Original Article

CHRONIC KIDNEY DISEASE AND RISK OF GLAUCOMA: A CASE-CONTROL STUDY

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ABSTRACT

Background: Glaucoma and chronic kidney disease (CKD) are major global health concerns with shared pathophysiological mechanisms including oxidative stress, inflammation, and microvascular damage. Despite growing evidence of their bidirectional relationship, limited research exists on their association in developing countries like Bangladesh. This study aimed to assess the association between chronic kidney disease and glaucoma risk among patients in Bangladesh.

Methods: A case-control study was conducted at National Institute of Ophthalmology and Bangabandhu Sheikh Mujib Medical University, Dhaka, from July 2023 to June 2024. The study included 115 physician-diagnosed glaucoma cases and 115 age- and sex-matched controls without glaucoma. Data were collected through structured interviews and medical record reviews. Multivariable logistic regression was performed to determine adjusted odds ratios (AOR) while controlling for potential confounders.

Results: CKD prevalence was significantly higher among cases (53.0%) compared to controls (13.0%, p<0.001). After adjusting for confounders, CKD patients demonstrated 5.31 times higher odds of developing glaucoma (AOR=5.31, 95% CI: 1.84-15.30, p=0.002). Other significant independent predictors included low monthly family income (AOR=5.88, 95% CI: 2.38-14.49), migraine (AOR=4.10, 95% CI: 1.31-12.85, p=0.016), myopia (AOR=7.73, 95% CI: 1.71-34.94, p=0.008), and history of ocular laser surgery (AOR=4.74, 95% CI: 1.60-14.02, p=0.005).

Conclusion: This study provides the first comprehensive evidence of a significant association between CKD and glaucoma risk in Bangladesh. CKD patients should receive routine glaucoma screening, and comprehensive prevention strategies targeting both conditions are needed.

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INTRODUCTION

Glaucoma represents one of the leading causes of irreversible blindness worldwide, with primary open-angle glaucoma (POAG) affecting 44.1 million people globally (1). This progressive optic neuropathy is characterized by retinal ganglion cell death, optic nerve head excavation, and visual field loss. The global burden of glaucoma is projected to reach 110-120 million cases by 2040, making it a significant public health concern. In Bangladesh, glaucoma affects approximately 3.2% of individuals aged 35 years and older, with an estimated 2 million patients nationwide (2).

The pathophysiology of glaucoma involves elevated intraocular pressure and disrupted vascular supply to the optic nerve head. When aqueous humor drainage is compromised, increased intraocular pressure compresses blood vessels supplying the optic nerve, leading to progressive nerve damage and peripheral vision loss (3). The insidious nature of the disease means that 50% of affected individuals remain undiagnosed, particularly in early stages when symptoms are absent (4).

Chronic kidney disease (CKD) has emerged as a rapidly increasing global public health issue, affecting approximately 8-16% of the worldwide population (5). In Bangladesh, CKD prevalence is notably higher at 22.48%, with one-third of the rural population at risk, largely remaining undiagnosed (6). The condition is characterized by reduced kidney function or kidney damage persisting for three months or more, ranking as the 18th leading cause of death globally according to the 2019 Global Burden of Disease Study (7).

Recent evidence suggests a significant association between CKD and glaucoma, supported by their shared pathophysiological mechanisms, including oxidative stress, inflammation, endothelial dysfunction, and microvascular damage (8). Both conditions share common risk factors such as advanced age, hypertension, and diabetes mellitus. Research from Singapore's National University demonstrated that CKD patients have an 18% higher incidence of glaucoma, with this risk increasing to 42% among diabetic CKD patients (9). Conversely, glaucoma patients showed a 3.6-fold higher risk of developing incident CKD over 10-15 years of follow-up.

The eye-kidney connection is supported by structural similarities between the glomerulus and choroid, both featuring extensive vascular networks susceptible to similar pathological processes (10). Despite growing evidence of this bidirectional relationship, comprehensive studies examining the association between CKD and glaucoma risk remain limited, particularly in developing countries like Bangladesh, where both conditions impose substantial healthcare burdens. Given the increasing prevalence of both CKD and glaucoma globally and the lack of adequate research on their relationship in Bangladesh, this study aimed to assess the association between chronic kidney disease and glaucoma risk.

