

Dyslipidemia in Primary Open Angle Glaucoma

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Abstract

Glaucoma is the leading cause of irreversible blindness worldwide. Primary Open Angle Glaucoma (POAG) is usually asymptomatic till advanced stages of the disease. Intraocular pressure (IOP) is the primary risk factor for development of POAG. But in spite of control of IOP, some cases progress which strengthens the view that there must be other independent risk factors in the pathogenesis of glaucoma. Serum lipids have been found to be associated with glaucoma in few studies. We conducted a study to assess the relation between dyslipidemia and glaucoma on 100 cases of glaucoma and 100 age-matched controls. Detailed ophthalmic examination was done in all subjects and fasting lipid profile was compared between cases and controls. Levels of total cholesterol, total triglycerides and LDL were significantly higher in cases than in controls with a p value < 0.0001 . We conclude that dyslipidemia is an independent risk factor for POAG.

Key Words

Dyslipidemia, Glaucoma, Intraocular pressure, Primary Open Angle Glaucoma

Introduction

Glaucoma is the leading cause of irreversible visual disability in the world (1,2). Quigley *et al.* estimated that by 2020, 79.6 million people will suffer from glaucoma, and 74% will have primary open-angle glaucoma (POAG) (3). The exact mechanism by which the anatomic and functional damage occurs in patients with POAG remains unknown. Established risk factors include elevated intraocular pressure (IOP), old age, ethnic background, and family history of glaucoma (4-6). However, other potential risk factors for glaucoma may exist, and these should be explored to develop interventions that can reduce the incidence of this disorder.

Recent epidemiologic studies have suggested that hyperlipidemia may be associated with glaucoma. For instance, the study by Lin and colleagues, which used the National Health Insurance Database, indicated that hyperlipidemia increases the odds of developing POAG (7). The present study attempts to establish a relation between serum lipids and its components with POAG.

Material and Methods

In this case-control study, we investigated a total of 200 North Indian subjects comprising 100 patients with

POAG documented by clinical tests using standard ophthalmologic equipment and 100 age-matched controls. All participants were over 20 years of age. Inclusion criteria for POAG group (cases) were: an untreated Intraocular pressure (IOP) of 21 mmHg or more with a non-contact tonometer, open anterior chamber angles on gonioscopy; glaucomatous optic disc changes (increased cup/disc ratio, thinning of the neuro retinal rim, notching) on ophthalmoscopy and visual field defects characteristic of glaucoma by standard automated perimetry with the Humphrey Visual Field Analyser. Exclusion criteria for the POAG group were: history of ocular trauma, ocular surgery and any systemic or local condition causing secondary glaucoma. Persons taking lipid lowering drugs like statins were also excluded. Inclusion criteria for control subjects were IOP below 21 mm Hg, no glaucomatous changes in the optic disc, no visual field loss characteristic for glaucoma and no pseudoexfoliation material in the lens capsule or near the pupil. The exclusion criteria were: high myopia ($>5D$), history of intraocular surgery, subluxated, traumatic, and complicated cataracts.

Demographic data including age, gender, address was noted. Ophthalmic examination was performed like visual

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acuity using Snellen's chart, anterior segment examination, slit lamp examination, pupillary reactions, Van-Herrick's grading, intraocular pressure measurement using Non-Contact Tonometer. Gonioscopy was done to evaluate the angle structures. Fundus examination and visual field charting were performed. Primary open angle glaucoma was diagnosed on the basis of raised IOP, optic nerve head changes detected by direct ophthalmoscopy and visual field defects.

Twelve hour fasting blood samples were collected for measuring serum lipids and assessed using enzymatic method (autoanalyzer). The lipid profile included total cholesterol, triglycerides (TGL), Low Density Lipoproteins (LDL) and High Density Lipoproteins (HDL). Reference values for lipids were taken from National Cholesterol Education Program: Adult Treatment Panel III (NCEP: ATP III) guidelines, according to which Hypercholesterolemia is defined as total cholesterol > 200 mg/dl, Hypertriglyceridemia, when triglycerides > 150 mg/dl, LDL > 130 mg/dl were considered high and HDL < 40 mg/dl were considered low (8).

Mean, Standard deviation and standard error of means were calculated. Statistical analysis was performed using unpaired t-test and chi square test using SPSS software. P value < 0.05 was considered significant.

Results

A total of 200 participants (100 in the glaucoma group and 100 in the control group) were included in our study. Demographic parameters of the study population are shown in *Table 1*. The maximum number of cases and controls were between the ages of 50-70 years.

High Cholesterol (>200mg/dl) was seen in 51 cases, whereas in controls, 18 individuals had high cholesterol. High Triglycerides (>150mg/dl) was seen in 42 cases whereas 13 controls had high triglycerides. LDL was high (> 130 mg/dl) in 60 cases and 18 controls. HDL was low (< 40mg/dl) in 68 cases and 57 controls (*Table 2*). 74% of subjects with hypercholesterolemia, 76% of subjects with hypertriglyceridemia and 77% with HDL had glaucoma.

In cases, mean total cholesterol was 217.15 ± 6.29 mg/dl; mean triglycerides were 156.05 ± 7.91 mg/dl; mean LDL level was 144.1 ± 4.24 mg/dl and mean HDL was 37.28 ± 4.43 mg/dl. In controls, mean total cholesterol was 174.95 ± 5.23 mg/dl; mean triglycerides were 112.70 ± 8.67 mg/dl; mean LDL level was 109.8 ± 6.27 mg/dl and mean HDL was 38.46 ± 4.18 mg/dl (*Table 3*).

