International Journal of Life Sciences, Biotechnology and Pharma Research Vol. 13, No. 9, September 2024 Online ISSN: 2250-3137
Print ISSN: 2977-0122

DOI: 10.69605/ijlbpr_13.9.2024.84

Original Research

Severity Of Primary Open-Angle Glaucoma In Patients With Diabetes And Hypertension: A Prospective Hospital-Based Study

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Received Date: 15 July, 2024 Accepted Date: 20 August, 2024

Abstract
Aims: To correlate the severity of primary open-angle glaucoma (POAG) with diabetes (DM) and hypertension (HTN).
Settings and Design: Prospective, comparative, observational study in a tertiary care centre.
Methods and Material: 200 newly diagnosed POAG patients were divided into four groups of 50 patients each, Group 1 (Controls: without DM andHTN), Group 2 (DM), Group 3 (HTN), and Group 4 (DM and HTN). The worst affected eye of each patient was enrolled. The severity of POAG was based on visual field defects (VFD) on 24-2 perimetry.
Statistical analysis was done using SPSS version 20 (IBM Corporation, Armonk, NY, USA). Continuous data were presented as mean±standard deviation and categorical data as percentages.Comparison between groups was performed using the Chi-Square test for qualitative and T-test or post-hoc Anova test for quantitative variables. The p-value ≤ 0.05 wasconsidered statistically significant.
Results: VFD in group 2 (MD = -10.527±5.367dB), Group 3 (MD= -10.296±5.632 dB), andGroup4(MD=-12.495±7.072dB) was statistically significant ($p<0.05$) in comparison with Group 1(MD=-5.891±4.689). 72% of patients in Group 1 had mild VFD whereas 84% in Group 2, 82% in Group 3, and 86% in Group 4 had moderate/severe VFD. The difference was statistically significant ($p<0.05$).
Conclusions: DM and HTN were significantly associated with the severity of POAG. Patients of POAG with DM or with HTN or with both DM and HTN had a more severe form of POAG when compared with the POAG patients without any DM or HTN.
Key-words: Primary open-angle glaucoma; diabetes mellitus; hypertension
Key Messages: Diabetes and hypertension, the potential vascular risk factors of POAG correlate with the severity of glaucoma at presentation. Physicians and ophthalmologists need to work in coordination to retard the progression of this irreversible but preventable blinding disease.

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Introduction

Primary open-angle glaucoma (POAG),associated with characteristic atrophy of the optic disc, visual field loss, and open-angle accounts for nearly three-quarters of all glaucomas.[1,2] The vascular theory of glaucoma postulates that impairment of the microvascular network at the optic nerve head (ONH) region, results in reduced nutritional support to the retinal ganglion cell axons and leads to retinal ganglion cell degeneration. Diabetesmellitus (DM) and hypertension (HTN) affect microvascular circulation and contribute directly or indirectly to the ischemic events at the ONH region, resulting in the development and progression of optic nerve damage in POAG.[3,4]

Subjects and Methods

After taking permission from the institutional ethical committee, the present prospective, comparative, observational study was conducted in a Regional Institute of Ophthalmology, in Northern India. The worst eye of 200 newly diagnosed cases of POAG was enrolled in the study after they gave written informed consent in their vernacular language as per the Declaration of Helsinki.

Patients were divided into four groups of 50 patients each, Group 1 (Controls: POAG patients without DM and HTN), Group 2 (POAG patients with DM), Group 3 (POAG patients with HTN), and Group 4 (POAG patients with both DM and HTN). Patients with secondary glaucoma, diabetic or hypertensive

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DOI: 10.69605/ijlbpr_13.9.2024.84

retinopathy, with a history of intraocular surgery or ocular trauma, were excluded from the study.

Detailed history and comprehensive examination including best-corrected visual acuity, intraocular pressure (IOP)measurementby applanation tonometry, slit-lamp biomicroscopy, gonioscopy with three mirror Goldmann Gonio lens, specular microscopy, indirect dilated slit-lamp biomicroscopy optic disc assessment with +90 D Lens, optical coherence tomography (OCT) for retinal nerve fibre layer (RNFL) analysis with RS 330 NIDEK machine, 24-2 visual field analysis using Automated Humphrey perimetry of each patient was documented. Average RNFL thickness, central macular thickness (CMT) on OCT and mean deviation (MD), pattern standard deviation (PSD), and visual field index (VFI) on 24-2 perimetry were analyzed and compared among the groups. The severity of POAG based on visual field defect (VFD) was sub-grouped into mild (MD < -6dB), moderate (MD -6dB to -12dB), and severe (MD > -12dB) POAG.

