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ORIGINAL ARTICLE

Systemic Hypertension as a Risk Factor for Primary Open-Angle Glaucoma in Adults

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ABSTRACT

Background: Primary open-angle glaucoma (POAG) is a leading cause of irreversible blindness worldwide. While elevated intraocular pressure is a known risk factor, vascular components such as systemic hypertension have also been implicated in its pathogenesis.

Objective: To determine the association between systemic hypertension and primary open-angle glaucoma in adults.

Methods: This case-control analytical study was conducted at Sahiwal Teaching Hospital, Sahiwal from February 2023 to July 2023. A total of 325 participants were included, comprising 162 cases (patients with POAG) and 163 controls (individuals without POAG), matched for age and gender. Demographic and clinical data were obtained using a structured questionnaire. This included information on age, gender, duration of hypertension, medication use, and lifestyle factors. Blood pressure was measured using a calibrated mercury sphygmomanometer in a sitting position after a five-minute rest.

Results: Systemic hypertension was present in 66.7% of patients with POAG compared to 45.4% of controls ($p < 0.001$). The unadjusted odds ratio for POAG in hypertensive individuals was 2.43 (95% CI: 1.57–3.78, $p < 0.001$). After adjusting for age, gender, and smoking status, systemic hypertension remained independently associated with POAG (adjusted OR = 2.18, 95% CI: 1.35–3.52, $p = 0.002$). Additionally, a longer duration of hypertension (>10 years) and the use of multiple antihypertensive medications were more frequent among POAG patients ($p = 0.03$ and $p = 0.02$, respectively).

Conclusion: It is concluded that systemic hypertension is significantly associated with primary open-angle glaucoma in adults. Prolonged duration and severity of hypertension further increases the risk. These findings emphasize the need for integrated cardiovascular and ophthalmologic screening in hypertensive individuals to enable early detection and prevention of glaucomatous vision loss.

Keywords: POAG, Patients, Retinal, Cells, Chronic, Neuropathy

INTRODUCTION

Primary open-angle glaucoma (POAG) is a chronic, progressive optic neuropathy characterized by the degeneration of retinal ganglion cells, optic nerve head cupping, and corresponding irreversible visual field defects[1]. It is the most prevalent subtype of glaucoma globally and a major cause of irreversible blindness, particularly among individuals aged over 40. The condition is typically asymptomatic in its early stages, often leading to delayed diagnosis and substantial visual impairment by the time patients seek clinical attention. This silent progression highlights the importance of identifying both modifiable and non-modifiable risk factors to enable early detection, prevention, and targeted interventions[2]. Traditionally, elevated intraocular pressure (IOP) has been considered the principal modifiable risk factor for POAG, forming the basis for most therapeutic strategies[3]. However, it is increasingly evident that glaucoma is a multifactorial disease, with many patients developing glaucomatous optic neuropathy even in the presence of normal IOP a condition known as normal-tension glaucoma (NTG). This observation has prompted an investigation into alternative mechanisms and systemic contributors to optic nerve damage, including vascular, genetic, and metabolic factors[4].

Among these, systemic hypertension has emerged as a potentially significant but controversial risk factor. Hypertension is one of the most prevalent chronic diseases globally, affecting approximately 1.28 billion adults as of the latest WHO estimates[5]. It is well-known for its deleterious effects on target organs, including the brain, kidneys, and heart. Similarly, its impact on the microvascular circulation of the eye, particularly the optic nerve head, has garnered increasing attention in ophthalmological research. The proposed pathophysiological link between systemic hypertension and POAG centers around vascular dysregulation. Chronically elevated blood pressure may lead to arteriosclerotic changes in the small vessels supplying the optic nerve, resulting in compromised autoregulation, ischemia, and oxidative stress[6]. Additionally, elevated systemic blood pressure can increase episcleral venous pressure, subsequently impairing aqueous humor outflow and elevating IOP. Nocturnal hypotension, a common phenomenon in treated hypertensive patients, may exacerbate this process by inducing ischemic damage during the night when optic nerve perfusion is already reduced[7].

Several epidemiological studies have investigated the association between hypertension and POAG, but results have remained inconsistent. Some studies suggest a positive association, where hypertension increases the risk of POAG due to the mechanisms described above. Others report an inverse or U-shaped relationship, indicating that both very high and very low blood pressure levels may contribute to glaucoma progression[8]. Moreover, certain findings imply that the duration and control of hypertension, as well as the class of antihypertensive medication used, may modulate this risk. For instance, beta-blockers may reduce IOP while calcium channel blockers may impair optic nerve perfusion, complicating the risk profile further[9]. There is also growing concern about the implications of aggressive antihypertensive therapy. Excessive blood pressure reduction, especially during nocturnal periods, may result in optic nerve hypoperfusion, accelerating glaucomatous damage despite controlled IOP[10]. This phenomenon underscores the importance of individualized blood pressure targets in patients with glaucoma or those at high risk[11]. In Pakistan and other low- to middle-income countries, the dual burden of non-communicable diseases like hypertension and avoidable visual disability due to glaucoma presents a unique public health challenge. The lack of awareness, limited access to eye care, and poor blood pressure control further compound the issue[11].

