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Ocular Surface Health in Glaucoma Therapy: a consistently undervalued area of study

M N Islam[1]

Glaucoma remains a chronic, progressive optic neuropathy requiring lifelong management, most often through topical anti-glaucoma medications (AGMs). While the ophthalmic community has focused largely on intraocular pressure (IOP) control as the central therapeutic target, the silent and cumulative impact of these medications on the ocular surface has frequently been underestimated. The case series by Tania Rahman Chhara, Masmum Sababa, Syed Jahangir Kabir, Md Iftekher Iqbal, Samia Mazumder Koli published in this issue, brings overdue attention to this neglected but clinically significant dimension of glaucoma care.

The authors have presented three instructive cases highlighting distinct manifestations of ocular surface disease (OSD) associated with long-term AGM use—ranging from brimonidine-induced blepharoconjunctivitis and brinzolamide-related periocular dermatitis to netarsudil-associated reticular corneal epithelial edema. Each case demonstrates how even widely accepted medications can elicit unpredictable and sometimes visually threatening surface toxicity. Their careful documentation, thoughtful discussion, and literature correlation make this series both educational and clinically valuable for practitioners in our region.

This report underscores a crucial message: ocular surface integrity is as vital to long-term glaucoma management as intraocular pressure control itself. Chronic exposure to preservatives such as benzalkonium chloride (BAK), combined with multiple topical agents, can set in motion a cascade of tear-film instability, inflammation, and conjunctival fibrosis. The result is not only patient discomfort and poor adherence but also compromised outcomes of future filtration surgeries. A fact too often realized only after failure has occurred.

The study also reminds us that the condition (Ocular Surface Disease, or OSD) can manifest in many different forms, or present with a great diversity of symptoms and signs. It can masquerade as allergic conjunctivitis, chronic blepharitis, or even mimic infectious keratitis. Thus, a high index of suspicion, periodic ocular surface evaluation, and open communication with patients about their symptoms are indispensable. When intolerance is suspected, timely intervention—by switching to preservative-free formulations, reducing drug load, or using combination preparations—can avert irreversible surface damage.

In the broader context of glaucoma care in Bangladesh, this work carries special importance. Many of our patients are on long-term topical therapy with limited access to preservative-free options or adequate follow-up. Incorporating structured ocular surface assessment into routine glaucoma clinics would therefore be a simple yet transformative step. Moreover, multidisciplinary collaboration between glaucoma and cornea specialists can significantly improve outcomes for patients suffering from OSD secondary to medical therapy.

I commend Dr. Tania Rahman Chhara and colleagues for their meticulous clinical observation and contribution to local evidence on this under-recognized topic. Their work is a timely

reminder that successful glaucoma management is not defined solely by a lower IOP—but by a comfortable, functional eye capable of sustaining vision for life.

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Association of Serum Uric Acid Level with Primary Open-Angle Glaucoma

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Abstract

Background: Uric acid (UA) is a natural antioxidant molecule and has been proposed to have a neuroprotective effect against oxidative damage. Uric acid level in the serum of primary open-angle glaucoma (POAG) patients and healthy controls may be correlated with POAG.

Objective: The study aims to determine the uric acid level in the serum of primary open-angle glaucoma (POAG) patients and healthy controls to understand the correlation with POAG.

Methods: A case-control study was conducted among 92 patients, and there were two groups. Group A-46 patients with POAG were selected (case), and Group 46 normal patients (control) were selected following the inclusion and exclusion criteria. Color Fundus Photography (CFP), visual field analysis, and OCT of Optic Nerve head (ONH) & Retinal nerve fiber layer thickness (RNFL) were conducted. Serum uric acid level and serum creatinine level were determined. SPSS version 22 was used to analyze the data.

Results: The POAG group serum uric acid (4.58 ± 1.46mg/dl) was lower (14%, p=0.040) compared to the control group(5.23 ± 1.51mg/dl). The UA/creatinine ratio was 17.46% lower (p =0.031) in patients with POAG (5.27 ± 2.05mg/dl), compared to the control group (6.19 ± 1.95mg/dl). The mean level of UA was lowest in the severe POAG group (4.34 ± 1.41mg/dl), followed by the moderate POAG group (4.62 ± 0.93mg/dl), and the mild POAG group (4.76 ± 1.50mg/dl). No statistically significant difference was observed without significant differences (p =0.723). No gender difference is found regarding the UA ratio, although a Pearson correlation (r=-0.278; p=0.008) between vertical cup disc ratio (VCDR) in the male subgroup was significantly associated (r=-0.453; p=0.001). IOP and UA levels were negatively correlated for the male subgroup (r =-0.349, p = 0.015). Significant negative correlation between UA and VCDR was found (B = -1.69, p = 0.044).

Conclusion: Serum uric acid level is decreased in primary open-angle glaucoma and is negatively correlated with disease severity.

Keywords: Glaucoma, OCT, RNFL, uric acid, visual field, primary open-angle glaucoma

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Introduction

Primary open angle glaucoma (POAG) is the second leading cause of blindness worldwide after cataracts and around 57.5 million people worldwide are affected by POAG with a global prevalence of 2.2%.[1-4] Age-adjusted prevalence of low vision is about 12.1% and blindness is around 1.0%, and glaucoma is 0.8% is the third leading cause of eye disease in Bangladesh.[5] In Bangladesh about one million people are suffering from POAG.[6] Several contributing variables are related to POAG. Oxidative DNA damage causes trabecular meshwork (TM) degeneration, resulting in an increase in IOP, which leads to retinal ganglionic cell (RGC) damage.[7] Unbalance between the levels of ROS and antioxidant agents also negative for POAG.[8] Uric acid is a major antioxidant that protects cardiac, vascular, and neural cells from oxidative injury.[9-10] UA acts playing direct scavenging oxidizing role as singlet 02, HOCl, and peroxyl radicals as well as reserves the peroxidase activity of both SOD 1 and SOD 3.UA can also effectively prevent the cytoskeleton from the insults caused by peroxynitrite-induced inactivation of cellular enzymes. UA can also indirectly confer neuronal protection via the activation of astroglia.[11] Thats why UA is an attractive antioxidant system for the optic nerve, since neurons are remarkably susceptible to oxidative stress. Decreased serum uric acid level has already found in aqueous humor of both POAG and PACG patients.[12] The aim of this study is to measure UA levels in the blood POAG patients and healthy controls. Analysis of potential association between serum UA levels and visual field and optical coherence tomography (OCT) in POAG-affected eyes also main areas of focus in the study.

Method

A case-control study was conducted in department of Ophthalmology of Bangladesh Medical University A total of 92 patients included from June 2021-May 2022 and there were two groups. Group A-46 patients with POAG (case), and Group B-46 normal patients (control) were selected following the inclusion and exclusion criteria. Institutional Ethical Review Committee (IERC) approval was obtained.

Selection of patient for POAG: Inclusion criteria included: All eyes with a diagnosis of POAG, under IOP-lowering agents, and following surgery: Age –≥40 years, IOP ≥21 mmHg, Glaucomatous optic nerve head changes and visual field defect, Open iridocorneal angle assessed with Gonioscopy, and normal anterior chamber depth is considered for the patient's criteria.

Selection of patient for Healthy control: Normal controls were consecutively recruited from individuals who participated in health screenings during the study period. Age – ≥40 years, no family history or personal history of glaucoma, Intraocular pressure (IOP) <21 mmHg, Anterior chamber angle open, & vertical cup disc ratio ≤ 0.5.

Clinical examination procedure

All patients underwent a complete clinical evaluation including history, physical examination, relevant ocular examinations, fundus examination, some special ocular examinations like – IOP, visual field analysis, and gonioscopy. IOP was measured in primary gaze by Goldmann applanation tonometer. Angle assessment conducted by gonioscopy. Visual field examination was performed with central 24-2 program; SITA Strategy-Humphrey II 740 Visual Field Carl Zeiss Meditec, Jena, Germany) on both eyes. Visual fields were not analyzed in the presence of artifacts, learning effects, or defects indicating diseases other than glaucoma, such as homonymous hemianopia. In the POAG group, the severity of glaucoma damage was graded according to MD. Eyes with MD ≤ 6 dB were rated as affected by mild glaucoma, 6 Db<MD≤ 12Dbwhile those with MD >12 dB were rated as affected by severe glaucoma. Both eyes of each participant were dilated with Tropicamide 1% drops 10 to 15 min before OCT scanning with NIDEK RS 330. The Optic Disc Cube 200 × 200 protocol, specifically designed to position the cube scan on the ONH, was used. VCDR and average RNFL thickness was measured. A peripheral blood sample was collected from each participant at baseline, and tested for UA levels. Serum uric acid was measured by the uricase method and carried out by an automated analyzer. Serum creatinine level was measured by the enzymatic method and carried out by an automated analyzer.

Data analysis

Data were analyzed by SPSS 22. Unpaired-t test was used to compare two means of two groups, the ANOVA test was used to compare three means of three groups and the chi-square test had used to measure the association between two qualitative variables. The associations between ocular parameters in POAG and Healthy control had analyzed using Pearson's correlation.

Results

In POAG patients about 56% were male (n=25), and 44% were female (n=21)) and control participants 50% were male (n= 23), & 50% were female (n = 23). The mean age was 56.67±9.11 years in the POAG group and 51.3±9.38 years in the control group.

Table 1. Demographics, creatinine, UA and UA/Cr ratio of the patients with POAG

	POAG group (n=46)	Control group (n=46)	P value
Age	56.67±9.11	51.3±9.38	0.006^{s}
Gender (Male/Female)	25/21	23/23	0.676^{ns}
BMI (kg/m^2)	25.28±2.37	25.8±2.58	0.316^{ns}
S. Uric Acid (mg/dl)			
Male	4.83±1.41	5.86±1.1	0.009^{s}
Female	4.29±1.5	4.6±1.61	0.513^{ns}
Total	4.58±1.46	5.23±1.51	0.040^{s}
S. Creatinine (mg/dl)			
Male	1.05±0.29	0.91±0.15	0.043^{s}
Female	0.79±0.23	0.8±0.18	0.872^{ns}
Total	0.96±0.29	0.86±0.17	0.046^{s}
Uric Acid: Creatinine			
Male	5.04±1.91	6.49±1.43	0.004^{s}
Female	5.55±2.22	5.88±2.35	0.635^{ns}
Total	5.27±2.05	6.19±1.95	0.031^{s}

The UA levels of the POAG group were approximately 14.19% lower (p =0.04) than those of the control group. The mean serum UA of the total was 4.58±1.46 mg/dl in group A and 5.23±1.51 mg/dl in group B. The UA/Cr ratio was 17.46% lower (p = 0.031) in patients with POAG compared with the control group. The

mean serum UA/Cr ratios were 5.27±2.05 mg/dl in group A and 6.19±1.95 mg/dl in group B. In the male subgroup, the UA levels and UA/Cr ratios were significantly lower in POAG participants compared with controls (p = 0.009 and p = 0.004, respectively). In the female subgroup, the UA levels and UA/Cr ratios were not significantly different in POAG patients compared with controls (p = 0.513and p = 0.635 (Table-1).

Table II: Comparison of UA, UA/Cr ratio in subjects with POAG (group A), stratified according to the severity.

	Mild (n=29)	Moderate (n=5)	Severe (n=11)	p-value
Uric acid level				
Male	4.85±1.41	4.70±1.22	4.58±1.93	0.935^{ns}
Female	4.63±1.68	4.5±0.70	4.15±0.95	0.806^{ns}
Total	4.76±1.50	4.62±0.93	4.34±1.41	0.723^{ns}
Uric Acid: Creatine				
Male	5.08±1.99	5.04±0.56	4.86±2.42	0.976^{ns}
Female	6.01±2.64	5.24±1.18	4.89±2.35	0.659^{ns}
Total	5.45±2.28	5.06±1.25	4.88±2.32	0.750^{ns}

The MD, the POAG participants were divided into three subgroups with varying degrees of disease severity: 29 were divided into mild, 5 into moderate, and 11 into severe POAG. The mean UA level was lowest in the severe POAG group (4.34±1.41mmol/l), followed by the moderate POAG group (4.62±0.93 mmol/l) and then the mild POAG group (4.76±1.50 mmol/l), but the differences were not significant between the three groups (p =0.723)). The mean UA/Cr ratio was lowest in the severe POAG group (4.88±2.32) and the moderate POAG group (5.06±1.25) compared with the mild POAG group (5.45±2.28) (Table-3).

Table III: Multi Linear regression analysis of uric acid and uric acid: creatinine ratio with other parameters of POAG patients.

Variables	Serum uric acid (mg/dl)					
	Total		Male		Female	
	R	*P* value	R	*P* value	R	*P* value
IOP (mm of hg)	-0.178	0.090^{ns}	-0.349	0.015^{s}	-0.070	0.651^{ns}
VCDR	-0.278	0.008^{s}	-0.453	0.001^{s}	-0.147	0.341^{ns}
RNFL thickness (µm)	-0.166	0.275^{ns}	-0.133	0.536^{ns}	-0.047	0.840^{ns}
MD	-0.176	0.269^{ns}	-0.141	0.520^{ns}	-0.011	0.963^{ns}
Uric acid: Creatinine ratio						
IOP (mm of hg)	-0.168	0.109^{ns}	-0.333	0.021^{s}	-0.051	0.742^{ns}
VCDR	-0.319	0.002^{s}	-0.504	0.001^{s}	-0.109	0.480^{ns}
RNFL thickness (µm)	-0.022	0.886^{ns}	-0.039	0.920^{ns}	0.116	0.873^{ns}
MD	-0.011	0.941^{ns}	-0.021	0.858^{ns}	0.038	0.617^{ns}

Significant negative correlations were observed between IOP and UA levels in male subgroup (r = -0.349, p = 0.015). In addition, significant negative correlations were observed between VCDR and UA levels in all participants (r = -0.278, p = 0.008), and in the male subgroup (r = -0.453, p = 0.001), but not in the female subgroup (r = -0.147, p = 0.341). There were no significant correlations between UA levels and MD or RNFL thickness. Significant negative correlations were observed between IOP and UA/Cr in male subgroup (r = -0.333, p = 0.021). In addition, significant negative correlations were observed between VCDR and UA/Cr in all participants (r = -0.319, p = 0.002), and in the male subgroup (r = -0.504, p = 0.001), but not in the female subgroup (r=0.109, p=0.480). Table IV shows Multiple linear regression associations between UA and UA/Cr ratio with ocular parameters (n=46). In the total POAG group, there was a significant correlation between UA and VCDR (β=-1.690, p=0.044). In the male POAG group, there was a significant correlation between UA and VCDR (β=-1.663, p=0.041). There were no significant correlations between UA levels or UA/Cr ratios and VCDR or MD in the female group.

Table IV: Multiple linear regressions associations between uric acid and uric acid: creatinine with ocular parameters (n=46)

	Total POAG β (p value)		Male POAG β (p value)		Female POAG β (p value)	
	UA	UA/Cr ratio	UA	UA/Cr ratio	UA	UA/Cr ratio
VCDR	-1.690(0.044^{s})	-1.046(0.079^{ns})	-1.663(0.041^{s})	-1.101(0.070^{ns})	-1.660(0.527^{ns})	-0.796(0.839^{ns})
MD	-0.001(0.950^{ns})	-0.012(0.676^{ns})	0.00(0.996^{ns})	-0.013(0.736^{ns})	-0.013(0.708^{ns})	0.001(0.980^{ns})

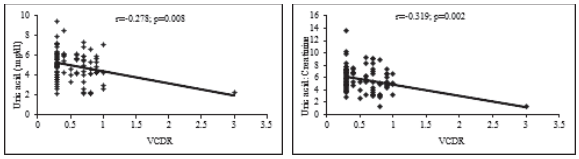

Figure 1: Negative significant Pearson correlation between VCDR with UA/Cr ratio.

Discussion

Study aim was to measure the serum UA level in POAG patients and in normal persons without POAG and also to compare the serum UA level between two groups and determine relationship between serum UA concentration and glaucoma severity.

Oxidative stress has been proposed as an etiologic factor in the pathophysiology of glaucomatous RGC death.[13] Mironczuk-Chodakowska et al., (2018) showed UA is one of the major non-enzymatic

antioxidants present in the human body. UA is one of the low molecular weight organic compounds and is the end product of an exogenous pool of purines and endogenous purine metabolism. The exogenous pool varies significantly with diet, and animal proteins contribute significantly to this purine pool. The endogenous production of uric acid is mainly from the liver, intestines, and other tissues like muscles, kidneys, and the vascular endothelium.[14] In addition, live and dying cells degrade their nucleic acids, adenine, and guanine into uric acid.[15] Previously potential roles for high levels of UA included- reduced risk for cancer and related mortality.[16] improved cognitive function, neuroprotective effects in stroke[17], protection against neurodegenerative diseases such as multiple sclerosis, Parkinson's disease, and Alzheimer's disease has been proved.[18]

In this present study, it was observed that the UA levels of the POAG group were approximately 14.19% lower ($p = 0.04$) than those of the control group. A similar pattern was observed when UA was compared between the POAG and control groups with respect to gender. In the male subgroup, the UA level was significantly lower($P<0.05$) in POAG participants compared with controls. Li et al. (2019) investigated serum UA concentrations in the Chinese population and found in the POAG group was approximately 12.77% lower than that of the control group, which supports the present study.[19] A comparable pattern was also observed when UA levels were compared between the POAG and control groups in male subjects, which closely resembled the present study. Similar observations regarding POAG patients showed significantly ($p<0.05$) lower levels of mean serum UA than healthy controls were also observed by Tang et al., (2021), Serra et al., (2021), and Li et al., (2017).[20] Glaucoma patients may have the high oxidative stress due to depletion of UA either by enhancing its consumption or by inhibiting its synthesis. Fabbrini et al. (2014) reported that subjects with a high UA level had 20.0–90.0% greater systemic nonenzymatic antioxidant capacity and lower levels of 30.0% of oxidative stress markers than those with lower UA levels.[21]

The UA/Cr ratio was approximately 17.46% lower ($p<0.05$) in patients with POAG compared with the control group. A comparable trend was observed when UA/Cr ratios were compared between the POAG and control groups with respect to gender. In the male subgroup, the UA/Cr ratios were significantly lower($p<0.05$) in POAG participants compared with controls. Based on disease severity according to their mean deviation (MD) in this current study, it was observed in patients with primary open angle glaucoma that 63.0% of patients had mild, 10.9% moderate, and 23.9% severe glaucoma. We found the mean UA level and UA/Cr ratios were lowest in the severe POAG group, followed by the moderate POAG group, and then the mild POAG group. But the difference is not significant possibly due to the small sample size. The mean serum UA levels significantly decreased with increasing glaucoma severity($p<0.05$). A possible explanation for the above finding could be that the progression of POAG is somehow related to increased activation of the oxidative stress system, thus causing a progressive consumption of UA and a consequent decrease in its serum level.

