Research Square

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Renal Function Markers Predict Risk of Specific Fundus Lesions in CKD: A Cross- Sectional Risk-Stratification Study

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Abstract

Objectives

To investigate the association between renal function markers and fundus damage in patients with chronic kidney disease(CKD).

Methods

Basic demographic information, renal function parameters, and data related to fundus lesions were collected. The correlations between kidney disease and ocular disease, as well as the associations between renal function markers and various ocular pathologies, were analyzed.

Results

Analysis of odds ratios (OR) between ocular and renal variables revealed a significantly increased risk of ocular diseases in patients with kidney disease, with particularly elevated risks for retinal hemorrhage and macular edema. Boxplot analyses further demonstrated that specific fundus phenotypes, such as retinal exudates, retinal hemorrhage, and macular edema, were significantly associated with markers of renal impairment, including estimated glomerular filtration rate (eGFR), serum creatinine, blood urea nitrogen, urinary protein, and urinary microalbumin. Further analysis of eGFR data indicated that for every 10 ml/(min·1.73 m²) decrease in eGFR, the risks of retinal hemorrhage, diabetic retinopathy, macular edema, hypertensive retinopathy, and retinal exudates increased by 27%, 25%, 20%, 20%, and 12%, respectively.

Conclusions

Patients with kidney disease have a significantly increased risk of developing ocular diseases, particularly retinal hemorrhage and macular edema. There are significant differences in specific fundus phenotypes according to markers of renal impairment, suggesting that renal dysfunction may indirectly elevate the risk of retinal lesions and macular edema by affecting systemic vascular health. Moreover, a decline in eGFR is closely associated with increased risks of various ocular diseases.

Introduction

The interplay between chronic kidney disease (CKD) and ocular diseases has increasingly become a focus of interdisciplinary research. Globally, CKD affects approximately 850 million individuals suffering from the disease. Notably, over 40% of patients are already in the middle or late stages of CKD at the time of initial diagnosis, partly due to the suboptimal sensitivity of traditional renal function markers (such as serum creatinine) for early disease detection [1,2]. This limitation underscores the urgent need for more effective early diagnostic approaches.

Recent studies have highlighted the retina as a window into the systemic microcirculation [3,4,5], suggesting that retinal lesions (such as exudates and hemorrhages) may offer novel avenues for early CKD screening. Anatomically, the retinal and glomerular microvasculature share similar vascular networks and certain pathological regulatory pathways (e.g., involving vascular endothelial growth factor and inflammation) [6]. Clinical research has also provided compelling evidence for this association: patients with diabetic retinopathy (DR) have a 2.4-fold increased risk of developing diabetic nephropathy compared to the general population [7], while the incidence of retinal arteriolosclerosis in patients with hypertensive nephropathy is significantly higher than in the general population [8].

However, current research on the relationship between CKD and ocular diseases remains limited. Most studies focus on single ocular indicators or specific types of eye diseases, lacking comprehensive investigations into the phenotypic differences of ocular diseases among CKD patients with varying etiologies and disease stages. Systematic analyses of the relationships between multidimensional renal function markers and a broad spectrum of fundus phenotypes are yet to be conducted. This study adopts a cross-sectional design to systematically explore the strength of associations between renal impairment and various ocular diseases. The findings are expected to provide a scientific basis for establishing an eye-kidney comorbidity warning system in clinical practice and to inform the development of individualized and precise treatment strategies.

Methods

2.1 Study Population

This is a retrospective, single-center, cross-sectional study. A total of 641 patients who underwent nephrology-ophthalmology consultations at the First Affiliated Hospital of Guangzhou Medical University from January 2020 to April 2023 were enrolled. Inclusion criteria were a diagnosis of kidney disease (including chronic kidney disease, diabetic nephropathy, glomerulonephritis, etc.) and completion of fundus examinations. Patients with other severe systemic diseases (such as malignancies, autoimmune diseases) or ocular lesions due to other causes (such as trauma or surgical history) were excluded.

