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A Prospective Study On The Prevalence Of Retinal Lesions Among The Hypertensive Patients

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ABSTRACT

To estimate the prevalence of retinal lesions among patients with hypertension. Hypertensive patients of both the genders above 18 years of age, who were willing to participate in the study, were included and patients who were having diabetes, previous retinal abnormalities and below 18 years of age were excluded from this study. The hypertensive patients were screened for the presence of retinal lesions and were categorised based on the severity of damage to the retinal arterioles and veins. In this study, about 876 patients who were diagnosed with hypertension were recruited and screened for retinal lesions. After screening, around 125 (14.3%) patients were observed with retinal lesions. In case of severity of retinal lesions in the hypertensive patients, most of the patients were found to be in Grade-I (40.8%) followed by Grade-II (37.6%). After treating with various types of treatment approaches, about 40 patients who were observed with retinal lesions of Grade-I severity were returned to a healthy state, and about 27 patients who were with retinal lesions of Grade-II severity were recovered to Grade-I. About six patients with retinal lesions of Grade-III was improved to Grade-II, and no patient recovered with the retinal lesions of Grade-IV severity. In this study, the prevalence of retinal lesions among the hypertensive patients was observed to be 14.3%, and the males were found to be more predominant with retinal lesions when compared to the females. It is the responsibility of the clinical pharmacist to create awareness among the hypertensive patients regarding the occurrence of hypertensive retinopathy as it may cause severe complications if left untreated. Hence, regular follow-ups are required for hypertensive patients, which may help to prevent retinal complications.

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INTRODUCTION

Hypertension (HTN) affects several systems such as cardiovascular, renal, cerebrovascular, and ocular when it is uncontrolled (Modi and Arsiwalla, 2020; Kabedi *et al.*, 2014). It usually affects the eyes, causing three types of ocular damage that includes choroidopathy, retinopathy and optic neuropathy (Henderson *et al.*, 2011). Among these visual damages, hypertensive retinopathy is more prominent due to the poorly controlled systemic hypertension that causes damage to the retinal

microcirculation thereby increasing the cardiovascular risk in hypertensive patients (Chatterjee *et al.*, 2002).

Hypertensive retinopathy (HR) occurs due to elevated blood pressure that damages the blood vessels in the retina. There has been significant evidence that hypertensive retinopathy acts as a predictor of systemic morbidity and mortality due to the target-organ damage (Kabedi *et al.*, 2014). Most of the studies reported that the incidence of retinopathy increases as the duration and severity of hypertension increases (Erden and Bicakci, 2012). Apart from the elevated blood pressure other factors play an important role in the development of hypertensive retinopathy which includes genetic factors, smoking, renal dysfunction, increased plasma leptin levels and end-organ damage (Grosso, 2005; Chobanian, 2001). Hypertension is a global problem that affects up to 50 million people in the United States and approximately one billion worldwide and is the single most important modifiable risk factor for stroke (Wolf-Maier *et al.*, 2003; Gorelick, 2002).

Various phases in the hypertensive retinopathy include vasoconstrictive phase (vasospasm & retinal arteriole narrowing), sclerotic phase (arteriolar narrowing, arteriovenous (AV) crossing changes, widening & accentuation of light reflex) and exudative phase (retinal haemorrhage, hard exudate formation, necrosis of smooth muscle cells & retinal ischemia) (Chaine and Kohner, 1983; Henderson *et al.*, 2011). Hypertensive retinopathy is usually asymptomatic; hence the diagnosis is based on the fundoscopic features that involve the AV crossing changes, arterial changes, retinal changes, macular changes and optic nerve changes. The changes can be retinal haemorrhages (Dot-blot haemorrhages or Flame shaped haemorrhages) and retinal exudates (Hard or Soft exudates). As the disease progresses, the blood may leak into the retina, and these changes may lead to a gradual loss of vision (Chatterjee *et al.*, 2002).

