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Research Article

Association of Trabecular Meshwork-Related Gene Variants with Glaucoma: Insights from the Belagavi Region of Karnataka

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Abstract

Background: Primary Open-Angle Glaucoma (POAG) is a chronic, progressive optic neuropathy and a leading cause of irreversible blindness worldwide. Genetic predisposition plays a crucial role in POAG pathogenesis, with variants in MYOC, OPTN and MMP9 genes implicated in disease susceptibility. However, their contribution in the Indian population remains poorly understood. This study investigated the association of selected Single Nucleotide Polymorphisms (SNPs) in MYOC (rs74315339, rs74315330), OPTN (rs11258194, rs2234968) and MMP9 (rs17576, rs2250889) with POAG in a Belagavi region.

Methods: A case-control study was conducted including 24 POAG patients and 20 age- and sex-matched healthy controls. Genomic DNA was extracted from peripheral blood and genotyping was performed using PCR followed by Restriction Fragment Length Polymorphism (RFLP) analysis. Allele and genotype frequencies were compared using chi-square tests, with $p < 0.05$ considered statistically significant.

Results: The mean age of POAG patients was 64.1 ± 10.8 years, with a male-to-female ratio of 1.7:1. Genotypic analysis revealed significant associations of OPTN rs2234968 and MYOC rs74315339 with POAG. The A/G genotype of OPTN rs2234968 was observed in 23.8% of cases versus 14.3% of controls ($\chi^2 = 7.22$, $p = 0.027$). Similarly, the C/A genotype of MYOC rs74315339 was more frequent in cases (70.8%) than controls (50%) ($\chi^2 = 6.41$, $p = 0.041$). OPTN rs11258194, MYOC rs74315330 and MMP9 rs2250889 were monomorphic, while MMP9 rs17576 showed no significant association.

Conclusion: This study provides the first evidence of OPTN rs2234968 and MYOC rs74315339 polymorphisms distribution in the Belagavi region Karnataka India. Population-specific variability highlights the need for larger, multicentric studies and functional validation to establish their role in POAG pathogenesis.

Keywords: Primary Open-Angle Glaucoma (POAG); Myocilin; Optineurin; Restriction Fragment Length Polymorphism (RFLP); Genotype

Introduction

Glaucoma is a multifactorial optic neuropathy characterized by progressive degeneration of retinal ganglion cells, optic nerve damage and corresponding visual field loss. It is the second leading cause of irreversible blindness globally, affecting an estimated 76 million individuals as of 2020, a figure projected to rise to over 111.8 million by 2040 [1]. Among the various subtypes of glaucoma, primary open-angle glaucoma (POAG) is the most common, particularly in individuals over 40 years of age [2].

Although elevated Intraocular Pressure (IOP) is a major risk factor, it is now well established that glaucoma is not solely an ocular hypertensive disease but also has a significant genetic component [3]. The pathophysiology of POAG involves complex interactions between environmental and genetic factors, making it imperative to explore the genetic underpinnings of the disease for better diagnosis, prevention and management [4].

Recent advances in molecular genetics have led to the identification of several genes implicated in POAG, including Myocilin (MYOC), Optineurin (OPTN) and Matrix Metalloproteinase 9 (MMP9) [5,6]. MYOC mutations were among the first to be linked to POAG and are particularly associated with juvenile-onset glaucoma [7]. The gene encodes a protein involved in the regulation of intraocular pressure through aqueous humor outflow. OPTN, initially associated with normal-tension glaucoma, plays a role in neuroprotection and apoptosis and is believed to affect the survival of retinal ganglion cells [8]. MMP9 encodes an enzyme involved in extracellular matrix remodeling and has been hypothesized to influence the biomechanical properties of the optic nerve head, potentially contributing to glaucoma pathogenesis [9]. Single Nucleotide Polymorphisms (SNPs) in these genes may act as genetic markers for disease susceptibility, although results across populations have been inconsistent, underscoring the need for population-specific investigations.

In addition to MYOC and OPTN, matrix metalloproteinases, particularly MMP9, have emerged as potential contributors to glaucoma pathogenesis due to their role in Extracellular Matrix (ECM) remodeling and IOP regulation. MMP9 dysregulation may contribute to increased resistance and elevated IOP, a key risk factor in POAG [10,11]. Several studies have reported altered MMP9 expression in glaucomatous eyes, indicating a genetic and molecular involvement in disease progression [12,13].