2.2 Data Collection

Collected data included basic demographic information (such as sex and age), visual acuity, refraction, intraocular pressure, slit-lamp anterior segment examination, Scanning Laser Ophthalmoscope(SLO) and macular optical coherence tomography (OCT). Laboratory tests included serum creatinine, blood urea nitrogen, urinary protein, urinary N-acetyl-β-D-glucosaminidase (NAG), and urinary microalbumin. All ocular symptoms were evaluated and diagnosed by attending or senior ophthalmologists, while the type of kidney disease was diagnosed by attending or senior nephrologists. The estimated glomerular filtration rate (eGFR) was calculated using the 2021 Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) Eq. 9.

2.3 Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics 25.0. A p-value < 0.05 was considered statistically significant. All quantitative data are presented as mean ± standard deviation. Pearson correlation analysis was used to assess the relationships between ocular and renal symptoms. Ocular parameters included lens opacity, anterior segment findings, vitreous liquefaction and opacities, arteriovenous crossing changes, macular foveal reflex, retinal hemorrhage, and retinal exudates. Renal parameters included diabetic retinopathy, kidney disease, chronic renal failure, acute renal failure, chronic glomerulonephritis, uremia, and chronic kidney disease. Boxplot analysis (Mann-Whitney U test) was used to compare differences in renal function markers among different ocular disease groups. Furthermore, multivariate logistic regression was performed to assess the association between eGFR levels and DR, categorizing eGFR into three clinically relevant groups: ≥90, 60–89, and < 60 ml / (min·1.73 m²), with eGFR ≥ 90 ml/(min·1.73 m²) as the reference. To control for confounding factors, age, hypertension, and hyperlipidemia were included as covariates in the regression model. Results are presented as odds ratios (OR) with 95% confidence intervals (CI), and a p-value < 0.05 was considered statistically significant.

Results

3.1 Dataset Summary

A total of 641 patients were included in this study, with a mean age of 54.75 ± 16.16 years. Among them, 56.3% (n = 361) were male and 43.7% (n = 280) were female. The types of kidney disease among the patients were classified according to disease course as chronic kidney disease (CKD, stages 1–5) and acute kidney disease; and according to etiology as diabetic nephropathy, hypertensive nephropathy, obstructive nephropathy, membranous nephropathy, and chronic glomerulonephritis.

The main types of fundus lesions included diabetic retinopathy, hypertensive retinopathy, retinal hemorrhage, macular edema, and retinal exudates. The general demographic and clinical characteristics of the patients are summarized in Table_1, Figure_1.

3.2 Odds Ratios for Kidney–Ocular Disease Associations

In this study, we explored the associations between different types of kidney disease and ocular diseases, and quantified the strength of these associations by calculating odds ratio (OR). Significant correlations were observed between various ocular diseases and kidney diseases. Diabetic nephropathy was significantly associated with multiple ocular manifestations, including lens opacity, retinal hemorrhage, and macular edema. Chronic kidney disease was mainly associated with retinal hemorrhage, retinal exudates, and macular edema. The associations between different types of kidney disease and ocular manifestations varied: hypertensive nephropathy was primarily associated with retinal hemorrhage, while chronic glomerulonephritis was significantly associated with lens opacity, among others (Figure_2).

1. **Diabetic Nephropathy:**
Patients with diabetic nephropathy had significantly higher risks of developing lens opacity (OR = 1.74, $p < 0.05$), retinal hemorrhage (OR = 5.87, $p < 0.01$), retinal exudates (OR = 4.22, $p < 0.01$), macular edema (OR = 2.63, $p < 0.01$), and vitreous opacity (OR = 1.64, $p < 0.05$) compared to those without diabetic nephropathy.

2. **Chronic Kidney Disease:**
Patients with chronic kidney disease had significantly higher risks of retinal hemorrhage (OR = 5.20, $p < 0.01$), retinal exudates (OR = 2.25, $p < 0.01$), and macular edema (OR = 4.93, $p < 0.01$) compared to those without chronic kidney disease.