The purpose of screening for hypertensive retinopathy is that retinal vessels are the only blood vessels visible on routine examination. The effects of elevated pressure in the eye are visible as hypertensive retinopathy and choroidopathy, which reflects the vascular changes occurring in other systems. Thereby, hypertensive patients should be screened efficiently to reduce the risk of ocular and systemic morbidity and mortality (Henderson *et al.*, 2011; Fraser-Bell *et al.*, 2017).

Hence, in this study, we attempted estimating the prevalence of retinal lesions among patients with hypertension.

MATERIALS AND METHODS

This study was conducted at Akira Eye Hospitals, Rajahmundry. After getting the ethical clearance from the Institutional Ethics Committee (IEC), the data was collected by strictly adhering to the inclusion and exclusion criteria by using a previously designed patient data collection form. Hypertensive patients of both the genders and above 18 years of age, who were willing to participate in the study, were included and patients who were having diabetes, previous retinal abnormalities and below 18 years of age were excluded from this study. The hypertensive patients were screened for the presence of retinal lesions and were categorised based on the severity of damage to the retinal arterioles and veins.

The diagnosis was made using fundus examination with indirect ophthalmoscopy with the 90-D lens. An ophthalmoscope is a painless technique which examines retina at the back of the eye for the signs of narrowing of blood vessels. Patients were categorised based on the elevated blood pressures which include Pre-hypertension (Stage 1: 120/80 mmHg to 139/89 mmHg), mild hypertension (Stage 2: 140/90 mmHg to 159/99 mmHg), moderate hypertension (Stage 3: 160/100 mmHg to 179/109 mmHg), severe hypertension (Stage 4: 180/110 mmHg or higher). The severity of retinal lesions was categorised using a traditional classification provided by Keith Wagner Barker that includes Grade-I (Slight constriction of retinal arterioles), Grade-II (Grade-I + focal narrowing of retinal arterioles + AV nicking), Grade-III (Grade-II + flame-shaped haemorrhages + cotton-wool spots + hard exudates) and Grade-IV (Grade-III + optic disc swelling) (Modi and Arsiwalla, 2020).

Procedure

To conduct a good peripheral eye examination, the patient's eyes must be well dilated using 1% tropicamide and 2.5% phenylephrine. Testing was done by using a slit-lamp with a 90-D (diopter) lens or an improved digital lens that can be used to identify the affected areas. For an optimal view in the ophthalmoscope, the patient was asked to lay flat in a reclining chair. The height of the chair was adjusted so that the optometrist can observe the superior retina and inferior retina of the patient. The 90-D lens was used to evaluate macular and peripheral pathology. The lens was held up towards right-side to minimise the distortions and moved in and out to focus on the retina. The pupillary distance and height of the beam were adjusted so that a full beam on each eye can be seen. A light aperture to the larger pupils and smallest aperture to the smaller

Table 1: Gender wise categorization of hypertensive patients based on retinal lesions

Gender	With retinal lesions (%)	Without retinal lesions (%)	Total (%)	χ2-value	p-value
Male	71 (56.8)	456 (60.7)	527 (60.2)	0.686	0.407
Female	54 (43.2)	295 (39.3)	349 (39.8)		
Total	125 (100)	751 (100)	876 (100)		

Table 2: Categorizationof hypertensive patients with retinal lesions based on age, stages of hypertension and severity of retinal lesions.

