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Original Research Article

Evaluation of Hypertensive Retinopathy in Patients of Essential Hypertension with High Serum Lipids: A Clinical Study

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Abstract

Background: In this study, we wanted to evaluate the different phases of hypertensive retinopathy fundus findings and correlate the findings with lipid profile (LDL, HDL, VLDL, triglycerides and total cholesterol) in essential hypertensive patients.

Materials and Methods: This was a hospital based prospective observational study conducted among 80 patients who presented with essential hypertension after thorough evaluation by the physician to the Department of Rangaraya Medical College Kakinada, from December 2019 to August 2021 after obtaining clearance from Institutional Ethics Committee and written informed consent from the study participants.

Results: In hypertensive retinopathy and duration of hypertension, duration in years the p value < 0.0001, was statistically significant. In relationship between dyslipidaemia and duration of hypertension, the p = 0.0001*, was statistically significant. In relationship between LDL with grades of retinopathy the p = 0.0001*, was statistically significant. Total cholesterol showed significant relation with grades of retinopathy. Triglycerides showed statistically significant relationship with grades of retinopathy. HDL showed statistically significant relationship with grades of retinopathy. In relationship between dyslipidaemia and grades of retinopathy, p = 0.0001*, statistically significant.

Conclusion: The blood pressure in malignant hypertension should be lowered gradually to allow sufficient time for the auto regulation of the blood flow to adapt itself. Therapy must be initiated as soon as possible to prevent the development of hypertensive retinopathy. Hence, physicians and the ophthalmologists must pursue a joint and coordinated approach to prevent visual loss and risk factors from hypertension.

Keywords: Hypertensive, Retinopathy, Patients, High Serum Lipids.

Introduction

Systemic hypertension is the most common disease of adults. Essential hypertension or primary hypertension is of unknown aetiology and diagnosed

when average blood pressure measures > 140 mmHg systolic or > 90 mmHg diastolic. In patients with borderline hypertension, relative danger of cardiovascular illness and final stage renal disease is nearly double than that of patients with optimal blood pressure. Primary hypertension is also called as essential hypertension. As blood pressure crosses the critical limit, there will be failure in auto regulation of retinal circulation. One of the important risk factors in patients of hypertension is dyslipidaemia or hyperlipidaemia. Hypertension along with hyperlipidaemia accelerates atherosclerosis, cause degeneration changes of walls of large and medium sized arteries, which triggers cerebrovascular haemorrhage, ischemic heart disease, stroke, cardiac arrest. Hypertension can result from many causes, but majority are due to essential hypertension. The only organ in the body where vascular changes is visualised directly is eye. Early evaluation of change in lipid parameters not only prevents fundus changes but also prevents other clinical complications like stroke, cardiac failure etc...

Aims and Objectives

To evaluate different phases of hypertensive retinopathy fundus findings and to correlate findings with lipid profile (LDL, HDL, VLDL, triglycerides and total cholesterol) in essential hypertensive patients.

Materials and Methods

This was a hospital based prospective observational study conducted among 80 patients who presented with essential hypertension after thorough evaluation by the physician to the Department of Rangaraya Medical College Kakinada, from December 2019 to August 2021 after obtaining clearance from Institutional Ethics Committee and written informed consent from the study participants.

Inclusion Criteria

Patients diagnosed with essential hypertension after detailed evaluation by physician and were having high serum lipids.

Exclusion Criteria

Patients suffering from:

- Diabetes
- High myopia
- People with hazy ocular media.
- Other retinal vascular diseases.
- Secondary hypertension.

Statistical Methods

Data was entered in MS Excel and analysed using Statistical Package for Social Sciences (SPSS) software. Results were presented as tables.

