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Original Research Article

Ocular associations in hyperlipidaemia: A rural hospital based study

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ABSTRACT

Background: The incidence of hypercholesterolemia is ever increasing as the co morbid conditions such as diabetes mellitus, hypertension, stressful life is on a rise. Ocular conditions associated with hypercholesterolemia are issues which are minimally discussed.

Materials and Methods: This prospective cross-sectional study was conducted from January 2019 to June 2019. Complete eye examination was performed including visual acuity examination, refraction, tear film evaluation, slit lamp examination, measurement of intraocular pressure using rebound tonometer, gonioscopy, direct and indirect ophthalmoscopy

Results: Total of 81 patients were examined, out of which males were 55, females were 26. Most common ocular finding was Xanthoma and Xanthelasma in 61(70%) patients. Arcus juvenalis was noted in 12 (14.63%), Lipid keratopathy in 23(29.26%). Other comorbidities associated were Hypertensive Retinopathy, diabetic retinopathy, Pre senile cataract, Primary open angle Glaucoma, Branch retinal vein occlusion which has indirect causal relationship.

Conclusion: Along with systemic workup, Hypercholesterolemia also warrants a routine detailed ocular examination even if the patient is asymptomatic. This aids in early diagnosis and management of the co-existing ocular morbidities.

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1. Introduction

Hypercholesterolemia is defined as increased total cholesterol concentration more than 220mg/dl or hypertriglyceridemia more than 150mg/dl or low- high density lipoprotein cholesterol level (HDL-C) less than 35mg/dl.¹ High blood cholesterol is a modifiable risk factor for cardiovascular disease. It is estimated to be responsible for more than 10% of global cardiovascular deaths in 2010.¹

Increase in the incidence of diabetes mellitus, hypertension, obesity along with sedentary stressful lifestyle, altered dietary intake, has increased the incidence

of hypercholesterolemia. Improved health care reach is also an important contributory factor.

The burden of increased cholesterol is ever increasing and is an important predictor of future cardiovascular events. Increased cholesterol is an important biomarker to prove the value in assessment of intervention aimed at decreasing unfavourable risk factors and long-term maintenance of life style modifications.

Hypercholesterolemia is commonly diagnosed in routine blood examination but ocular examination is not done as a protocol in such patients. The aim of this study is to study the ocular features seen in hypercholesterolemia and to emphasize the need for concurrent ocular examination as a protocol in patients diagnosed with hypercholesterolemia.

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2. Materials and Methods

A time based cross-sectional study was done from Jan 2019 to June 2019. Study was conducted in Ophthalmology OPD at Adichunchanagiri institute of medical sciences, B G Nagara. All patients were referred from Medicine department after diagnosing with elevated cholesterol levels during routine blood examination. Patients between the age of 18- 60 years were included in the study. Patients with history of trauma, post-keratoplasty, patients below 18 years, were excluded from the study.

A detailed history of diabetes mellitus, hypertension, drug history, family history of diabetes mellitus, hypertension, familial hypercholesterolemia, obesity, were taken. Systemic examination included BMI calculation, measurement of blood pressure.

A complete routine ocular examination was done including assessment of visual acuity, refraction, tear film assessment, examination of lids and adnexa, slit lamp examination, IOP, Gonioscopy, colour vision assessment, tear film analysis, detailed fundus examination by direct and indirect ophthalmoscopy was done.

This study was conducted after obtaining ethical committee clearance from the institution along with informed consent from the patients.

There was no drug trial done or other modalities of treatment imposed upon the patients.

3. Results

1. A total of 81 patients were included in the study, out of which 55 (67.90%) were males and 26 (32.09%) were females.
2. Total of 23 patients (28.39%) belonged to the age group less than 40 years, 58 patients (71.60%) were above the age of 40 years.
3. The ocular morbidities with direct causal relationship in patients with hypercholesterolemia (ie the cause of which can be directly attributed to the raised cholesterol levels) are as follows. There were multiple ocular morbidities present in a same person too
 - (a) 61 out of 81 (75.30%) had xanthomas and xanthelasmas.
 - (b) Arcus juvenalis was present in 12(14.81%) patients (patients > 40 years).
 - (c) 23 patients (28.39%) had lipid keratopathy,,
 - (d) 1 patient had adult-onset Coats's disease (1.23%),
 - (e) 13 (16.04%) patients presented with pinguecula
 - (f) Yellow patches in the sclera were found in 4 (4.93%) patientss
 - (g) Asteroid hyalosis was detected in 6 (7.4%) patients
 - (h) Macular drusens were present in 12 (14.81%) patients

4. The patients with co-morbidities associated with hypercholesterolemia but without direct causal relationship were found with the following ocular conditions i.e., these might or might not be due to hypercholesterolemia alone y

