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Original Research Article

TO INVESTIGATE THE CORRELATION BETWEEN FUNDUS CHANGES AND SERUM LIPID PROFILE IN INDIVIDUALS DIAGNOSED WITH ESSENTIAL HYPERTENSION

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Abstract

Background: Aim: To investigate the correlation between fundus changes and serum lipid profile in individuals diagnosed with essential hypertension. **Materials and Methods:** The present investigation was conducted as a prospective study within the Ophthalmology department. A pre-established template was employed for the purpose of inputting data. A total of 120 consecutive individuals who received a diagnosis of primary essential hypertension were included as participants in this study. A comprehensive ophthalmological examination was performed on all subjects, totaling 240 eyes. The classification of fundus changes was conducted based on the systems developed by Keith, Wagener, and Barker (KWB), as well as the Modified Scheie's grading system. **Results:** Total of 120 patients, 29 individuals exhibited normal fundus, while 26 patients displayed grade 1 hypertensive retinopathy (HR). Furthermore, 52 patients were found to have grade 2 HR, whereas 13 patients exhibited both grade 3 and grade 4 HR. There was a strong positive correlation observed between the elevation in total serum cholesterol levels and the progression of retinopathy, with a statistically significant p-value of less than 0.015. There was a positive correlation observed between serum triglyceride levels and the progression of retinopathy, with statistical significance ($p<0.04$). The study found no statistically significant correlation between the serum levels of HDL-cholesterol and the grades of retinopathy ($p<0.23$). There was no statistically significant association between the serum levels of LDL Cholesterol and the grades of retinopathy ($p<0.36$). **Conclusion:** Our study revealed a positive correlation between the incidence of hypertensive retinopathy and elevated levels of serum total cholesterol and serum triglycerides. Nevertheless, a lack of association was observed between LDL-cholesterol and HDL-cholesterol levels and the occurrence of hypertensive retinopathy.

INTRODUCTION

Hypertension, commonly referred to as HT, is a prevalent medical condition that impacts a significant portion of the population, with an estimated 50 million individuals affected in the United States alone and approximately one billion individuals worldwide. This condition is often characterised as a silent killer. Hence, in order to effectively identify and diagnose end organ damage associated with hypertension prior to the onset of symptoms, it is crucial to emphasise the significance of optimising risk stratification strategies. The retina serves as a valuable tool for investigating human circulation. The visualisation of retinal arteries can be achieved rapidly and without invasive procedures, and these arteries exhibit similar anatomical and physiological characteristics as the microcirculation in the brain and heart.[1] Hypertension (HT) has an impact on various organ systems, including the kidney, retina, heart, and brain. In the context of hypertensive individuals, it is noteworthy that inflammatory pathways play a substantial role in the vascular beds.[2] Hypertensive retinopathy (HR) is considered to be a critical vascular complication associated with hypertension. The management of retinal circulation in the automotive industry is ineffective when blood pressure exceeds critical thresholds. The sole

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consideration of elevated blood pressure does not fully encompass the extent of retinopathy. In addition to the impact of high blood pressure, there are other potential factors that may contribute to the development of HR.[3] Multiple studies have demonstrated a significant and positive correlation between serum and plasma total cholesterol concentrations and the development of coronary artery atherosclerosis. This association has been observed across a wide range of total cholesterol levels and low-density lipoprotein (LDL) cholesterol.[4] The presence of hyperlipidemia is widely acknowledged as a substantial risk factor among individuals diagnosed with hypertension.[5] Dyslipidemia is recognised as a risk factor for retinopathy and other ocular abnormalities. Hypertensive treatment initiation (HTi) poses challenges when it is linked with comorbidities such as diabetes. The established relationship between its function and the occurrence of diabetes retinopathy and maculopathy associated with age has been extensively documented.[6,7] Dyslipidemia has the potential to act as a predisposing, aggravating, or complicating factor in individuals with hypertension. Having knowledge about different ocular manifestations, the range of observations, and their correlation with lipid profile components (such as LDL, HDL, VLDL, Total Cholesterol, and Triglycerides) can be advantageous in determining the level of risk and customising treatment for hypertension and lipid reduction. Given these circumstances, the primary objective of the present study was to assess the impact of dyslipidemia on ocular fundus alterations in individuals with hypertension. Additionally, the study aimed to establish a relationship between the observed fundus changes and the various components of the lipid profile, namely low-density lipoprotein (LDL), high-density lipoprotein (HDL), very low-density lipoprotein (VLDL), total cholesterol, and triglycerides.