Results

Table 1

	< 5	**5 – 10**	**11 – 15**	**16 – 20**	**Total**
Normal	32	3	0	0	35
Grade 1	11	5	0	0	16
Grade 2	8	5	2	1	16
Grade 3	4	3	2	2	11
Grade 4	0	0	0	2	2
Total	55	16	4	5	80
	Chi Square Test = 53.5, p =< 0.0001, Statistically Significant				
Hypertensive Retinopathy and Duration of Hypertension (Duration in Years)					
	Grade 1	**Grade 2**	**Grade 3**	**Grade 4**	**Normal**
29 – 40	2	0	0	0	9

41 – 50	2	2	1	0	7
51 – 60	9	7	6	2	16
61 – 70	3	6	1	0	3
71 – 80	0	1	2	0	0
81 – 90	0	0	1	0	0
Chi Square Test = 31.43, p = 0.04*, Statistically Significant					
Retinopathy and Age Distribution					

In hypertensive retinopathy and duration of hypertension (duration in years p = < 0.0001, was statistically significant.
In retinopathy and age distribution, p = 0.04*, was statistically significant.

Table 2

	Dyslipidaemia				**Total**	
	Yes		**No**			
	N	**%**	**N**	**%**	**N**	**%**
Male	32	71.1 %	22	62.9 %	54	67.5 %
Female	13	28.9 %	13	37.1 %	26	32.5 %
Total	45	100.0 %	35	100 %	80	100 %
Chi Square Test = 0.60, p = 0.43, Not Statistically Significant						
Relationship between Gender Distribution And Dyslipidaemia						
	Dyslipidaemia				**Total**	
	Yes		**No**			
	N	**%**	**N**	**%**	**N**	**%**
< 5	23	51.1 %	32	91.4 %	55	68.7 %
6 – 10	13	28.9 %	3	8.6 %	16	20 %
11 – 15	4	8.9 %	0	0.0 %	4	5 %
16 – 20	5	11.1 %	0	0.0 %	5	6.2 %
Total	45	100.0 %	35	100.0 %	80	100 %
Mean ± SD	6.8 ± 4.79		3.65 ± 1.34		5.42 ± 4.0	
Chi Square Test = 15.71, p = 0.0001*, Statistically Significant						
Relationship between Dyslipidaemia And Duration Of Hypertension						

Males accounted for 54 (67.5 %) and females accounted for 26 (32.5 %).
In relationship between dyslipidaemia and duration of hypertension, p = 0.0001*, was statistically significant.

Table 3

	Dyslipidaemia				**Total**	
	Yes		**No**			
	N	**%**	**N**	**%**	**N**	**%**
29 – 40	2	4.4 %	9	25.7 %	11	13.8 %
41 – 50	5	11.1 %	7	20.0 %	12	15 %
51 – 60	24	53.3 %	16	45.7 %	40	50 %
61 – 70	10	22.2 %	3	8.6 %	13	16.3 %
71 – 80	3	6.7 %	0	0.0 %	3	3.7 %
81 – 90	1	2.2 %	0	0.0 %	1	1.3 %

Total	45	100 %	35	100 %	80	100 %
Mean ± SD	59.52 ± 9.18		47.74 ± 9.69		54.31 ± 11.01	
Chi Square Test = 13.11, p = 0.02*, Statistically Significant						
Relationship between Dyslipidaemia And Age Distribution						
	Dyslipidaemia				Total	
	Yes		No			
	N	%	N	%	N	%
Grade 1	16	35.6 %	0	0.0 %	16	20 %
Grade 2	16	35.6 %	0	0.0 %	16	20 %
Grade 3	11	24.4 %	0	0.0 %	11	13.8 %
Grade 4	2	4.4 %	0	0.0 %	2	2.5 %
Normal	0	0.0 %	35	100.0 %	35	43.7 %
Total	45	100.0 %	35	100.0 %	80	100 %
Chi Square Test = 80, p = 0.0001*, Statistically Significant						
Relationship between Dyslipidaemia And Grades Of Retinopathy						

Maximum no of patients belonged to 51 to 60 years of age group (50 %) followed by 61 to 70 years (16.3 %) and 41 to 50 years (15 %) and 29 to 40 years (13.8 %) then 71 to 80 years (3.7 %) and then by 81 to 90 years (1.3 %) age group.