- (a) 1 (38.27%) patients presented with diabetic retinopathy
- (b) 22 (27.1%) patients had hypertensive retinopathy,
- (c) 15 (18.52%) had mixed retinopathy
- (d) Around 14 (17.28%) patients had presenile cataract
- (e) 7 (8.64%) patients had primary open angle glaucoma and
- (f) (7.40%) patients had branch retinal vein occlusion
- (g) 7 (8.64%) patients had dry eye

Table 1: Showing the ocular morbidities with direct causal relationship in patients with hypercholesterolemia

Ocular morbidity	Number of patients (%)
Xanthoma & xanthelasma	61 (75.30%)
Arcus juvenilis	12 (14.81%)
Lipid keratopathy	23 (28.39%)
Adult-onset Coats's disease	1 (1.23%)
Pinguecula	13 (16.04%)
Yellow patches on the sclera	4 (4.93%)
Asteroid hyalosis	6 (7.40%)
Macular drusens	12 (14.81%)

Table 2: Showing the patients with co-morbidities associated with hypercholesterolemia but without direct causal relationship

Ocular comorbidities without causal relationship	Number of patients (%)
Diabetic retinopathy	31 (38.27%)
Hypertensive retinopathy	22 (27.1%)
Mixed retinopathy	15 (18.62%)
Presenile cataract	14 (17.28%)
Branch retinal vein occlusion	6 (7.40%)
Primary open angle glaucoma	7 (8.6%)

Table 3: Age and sex distribution

Sex	Number of patients (%)	18-40 years (%)	41-80years (%)
Male	55 (67.90%)	17 (20.9%)	38 (46.9%)
Female	26 (32.09%)	06 (7.4%)	20 (24.69%)
Total	81 (100%)	23 (28.39%)	58 (71.6%)

4. Discussion

It is recognized that lipids play a key role as structural and signalling molecules. Given that lipid intake is most dependent on food composition, the dietary regimen could contribute to induction or prevention of ocular diseases.

Hypercholesterolemia is identified factor of premature vessel atherosclerosis. Endothelial damage in atherosclerosis is characterized by abnormal vascular functionality.

Despite the fact that alterations in the cardio-vascular system, skin changes and digestive symptoms are well-known and expected, the ocular lesions in hyperlipidaemia are often forgotten. However, there are reports describing the ocular lesions in hyperlipoproteinemia, such as xanthelasma (a deposition of lipid the in eyelid), lipid keratopathy (corneal arcus), retinal artery and vein occlusions, ischemic optic neuropathy, cataract and even dry eye.²⁻⁴

In our study total of 81 patients were included, out of which 55 (67.90%) were males and 26 (32.09%) were females.

Total of 23 patients (28.39%) belonged to the age group less than 40 years out of which 17(20.9%) were males and 6 (7.4%) were females, 58 patients (71.60%) were above the age of 40 years which had 38 (46.9%) males and 20(24.69%) females.

In both the groups, males were more affected than females.

In the age group less than 40 years, common ocular conditions associated were pinguecula, pre senile cataract and arcus juvenalis. Very few young adults presented with diabetic retinopathy and yellow patches in the sclera. In the age group above 40, xanthomas and xanthelasmas were common manifestation. Primary open angle glaucoma, branch retinal vein occlusion, hypertensive retinopathy, diabetic retinopathy and mixed retinopathy were other manifestations in the patients above 40 years of age.

In a Lipid Research Clinics population survey, both xanthelasma and corneal arcus were associated with increased levels of plasma cholesterol and low-density lipoprotein cholesterol (LDL-C), especially in young males. Xanthelasma and corneal arcus were highly associated with each other, especially in young people.⁵

In our study, 14 (17.28%) patients had presenile cataract similar to a study conducted by SW Nam, et al, where risk factors for pre senile cataract was studied, around 16.92% of participants had dyslipidaemia in which there was a significant correlation between increased LDL, and triglyceride values ($p=0.3$; $p=0.09$) There could be other direct or indirect causal relationship between hyperlipidaemia and the presenile cataract.⁶

In contrast to study done by Wang S et al, there was no significant correlation between dyslipidaemia and posterior subcapsular cataract($p=0.6$) but there was a significant correlation between the dyslipidaemia and cortical cataracts ($p=0.02$).¹

In our study, there were multiple ocular morbidities present in a same person and morbidities with direct causal relationship to hyperlipidaemia were as follows; 61 out

of 81 (75.30%) had xanthomas and xanthelasmas, Arcus juvenalis was present in 12(14.81%) patients (patients > 40 years). 23 patients (28.39%) had lipid keratopathy, 1 patient had adult-onset Coats's disease (1.23%), 13 (16.04%) patients presented with pinguecula, yellow patches in the sclera were found in 4 (4.93%) patients, Asteroid hyalosis was detected in 6 (7.4%) patients, Macular drusens were present in 12 (14.81%) patients.