In the Indian context, studies investigating the role of MYOC and OPTN mutations in POAG have yielded varied results. Kaur, et al., analyzed 251 Indian POAG patients and identified MYOC mutations in 0.8% and OPTN mutations in 0.4% of cases, suggesting a relatively low prevalence of these mutations in the Indian population [14]. Mukhopadhyay, et al., identified two disease-associated MYOC mutations (Gln48His and Pro370Leu) in Indian POAG patients, highlighting the gene's variable contribution to disease pathogenesis in this population [15]. Several other studies have reported the presence of MYOC and OPTN variants in Indian POAG patients, but the overall contribution of these genes to POAG pathogenesis in India remains unclear [15,16]. The low mutation frequency observed in these studies may indicate a polygenic or multifactorial basis of POAG in the Indian population, potentially involving other genes or environmental interactions that require further investigation.

There is a scarcity of comprehensive genetic studies on MYOC, OPTN and MMP9 polymorphisms in the Indian population, leading to limited understanding of their collective role in the pathogenesis of POAG in Indian patients. Given the genetic diversity of the Indian population and the high burden of undiagnosed glaucoma, there is the requirement of studies to elucidate the role of MYOC and OPTN polymorphisms in POAG among Indian patients, which could facilitate early diagnosis, risk stratification and the development of targeted therapeutic interventions.

Although several studies have explore MYOC, OPTN and MMP9 variants in India population, no such study has been reported from the Belagavi region, a region with distinct genetic and environmental characteristics. There for present study aimed to evaluate the association of MYOC and OPTN gene polymorphisms with primary open-angle glaucoma in this population.

Materials and Methods

Study Population

The study was conducted at the Prabhakar Kore's Basic Science Research Center, Belagavi, India to study the association of the single nucleotide polymorphism with POAG. The inclusion criteria for cases comprised patients diagnosed with glaucoma, were ≥18 years of age, had IOP >21 mmHg, demonstrated open angles on gonioscopy, had characteristic glaucomatous optic nerve head changes such as a cup-to-disc ratio >0.4, glaucomatous visual field defects, and/or other optic disc changes including polar notching, deep cupping, peripapillary hemorrhages or thinning of the neuroretinal rim. Patients were excluded if they IOP<21 mmHg, neovascular glaucoma or any other ocular conditions that could confound the diagnosis of glaucoma, such as age-related macular degeneration, diabetic retinopathy, retinal abnormalities or high myopia. Cases with a history of ocular or head injury were also excluded. For control, the inclusion criteria comprised IOP <21 mmHg, no family history of glaucoma, normal anterior segment and optic disc features and no glaucomatous or retinal abnormalities. Individuals were excluded from if they had any ocular disease other than simple cataract, IOP >21 mmHg, cup-to-disc ratio >0.4, a family history of glaucoma or high myopia.

Cases and controls were age and sex-matched. Ethical approval was obtained from the Institutional Ethics Committee of Prabhakar Kore's Basic Science Research Center, Belagavi (Letter No.: KLESKF/IEC/23/13) and informed consent was collected from all participants.

Sample Collection and Genomic DNA Preparation

Peripheral blood samples (10 mL) were collected of all 44 participants in EDTA-containing vacutainer tubes from patients with POAG (cases)and individuals (control) meeting the inclusion and exclusion criteria and stored at 4°C, following the protocol described by Malinowska, et al. [17]. Genomic DNA was extracted from fresh peripheral blood of glaucoma patients and healthy controls using the QIAamp DNA Blood Mini Kit (Qiagen), according to the manufacturer's instructions. DNA concentration and purity were assessed using a NanoDrop2000c spectrophotometer (JH Bio) and integrity was confirmed by 0.8% agarose gel electrophoresis. The extracted DNA was resuspended in TE buffer (10 mM Tris-HCl, 1 mM EDTA, pH 8.0 for subsequent PCR amplification and analysis [18].

