 94 (26.9%), and 46 (13.2%) had proteinuria of < +1, +1 ≤ +2 and > +2 respectively.

There was no statistically significant difference between age, gravida, parity of the patients and grades of retinopathy. There was a statistically significant difference between the severity of hypertensive disease and grades of hypertensive retinopathy (p<0.001). A higher percentage of Grades III-IV hypertensive retinopathy was observed in patients who had severe hypertension (eclampsia). Significantly higher percentage patients had hypertensive retinopathy that had proteinuria ≥ +1 as compared to patients who had proteinuria < 1 (p<0.05). There was a statistically significant difference between SBP and grades of hypertensive retinopathy. A higher percentage of Grades III-IV hypertensive retinopathy was observed in patients who had SBP > 180 mm of Hg (Table 2). There was a statistically significant difference between DBP and grades of hypertensive retinopathy (P<0.05). A higher percentage of Grades III-IV hypertensive retinopathy was observed in patients who had DBP > 110 mm of Hg.

Table 1: Association between age, obstetric variables, and severity of hypertension with hypertensive retinopathy (N=350)

Characteristics	Within normal limits n (%)	Grades of hypertensive retinopathy			p-value (Fisher exact Test)
		Grade I n (%)	Grade II n (%)	Grade III-IV n (%)	
Age (in years)					
20-24	97 (62.2)	47 (30.1)	11 (7.1)	1 (0.6)	0.7546
25-30	82 (62.1)	31 (23.5)	16 (12.1)	3 (2.3)	
30-34	34 (63.0)	12 (22.2)	6 (11.1)	2 (3.7)	
35-40	5 (62.5%)	2 (25.0%)	1 (12.5%)	0 (0.0)	
Gravida					
Primi	122 (60.1)	58 (28.6)	18 (8.9)	5 (2.5)	0.5143
Multi	96 (65.3)	34 (23.1)	16 (10.9)	1 (0.7)	

Para					
Primi	117(61.9)	50 (26.5)	19 (10.1)	3 (1.6)	0.9836
Multi	101(62.7)	42 (26.1%)	15 (9.3)	3 (1.9%)	
Severity of hypertension					
Gestational HTN	160 (76.2)	42 (20)	8 (3.8)	0 (0)	<0.0001
Pre-eclampsia	47 (44.3)	35 (33)	22 (20.8)	2 (1.9)	
Eclampsia	11 (32.4)	15 (44.1)	4 (11.8)	4 (11.8)	
Urine albumin					
Less than or =1	207 (98.6)	3 (11.7)	0 (0)	0 (0)	<0.05
1-2	11 (11.7)	55 (58.5)	27 (28.7)	1 (1.1)	
2+	0 (0)	34 (73.9)	7 (15.2)	5 (10.9)	

Table 2: Association between systolic and diastolic blood pressures with hypertensive retinopathy (N=350)

Characteristics	Within normal limits n (%)	Grades of hypertensive retinopathy			p-value (Fisher exact test)
		Grade I n (%)	Grade II n (%)	Grade III-IV n (%)	
Systolic BP (mmHg)					
100-120	16 (69.6)	6 (26.1)	1 (4.3)	0 (0)	<0.05
121-140	30 (41.1)	25 (34.3)	15 (20.6)	3 (4.1)	
141-160	166 (70.6)	56 (23.8)	12 (5.1)	1 (0.4)	
161-180	6 (40)	4 (26.7)	4 (26.7)	1 (6.7)	
>180	0 (0)	1(25)	2 (50)	1 (25)	
Diastolic BP (mmHg)					
<80	38 (77.6)	9 (18.4)	2 (4.1)	0 (0)	<0.05
81-90	126 (65.3)	50 (25.9)	16 (8.5)	1 (0.5)	
91-100	6 (37.5)	7 (43.8)	2 (12.5)	1 (6.3)	
101-110	46 (55.4)	24 (28.9)	10 (12)	3 (3.6)	
>110	2 (22.2)	2 (22.2)	4 (44.4)	1 (11.1)	

Discussion

The present study was undertaken to find the prevalence of retinal changes in PIH and the association between the retinal changes and severity of PIH in 350 pregnant women. In the present study, the prevalence of Grade III/IV hypertensive retinopathy was significantly higher in eclampsia as compared to gestational hypertension and preeclampsia. The prevalence of Grade III/IV hypertensive retinopathy was significantly higher in patients who had systolic blood pressure > 180 mm of Hg, diastolic blood pressure > 110 mm of Hg and proteinuria ≥ 1+. In the present study, the mean age of the patients was 25.8 ± 3.9 years with ages ranging from 20-40 years. Mean ages of were between 25.1 years and 30.2 years in other studies [9-11, 15-19]. Like in our study, age was not significantly associated with hypertensive retinopathy [10, 17, 20].