Categories		Male (%)	Female (%)	Total (%)	χ2-value	p-value
Age group	31-40	9 (12.6)	7 (12.9)	16 (12.8)	1.50	0.8
	41-50	14 (19.7)	8 (14.8)	22 (17.6)		
	51-60	19 (26.7)	18 (33.3)	37 (29.6)		
	61-70	18 (25.3)	14 (25.9)	32 (25.6)		
	71-80	6 (8.4)	5 (9.2)	11 (8.8)		
	81-90	5 (7.0)	2 (3.7)	7 (5.6)		
	Total	71(100)	54(100)	125(100)		
Hypertension stage	Pre	9 (12.6)	13 (24.0)	22 (17.6)	2.4	0.48
	Primary	33(46.7)	25 (46.5)	58 (46.4)		
	Secondary	22(30.9)	15 (27.7)	37 (29.6)		
	Tertiary	7 (9.8)	1 (1.8)	8 (6.4)		
	Total	71(100)	54(100)	125 (100)		
Severity of Retinal Lesions	Grade I	30 (42.2)	21 (38.8)	51 (40.8)	0.5	1.74
	Grade II	27 (38.0)	20 (37.0)	47 (37.6)		
	Grade III	13 (18.3)	10 (18.5)	23 (18.4)		
	Grade IV	1 (1.4)	3 (5.5)	4 (3.20)		
	Total	71(100)	54(100)	125(100)		

Table 3: Categorization of the severity of retinal lesions basedon the stages of hypertension

Stages of Hypertension	Grade-I (%)	Grade-II (%)	Grade-III (%)	Grade-IV (%)	Total (%)	χ2 value	p-value
Pre	14(27.6)	8 (17.1)	0 (0)	0 (0)	22 (17.6)	31.8	<0.0001
Primary	31(60.7)	21(44.6)	5 (21.7)	1 (25)	58 (46.4)		
Secondary	6(11.7)	18(38.2)	11(47.8)	2 (50)	37 (29.6)		
Tertiary	0 (0)	0 (0)	7 (30.5)	1 (25)	8 (6.4)		
Total	51(100)	47(100)	23(100)	4(100)	125(100)		

Table 4: Categorization of the severity of retinal lesions based on the duration of hypertension

Duration of hypertension	Grade-I (%)	Grade-II (%)	Grade-III (%)	Grade-IV (%)	Total (%)	p-value
$\leq$ 10years	31 (60)	17 (36.1)	5(21.7)	0	53(42.4)	<0.0001
11-20years	17 (33.3)	24 (51.0)	6(26)	0	47(37.6)	
21-30 years	3 (5.8)	6 (12.7)	6(26)	2(50)	17(13.6)	
31-40 years	0 (0)	0 (0)	6(26)	2(50)	8(6.4)	
Total	51 (100)	47 (100)	23 (100)	4 (100)	125 (100)	

Table 5: Mean and standard deviation of the blood pressure of hypertensive patients withretinal lesions before and after the treatment

Grade of Retinal Lesions	V_0 Mean ($\pm$SD)	V_1 Mean ($\pm$SD)
Grade-I	149.1/92.0 ($\pm$11.1/6.5)	134.2/86.8 ($\pm$11.0/4.8)
Grade-II	154.8/90.6 ($\pm$17.9/11.06)	140.9/87.2 ($\pm$15.2/6.2)
Grade-III	177.3/104.9 ($\pm$26.9/17.7)	153.2/97.5 ($\pm$18.4/10.0)
Grade-IV	180/115 ($\pm$0/7.0)	180/115 ($\pm$0/7.0)

pupils were set. A white filter with good intensity was used to improve the field view. Scleral depressors were used to depress the sclera, which allows a dynamic view of the retina and finally the readings were recorded.

Statistical Analysis

Percentage, mean and standard deviations were calculated, and statistical analysis was performed by using software SPSS 21.0. Chi-square test was performed, and p-values were obtained at a 95% confidence interval for the interpretation of the results.

RESULTS AND DISCUSSION

In this study, about 876 patients who were diagnosed with hypertension were recruited and screened for retinal lesions. After screening, around 125 (14.3%) patients were observed with retinal lesions. Table 1 represents the categorisation of hypertensive patients with retinal lesions based on their gender were, males (56.8%) were more prone to retinal lesions when compared to females (43.2%).