3. **Hypertensive Nephropathy:**
Patients with hypertensive nephropathy had a significantly lower risk of retinal hemorrhage (OR = 0.49, $p < 0.01$) compared to those without hypertensive nephropathy.

4. **Chronic Glomerulonephritis:**
Patients with chronic glomerulonephritis had significantly lower risks of lens opacity (OR = 0.53, $p < 0.05$), retinal hemorrhage (OR = 0.46, $p < 0.05$), and retinal exudates (OR = 0.47, $p < 0.05$) compared to those without chronic glomerulonephritis.

3.3 Renal Markers and Fundus Lesions

Boxplot analyses revealed significant differences in renal function markers among patients with different ocular disease statuses:

1. **eGFR Distribution:**
The eGFR values in the hypertensive retinopathy group ($p < 0.01$), retinal exudate group ($p < 0.01$), retinal hemorrhage group ($p < 0.01$), diabetic retinopathy group ($p < 0.01$), and macular edema group ($p < 0.01$) were all significantly lower than those in their respective control groups without these lesions, suggesting an association between ocular disease and renal dysfunction (Figure_3A).

2. **Urinary Microalbumin:**
Urinary microalbumin levels were significantly higher in the retinal hemorrhage group compared to the non-hemorrhage group ($p < 0.01$), with the most pronounced difference observed in the retinal hemorrhage group. This suggests that combined assessment of urinary microalbumin and retinal hemorrhage may serve as an early warning indicator (Figure_3B).

3. **Serum Creatinine:**
Serum creatinine levels were significantly higher in patients with hypertensive retinopathy ($p < 0.01$), retinal exudates ($p < 0.01$), and macular edema ($p < 0.01$) compared to those without retinal lesions, indicating a close relationship between renal impairment and these ocular diseases.

4. **Urinary Protein:**
Urinary protein levels were significantly higher in patients with diabetic retinopathy ($p < 0.05$) and retinal exudates ($p < 0.01$) compared to control groups without these lesions, suggesting that glomerular permeability may be affected by ocular disease.

5. **Blood Urea Nitrogen:**
Blood urea nitrogen levels were significantly higher in patients with retinal hemorrhage compared to those without hemorrhage ($p < 0.05$), indicating possible impairment of glomerular filtration function.

3.4 Ocular Signs Linked to eGFR Decline

Multivariate logistic regression analysis demonstrated that eGFR is a significant risk factor for the development of various ocular diseases. The relationship between declining eGFR and the odds ratios for ocular symptoms is shown in Table_2 and Figure_4.

1. **Declining eGFR independently increases the risk of multiple ocular diseases.** For every 10 ml/(min·1.73 m^2) decrease in eGFR, the risks of retinal hemorrhage, diabetic retinopathy (DR), macular edema, hypertensive retinopathy, and retinal exudates increased by 27%, 20%, 20%, 14%, and 12%, respectively, all of which were statistically significant ($p < 0.05$). This indicates that renal dysfunction significantly exacerbates the risk of ocular complications.

2. **The extent of risk increase differs among ocular disease.** The risk increase was most pronounced for retinal hemorrhage (OR = 1.27), followed by DR (OR = 1.25) and macular edema (OR = 1.25), while the risk increases for retinal exudates and hypertensive retinopathy were relatively lower (OR = 1.12 and 1.20, respectively), suggesting that declining eGFR has a more pronounced impact on certain ocular diseases.

3. **A dose-dependent relationship exists between eGFR decline and ocular disease risk.** As also shown in the Appendix Table 2, with each fixed unit decrease in eGFR, the risks of multiple ocular diseases showed a consistent upward trend, and the 95% confidence intervals did not include 1 ($p < 0.05$), further supporting the clinical value of eGFR as a predictive marker for ocular complications.

3.5 Diagnostic Performance of Renal Markers and Age for Ocular Signs

Receiver Operating Characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance of eGFR, urinary microalbumin, and age in predicting the presence of various ocular signs (Figure 5). For predicting retinal hemorrhage, eGFR demonstrated the highest discriminatory ability (Area Under the Curve [AUC] = 0.67), followed by urinary microalbumin (AUC = 0.65). Similar analyses for macular edema revealed AUCs of 0.62 for both eGFR and urinary microalbumin. When predicting retinal exudates, the AUCs were 0.67 (eGFR), 0.65 (urinary microalbumin), and 0.45 (age).