Few studies noted that percentage of primigravidae was between 43.5% and 70.0% which is similar with our study [9, 10, 15, 17, 21, 22]. Kamath RK and Nayak SR and Bharathi NR *et al.* reported 65.0% and 70.0% primigravidae respectively which were higher than our study [16, 23]. In the present study, there was no statistically significant between parity of the patients and grades of retinopathy which is similar to the findings of Reddy SC *et al.*, and Krishnakumar S and Chatterjee P studies [10, 17]. Das KA and Jaisal P reported a statistically significant difference between parity of the patients and grades of retinopathy (p-value < 0.002) [20]. In the present study of 350 patients, 60.0%, 30.3% and 9.7% had gestational hypertension, preeclampsia and eclampsia respectively which were comparable to study by Shah AP *et al.*, who reported 61.3%, 32.7% and 6.0% gestational hypertension, preeclampsia and eclampsia respectively [9]. In the present study, there was a statistically significant difference between the severity of hypertensive disease and grades of hypertensive retinopathy. Patients who had severe hypertension (eclampsia) had a higher percentage of Grades III-IV hypertensive retinopathy (p-value < 0.0001). Our findings are comparable to studies conducted by Reddy SC

et al., (p-value = 0.024), Shah AP *et al.*, (p-value = 0.004) and Krishnakumar S and Chatterjee P (p-value = 0.0139) studies [9, 10, 17].

The prevalence of retinal changes was 37.7% in our study. Ranjan R *et al.*, Varija T *et al.*, and Tadin I *et al.* reported retinal changes in 40.0%, 42.7%, and 45.0% patients respectively which are similar to our study [11, 18, 22]. Reddy SC *et al.*, Kamath RK and Nayak SR and Javadekar SD *et al.* reported retinal changes in 59.0%, 60.0%, and 72.0% patients respectively which are higher than our study [10, 23, 24]. whereas Shah AP *et al.* reported retinal changes in 12.0% patients which is lower than our study [9]. Tadin I *et al.*, reported that 25.0%, 15.0% and 5.0% had Grade I, Grade II and Grade III retinopathy respectively [18]. In the present study, 26.3%, 9.7%, 1.4% and 0.3% patients had Grade I, Grade II and Grade III and IV hypertensive retinopathy respectively. Tadin I *et al.*, and Krishnakumar S and Chatterjee P stated that the degree of retinopathy was directly proportional to the severity of hypertension [17-18]. Landesman R *et al.*, also reported a correlation between the degree of retinopathy and the severity of hypertension. Our study substantiated these findings. [25] Few studies have reported a statistically significant association between high systolic blood pressure and the severity of the retinal changes which is similar to the present study [9, 10-18, 21]. Reddy SC *et al.*, Shah AP *et al.*, Bhandhari AJ *et al.*, Mithila R *et al.*, and Tadin I *et al.*, reported a statistically significant association between proteinuria and severity of retinopathy [9, 10, 15, 18, 26]. Our study substantiated these findings.

The retinal changes were observed in 132/350 (37.7%) pregnant women. A higher percentage of Grades III-IV hypertensive retinopathy was observed in pregnant women who had severe hypertension (eclampsia), systolic blood pressure > 180 mm of Hg, diastolic blood pressure > 110 mm of Hg and proteinuria ≥1+. The retinopathy may indicate similar changes in the placenta; hence, it gives a reasonable idea of the state of placental circulation and fetal

wellbeing. The presence of macular edema, papilloedema or retinal detachment is the warning signs for termination of pregnancy to save the vision of the mother. Fetal and maternal complication can be avoided if retinopathy is detected early. The pregnant women with hypertension should be screened for funduscopy. This study is mainly limited by the small sample size and the single centre design, which increases the risk of a Type II error. As a consequence, these findings need to be confirmed in larger populations. Multicentric prospective studies with a large sample size should be undertaken to substantiate the research findings described in this paper. In conclusion, there was a statistically significant difference between the severity of the hypertensive disease, systolic blood pressure, diastolic blood pressure, proteinuria and grades of hypertensive retinopathy. A higher percentage of Grades III-IV hypertensive retinopathy was observed in patients who had severe hypertension (eclampsia), systolic blood pressure > 180 mm of Hg, diastolic blood pressure > 110 mm of Hg and proteinuria $\geq 1+$.

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