Table 2 represents the categorisation of hypertensive patients with retinal lesions based on their age group, stages of hypertension and severity of retinal lesions. Based on the age-wise classification, the majority of the subjects were found to be in the age group of 51-60 years (29.6%) followed by the age group 61-70 years (25.6%). In the aspect of the stages of hypertension, most of the patients were found to be with primary hypertension (46.4%) followed by secondary hypertension (29.6%). In the case of severity of retinal lesions in hypertensive patients, most of the patients were found to be in Grade-I (40.8%) followed by Grade-II (37.6%).

Table 3 represents the categorisation of the severity of retinal lesions based on the stages of hypertension where, majority of the pre-hypertension (27.6%) and primary hypertension (60.7%) patients were observed to be with Grade-I severity. Most of the secondary hypertension (38.2%) and tertiary hypertension (30.5%) patients were observed to be with Grade-II and Grade-III severity respectively.

Table 4 represents the categorisation of the severity of retinal lesions based on the duration of hypertension where a majority of the hypertensive patients with a duration of $\leq$ 10 years (31 patients) were observed with a retinal lesion of Grade-I severity. Most of the patients with < 10 years of duration were observed to be with retinal lesions of Grade-II and Grade-III severity. It is crucial to assess the risk factors of retinopathy in hypertensive patients in order to reduce the incidence of hypertensive retinopathy associated with cardiovascular and cerebrovascular diseases. Thus on the categorisation of hypertensive patients with retinal lesions based on their predisposing factors, the significant risk factors for the development of retinopathy was observed in patients with prolonged hypertension (57.6%) followed by alcoholism (45.6%) and smoking (32.8%) while a delayed diagnosis of hypertension (20.1%), non-compliance (12.8%) and age above 60 years (14.4%) were observed to be the minor risk factors.

Table 5 represents the mean and standard deviation

of systolic and diastolic pressures at baseline and after the treatment in hypertensive retinopathy patients based on the grade of retinal lesions. After treating with various types of treatment approaches, about 40 patients who were observed with retinal lesions of Grade-I severity were returned to a healthy state, and about 27 patients who were with retinal lesions of Grade-II severity were recovered to Grade-I. About six patients with retinal lesions of Grade-III was improved to Grade-II and no patient was recovered with the retinal lesions of Grade-IV severity.

The main aim of the study is to estimate the prevalence of retinal lesions among patients with hypertension. A total of 876 patients who were diagnosed with hypertension were screened for retinal abnormality. Among them, 125 patients were found to be with retinal lesions, and the prevalence was found to be 14.3%. In this study, majority of the patients with retinal lesions were found to be males (56.8%) when compared to females (43.2%). Current studies suggest that oestrogen may modulate vascular endothelial function resulting in vasodilation which in females contributes to lower blood pressures (August, 1999; Mendelsohn and Karas, 1999; Reckelhoff and Granger, 1999).Based on genetic polymorphisms, studies have shown that ACE I/D (Angiotensin-converting enzyme insertion /deletion) genotype was associated with increased diastolic blood pressure in males but not in females (O'Donnell *et al.*, 1998). Thus, males are more prone to hypertension due to lack of oestrogen and other factors like elevated stress levels, alcohol intake and consumption of tobacco which may increase the risk of developing retinal lesions.

According to the age-wise categorisation, most of the patients with retinal lesions were found to be elderly. The chance of the occurrence of retinal lesions increases as the age of the patient increases and this finding was similar to the study done by Tien Wong et al. According to the various studies in different parts of the world, the prevalence of retinopathy in hypertensive patients is high in the age group of above 40 years between 5.4% to 25.6% (Dibonito *et al.*, 2003; Ong *et al.*, 2013).