METHODS

Study design, place and period

A case-control study was conducted to assess the association between chronic kidney disease and risk of glaucoma among patients attending the outpatient and inpatient departments of National Institute of Ophthalmology & Hospital (NIO) and Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. The study was carried out over a one-year period from July 1, 2023, to June 30, 2024. Cases were defined as patients previously diagnosed with glaucoma by ophthalmologists based on their clinical reports, while controls were individuals without glaucoma, matched for age (±5 years) and sex, attending the same institutions during the study period. Both study hospitals were selected purposively as tertiary care centers serving patients from greater Dhaka city and various regions of the country.

Sample size and sampling

Sample size was calculated using the standard formula for case-control studies (11):

$$n = \frac{(r+1)}{r} \frac{p(1-p)(Z_\beta + Z_{\frac{\alpha}{2}})^2}{(p_1 - p_2)^2}$$

Here, r represents the ratio of controls to cases, p is the pooled proportion, and (p_1-p_2) represents the effect size. Based on a previous study by Tham et al. (9), the proportion of stage I chronic kidney disease was 29.2% (p_1=0.292) among open-angle glaucoma patients and 48.8% (p_2=0.488) among controls. With r=1, α=0.05, and 80% power, the calculated sample size was 96 per group. Considering a 20% non-response rate, the final sample size was determined as 115 cases and 115 controls, totaling 230 participants. A purposive sampling technique was employed for participant selection. Physician-diagnosed glaucoma patients were included as cases. Those who had glaucoma secondary to other eye diseases were excluded. Individuals without a history of glaucoma from the same institute were included as controls. Both cases and controls, who were unwilling to participate or had severe mental illness, were excluded.

Data collection

Data collection utilized two primary instruments: a pre-tested semi-structured questionnaire and a checklist. The questionnaire was developed in both English and Bengali, covering socio-demographic characteristics, factors related to glaucoma, and other associated risk factors. The checklist was used to collect information regarding CKD stage, duration, types of glaucoma, comorbidities, and history of medication use, particularly corticosteroids, anti-hypertensive drugs, and oral hypoglycemic agents. Data were collected through face-to-face interviews lasting approximately 20 minutes per participant. Medical records were reviewed to supplement the checklist information. Pre-testing was conducted at Dhaka Medical College and Hospital with 30 interviews (15 cases and 15 controls) to refine the instruments before actual data collection.

Data analysis

Data were analyzed using IBM SPSS version 24 software. Descriptive statistics included frequency distributions, means, standard deviations, median, and interquartile range for participant characteristics. Normality of continuous data was assessed using box plots and Shapiro-Wilk tests. Inferential statistics comprised chi-square tests for categorical variables and independent samples t-tests and Mann-Whitney U test for continuous variables to examine associations between cases and controls. Potential factors were selected for multivariable analysis from bivariate analyses. Multivariable binary logistic regression was performed to calculate adjusted odds ratios with the primary aim of assessing the strength of association between chronic kidney disease and glaucoma risk, controlling for potential confounders.

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Ethical considerations

The study protocol received approval from the Protocol Approval Committee and the Institutional Review Board (IRB) of the National Institute of Preventive & Social Medicine (NIPSOM/IRB/2024/8). Written permissions were obtained from the administrative authorities of both BSMMU and NIO, as well as departmental heads of the ophthalmology departments. Informed written consent was obtained from all participants after verbally explaining the study's purpose and objectives. Participants were assured of voluntary participation, confidentiality, anonymity, and their right to withdraw from the study at any time without consequences.

RESULTS

The study included 230 participants, comprising 115 cases with glaucoma and 115 age- and sex-matched controls. The sociodemographic characteristics revealed that cases had a slightly higher mean age (47.23±13.03 years) compared to controls (44.12±12.31 years), though this difference was not statistically significant (p=0.064). The majority of participants in both groups were aged 30-59 years, with cases showing a higher proportion of participants aged 60-75 years (26.5% vs 16.7%). Gender distribution was equally matched between groups (53.0% male in each group). Significant differences were observed in residence patterns, with cases more likely to be from rural areas (42.6% vs 23.5%, p=0.002). Educational attainment differed markedly between groups, with cases having significantly lower educational levels, including a higher proportion of illiterate participants (31.3% vs 9.6%, p<0.001). Cases were more likely to be unemployed, businessmen, or homemakers, while controls were predominantly service holders (73.9% vs 32.2%, p<0.001). Monthly family income was significantly lower among cases, with 68.7% earning 10,000-39,000 Taka compared to only 22.6% of controls (p<0.001). Cases also had significantly more children (median 2 [IQR:2-3] vs 2[IQR:1-2], p=0.001), while other demographic characteristics such as marital status, family type, and number of family members showed no significant differences (Table 1).