Discussion

Based on a cohort of 641 CKD patients, this study is the first to comprehensively evaluate the association strength between serum creatinine, blood urea nitrogen, urinary protein, urinary microalbumin, and eGFR with retinal hemorrhage, exudates, macular edema, diabetic retinopathy, and hypertensive retinopathy. The results indicate that greater renal impairment increases the risk of fundus lesions, suggesting shared pathogenic mechanisms involving systemic microvascular disease, oxidative stress, and inflammatory pathways.

4.1 Kidney–Eye Disease Associations

This study systematically elucidates the clinical association strength between different types of kidney disease and specific ocular diseases. Notably, diabetic nephropathy (DN) showed a particularly strong association with retinal hemorrhage (OR = 5.87), retinal exudates (OR = 4.22), and macular edema (OR = 2.63), while CKD was strongly associated with retinal exudates (OR = 2.25) and macular edema (OR = 4.93).

These findings not only confirm the shared pathological basis of the renal and ocular microvascular systems but also reveal the heterogeneity in the mechanisms by which different types of kidney disease drive ocular pathology. From a pathophysiological perspective, diabetic nephropathy and retinal disease share hyperglycemia-induced endothelial injury pathways. Advanced glycation end products (AGEs) activate oxidative stress and inflammatory responses, disrupting both the glomerular filtration and blood-retinal barriers [10,11,12], which may explain the strong association between DN and retinal hemorrhage.

Recent mechanistic studies provide further biological explanations: uremic toxins (such as indoxyl sulfate) accumulated in CKD patients can activate the ROS-NFκB pathway, damaging the blood-retinal barrier and directly leading to vascular leakage and hemorrhage [13], which mechanistically aligns with the high risk of retinal hemorrhage and macular edema observed in this study. Our findings indicated a significantly lower risk of retinal hemorrhage in patients with hypertensive nephropathy (OR = 0.49, $p < 0.01$) compared to the reference group. This unexpected protective association warrants further exploration. While systemic hypertension is a risk factor for retinal hemorrhage, it is plausible that patients specifically identified with hypertensive nephropathy in our cohort are subject to distinct management strategies (e.g., more intensive blood pressure control or specific antihypertensive classes) that could mitigate hemorrhagic risk. Alternatively, The relatively weaker association between hypertensive nephropathy and retinal hemorrhage (OR = 0.49, $p < 0.01$) may suggest its pathology may focus more on arteriolosclerosis than microvascular leakage. This is consistent with the longitudinal findings of Sabanayagam et al., who reported that retinal arteriolar narrowing independently predicts renal function decline [14], but its impact on hemorrhagic lesions may be buffered by hemodynamic compensatory mechanisms. In contrast, the negative associations observed between chronic glomerulonephritis (CGN) and lens opacity (OR = 0.53, $p < 0.05$), retinal hemorrhage (OR = 0.46, $p < 0.05$), and retinal exudates (OR = 0.47, $p < 0.05$) may suggest that immune-mediated renal injury (such as complement activation or antibody deposition) affects the ocular microenvironment through unique pathways [15,16], indicating that immune regulation may counteract exudative processes.

Clinical studies have shown that patients with diabetic retinopathy (DR) have an increased risk of developing diabetic nephropathy, and the incidence of retinal arteriolosclerosis is higher in patients with hypertensive nephropathy [17,18,19]. These findings suggest that kidney and ocular diseases may share common pathophysiological mechanisms, such as microvascular disease, oxidative stress, and inflammatory responses [20], which may play a role in the development and progression of both conditions.