Moreover, Pearson correlations of the UA levels and UA/Cr ratios with the various ocular parameters showed a significant negative Pearson correlation of UA and UA/Cr ratio with VCDR respectively in total study subjects and in the male subgroup. There is also a significant negative correlation between the UA levels and UA/Cr ratios with IOP in the male subgroup. The new cases of POAG and treated cases of POAG patients, this might be a cause that serum uric acid levels do not correlate with intra-ocular pressure in total subjects. Tang et al., (2021) suggested that the topical drug effect is relatively small on plasma. So, plasma metabolites are essential to identify biological dysfunctions and provide information on metabolic alteration in POAG patients. However, there were no significant negative correlations between UA levels or UA/Cr ratios and IOP, VCDR, or MD in the female subgroup.

Serra et al. (2021) found a statistically significant negative correlation between the mean serum UA levels with MD, RNFL thickness, and VCDR parameters. Unexpectedly, this correlation was stronger for visual field parameters rather than for RNFL thickness. Actually, the investigators cannot rule out that the presence of motion artifacts on OCT images, due to inadvertent eye movements e.g. microsaccades and drift during the exam, may have reduced the reliability

of RNFL thickness values in their study [35]. The above findings are comparable with the present study.

As the correlation may also be affected by other factors, multivariate analyses were conducted to further investigate the association between UA levels and POAG. It was observed that there was a significant negative correlation between UA with VCDR (β =-1.690, p=0.044) in the total POAG group and in the male POAG group (β=-1.663, p=0.041). There were no significant negative correlations between UA levels or UA/Cr ratios and VCDR or MD in the female group. Li et al. (2019) observed in the overall POAG group, there was a significant negative correlation between UA levels and VCDR in total participants. In the male POAG subgroup, there was a significant negative correlation between UA levels and MD. However, there were no significant negative correlations between UA levels or UA/Cr ratio and VCDR or MD in the female subgroup. The above findings are comparable with the current study.

As our study showed, the number of male POAG participants was greater than the number of female participants. Serum UA level is not significantly lower(P=0.513) in female participants of the POAG group (4.29±1.5 mg/dl) in comparison to the control group (4.6±1.61 mg/dl) but lowered in the POAG group. and also, significantly not correlated with the severity. A possible explanation for this is due to the small sample size. The males had a higher risk of developing POAG than females in a population-based cross-sectional study of the Korean population, the prevalence of POAG was 5.5% in males versus 3.9% in females. The authors also illustrated the association between estrogen and the development of primary angle closure glaucoma in their previous study. As already aware, females have higher levels of estrogen than males across all different age groups. There is also evidence to suggest that estrogen is a protective factor against POAG in females and can also influence the levels of UA in the body. It has been shown that the UA level reference ranges differ in males and females. The normal range of UA was 3.7 to 9.2 mg/dL for males and 3.1 to 7.8 mg/dL for females. In addition, glaucoma prevalence is also higher in men than in women in Bangladesh.

Conclusion

The serum uric acid level is low in primary open angle glaucoma patients and is negatively correlated with disease severity. A possible involvement of serum uric acid levels in the pathogenesis of primary open angle glaucoma may present.

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Original Article

Treatment of Advanced Glaucoma Study (TAGS) – Primary Trabeculectomy vs Medical Therapy

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Abstract

Background: Advanced glaucoma remains a leading cause of irreversible blindness, particularly in low- and middle-income countries. The optimal initial treatment strategy, surgery versus medical therapy, remains uncertain.

Objective: This study aimed to compare the effectiveness and safety of primary trabeculectomy and primary medical therapy in newly diagnosed advanced primary open-angle glaucoma (POAG) in a Bangladeshi tertiary-care setting.

Methodology: This randomized controlled trial was conducted at Deen Mohd. Eye Hospital & Research Centre, Dhaka, January 2020 to December 2024. A total of 345 patients with advanced POAG were randomized to trabeculectomy (n = 172) or medical therapy (n = 173) groups. The primary outcome was intraocular pressure (IOP) reduction. The secondary outcomes included visual field mean deviation (VF MD), visual acuity, medication burden, and adverse events over 24 months. Data were analyzed using SPSS version 25.0, and statistical significance was set at $p < 0.05$.

Results: At 24 months, the mean IOP was significantly lower in the trabeculectomy group than in the medical therapy group (12.3 ± 4.9 mmHg vs 15.1 ± 4.2 mmHg; $p < 0.001$). The median number of topical glaucoma medications was 0 (IQR, 0–1) in the surgical arm vs. 2 (IQR, 1–3) in the medical arm ($p < 0.001$). VF MD loss was slightly less in the surgical arm (−14.5 ± 6.8 dB vs −16.2 ± 6.5 dB; p = 0.010). The rates of serious adverse events were comparable between the two groups (5.0 % vs. 4.0 %).

Conclusion: In Bangladeshi patients with advanced POAG, primary trabeculectomy provided superior IOP control and reduced dependence on topical medications while maintaining a safety profile comparable to that of primary medical therapy. These findings support early surgical intervention as a viable first-line treatment strategy in resource-constrained settings.

Keywords: Advanced glaucoma, trabeculectomy, medical therapy, intraocular pressure.

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Introduction

Glaucoma remains one of the leading causes of irreversible vision loss worldwide, with advanced disease contributing disproportionately to visual disability in low- and middle-income countries.[1] Primary open-angle glaucoma (POAG) predominates and is characterized by progressive optic neuropathy and corresponding visual field loss.[2] The principal therapeutic objective in POAG is sustained reduction of intraocular pressure (IOP), the only modifiable risk factor known to slow disease progression. Management traditionally begins with topical medications, while surgery, such as trabeculectomy, is reserved for eyes that are unresponsive to medical therapy or present at an advanced stage.[3]

For patients presenting with advanced glaucoma at diagnosis, the optimal initial management strategy—whether early surgical intervention or primary medical therapy—remains subject to debate. The Treatment of Advanced Glaucoma Study (TAGS) from the UK was designed to address this very question and found that primary trabeculectomy achieved lower mean IOP than primary medical therapy over two years while maintaining vision-related quality of life.[4,5] Subsequent longer-term follow-up confirmed sustained IOP control and reduced topical therapy burden in the surgical arm, although differences in visual-field outcomes remained modest.[6]

Despite these findings, extrapolating TAGS results to resource-limited settings is challenging. In Bangladesh, late presentation is common and long-term adherence to topical therapy is difficult due to cost, availability and socio-economic constraints.[7] Advanced glaucoma frequently manifests at tertiary referral centers, and limitations in access to subspecialty care and high surgical caseloads may influence outcomes.[8] In such contexts, primary trabeculectomy may offer more rapid and sustained IOP reduction, potentially mitigating further visual-field

loss during the vulnerable early treatment phase.

Previous randomized and observational studies globally have shown trabeculectomy to be effective in achieving lower IOP compared with pharmacologic therapy; however, postoperative complications, variability in surgeon experience and follow-up adherence remain important considerations.[9,10] Meanwhile, medication-based regimens often require lifelong strict adherence and may be associated with ocular-surface toxicity and drop-related adverse effects.[11] Evidence from Asian populations remains limited, and regional anatomic, economic and healthcare-delivery differences may influence treatment response and complication rates.[12]

The present study, therefore, undertakes a Bangladeshi adaptation of the TAGS trial design, comparing the effectiveness and safety of primary trabeculectomy versus primary medical therapy among patients with newly diagnosed advanced POAG. The study aims to evaluate IOP reduction, visual-field preservation, medication requirement and adverse-event profiles over 24 months in a real-world Bangladeshi tertiary-care setting. Such contextualized evidence is essential to inform national clinical guidelines and policy decisions in countries where late presentation is common and long-term topical therapy adherence remains a critical barrier to care.

Materials and Methods

This prospective randomized controlled trial was conducted at Deen Mohd. Eye Hospital & Research Center, Dhaka, Bangladesh. This study aimed to compare the effectiveness of primary trabeculectomy and primary medical therapy in newly diagnosed advanced primary open-angle glaucoma (POAG) from January 2020 to December 2024. A total of 345 eligible patients were enrolled and randomized (1:1) to trabeculectomy (n = 172) or medical therapy (n = 173) groups using computer-generated concealed allocation. Eligible participants were adults aged ≥40 years with newly diagnosed, untreated advanced POAG characterized by a mean deviation worse than –12 dB on standard automated perimetry, intraocular pressure (IOP) ≥21 mmHg on at least two visits, and open angles on gonioscopy. Patients were excluded if they had previous ocular surgery (except for uncomplicated cataract extraction), secondary glaucoma (such as neovascular, uveitic, or angle-closure), coexisting ocular diseases that could impair vision (e.g., macular degeneration or diabetic retinopathy), systemic contraindications to surgery or glaucoma medications, or inability to comply with follow-up. Baseline assessments included demographic data, best-corrected visual acuity (BCVA, logMAR), slit-lamp biomicroscopy, gonioscopy, Goldmann applanation tonometry, fundus examination, and Humphrey 24-2 visual field testing. Trabeculectomy with mitomycin-C was performed following a standardized protocol with postoperative corticosteroids tapered over eight weeks. The medical therapy group received stepwise topical treatment beginning with prostaglandin analogs, followed by beta-blockers, carbonic anhydrase inhibitors, or alpha-agonists, as required. Follow-up visits were scheduled at 1 week, 1 month, 6 months, 12 months, and every 6 months up to 24 months to assess the IOP, BCVA, and visual field indices. The data were analyzed using SPSS version 25.0. Statistical significance was set at $P < 0.05$. Informed consent was obtained, and confidentiality was maintained throughout the study.

Results

Table I: Baseline Characteristics of Study Participants (n = 345)

Variable	Trabeculectomy (n = 172)	Medical therapy (n = 173)
Age (years), mean ± SD	66.4 ± 11.7	66.6 ± 11.9
Male patients	106 (61.6)	101 (58.4)
Bilateral advanced glaucoma	68 (39.5)	67 (38.7)
Mean (SD) Baseline IOP (mmHg)	19.6 ± 6.1	19.2 ± 5.8
Mean (SD) Baseline VF mean deviation (dB)	−15.0 ± 6.4	−15.4 ± 6.3
Mean (SD) Baseline logMAR visual acuity	0.15 ± 0.25	0.16 ± 0.26

Table I presents the demographic and baseline clinical characteristics of the participants. The mean age was 66.5 ± 11.8 years, and approximately 60 % of participants were male. Bilateral advanced glaucoma was observed in 39 % of the cohort. Both treatment arms were similar with respect to baseline IOP (19.4 mmHg), VF mean deviation (−15.2 dB), and visual acuity (0.16 logMAR), indicating balanced randomization.

Table II: Primary Clinical Outcomes at 24 Months (n = 345)

Outcome	Trabeculectomy (n = 172)	Medical therapy (n = 173)	Mean difference (95 % CI)	p-value
Mean IOP (mmHg)	12.3 ± 4.9	15.1 ± 4.2	−2.8 (−3.9 to −1.7)	< 0.001
Change in IOP from baseline (mmHg)	−7.3 ± 6.2	−4.1 ± 5.9	−3.2 (−4.4 to −2.0)	< 0.001
VF mean deviation (dB)	−14.5 ± 6.8	−16.2 ± 6.5	+1.7 (0.4 to 3.0)	0.01
Change in VF from baseline (dB)	+0.5 ± 2.1	−0.8 ± 2.3	+1.3 (0.5 to 2.1)	0.004
logMAR visual acuity	0.18 ± 0.26	0.12 ± 0.24	+0.06 (0.01 to 0.11)	0.02
Mean number of topical glaucoma agents	0.5 ± 0.8 (median 0 [IQR 0 −1])	2.2 ± 1.1 (median 2 [IQR 1 −3])		<0.001

Table II shows the primary clinical outcomes at 24 months. The trabeculectomy group achieved a significantly lower mean IOP (12.3 ± 4.9 mmHg) than the medical-therapy group (15.1 ± 4.2 mmHg; $p < 0.001$). The reduction in IOP from baseline was greater after trabeculectomy (−7.3 mmHg vs −4.1 mmHg; $p < 0.001$). The mean VF mean deviation at 24 months was slightly better in the trabeculectomy arm (−14.5 ± 6.8 dB) than in the medical arm (−16.2 ± 6.5 dB; $p = 0.010$). A small but statistically significant difference in logMAR visual acuity was observed, favoring the medical group ($p = 0.020$). The surgical group required markedly fewer topical medications (median 0 vs 2; $p < 0.001$).

long-term drop use. There were no treatment-related deaths or vision-threatening infections.

Discussion

The present randomized controlled trial compared primary trabeculectomy with primary medical therapy for newly diagnosed advanced primary open-angle glaucoma (POAG) in a Bangladeshi population. The findings demonstrate that trabeculectomy achieved significantly greater intraocular pressure (IOP) reduction and reduced dependence on topical medication, while maintaining comparable visual-field outcomes and overall safety. These results are consistent with previous international studies,

Table III: Safety and Adverse Events up to 24 Months (n = 345)

Adverse event	Trabeculectomy (n = 172)	Medical therapy (n = 173)	p-value
Any safety event (AE or SAE)	79 (45.9)	86 (49.7)	0.49
Serious adverse event (any cause)	9 (5.2)	7 (4.0)	0.62
Death (all -cause)	3 (1.7)	3 (1.7)	1
Ocular hypotony requiring intervention	9 (5.2)	0 (0.0)	0.002
Early bleb leak	14 (8.1)	0 (0.0)	< 0.001
Late bleb leak / blebitis	3 (1.7)	0 (0.0)	0.09
Corneal epithelial defect	4 (2.3)	2 (1.2)	0.44
Ocular -surface irritation or allergy	38 (22.1)	52 (30.1)	0.11

Table III: summarizes adverse events recorded through 24 months. Overall event rates were comparable between treatment arms (45.9 % vs 49.7 %, $p = 0.49$). Surgery-related complications occurred only in the trabeculectomy group, including ocular hypotony (5.2 %) and early bleb leaks (8.1 %), all of which were successfully managed without vision loss. Ocular-surface irritation and drop-related allergies were more frequent among patients on medical therapy (30.1 %), reflecting preservative exposure and particularly the Treatment of Advanced Glaucoma Study (TAGS) conducted in the United Kingdom, which reported a similar magnitude of IOP reduction with trabeculectomy compared with medical therapy at both two- and five-year follow-up.[5,6]

In the current study, the mean IOP at 24 months was 12.3 mmHg in the trabeculectomy group and 15.1 mmHg in the medical group, representing a mean between-group difference of approximately 2.8 mmHg.

This outcome parallels the findings of King et al., who reported a 2.9 mmHg difference favoring trabeculectomy at 24 months.[5] The long-term TAGS follow-up further confirmed the persistence of this pressure differential over five years.[6] Such sustained IOP control is crucial, as evidence from major longitudinal trials has consistently shown that even small increments in IOP can substantially increase the risk of glaucomatous progression.[13,14] The Early Manifest Glaucoma Trial (EMGT) demonstrated that each 1 mmHg reduction in mean IOP lowered the risk of disease progression by nearly 10 %.[15] Therefore, the magnitude of IOP lowering achieved through trabeculectomy in this cohort is likely to translate into meaningful long-term visual preservation.

Visual-field mean deviation (VF MD) changes in this study were modest in both groups, with a slightly smaller decline in the surgical arm. This finding aligns with the TAGS five-year results and earlier findings from the Collaborative Initial Glaucoma Treatment Study (CIGTS), which demonstrated that while surgical and medical treatments can yield similar visual outcomes, surgery achieves lower IOP more consistently.[2,9] The slightly improved VF MD observed in the trabeculectomy arm may reflect not only greater IOP reduction but also reduced diurnal fluctuation, a parameter increasingly recognized as a risk factor for progression.[16]

Visual-acuity outcomes in the present trial showed a small difference (0.06 logMAR) favoring medical therapy, consistent with prior reports suggesting that postoperative cataract progression or transient hypotony may marginally affect central vision after trabeculectomy.[5] Importantly, this difference was clinically negligible and did not affect overall visual function or patient safety. The preservation of vision despite more intensive surgical intervention highlights the advances in surgical technique and postoperative management that minimize visual compromise following trabeculectomy.

A particularly relevant finding for the Bangladeshi context is the dramatic reduction in medication burden after surgery. At 24 months, the median number of topical agents in the trabeculectomy group was zero compared with two in the medical group. Similar patterns were observed in the TAGS trial and the CIGTS.[5,9] This finding carries important clinical and public-health implications in low- and middle-income countries, where chronic medication adherence is often limited by cost, accessibility, and patient education barriers.[7] Reduced dependence on multiple medications may improve long-term adherence, minimize ocular-surface toxicity, and decrease financial strain on patients.

Safety outcomes were broadly comparable between the two treatment modalities. The overall rate of adverse events did not differ significantly, and no treatment-related mortality occurred. Bleb-related complications and hypotony were observed exclusively in the surgical arm but were successfully managed without long-term sequelae. These findings align closely with previous, large, peer-reviewed reports that emphasize how trabeculectomy-related complications —while not uncommon—are generally manageable when the procedure is performed by experienced surgeons and supported by structured postoperative care.[17,18] Conversely, ocular-surface irritation and allergy were more frequent among patients receiving long-term topical therapy — a well-documented effect of preservatives such as benzalkonium chloride in anti-glaucoma medications.[10]

When interpreted collectively, these data reinforce that primary trabeculectomy is a safe and effective option for patients with advanced POAG, particularly where late presentation and medication non-adherence are prevalent. The current findings also expand the evidence base to a South Asian population, demonstrating that the physiological response to trabeculectomy and the relative safety profile remain consistent across geographic and ethnic groups. This consistency supports the external validity of major multicenter trials such as TAGS and CIGTS, confirming that their results are generalizable beyond Western populations.[9]

The implications for clinical practice in Bangladesh and comparable resource-limited settings are significant. The high prevalence of late-stage presentation, coupled with socioeconomic barriers to lifelong medical therapy, argues for consideration of early surgical intervention in selected patients. Modern trabeculectomy, when performed with meticulous technique and appropriate postoperative care,

provides durable IOP control with minimal long-term morbidity. Furthermore, expanding access to standardized surgical training and postoperative follow-up programs could further enhance outcomes in such environments.