Results

Mean age of patients in Group 2, Group 3, and Group 4 (60.02±10.69, 59.46±9.06, 60.90±9.80 years respectively) was comparable to that of Group 1 (58.78±9.85 years) (p=0.744). Out of 200 POAG patients, 48.5% were females and 51.2% were males. Male predominance was observed in Group 1 (54%), Group 2 (54%), and Group 3 (52%) whereas in Group 4, 54% were females[Table 1].The worst affected eye was the right eye in 113 patients (56.52%). The right eye was affected more in Group 1 (52%), Group 2 (62%), and Group 4 (62%) whereas Group 3 showed equal involvement of bothright eye and left eye.

A statistically significant difference (p<0.05) was observed in mean RNFL thickness and mean CMT in group 2 (70.040±8.974 μm,209.100±21.937 μm respectively), Group 3 (71.620±10.026 μm, 194.780±35.642 μm respectively) and Group 4 (65.900±11.638 μm,215.700±22.000 μm respectively) in comparison with Group 1 (80.680±10.561 μm, 230.400±21.835 μm respectively)[Table 2].

A statistically significant difference (p<0.05) was observed in MD, PSD, and VFI in group 2 (-10.527±5.367 dB, 6.039±3.377 dB, 76.380±15.914% respectively), Group 3 (-10.296±5.632 dB, 7.136±3.494 dB, 75.500±18.914% respectively) and Group 4 (-12.495±7.072 dB, 7.127±3.861 dB, 71.180±17.278% respectively) in comparison with Group 1 (-5.891±4.689 dB, 3.417±2.881 dB, 88.480±14.779% respectively) on 24-2 perimetry [Table 3].

72% of patients in Group 1 had mild VFD whereas 84% in Group 2 (OR:13.50, 95 % CI: 5.08-35.83), 82% in Group 3 (OR:11.71, 95% CI: 4.53-30.72), and 86% in group 4 (OR:15.79, 95% CI: 5.75-43.35) had moderate/severe VFD. The difference was statistically significant (p=0.001) [Table 4].

Table: 1 Demographic Profile Of The Study Groups

Variables	Groups				Total	p-value*
	Group 1 (Controls)	Group 2 (DM)	Group 3 (HTN)	Group 4 (DM and HTN)		
Female	23(46%)	23(46%)	24(48%)	27(54%)	97(48.5%)	>0.05
Male	27(54%)	27(54%)	26(52%)	23(46%)	103(51.5%)	>0.05
Total	50	50	50	50	200	
Mean age (in years)±SD	58.78±9.85	60.02±10.69	59.46±9.06	60.90±9.80	59.79±9.82	>0.05

*p>0.05 was taken as not significant.

Table: 2 Comparison Of Oct Parameters Of The Study Groups With The Control Group

Variables	Groups				p-value*
	Group 1 (Controls)	Group 2 (DM)	Group 3 (HTN)	Group 4 (DM and HTN)	
Average RNFL thickness (μm)	80.68±10.56	70.04±8.974	71.62±10.026	65.90±11.638	<0.05
Central macular thickness (μm)	230.40±21.835	209.10±21.94	194.78±35.64	215.70±22.00	<0.05

*p<0.05 was taken as significant.

Table: 3 Comparison Of 24-2 Perimetry Parameters Of The Study Groups With The Control Group

Parameters	Groups (Mean±SD)				p-value*
	Group 1 (Controls)	Group 2 (DM)	Group 3 (HTN)	Group 4 (DM and HTN)	
24-2 MD (dB)	-5.891±4.69	-10.527±5.367	-10.296±5.63	-12.495±7.07	<0.05
24-2 PSD (dB)	3.417±2.88	6.039±3.377	7.136±3.494	7.127±3.861	<0.05

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DOI: 10.69605/ijlbpr_13.9.2024.84

24-2 VFI (%)	88.480±14.78	76.38±15.914	75.50±18.914	71.18±17.278	<0.05

*p<0.05 was taken as significant.