4.2 eGFR Decline and Ocular Risk

Systemic vascular endothelial dysfunction resulting from renal impairment may be an important underlying mechanism linking kidney and ocular diseases. Our results demonstrate a significant association between declining eGFR and the risk of various fundus lesions in CKD patients. Specifically, for every 10 ml/(min·1.73 m²) decrease in eGFR, the risks of retinal hemorrhage, diabetic retinopathy, macular edema, hypertensive retinopathy, and retinal exudates increased by 27%, 25%, 20%, 20%, and 12%, respectively. This finding is highly consistent with large-scale epidemiological studies, such as the CRIC Study by Juan E. Grunwald et al. (n = 1904), which found that patients with GFR < 30 ml/min/1.73 m² had a threefold increased risk of retinopathy [21].

As renal function declines, the kidneys are less able to clear metabolic waste and toxins, leading to their accumulation, which in turn induces oxidative stress and inflammation, damaging systemic vascular endothelial cells [22,23]. As part of the systemic microvascular system, retinal vessels are similarly affected [24], resulting in retinal microvascular disease. Thus, a decrease in eGFR not only reflects the degree of renal impairment but may also indirectly indicate the extent of systemic vascular endothelial dysfunction [25], closely linking it to the risk of fundus lesions.

Our forest plot analysis further showed that specific fundus phenotypes, such as retinal exudates, retinal hemorrhage, and macular edema, were significantly different in relation to eGFR, serum creatinine, blood urea nitrogen, urinary protein, and urinary microalbumin (Figure_5). This suggests that renal dysfunction may increase the risk of retinal lesions and macular

edema by affecting systemic vascular health. As a key indicator of renal function, eGFR decline is closely associated with increased risk of multiple ocular diseases. Our quantitative analysis found that for every 10 ml/(min·1.73 m²) decrease in eGFR, the risks of retinal hemorrhage, macular edema, hypertensive retinopathy, and retinal exudates increased by 27%, 20%, 14%, and 12%, respectively. This provides important quantitative evidence for clinicians, highlighting that monitoring renal function is crucial for managing kidney disease and for early screening and intervention of ocular diseases. In particular, patients with declining renal function should undergo more frequent fundus examinations to facilitate early detection and intervention of ocular disease.

4.3 Ocular Signs as Early Renal Indicators

By analyzing the distribution differences of various renal function markers in the presence of different fundus lesions, this study reveals the potential early warning value of five ocular manifestations—retinal exudates, retinal hemorrhage, macular edema, lens opacity, and vitreous opacity—for different renal function markers. Our results suggest that the presence of retinal exudates, retinal hemorrhage, or macular edema is associated with significantly lower eGFR compared to patients without these ocular symptoms, indicating a strong correlation between multiple types of retinal microvascular injury and renal function decline, whereas lens opacity and vitreous opacity do not reflect renal function status. This finding is consistent with the results of the multicenter cohort study by Juan E. Grunwald et al. [26]. Anatomically, since the kidney and retina develop during the same embryonic stage, the retinal and glomerular microvasculature share significant similarities in structure, function, and pathological mechanisms [27,28,29,30], including common regulatory pathways and the renin-angiotensin-aldosterone system (RAAS) [31,32]. These lines of evidence suggest that the eye-kidney association is largely based on their shared microvascular architecture, and our study further demonstrates that retinal lesions can serve as indicators of eGFR decline, providing a foundation for future research on eye-kidney comorbidity.

Our findings indicate that different retinal signs may reflect abnormalities in different renal function markers. For example, patients with retinal hemorrhage had significantly higher blood urea nitrogen and urinary microalbumin levels. Urinary microalbumin is an early marker of glomerular filtration membrane damage and systemic microvascular endothelial injury; its elevation indicates glomerular microvascular disease [33,34]. In this study, the difference in urinary microalbumin was most pronounced in the retinal hemorrhage group. As a severe manifestation of retinal microvascular disease, retinal hemorrhage may share a common pathophysiological basis with elevated urinary microalbumin. Therefore, combined assessment of urinary microalbumin and retinal hemorrhage may facilitate early identification of eye-kidney comorbidity. In patients with kidney disease, non-invasive and convenient retinal examination may indirectly reflect the type of renal impairment, thereby enhancing the comprehensive management of kidney disease in clinical practice.