Polymerase Chain Reaction (PCR) Amplification

PCR amplification of selected Single Nucleotide Polymorphisms (SNPs) in the MYOC, OPTN and MMP9 genes was carried out for all 44 samples using gene-specific primers (details provided in Table 1). Each 25 μL reaction contained 50-100 ng of genomic DNA, 10 pmol of each primer, 200 μM of each dNTP, 1.5 mM$MgCl_2$, 1X Taq DNA polymerase buffer and 1 unit of Taq DNA polymerase (Thermo Fisher Scientific). The amplification was performed in a thermal cycler under the following cycling conditions: an initial denaturation at 95°C for 5 minutes, followed by 35 cycles of denaturation at 95°C for 30 seconds, annealing at optimized temperatures specific to each primer set for 30 seconds and extension at 72°C for 45 seconds. A final extension step was carried out at 72°C for 7 minutes.

Gene	SNP (rsID)	Primer Sequence (5′–3′)	Amplicon Size (bp)	Tm (°C)	Restriction Enzyme	Fragment Sizes (bp)
OPTN	rs11258194	F: TCCACTTTCCTGGTGTGTGA R: TTTCCAAGCTCTTCCTTCAA	218	51	StuI	T/T: 218 A/T: 218 + 174 + 44 A/A: 174 + 44
	rs2234968	F: GGGGGACAGCTCTATTTTCA R: CTGCTCACCTTTCAGCTGGT	224	51	HpyCH4V	A/A: 150+ 70 A/G: 224+ 150+ 70 G/G: 224
MYOC	rs74315339	F: GGCTGGCTCCCCAGTATATAT R: GATGACTGACATGGCCTGG	334	53	HpyCH4V	C/A: 334+268+66 A/A:334 C/C:268+66
	rs74315330	F: ATACTGCCTAGGCCACTGGA R: CAATGTCCGTGTAGCCACC	198	63	AlwNI	G/A: 198+159+39 A/A:198 G/G:159+39
MMP9	rs2250889	F: GTATTTGTTCAAGGATGGGTG R: AGACGTTTCGTGGGTTAT	122	56	NlaIV	C/G: 181+172+13 G/G: 181+172+119+62+13 C/C: 172+119+62+13
	rs17576	F: TCACCCTCCCGCACTCTGG R: CGGTCGTAGTTGGCGGCGGTGG	300	68	Bsob1	A/A: 211 A/G : 222+172+50 G/G: 172+50
Abbreviations: SNP, single nucleotide polymorphism; rs, reference SNP, A, adenine; T, thymine; C, cytosine; G, guanine; F, forward; R, reverse; bp, base pair; Tm, melting temperature						

Table 1: Primer sequences, amplicon size and restriction enzymes used for genotyping SNPs in OPTN, MYOC and MMP9 genes.

RFLP Analysis and Genotype Determination

PCR-amplified products of all 44 samples were digested using gene-specific restriction enzymes selected based on the SNPs of interest [19]. Each reaction mixture included 10μL of PCR product, 1X reaction buffer and 5-10 units of restriction enzyme, followed by incubation at 37°C for 4-16 hours under optimal conditions. The resulting DNA fragments were separated by electrophoresis on 6% polyacrylamide gels, stained with ethidium bromide and visualized under ultraviolet illumination using a UV transilluminator. Genotypes were assigned by analyzing the banding patterns. Alleles were scored accordingly and the number of samples with each genotype was documented for further analysis.

Statistical Analysis

Descriptive statistics were used to summarize demographic and clinical variables, with results expressed as mean ± Standard Deviation (SD) for continuous variables and number (percentage) for categorical variables. Genotype and allele frequencies were calculated and compared between glaucoma patients and controls using the Chi-square test. A p-value < 0.05 was considered statistically significant.

Results

Characteristics of Study Population

A total of 44 individuals were enrolled in the study, comprising 24 patients diagnosed POAG and 20 age- and sex-matched healthy controls. The demographic and clinical characteristics of the study population have been given in Table 2. The mean age of the patients with POAG was 64.1 ± 10.8 years, while that of the control group was 62.9 ± 10.8 years (p = 0.929). Among the POAG group, 15 (62.5%) were male and 9 (37.5%) were female, compared to 10 (50%) males and 10 (50%) females in the control group (p = 0.404). The average IOP in cases was 27.9 ± 8.9 mmHg, whereas it remained below 20 mmHg in the control group (p< 0.001). The mean cup-to-disc ratio in POAG patients was reported to be 0.8 ± 0.1in right eye and 0.7 ± 0.1 in left eye.