Level of mean cholesterol, triglycerides, and LDL were significantly higher in cases than in controls with *p* value < 0.0001 taking confidence interval 95%. Level of HDL

Table 1: Baseline Characteristics of Study Participants

Characteristics	Cases (n=100)	Controls (n=100)	<i>p</i> -value
Range of age (in years)	31 - 82	28- 74	
Mean age (in years)	56.36 ± 7.91	54.33 ± 9.78	.1081
Gender (Male: Female)	41:59	53:47	.1192
Locality (Urban: Rural)	67:33	56:44	.1463

Table 2: Dyslipidemia in Cases and Controls

Lipid Parameters	Cases (n=100)	Controls (n=100)	<i>p</i> -value
High Cholesterol (>200mg/dl)	51	18	< .0001
High Triglycerides (>150mg/dl)	42	13	< .0001
High LDL (> 130 mg/dl)	60	18	< .0001
Low HDL (< 40mg/dl)	68	57	.1442

Table 3: Serum Lipid Values in Cases and Controls

Serum Lipid Parameters	Cases (n=100)	Controls (n=100)	<i>p</i> -value
Mean Cholesterol (mg/dl)	217.15 ± 6.29	174.95 ± 5.23	< .0001
Mean Triglycerides (mg/dl)	156.05 ± 7.91	112.70 ± 8.67	< .0001
Mean LDL (mg/dl)	144.1 ± 4.24	109.8 ± 6.27	< .0001
Mean HDL (mg/dl)	37.28 ± 4.43	38.46 ± 4.18	.0541

was lower in cases than in controls but it was not statistically significant ($p = 0.0541$).

Discussion

Many risk factors for the development of POAG have been identified. Many studies have reported an association between hyperlipidemia and POAG. Lipid peroxidation leading to oxidative stress may directly damage trabecular meshwork and endothelium of blood vessels supplying the optic nerve head or atherosclerotic changes due to high cholesterol may affect ocular perfusion. Excess lipid levels could increase episcleral venous pressure and blood viscosity, resulting in a consequent decrease in outflow facility. The higher values of total cholesterol, particularly atherogenic LDL fraction, may have certain influence in glaucoma (9). Egorow *et al.* found that patients with glaucoma may have atherogenic hyperlipidaemia with lower antioxidative activity (10). The statins in usage longer than 23 months may significantly reduce the risk of glaucoma (11).

In a case control study, Davari *et al.* found that there was a positive association between POAG and dyslipidemia (hypercholesterolemia and hypertriglyceridemia). They concluded that hyperlipidemia can be a risk factor for POAG (12). Our present study also suggests similar findings. In this study, 51% of glaucoma cases had hypercholesterolemia as compared to 18% of normotensive controls. Similarly, 42% of glaucoma cases and 13% of normotensive controls had hypertriglyceridemia. More than 74% of subjects with hypercholesterolemia and more than 76% of subjects with hypertriglyceridemia had glaucoma in this study.

In a similar study in 2009, by Pavljasevic and Asceric in Bosnia and Herzegovina, the researchers found that blood cholesterol levels for patients in the test group were higher compared to those of the control group (13). In the present study, we observed that mean serum cholesterol levels in glaucoma cases was 217.15 ± 6.29 mg/dl while in controls it was 174.95 ± 5.23 mg/dl.

The Beijing eye study on 3251 individuals (aged >45 years) showed that in dyslipidemic patients, IOP was significantly increased (14). In the present study, we found that glaucoma cases had significantly more dyslipidemia as compared to normotensive controls.

Maybe, the relationship between lipids and glaucoma is due to the association of this disorder with other cardiac risk factors such as diabetes and hypertension. A cohort study was conducted in Michigan university in people

aged >40 years to assess the elements of metabolic syndrome and glaucoma. The results showed that risk of glaucoma increased if dyslipidemia is associated with diabetes or hypertension (15). These results point to a combined effect of dyslipidemia with hypertension or diabetes in pathogenesis of glaucoma. In our study we find that dyslipidemia is an independent risk factor for glaucoma after removing these confounding factors; as there is a significant relationship between high cholesterol, LDL, and triglyceride to POAG.

Further research will help us in understanding the mechanisms by which dyslipidemia leads to development of POAG. Various studies showing increased levels of lipid peroxides in the aqueous humor, trabecular meshwork and Schlemm's canal in POAG cases compared with control eyes suggest that lipid peroxidation by increasing oxidative stress is responsible for destruction of the trabecular meshwork and Schlemm's canal (16-18).

Wang and Bao (19) performed multiple distinct meta-analyses to clarify the association of hyperlipidemia and blood lipid levels with glaucoma, OHT and IOP. They included all the papers that assessed the correlation between hyperlipidemia and glaucoma. They detected a marked association between hyperlipidemia and glaucoma with significant heterogeneity among studies. They concluded that the evidence suggests that hyperlipidemia is significantly associated with an increased risk of glaucoma. Our current study also showed similar findings.

Conclusion

The current evidence suggests that dyslipidemia is significantly associated with an increased risk of glaucoma. These study findings provide the clinicians with useful information about the treatment of hyperlipidemia to prevent the incidence of glaucoma.

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