MATERIALS AND METHODS

The present investigation was conducted as a prospective study within the Ophthalmology department. A pre-established template was employed for the purpose of inputting data. A total of 120 consecutive individuals who received a diagnosis of primary essential hypertension were included as participants in this study. A comprehensive ophthalmological examination was performed on all subjects, totaling 240 eyes. The classification of fundus changes was conducted based on the systems developed by Keith, Wagener, and Barker (KWB), as well as the Modified Scheie's grading system. The investigations conducted in this study encompassed a range of diagnostic tests, including a complete blood count to measure haemoglobin levels, total leukocyte count, differential leukocyte count, and erythrocyte sedimentation rate. Additionally, urine samples were subjected to routine analysis and microscopic examination. Random blood sugar levels and fasting serum lipid profiles were also assessed. Additional diagnostic tests, such as blood urea and serum creatinine measurements, chest X-ray, electrocardiogram (ECG), echocardiogram (ECHO), and computed tomography (CT) scan, were performed in accordance with the clinical diagnosis and suspicion of dysfunction in vital organs. Visual fields, specifically Humphreys Field analysis, will be conducted if deemed necessary. The study excluded individuals who were normotensive, had diabetes or other systemic diseases, had high myopia, had hazy ocular media in both eyes, or had other retinal vascular disorders. The comprehensive hypertensive status of all study participants was recorded, including information such as age of onset, duration of the disease, presence of associated conditions (such as diabetes, renal, cardiovascular, and cerebrovascular disease), medications taken (including antihypertensive drugs and lipid lowering drugs), family history, and other risk factors like smoking, alcohol consumption, and tobacco use. Additionally, a thorough ophthalmic examination was conducted on each patient, which involved assessing parameters such as best corrected visual acuity, refraction, slit lamp examination of the anterior segment, dilation of pupils using tropicamide eye drops after anterior segment examination, and evaluation of the dilated fundus using direct ophthalmoscope, indirect ophthalmoscope, and slit lamp biomicroscopy with the use of 90D or 78D lens. The results of the dilated fundus examination were documented on an Amsler chart, and the staging of hypertensive retinopathy (HR) was determined using the Modified Keith Wagener-Barker Classification [7]. Following a thorough evaluation, the patient was provided with counselling and recommended an appropriate course of treatment.

Statistical Analysis

The statistical data analysis was conducted utilising SPSS Software version 25.0. The normality distribution was assessed using D'Agostino's test. The data, both categorical and numerical, was represented using frequencies (n) and proportions (%), as well as mean and standard deviation (SD). The categorical data included demographic variables such as age, gender, grading of retinopathy, duration of hypertension, and lipid profile distributions. The analysis of categorical data was conducted using either the Fisher exact test or the chi-square test (χ^2), depending on appropriateness. An analysis of variance (ANOVA) test was conducted to compare retinopathy across different grades, taking into consideration various quantitative variables. The Spearman rank correlation test was utilised to assess the association between the grade of fundus retinopathy and lipid profile parameters. A significance level of $p<0.05$ was used to determine statistical significance.

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RESULTS

Table 1 presents the age distribution among the 120 subjects. A total of 18.33% of the participants fell within the age range of 20-40 years, while 60.83% of the participants were aged between 40-60 years. The remaining 20.83% of the participants were above the age of 60. The study observed a gender distribution across all subjects, with a male to female ratio of 1.40:1.