Table 4

Retinopathy Grades	**LDL (Mean ± SD)**
Grade 1	122.87 ± 8.21
Grade 2	147.56 ± 29.98
Grade 3	154.54 ± 32.67
Grade 4	164 ± 0
Normal	127.22 ± 18.82
F Value = 6.48, p = 0.0001*, Statistically Significant	
Relationship between LDL with Grades Of Retinopathy	
Retinopathy Grades	**Total Cholesterol (Mean ± SD)**
Grade1	192.12 ± 20.23
Grade 2	206.37 ± 28.83
Grade 3	211.81 ± 32.86
Grade 4	210± 0
Normal	185.94 ± 22.99
F Value = 3.41, p = 0.01*, Statistically Significant	
Relationship between Total Cholesterol with Retinopathy	
Retinopathy Grades	**Triglycerides (Mean ± SD)**
1st Grade	135.75 ± 23.57
Grade 2	158.62 ± 25.55
Grade 3	158.09 ± 19.98
Grade 4	139 ± 0
Normal	140.34 ± 22.04
F Value = 3.41, p = 0.01*, Statistically Significant	

Relationship between Triglycerides with Retinopathy	
Retinopathy grades	**HDL (Mean ± SD)**
1st Grade	40.43 ± 10.05
Grade 2	40.12 ± 9.27
Grade 3	45.81 ± 11.16
Grade 4	42 ± 0
Normal	35.97 ± 7.52
F Value = 2.82, p = 0.02*, Statistically Significant	
Relationship between HDL with Retinopathy	

LDL is showing significant relationship with grades of retinopathy in our study.
Total cholesterol is showing significant relation with grades of retinopathy.

Triglycerides is showing statistically significant relationship with grades of retinopathy.

HDL is showing statistically significant relationship with grades of retinopathy.

Discussion

Blood pressure

Prolonged uncontrolled systemic hypertension may result in visual impairment or blindness. It was well understood that hypertension aggravates atherosclerosis and vice versa. Similarly, prolonged uncontrolled systemic hypertension results in retinal arteriolosclerosis. Systemic hypertension is related to both the processes of atherosclerosis and arteriolosclerosis.

A high blood cholesterol concentration in the form of low-density lipoproteins is primary causal factor in atherosclerosis affecting the arteries of larger calibre and the central retinal artery before its bifurcation, whereas the arteriolosclerosis develops in the retinal arterioles. It therefore, leads to hypothesize that the co-existence of atherosclerosis with systemic hypertension affects the development of arteriolosclerosis and consequent fundus changes of the eye.

Routine ophthalmoscope examination to detect signs of retinopathy in people with hypertension is recommended by National Committee on the prevention, diagnosis, evaluation, and hypertension treatment in United States & British Society [1,2] of Hypertension for risk stratification and treatment decisions.

In this study, the mean SBP found in normal cases was 149.42 ± 10.55mm Hg, the mean SBP found in grade 1 retinopathy was 159.37 ± 17.68, in grade 2 retinopathy the mean SBP was 166.25 ± 16.27 mm Hg, in grade 3 retinopathy, the mean SBP was 180 ± 16.12 mm Hg, in grade 4 retinopathy, the mean SBP was 190 ± 0 mm Hg. The difference in mean SBP was statistically significant across the groups.

In the present study, the mean DBP observed in normal cases was 92.85 ± 4.58mmHg, In grade 1 retinopathy, the mean DBP was 96.87 ± 6.02mmHg, In grade 2 retinopathy, the mean DBP was 93.87 ± 24.71 mmHg, In grade 3 retinopathy, the mean DBP was 97.27 ± 12.72 and in grade 4 retinopathy, the mean DBP was 110 ± 0 mmHG and no statistically significant difference was observed across the groups.