In summary, this study corroborates previous international evidence that primary trabeculectomy offers superior IOP control and reduced medication burden compared with primary medical therapy, without compromising visual outcomes or safety. These findings advocate for reconsideration of treatment algorithms in regions like Bangladesh, where early surgical management may be a more practical and sustainable approach for patients presenting with advanced glaucoma.

Limitations of the study

There were some limitations of this study.

1. The single-center design may limit the generalizability of the findings to other settings, such as rural hospitals with different levels of surgical experience and patient follow-up.
2. The 24-month follow-up period may be insufficient to observe long-term differences in visual-field outcomes and cataract progression.

Conclusion

Primary trabeculectomy achieved greater intraocular pressure reduction and comparable visual field preservation compared to primary medical therapy in Bangladeshi patients with advanced POAG. The surgical approach significantly reduced the need for topical medication without increasing the rate of serious adverse events. These outcomes confirm that trabeculectomy can be a safe and effective first-line option for advanced glaucoma when performed using standardized protocols. In resource-limited settings, where late presentation and adherence challenges are common, early trabeculectomy may provide a more sustainable and effective pathway for long-term glaucoma control.

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Conflicts of interest

There are no conflicts of interest.

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Original Article

Prevalence of Neovascular Glaucoma in Retinal Diseases in a Tertiary eye care Centre of Bangladesh

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Abstract

Background: Neovascular glaucoma (NVG) is a severe sight-threatening condition resulting from retinal ischemia, leading to neovascularization in the anterior segment of the eye. The burden of retinal diseases is particularly significant in low- and middle-income countries including Bangladesh due to limited access to early screening.

Aim: To determine the prevalence of neovascular glaucoma in retinal diseases and assess its associated sociodemographic factors, visual status, and management practices among patients in a tertiary eye care center in Bangladesh.

Result: Among 38 respondents with retinal diseases, the prevalence of NVG was 97.4%, primarily linked to diabetic retinopathy 57.9% and central retinal vein occlusion 26.3%. Respondents had a mean age ± SD is 53.32 ± 9.433 years, with nearly equal gender distribution. Visual complaints were dominated by blurred vision, redness, and pain 71.1%. Comorbidities included diabetes 47.5% and hypertension 42.4%. Anterior segment findings highlighted iris neovascularization 78.9%, while posterior findings included hemorrhages 34.2% and macular edema 10.5%. Gonioscopy findings showed open angles in 63.2% and neovascularization in 28.9%. The most frequent intraocular pressure (IOP) reading status for the right eye was 35 mm of Hg, observed in 10.5% of cases, while the left eye had the highest frequency at 20 mm of Hg, occurring in 13.2% of cases. The post-surgical management of IOP in the cohort. A significant proportion, 34.2%, underwent post-surgical IOP monitoring, while 65.8% did not. Similarly, only 15.8% of patients received medications for IOP management post-surgery, indicating that the majority, 84.2%, did not require such intervention.

Methods: This cross-sectional study was conducted at Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, from October 2022 to November 2024. Patients aged ≥18 years with retinal diseases were included, while those with unrelated glaucoma or incomplete data were excluded. Data were collected using a pre-tested questionnaire and detailed ophthalmological evaluations, including gonioscopy and visual acuity assessments. Statistical analyses were performed using Statistical Package for Social Sciences (SPSS) version 26.0. Findings were presented by frequency and percent table.

Conclusion: Neovascular glaucoma is highly prevalent among patients with retinal diseases, particularly those with diabetic retinopathy and retinal vein occlusion in Bangladesh. Early detection and comprehensive management are crucial to mitigating its impact and preventing blindness in resource-limited settings.

Keywords: Neovascular glaucoma; Retinal diseases; Diabetic retinopathy; Central retinal vein occlusion; Gonioscopy; Visual impairment.

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Introduction

Pathogenesis of Neovascular Glaucoma is a serious form of glaucoma indicated by the development of abnormal blood vessels in the eye, usually caused by retinal ischemia, important to raised intraocular pressure and potential vision loss. It is a severe form of secondary glaucoma categorized by the proliferation of new blood vessels on the iris and within the anterior chamber angle, frequently important to significant visual impairment. This condition characteristically arises from retinal ischemia related with diseases such as proliferative diabetic retinopathy (PDR) and central retinal vein occlusion (CRVO) [1].

In Bangladesh, the prevalence of glaucoma among persons aged 40 years and older is approximately 2.1%, with primary open-angle glaucoma being the most common procedure [2]. Exact data on the prevalence of NVG in the Bangladeshi residents remain inadequate. Given the rising incidence of diabetes and associated problems in the region, it is believable that the prevalence of NVG is also growing.

Studies from adjacent countries provide some perceptions. For example, research from India designates that the prevalence of NVG among patients

with PDR can be as high as 21.3% [3]. Moreover, a hospital-based study stated that retinal vein occlusion accounted for 53% of NVG cases, followed by proliferative diabetic retinopathy at 41% [4].

Neovascular glaucoma is an upsetting difficulty of retinal ischemia, usually arising from complaints like proliferative diabetic retinopathy (PDR) or central retinal vein occlusion. It's characterized by the growth of new blood vessels in the iris and angle of the anterior chamber [5,6]. Though NVG accounts for a small proportion of all glaucoma cases worldwide, it significantly underwrites to blindness due to its rapid development and confrontation to conventional treatment [7].

In Bangladesh, the burden of retinal diseases is increasing in tandem with growing rates of diabetes and hypertension. A recent population-based study originates that diabetic retinopathy (DR) affects nearly 12% of persons with diabetes, with proliferative stages being a major contributor to NVG growth [8]. Despite this, there is incomplete complete data on the prevalence of NVG among patients with retinal diseases in the country. Understanding these tendencies is vital for the deterrence of permanent visual damage and blindness.

Data from India, a bordering country with similar healthcare contests, highlight the significant influence of NVG on patients with progressive retinal circumstances. Studies have stated NVG prevalence rates of up to 18% in PDR cases and 20–30% in retinal vein occlusions [9]. Still, management consequences remain suboptimal due to late presentation and limited access to specialized care [10].

This study aims to determine the prevalence of NVG among patients with retinal diseases and to assess associated sociodemographic factors, visual status, and management practices in a tertiary eye care center in Bangladesh.

Materials and Methods

This cross-sectional study was conducted at Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, over a two-year period from October 2022 to November 2024. The study included patients aged 18 years and older diagnosed with retinal diseases and those with confirmed diagnoses of NVG or at risk of NVG due to underlying retinal conditions. Patients with incomplete clinical records, secondary glaucoma unrelated to neovascularization or retinal diseases, or those unwilling to provide informed consent were excluded. Ethical approval was obtained from the Institutional Review Board of BSMMU, and written informed consent was secured from all participants.

Data were collected using a pre-tested, semi-structured questionnaire that captured sociodemographic details, clinical history, visual status, and management practices. Data was analyzed by using SPSS software (version 26.0) and findings were presented by frequency and percent table. Comprehensive ophthalmological evaluations, including gonioscopy and visual acuity assessments using Snellen's chart, were conducted. Anterior and posterior segment findings were documented to identify features associated with NVG.

Descriptive statistics summarized categorical variables as frequencies and percentages, while continuous variables were expressed as means and standard deviations. Results are presented in tabular and graphical formats to ensure clarity and comprehensiveness.

Results

Among the 38 respondents, the mean age was 53.32 ± 9.433 years, ranging from 34 to over 65 years. Gender distribution was nearly equal, with 52.6% male and 47.4% female.

NVG was diagnosed in 97.4% of respondents. Diabetic retinopathy was the leading cause, accounting for 57.9% of cases, followed by central retinal vein occlusion 26.3%, old hemi-retinal vein occlusion 7.9%, and branch retinal vein occlusion 2.6%. Miscellaneous conditions were identified in 5.3% of cases.

The most frequent IOP reading for the right eye was 35 mm of Hg, observed in 10.5% of cases, while the left eye had the highest frequency at 20 mm of Hg, occurring in 13.2% of cases.

The post-surgical management of intraocular pressure in the cohort. A significant proportion, 34.2%, underwent post-surgical IOP monitoring, while 65.8% did not. Similarly, only 15.8% of patients received medications for IOP management post-surgery,

indicating that the majority, 84.2%, did not require such intervention.

Anterior segment findings showed iris neovascularization in 78.9% of cases, with flare, pupil reactivity, and surface abnormalities each reported in 5.3%. Posterior segment findings included hemorrhages along the disc or elsewhere in 34.2% of cases, macular edema in 10.5%, and retinal detachment in 10.5%.

Gonioscopy findings revealed that 63.2% of respondents had an open angle, while 15.8% had a closed angle with new vessel growth. New vessels in the angle were observed in 7.9%, and narrow angles with new vessels in 5.3%.

Visual acuity assessments revealed that 6/60 was the most common in the right eye 28.9% and the left eye 26.3%. Severe impairments, such as no perception of light (NPL), were noted in 15.8% of the right eyes and 2.6% of the left.

Management strategies were diverse, with 39.5% receiving conservative treatment, 28.9% undergoing surgical interventions, and 28.9% receiving a combination of both.

Table 1: Distribution of the respondents by Socio Demographic Variables

Age	Frequency	Percent
34-44	5	13.2
45-54	17	44.7
55-64	12	31.6
65+	4	10.5
Total	38	100.0
Mean±SD	53.32±9.433	
Gender		
Male	20	52.6
Female	18	47.4
Total	**38**	**100.0**

Table 1. The age of the respondents ranged from 34 to 65 years and above, with a mean age of 53.32 ± 9.433 years. The majority 44.7% were aged between 45 and 54 years. The gender distribution was nearly equal, with 52.6% male and 47.4% female.

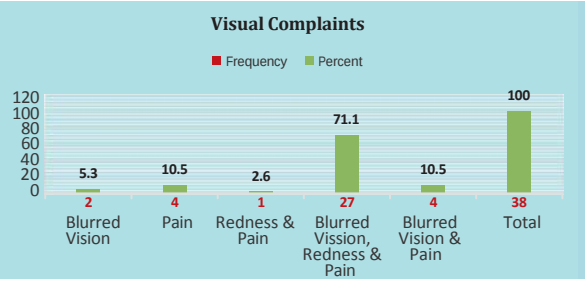

Figure 1: Distribution of Respondents by Visual Complaints

Figure 1 highlights the visual complaints reported by the 38 respondents. The majority (71.1%) experienced a combination of blurred vision, redness, and pain. Blurred vision and pain together were reported by 10.5%, while 5.3% had only blurred vision. Pain alone accounted for 10.5% of cases, and 2.6% reported redness and pain.

Table 2: Distribution of Respondents by Family and Personal History of Other Comorbidities

Family History				Personal History			
Comorbidities	N	Percent	Percent	Comorbidities	N	Percent	Percent
Other disease	20	40.00%	87.00%	Other diseases	1	1.70%	2.70%
Diabetes	20	40.00%	87.00%	Diabetes	28	47.50%	75.70%
Hypertension	12	24.00%	52.20%	Hypertension	25	42.40%	67.60%
Total	50	100.00%	217.40%	Cardiovascular	5	8.50%	13.50%
				Total	59	100%	159.50%

* Dichotomy group tabulated at value 1. Multiple response.

Table 2 shows the prevalence of comorbidities among respondents, considering both family and personal medical histories. In family history, 40% reported eye diseases and diabetes, 24% hypertension, with a total exceeding 100% due to multiple responses. For personal medical history, diabetes 47.5% was most common, followed by hypertension 42.4%, cardiovascular disease 8.5%, and other eye diseases 1.7%. Again, the total percentage exceeded 100% due to multiple comorbidities.

Table 3: Distribution of Respondents by Anterior and Posterior Segment Findings

Anterior Segment	Frequency	Percent	Posterior	Frequency	Percent
Corneal Opacity	1	2.6	Macular Edema	4	10.5
Flare	2	5.3	Hemorrhages	1	2.6
Pupil Reactivity	2	5.3	Retinal	4	10.5
Iris	30	78.9	Disc or else where	8	21.1
Surface	2	5.3	Hemorrhages &	13	34.2
Anterior Chamber Cell,					

Flare, Pupil Reactivity & Iris Neovascularization margin	1	2.6	Macular Edema, Hemorrhages & Disc or else where	1	2.6
			Exudates,	2	5.3
			Retinal	2	5.3
			Hemorrhages,	1	2.6
			Other	2	5.3
Total	**38**	**100**	**Total**	**38**	**100**

Table 3 summarizes the anterior and posterior segment findings among the 38 respondents. Most respondents 97.4% had a retinal disease, with diabetic retinopathy being the most prevalent 39.5%. Central retinal vein occlusion 28.9% was the second most common. Most respondents suffered for 1-3 years 84.2%. Anterior segment findings primarily included iris neovascularization at the margin 78.9%, while posterior segment findings were more diverse, with hemorrhages along with disc or elsewhere being the most common 34.2%.

Table 4: Diagnosis and Causes of Neovascular Glaucoma among Respondents

Neo-vascular glaucoma diagnosed by healthcare professional	**Frequency**	**Percent**
Yes	37	97.4
No	1	2.6
Total	**38**	**100.0**
Cause of your neo-vascular glaucoma		
Diabetic Retinopathy	22	57.9
Central Retinal Vein Occlusion	10	26.3
Old Hemi retinal vein Occlusion	3	7.9
Other	2	5.3
Brach retinal vein occlusion	1	2.6
Total	**38**	**100.0**

Table 4 shows the diagnosis and underlying causes of neovascular glaucoma among 38 respondents. Almost 97.4% were diagnosed, while 2.6% were not. Diabetic retinopathy was the most common cause 57.9%, followed by central retinal vein occlusion 26.3%, old hemi-retinal vein occlusion 7.9%, branch retinal vein occlusion 2.6%, and other miscellaneous causes 5.3%.

Table 5: Distribution of types of Retinal Diseases among Respondents

Any retinal diseases	**Frequency**	**Percent**
Yes	37	97.4
No	1	2.6
Total	**38**	**100.0**
Type of retinal disease		
Diabetic Retinopathy	15	39.5
Retinal Detachment	3	7.9
Central Retinal Vein Occlusion	11	28.9
Old Hemi retinal vein occlusion	4	10.5
Other	3	13.2
Total	**38**	**100.0**

Table 5 shows the prevalence and types of retinal diseases among 38 respondents. The vast majority, 97.4%, reported having a retinal disease. Diabetic retinopathy was the most prevalent at 39.5%, followed by central retinal vein occlusion 28.9%, old hemi-retinal vein occlusion 10.5%, retinal detachment 7.9%, and other 13.2%.

Table 6: Distribution of Respondents by Visual Acuity in Right and Left Eyes

Right Eye: (Snellen Chart Notation)	**Frequency**	**Percent**	**Left Eye: (Snellen Chart Notation)**	**Frequency**	**Percent**
6/60	11	28.9	3/60	1	2.6
6/36	4	10.5	6/60	10	26.3
6/00	2	5.3	CF1ft	3	7.9
6/12	2	5.3	6/12	5	13.2
3/60	2	5.3	6/36	2	5.3
NPL (No	6	15.8	6/18	3	7.9
CF1ft	2	5.3	6/24	2	5.3
6/18	2	5.3	CF2ft	1	2.6
CF2ft	3	7.9	2/60	1	2.6
CF3ft	3	7.9	CF3ft	3	7.9
			CF5ft	1	2.6
			6/90	3	7.9
			4/60	1	2.6
Hand Movement	1	2.6	Hand Movement	1	2.6
			NPL	1	2.6
Total	**38**	**100.0**	**Total**	**38**	**100.0**

Table 6 shows the distribution of visual acuity for the right and left eyes of 38 respondents, based on Snellen Chart Notation. For the right eye, 6/60 was the most common acuity 28.9%, followed by NPL 15.8%. Other acuities like CF3ft, CF2ft, and Hand Movement were less frequent. For the left eye, 6/60 was also the most prevalent 26.3%, followed by 6/12 13.2% and 6/90 (7.9%). Other acuities like CF3ft and NPL were less common.

Table 7: Distribution of most recent intraocular pressure reading status of right and left eye.

Most recent reading status Right eye (mm of Hg)	Frequency	Percent	Most recent reading status Left eye (mm of Hg)	Frequency	Percent
10	1	2.6	11	1	2.6
12	2	5.3	12	3	7.9
15	3	7.9	15	1	2.6
18	3	7.9	16	2	5.3
20	1	2.6	17	2	5.3
21	2	5.3	18	3	7.9
22	3	7.9	19	1	2.6
24	1	2.6	20	5	13.2
25	2	5.3	21	2	5.3
27	2	5.3	22	1	2.6
28	2	5.3	23	1	2.6
30	3	7.9	24	2	5.3
32	1	2.6	25	2	5.3
35	4	10.5	26	1	2.6
40	2	5.3	27	1	2.6
42	1	2.6	29	1	2.6
45	3	7.9	30	2	5.3
50	1	2.6	35	3	7.9
52	1	2.6	36	1	2.6
			40	1	2.6
Total	**38**	**100.0**	45	2	5.3
			Total	**38**	**100.0**

Table 7 presents the distribution of most recent readings for right and left eyes, measured in millimeters of Hg. Both eyes exhibited a range of readings, with the right eye showing a slightly wider range than the left. The most frequent reading for the right eye was 35 mm of Hg, observed in 10.5% of cases, while the left eye had the highest frequency at 20 mm of Hg, occurring in 13.2% of cases.