Table 1. Comparison of sociodemographic characteristics between cases and controls

Characteristics	Type of Participant		p-value*
	Case; n (%)	Control; n (%)	
Age (years), Mean ±SD	47.23 ±13.03	44.12 ±12.31	0.064
Age groups (years)			
20 – 29	12 (10.6)	14 (12.3)	0.194
30 – 59	71 (62.8)	81 (71.1)	
60 – 75	30 (26.5)	19 (16.7)	
Sex			
Male	61 (53.0)	61 (53.0)	1.000
Female	54 (47.0)	54 (47.0)	
Residence			
Rural	49 (42.6)	27 (23.5)	0.002
Urban	66 (57.4)	88 (76.5)	
Educational qualification			
Illiterate	36 (31.3)	11 (9.6)	<0.001
Primary	11 (9.6)	13 (11.3)	
Secondary	15 (13.0)	5 (4.3)	
SSC	20 (17.4)	2 (1.7)	
HSC	8 (7.0)	21 (18.3)	
Graduation	25 (21.7)	44 (38.3)	
Post-graduation	0 (0.0)	19 (16.5)	
Occupation			
Unemployed	11 (9.6)	7 (6.1)	<0.001
Service holder	37 (32.2)	85 (73.9)	
Businessman	30 (26.1)	8 (7.0)	
Homemaker	37 (32.2)	15 (13.0)	
Monthly family income (Taka)			
10000 – 39000	79 (68.7)	26 (22.6)	<0.001

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40000 and above	36 (31.3)	89 (77.4)	
Marital status			
Married	104 (90.4)	98 (85.2)	0.226
Single	11 (9.6)	17 (14.8)	
Family type			
Nuclear	73 (63.5)	70 (60.9)	0.683
Joint	42 (36.5)	45 (39.1)	
Number of family members, median (IQR)	5 (4 – 6)	5 (4 – 6)	0.624
Number of children, median (IQR)	2 (2 – 3)	2 (1 – 2)	0.001

*p-values were determined by Independent Samples t-test, Chi-square test and Mann-Whitney U test as appropriate

Personal habits and comorbidities analysis revealed substantial differences between cases and controls. Tobacco consumption was significantly higher among cases, with 53.0% being ever consumers compared to 29.6% of controls (p<0.001). Among tobacco users, the duration of consumption was longer in cases (13.21±4.87 years' vs 10.59±4.48 years, p=0.010). The prevalence of chronic kidney disease was markedly higher in cases (53.0%) compared to controls (13.0%, p<0.001), representing the primary exposure of interest. Several comorbidities were significantly more prevalent among cases, including diabetes mellitus (52.2% vs 29.6%, p<0.001), hypertension (69.6% vs 45.2%, p<0.001), migraine (93.9% vs 63.5%, p<0.001), myopia (96.5% vs 75.7%, p<0.001), and obstructive sleep apnea (18.3% vs 7.8%, p=0.019). Dyslipidemia showed no significant difference between groups (49.6% vs 40.0%, p=0.145) (Table 2).

Table 2. Comparison of personal habits and comorbidities between cases and controls

Characteristics	**Type of Participant**		**p-value**
	Case; n (%)	**Control; n (%)**	
Personal habit			
Tobacco consumption			
Ever consumer	61 (53.0)	34 (29.6)	<0.001
Never consumer	54 (47.0)	81 (70.0)	
Type of tobacco consumed			
Smoked	25 (41.0)	12 (35.3)	0.327
Smokeless	30 (49.2)	21 (61.8)	
Duration of tobacco consumption (Years), Mean±SD	13.21 ±4.87	10.59 ±4.48	0.01
Comorbidities			
Chronic Kidney Disease	61 (53.0)	15 (13.0)	<0.001
Diabetes mellitus	60 (52.2)	34 (29.6)	<0.001
Dyslipidemia	57 (49.6)	46 (40.0)	0.145
Hypertension	80 (69.6)	52 (45.2)	<0.001
Migraine	108 (93.9)	73 (63.5)	<0.001
Myopia	111 (96.5)	87 (75.7)	<0.001
Obstructive sleep apnea	21 (96.5)	9 (7.8)	0.019

*p-values were determined by Independent Samples t-test, and Chi-square test as appropriate

The distribution of chronic kidney disease stages among participants with CKD showed that the majority of cases were mild, with Stage 2 being most common (59.02% of cases and 73.33% of controls), followed by Stage 1 (21.31% of cases and 13.33% of controls). Controls with CKD were predominantly in earlier stages (Stage 1 and 2), indicating that more severe kidney dysfunction was associated with glaucoma development (Figure 1).