In HegdePP et al., [3] study they observed a significant difference across the severity of HTN and the occurrence of retinopathy, a finding which was in consonance with the present study. Here they have also concluded saying that the current level, but not previous blood pressure levels is associated with other symptoms of focal arteriolar narrowing, retinal haemorrhage, micro aneurysms,

and cotton-wool spots may also indicate more seriousness of HT in recent time.

Lipid parameters

HDL

In my study, the mean HDL value observed in normal cases was 35.97 ± 7.52, In grade 1 retinopathy, the mean HDL was 40.43 ± 10.05, In grade 2 retinopathy, the mean HDL was 40.12 ± 9.27, In grade 3 retinopathy, the mean HDL was 45.81 ± 11.16 and in grade 4 retinopathy, the mean HDL was 42 ± 0 and a statistically significant difference was observed across the groups.

In the study done by HegdePP et al., [3] the retinopathy group had mean HDL-cholesterol values of 41.18 and 47.76 for no retinopathy group. The serum HDL-cholesterol and retinopathy were not significantly linked.

Bastola et al. [4] also showed similar findings which are in consonance with the present study.

In a study done by Akshar V Soni serum HDL-cholesterol values for retinopathy group were 42.70 and that for no retinopathy group was 43.6. [5]

Except the study by Karaca et al. [6] no further research has shown that serum HDL cholesterol is correlated with HR until recently LDL:

In this study, the mean LDL value observed in normal cases was 127.22 ± 18.82, In grade 1 retinopathy, the mean LDL was 122.87 ± 8.21, In grade 2 retinopathy, the mean LDL was 147.56 ± 29.98, In grade 3 retinopathy, the mean LDL was 154.54 ± 32.67 and in grade 4 retinopathy, the mean LDL was 164 ± 0 and a statistically significant difference was observed across the groups.

In the study done by HegdePP et al. [3] no statistically significant link between the serum levels of low-density lipoprotein cholesterol and retinopathy grades was found ($p < 0.671$). This finding in our research contrasts with the findings of other researchers, where serum LDL cholesterol and retinopathy are significantly correlated.

Badhu et al. [7] and Bastola et al. [4] also showed a significant correlation between high serum LDL-cholesterol and HR. In a study done in a medical college in Kota, they found a significant association between high serum LDL-cholesterol and the severity of the retinopathy, ($p < 0.0001$).

Total cholesterol

In this study, the mean total cholesterol value observed in normal cases was 192.12 ± 20.23, In grade 1 retinopathy, the mean TC was 192.12 ± 20.23, In grade 2 retinopathy, the mean TC was 206.37 ± 28.83, In grade 3 retinopathy, the mean TC was 211.81 ± 32.86 and in grade 4 retinopathy, the mean TC was 210 ± 0 and a statistically significant difference was observed across the groups.

In study done by HegdePP et al. [3] increase in serum TC levels correlated well with increasing grades of retinopathy which was statistically significant ($p < 0.013$).

In a study done by Akshar V Soni, [5] increased incidence of HR was observed in patients having high serum total cholesterol level and this association was statistically significant ($p < 0.0001$).

In Gupta et al. [8] study, the disparity between average serum cholesterol level ($p < 0.001$) of persons with no fundus changes and others with varying degrees of HR has also been shown to be statistically significant.

In another study by Hanff et al. [9] also revealed there was an increased incidence of HR inpatients having raised cholesterol level and this association was statistically significant ($p < 0.0008$).

In the study done by Cuspidiet al. [10] described the prevalence of advanced retinal microvascular lesions and their associations with cardiac and extra cardiac signs of target organ damage (TOD) in a large selected hypertensive population.

Triglycerides

In our study, the mean triglycerides value observed in normal cases was 140.34 ± 22.04, In grade 1 retinopathy, the mean triglycerides were 135.75 ± 23.57, In grade 2 retinopathy, the mean triglycerides were 158.62 ± 25.55, In grade 3 retinopathy, the mean triglycerides was 158.09 ± 19.98 and in grade 4 retinopathy, the mean triglycerides was 139 ± 0. A statistically significant difference was observed across the groups.