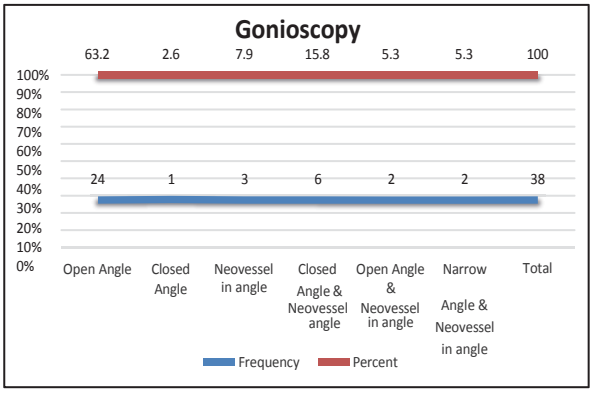

Figure 2: Distribution of Respondents by Gonioscopy Findings

Figure 2 presents the majority 63.2% had an open angle, while 7.9% showed neo vessel growth. Other findings included combinations of closed angle and neo vessel growth 15.8%, open angle with new vessels 5.3%, and narrow angle with new vessels 5.3%. Only 2.6% had a closed angle without additional findings.

Table 8: Distribution of Respondents by type of Management

Type of management		
Conservative (medications, lifestyle modifications)	15	39.5
Surgical	11	28.9
Both	11	28.9
N/A	1	2.6
Total	**38**	**100.0**

Table 8 details regarding management, 39.5% were managed conservatively, 28.9% surgically, 28.9% received both, and 2.6% had no specific management.

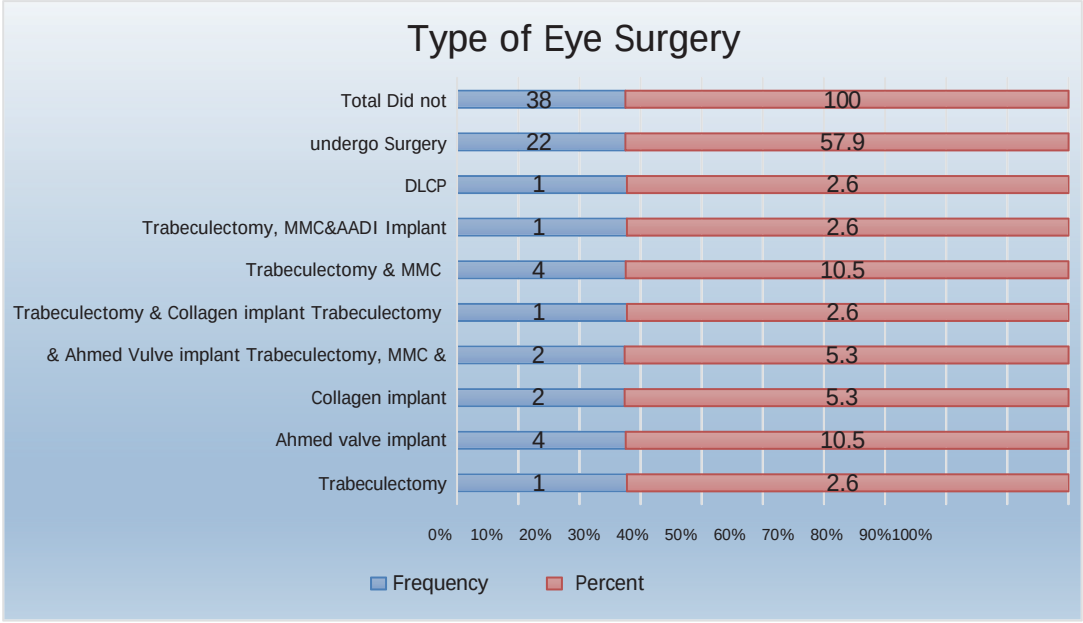

Figure 3: Distribution of Respondents by Type of Eye Surgery related to NVG

Figure 3 displays the types of eye surgeries related to NVG's performed on 38 respondents. 57.9% did not undergo surgery. Among those who did, Ahmed valve implant and trabeculectomy with Mitomycin C (MMC) were the most common 10.5% each. Other procedures included trabeculectomy with various combinations and implants, as well as Diode laser cyclophotocoagulation (DLCP).

Table 9: Distribution of Post-Surgical Intraocular Pressure Monitoring and Medication Management

Pressure Monitoring and Medication Management	Intraocular pressure measure since surgery		Medication for IOP management	
	Frequency	Percent	Frequency	Percent
Yes	13	34.2	6	15.8
No	25	65.8	32	84.2
Total	**38**	**100.0**	**38**	**100.0**

Table 9 summarizes the post-surgical management of IOP in a cohort of 38 patients. A significant proportion, 34.2%, underwent post-surgical IOP monitoring, while 65.8% did not. Similarly, only 15.8% of patients received medications for IOP management post-surgery, indicating that the majority 84.2% did not require such intervention.

Discussion

This study investigated the prevalence of neovascular glaucoma among patients with retinal diseases at a tertiary eye care center in Bangladesh. The findings revealed a remarkably high prevalence of NVG 97.4%, underscoring the significant burden of this sight-threatening condition in this population. This study aligns with previous studies conducted in developing countries, which have similarly reported high NVG prevalence among patients with retinal diseases [5]

The high prevalence of diabetic retinopathy 57.9% as the causing of NVG is uniform with the rising incidence of diabetes in Bangladesh [6] and its well-established correlation with NVG development [7]. The predominance of NVG in patients with DR 57.9% mirrors current literature, which identifies proliferative PDR as a major risk factor for NVG due to ischemia-induced angiogenesis [8; 11]. Likewise, CRVO accounted for 26.3% of cases, reliable with Indian studies that characteristic a significant percentage of NVG cases to retinal vein occlusion [12]. These data highlight the importance of addressing complete comorbidities like diabetes and hypertension, which were prevalent in 47.5% and 42.4% of respondents,

consistently, and are known to worsen retinal vascular circumstances.

Visual acuity assessments exposed severe damage in many patients, with 15.8% of right eyes showing NPL. These findings focus on the overwhelming impact of NVG on vision and excellence of life. Prior studies have equally recognized high rates of vision loss in NVG, mainly in patients awarding late or with progressive disease [10; 13].

Management strategies for NVG in this cohort diverse, with 39.5% receipt conservative treatment and 28.9% undergoing surgical interventions. The difficulty of NVG needs a multimodal method, frequently combination medical therapy, laser treatment, and surgery. Current progressions in anti-VEGF therapies and minimally invasive glaucoma surgeries (MIGS) have prolonged treatment choices, contribution possible assistances in governing intraocular pressure and neovascularization [14].

The considerable prevalence of NVG amongst patients with retinal diseases in Bangladesh underlines the necessity for improved screening and management protocols. Applying monotonous ophthalmic evaluations for persons with DR and CRVO, attached with timely therapeutic interventions, could mitigate the development to NVG. Public health initiatives concentrating on the management of systemic risk issues, such as diabetes and hypertension, are also authoritative in dropping the incidence of NVG [15].

The study also highlighted the significant visual impairment experienced by patients. Visual acuity ranged from 6/60 to no light perception, emphasizing the severe impact of NVG on vision. This aligns with the known pathophysiology of NVG, where improved IOP and retinal ischemia can lead to irreversible vision loss [16].

Conclusion

The results highlight the critical requirement for complete strategies to address NVG in patients with retinal diseases in Bangladesh. Initial discovery, rapid intervention, and actual management of systemic comorbidities are important to stop vision loss and recover patient outcomes. Collective efforts between healthcare providers and policymakers are essential to improve access to progressive therapies and implement public health actions aimed at dropping the burden of NVG.

Declaration of Interest Statement

The authors report no conflict of interest.

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Association of Estimated Glomerular Filtration rate (eGFR) with Primary Open Angle Glaucoma (POAG)

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Abstract

Background: Primary open-angle glaucoma (POAG) is a leading cause of irreversible blindness worldwide. Emerging evidence suggests a systemic link between POAG and chronic kidney disease (CKD) through shared mechanisms such as vascular dysfunction, oxidative stress, and renin–angiotensin system dysregulation.

Aim: This study aims to analyze the association between eGFR and primary open angle glaucoma.

Method: A group of patients aged ≥40 years who were diagnosed with POAG and without POAG and attending the Department of ophthalmology at BMU comprised the study patients. The study period was one and half year. eGFR was measured in both the groups. Statistical analysis of the result was conducting using computer based soft-ware, SPSS 27. A probability "P" value of 0.05or less was considered significant.

Results: The mean age of POAG patients was significantly higher than controls (56.83±7.73 vs. 49.20±7.08 years; $p < 0.001$). Mean eGFR was significantly lower in POAG patients (69.9±17.1 vs. 98.2±14.1 mL/min/1.73 m²; $p < 0.001$), while mean serum creatinine was higher (1.19±0.92 vs. 0.81±0.17 mg/dL; $p = 0.017$). Univariate analysis identified both older age (OR=1.14 per year, 95% CI: 1.06–1.23, $p < 0.001$) and reduced eGFR (OR=22.4, 95% CI: 6.18–81.17, $p < 0.001$) as significant predictors. Multivariate regression confirmed reduced eGFR as an independent risk factor for POAG (adjusted OR=17.5, 95% CI: 3.61–84.71, $p < 0.001$). No significant associations were observed for sex, diabetes, or hypertension.

Conclusion: This study demonstrates that reduced eGFR is strongly and independently associated with POAG, while traditional risk factors such as age lose significance after adjustment.

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Keywords: Primary open-angle glaucoma, chronic kidney disease, eGFR, serum creatinine, risk factors

Introduction

Glaucoma causes blindness which encompasses a group of pathological condition affecting the optic nerve head and is characterized by progressive retinal ganglionic cell loss, cupping of the optic nerve head and visual field defect.[1.]

In 2022, its incidence among individuals aged 40 to 79 years was estimated at 23.46 cases per 10,000 person-years with a 95% confidence interval ranging from 15.68 to 32.91.[2.]

Two major mechanisms of glaucoma pathogenesis have been proposed: (1) the mechanical theory, which focuses on the role of high intraocular pressure (IOP). and (2) the ischemic theory, which emphasizes disturbance of blood flow.[3]

Another common and progressive disease that affects 8–16% of the world's population and is costly to treat in terms of both morbidity and mortality is kidney disease. Numerous ocular conditions, have been linked to kidney disease including glaucoma. These two diseases share several risk factors such as diabetes, hypertension and cardio-vascular disease by means of microvascular dysfunction and ischemia.[4]

The glomerulus and choroid exhibit structurally analogous extensive vascular networks and comparable mechanisms contribute to the pathogenesis of kidney disease and glaucoma, including renin-angiotensin-aldosterone system (RAAS) dysfunction, oxidative stress, inflammation, atherosclerosis, endothelial dysfunction, and vascular remodeling.[5]

Components of the RAAS in cultured human non-pigmented ciliary epithelial cells have been identified as responsible for the formation and secretion of aqueous humor. In contrast, Angiotensin II has been shown to reduce trabecular aqueous outflow by promoting cellular proliferation and enhancing

collagen deposition in the trabecular meshwork. This indicates that the ocular RAAS may be implicated in the formation and drainage of aqueous humor and regulation of IOP.[6]

In kidney disease, oxidative stress plays an important role in the process of renal fibrosis, which is common final pathway of renal disease.[7]

Topical carbonic anhydrase inhibitors (CAI) are most commonly used as antiglaucoma medication and are generally regarded as safe and unrelated to systemic side effects.[8]

However, oral forms of CAI result in numerous systemic adverse effects, such as metabolic acidosis, nephrolithiasis, blood dyscrasias and fatigue. For this reason, there has been a concern that topical CAIs could cause systemic side effects. In the present study, topical CAI was associated with the development of kidney disease.[9]

Kidney function was assessed by estimating the glomerular filtration rate (eGFR), with lower eGFR values reflecting reduced kidney performance. The eGFR was derived from serum creatinine levels using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula:

$GFR = 141 \times \min(Scr/\kappa,1)^{\alpha} \times \max(Scr/\kappa,1)^{-1.209} \times 0.993^{Age} \times 1.018$ (If female) x 1.159 (if black)

Where Scr is serum creatinine, κ is 0.7 for females and 0.9 for males, α is-0.329 for females and -0.411 for males, min indicates the minimum of Scr/κ or1, and max indicates maximum of Scr/κ or 1.[10]

Kidney function status is further stratified into normal (eGFR>90 mL/min/1.73 m^2), mild (eGFR 60–89 mL/min/1.73 m^2), moderate (eGFR 45–59 mL/min/1.73 m^2) and severe decline (eGFR<45 mL/min/1.73 m^2.[10]

In summary, glaucoma and kidney disease share overlapping risk factors and pathogenic mechanisms, with impaired renal function- measured by estimated glomerular filtration rate (eGFR)- emerging as a potential contributor to primary open-angle glaucoma.

Materials and Methods

For this observational, Cross-sectional study, 35 patients with POAG and 35 patients without POAG were recruited from Institute of Bangladesh Medical University (BMU) , Department of ophthalmology, from January 2024 to May 2025.

Diagnosed case of POAG, aged ≥ 40 years of both sexes were included, but patients with angle closer glaucoma, secondary glaucoma, Patient with angle closure glaucoma, secondary glaucoma, normal tension glaucoma, neovascular glaucoma, Patients with neurological disease that can potentially affect visual acuity or visual field eg. Pituitary adenoma, craniopharyngioma etc., Patients with other ocular disease that is responsible for optic nerve damage eg. NAION, Optic neuritis etc. were excluded from the study sample.

Complete clinical evaluations include history, relevant ocular examination and some special ocular examination like IOP, gonioscopy were done.

Statistical analysis of the result was done by using computer-based software, SPSS 27 (SPSS inc, Chicago, IL, USA). The independent t-test was used to see the association and logistic regression was also done.

A probability P value of 0.005 or less was considered as significant.

Ethical consideration

The research protocol was approved by the Institutional Review Board (IRB) of BMU before the commencement of the study. The purpose and procedures were briefly explained to all participants and informed written consent (English/Bengali version) was obtained from each patient. Confidentiality was strictly maintained.

Result

Table I : Distribution of the study participants according to their age (n=70).

Age (Years)	Group A (POAG) n (%)	Group B (Control) n (%)	*p* value
Age group			
40–45 years	4 (11.4%)	14 (40.0%)	0.002*
46–50 years	6 (17.1%)	8 (22.9%)	
51–55 years	2 (5.7%)	6 (17.1%)	
56–60 years	17 (48.6%)	6 (17.1%)	
>60 years	6 (17.1%)	1 (2.9%)	
Mean±SD age, years	56.83±7.73	49.20±7.08	<0.001‡

*Chi-square test ‡ Independent sample's t-test

The majority of POAG (Primary open-angle glaucoma)

participants were aged 56–60 years (48.6%), whereas the control group had the highest proportion in the 40–45 years category (40.0%). A statistically significant difference was observed in age distribution between the groups (p=0.002). The mean age was significantly higher in the POAG group (56.83±7.73 years) compared to the control group (49.20±7.08 years; p<0.001).

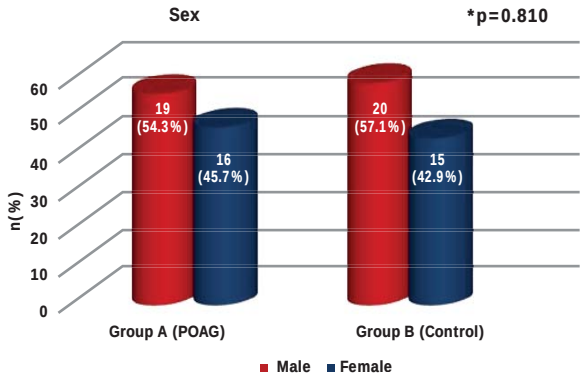

Figure 4.1: Distribution of the study participants according to their sex (n=70).

The distribution of male and female participants was comparable between the POAG and control groups, with no statistically significant difference (p = 0.81). Males constituted 54.3% of the POAG group and 57.1% of the control group.

Table II: Estimated glomerular filtration rate between two groups in the study (n=70).

Kidney function status	Group A (POAG) n (%)	Group B (Control) n (%)	*p* value
Stages of Kidney function by eGFR (mL/min/1.73m²)			
Normal (>90mL/min/1.73m²)	4 (11.4%)	26 (74.3%)	<0.001*
Mild (60–89mL/min/1.73m²)	23 (65.7%)	9 (25.7%)	
Moderate (45–59mL/min/1.73m²)	7 (20.0%)	0 (0.0%)	
Severe (<45mL/min/1.73m²)	1 (2.9%)	0 (0.0%)	
Mean eGFR (mL/min/1.73m²)	69.94±17.06	98.23±14.12	<0.001‡
Mean Serum creatinine (mg/dl)	1.19±0.92	0.81±0.17	0.017‡

*Chi-square test

‡ Independent sample's t-test

Normal kidney function (eGFR >90) was significantly more common in the control group than in the POAG group (74.3% vs. 11.4%; p<0.001). The POAG group also had significantly lower mean eGFR (69.94±17.06 vs. 98.23±14.12; p<0.001) and higher serum creatinine (1.19±0.92 vs. 0.81±0.17; p=0.017).

Table III: Distribution of co-morbidities between study groups (n=70).

Co-morbidities	Group A (POAG) n (%)	Group B (Control) n (%)	*p* value*
DM	7 (20.0%)	12 (34.3%)	0.179
HTN	8 (22.9%)	10 (28.6%)	0.584

*Chi-square test No significant differences were observed between the groups regarding the presence of diabetes or hypertension. DM was present in 20.0% of POAG cases and 34.3% of controls (p=0.179), while HTN affected 22.9% and 28.6%, respectively (p=0.584).

Table IV: Univariate logistic regression of risk factors for primary open-angle glaucoma (POAG) (n=70).