The patients with co-morbidities associated with hypercholesterolemia but without direct causal relationship were found with the following ocular conditions i.e., these might or might not be due to hypercholesterolemia alone- 31 (38.27%) patients presented with diabetic retinopathy, 22 (27.1%) patients had hypertensive retinopathy, 15 (18.52%) had mixed retinopathy, 14 (17.28%) patients had presenile cataract, 7 (8.64%) patients had primary open angle glaucoma, 6(7.40%) patients had branch retinal vein occlusion, 7 (8.64%) patients had dry eye.

In our study, 7 (8.64%) patients out of 81 had primary open angle glaucoma, which was in contrast to another study done by Dube M et al, whereas there was a significant relationship between high cholesterol, LDL, and triglyceride and low HDL to POAG. HDL was found to be lower in cases than controls but this was not statistically significant. Dyslipidaemia could be an independent risk factor for POAG.⁷

There was no single case of angle closure glaucoma in our study which was associated with hyperlipidaemia. Similarly in study done by Wang S, et al, there were no significant correlation between the dyslipidaemia and angle closure glaucoma ($p=0.6$).¹

In our study, total of 37 patients (41%) out of which 22 (27.1%) patients had hypertensive retinopathy in various stages, 15 (18.52%) had mixed retinopathy associated with hyperlipidaemia.

Similarly, in a study done by Soni A V et al, there was an increased incidence of hypertensive retinopathy in patients having high serum total cholesterol level and this association was statistically significant ($P < 0.0001$).⁸ In another study, Gupta R P et al⁹ also showed that there was an increased incidence of hypertensive retinopathy in patients having high serum cholesterol level and this association was statistically significant ($P < 0.0008$).⁹ Similarly, Bastola et al in their study, also showed that there was a statistically significant difference in the mean serum cholesterol level ($F = 10.38$; $P < 0.001$) of patients with normal fundus and in those with different grades of hypertensive retinopathy.¹⁰

In our study, around 31 (38.27%) patients presented with diabetic retinopathy in various stages and 15 (18.52%) had mixed retinopathy. Hard exudates were prominently seen in most cases. Totally around 46(51.11%) patients had diabetic retinopathy.

In a study done by Bhowmik et al, Type 2 diabetes mellitus was significantly associated with high Total-Cholesterol ($p < 0.001$), high Triglyceride ($p < 0.001$) and low HDL-C ($p = 0.044$). Prediabetes showed a significant association with high triglycerides ($p < 0.001$) and low HDL-C ($p = 0.011$).¹¹ Diabetic retinopathy remains the most common cause of legal blindness in adults in developed countries. Lipid-lowering therapy may be an effective adjunctive agent for DR, particularly for patient with DME requiring laser treatment.¹² This can be an indication of association between diabetes mellitus, diabetic retinopathy and dyslipidaemia.

In our study only 6 (7.40%) patients had branch retinal vein occlusion. These patients also had mixed retinopathy, systemic diabetes mellitus and hypertension. In a study done by Wang S et al, there was no significant correlation ($p=0.21$) between retinal venous occlusion and dyslipidemia.¹ The venous occlusions can be due to multifactorial reasons, can be attributed to systemic diabetes mellitus, hypertension and hyperlipidaemia can be a contributing factor.

In our study, 7 (8.64%) patients had dry eye. This could be mostly attributed to meibomian gland dysfunction in all 7 patients. In a similar study done by Aldaas K et al, 8.6% patients with dyslipidaemia were associated with diagnosis of dry eye disease. A hypothetical mechanism relates to the proinflammatory characteristics of LDL as inflammation is known to contribute to the pathogenesis of MGD and DED.¹³

Those with dyslipidaemia and treated with statins (HMG-CoA Reductase inhibitors) can contribute to dry eye disease. HMG-CoA reductase expression has been identified within the sebaceous cells of meibomian glands in human eyelid tissue. Thus, it is possible that statin use could alter cholesterol synthesis and lipid homeostasis within the meibomian glands, leading to destabilization of the tear film and subsequent DED.¹⁴

Potential limitations of our study are that sample size is relatively small, and study should be done on a larger population to extrapolate results. Also, these comorbidities have multiple contributing factors and direct causal association could not be established with a small sample size.

5. Conclusion

Hyperlipidaemia is intricately related with other metabolic disorders such as diabetes mellitus, hypertension, obesity and cardiac diseases. It can also have potential vision threatening complications. Hence a routine ocular examination should be a part of dyslipidaemia evaluation for early intervention and prevention of sight threatening complications.

6. Source of Funding

None.

7. Conflicts of Interest

The authors declare no conflict of interest.

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