Characteristic	**POAG Cases**	**Control**	***p*-value**
	(N= 24)	**(N= 20)**	
Age (years), mean ± SD	64.1 ± 10.8	62.9 ± 10.8	0.929
Sex, n (%)			
Female	9 (37.5%)	10 (50.0%)	0.404
Male	15 (62.5%)	10 (50.0%)	
Residential location, n (%)			
Urban	11 (45.8%)	14 (70%)	0.577
Rural	13 (54.2%)	6 (30%)	
Comorbidities, n (%)			
Angioplasty	1 (2.6%)	0	0.729
Asthma	1 (2.6%)	0	
Cataract	16 (41%)	3 (27.3%)	
Diabetes mellitus	6 (15.4%)	1 (9.1%)	
Hypertension	11 (28.2%)	5 (20.0%)	
Thyroid disorders	2 (5.1%)	2 (18.2%)	
Myopia bilateral	1 (2.6%)	0	
Pterygium	1 (2.6%)	0	
Intraocular Pressure (mmHg)			
Right eye	27.9 ± 8.9	15.8 ± 2.8	<0.001*
Left eye	28.3 ± 8.7	16.0 ± 3.0	<0.001*
Affected eye, n (%)			
Left eye only	7 (29.2%)	NA	-
Right eye only	4 (16.7%)	NA	
Bilateral	13 (54.2%)	NA	
Central corneal thickness (μm)			

Right eye	541.1 ± 18.8	NA	-
Left eye	542.4 ± 18.4	NA	
Cup-to-disc ratio			
Right eye	0.8 ± 0.1	NA	-
Left eye	0.7 ± 0.1	NA	
SD: Standard Deviation; POAG: Primary Open-Angle Glaucoma; N/n: Number of participants; NA: Not Applicable; mmHg, millimeter of mercury; μm: Microns			

Table 2: Demographic data and clinical characteristics of the study population.

Comparison of Genotype Frequencies Between POAG Cases and Controls for Selected SNPs

OPTN rs11258194 showed no polymorphism in the study population. All individuals in both groups were homozygous for the T/T genotype. For OPTN rs2234968, the A/A genotype was found in 50% of POAG cases and 55% of controls. The heterozygous A/G genotype was observed in 45.8% of cases and 40% of controls, while the G/G genotype was rare in both groups (4.2% in cases, 5% in controls). Allele frequencies for the A allele were 72.9% in cases and 75% in controls, while the G allele was 27.1% and 25%, respectively. No statistically significant difference was observed ($\chi^2 = 0.115$, $p = 0.944$) (Fig. 1). In MYOC rs74315339, the C/A genotype was most common among both cases (58.3%) and controls (60%), followed by C/C in 41.7% of cases and 20% of controls. The A/A genotype was present only in controls (20%). The allele frequencies were similar across groups (cases: C = 70.8%, A = 29.2%; controls: C = 50%, A = 50%). The difference in genotype distribution showed a trend toward significance ($\chi^2 = 5.00$, $p = 0.082$), suggesting possible association pending validation in a larger sample. For MYOC rs74315330, no polymorphism was observed; all individuals were homozygous for the A/A genotype (Fig. 1). MMP9 rs2250889 showed no variation, with all individuals being homozygous for the C/C genotype. For MMP9 rs17576, the A/G genotype was the most frequent among both cases (58.3%) and controls (50%). A/A genotype was present in 20.8% of cases and 20% of controls, while the G/G genotype was observed in 20.8% and 30% of cases and controls, respectively. Allele frequencies for the A allele were 50% in cases and 45% in controls and for the G allele, 50% and 55%, respectively. The distribution was not significantly different ($\chi^2 = 0.464$, $p = 0.793$) (Fig. 1).