Objective: To determine the association between systemic hypertension and primary open-angle glaucoma in adults.

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METHODOLOGY

This case-control analytical study was conducted at Sahiwal Teaching Hospital, Sahiwal from February 2023 to July 2023 A total of 325 participants were included, comprising 162 cases (patients with POAG) and 163 controls (individuals without POAG), matched for age and gender. The sample size was calculated using OpenEpi software, based on previous literature: 95% confidence level, 80% power, 25% exposure in controls, and an expected odds ratio of 2.0.

Inclusion Criteria: Participants aged 40 years or above, diagnosed with primary open-angle glaucoma based on clinical and visual field criteria, or healthy individuals undergoing routine eye check-ups without glaucomatous findings, were included.

Exclusion Criteria: Participants were excluded if they had secondary glaucoma (e.g., traumatic, uveitic), history of intraocular surgery other than uncomplicated cataract extraction, coexisting retinal or optic nerve diseases, neurological conditions affecting vision, or diabetes mellitus.

Data collection: Demographic and clinical data were obtained using a structured questionnaire. This included information on age, gender, duration of hypertension, medication use, and lifestyle factors. Blood pressure was measured using a calibrated mercury sphygmomanometer in a sitting position after a five-minute rest. Primary open-angle glaucoma was defined by open anterior chamber angles on gonioscopy, glaucomatous optic disc changes such as a cup-to-disc ratio greater than 0.6, corresponding visual field defects on Humphrey perimetry, and intraocular pressure greater than or equal to 21 mmHg. Systemic hypertension was defined as a history of hypertension, use of antihypertensive medication, or a blood pressure reading ≥140/90 mmHg on at least two separate occasions. All participants underwent a detailed ophthalmologic examination, including visual acuity testing, slit-lamp biomicroscopy, intraocular pressure measurement using Goldmann applanation tonometry, gonioscopy, and dilated fundus examination for optic nerve head assessment. Visual field analysis was performed using the Humphrey Field Analyzer.

Statistical Analysis: Data were analyzed using IBM SPSS Statistics version 17. Categorical variables were presented as frequencies and percentages, while continuous variables were expressed as mean ± standard deviation. The Chi-square test was used to assess associations between hypertension and POAG. Odds ratios with 95% confidence intervals were calculated to quantify the strength of association. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 325 participants were enrolled in the study, comprising 162 patients in the POAG group and 163 individuals in the control group. The mean age of participants was 59.3 ± 8.2 years in the POAG group and 58.6 ± 7.9 years in the control group (p = 0.43). Males constituted 54.3% of the POAG group and 51.5% of the control group (p = 0.61), indicating no significant gender difference between the groups. Systemic hypertension was significantly more prevalent in the POAG group (66.7%) compared to controls (45.4%), showing a strong association (p < 0.001). Other variables such as smoking history, BMI, and family history of glaucoma did not differ significantly between groups. However, a longer duration of hypertension (>10 years) was notably more common among POAG patients (35.1% vs. 18.9%, p = 0.03).

Table 1: Demographic Characteristics of Study Participants

Variable	POAG Group (n=162)	Control Group (n=163)	p-value
Age (years), mean ± SD	59.3 ± 8.2	58.6 ± 7.9	0.43
Male gender, n (%)	88 (54.3%)	84 (51.5%)	0.61
Systemic hypertension, n (%)	108 (66.7%)	74 (45.4%)	<0.001
Smoking history, n (%)	49 (30.2%)	45 (27.6%)	0.63
Body Mass Index (kg/m²), mean ± SD	26.1 ± 3.7	25.7 ± 3.9	0.29
Family history of glaucoma, n (%)	21 (13.0%)	17 (10.4%)	0.45
Duration of hypertension >10 yrs*	38 (35.1%)	14 (18.9%)	0.03

In multivariate logistic regression analysis, systemic hypertension remained an independent and statistically significant risk factor for primary open-angle glaucoma (adjusted OR = 2.18, 95% CI: 1.35–3.52, p = 0.002). Age showed a non-significant association with POAG (adjusted OR = 1.02, p = 0.24), indicating minimal impact. Male gender also did not significantly influence the risk (adjusted OR = 1.11, p = 0.61), nor did smoking status (adjusted OR = 0.93, p = 0.74).