Variables	Odds ratio	95% CI		*p* value
		Lower	Upper	
Sex (Female)	1.123	0.437	2.885	0.810
Age	1.143	1.062	1.231	<0.001
Age group				
40–45 years (Ref)				
46–50 years	2.625	0.566	12.179	0.218
51–55 years	1.167	0.166	8.186	0.877
56–60 years	9.917	2.327	42.254	0.002
>60 years	21	1.922	229.39	0.013
eGFR (Mild to severe)	22.389	6.176	81.169	<0.001
DM				
No	-	-	-	-
Yes	0.479	0.162	1.415	0.183
HTN				
No	-	-	-	-
Yes	0.741	0.252	2.175	0.585

Univariate logistic regression showed that age was significantly associated with increased odds of POAG (OR=1.143, 95% CI: 1.062–1.231, p<0.001). Compared to the 40–45 years group, participants aged 56–60 years (OR = 9.917, p=0.002) and above 60 years (OR=21.00, p=0.013) had significantly higher odds. Reduced eGFR was also a strong predictor (OR=22.389, 95% CI: 6.176–81.169, p<0.001). No significant association was found for sex, diabetes, or hypertension.

Table V: Multivariate logistic regression of risk factors for primary open-angle glaucoma (POAG) (n=70).

Variables	Odds ratio	95% CI		*p* value
		Lower	Upper	
Age	1.208	0.821	1.775	0.337
Age group				
40–45 years (Ref)				
56–60 years	.148	0	97.75	0.564
>60 years	.106	0	1633.98	0.648
eGFR (Mild to severe)	17.475	3.605	84.709	<0.001

In multivariate logistic regression analysis, reduced kidney function (eGFR <90 mL/min/1.73m²) remained a significant independent predictor of POAG (OR=17.475, 95% CI: 3.605–84.709, p<0.001). Age and age group categories did not show significant associations with POAG after adjustment (p>0.05).

Discussion

In this cross-sectional comparative study, POAG patients were notably older (mean 56.83±7.73 years) than controls (49.20±7.08 years, p<0.001), with 65.7% of cases in the 56–60-year age bracket (versus 40.0% of controls in the 40-45 years of age). This age difference aligns with the well-known age-related risk for glaucoma. A previous study in Korea also found that patients with primary open angle glaucoma had a higher mean age compared to POAG absent group (57.21 years vs 53.75 years, p<0.001).[11]Notably, our patients' mean age (~57) is somewhat younger than in many population-based studies (often 60-70+ years), which might reflect regional demographics or earlier presentation of glaucoma in our setting.[12,13] Recent meta-analysis confirmed that age is a major risk factor for POAG, with those over 80 years having the highest disease rates (9.2% prevalence).[14]A large population-based survey in Bangladesh reported that glaucoma risk increased with each additional age increment (OR:1.1 per 5 years).[15]

There was a striking difference in kidney function between POAG patients and controls in our study. Normal renal function (eGFR >90 mL/min/1.73 m²) was observed in only 11.4% of POAG cases, compared to 74.3% of controls (p<0.001). Most POAG patients had mild-to-moderate reductions in eGFR and one had severe impairment, whereas almost three-quarters of controls had eGFR in the normal range. Consistently, the mean eGFR in the POAG group was significantly lower than in controls (69.94 ± 17.06 vs 98.23 ± 14.12 mL/min/1.73 m², p<0.001).

Moreover, mean serum creatinine was higher among POAG patients (1.19 ± 0.92 mg/dL) than controls (0.81 ± 0.17 mg/dL, p = 0.017). These findings indicate that reduced kidney function is associated with the presence of POAG. In other words, our glaucoma patients tended to have poorer renal function relative to controls. This novel observation is in line with emerging research suggesting a link between chronic kidney disease (CKD) and glaucoma. For example, Ro et al. (2022) conducted a nationwide cohort study in South Korea and found that a history of CKD was associated with a significantly higher risk of developing open-angle glaucoma over 12 years (adjusted hazard ratio ~1.55).Notably, the risk of POAG in that study increased with CKD severity- advanced CKD (stages 4–5) carried an HR of 1.861.[16] Moon et al. (2021) investigated glaucoma incidence among Korean patients with end-stage renal disease (ESRD) and kidney transplant recipients. While raw rates of POAG appeared higher in ESRD patients, adjusted analyses showed that the increased risk was not statistically significant for open-angle glaucoma, though it remained significant for angle-closure glaucoma.[17]

The prevalence of two common systemic comorbidities- diabetes mellitus (DM) and hypertension (HTN) wan analyzed in POAG patients versus controls. Diabetes was present in 7 out of 35 POAG cases (20.0%) compared to 12 out of 35 controls (34.3%), and hypertension in 8 POAG cases (22.9%) versus 10 controls (28.6%). Although numerically both conditions were actually more frequent in the control group, the differences were not statistically significant (DM: p=0.179, HTN: p=0.584). But a meta-analysis by Bonovas et al. (2004), which pooled data from 12 studies, found that diabetes was associated with about a 50% higher odds of POAG (OR ≈1.5, 95% CI 1.16–1.93).[18] Similarly, a recent systematic review and meta-analysis concluded that hypertension significantly increases the risk of POAG, reporting a pooled risk ratio of 1.69 (95% CI 1.50–1.90) for hypertensive individuals compared to normotensives.[19]

Univariate analysis identified older age and reduced eGFR as significant risk factors for primary open-angle glaucoma (POAG). Each additional year of age was associated with about a 14% increase in the odds of

having POAG (OR:1.14 per year, 95% CI: 1.06–1.23, p<0.001) and individuals in the oldest age group (>60 years) had markedly higher odds (21-fold) compared to those aged 40–45. Similarly, impaired kidney function was a strong predictor: participants with reduced eGFR (<90 mL/min/1.73 m²) had dramatically higher odds of POAG (OR≈22.4, 95% CI: 6.18–81.17, p<0.001).

In the multivariate logistic regression (adjusting for all factors), only eGFR remained an independent predictor of POAG (adjusted OR≈17.5, 95% CI: 3.61–84.71, p<0.001), while the effect of age was attenuated and no longer statistically significant after adjustment (adjusted p>0.05). In a Taiwanese nationwide cohort study of over 1.4 million participants, patients with chronic kidney disease (CKD) had a significantly higher risk of new-onset glaucoma, with an adjusted hazard ratio (aHR) of1.29 (95% CI: 1.26–1.32, p<0.001).[20] Sex, diabetes, and hypertension remained non-significant in the multivariate model, which is not unexpected since they were weak univariate factors. Our adjusted analysis concurs that, after accounting for age and eGFR, there was no evidence that being male or female altered risk, nor that the presence of DM or HTN affected odds of POAG. This implies that in our dataset, these factors were neither confounders nor independent predictors in the development of POAG. It is worth noting that in some other multivariate analyses (e.g., the Korean KNHANES data), factors like male sex or hypertension did come out as independent predictors.[21] The difference could be due to population variance or because our study was not powered to detect small effects.

Conclusion

This cross-sectional study demonstrates a strong association between reduced estimated glomerular filtration rate (eGFR) and primary open-angle glaucoma (POAG). POAG patients had significantly lower mean eGFR and higher serum creatinine levels compared to controls, indicating poorer renal function. Univariate analysis showed both older age and reduced eGFR were significant risk factors for POAG; however, multivariate analysis confirmed that only reduced eGFR remained an independent predictor. These findings suggest that impaired kidney function may play a crucial role in the development of POAG, supporting the hypothesis of shared systemic mechanisms between ocular and renal disease.

Limitations

This study although shows multivariate analysis was used, residual confounding (e.g., lifestyle factors, medication use, socioeconomic status) may have influenced outcomes. Our study is the cross-sectional study which can identifies associations but cannot establish causality between reduced eGFR and POAG. Age was not perfectly matched between the POAG and control groups, which may have influenced observed associations despite statistical adjustments.

Recommendations

Patients with chronic kidney disease or reduced eGFR should be considered at higher risk for glaucoma and may benefit from regular ophthalmic screening for early detection of POAG. Patients diagnosed with POAG should have their eGFR routinely tested to assess kidney function and identify potential systemic risk factors contributing to disease progression. Closer collaboration between ophthalmologists, nephrologists, and primary care physicians is recommended to ensure systemic risk factors are evaluated alongside ocular assessments.

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Glaucoma : Current and New Therapeutic Approaches

M S I Prodhan[1]

Abstract

Glaucoma is identified by the loss of retinal ganglion cells (RGCs). The primary approach to managing glaucoma is to control intraocular pressure (IOP). Lately, there has been an increasing focus on neuroprotective therapies for glaucoma because of the limited effectiveness of standard methods in reducing IOP and preventing ongoing vision deterioration in certain glaucoma patients. Various drug-based techniques with neuroprotective properties have demonstrated the ability to decrease the mortality of retinal ganglion cells. This study will analyze the currently recommended drug-based techniques for neuroprotection in the prospective treatment of glaucoma.

Keywords: Glaucoma therapeutic approaches; neuroprotection; neurodegeneration; oxidative stress; neuroinflammation; excitotoxicity.

1. Introduction

Glaucoma is a group of long-lasting and worsening optic neuropathies that are identified by the reduction of retinal ganglion cells and the consequent problems with vision.[1] Despite the current lack of complete understanding regarding the precise etiology of the disease, it has been firmly established that altering intraocular pressure (IOP) represents the sole adjustable risk factor for mitigating the potential visual impairment associated with glaucoma. The primary approach for managing adult glaucoma is through medical care, which has shown significant and rapid breakthroughs in therapeutic interventions for this illness.[2] Lately, there has been an increasing focus on retinal ganglion cells (RGCs) and the specific processes that make them vulnerable to damage and deterioration in the retina and optic nerve. Additionally, there is progress being made in developing medications that protect the nervous system from damage caused by glaucoma. These treatments could be employed in addition to ocular hypotensive methods to better preserve RGCs and minimize visual loss.[3]

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2. Present IOP-Reducing Medications

In the management of glaucoma, drugs that reduce IOP play a pivotal role. The

selection of medication is contingent upon the individual patient's unique requirements, the precise classification of glaucoma, and any existing contraindications, necessitating constant surveillance to ascertain the efficacy of the treatment and mitigate potential adverse reactions.

2.1. Beta Adrenergic Antagonists (β-Blockers)

The identification of Beta-adrenergic antagonists (β-blockers) as a potential therapeutic approach for glaucoma was fortuitous and sprang from cardiovascular investigations. During the late 1960s and early 1970s, β-blockers were predominantly formulated and employed for the treatment of cardiovascular ailments such as hypertension and arrhythmias.[4] Researchers noted that these drugs also influenced IOP, prompting additional investigations into their potential applications in ophthalmology. They prevent sympathetic nerve terminals in the ciliary body's epithelium from functioning, and blocking adrenergic β-receptors in the ciliary body leads to a reduction of the generation of aqueous humor. This inhibition results in a reduction of the synthesis of aqueous humor. β-blockers can be categorized into two primary categories: nonselective and cardioselective, sometimes known as β1 selective. Individuals with asthma and chronic obstructive pulmonary disease (COPD) have been found to exhibit a higher level of tolerance towards the latter category. β-blockers offer various benefits, such as their cost-effectiveness and the simplicity of once daily administration.[5] Research findings indicate that timolol, a β-blocker commonly used, possesses the capacity to substantially diminish IOP by approximately 20–35%.[6] It emerged as the primary medical therapy for glaucoma and ocular hypertension (OHT) and continued to be the unquestioned first option until the prostaglandin analogues were introduced in 1996.[7]

2.2. Adrenergic Agonists

Adrenergic agonists work by inhibiting the synthesis of aqueous humor and enhancing the drainage of uveoscleral fluid from the eye. In practical settings, selective drugs have largely replaced nonselective adrenergic agonists. Currently, brimonidine, which was introduced in the mid-1990s, stands out as the sole medication utilized for long-term treatments in this category. Several studies have shown that giving alpha-agonists can change the amounts and activities of matrix metalloproteinases and the tissue inhibitors that go with them. These proteins have a significant impact on the degradation of the extracellular matrix, which makes it possible for more fluid to flow through the uveoscleral pathway.[8] A smaller-scale randomized controlled trial was performed to see how brimonidine treatment affected the sensitivity of contrast in people who had just been diagnosed with glaucoma. The results of this study demonstrated that those who received brimoni-dine exhibited a statistically significant enhancement in contrast sensitivity compared to those who were administered timolol. The aforementioned observation, regardless of any drop in intraocular pressure, implies the existence of a neuroprotective mechanism in glaucoma.[9] Nevertheless, it is advisable to refrain from utilizing alpha2-adrenergic agonists for topical therapy in pediatric patients below the age of 12, owing to the potential for significant adverse reactions. In certain instances, these deleterious consequences can be highly severe, potentially resulting in a state of unconsciousness in infants and toddlers.

2.3. Carbonic Anhydrase Inhibitors (CAIs)

Carbonic anhydrase inhibitors (CAIs) function by suppressing the activity of the enzyme carbonic anhydrase. This leads to a decrease in the secretion of bicarbonate and aqueous humor. Medications with a significant historical lineage have been used to treat open-angle glaucoma (OAG). Systemic CAIs, such as acetazolamide and methazolamide, have demonstrated efficacy in decreasing IOP in patients with glaucoma with reports demonstrating the efficacy of acetazolamide in reducing IOP as early as 1954. However, their administration is linked to notable adverse effects, including fatigue, abnormal sensations, nausea, dizziness, hypokalemia, nephrolithiasis and weight loss. Stevens-Johnson syndrome, toxic epidermal necrolysis, and aplastic anemia are infrequent yet severe consequences that may manifest.[10] The development of topical CAIs, like dorzolamide and brinzolamide has been focused on achieving localized administration in order to minimize the occurrence of systemic side effects. These pharmaceuticals have subsequently emerged as a noteworthy classification, including easily obtainable formulations that have been formulated in conjunction with other prescribed drugs to mitigate IOP.[11] Dorzolamide–timolol (Cosopt, FDA authorized in 1998) and brinzolamide–brimonidine (Simbrinza, FDA approved in 2013) are combination medicines that are commonly used to reduce IOP and enhance patient adherence.[12] Switching from a combination of four drugs to a combination of latanoprost–timolol and brinzolamide–brimonidine resulted in significant improvements in IOP and patient adherence. A further study demonstrated that the combination of brinzolamide–brimonidine with a prostaglandin analogue resulted in a more effective reduction of IOP compared to using a prostaglandin analogue alone.[13] Both the combination therapy of brinzolamide–brimonidine and dorzolamide–timolol, when provided as a single drop, were found to be equally effective as each of the individual component medicines when administered separately. CAIs may be employed when second-line beta blockers are contraindicated, although they are frequently more effective when prescribed in conjunction with a beta-blocker.[14]

2.4. Prostaglandin Analogues (PGAs)

Prostaglandin analogues (PGAs), including tafluprost, latanoprost, travoprost, bi matoprost, have shown more effective than carbonic anhydrase inhibitors, β-blockers, and α-2 agonists.[15] Five classes of prostaglandins exist: prostaglandin E2 (PGE2), F2 (PGF2), I2 (PGI2), D2 (PGD2), and thromboxane A (TXA2). The utilization of PGF2 and prostaglandin FP agonists has resulted in a reduction of IOP. In order to achieve this particular impact, the uveoscleral outflow is augmented in an atypical manner. This process can also be achieved by activating prostaglandin receptors located in the ciliary muscle, iris root, and sclera by relaxing the smooth muscle, modifying the cytoskeleton, and remodeling the extracellular matrix in the uveoscleral pathway.[16] Furthermore, it could

potentially improve the outflow of aqueous humor by activating the FP receptors found in the trabecular meshwork. PGAs are the most effective medications for lowering intraocular pressure (IOP), followed by β-blockers, α-2 agonists, and carbonic anhydrase inhibitors.[17] Several studies have provided evidence indicating that latanoprost (FDA approved in 1996) demonstrates enhanced effectiveness in the reduction of IOP and that bimatoprost exhibits greater efficacy in the reduction of IOP in comparison to latanoprost.[18] Nevertheless, there have been different research outcomes that indicate similar efficacy between the two drugs.[19] Adverse effects on the eyes may include redness of the conjunctiva, increased growth of eyelashes, and various forms of pain such as eye irritation, itching, tears, a sensation of a foreign object in the eye, the formation of cysts in the iris, swelling of the macula, inflammation of the front part of the eye, and the reactivation of herpes simplex keratitis. PGAs have a very safe profile when it comes to systemic side effects. These drugs are non-toxic to the circulatory and respiratory systems and have no negative side effects.[20]

2.5. Muscarinic Receptor Agonist

Activation of muscarinic receptors in the ciliary muscle leads to an increased outflow of aqueous humor from the eye. The duration of this impact normally ranges from three to five hours. Hence, the administration of pilocarpine eye drops necessitates a minimum of four daily doses, posing challenges for patients in adhering continuously to the recommended therapeutic regimen.[21] Moreover, the administration of pilocarpine has the potential to elicit extensive parasympathetic reactions, including bronchospasm, heightened salivation, gastrointestinal disturbances, perspiration, and bradycardia, as a result of its activation of the cholinergic system.[22]

2.6. Hyperosmotic Agent

Hyperosmotic drugs function by diminishing the quantity of aqueous fluid present in the ocular cavity, hence leading to a reduction in IOP. These medications are commonly employed in urgent scenarios or as a preoperative measure to transiently reduce IOP.[23] This category of pharmaceuticals encompasses orally delivered substances such as glycerin, isosorbide, and mannitol, which is supplied intravenously.

2.7. Rho Kinase Inhibitor

Rho kinase (ROCK) is a serine/threonine protein kinase that serves as an important

downstream mediator of Rho signaling.[24] It reduces the density of actin stress fibers, which directly affects the cytoskeleton of the trabecular meshwork and Schlemm's canal and improves the outflow facility. This differs from the intended goal of other glaucoma medications. Investigation into Rho kinase commenced in the late 1990s and has persisted up to the present day. Recent studies have produced a wealth of information regarding the various possible therapeutic applications of ROCK inhibitors in treating glaucoma, namely in maintaining IOP and in treating neurodegenerative disease.[25] There is a limited amount of research examining the therapeutic impact of a Rho kinase inhibitor on diabetic retinopathy and its ability to promote repair in the corneal endothelium. In 2014, Ripasudil was approved in Japan for the particular treatment of ocular hypertension and glaucoma. Then, the efficacy of Rho-kinase inhibitors as a anti-glaucoma drugs was validated with the release of Netarsudil in 2017. This drug was licensed in the United States in a 0.02% formulation.[26] Rhopressa, a Rho kinase inhibiting drug consisting of Netarsudil, gained FDA approval in December, 2017.[27] Currently, ROCK inhibitors are primarily used in combination with other primary drugs for glaucoma treatment to guarantee a sufficient reduction in IOP.[28]

2.8. Fixed Combinations

Regarding the treatment of ocular hypertension and glaucoma, fixed combinations of medications that decrease IOP are now increasingly being used. These combinations provide various potential benefits compared to using the individual medications separately, such as increased convenience, enhanced adherence, reduced exposure to preservatives, and potential cost savings.[29] The current meta-analysis revealed that the utilization of fixed combinations with timolol, specifically dorzolamide/timolol, brinzolamide/ timolol, and brimonidine/timolol, can lead to a reduction in IOP of over 30%.[30]

3. Beyond IOP: Mechanisms of Neurodegeneration in Glaucoma

Neuroprotective treatments for glaucoma can help to avoid the death of retinal ganglion cells and damage to

the optic nerve by reducing ischemia and oxidative damage. While IOP is the sole identified variable that can be changed to lower the risk of glaucoma, emerging research indicates that injury to the optic nerve can persist even when IOP is effectively reduced.[31] There is a tremendous therapeutic need for neuroprotective methods that especially focus on the retinal ganglion cell and the underlying neurodegenerative processes.