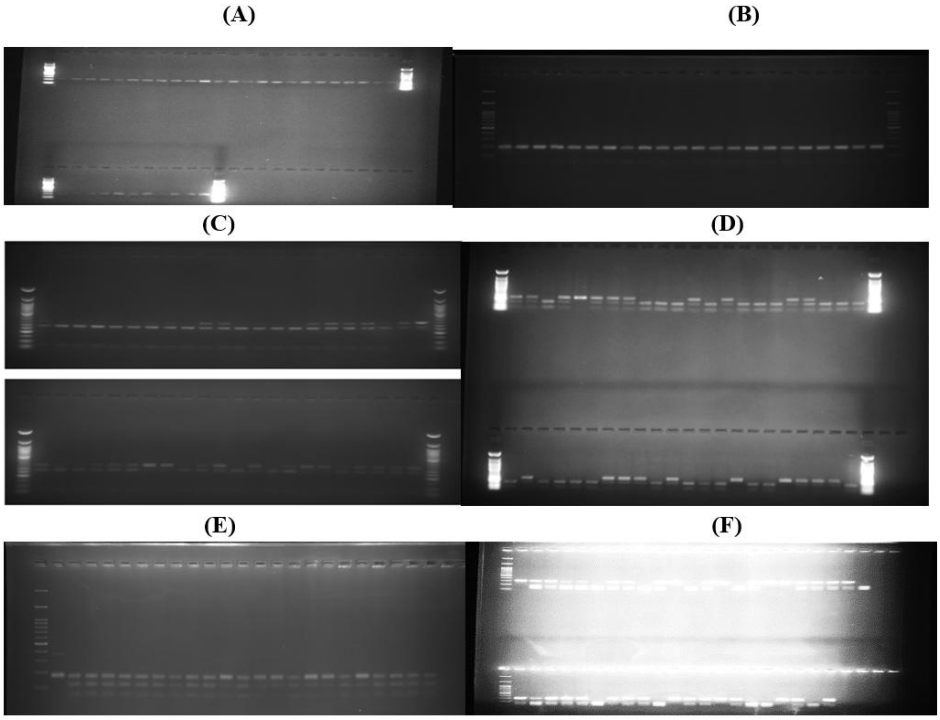

Figure 1: RFLP gel electrophoresis patterns showing genotype distributions for SNPs analyzed in the study. DNA was amplified by PCR and digested with specific restriction enzymes followed by separation on 3% agarose gels. (A)OPTN rs11258194 (T/T genotype – monomorphic), (B)OPTN rs2234968 – lanes show A/A, A/G and G/G genotypes distinguished by distinct fragment patterns, (C)MYOC rs74315339 – lanes represent heterozygous (C/A), homozygous wild-type (C/C) and A/A genotypes, (D)MYOC rs74315330 (A/A genotype – monomorphic), (E)MMP9 rs2250889 (C/C genotype – monomorphic), (F)MMP9 rs17576 – shows A/A, A/G and G/G genotypes based on specific banding patterns.

Association of OPTN, MYOC and MMP9 Gene Polymorphisms with POAG

Among the six SNPs examined, rs2234968 (OPTN) and rs74315339 (MYOC) showed statistically significant associations with POAG, while the other SNPs did not exhibit any meaningful differences between cases and controls (Table 3). The OPTN rs11258194 SNP was monomorphic in our study population, with all individuals (both cases and controls) exhibiting the T/T genotype, indicating no association with POAG. In contrast, the rs2234968 SNP showed a statistically significant association with disease status. The heterozygous A/G genotype was observed only among POAG cases and was absent in controls. Allele frequency analysis revealed a higher frequency of the G allele in cases (23.8%) compared to controls (14.3%) ($p = 0.027$), suggesting a possible role in disease susceptibility (Table 3). For the MYOC gene, rs74315330 was found to be monomorphic, with all participants exhibiting the A/A genotype. However, rs74315339 demonstrated a significant difference in allele distribution between cases and controls. The C allele was more frequent in POAG cases (70.8%) than in controls (50%), while the A allele was more prevalent in controls (50%) compared to cases (29.2%) ($p = 0.0405$), indicating a potential association with POAG risk (Table 3). Analysis of the MMP9 rs2250889 SNP revealed it to be monomorphic (C/C) across both groups, showing no association with POAG. Meanwhile, rs17576 did not show a statistically significant difference between cases and controls. However, a slightly higher G allele frequency was observed in controls (55%) compared to cases (50%), hinting at a potential protective effect, though this was not statistically significant ($p = 0.7752$) (Table 3).