4. 4 Limitations

This study provides new evidence for the association between kidney disease and ocular disease, particularly in quantifying the relationship between renal function markers and fundus lesions. However, several limitations should be noted. First, as a cross-sectional study, causality between renal function decline and ocular disease cannot be established. Second, being a single-center study, the generalizability of the results may be limited. Additionally, the study did not include dynamic data on changes in renal function markers, precluding further exploration of the impact of renal function changes on the progression of ocular disease. Future research should employ longitudinal designs and include data from multiple centers to further investigate the pathophysiological mechanisms linking kidney and ocular diseases.

Conclusion

This study reveals the multi-layered pathological nature of the association between declining renal function and ocular disease, analyzes the associations between different types of kidney disease and ocular symptoms, and quantifies the specific risks of various ocular lesions associated with renal function decline. These findings provide new insights for the clinical management of patients with kidney disease, may enhance clinical awareness of eye-kidney comorbidity, and offer further clinical evidence for future research on the eye-kidney connection.

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the First Affiliated Hospital of Guangzhou Medical University (Approval No. : ES-2024-157-01), and all procedures adhered to the principles of the Declaration of Helsinki.

Disclosure of interest

The authors report no conflict of interest.

Clinical trial number

Not applicable.

Consent to participate

This retrospective case analysis has obtained ethical approval from the Ethics Committee of the First Affiliated Hospital of Guangzhou Medical University (Approval No.: ES-2024-157-01). In accordance with the approval decision of this ethics committee, informed consent for this study has been waived.

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Author Contribution

Yuran Chen: Writing-Original Draft, Investigation, Data Curation, Project administration. Min Hu: Writing-Review & Editing, Methodology, Formal analysis, Data Curation, Visualization. Weiwei Dai: Writing-Review& Editing, Conceptualization, Methodology. Chaokui Huo: Writing- Review & Editing, Conceptualization, Methodology. Wai Cheng Iao: Writing-Review & Editing, Conceptualization, Methodology. Huayin Chen: Writing-Review & Editing, Investigation. Jianmei Lu: Writing-Review & Editing, Investigation Hao Cheng: Writing-Review & Editing, Conceptualization, Methodology, Supervision, Resources. Danmin Cao: Writing-Review & Editing, Conceptualization, Methodology, Supervision, Resources, Funding acquisition.

Data Availability

The data that support the findings of this study are available from the corresponding author, Cao DM, upon reasonable request.

References

1. Jager KJ, Kovesdy C, Langham R, Rosenberg M, Jha V, Zoccali C. A single number for advocacy and communication-worldwide more than 850 million individuals have kidney diseases. Kidney Int. 2019;96(5):1048–50.

10.1016/j.kint.2019.07.012.