HegdePP et al. [3] study showed positive correlation of serum triglycerides levels with increasing severity of retinopathy, and it was statistically significant ($p < 0.039$).

Similar observations were made in studies done by Gupta et al.,[8] and by Holmes et al. [11] reported similar association between serum triglycerides levels and HR changes which was statistically significant ($p < 0.01$).

Mean triglycerides levels were also found to be high in grade II and higher HR patients in a study carried out by Tada et al. [12] Another study proved that serum triglycerides were associated with first cardiovascular events among high-risk diabetes patients with hypercholesterolemia and retinopathy. [13]

Dyslipidaemia

In our study dyslipidaemia is seen in 56.2 % of the subjects and 43.7 % of the subjects had a normal lipid profile. The mean duration of dyslipidaemia was 6.8 ± 4.79 years. There was a statistically alterations in mean duration of dyslipidaemia across the groups.

In this study it was observed that, there was major link between cases with dyslipidaemia and retinopathy severity and the similar conclusion was drawn in the study done by HegdePP et al. [3] as well. They have concluded saying that the hypertensive retinopathy signs were closely related, though not reliably, to an increase in blood pressure, serum lipids and other atherosclerosis risk factors. However, this analysis found that the serum lipids in hypertensive patients with fundus changes were significantly increased. Serum cholesterol and serum lipids were elevated while free fatty acids were normal, relative to normal people with HT without retinopathy.

According to the study by Adhikari et al. [14] hypertension duration has been demonstrated to be closely linked to development of hypertensive retinopathy. Obesity and raise in all lipid profile indicators were found to be substantially linked to retinopathy in hypertension patients and the overall association of serum triglycerides with retinopathy was found significant ($p < 0.0001$). Further to this observation, a longer period of diabetes, poorer glycaemic and lipid control, and higher BP level were the main predictors of development of HR.

In Popescu T et al. [15] study they have observed that dyslipidaemia correlates well with the presence and severity of retinopathy, especially HDL-C and LDL-C. Although triglycerides were higher in patients with retinopathy, there was no statistical significance. However, the association between dyslipidaemia and HR requires further studies to determine its role in pathogenesis and the influence of treatment of dyslipidaemia on HR. Dyslipidaemia has an important part in pathogenesis of HR.

In view of the high prevalence of HR in our setting, we can confidently conclude that regular ophthalmological check-up of hypertensive patients are a must. A routine lipid profile can reduce ocular morbidity in

all hypertensive patients. One study assessed the association between hypertensive retinopathy and variable lipid profile in patients with essential hypertension. [16]

FBS

In the present study, the mean FBS value observed in normal cases was 85.60 ± 10.25, In grade 1 retinopathy, the mean FBS was 94.06 ± 7.10, In grade 2 retinopathy, the mean FBS was 84.25 ± 10.55, In grade 3 retinopathy, the mean FBS was 95.09 ± 9.30 and in grade 4 retinopathy, the mean FBS was 98 ± 0 and a statistically significant difference was observed across the groups.

In Gupta R et al. [8] study, they have observed that there wasn't any significant association between the levels of FBS and HR and this finding is discordant with the finding made in the present study.

Ocular findings

Direct ophthalmoscope is a low cost, readily available, non-invasive and portable equipment that allows changes in the retinal vasculature and optic nerve to be seen in real time. That is why, in certain cases, an ophthalmologist is the first doctor to diagnose hypertensive patients who are asymptomatic.

Blood supply to retina, choroid and the optic nerve are different. Recent research has indicated that fundus alterations in systemic hypertension can be classified into following categories:

(1) Retinopathy caused by hypertension (2) Choroidopathy due to hypertension and

(3) Hypertensive optic neuropathy.

Individuals with acute hypertension (Malignant hypertension) particularly young patients with eclampsia, pre-eclampsia, renal disorders and accelerated essential hypertension can develop choroidopathy due to hypertension.