SNP	Genotype Frequency (Cases / Controls)	Allele Frequency (Cases / Controls)	Chi-square	*p*-value	Genotype Association with POAG	Observation
OPTN rs11258194	T/T: 24 / 20 A/T: 0 / 0 A/A: 0 / 0	T: 100% / 100% A: 0% / 0%	0	1.000	No association	Monomorphic: T/T genotype observed in both cases and controls
OPTN rs2234968	A/A: 12 / 11 A/G: 11 / 8 G/G: 1 / 1	A: 76.2% / 85.7% G: 23.8% / 14.3%	7.222	0.027	Significant association	Higher G allele frequency in cases; $p = 0.027$
MYOC rs74315339	C/A: 14 / 12 A/A: 0 / 4 C/C: 10 / 4	C: 70.8% / 50% A: 29.2% / 50%	6.415	0.0405	Significant association	Higher C allele frequency in cases; $p = 0.0405$
MYOC rs74315330	A/A: 24 / 20 G/A: 0 / 0 G/G: 0 / 0	A: 100% / 100% G: 0% / 0%	0	1.000	No association	Monomorphic: A/A genotype in all subjects
MMP9 rs2250889	C/C: 24 / 20 C/G: 0 / 0 G/G: 0 / 0	C: 100% / 100% G: 0% / 0%	0	1.000	No association	Monomorphic: C/C genotype in all subjects
MMP9 rs17576	A/A: 5 / 4 A/G: 14 / 10 G/G: 5 / 6	A: 50% / 45% G: 50% / 55%	0.509	0.7752	No significant association	G allele slightly more frequent in controls; $p = 0.7752$
SNP: Single Nucleotide Polymorphism; RS: Reference SNP, A: Adenine; T: Thymine; C: Cytosine; POAG: Primary Open-Angle Glaucoma						

Table 3: Genotypic and allelic distribution of OPTN, MYOC and MMP9polymorphisms and their association in POAG cases and controls.

Discussion

It is known that the genomic construction of prevalent adult-metabolic disorders, is influenced by complex gene-gene and gene–environment interplay. The development of POAG may be influenced by lifestyle associated risk factors like smoking and the use of postmenopausal hormones, as well as nutritional factors like dietary fat and antioxidant intake [20]. POAG is a complex, multifactorial optic neuropathy characterized by progressive retinal ganglion cell loss and associated visual field defects.

Although elevated IOP remains the most significant risk factor, accumulating evidence suggests that genetic predisposition plays a critical role in POAG pathogenesis [21]. This is the first study which evaluated the association of selected SNPs in three genes implicated in POAG pathophysiology, OPTN, MYOC and MMP9, in a region of Belagavi. Our findings highlight valuable regional data to understand distinct genotypic and allelic patterns that may contribute to the underlying mechanisms of POAG in this population.

The myocilin protein, encoded by MYOC, is expressed all over the body along with Trabecular Meshwork (TM) tissue of the eyes. Increased Intraocular Pressure (IOP) is the primary risk factor for glaucoma and TM primarily regulates IOP [22]. It also known that OPTN has a role in a number of vital cellular processes, including vesicle transport, autophagy and NF-κB control. It was recently discovered that both normal tension glaucoma can result from a mutation in the OPTN interacting protein, specifically the duplication of the TANK Binding Protein 1 (TBK1) gene [23]. MMPs are believed to be crucial for a number of biological functions, including host defense, migration, angiogenesis, differentiation, cell proliferation, death and also in breaking of extracellular matrix . MMPs are found in practically every intraocular tissue and have a role in both pathological and normal processes in the eye. Glaucoma, a progressive neurodegenerative eye disease, is similarly linked to MMPs. The pathogenic mechanisms of glaucoma, intraocular pressure regulation and retinal ganglion cell death, are impacted by MMP activity [24].

Among the OPTN gene variants analyzed, rs11258194 was found to be monomorphic, exhibiting only the T/T genotype in both patients and controls. This observation is consistent with earlier studies reporting low polymorphic variability for this SNP in certain ethnic populations [25,26]. Conversely, rs2234968 showed a significant association with POAG, as the heterozygous A/G genotype was observed exclusively in POAG patients. The G allele was also more prevalent in the patient group compared to controls (23.8% vs. 14.3%; $p = 0.027$), suggesting its potential role as a risk allele. These findings align with previous reports that have implicated OPTN variants in glaucoma, although the precise pathogenic mechanism remains elusive [8,27]. OPTN is involved in autophagy and neuroprotection and mutations may impair cellular stress responses, contributing to retinal ganglion cell apoptosis [28].

