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ORIGINAL ARTICLE

Is the primary open angle glaucoma finding connected with kidney function? Results from several Basra City hospitals

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ABSTRACT

BACKGROUND: Chronic kidney disease (CKD) is defined as a GFR of under sixty milliliter/minute per 1.73 m^2 of the body or a urine albumin excretion of more than thirty milligrams per gram that has lasted for more than three months and has negative health effects; on another hand primary open-angle glaucoma (POAG) is a chronic, progressive optic neuropathy resulting in retinal ganglion cell (RGC) death and irreversible visual impairment. The aim of this study was to investigate the connection between CKD and POAG.

METHODS: Three thousand and two hundred people are included in this investigation; they are split into 2 groups. POAG (N.=186) and non-POAG (N.=3014). This study is carried out at multiple medical centers in Basra City (Iraq).

RESULTS: We found that POAG patients were significantly older than non-POAG patients. Moreover, male gender, hypertension, and diabetes were significantly more frequent among POAG patients. However, compared to non-POAG patients, POAG patients had a considerably greater IOP. According to this study, POAG patients had significantly increased occurrence of CKD. In addition, POAG patients had a significantly greater level of urea and creatinine than non-POAG patients. However, eGFR was considerably lower in POAG individuals compared to non-POAG patients. Patients with POAG experienced higher rates of proteinuria than non-POAG patients, although nothing had changed that would be considered statistically significant. The prevalence of POAG and CKD stages are significantly correlated.

CONCLUSIONS: Based on our research, we can say that kidney function and POAG were significantly correlated.

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KEY WORDS: Glaucoma, open-angle; Renal insufficiency, chronic; Glomerular filtration rate.

Chronic kidney disease (CKD) is defined as a GFR of under sixty milliliter/minute per 1.73 m^2 of the body or a urine albumin excretion of more than thirty milligrams per gram that has lasted for more than three months and has negative health effects.[1, 2] CKD is a significant condition that has a negative impact on many people's health and is linked to kidney and cardiovascular complications as well as early death.[3-5] In both Western and Asian populations, in the USA, the frequency of CKD among people of thirty years of age and older is predicted to reach 16.7precent in 2030 and 14.4 percent in 2020.[6]

Furthermore, glaucoma is the primary cause of irreversible blindness around the globe. In 2040,[7, 8] there will be 110-120 million glaucoma patients globally. This is because glaucoma affects persons between the ages of 40 to 80; between three and four percent of the time worldwide. Glaucoma signs include associated cupping of the optic nerve head and the degeneration of retinal ganglion cells

Increases in IOP are associated with glaucoma, however, nothing is known about its etiology and pathophysiology. Genetic predispositions,[9, 10] vascular deficiencies,[9, 11] oxidative stress,[12, 13] elevated trans-lamina cribrosa pressure,[14] *Helicobacter pylori* infections, and metabolic illnesses, such as CKD, are a few examples of additional variables. The pathophysiology, histology, and physiology of kidney and eye diseases are significantly similar, raising the possibility that they are closely interrelated.[15]

For instance, the choroid and glomerulus have architecturally comparable vast vascular networks, and similar mechanisms, such as inflammation, oxidative stress, endothelial dysfunction, atherosclerosis, and vascular remodeling, that lead to the development of several eye illnesses, such as chronic kidney disease.[16] Numerous eye conditions are related to CKD, including glaucoma, retinal vein occlusion, cataract, age-related macular degeneration, ocular surface disease. Last but not least vision impairment[17, 18] diabetic retinopathy[19, 20] and increased intraocular pressure[21] suggest that patients like those should have regular eye exams. The prevalence of ocular pathology varies with racial groups, indicating the effect of social and genetic differences.[22]

Recent research has demonstrated the presence of an active local intraocular RAS in the human eye. Mounting data suggests that antihypertensive medications that target the renin-angiotensin system can also reduce IOP. Additionally, they appear to function as neuroprotective drugs against the ganglion cells in the retina dying *in vivo*. The important peptide in the circulatory renin-angiotensin system is traditionally angiotensin II (Ang II), a highly vasoconstrictive substance. The ultimate impact of renin-angiotensin system activation at the tissue level, however, is more intricate, since it depends not only on Ang II's biological activity but also on the actions of other byproducts of angiotensinogen metabolism, which frequently have opposing effects to Ang II action.[23, 24] The aim of this study was to detect the relation between open angle glaucoma (OAG) and CKD.