3.1. Neurodegenerative Processes

Similar to other diseases, glaucoma exhibits an increased prevalence with advancing age, advances gradually and subtly, and is influenced by genetic factors. A retrospective study revealed that patients with primary open-angle glaucoma (POAG) were more likely to acquire Alzheimer's disease (AD) compared to people without POAG.[32] There is also increasing evidence that glaucomatous neuropathy affects not just the retina, but also the central nervous system (CNS).[33]

3.2. Oxidative Stress

Inflammation, hypoxia, ischemia, and mitochondrial malfunction can induce heightened oxidative stress, which can lead to glaucoma. The presence of mitochondrial damage and loss in the trabecular meshwork (TM) leads to both degenerative and apoptotic processes, ultimately resulting in cell loss.[34] Oxidative stress can directly damage RGCs as well.[35] Increasing evidence suggests that oxidative stress is a significant factor in the neuronal cell death that happens during glaucomatous neurodegeneration.[36] This oxidative stress impairs cellular homeostasis and disrupts normal cellular functions, contributing to a cascade of detrimental effects on the optic nerve and retinal tissues. Additionally, oxidative stress exacerbates the inflammatory response, further aggravating tissue damage and promoting the progression of glaucoma. Therefore, researchers are exploring antioxidant therapies and protective agents as a potential strategy to target oxidative stress, mitigate the progression of glaucomatous damage, and preserve visual function.

3.3. Neuroinflammation

Neuroinflammation is now recognized as a crucial role in the development of glaucoma due to the participation of immune and glial cells in the early stages of the illness. Astrocytes, microglia, and invading monocytes play important roles in the neuroinflammatory process in glaucoma.[37] Glaucoma donor tissue exhibits an elevated presence of microglia in the inner retina and optic nerve, as well as an increase in GFAP, indicating reactive restructuring of astrocytes and Muller glia.[38] The glial responses in glaucoma and their association with RGCs and systemic immunity have been most accurately characterized in animal models.[39]

3.4. Autophagy

Autophagy contributes to the development of glaucoma. Cellular stress, such as hunger, hypoxia, and oxidative damage, triggers a significant reaction.[40] Nevertheless, numerous studies present contradictory information regarding whether this response is harmful or beneficial.[41] Among all conditions, a lack of nutrition (particularly amino acids) is the most important factor in autophagy activation. Autophagy levels decrease with the natural process of human aging in all investigated tissues, including the brain and retina.

3.5. Excitotoxicity

Glutamate is a highly toxic substance for the nervous system, glutamate transporters play a crucial role in preventing retinal damage from excessive neural stimulation. Excitotoxicity has been implicated in various eye diseases, such as retinal or choroidal artery occlusion-induced ischemia, glaucoma, and diabetic retinopathy. Considering the highly toxic nature of glutamate in the nervous system, the role of glutamate transporters is essential in reducing damage to the retina induced by excessive neuronal stimulation. Both experimental and clinical cases of glaucoma exhibit increased amounts of glutamate in the vitreous.[42] Excessive levels of glutamate cause an over activation of NMethyl- D-aspartate (NMDA) receptors, particularly impacting RGCs death.[43]

3.6. Decreased Ocular Perfusion

Numerous chronic neurodegenerative disorders have been linked to vascular factors. The level of ocular perfusion is affected by the resistance to blood flow and determines the amount of blood and oxygen that reaches the optic nerve head.[44] Therefore, there is a generally held belief that a decrease in ocular perfusion pressure may heighten the susceptibility of the optic disc, resulting in an elevated likelihood of

glaucoma onset or advancement.[45]

4. Exploring the Frontiers of Neuroprotection Treatments

Currently, glaucoma is acknowledged as a long-lasting neurodegenerative illness that impacts the complete visual pathway extending from the eye to the visual cortex. It is a prominent factor contributing to decreased eyesight in the senior population worldwide, and its impact as a social health concern is expected to worsen over time. Given its neurodegenerative character, pharmacological treatments applied to several degenerative brain diseases could also help in treating glaucoma and other visual neuropathies.[46] Neuroprotection has gained significant interest in recent years as a new method to prevent or slow down the progression of structural and functional damage caused by glaucoma, with a specific emphasis on delaying the degeneration of RGCs[47] (Table 1).

Table 1 : Neuroprotective treatments.

Pathological Mechanism	Result or Impact	Neuroprotective Interventions
Deprivation of Neurotrophins	Glutamate NMDA Receptors Activation, Calcium Influx of RGCs	Neurotrophins
Glutamate Increase	Increased activation of NMDA receptors	Coenzyme Q10, Memantine
Glutamate NMDA Receptors Activation	Leads to calcium influx into RGCs	Brimonidine, BDNF-TrkB signaling
Calcium Influx of RGCs	Leads to an increase in free radicals (e.g., NO), Mitochondrial Dysfunction	Calcium channel blockers
Oxidative Stress	Leads to RGCs death	Antioxidant (e.g., EPO), NOS inhibitors
Decreased Ocular Perfusion	Leads to RGCs death	Gingko biloba extract
Neuroinflammation	Leads to RGCs death	
Mitochondrial Dysfunction	Leads to excitotoxicity and RGCs death	Citicoline
RGCs Death	Final outcome	

4.1. Nitric Oxide

Nitric oxide (NO) makes trabecular meshwork (TM) cells relax and Schlemm's canal (SC) cells more permeable. It has diverse biological functions in the ocular system, such as regulating vascular tone and performing several additional jobs processing visual stimuli[48] promoting immunological cytotoxicity and managing IOP. Healthy individuals exibit higher levels of NO production in comparison to ocular hypertensive patients. Moreover, the existing literature indicates that NO has a dual role in optic neuropathy on cultured neurons. Low levels of NO have been found to have neuroprotective benefits, while high levels of NO have been associated with neurodegenerative consequences.[49]

4.2. Rho Kinase Inhibitor

As mentioned in Section 2.7, Rho kinase inhibitors are employed in the management of neurodegenerative disorders. They have been observed to prevent the programmed cell death of RGCs caused by axotomy, and also provide protection against the loss of neurons in vivo.[50]

4.3. Coenzyme Q10

Coenzyme Q10 has been extensively used to treat a range of illnesses, such as Leber hereditary optic neuropathy, cerebral ischemia, Parkinson's disease, and Huntington's disease.[51] It has demonstrated efficacy in reducing apoptosis and the loss of RGCs in animal models. When administered directly into the eye, it prevented the death of RGCs through the regulation of mitochondrial depolarization.[52]

4.4. Citicoline (Cytidine-5′-Diphosphocholine)

Citicoline is a naturally occurring chemical that plays a role in the production of phospholipids' membranes, specifically phosphatidylcholine. The effects of citicoline are caused by a lot of different metabolic pathways, such as cholinergic and dopaminergic transmission, phospholipid homeostasis, and mitochondrial dynamics. These mechanisms play a role in the complex process of visual transmission. Citicoline's neuroprotective effect is due to its ability to decrease glutamate excitotoxicity and oxidative stress, improve mitochondrial function[53], and enhance neurotrophin levels. However, current research does not provide enough support to conclude that citicoline effectively slows down the course of glaucoma.[54]

4.5. Gingko Biloba Extract (GBE)

Ginkgo is a prehistoric tree species that closely resembles plants that existed 270 million years ago. The cultivation of this tree is extensive in China, and it was introduced at an early stage in traditional Eastern medicine to address a range of issues, including asthma, vertigo, tiredness, tinnitus, and circulatory ailments. Current medical science has scientifically

proven the positive effects of ginkgo biloba extract, derived from the leaves of the ginkgo biloba tree, on cognitive impairment and dementia. Because Alzheimer's disease and glaucoma share molecular and mechanical similarities, researchers have investigated ginkgo for glaucoma.[55] Studies conducted on animal models have demonstrated that GBE possesses neuroprotective, antioxidant, and anti-inflammatory characteristics, specifically targeting RGCs. It also demonstrated that GBE enhances the flow of blood in the eyes. However, the impact of GBE on the visual field remains uncertain.

4.6. Tumor Necrosis Factor-α Inhibitors

Tumor necrosis factor α (TNF-α) has been shown to be involved in pathways leading to the death of RGCs death in animal and on vitro glaucoma models.[56] It stimulates the processes that lead to the death of mitochondria in cells and triggers the production of reactive oxygen species (ROS), play a vital function in the immune response and are responsible for a apoptosis and inflammation and potentially influence axonal degeneration on glaucomatous eyes as well. It is feasible to repair damaged neuronal tissue caused by inflammation in glaucomatous eyes by blocking TNF, which is the key factor in both inflammatory and cell death signaling in RGCs, as well as axon injuries in on vivo models of glaucoma.[57]

4.7. Nuclear Factor Kappa B (NF-κB) Inhibitors

The nuclear factor-kappaB (NF-κB) is a crucial molecule that activates the transcription of genes involved in inflammation. It has been found to be significantly impacted in astroglia damaged by glaucoma.[58] Research has demonstrated the crucial involvement of astroglial NF-κB in the inflammatory and degenerative effects of experimental glaucoma, and its ability to offer neuroprotection by modulating the immune response.[59]

4.8. Memantine

Memantine can help to treat Alzheimer's disease and Parkinson's disease.[60] It is a non-competitive open-channel blocker that only inhibits NMDA-receptor function when glutamate levels are abnormally high, leaving normal physiological levels necessary for synaptic action unaffected, and has been discovered to be very successful as a neuroprotective drug in both acute and chronic animal models of RGC death.[61] Regrettably, in two clinical trials, the administration of memantine on a daily basis for a duration of 4 years did not have any effect in terms of preventing or slowing down the progression of open-angle glaucoma in patients.[62]

4.9. Calcium Channel Blockers (CCBs)

Calcium channel blockers (CCBs) are authorized for the management of hypertension and cerebral impairment. They enhance vasodilation, reduce vascular resistance, and ultimately lower blood pressure while increasing blood flow.[63] Studies have demonstrated that CCBs possess therapeutic efficacy in the treatment of glaucoma. Nifedipine, verapamil, diltiazem, and nilvadipine[64] have been found to decelerate the advancement of visual field deterioration in patients with normal tension glaucoma (NTG). Furthermore, the administration of nifedipine and brovincamine resulted in an augmentation of peripheral blood circulation in the optic disc.[65]

4.10. Platelet-Derived Growth Factor (PDGF)

Platelet-derived growth factor (PDGF) plays a crucial role in the neuroprotective impact of mesenchymal stem cells on RGCs in both retinal explants and experimental glaucoma.[66] Additionally, it has been observed to increase neuronal survival in many damage models, such as excitotoxicity and oxidative stress.[67] These findings recommend further exploration of PDGF treatment as a potential glaucoma therapy in the future.

4.11. Neurotrophic Factors

Brain-derived neurotrophic factor (BDNF), one of the neurotrophin families, has significantly low levels in the ocular fluids found in glaucoma patients.[68] This supports the idea that a lack of neurotrophic factors is a probable cause of glaucomatous optic neuropathy. Several published studies detail the connection between the absence of BDNF support for the RGCs and the initiation of their deaths. After 7 days of elevated IOP in a rat model of glaucoma, the natural production of brain-derived BDNF and neurotrophin-4/5 (NT-4/5) in the optic nerve was entirely depleted, which corresponds to the apoptosis of RGCs. Essentially, a lack of neurotrophic factors in the optic nerve is a contributing factor to the development and advancement of glaucomatous optic neuropathy (GON). Augmenting neurotrophic support

can potentially postpone RGC degeneration in individuals with glaucoma. Thus, directing attention towards modifying the problematic sequence around the converging endpoints could potentially be more effective in preventing the death of RGCs.[69]

4.12. Erythropoietin

Erythropoietin (EPO) is a hormone that can promote pleiotropic effects.[70] Multiple studies have documented an elevation in the EPO concentration in the fluid known as aqueous humor among individuals diagnosed with glaucoma. The increasing levels of aqueous EPO in glaucomatous eyes may be attributed to ischemia, hypoxia, or increased levels of reactive oxygen species (ROS) resulting from glaucomatous damage. EPO exhibits anti-inflammatory, antioxidative, and antiapoptotic effects, which make it a prospective therapeutic option for the treatment of glaucoma.[71]

5. A Multifaceted Approach: The Future of Glaucoma Management

5.1. Nanotechnology-Based Ophthalmic Delivery System

Novel drug carriers, including nanomicelles, nanoparticles (NPs), nanoemulsions (NEs), microemulsions, nanofibers, dendrimers, liposomes, niosomes, nanowafers, and microneedles (MNs), have been investigated for the treatment of both anterior and posterior ocular disorders.[72] An instance of the application of lipid-based nanoparticles (NPs) containing brimonidine and latanoprost is their usage in the treatment of glaucoma.[73]

5.2. Intracameral Implant

Bimatoprost implant (Durysta) is a biodegradable intracameral implant to reduce IOP in patients with open-angle glaucoma (OAG) or ocular hypertension (OHT).[74] The implant is a tiny cylinder with a diameter of around 200 µm and a length of about 1.1 mm. It contains 10 µg of bimatoprost and uses a drug delivery system for the eyes. This system is made of biodegradable polymers that have been proven to be safe for ocular tissues. The implant was specifically engineered to gradually release bimatoprost over a period of approximately 3–4 months. However, there have been reports that the implant has long-term effects on IOP. The most frequently reported adverse effect in patients was eye irritation. The FDA currently permits a single dose of the implant per eye through intracameral delivery, and it prohibits re-treatment.[75] The travoprost intracameral implant (iDose TR) is a small, biocompatible titanium reservoir that is secured to the sclera at the iridocorneal angle by an anchor that passes through the trabecular meshwork. The reservoir has 75 µg of a proprietary, preservative-free travoprost formulation, which is about 25,000 times more concentrated than the travoprost in travoprost ophthalmic solution.[76] For individuals with OHT or OAG, the FDA has approved a single injection per eye.

5.3. Genome-Wide Analyses

Prior genome-wide association studies have discovered significant loci linked to the

incidence of POAG.[77] Identifying risk loci could be used as targets for preventive therapies.

5.4. Stem Cell Therapy

Stem cell therapy offers the intriguing potential to regenerate and replenish RGCs, potentially leading to the restoration of eyesight that has been lost due to glaucoma. It could potentially contribute to the restoration of the trabecular meshwork using cell based functional methods. Existing evidence indicates the presence of a population of mature stem cells in the Schwalbe's ring and the anterior trabecular meshwork.[78]

6. Conclusions

The comprehension of the intricate pathophysiology of glaucoma is expanding, leading to a transformation in the emphasis on therapeutic interventions. Prospects for the future indicate the convergence of IOP-lowering, neuroprotection, and cellular resilience-building strategies into a unified approach that provides holistic management solutions and strives for individuality, precision, and efficacy to predominate. As research progresses, there is an increasing focus on the genetic and molecular underpinnings of the disease, which holds promise for the development of personalized medicine tailored to each patient's unique genetic profile. Furthermore, advances in imaging technologies and biomarker discovery are enhancing early detection and monitoring capabilities, allowing for more timely and targeted interventions. Ultimately, these

advancements aim to preserve vision and improve the quality of life for patients with glaucoma, marking a significant shift towards more comprehensive and patient-centered care in ophthalmology.

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Topiramate induced acute angle closure and high myopia: A case report

R Das[1], S M Noman[2], Z Khaled[3]

Abstract

Purpose: To report a case of Topiramate induced acute angle closure Glaucoma and High Myopia .

Case Presentation : A 24 year old unmarried female complaints of sudden onset of severe dimness of vision 7 days prior to which she was taking tab Topiramate 25 mg twice daily for migraine prophylaxis. Visual acuity reduced to counting finger. Retinoscopy shows -8.00 diopter myopia and vision was improving to 6/6(p) with subjective refraction. Slit Lamp examination reveals severe shallowing of anterior chamber, forward movement of lens iris diaphragm . Intraocular pressure was 25 mm Hg both eyes. Gonioscopy shows appositional angle closure. B-scan USG shows Choroidal effusion. UBM shows thickening of cilliary body. All those changes, both anatomical changes resolved, and refractive status improved to -1.00 D right eye, -1.5 D left eye. 3 days after discontinuation of the drug.

Conclusion: Neurologist, ENT specialist, Ophthalmologist or Internist whoever is prescribing Topiramate needs to be aware of the potential ocular side effects. Although relatively rare prompt diagnosis is key and urgent discontinuation of the drug is important to prevent permanent ocular damage and visual loss.

Key words: Topiramates, angle closure glaucoma, myopia

Introduction

Acute angle closure glaucoma is an ocular emergency. Late diagnosis and treatment can cause irreversible optic nerve damage and visual field defect. Angle closure glaucoma may be primary or secondary. Among the causes of secondary angle closure glaucoma drug induced AACG is one of the important cause though rare. Drug-induced AACG is an ophthalmic emergency which may lead to persistent visual loss if not treated urgently. Presenting symptoms include conjunctival hyperemia, acute onset of impaired vision, ocular, periocular pain, colored halos and headache.[17] On examination findings are elevated intraocular pressure (IOP) above 21mm Hg, conjunctival and cilliary congestion, a mid-dilated and fixed pupil and a shallow anterior chamber.[15,16] The hallmark of angle closure is the apposition or adhesion of the peripheral iris to the trabecular meshwork, then drainage of the aqueous humour through the angle is reduced and IOP rises.