Table: 4 Comparison Of Severity Of Visual Field Defect Of The Study Groups With The Control Gr

Severity of visual field defect	Groups								Total *	
	Group 1 (Controls)		Group 2 (DM) †		Group 3 (HTN) ‡		Group 4 (DM and HTN) §			
	No.	%	No.	%	No.	%	No.	%	No.	%
Mild	36	72.00	8	16.00	9	18.00	7	14.00	60	30.00
Moderate/ Severe	14	28.00	42	84.00	41	82.00	43	86.00	140	70.00
Total	50	100.00	50	100.00	50	100.00	50	100.00	200	100.00

Discussion:

The present study was conducted on the worst affected eye of 200 newly diagnosed cases of POAG. Patients were divided into four groups of 50 patients each, Group 1 (Controls: POAG patients without DM and HTN), Group 2 (POAG patients with DM), Group 3 (POAG patients with HTN), and Group 4 (POAG patients with both DM and HTN).

The risk of glaucoma increases with age.[5] In the present study, it was observed that the mean age of patients was 59.79±9.82 years. Similar results were reported in the previous studies done by Khatri et al. (54.4±15.9 years),Singh et al.(59.23±8.89 years),andShakya-Vaidya et al.(58.99±14.7 years) in patients with POAG.[6,7,8]

On OCT the mean RNFL thickness and mean CMT was significantly lower (p=0.001) in Group 2 (70.040±8.9738 µm and 209.1±21.937 µm) compared to Group1 (80.680±10.5607 µm and 230.40±21.835 µm)[Table 2]. Similarly, in Group 1 and Group 2 the difference in mean MD (-5.891±4.689 dB and -10.527±5.367 dB, p=0.001), mean PSD (3.417±2.881dB and 6.039±3.377 dB, p=0.001) and mean VFI (88.48±14.779 % and 76.38±15.914 %, p=0.001) on 24-2 perimetry was statistically significant[Table 3]. Also, our study showed that 84% of patients in Group 2 had moderate/severe VFD whereas 72% in Group 1 had mild VFD. This correlation was statistically significant[Odds ratio (OR)=13.5; 95% CI: 5.08-35.83; p=0.001][Table 4].

The findings of our study were consistent with the study conducted byKhatriet al.[6] which compared POAG patients with DM and without DM. They found that the mean VFD in patients with DM was −8.52 [95% confidence interval (CI): −13.4 to −3.64, p<0.05]. In contrast, patients without DM had a mean VFD of −4.85 (95% CI: −5.83 to −3.86, p<0.05), which was of significant statistical value to show that POAG was more severe among the diabetic group compared with that of the non-diabetic group. This study also showed that DM had higher chances of having severe VFD compared with the patients without DM (OR: 4.72, 95% CI: 1.69 to 13.2, p=0.0031).

A study done by Singhet al.[7] revealeda 15.6% increased incidence of POAG in diabetic patients. In a large U.S.-based prospective study done on a cohort of women by Pasquale et al,[9]a positive association was found between type 2 DM and POAG [Relative risk (RR) = 1.82, 95% CI: 1.23–2.70]. A meta-analysis done by Bonovaset al.[10]also suggested that diabetic patients were at a significantly increased risk of developing POAG (OR= 1.50, 95% CI: 1.16–1.93). One prospective study done by Ellis et al.[11] reported an age-adjusted rate ratio of 1.57 (95% CI: 0.99–2.48) for POAG among subjects with diabetes versus non-diabetic patients.

On OCT the mean RNFL thickness and mean CMT was significantly lower (p=0.001) in Group 3 (71.620±10.0263 µm and 194.78±35.642 µm) compared to Group 1 (80.680±10.5607 µm and 230.40±21.835 µm) [Table 2]. Similarly, in Group 1 and Group 3 the difference in mean MD (-5.891±4.689 dB and -10.296±5.632 dB, p=0.001), mean PSD (3.417±2.881dB and 7.136±3.494 dB, p=0.001) and mean VFI (88.48±14.779 % and 75.5±18.914%, p=0.002) on 24-2 perimetry was statistically significant[Table 3]. Also, our study showed that 82% of patients in Group 3 had moderate/severe VFD whereas 72% in Group 1 had mild VFD. This correlation was statistically significant (OR= 11.71; 95% CI: 4.53-30.72; p=0.001) thus concluding that POAG was more severe among the hypertensive group compared with that of the non-hypertensive group [Table 4].

Similar findings were reported by Khatri et al.[6]in their study which compared the severity of VFD among the POAG patients with and without HTN. This study found that the mean VFD in patients with HTN was −8.39 (95% CI: −11.1 to −5.64, p<0.05) in comparison with the patients without HTN who had a mean VFD of −4.85 (95% CI: −5.83 to −3.86). The results showed that patients with HTN had OR 2.75 (95% CI: 1.51 to 5.00, p=0.001) of having severe visual field changes in comparison with the patients without HTN.