Table 1: Age and gender distribution

Gender	Number	Percentage
Male	70	58.33
Female	50	41.67
Age groups		
20 – 40	22	18.33
40 – 60	73	60.83
Above 60	25	20.83
Mean Age	51.89 ±6.88	

Table 2: Fundus retinopathy grade

Retinopathy grade	Number	Percentage
Normal	29	24.17
Grade 1	26	21.67
Grade 2	52	43.33
Grade 3 and more	13	10.83

According to the data presented in Table 2, it can be observed that among the total of 120 patients, 29 individuals exhibited normal fundus, while 26 patients displayed grade 1 hypertensive retinopathy (HR). Furthermore, 52 patients were found to have grade 2 HR, whereas 13 patients exhibited both grade 3 and grade 4 HR.

Table 3: Retinopathy with Serum Total Cholesterol and Triglycerides

Cholesterol (mg/dl)	Fundus Retinopathy Grade				Total	Percentage
	Normal	Grade 1	Grade 2	Grade 3 and more		
<200 mg/dl (within normal limits)	25	15	27	8	75	62.5
>200mg/dl (above normal limits)	4	11	25	5	45	37.5
Triglycerides (mg/dl)						
<150 mg/dl(within normal limits)	24	21	32	8	85	70.83
>150mg/dl(above normal limits)	5	5	20	5	35	29.17

According to the data presented in Table 3, a total of 120 patients were included in the study. Among these patients, 75 individuals (62.5%) exhibited Total cholesterol levels that fell within the established normal range. Within this subgroup, 50 patients (66.67%) were found to have retinopathy, while the remaining 25 patients (33.33%) did not display any signs of retinopathy. Out of the total sample size of 45 patients, 37.5% exhibited Total cholesterol levels exceeding 200mg/dl. Among these patients, 91.11% were found to have retinopathy, while the remaining 9.89% did not exhibit any signs of retinopathy. In general, there was a strong positive correlation observed between the elevation in total serum cholesterol levels and the progression of retinopathy, with a statistically significant p-value of less than 0.015. Among a total of 120 patients, 85 individuals exhibited triglyceride levels that fell within the established normal range. Of these patients, 61 individuals, accounting for approximately 71.76% of the group, presented with retinopathy, while the remaining 24 patients, constituting approximately 28.24% of the cohort, did not display any signs of retinopathy. Out of the total sample size of 35 patients, it was observed that 30 patients (85.71%) exhibited retinopathy, while the remaining 5 patients (14.29%) did not display any signs of retinopathy. These findings were associated with triglyceride levels exceeding 150mg/dl. In general, there was a positive correlation observed between serum triglyceride levels and the progression of retinopathy, with statistical significance ($p<0.04$).

Table 4: Retinopathy with serum HDL and LDL Cholesterol

Serum HDL cholesterol(mg/dl)	Fundus retinopathy grade				Total	Percentage
	Normal	Grade 1	Grade 2	Grade 3 and more		
<40	8	11	31	4	54	45
40-60	18	12	17	9	56	46.67

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>60	3	3	4	0	10	8.33
Serum LDL Cholesterol (mg/dl)						
<50	1	0	6	1	8	6.67
50-100	7	8	9	4	28	23.33
>50	21	18	37	8	84	70