Table 2: Multivariate Logistic Regression Analysis

Variable	Adjusted OR	95% CI	p-value
Systemic Hypertension	2.18	1.35–3.52	0.002
Age	1.02	0.98–1.07	0.24
Gender (Male)	1.11	0.73–1.69	0.61
Smoking	0.93	0.61–1.42	0.74

Among hypertensive participants, those in the POAG group had a longer duration of hypertension compared to controls. Only 26.9% of POAG patients had hypertension for less than 5 years, versus 43.2% in the control group. Conversely, 35.1% of POAG patients had hypertension for more than 10 years, compared to just 18.9% of controls. This difference was statistically significant (p = 0.03)

Table 3: Association Between Duration of Hypertension and POAG

Duration of Hypertension	POAG Group (n=108)*	Control Group (n=74)*	p-value
<5 years	29 (26.9%)	32 (43.2%)	0.03
5–10 years	41 (38.0%)	28 (37.8%)	
>10 years	38 (35.1%)	14 (18.9%)	

*Only hypertensive participants included in this table.

Only 36.1% of POAG patients were managed with monotherapy compared to 55.4% in the control group. Notably, 25.0% of POAG patients were on three or more medications versus just 10.8% of controls.

Table 4: Number of Antihypertensive Medications Used by Participants

No. of Medications	POAG Group (n=108)*	Control Group (n=74)*	p-value
Monotherapy	39 (36.1%)	41 (55.4%)	0.02
Dual therapy	42 (38.9%)	25 (33.8%)	
≥3 medications	27 (25.0%)	8 (10.8%)	

*Only hypertensive participants included in this table.

DISCUSSION

This study aimed to evaluate the relationship between systemic hypertension and the risk of developing primary open-angle glaucoma (POAG) in adults. The findings revealed a statistically significant association, with hypertensive individuals having more than twice the odds of developing POAG compared to normotensive controls. The association observed in this study supports the hypothesis that vascular dysregulation plays a critical role in the pathogenesis of glaucoma[11]. Chronic hypertension may contribute to structural changes in the small vessels supplying the optic nerve, compromising autoregulation and perfusion pressure. These changes may eventually lead to ischemia and optic nerve head damage, especially in patients with elevated or even borderline intraocular pressure. Furthermore, elevated episcleral venous pressure in hypertensive individuals may impair aqueous outflow, contributing to increased intraocular pressure, a known risk factor for glaucomatous optic neuropathy[12]. An important observation in this study was that the duration of hypertension appeared to influence the risk of POAG. Participants with more than 10 years of hypertension had a significantly higher prevalence of POAG compared to those with shorter durations, which aligns with previous literature suggesting that cumulative vascular damage over time may exacerbate optic nerve susceptibility[13]. Similarly, patients on multiple antihypertensive medications (≥3 drugs) also showed a higher frequency of POAG, although this may reflect more severe or long-standing hypertension rather than a direct effect of the medications themselves. The literature on this association has been mixed. While some population-based studies, such as the Rotterdam Study and the Barbados Eye Study, reported a positive association between hypertension and

POAG, others found either a null or even inverse relationship depending on how blood pressure and glaucoma were measured and defined. The discrepancy may stem from differences in study design, patient populations, control for confounding variables, and the dynamic relationship between systemic blood pressure and ocular perfusion pressure[14]. This study also adds to growing concerns regarding nocturnal hypotension, a side effect of aggressive antihypertensive therapy. Though not directly evaluated in this study, previous evidence suggests that significant drops in blood pressure during the night can reduce optic nerve perfusion, especially in patients with normal-tension glaucoma[15]. The finding that POAG was more prevalent in those using multiple medications may indirectly reflect this phenomenon, though further studies using ambulatory blood pressure monitoring would be necessary to confirm this[16]. Our findings highlight the need for a multidisciplinary approach in managing patients with systemic hypertension who are at risk for glaucoma[17]. Ophthalmologists should routinely inquire about blood pressure history and medication use when assessing patients for glaucoma. Conversely, primary care physicians and cardiologists should consider regular eye screenings for their hypertensive patients, particularly those with longstanding disease[18]. There are several strengths to this study, including a reasonably large sample size, strict inclusion/exclusion criteria, and the use of standardized diagnostic procedures for POAG. However, the study also has limitations. The case-control design limits our ability to establish causality. Additionally, we did not assess diurnal blood pressure fluctuations or ocular perfusion pressure directly, which could have provided further insight into vascular mechanisms. Also, potential confounders such as socioeconomic status, diet, and medication adherence were not evaluated in depth.

CONCLUSION

It is concluded that systemic hypertension is significantly associated with an increased risk of developing primary open-angle glaucoma (POAG) in adults. The findings suggest that individuals with hypertension, particularly those with a disease duration longer than 10 years or requiring multiple antihypertensive medications, are at a higher risk of glaucomatous optic nerve damage. Systemic hypertension remained an independent risk factor for POAG even after adjusting for confounders such as age, gender, and smoking.

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