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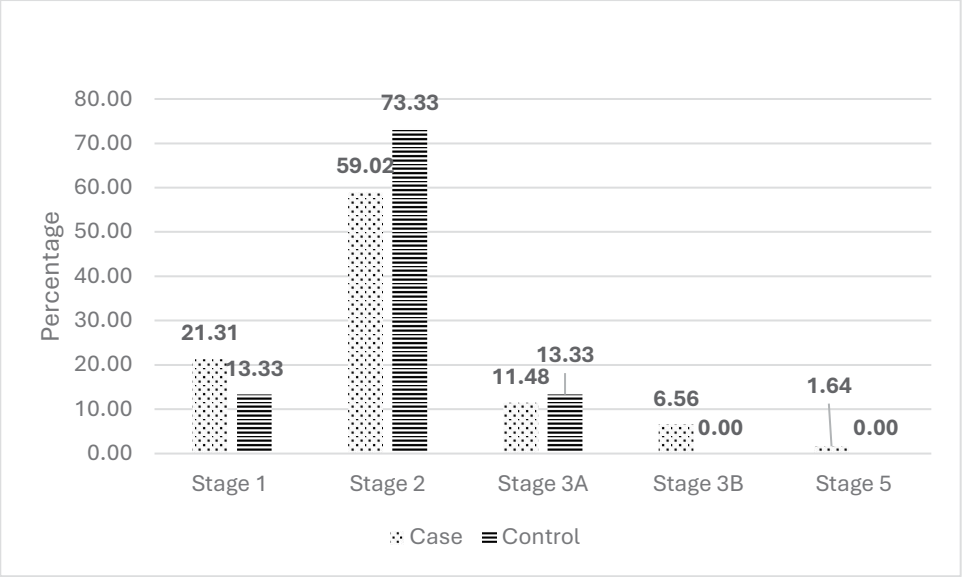

Figure 1. Comparison of CKD stages between case and controls [Stage 1 (normal or high): GFR >90ml/min; Stage 2 (mild): GRF = 60 – 89 ml/min; Stage 3A (moderate): GFR = 60 – 89 ml/min; Stage 3B (moderate): GFR = 45 – 59 ml/min; Stage 5 (end stage): GFR <15 ml/min]. Family history, trauma, surgical history, and medication-use patterns differed significantly between groups. Cases had a substantially higher prevalence of family history of glaucoma (71.3% vs 46.1%, p<0.001) and history of ocular trauma (71.3% vs 53.0%, p<0.001). History of laser surgery was more common among cases (37.4% vs 9.6%, p<0.001). Regarding medication history, cases showed significantly higher usage of corticosteroids (67.8% vs 33.9%, p<0.001), oral hypoglycemic agents (51.3% vs 27.0%, p<0.001), antihypertensive drugs (69.6% vs 46.1%, p<0.001), and antiplatelet agents (42.6% vs 13.9%, p<0.001), reflecting the higher burden of comorbidities and their management in the glaucoma group (Table 3).

Table 3. Comparison of factors related to glaucoma between cases and controls

Characteristics	Type of Participant		p-value
	Case; n (%)	Control; n (%)	
Family history of glaucoma	82 (71.3)	53 (46.1)	<0.001
History of ocular trauma	82 (71.3)	61 (53.0)	<0.001
History of laser surgery	43 (37.4)	11 (9.6)	<0.001
Drug history			
Corticosteroid	78 (67.8)	39 (33.9)	<0.001
Oral hypoglycemic agent	59 (51.3)	31 (27.0)	<0.001
Antihypertensive drug	80 (69.6)	53 (46.1)	<0.001
Antiplatelet agent	49 (42.6)	16 (13.9)	<0.001