Certain drugs like antidepressants, cold medications, or antihistamines can cause acute angle closure.

• Topiramate (Topamax; Ortho-McNeil Pharmaceutical, Raritan, NJ,USA) is an oral sulfamate medication used primarily for seizure treatment, for migraine prophylaxis, depression, and neuropathic pain induced AACG within the first 2 weeks after starting with almost all cases are bilateral AACG.[17]

• The exact mechanism of action is unknown, however, four properties that may contribute to Topiramate anti-epileptic and anti-migraine efficacy include a blockage of voltage-dependent sodium channels, an augmentation of gamma amino- butyrate acid activity at some subtypes of the GABA-A receptors, antagonism of AMPA/ kinate subtype of the glutamate receptor, and inhibition of the carbonic anhydrase enzyme, particularly isozymes II and IV[18]. We report a case of Topiramate induced 2ndary ocular hypertension and sudden onset of severe myopia. In this case prompt discontinuation of the drug causes reversal of myopia and resolution of angle closure within 72 hrs and could prevent from developing angle closure glaucoma. Sulpha drugs may induce AACG without pupillary block. Mechanisms in this type of angle closure include lenticular swelling, retinal edema, Choroidal effusion, and secondary shallowing of the anterior chamber. Basic mechanism is blockage of $Na^{\pm}k$ pump and water retention and swelling of cilliary body, followed by anterior rotation of the cilliary body, forward movement of lens iris diaphragm, that leads to acute angle closure glaucoma and high myopic shift.

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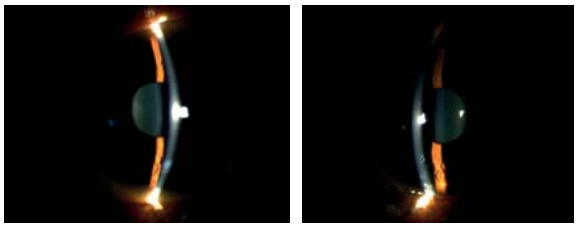
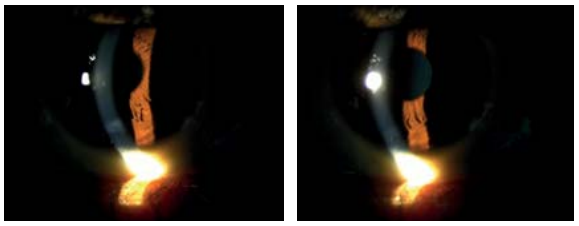
• Ecstasy, a synthetic amphetamine derivate, and marijuana induced recurrent bilateral AACG. Cocaine has indirect sympathomimetic activity and causes mydriasis. AACG has been reported following therapeutic or abuse intranasal application of cocaine[17]

Case Presentation: A 34 year old female complained of sudden severe dimness of vision. Her visual acuity on presentation was counting finger close to face. She gave history of taking Topiramate tab 25 mg twice daily as migraine prophylaxis prescribed by ENT specialist for 7 days prior to presentation.



1st day of presentation

1 day after stopping the drug, AC depth started increasing

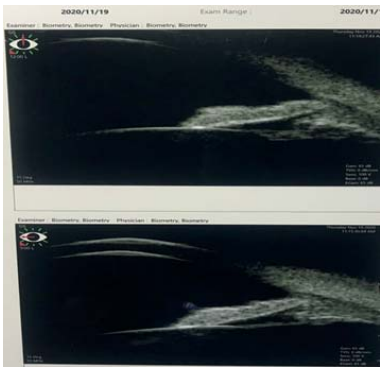


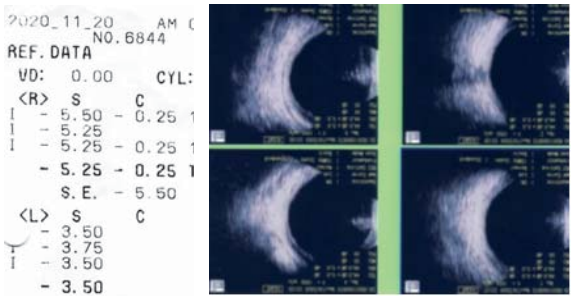
1 week after. AC become normal depth completely

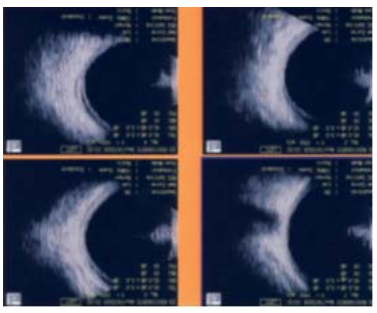
Retinoscopy shows -9.5D RE and -8.5D LE myopia both the eyes. On subjective refraction visual acuity improved to 6/6 part with -8.50D RE, -8.0D LE.

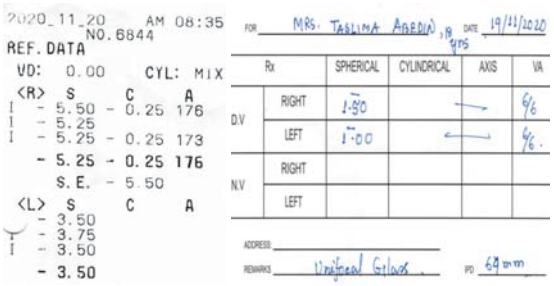
On slit lamp examination both eyes shows mild conjunctival and cilliary congestion, very shallow anterior chamber –lens iris diaphragm was coming forward to touch the cornea, mild AC reaction Intraocular pressure was 25mm Hg in both eyes. Gonioscopy shows Shaffer grade 1 throughout 360° .B scan shows mild Choroidal effusion. UBM shows cilliary body swelling. Few cells and flare and thin exudative membrane were there in anterior chamber of LE.

Topiramate therapy has been discontinued immediately. Brinzolamide eye drop 3 times a day, Neopred eye drop prescribed 6 times a day LE prescribed in both eyes. On following day morning her visual acuity improved to 6/6 with -5.5 D in RE and with-3.5 D in LE,. Anterior chamber started becoming deeper than before. Lens- iris diaphragm started moving backwards a bit. On the same day evening her visual acuity improved to 6/6 with -2D in RE and -1.75 D in LE.









On 3 days after follow up her visual acuity becomes 6/6 unaided, Anterior chamber was formed and deep, exudative membrane was resolved in LE, IOP reduced to 10 mmHg both eyes, Choroidal effusion has been resolved completely in B scan. One weeks later gonioscopy shows Shaffers grade 4 throughout 360° of the angle**.**

Discussion

Topiramate is used for the treatment of epilepsy, as weight reduction agent in bipolar disorder, to treat depression and neuropathic pain and as prophylaxis for migraine. Case reports on ocular side effects of this drug was there date back to 2001 [1-3] In September 2001 Ortho-McNeil Pharmaceuticals sent out a Page 1 of 3 safety alert to healthcare professionals indicating 23 cases of secondary angle-closure glaucoma related to Topiramate use based on post-marketing experience in more than 825,000 patients. (Hulihan J: Important drug warning [letter]. Available at: http://www.fda.gov/medwatch/SAFETY/2001/topamax_deardoc.PDF). The majority of reported adverse events have occurred in female patients (up to 89%) [4].Our case is a female patient. Ocular side effects have also been reported in children [5]. In the "certain" category of the World Health Organisation classification system adverse ocular side effects associated with topiramate include abnormal vision, acute IOP elevation, acute myopia (up to 8.75 dioptres), diplopia, nystagmus and shallow anterior chamber with angle-closure. "Probable/ likely" include blepharospasm, myokymia, oculogyric crisis, suprachoroidal effusions and "possible" are congenital ocular abnormalities, periorbital oedema and scleritis [6]. High frequency ultrasound biomicroscopy, anterior segment ocular coherence tomography and B-scan ultrasound have helped establish and document the underlying mechanism of the myopia and angle-closure glaucoma [7-9] – uveal effusions and ciliary body oedema result in antero-lateral rotation of the ciliary body, anterior displacement of the lens-iris diaphragm which contributes to the myopic shift, anterior chamber shallowing and secondary appositional angle closure. The effusion and oedema also lead to relaxation of the lens zonules resulting in thickening of the lens further narrowing the angle. Though the exact mechanism is unclear the fluid movement leading to effusions is thought to be related to drug induced changes in membrane potential [8]. In reported cases of angle-closure glaucoma topiramate doses varied from 50 mg or less to 100 mg or more, 5 reported cases were precipitated within hours after doubling the dose, 85% of cases occurred in the first 2 weeks of treatment with the drug [10]. Fraunfelder et al [10] advise the following management strategy for topiramate-associated angle-closure glaucoma: Stoppage of the drug in the first instance, the prescribing doctor should be consulted. Medical therapy such as oral medications and aqueous suppressants should be given. Laser iridotomy or peripheral iridectomy are not helpful as topiramate angle closure is not pupil block related.

Topical miotics may be contraindicated as they could precipitate a relative pupil block.

Topical cycloplegic agents may be given as they possibly lower IOP by retracting ciliary processes. Care should be taken with acetazolamide as it is also a sulfa-based drug and has been reported to cause angle closure glaucoma in a similar manner to topiramate [11].

In this case the Topiramate induced anatomical changes has been reversed after stopping the drug immediately , before inducing angle closure glaucoma and any permanent ocular damage could prevented to happen. But the rapid onset of severe visual disturbance was much distressing to the patient. And as visual acuity was improved to 6/6 (p) with refraction, it was reasonable to counsel the patient about the better prognosis. As the half life of the drug is about 21-24 hrs,[12] ,rapid visual recovery usually occurs although in some cases it can take several weeks[10]. If unrecognised as a drug-related event serious outcomes could occur (7 cases of permanent visual loss following angle-closure glaucoma have been reported) [10]. Ocular examination before starting Topiramate cannot identify eyes at risk [8].

Patients commencing Topiramate should therefore be advised to immediately report any symptoms of eye pain or blurred vision especially in the first few weeks of treatment.

Conclusion

Drug-induced AACG may be preventable if patients at risk are recognized earlier and properly treated. The causative drug should stop immediately. Delayed recognition and treatment may lead to permanent visual loss due to corneal decompression, optic nerve ischemia and retinal vein thrombosis due to high IOP. Both patients and treating physicians should be aware of the potential of the above drugs to cause AACG.(AAO)[17].

Ophthalmologists, Neurologist, ENT specialist, Internist whoever is prescribing Topiramate need to be aware of the potential ocular side effects of it and counsel the patient about those side effects and to consult an ophthalmologist immediately if any symptoms of vision loss develops specially within initial few days. Although relatively rare prompt recognition is key. So appropriate management can be instituted and visual outcome can be regained and serious complications like permanent visual loss can be prevented.

Abbreviation

IOP, Intraocular pressures.

Consent

The author obtained written informed consent from the patient for the publication of this case report.

Competing interests.

The author declares there are no competing interests.

Author contribution

RD is the sole author of this work. All other authors have helped in the medical care of the patient, analysed and interpreted the patient"s data, performed the literature search and case write-up.

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18. Journal of clinical and diagnostic research

Reversible bilateral Angle Closure Glaucoma introduced by Topiramate: A case report

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Abstract

Purpose: To report a case of reversible bilateral angle-closure glaucoma induced by topiramate and to emphasize the importance of early recognition and management of this potentially vision-threatening but reversible condition.

Methods: After detailed history taking and meticulous examination, the patient was diagnosed as a case of topiramate induced bilateral secondary angle closure glaucoma.

A case of 20 year old female complaints of sudden onset of severe dimness of vision was attended in our hospital.

Visual acuity reduced to counting finger. Retinoscopy shows -3.5.00 diopter myopia and vision was improving to 6/9 with subjective refraction. Slit Lamp examination reveals severe shallowing of anterior chamber, forward movement of lens-iris diaphragm. Intraocular pressure was 25 mm of Hg both eyes. Gonioscopy shows appositional angle closure. Ultrasound bio microscopy shows bilateral cilio-choroidal effusion. Three days after discontinuation of the drug, anatomical changes resolved and refractive status improved to -1.00 D right eye, -1.5 D left eye.

Following diagnosis confirmation, treatment was started with topical cycloplegic, high doses of oral steroids, combination of topical brimonidine and timolol. After seven days, the angle anatomy restored to normal and the IOP decreased. This cilio-choroidal effusion was resolved on ultrasonography biomicroscopy.

Conclusion: Topiramate induced bilateral angle-closure glaucoma is a rare but reversible adverse effect. Prompt recognition, immediate drug discontinuation and appropriate medical therapy are essential to restore vision and prevent permanent glaucomatous damage.

Key Words: Topiramate, angle closure glaucoma, myopic shift.

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Introduction

Topiramate is a sulfamate-substituted monosaccharide widely used for the treatment of epilepsy, migraine prophylaxis and certain psychiatric disorders. Although it is generally well tolerated, one of its rare but serious adverse effects is bilateral acute angle closure glaucoma (AACG).[1] The mechanism differs from primary pupillary block glaucoma; it is attributed to ciliochoroidal effusion leading to forward rotation of the ciliary body, anterior displacement of the lens–iris diaphragm, shallowing of the anterior chamber, and secondary angle closure.[2-3]

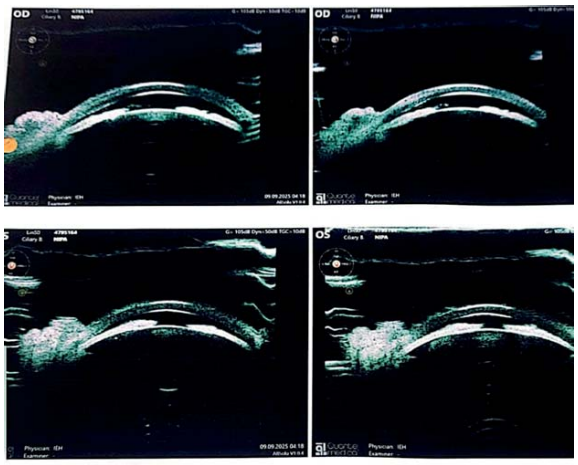
This drug-induced reaction is typically bilateral, acute in onset, and reversible if recognized early.[4] It usually occurs within the first two weeks of starting topiramate or following a dosage increase.[5] Patients present with sudden blurred vision, ocular pain, headache, halos, and myopic shift.[6] Because the mechanism is non-pupillary block, miotics and laser iridotomy are ineffective, and management instead focuses on discontinuing topiramate, using cycloplegics, corticosteroids and intraocular pressure (IOP)-lowering agents.[7]

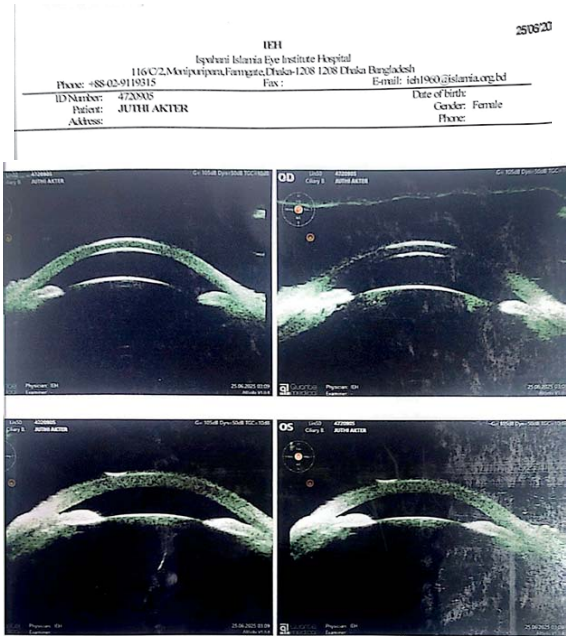
We report a case of otherwise healthy woman who developed reversible bilateral angle closure glaucoma with myopic shift following topiramate use, highlighting the importance of prompt recognition and treatment to prevent permanent visual loss.

Case Report

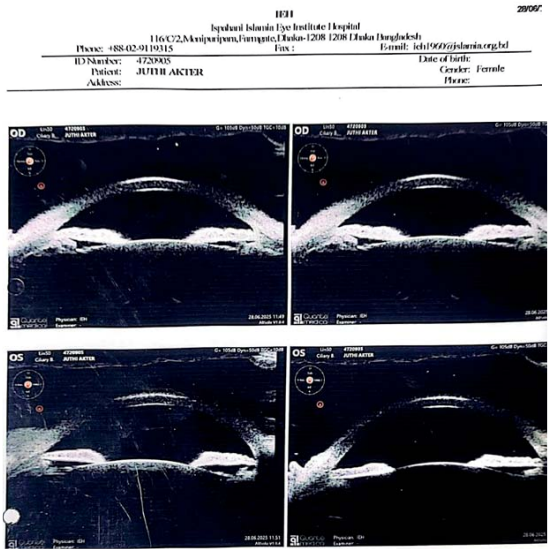
In this case report, we discuss a 20-year-old female patient with a history of recurrent migraine headaches, was started on topiramate 50 mg by her neurologist. She had no prior ocular history and no family history of glaucoma.

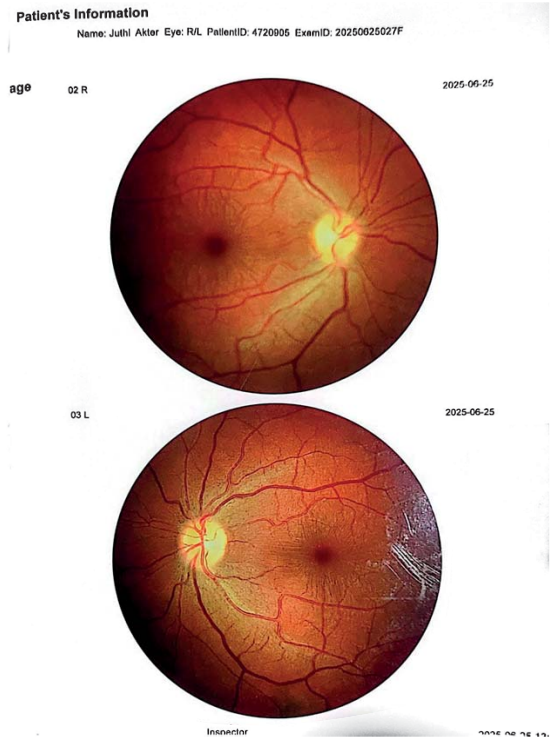
Five days after initiating the medication, she developed acute bilateral ocular pain, blurred vision and severe eyeache. She presented to our glaucoma department with these complaints.