Materials and methods

Study design

This study is a case-control study, retrospective analytical one that is conducted on 3200 participants, separated into 2 groups POAG (N.=186), and No POAG (N.=3014). This study is carried out at multiple medical centers in Basra City. Informed consent to participate in the study is taken from all the participants and all investigations are performed in accordance with relevant guidelines and regulations and participants were not exposed to any harm or unintended effect. Age of participants ranges from 40-70 years both male and female. The research followed the tents of the Declaration of Helsinki. The Ethics Committee of Basrah University of Medicine approved this study. The institutional ethical committee at Basrah University of Medicine approved all study protocols (IR.SBMU.MSP.REC.1396.900). Accordingly, written informed consent taken from all participants before any intervention

Inclusion criteria

All patients enrolled in this study are:

- asked for sociodemographic status including age, sex, residence, lifestyle, BMI, smoking status;
- exposed to laboratory investigations, *e.g.*, kidney function tests including creatinine, urea, glomerular filtration rate (GFR), proteinuria, complete blood count (CBC);
- exposed to medical examination complete data on primary open-angle glaucoma, relevant systemic diseases for example, the presence of body mass index, diabetes, hyperlipidemia, hypertension, smoking status and history of cardiovascular disease (CVD).

Data were collected within one year when patients confirmed CKD, full investigation had done and, ocular examination to detect glaucoma and questions related to different risk factors mentioned before. Every interview with each patient take from 30 to 45 minutes.

Statistical analysis

All data are collected, tabulated, and statistically analyzed utilizing SPSS 27.0 software (IBM, Armonk, NY, USA). Normality of the data distribution was assessed using the Shapiro-Wilk Test. Categorical data were presented as frequencies and relative percentages. The χ^2 was employed to ascertain differences between qualitative variables as appropriate. Quantitative data were reported as mean±SD (standard deviation). For parametric data, the independent *t*-test was utilized to determine differences between quantitative variables in distinct groups, and logistic regression to detect the main risk factors associated with increased risk of open angle glaucoma.

Results

It was found that POAG patients were significantly older than non-POAG patients. Moreover, male gender, hypertension, and diabetes were significantly more frequent among POAG patients, but IOP was significantly higher among POAG patients than non-POAG patients (Table I, II).

TABLE I.—*Baseline characteristics.*

Parameters	POAG (N.=186)	No POAG (N.=3014)	P
Age (years)	57.36±9.14	54.7±8.65	<0.001*
BMI (kg/m²)	27.14±2.83	26.87±3.03	0.237
Gender, N. (%)			
Male	115 (61.8)	1638 (54.3)	0.046*
Female	71 (38.2)	1376 (45.7)	
Comorbidities, N. (%)			
Smoking	45 (24.2)	795 (26.4)	0.511
Hypertension	86 (46.2)	1042 (34.6)	0.001*
Diabetes	42 (22.6)	486 (16.1)	0.021*
Hyperlipidemia	44 (23.7)	545 (18.1)	0.057
IOP (mmHg)	14.24±0.217	14.13±0.105	0.001*

Qualitative data were represented as numbers and percentages and tested χ^2 test; quantitative data were described as mean±SD and tested using the independent *t*-test.
BMI: Body Mass Index; IOP: intraocular pressure; POAG: primary open-angle glaucoma.
*Statistically significant difference.