According to the categorisation of retinal lesions based on the stages of hypertension, most of the patients were observed with primary hypertension, followed by secondary hypertension. Patients with severely elevated blood pressure (i.e., > 240 mm Hg) had more extensive areas of retinal exudates which indicate the high intravascular pressure in the large arterioles of the peripapillary area which is high enough to break the blood-retinal barrier. Severe hypertension leads to the exudative stage and finally to a malignant stage with macular oedema (Ahn *et al.*, 2014). According to the categorisation of patients based on the severity of the lesion, most of the patients were observed with Grade-I, followed by Grade-II. Most of the pre-hypertensive and primary hypertensive patients were observed with retinal lesions of Grade-I severity. Most of the secondary and tertiary hypertensive patients were observed with retinal lesions of Grade-II and Grade-III respectively. Majority of the patients with $\leq$10 years of the past medical history of hypertension were found to be with retinal lesions of Grade-I. Most of the patients with more than 10 years of the recent medical history of hypertension were found to be with retinal lesions of Grade-II, Grade-III and Grade-IV respectively. Elevated acute blood pressure causes reversible vasoconstriction in retinal blood vessels. And in cases of prolonged hypertension, exudative vascular changes causes endothelial damage and necrosis (Klein *et al.*, 1993). According to the study conducted by Besharaty et al., the risk of retinopathy was higher in patients suffering from hypertension for more than a decade than those with hypertension for less than a decade. This is due to the longer duration of hypertension associated with changes in the retinal blood vessels and optic nerve (Besharati *et al.*, 2006). According to Erden et al., the severity and duration of hypertension are directly proportional to the incidence of hypertensive retinopathy (Erden and Bicakci, 2012).

Hypertensive retinopathy is managed primarily by controlling hypertension. While the retinal lesions are treated with laser or with intravitreal injections of corticosteroids or antivascular endothelial growth factor drugs (e.g. Ranibizumab, pegaptanib,bevacizumab) (Klein *et al.*, 1993), most of the patients with hypertensive retinopathy do not cause vision loss as long as the hypertension is treated and if the blood pressure remains untreated, it may lead to vision loss within a short period (Do *et al.*, 2015; Wolz *et al.*, 2017). In this study, all the hypertensive patients who were observed with retinal lesions were treated with various types of antihypertensive drugs like beta-blockers, calcium channel blockers, ACE inhibitors, diuretics and angiotensin blockers. Most of the patients were prescribed with beta-blockers, followed by calcium channel blockers. The retinal lesions were usually treated using drugs, surgeries and lifestyle modifications to obtain better outcomes in reducing retinal abnormalities thus a categorisation was done based on the treatment strategies in the study participants depending on the severity of retinal lesions. Most of the patients were

under pharmacological treatment (78.4%) followed by a surgical type of approach (21.6%) in this study.

CONCLUSIONS

In this study, the prevalence of retinal lesions among the hypertensive patients was observed to be 14.3%, and the males were found to be more predominant with retinal lesions when compared to the females. The elevated blood pressure for a prolonged duration in hypertensive patients impacts the severity of retinal lesions increasing the risk of retinopathy. It is the responsibility of the clinical pharmacist to create awareness among the hypertensive patients regarding the occurrence of hypertensive retinopathy as it may cause severe complications if left untreated. Hence, regular follow-ups are required for hypertensive patients, which may help to prevent retinal complications.

Conflict of Interest

None.

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REFERENCES

Ahn, S. J., Woo, S. J., Park, K. H. 2014. Retinal and Choroidal Changes With Severe Hypertension and Their Association With Visual Outcome. *Investigative Ophthalmology & Visual Science*, 55(12):7775–7785.

August, P. 1999. Hypertension in Men. *The Journal of Clinical Endocrinology & Metabolism*, 84(10):3451–3454.

Besharati, M. R., Rastegar, A., Shoja, M. R., Maybodi, M. E. 2006. Prevalence of retinopathy in hypertensive patients. *Saudi Medical Journal*, 27(11):1725–1728.

Chaine, G., Kohner, E. M. 1983. Hypertensive retinopathy. *Journal francais d'ophtalmologie*, 6(12):995–1005.

Chatterjee, S., Chattopadhya, S., Hope-Ross, M., Lip, P. L. 2002. Hypertension and the eye: changing perspectives. *Journal of Human Hypertension*, 16(10):667–675.