Multivariable logistic regression analysis identified several independent factors associated with glaucoma. The presence of chronic kidney disease emerged as the strongest predictor, with participants having CKD showing 5.31 times higher odds of developing glaucoma compared to those without CKD (AOR=5.31, 95% CI: 1.84-15.3, p=0.002). Low monthly family income (less than 40,000 Taka) was associated with dramatically increased odds of glaucoma (AOR=5.88, 95% CI: 2.38-14.49, p<0.001). Other significant independent predictors included migraine (AOR=4.10, 95% CI: 1.31-12.85, p=0.016), myopia (AOR=7.73, 95% CI: 1.71-34.94, p=0.008), and history of ocular laser surgery (AOR=4.74, 95% CI: 1.60-14.02, p=0.005) (Table 4).

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Table 4. Multivariable logistic regression table exploring factors associated with Glaucoma

Factor	Reference Category	Adjusted Odds Ratio (95%CI)	p-value
Chronic Kidney Disease (%)	Absent	5.31 (1.84 – 15.3)	0.002
Residence (Rural)	Urban	0.98 (0.4 – 2.4)	0.962
Education (No formal education)	Having formal education	1.93 (0.63 – 5.85)	0.248
Occupation (Unemployed)	Employed	1.52 (0.6 – 3.81)	0.375
Monthly family income (Less than 40000)	40000 and above	5.88 (2.38 – 14.49)	<0.001
Tobacco consumption (Ever consumed)	Never consumed	1.29 (0.56 – 3.01)	0.551
Diabetes (%)	Absent	0.38 (0.05 – 2.96)	0.359
Hypertension (%)	Absent	1.33 (0.12 – 14.9)	0.815
Migraine (%)	Absent	4.1 (1.31 – 12.85)	0.016
Myopia (%)	Absent	7.73 (1.71 – 34.94)	0.008
Obstructive Sleep Apnea (%)	Absent	1.52 (0.46 – 4.97)	0.491
Family history of glaucoma (%)	Absent	1.63 (0.7 – 3.76)	0.256
History of ocular trauma (%)	Absent	0.82 (0.34 – 1.97)	0.656
History of ocular laser surgery (%)	Absent	4.74 (1.6 – 14.02)	0.005
History of taking steroid (%)	Absent	1 (0.41 – 2.4)	0.993
History of taking oral hypoglycemic drug (%)	Absent	1.5 (0.18 – 12.36)	0.707
History of taking anti-platelet drug (%)	Absent	2.31 (0.71 – 7.56)	0.165
History of taking antihypertensive drug (%)	Absent	0.69 (0.07 – 6.87)	0.753

DISCUSSION

Our case-control study provides compelling evidence for a significant association between chronic kidney disease and glaucoma risk, with CKD patients demonstrating 5.51 times higher odds of developing glaucoma compared to those without CKD. This finding aligns with previous research from South Korea in 2022, where Ng et al. reported that glaucoma consecutively developed in 4.3% of the CKD group compared to 2.8% in controls, with CKD increasing glaucoma risk (Odds Ratio [OR] = 3.67, 95% CI = 2.16-6.24) (12). Similarly, Cho et al. demonstrated that patients with CKD stages 1-3 and 4-5 had greater glaucoma risk compared to those without CKD, with advanced CKD showing considerably higher cumulative incidence than mild to moderate CKD (13).

Our analysis of sociodemographic characteristics revealed important patterns, with glaucoma cases predominantly from rural areas (42.6% vs 23.5%) and having significantly lower educational attainment and monthly family income. These findings contrast with the South Korean study by Ng et al.(12), which found higher income families had greater glaucoma prevalence, likely reflecting the substantial economic differences between developed and developing countries. We observed that the mean age of cases (47.23±13.03 years) was slightly higher than controls (44.12±12.31 years), though not statistically significant, which differs from other studies where glaucoma prevalence increased markedly with age, particularly in the 70-79 age group.

The family history of glaucoma emerged as a significant risk factor in our study, with 71.3% of cases having a positive family history compared to 46.1% of controls. This finding is consistent with McNaught et al.(14), who reported that approximately 50% of primary glaucoma patients had positive family history, with first-degree relatives having a nine-fold increased risk. The genetic predisposition to glaucoma underscores the importance of family screening programs, particularly given that more than 50% of glaucoma cases remain undiagnosed.