Our results are also supported by the findings of many studies in the literature that have demonstrated that HTN is a risk factor for OAG.[12,13,14,15,16] However, Barbados Eye and the Proyecto VER studies failed to demonstrate a significant relationship between BP and POAG.[12,18] Jasmine Mary Jacob et al.[19] reported a statistically significant association between hypertension and POAG (p=0.02) and odds

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DOI: 10.69605/ijlbpr_13.9.2024.84

ratio 2.2(95% CI:1.1-4.2) in their study. This was similar toobservations of the Blue Mountains Eye Study (OR: 1.56, 95% CI: 1.01–2.40).[12]Bonomi et al.[14] also found that POAG is more prevalent among patients with lower perfusion pressures.

Newman-Casey et al.[20] found in their study that out of 2,182,315 enrollees who met the inclusion criteria, 55,090 (2.5%) had open-angle glaucoma (OAG). After adjustment for confounding factors, patients with DM (hazard ratio=1.35, 95% CI: 1.21 to 1.50) or HTN (hazard ratio =1.17, 95% CI: 1.13 to 1.22) alone or in combination (hazard ratio =1.48, 95% CI: 1.39 to 1.58) had an increased hazard of developing OAG relative to persons with neither of these conditions. They also reported that people with DM alone had a 35% increased risk of developing OAG and those with HTN alone had a 17% increased risk. For people with both DM and HTN, there was a 48% increased risk of developing OAG. Another study by Shakya-Vaidya et al.[8]reported that the overall odds of POAG increased 2.72-fold among hypertensive and 3.50-fold among diabetic patients. Jasmine Mary Jacob et al.[19] in their study reported a more than two-fold increased risk of POAG among patients with hypertension and diabetes.

In our study, we also compared patients having both DM and HTN (Group 4) with patients without DM and HTN (Group 1: Controls). On OCT the mean RNFL thickness and mean CMT was significantly lower (p=0.001,0.027 respectively) in Group 4 (65.900±11.6378 μm and 215.7±22 μm) compared to Group 1 (80.680±10.5607 μm and 230.40±21.835 μm)[Table 2]. Similarly, in Group 1 and Group 4 the difference in mean MD (-5.891±4.689 dB and -12.495±7.072 dB, p=0.001), mean PSD (3.417±2.881dB and 7.127±3.861 dB, p=0.001) and mean VFI (88.48±14.779 % and 71.180±17.278 %, p=0.001) on 24-2 perimetry was statistically significant[Table 3]. Also, our study showed that 86% of patients in Group 4 had moderate/severe VFD whereas 72% in Group 1 had mild VFD. This correlation was statistically significant (OR= 15.79; 95% CI: 5.75-43.35; p=0.001) thus concluding that POAG was more severe among the diabetic and hypertensive group compared with that of the non-diabetic, non-hypertensive group [Table 4].

Similar findings were reported byKhatri et al.[6]in their study which also compared patients with DM and HTN with participants without DM and HTN. This study found that the mean VFD with both DM and HTN was −9.08 (95% CI: −16.9 to −1.27 $p<0.05$). In contrast, the patients without DM and HTN had a mean VFD of −4.85 (95% CI: −5.83 to −3.86, $p<0.05$). The comparison showed that the participants with DM and HTN had higher chances of having severe VFD compared with the participants without DM and HTN (OR 19.9, 95% CI: 2.52 to 156.8, p=0.0046).

Limitations: Our study has some limitations. Firstly, this is a single-centre study. Secondly, the sample size is small. Thirdly, we did not consider the duration of DM/HTN. Fourthly, we included only mild or well-controlled DM/HTN patients without diabetic/hypertensive retinopathy. Studies are available in the literature showing a significant association of POAG with DM and HT. Nevertheless, this study attempted to find the association of diabetes and hypertension with the severity of POAG. We believe that our results need to be confirmed in a larger longitudinal study to further aid in understanding the complex relationship of DM/HTN with POAG.

Conclusion: Our study confirms that there is a significant association between diabetes and hypertension with the severity of primary open-angle glaucoma. Patients of POAG with DM or with HTN or with both DM and HTN have more severe POAG compared to POAG patients without any DM or HTN. Early identification and management of these modifiable risk factors by health care professionals and awareness, strict control, and regular follow-up by the patients can play a significant role in the prevention and progression of this eventually blinding disease.

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