According to the data presented in Table 4, Among the cohort of 120 patients, a total of 54 individuals (45%) exhibited HDL Cholesterol levels below 40 mg/dl. Within this subgroup, 46 patients (85.19%) presented with retinopathy, while 8 patients (14.18%) did not exhibit any signs of retinopathy. Out of the total sample size of 56 patients, it was observed that 38 patients (67.86%) exhibited retinopathy, while 18 patients (32.14%) did not exhibit any signs of retinopathy. It is worth noting that all patients had HDL cholesterol levels within the normal range of 40-60mg/dl. Out of the total sample size of 10 patients, it was observed that 70% (n=7) had retinopathy while 30% (n=3) did not exhibit any signs of retinopathy. These patients were identified based on their HDL cholesterol levels, which were measured to be equal to or greater than 60mg/dl. In general, the study found no statistically significant correlation between the serum levels of HDL-cholesterol and the grades of retinopathy ($p<0.23$). Among the cohort of 120 patients under investigation, a total of 8 individuals (6.67%) exhibited LDL Cholesterol levels below 50mg/dl. Within this subgroup, 7 patients (87.5%) presented with retinopathy, while 1 patient (12.5%) did not exhibit any signs of retinopathy. A total of 28 individuals exhibited LDL Cholesterol levels ranging from 50 to 100 mg/dl. Among these patients, 21 individuals (constituting 75% of the sample) presented with retinopathy, while the remaining 7 patients (25% of the sample) did not exhibit any signs of retinopathy. Out of the total sample size of 84 patients, representing 70% of the population, LDL Cholesterol levels exceeding 100mg/dl were observed. Among these patients, 63 individuals, accounting for 75% of the aforementioned subgroup, exhibited retinopathy, while the remaining 21 patients, constituting 25% of the subgroup, did not display any signs of retinopathy. The analysis revealed that there was no statistically significant association between the serum levels of LDL Cholesterol and the grades of retinopathy ($p<0.36$).

Table 5: Retinopathy with Cholesterol: HDL and LDL: HDL ratio

Cholesterol: HDL(mg/dl)	**Fundus Retinopathy Grade**				**Total**	**Percentage**
	Normal	Grade 1	Grade 2	Grade 3 and more		
<2.5	9	1	3	0	13	10.83
2.5-5	18	15	27	6	66	55
>5	2	10	22	7	41	34.17
Serum LDL: HDL ratio(mg/dl)						
0-2	10	6	18	4	38	31.67
>2	19	20	34	9	82	68.33

According to the data presented in Table 5, it was observed that among the 120 patients included in the study, a total of 13 patients (10.83%) exhibited a Cholesterol: HDL ratio below 2.5. Among these patients, 4 individuals (30.77%) were found to have retinopathy, while the remaining 9 patients (69.23%) did not exhibit any signs of retinopathy. Out of the total sample size of 66 patients, it was observed that those with a Cholesterol: HDL ratio falling within the normal range of 2.5-5 comprised 48 patients (72.73%) who exhibited retinopathy, while the remaining 18 patients (27.27%) did not display any signs of retinopathy. Out of the total sample size of 41 patients, it was observed that the Cholesterol: HDL ratio exceeded 5 in all cases. Among these patients, 39 individuals (95.12%) were found to have retinopathy, while the remaining 2 patients (4.88%) did not exhibit any signs of retinopathy. In general, there was a positive correlation observed between the increasing levels of the Cholesterol: HDL ratio and the severity of retinopathy. This correlation was found to be statistically significant ($p<0.011$).

Among the cohort of 120 patients, a total of 38 individuals (31.67%) exhibited a low-density lipoprotein (LDL) to high-density lipoprotein (HDL) ratio falling within the range of 0-2. Within this subgroup, 28 patients (73.68%) were diagnosed with retinopathy, while the remaining 10 patients (26.32%) did not exhibit any signs of retinopathy. Among the subsequent cohort of 82 individuals, comprising 68.33% of the total sample, it was observed that their serum LDL: HDL ratio exceeded 2. Within this subgroup, 76.83% of patients exhibited retinopathy, while 23.17% did not. In general, our findings indicate that there is no statistically significant association between the serum levels of LDL: HDL ratio and the grades of retinopathy ($p<0.31$).