Chobanian, A. V. 2001. Control of Hypertension — An Important National Priority. *New England Journal of Medicine*, 345(7):534–535.

Dibonito, P., Difraia, L., Digennaro, L., Russo, P., Scala, A., Iovine, C., Vaccaro, O., Capaldo, B. 2003. Impact of known and unknown diabetes on in-hospital mortality from ischemic stroke. *Nutrition, Metabolism and Cardiovascular Diseases*, 13:148–153.

Do, D. V., Wang, X., Vedula, S. S., Marrone, M., Sleilati, G., Hawkins, B. S., Frank, R. N. 2015. Blood pressure control for diabetic retinopathy. *The Cochrane Database of Systematic Reviews*, 1.

Erden, S., Bicakci, E. 2012. Hypertensive Retinopathy: Incidence, Risk Factors, and Comorbidities. *Clinical and Experimental Hypertension*, 34(6):397–401.

Fraser-Bell, S., Symes, R., Vaze, A. 2017. Hypertensive eye disease: a review. *Clinical & Experimental Ophthalmology*, 45(1):45–53.

Gorelick, P. B. 2002. New horizons for stroke prevention: PROGRESS and HOPE. *The Lancet Neurology*, 1(3):149–156.

Grosso, A. 2005. Hypertensive retinopathy revisited: some answers, more questions. *British Journal of Ophthalmology*, 89(12):1646–1654.

Henderson, A. D., Bruce, B. B., Newman, N. J., Biousse, V. 2011. Hypertension-related eye abnormalities and the risk of stroke. *Reviews in Neurological Diseases*, 8(1-2):1–9.

Kabedi, N. N., Mwanza, J.-C., Lepira, F. B., Kayembe, T. K., Kayembe, D. L. 2014. Hypertensive retinopathy and its association with cardiovascular, renal and cerebrovascular morbidity in Congolese patients : cardiovascular topic. *Cardiovascular Journal Of Africa*, 25(5):228–232.

Klein, R., Klein, B. E., Moss, S. E., Wang, Q. 1993. Blood pressure, hypertension and retinopathy in a population. *Transactions of the American Ophthalmological Society*, 91:207–226.

Mendelsohn, M. E., Karas, R. H. 1999. The Protective Effects of Estrogen on the Cardiovascular System. *New England Journal of Medicine*, 340(23):1801–1811.

Modi, P., Arsiwalla, T. 2020. Hypertensive Retinopathy. *StatPearls, Treasure Island*.

O'Donnell, C. J., Lindpaintner, K., Larson, M. G., Rao, V. S., Ordovas, J. M., Schaefer, E. J., Myers, R. H., Levy, D. 1998. Evidence for Association and Genetic Linkage of the Angiotensin-Converting Enzyme Locus With Hypertension and Blood Pressure in Men but Not Women in the Framingham Heart Study. *Circulation*, 97(18):1766–1772.

Ong, Y.-T., Wong, T. Y., Klein, R., Klein, B. E., Mitchell, P., Sharrett, A. R., Couper, D. J., Ikram, M. K. 2013. Hypertensive Retinopathy and Risk of Stroke. *Hypertension*, 62(4):706–711.

Reckelhoff, J. F., Granger, J. P. 1999. Role Of Androgens In Mediating Hypertension And Renal Injury. *Clinical and Experimental Pharmacology and Phys-*

iology, 26(2):127–131.

Wolf-Maier, K., Cooper, R. S., Banegas, J. R. 2003. Hypertension prevalence and blood pressure levels in 6 European countries, Canada, and the United States. *ACC Current Journal Review*, 12(4):32–32.

Wolz, J., Audebert, H., Laumeier, I., Ahmadi, M., Steinicke, M., Ferse, C., Michelson, G. 2017. Telemedical assessment of optic nerve head and retina in patients after recent minor stroke or TIA. *International Ophthalmology*, 37(1):39–46.