2. Webster AC, Nagler EV, Morton RL, Masson P. Chronic Kidney Disease. Lancet. 2017;389(10075):1238–52. 10.1016/S0140-6736(16)32064-5.
3. Cabrera DeBuc D, Somfai GM, Koller A. Retinal microvascular network alterations: potential biomarkers of cerebrovascular and neural diseases. Am J Physiol Heart Circ Physiol. 2017;312(2):H201–12. 10.1152/ajpheart.00201.2016.
4. Courtie E, Veenith T, Logan A, Denniston AK, Blanch RJ. Retinal blood flow in critical illness and systemic disease: a review. Ann Intensive Care. 2020;10(1):152. 10.1186/s13613-020-00768-3. Published 2020 Nov 12.
5. Cabrera DeBuc D, Somfai GM, Koller A. Retinal microvascular network alterations: potential biomarkers of cerebrovascular and neural diseases. Am J Physiol Heart Circ Physiol. 2017;312(2):H201–12. 10.1152/ajpheart.00201.2016.
6. Sun C, Wang JJ, Mackey DA, Wong TY. Retinal vascular caliber: systemic, environmental, and genetic associations. Surv Ophthalmol. 2009;54(1):74–95. 10.1016/j.survophthal.2008.10.003.
7. Gupta M, Rao IR, Nagaraju SP, Bhandary SV, Gupta J, Babu GTC. Diabetic Retinopathy Is a Predictor of Progression of Diabetic Kidney Disease: A Systematic Review and Meta-Analysis. Int J Nephrol. 2022;2022:3922398. 10.1155/2022/3922398. Published 2022 Apr 29.
8. Kabedi NN, Mwanza JC, Lepira FB, Kayembe TK, Kayembe DL. Hypertensive retinopathy and its association with cardiovascular, renal and cerebrovascular morbidity in Congolese patients. Cardiovasc J Afr. 2014;25(5):228–32. 10.5830/CVJA-2014-045.
9. Inker LA, Titan S. Measurement and Estimation of GFR for Use in Clinical Practice: Core Curriculum 2021. Am J Kidney Dis. 2021;78(5):736–49. 10.1053/j.ajkd.2021.04.016.
10. Wong CW, Wong TY, Cheng CY, Sabanayagam C. Kidney and eye diseases: common risk factors, etiological mechanisms, and pathways. Kidney Int. 2014;85(6):1290–302. 10.1038/ki.2013.491.
11. Srejovic JV, Muric MD, Jakovljevic VL, et al. Molecular and Cellular Mechanisms Involved in the Pathophysiology of Retinal Vascular Disease-Interplay Between Inflammation and Oxidative Stress. Int J Mol Sci. 2024;25(21):11850. 10.3390/ijms252111850. Published 2024 Nov 4.
12. Wang X, Wang T, Lam E, Alvarez D, Sun Y. Ocular Vascular Diseases: From Retinal Immune Privilege to Inflammation. *Int J Mol Sci*. 2023;24(15):12090. Published 2023 Jul 28. 10.3390/ijms241512090
13. Adijiang A, Higuchi Y, Nishijima F, Shimizu H, Niwa T. Indoxyl sulfate, a uremic toxin, promotes cell senescence in aorta of hypertensive rats. Biochem Biophys Res Commun. 2010;399(4):637–41. 10.1016/j.bbrc.2010.07.130.
14. Sabanayagam C, Shankar A, Klein BE et al. Bidirectional association of retinal vessel diameters and estimated GFR decline: the Beaver Dam CKD Study [published correction appears in Am J Kidney Dis. 2018;72(1):157. 10.1053/j.ajkd.2018.05.001.]. *Am J Kidney Dis*. 2011;57(5):682–691. doi:10.1053/j.ajkd.2010.11.025.
15. Pickering MC, D'Agati VD, Nester CM, et al. C3 glomerulopathy: consensus report. Kidney Int. 2013;84(6):1079–89. 10.1038/ki.2013.377.
16. Rohrer B, Long Q, Coughlin B, et al. A targeted inhibitor of the complement alternative pathway reduces RPE injury and angiogenesis in models of age-related macular degeneration. Adv Exp Med Biol. 2010;703:137–49. 10.1007/978-1-4419-5635-4_10.
17. Kulkarni A, Thool AR, Daigavane S. Understanding the Clinical Relationship Between Diabetic Retinopathy, Nephropathy, and Neuropathy: A Comprehensive Review. Cureus. 2024;16(3):e56674. 10.7759/cureus.56674. Published 2024 Mar 21.
18. Saini DC, Kochar A, Poonia R. Clinical correlation of diabetic retinopathy with nephropathy and neuropathy. Indian J Ophthalmol. 2021;69(11):3364–8. 10.4103/ijo.IJO_1237_21.
19. Wang L, Wang JY, Chen C, et al. OCTA evaluates changes in retinal microvasculature in renal hypertension patients. Sci Rep. 2024;14(1):28910. 10.1038/s41598-024-68690-3. Published 2024 Nov 21.
20. Goyal JL, Gupta A, Gandhi P. Ocular manifestations in renal diseases. Indian J Ophthalmol. 2023;71(8):2938–43. 10.4103/IJO.IJO_3234_22.