We found that ocular trauma history was significantly more prevalent among cases (71.3% vs 53.0%), supporting the established relationship between trauma and secondary glaucoma development. According to Ng and Lau(15), glaucoma can develop rapidly following eye damage or gradually over months to years due to tears in the ciliary body muscle fibers affecting the trabecular meshwork. Our observation of a higher prevalence of laser surgery history among cases (37.4% vs 9.6%) may reflect both therapeutic interventions for existing glaucoma and potential iatrogenic risk factors.

Our analysis of comorbidity patterns revealed that diabetes mellitus, hypertension, migraine, and myopia were significantly more prevalent among glaucoma cases. The association with diabetes (52.2% vs 29.6%) aligns with Zhao and Chen's findings (16) suggesting

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diabetes as a glaucoma risk factor, particularly as hyperglycemia results in heightened sensitivity to intraocular pressure and increased neuronal injury risk. We observed hypertension in 69.6% of cases versus 45.2% of controls, consistent with Zhao et al (17), who found hypertension significantly associated with glaucoma development (HR = 1.16, 95% CI = 1.05–1.28). The mechanism likely involves microvascular circulatory disturbances and decreased ocular perfusion to the optic disc.

The strong association between myopia and glaucoma (96.5% vs 75.7%) that we identified supports Marcus et al. (18), who demonstrated that myopia, particularly high myopia with increased axial length, represents a significant glaucoma risk factor. The optic nerve head in myopic eyes may be structurally more susceptible to glaucomatous damage due to connective tissue changes. Similarly, our finding of a relationship between migraine and glaucoma (93.9% vs 63.5%) suggests shared vascular pathophysiology, as suggested by Chen, Li and Kao (19) with compromised blood flow being a common mechanism.

Our medication history analysis revealed significantly higher corticosteroid use among cases (67.8% vs 33.9%), which is consistent with the established mechanism of steroid-induced elevation of intraocular pressure through decreased aqueous outflow facility (20). The higher usage of oral hypoglycemic agents and antihypertensive medications among cases likely reflects the greater burden of diabetes and hypertension in this population.

We found that tobacco consumption was significantly higher among cases (53.0% vs 29.6%), with longer duration of use, supporting Pérez-de-Arcelus et al. (21), who identified smoking as an environmental stressor that may increase glaucoma development risk. This finding has important public health implications given the preventable nature of tobacco exposure.

Our multivariable analysis strengthened the study's conclusions by demonstrating that CKD remained independently associated with glaucoma even after controlling for potential confounders, including demographics, comorbidities, and medication use. Other independent predictors included low family income, migraine, myopia, and history of ocular laser surgery, while several factors that showed univariate associations did not retain significance in the adjusted model.

Our study has several important limitations. The findings may not be representative of the general Bangladeshi population as we recruited participants only from two specialized hospitals in Dhaka city. The small sample size and potential recall bias during face-to-face interviews represent additional constraints. Selection bias may have occurred as we conveniently selected controls from the same hospitals, potentially underestimating the true association. The absence of laboratory investigations due to resource constraints limited our depth of CKD characterization, and the cross-sectional nature of the case-control design prevents establishment of temporal relationships between CKD and glaucoma development.

CONCLUSION

This case-control study demonstrates a significant association between chronic kidney disease and glaucoma risk in Bangladesh, with CKD patients having 5.51 times higher odds of developing glaucoma. The findings reveal that glaucoma cases were characterized by lower socioeconomic status, rural residence, and higher prevalence of comorbidities including diabetes, hypertension, migraine, and myopia. Family history of glaucoma, ocular trauma, and medication use patterns further distinguished cases from controls. These results provide the first comprehensive evidence of the CKD-glaucoma relationship in the Bangladeshi context, where both conditions represent significant public health challenges. The study recommends implementation of comprehensive awareness programs to reduce CKD prevalence among at-risk populations and establishment of routine glaucoma screening protocols for CKD patients, particularly those with advanced kidney disease. Healthcare providers should maintain heightened vigilance for glaucoma development in patients with CKD, diabetes, hypertension, and family history of glaucoma. Policy-level interventions targeting tobacco cessation, improved access to eye care services in rural areas, and early detection programs for both CKD and glaucoma are essential. Future population-based studies with larger sample sizes and longitudinal designs are needed to better understand the temporal relationship and underlying mechanisms linking these conditions, ultimately improving prevention and management strategies for both diseases in Bangladesh and similar developing countries.

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