TABLE II.—*Renal function findings.*

Parameters	POAG (N.=186)	No POAG N.=3014)	P
CKD, N. (%)	29 (15.6)	265 (8.8)	0.002*
Renal function			
Creatinine (mg/dL)	0.908±0.412	0.842±0.389	0.012*
Urea (mg/dL)	42.06±11.63	39.98±11.29	0.015*
eGFR (mL/min/1.73m²)	82.49±15.51	87.32±12.65	0.001*
Proteinuria, N. (%)	4 (2.2)	41 (1.36)	0.374

Qualitative data were represented as numbers and percentages and tested χ^2 test; quantitative data were described as mean±SD and tested using the independent *t*-test.
eGFR: estimated glomerular filtration rate; CKD: chronic kidney disease; POAG: primary open-angle glaucoma.
*Statistically significant difference (Mann Whitney Test).

This study revealed that CKD was significantly more frequent among POAG patients. Moreover, creatinine and urea were significantly greater among POAG patients than non-POAG patients. However, eGFR was significantly lower among POAG patients than non-primary open-angle glaucoma patients. Proteinuria was more frequent among POAG patients compared to non-POAG patients but without a statistically significance difference (Figure 1).

Table III shows that there is a significant association between CKD stages and primary open-angle glaucoma prevalence.

Discussion

The chronic, progressive optic neuropathy known as primary open angle glaucoma (POAG) causes irreversible vision impairment and the death of

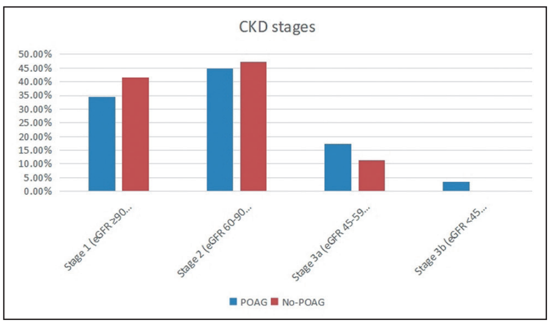

Figure 1.—CKD stages distribution among CKD patients according to e GFR between the two studied groups, showing that advanced CKD stages were significantly more prevalent among primary open-angle glaucoma patients (P=0.017).
CKD: chronic kidney disease; GFR: glomerular filtration rate.

Table III.—*Association between POAG prevalence and renal function.*

CKD stages	OR (95% CI)	P value
Stage 1	1.13 (0.347-2.26)	<0.001*
Stage 2	1.52 (1.10-2.715)	<0.001*
Stage 3a	2.10 (1.02-3.18)	0.008*
Stage 3b	3.51 (2.062-6.231)	0.026*
Proteinuria	1.18 (0.315-2.34)	0.411

OR: Odds Ratio; CI: confidence interval; CKD: chronic kidney disease; POAG: primary open-angle glaucoma.
*Statistically significant difference.

RGCs. While elevated IOP is a well-established causal risk factor for open-angle glaucoma, additional factors that are also significant in the onset and advancement of the illness include vascular dysfunction, myopia, perfusion pressure and systemic hypertension. CKD is a rapidly developing public health issue linked to both cardiovascular and renal complications as well as comorbid vision-threatening eye disorders such as cataracts, glaucoma, age-related macular degeneration, and diabetic retinopathy. CKD is described as a glomerular filtration rate lower than sixty milliliters per minute/1.73 meters square or if kidney injury signs are present in patients, or both, for at least three months.[25, 26]

Numerous investigations have documented the correlation between chronic kidney disease and POAG, even if the etiology of glaucoma remains unclear. Shim *et al.* showed that in a countrywide cross-sectional study carried out in Korea, lower eGFR levels were independently linked with POAG. Nevertheless, the majority of earlier research looked at glaucoma risk in CKD patients.[27]

Patients with POAG were found to be significantly older than those without POAG. Furthermore, among diabetes, Primary open-angle glaucoma patients, hypertension, and male gender were substantially more common. On the other hand, POAG patients had a considerably higher IOP than non-POAG individuals.