DISCUSSION

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The study encompassed a cohort of 120 individuals who had been diagnosed with primary essential hypertension. The individuals were initially classified into two groups: those with retinopathy and those without retinopathy. Among the retinopathy patients, further categorization was done based on the severity of retinopathy, resulting in four grades: grade I, II, III, and IV. The average age of patients in the current study population was 51.89 ±6.88 years, with a range of 20-69 years. Nguyen et al. (year) assert that the examination of retinal vasculature provides a direct and noninvasive means of studying the state of the human microcirculation in vivo, thus presenting a distinctive and readily accessible avenue for investigating health and disease [8]. The mean age of the study group in the research conducted by Bastola et al and Nguyen et al was found to be 58.5 years (standard deviation = 9.2 years; range = 33-48), 56.50±21.00 years, range = 35 to 78 years respectively.[8,9] Epidemiological studies have demonstrated that individuals aged 42 may experience symptoms of heartburn (HR) even in the absence of a history of hypertension (HT). The prevalence of retinopathy varied between 2% and 16% across different symptom presentations. The study group consisted of 70 male participants and 50 female participants. The consistent demonstration of variations in the prevalence of specific signs of human resources (HR) according to age and sex has not been observed in previous studies.[10-12] There has been a decrease in the number of HR trials that have been conducted. According to two reports, the incidence of diverse retinopathy symptoms exhibits a range of 6 to 10 percent over a period of five to seven years (13,14). Nevertheless, a study conducted by Rasoulinejad (15) found no significant association between retinopathy and smoking, dyslipidemia, or gender.

Our study revealed a noteworthy correlation between the severity of hypertension and retinopathy ($p<0.006$). The statistical analysis revealed a significant correlation ($p<0.001$) between different grades of retinopathy and the duration of hypertension. Multiple studies have demonstrated a strong correlation between retinopathy symptoms and elevated blood pressure.[10-13,15] Two studies have evaluated the impact of a history of high blood pressure on the occurrence of complex retinal signs. The present blood pressure level, as opposed to past levels, exhibits a correlation with additional symptoms such as focal arteriolar narrowing, retinal haemorrhage, microaneurysms, and cotton-wool spots. These symptoms may indicate a heightened severity of hypertension in recent periods.[16,17]

Numerous studies have demonstrated a positive correlation between elevated blood pressure levels and perturbations in lipid profiles. A study has provided evidence of a positive correlation between elevated cholesterol levels and blood pressure. While there is a growing understanding of the association between elevated levels of serum low density lipoprotein (LDL) and coronary artery disease, there is limited research on the potential significant increase in serum lipoprotein levels in individuals with high risk (HR) factors. Recent research has revealed that hypertensive patients with fundus changes have exhibited statistically significant improvements in serum lipids. The findings closely aligned with the outcomes of a previous study conducted in Nepal, which also utilised a smaller sample size.[18] There exists a correlation between HR signs and certain atherosclerosis risk factors, such as an increase in blood pressure and serum lipids, although this relationship is not consistently observed.[19] Nevertheless, the present study revealed a notable elevation in serum lipids among hypertensive individuals exhibiting fundus alterations. The levels of serum cholesterol and serum lipids were found to be elevated in individuals with HT without retinopathy, compared to individuals without the condition.[20] However, the levels of free fatty acids were within the normal range. The levels of free fatty acids, serum lipids, and serum cholesterol in individuals with HR have exhibited an elevation compared to the general population.

The study conducted by Adhikari et al. revealed a significant correlation between the duration of hypertension and the occurrence of hypertensive retinopathy. There was a significant correlation observed between retinopathy and the elevation of lipid profile parameters as well as obesity in hypertensive patients. Additionally, a significant association was found between serum triglycerides and retinopathy ($p<0.0001$).[21] In addition to this observation, it was found that a longer duration of diabetes, suboptimal glycemic and lipid control, and elevated blood pressure levels were the primary factors associated with the development of heart failure.[22]

In our investigation, we observed a strong positive correlation between the elevation of serum total cholesterol levels and the progression of retinopathy, as indicated by higher grades. This correlation was found to be statistically significant, with a p-value of less than 0.015. A study conducted by Akshar V Soni in Kota revealed a heightened occurrence of HR in patients with elevated serum total cholesterol levels, and this correlation demonstrated statistical significance ($p<0.0001$).[22] The study conducted by Gupta et al. demonstrated a statistically significant difference ($p<0.001$) in the mean serum cholesterol level between patients with normal fundus and those with varying degrees of HR.[23] Another study conducted by Hanff et al. also demonstrated a notable correlation between high serum cholesterol levels and an elevated incidence of HR inpatients. The statistical analysis of this association yielded a significant result ($p<0.0008$).[24] Cuspidi (25) conducted a study to examine the occurrence of advanced retinal microvascular lesions and their connections with cardiac and extracardiac indicators of target organ

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damage (TOD) in a sizable, specifically chosen hypertensive cohort.