On examination, her visual acquity was counting finger on both eyes which corrected to 6/9 both eyes with a correction of – 3.5 D B/E. Pupils were 5 mm round, regular and minimally reacting B/E, with no afferent pupillary defect. Intraocular pressure with Goldmann applanation tonometry was 25 mm of Hg in the R/E and 30 mm of Hg in L/E. Anterior segment examination was mild conjuctival congestion and markedly shallow anterior chambers B/E. There was no significant corneal oedema. On gonioscopy, there was 360 degree angle closure B/E (Shaffer Grade 0). Fundoscopy examination was unremarkable. Ultrasound bio microscopy confirmed ciliary body oedema and choroidal effusion B/E.





Discussion

Topiramate-induced AACG is an uncommon but increasingly recognized ophthalmic emergency.[8] The estimated incidence is low, but due to the widespread use of topiramate for neurological and psychiatric conditions, clinicians across specialties must remain vigilant.[9] The pathophysiology involves idiosyncratic uveal effusion causing swelling of the ciliary body and

choroid, which in turn displaces the lens–iris diaphragm anteriorly, resulting in angle closure and transient myopia.[10] This mechanism distinguishes it from classic angle closure caused by pupillary block.

Characteristic imaging findings include shallow anterior chambers, thickened choroid, and suprachoroidal effusions on ultrasound biomicroscopy or B-scan.[11] Prompt discontinuation of the offending drug is the cornerstone of management.[12] Topical and systemic IOP-lowering agents, cycloplegics (e.g., atropine), and systemic corticosteroids hasten recovery by reversing ciliary body edema.[13] Unlike primary AACG, laser peripheral iridotomy has no therapeutic role in this condition.[14]

Most cases show complete resolution within days to weeks after cessation of topiramate.[15] Awareness of this rare adverse effect among ophthalmologists, neurologists, and primary care physicians is crucial to ensure early diagnosis, appropriate management, and prevention of irreversible optic nerve damage.

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IOP control in pseudophakic Eye with AADI Bulb implantation –A case report

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Abstract

Intraocular pressure (IOP) management in pseudophakic eyes can be challenging, particularly in cases where traditional methods of control are insufficient. This case report explores the successful management of IOP in a pseudophakic eye through the implantation of an Ahmed Glaucoma Valve (AADI). The patient, a 17-year-old individual with a history of cataract surgery and subsequent elevated IOP, was presented with uncontrolled glaucoma despite maximal medical therapy. Following the AADI implantation, the patient demonstrated significant improvement in IOP control, without the need for additional interventions. This case highlights the effectiveness of the AADI in providing sustained IOP reduction in pseudophakic eyes, especially in patients with complex glaucoma. The report also discusses the surgical technique, postoperative management, and potential complications associated with this intervention. Our findings suggest that AADI implantation can be a viable option for IOP control in pseudophakic glaucoma patients who are refractory to medical treatment.

Case Summary: The patient, Md. Nizamul Haque, is a 17-year-old male with a history of congenital glaucoma. He underwent cataract surgery at the age of 6, with the implantation of a posterior chamber intraocular lens (PCIOL). Subsequently, he developed secondary glaucoma in both eyes. Upon presenting to our department, his intraocular pressure (IOP) was 26 mmHg in the right eye and 32 mmHg in the left eye, despite being on maximum anti-glaucoma medication. The cup-to-disc ratio was 0.75:1 in both eyes. His visual acuity was 6/36 in the right eye and 6/60 in the left eye. After evaluation, we decided to proceed with AADI implantation in both eyes under general anesthesia. The procedure was performed in the right and left eyes, respectively, seven days apart.

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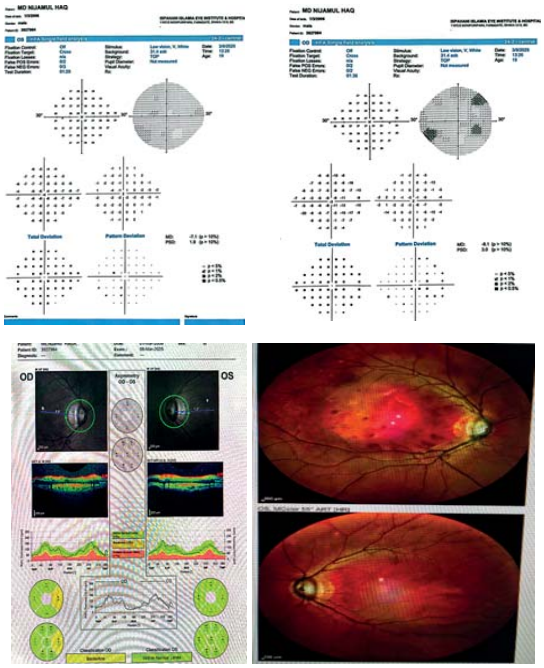

Fig: Investigation reports

Surgery Steps

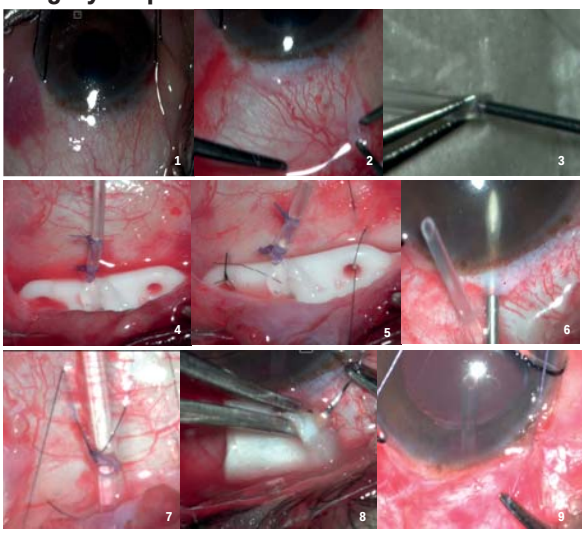

Figure: Steps of Surgery: 1. Corneal Countertraction, 2. Conjunctival dissection 3. Priming of implant 4. Insertion of implant 5. Fixation of Implant 6. Creation of Scleral tract or AC entry 7. Fixation of Tube 8. Scleral patch graft 9. Conjunctival closure.

Post Operative Outcome: On 3 months postoperative Follow up VA was 6/60 in both eyes and IOP was recorded 15 and 16

Respectively R/E and L/E. and at 6th months follow up VA was 6/60 (B/E) as previous visit and IOP was being maintained 13 mmhg R/E and 14 mmhg L/E. No further disc damage documented. No postoperative complications like hypotony, the AADI tube exposure, retraction, plate exposure, and plate displacement were seen.

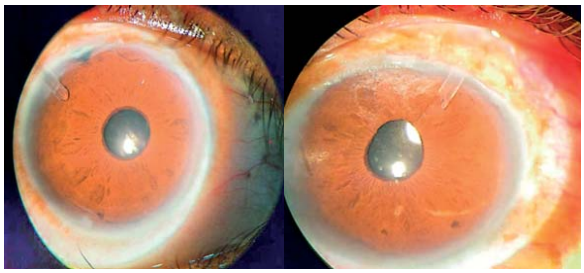

Figure: 6 month post-operative.

Discussion

Glaucoma is the leading cause of irreversible blindness in today's world, and its prevalence in India ranges from 2.2%to 5.8%.[1,2] Glaucoma drainage devices (GDDs) are used in patients with failed trabeculectomy, refractory glaucoma and patients with conjunctival scarring where trabeculectomy is not possible or has high risk of failure.[3] GDDs help to create alternate an pathway by channeling aqueous from the anterior chamber to an equatorial plate through a long tube and promotes bleb formationposteriorly.[4]

Ahmed glaucoma valve (AGV, New World Medical, Cucamonga, CA) was the only valved GDD available and the high cost of the device was a limiting factor in developing countries like Bangladesh.[5]. AADI developed by Aurolab, India, is an innovative proto type of non-valved Baerveldt implant (Abbott Medical Optics, Abbott Park, IL) and has gained increasing popularity over the last few years.[6]. AADI was traditionally used to manage patients with refractory glaucoma. They were usually used as secondary procedure after failed trabeculectomy and also as a primary procedure in refractory glaucoma. AADI channels the aqueous from the anterior chamber to the equatorial plate located subconjunctivally via a tube thus creating an alternate pathway. It's a non-valved device, thus the tube should be ligated to prevent early hypotony related complications. An encapsulated bleb that forms over the plate over a period of time helps in regulating the aqueous Drainage and IOP control.[7]. In our retrospective review of AADI in refractory glaucoma, we found that it was effective in reducing the IOP and reduced the need for antiglaucoma medications (AGMs) in 1 or 2 years. Cumulative failure rate of the AADI was defined as IOP > 18 mmHg or not reduced by 30% below baseline on 2 consecutive follow-up visits 3 after months, IOP ≤ 6 mmHg on 2 consecutive follow-up visits after 3 months, re-operation for glaucoma, or loss of light perception vision[8]. Common Postoperative outcome documented was postoperative hypotony, the AADI tube exposure, retraction, plate exposure, and plate displacement were seen and eventually bulb failure.

Conclusion

In conclusion, AADI is an affordable, non-valved glaucoma drainage device that has shown positive outcomes in treating cases of refractory glaucoma. While complications can occur both early and late, they are generally manageable with prompt and appropriate medical or surgical treatment.

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Management of Weill-Marchesani Syndrome with Secondary Glaucoma: A rare case report

F Yasmin[1], S M Noman[2], E Reza[3]

Abstract

Purpose: To describes clinical features and surgical management of a rare case of Weill-Marchesani Syndrome with secondary glaucoma who presented with poor vision.

Methodology

Case Report: A 30 years old male presented with bilateral dimness of vision for 1 year. His intraocular pressure was 45 mm of Hg in left eye and 36 mm of Hg in right eye. His vision in right eye 2/60 and PLPR positive in the left eye. To control intraocular pressure the pt underwent trabeculectomy in both eyes three years back. On slit lamp examination with the dilated pupil revealed dislocated microspherophakia in both the eyes. The patient was diagnosed Weill -Marchesani Syndrome based on ocular and systemic clinical findings including brachydactyly, short stature, thickened skin, joint stiffness. Microspherophakic lens was confirmed by anterior segment OCT. Subsequently patient was well managed by phaco emulsification with intraocular lens implantation. We follow up the patient at 1 monthly,3 monthly and 6 monthly and found well controlled intraocular pressure and normal anterior chamber depth in both eyes

Discussion: Weill -Marchesani Syndrome is a multisystem connective tissue disorder. First described in 1932 by George Weil, a French Ophthalmologist. It is characterized by significant ocular complications, ranging from severe myopia, microspherophakia, and vision loss and systemic complications are common and often very serious like skeletal/joint involvement, and cardiac problem facial structures are often involved.

Conclusion: Early diagnosis is critical not only for the management of systemic features but also for visual rehabilitation by joint collaboration of the cardiologist, rheumatologist, and by the ophthalmologist. Clear lens extruction with posterior chamber intraocular lens implantation should be carried out for well control of IOP and better visual prognosis.

Introduction

Weill-Marchesani syndrome (WMS) is a rare systemic connective tissue disorder, conceptually the converse of Marfan Syndrome.[1] Inheritance is AR or AD. WMS was first described by two ophthalmologist, Georges Weill and Oswald Marchesani in 1932.[2] Ocular abnormalities include ectopia lentis, microspherophakia, lens subluxation, high myopia, glaucoma, and corneal changes.[3,4] Microspherophakia is common, so the pupillary block with angle closure may ensue. Systemic abnormalities include short stature, progressive joint stiffness, short fingers and toes, thick skin, learning difficulties, mild mental retardation, and cardiac anomalies.[5,6] Weill-Marchesany Syndrome patients are often misdiagnosed by an ophthalmologist as high myopia or angle closure glaucoma. Here we report a rare case with Weill-Marchesani syndrome with surgical management of advanced glaucoma as WMS diagnosis not only assists in treatment and management of the patient but may also help identify others at-risk in family members.

Case History

A 30- years- old male presented at our hospital with bilateral dimness of vision for last years. The patient undergone glaucome surgeries in his both eyes 3 years back for raised intraocular pressure. Ocular examination further revealed his best corrected visual acuity was PLPR in the left eye with -10.0D not improved and in the right eye 2/60 with -8.0D improved to 6/36. On slit lamp examination anterior chamber was shallow in both eyes more in the left eye. The intraocular pressure was 36 mm of Hg in the right eye and 45 mm of Hg in the left eye. Although the patient had history of trabeculectomy in both eyes his IOP was high. Dilated fundus examination of both eyes revealed lens are smaller, spherical and equator is visible in the both eyes. Suspensory ligament of the lens is also visible. The cup to disc C:D ratio 0.9 in the left eye and 0.8 in the right eye. Humphrey visual field testing was done in both eyes that show narrow field and more marked in left eye. Anterior segment OCT was done that shows microspherophakia and its diameter both anteroposterior and horizontal is around 8 mm. On general examination, the patient is short(130cm),

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fingers and toe are short stubby. Based on history and clinical examination we diagnose the case as Weill-Marchesany Syndrome with secondary glaucoma due to pupillary block by the microspherophakic lens. After diagnosis we started anti- glaucome medications in both eyes and immediately undergo phacoemulsification and posterior chamber intraocular lens implantation in the better seeing right eye to prevent further damage of the optic nerve. An intraocular lens with +24.5D was successfully implanted in the posterior capsule with very caution. Surprisingly on first post-operative day IOP of the right eye become 22 mm of Hg from pre-operative IOP 35 mm of Hg and his vision improved to 6/24 with PH improved to 6/18. During follow -up after 1 week and after 1month IOP becomes 18 and 16 mm of Hg. Final vision after one month becomes 6/18 which is improved to 6/9 with -0.75D sph and N6 with +2.50Dsph. As IOP becomes nicely controlled in the right eye we decided to go for same surgery in the left eye after 7 days. Following surgery IOP becomes well controlled in that eye but vision not improved due to pre-existing glaucomatous optic atrophy. Subsequently in the 3 months,6 months and 1 year follow up the patient had normal IOP without any anti-glaucoma medication, anterior chamber depth was normal and intraocular lens was well placed in situ.

Fig1: The Patient

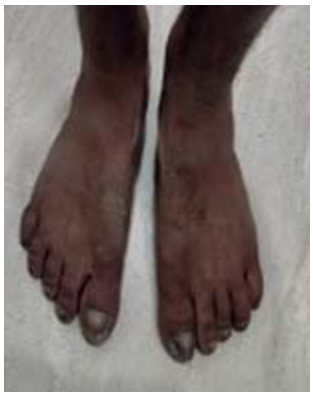

Fig2: Thick skin with short toes.

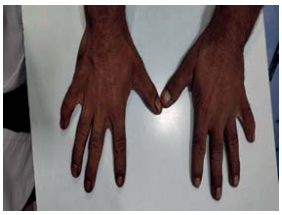

Fig 3: Short and stubby fingers.

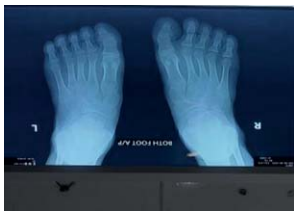

Fig 4: X-ray shows brachydactyly and joint thickness

Fig 5: Anterior segment photo showing microspherophakia

Fig 6: Anterior segment OCT showing microspherophakia

Discussion

The major systems involved in Weill-Marchesany syndrome are the ocular, cardiac and musculoskeletal systems. Severe myopia, lens microspherophakia, lens subluxation, secondary pupillary block glaucoma and secondary angle closure glaucoma are the ocular features of the disorder.

Diagnostic criteria for Weill Marchesany Syndrome are based on combination of characteristic clinical features and molecular genetic testing. The primary clinical findings are ocular abnormalities including microspherophakia, ectopia lentis, short stature, brachydactyly and joint stiffness. Diagnosis can be established in a proband with these suggestive findings or via genetic testing identifying pathogenic variants in genes like ADAMTS10, ADAMTS17, LTBP2,or FBN1.(Ben Yahia S, Jelliti B et all 2009:54:550-3. (PubMed)

Inheritence of the disease is autosomal dominant and autosomal recessive varients and carry a family history of this condition. Faivre et al. reported that autosomal recessive and autosomal dominant inheritance accounted for 45% and 39% of WMS cases respectively and the remaining cases are sporadic (6) Patients develop secondary glaucoma due to pupillary block and angle closure glaucoma eventually develop permanent damage of optic nerve. Our patient undergo trabeculectomy in both eyes but his IOP increased due to zonular relaxation leads to move the lens forwards. Microspherophakic lens removal is mandatory to reduce IOP. Our patient is one eyed patient so immediate clear lens extruction with intraocular lens implantation was advised immediately to save the better eye

Pre-operative careful evaluation and phacoemulcification with posterior chamber intraocular lens was implanted with caution. We follow up the patient upto 1year with stable IOP. WMS is a rare disease and there is no clinically accepted treatment

modatities, however removal of lens was recommended to control IOP and increase vision. In case of early glaucoma simple removal of lens could control IOP. If patient have advanced glaucoma lens removal with trabeculectomy should be performed. Subsequently we refer to the cardiologist and rheumatologist.

Conclusion

The major systems involved in Stickler syndrome are the ocular, auditory, orofacial, and musculoskeletal systems. Severe myopia with onset in the first decade of life, vitreous degeneration, spontaneous retinal detachment, chorioretinal degeneration, open angle glaucoma, and presenile cataracts are the ocular features of the disorder (Stickler et al., 1965; Rimoin and Lachman, 1993; Liberfarb et al., 2003).

Early diagnosis is critical. It is a mult- system pathology so very crucial to involve cardiologist, rheumatologist and Ophthalmologist. Proper genetic counselling is also very important for the patient's parents so that they can plan for the future of their child affected with Weill -Merchesany syndrome.

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