The results of this study were supported by Tham *et al.*[28] who, through a vast consortium of several Asian population-based research, sought to thoroughly examine the correlation between kidney function and POAG. They stated that there were notable differences in the study groups histories of sex, CVD, age, diabetes, hypertension, and hyperlipidemia.

Furthermore, these results also support those of Ro *et al.*,[29] who showed that hypertension, age, hyperlipidemia, diabetes, and history of cardiovascular disease did not significantly differ among the groups under investigation. If not, they stated that the groups that were studied did not differ in terms of sex.

According to this study, POAG patients had a significantly greater frequency of CKD. In addition, POAG patients had significantly higher levels of urea and creatinine than non-POAG patients. But when compared to non-POAG, the eGFR of POAG patients were significantly lower. Although no statistically significant change was seen, Primary open-angle glaucoma patients experienced proteinuria more frequently than non-POAG individuals.

The results were consistent with Tham *et al.*[28] which revealed a statistically significant difference in eGFR among the groups under investigation, creatinine and chronic kidney disease.

Similarly, Shim and colleagues in a Korean population, a significant correlation between decreased eGFR and POAG has been previously found.[27]

Chou *et al.*,[30] Propensity score matched the Chinese cohort observationally by 15,185. In comparison to individuals without ocular problems, POAG patients and 15,185 controls, who also included POAG patients, had increased acute renal failure and risks of end-stage renal disease.

A recent population-based cross-sectional study from (South Korea) showed a beneficial association between lower eGFR and primary open-angle glaucoma validated this link.[31]

It was discovered that the distribution of CKD stages among CKD patients was based on eGFR, demonstrating that POAG patients had a significantly higher prevalence of late CKD stages (P=0.017). The prevalence of POAG and chronic kidney disease stages are significantly correlated.

Primary OAG (POAG) prevalence was not correlated with poorer eGFR or CKD, according to a review of numerous Asian population-based studies. Nevertheless, subgroup analysis showed that East Asians, particularly Korean and Chinese people, had a significant correlation between lower eGFR and POAG prevalence.[28]

Furthermore, the findings of this study are consistent with Ro *et al.*[29] findings, which showed that the CKD group (P<0.001) had a considerably increased chance of acquiring OAG during the twelve-year follow-up period compared to the control group. An increased incidence of OAG was linked to higher CKD stages (CKD group 1: P=0.005; CKD group 2: P<0.001). Low income, older age, hypertension, rural residency, hyperlipidemia, and an elevated risk of OAG was also linked to diabetes mellitus.

Given the genetic similarities among these three ethnic groups, more assessment among Japanese will assist in determining whether this is unique to East Asians in general.[32]

Ro *et al.*[29] in a twelve-year nationwide cohort study showed that OAG is a greater risk with CKD. Furthermore, the risk of OAG is significantly elevated for individuals suffering from more intense illness. This suggests that OAG and reduced eGFR are related.

This population-based research of individuals in South Korea demonstrated an independent relationship between low eGFR levels and POAG.[27]

Cho *et al.*[33] conducted a national, population-based, retrospective, longitudinal Korean cohort of 17,971 controls and 3640 patients with CKD. 4.3% of the chronic kidney disease group and 2.8 percent of the control group developed glaucoma. The chance of developing glaucoma was elevated by CKD. In the study by Park *et al.*,[34] POAG was linked to an increased chance of progressing in CKD in a retrospective, longitudinal population, reported.

Limitations of the study

This study is considered a retrospective study. Further prospective studies are needed to detect cause-effect relationship and time sequence of occurrence of primary angle glaucoma in CKD.

Conclusions

It can be concluded that there was a significant relationship between primary open-angle glaucoma and kidney function.

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Conflicts of interest

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Authors' contributions

Heba A. Al Bayati and Firas S. Alfuriaji have given substantial contributions to study design, and manuscript writing, Heba A. Al Bayati to study conception, data acquisition and investigation, Firas S. Alfuriaji to study supervision and validation, data acquisition, curation and analysis, manuscript writing, revision and editing. Both authors read and approved the final version of the manuscript.

History

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