The findings of our study demonstrated a significant positive correlation between serum triglyceride levels and the severity of retinopathy ($p<0.04$). In line with findings from the Gupta study, a separate investigation conducted by Holmes et al. (2018) revealed a comparable correlation between serum triglyceride levels and changes in heart rate, with statistical significance (p0.01).[26] Tada et al. (27) conducted a study which revealed elevated levels of triglycerides in patients with grade II and higher HR. A separate investigation has provided evidence supporting the association between serum triglycerides and initial cardiovascular events in individuals with high-risk diabetes, hypercholesterolemia, and retinopathy.[28]

The present study did not find a statistically significant association between serum HDL cholesterol levels and retinopathy. In the study conducted by Gupta et al., it was observed that the average serum HDL-cholesterol level for the retinopathy group was 38.68, while for the group without retinopathy, it was 39.[23] Bastola et al (year) also demonstrated comparable results.[9] According to a study conducted by Soni (year not provided), the serum HDL-cholesterol levels for the retinopathy group were recorded as 42.70, while the no retinopathy group exhibited a value of 43.61.[21] With the exception of the study conducted by Karaca et al.[29], there has been a lack of additional research demonstrating a correlation between serum HDL cholesterol and heart rate (HR) until more recently.

In the present study, we observed no statistically significant association between the serum levels of low-density lipoprotein (LDL) cholesterol and the severity of retinopathy, as indicated by the grades assigned ($p<0.36$). The present study's findings diverge from those of previous researchers, who have observed a significant correlation between serum LDL cholesterol and retinopathy. The study conducted by Gupta et al. demonstrated a substantial correlation between serum LDL-cholesterol levels and the severity of retinopathy ($p<0.01$).[23] The studies conducted by Badhu et al and Bastola et al demonstrated a notable association between elevated levels of serum LDL-cholesterol and heart rate (HR) [9,18]. A significant correlation was observed between elevated serum LDL-Cholesterol levels and the severity of retinopathy in a study conducted at a medical college in Kota ($p<0.0001$).[21]

In our investigation, we observed that the association between the LDL: HDL-Cholesterol ratio and the outcome variable did not exhibit statistical significance ($p<0.36$). The statistical significance ($P<0.0001$) of the association between the LDL:HDL-Cholesterol ratio was observed in a study conducted by Gupta et al.[23] To date, there have been no documented reports of such a correlation in the existing body of literature. The current study revealed a significant increase in mean serum cholesterol level and mean triglyceride levels among individuals with grade 2 or higher grades of HR. Nevertheless, additional research is needed to investigate the correlation between dyslipidemia and heart rate (HR) in order to ascertain its involvement in the development of disease and the potential effects of dyslipidemia treatment on HR. Dyslipidemia plays a significant role in the pathogenesis of heart disease. Given the elevated frequency of hypertensive retinopathy (HR) within our specific context, it is justifiable to assert that routine ophthalmic examinations for individuals with hypertension are imperative. Performing a regular lipid profile has the potential to decrease ocular morbidity in hypertensive individuals across the board.

CONCLUSION

Our study revealed a positive correlation between the incidence of hypertensive retinopathy and elevated levels of serum total cholesterol and serum triglycerides. Nevertheless, a lack of association was observed between LDL-cholesterol and HDL-cholesterol levels and the occurrence of hypertensive retinopathy. Dyslipidemia is a significant risk factor for both the prevalence and severity of retinopathy, as well as other forms of end organ failure.

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