Hypertensive optic neuropathy pathological processes are not completely known. The accumulation of axoplasma in the region of the lamina retinalis and choroidalis could be the cause.

Coming to the ocular findings, adnexa was normal in OD and OS in 100 % of the patient. Arcus was seen in the cornea in OD and OS in 5 % of the patients. Pterygium was seen in OD 1.3 % of the subjects; anterior chamber was normal in all the patients. In the lens CAT was seen in 2.5 % on the OD and in 3.7 % in OS, RRR was seen 100 % of the subjects in OD and OS.

Retinopathy

There are two types of lesions in retinopathy due to hypertension lesions: vascular and extra vascular. Arteriolar changes in the retina, "focal intra retinal peri arteriolar transudates" (FIPTS), cotton wool spots, capillary changes in retina, venous changes in retina, and increased retinal vascular bed permeability are all examples of retinal vascular lesions. Haemorrhages in the retina, retinal and macular oedema, retinal lipid deposits (hard exudates), and retinal nerve fibre loss are all extra vascular retinal lesions.

For the purposes of heart risk stratification and hypertension treatment decisions, hypertensive patients should have a routine ophthalmoscopic examination. Hypertensive retinopathy predicts CHD in high-risk men regardless of blood pressure or other CHD risk factors. Microvascular changes in the retina are blood pressure indicators damage.

Microvascular changes have recently been shown to predict stroke even when blood pressure and other cardiac risk factors are not measured. These factors emphasise the importance of an ophthalmologist's ophthalmoscope examination of hypertensive patients. The pupils were fully dilated, and routine direct ophthalmoscope was performed on

all cases of hypertension that came to the eye OPD, KMCTH.

Hypertensive fundus changes are classified and graded in a variety of ways. The KWB classification is used in this study because it is the most widely accepted and simple to follow. However, ophthalmologically, distinguishing between Grade I and Grade II retinal changes is frequently difficult. Furthermore, the clinical significance of these changes is nearly identical. Another issue with grading fundus changes is that some of the changes in retina present in hypertension do not fit into any of the classifications. As a result, these retinal changes were given their own heading.

Grade 1 retinopathy was seen in 20 % of the cases, grade 2 retinopathy was seen in 20 % of the cases, grade 3 retinopathy was seen in 13.85 of the cases, grade 4 retinopathy was seen in 2.5 % of the cases and the retinopathy finding was normal in 43.7 % of the subjects.

In this study, it was observed that there was no dyslipidaemia in all the normal cases, and in all the cases with retinopathy irrespective of the grades, retinopathy was seen, and the difference observed was statistically significant.

In the study done by Kulakari v et al. [17] and Hedge PP et al. it was observed that majority of cases of retinopathy are of grade 1 and 2 and the findings are similar and in consonance with the present study.

Conclusion

Hypertension is a multifactorial condition. It's defined as a persistently high blood pressure reading of 140/90 mmHg on 2 or greater blood pressure readings. The arteries, veins, choroids, and optic nerve are all affected. Changes in the fundus could be a reflection of changes in other body organs such as the heart, brain, and kidneys. The direct ophthalmoscope is the best tool for detecting fundus changes. In our data, we discovered that hypertension retinopathy is correlated with duration and severity of hypertension. As sustained in many studies that blood pressure control can reduce the incidence of retinopathy because of hypertension, and it must be obtained as early as possible. Dyslipidaemia was significantly correlated with occurrence of hypertensive retinopathy, but this significance decreases with the severity of retinopathy. This is a strong indication towards a good lipid control. The blood pressure in malignant hypertension should be lowered gradually to allow sufficient time for the auto regulation of the blood flow to adapt itself. If the BP is lowered suddenly, irreversible blindness may occur. So, therapy must be initiated as soon as possible to prevent the development of hypertensive retinopathy. Hence, physicians and the ophthalmologists must pursue a joint and coordinated approach to prevent visual loss and risk factors from hypertension.

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