For the MYOC gene, our analysis of rs74315330 revealed a monomorphic pattern (A/A genotype only), indicating no association with POAG in our study region. However, the rs74315339 SNP showed significant genotypic and allelic variation between cases and controls. The C allele was found to be substantially more frequent among patients (70.8%) than controls (50%) ($p = 0.0405$), suggesting a possible pathogenic role. Previous studies have established the involvement of MYOC mutations, particularly in the coding region, in early-onset and familial POAG cases [7,15]. The MYOC gene product, myocilin, is thought to be involved in trabecular meshwork function and aqueous humor outflow regulation. Pathogenic variants may lead to protein misfolding and endoplasmic reticulum stress, thereby contributing to elevated IOP and optic nerve damage.

In the context of MMP9, rs2250889 was monomorphic in both groups, suggesting no contribution to POAG susceptibility in our region. However, rs17576 demonstrated a non-significant trend, with the G allele being slightly more frequent in controls (55%) compared to cases (50%). Although not statistically significant, this distribution hints at a possible protective role of the G allele. MMP9 encodes an enzyme that modulates Extracellular Matrix (ECM) turnover, which is crucial for maintaining trabecular meshwork architecture and function. Dysregulation of MMP activity can lead to ECM accumulation and impaired aqueous outflow, thereby increasing IOP [29,30]. Several studies have reported altered MMP9 expression in glaucomatous eyes, supporting its potential involvement in disease pathophysiology [31,32].

The findings of this study are particularly relevant in the Indian context, where the prevalence and genetic profile of POAG may differ from Western populations. Kaur, et al., observed MYOC mutations in only 0.8% and OPTN mutations in 0.4% of Indian POAG patients, indicating low mutation frequency [14]. Mukhopadhyay, et al., similarly reported several rare MYOC variants in Indian patients, though their functional significance remains uncertain [15]. The low prevalence of canonical mutations underscores the need to explore additional genetic loci and ethnic-specific variants that may contribute to POAG in India. Our study adds to this growing body of evidence by identifying potentially relevant SNPs in a local patient region.

Moreover, the identification of a significant association between rs2234968 in OPTN and rs74315339 in MYOC with POAG highlights the importance of examining non-coding and regulatory variants that may modulate gene expression or splicing. The

functional consequences of these polymorphisms are yet to be elucidated and warrant further investigation using transcriptomic and proteomic approaches. In addition, environmental and epigenetic factors may interact with genetic predispositions to influence disease onset and progression, further complicating the genotype-phenotype correlation.

A key limitation of the current study is the relatively small sample size, which may restrict the statistical power and generalizability of the findings. Larger, multicentric studies with well-matched controls are needed to validate these associations. Furthermore, functional assays are essential to determine the biological relevance of identified SNPs. The role of gene-gene and gene-environment interactions also remains an open area for research.

The present study underscores the potential involvement of OPTN rs2234968 and MYOC rs74315339 polymorphisms in the pathogenesis of POAG in an Belagavi region. These findings pave the way for future investigations into the functional implications of these variants, which may reveal novel molecular mechanisms and therapeutic targets. Moving forward, genome-wide association studies and next-generation sequencing approaches can offer a comprehensive overview of genetic contributors to POAG. Integrating genetic data with clinical parameters and biomarkers may enable personalized risk stratification and early intervention strategies. Such efforts are crucial for developing targeted therapies and improving clinical outcomes in POAG patients, particularly in genetically diverse populations such as India.

Conclusion

The present study provides evidence for a potential association between specific genetic polymorphisms and the risk of developing POAG in an Belagavi region. While other SNPs such as OPTN rs11258194, MYOC rs74315330 and MMP9 rs2250889 appeared monomorphic and showed no association, MMP9 rs17576 revealed a trend suggestive of a protective effect of the G allele. These findings contribute to the growing body of genetic research on POAG and underscore the importance of population-specific studies in understanding the disease's molecular underpinnings. Further large-scale and functional studies are warranted to validate these associations and explore their biological significance. This could pave the way for the development of genetic screening tools and personalized management strategies for glaucoma, particularly in genetically diverse populations such as those in India.

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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Data Availability Statement

Not applicable.

Ethical Statement

The project did not meet the definition of human subject research under the purview of the IRB according to federal regulations and therefore, was exempt.

Informed Consent Statement

Informed consent was taken for this study.

Authors' Contributions

All authors contributed equally to this paper.

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