21. Grunwald JE, Alexander J, Maguire M, et al. Prevalence of ocular fundus pathology in patients with chronic kidney disease. Clin J Am Soc Nephrol. 2010;5(5):867–73. 10.2215/CJN.08271109.
22. Gyurászová M, Gurecká R, Bábíčková J, Tóthová Ľ. Oxidative Stress in the Pathophysiology of Kidney Disease: Implications for Noninvasive Monitoring and Identification of Biomarkers. Oxid Med Cell Longev. 2020;2020:5478708. 10.1155/2020/5478708. Published 2020 Jan 23.
23. Frąk W, Dąbek B, Balcerczyk-Lis M, et al. Role of Uremic Toxins, Oxidative Stress, and Renal Fibrosis in Chronic Kidney Disease. Antioxid (Basel). 2024;13(6):687. 10.3390/antiox13060687. Published 2024 Jun 3.
24. Fursova AZ, Derbeneva AS, Vasilyeva MV, Tarasov MS, Nikulich IF, Gamza YA. Osobennosti strukturnykh i mikrovaskulyarnykh izmenenii setchatki i khorioidei pri khronicheskoi bolezni pochek [Structural and microvascular changes in the retina and choroid in patients with chronic kidney disease]. Vestn Oftalmol. 2021;137(6):99–108. 10.17116/oftalma202113706199.
25. Inker LA, Titan S. Measurement and Estimation of GFR for Use in Clinical Practice: Core Curriculum 2021. Am J Kidney Dis. 2021;78(5):736–49. 10.1053/j.ajkd.2021.04.016.
26. Grunwald JE, Alexander J, Maguire M, et al. Prevalence of ocular fundus pathology in patients with chronic kidney disease. Clin J Am Soc Nephrol. 2010;5(5):867–73. 10.2215/CJN.08271109.
27. Kannenkeril D, Frost S, Nolde JM, et al. Microvascular changes at different stages of chronic kidney disease. J Clin Hypertens (Greenwich). 2021;23(2):309–16. 10.1111/jch.14138.
28. Grunwald JE, Alexander J, Ying GS, et al. Retinopathy and chronic kidney disease in the Chronic Renal Insufficiency Cohort (CRIC) study. Arch Ophthalmol. 2012;130(9):1136–44. 10.1001/archophthalmol.2012.1800.
29. Goyal JL, Gupta A, Gandhi P. Ocular manifestations in renal diseases. Indian J Ophthalmol. 2023;71(8):2938–43. 10.4103/IJO.IJO_3234_22.
30. Bodaghi B, Massamba N, Izzedine H. The eye: a window on kidney diseases. Clin Kidney J. 2014;7(4):337–8. 10.1093/ckj/sfu073.
31. Wilkinson-Berka JL, Agrotis A, Deliyanti D. The retinal renin-angiotensin system: roles of angiotensin II and aldosterone. Peptides. 2012;36(1):142–50. 10.1016/j.peptides.2012.04.008.
32. Farrah TE, Dhillon B, Keane PA, Webb DJ, Dhaun N. The eye, the kidney, and cardiovascular disease: old concepts, better tools, and new horizons. Kidney Int. 2020;98(2):323–42. 10.1016/j.kint.2020.01.039.
33. Singh A, Satchell SC. Microalbuminuria: causes and implications. Pediatr Nephrol. 2011;26(11):1957–65. 10.1007/s00467-011-1777-1. Epub 2011 Feb 8. PMID: 21301888; PMCID: PMC3178015.
34. Prasad RM, Bali A, Tikaria R. Microalbuminuria. StatPearls. Volume 30. Treasure Island (FL): StatPearls Publishing; 2023.

Tables

Table_1. Demographic and Clinical Characteristics of the Study Population

Characteristics		n (%)
Demographics	Female	280 (43.7%)
Renal observations	Diabetic Nephropathy	122 (19.3%)
	Hypertensive Nephropathy	103 (16.3%)
	Obstructive Nephropathy	2 (0.3%)
	Membranous Nephropathy	3 (0.5%)
	Chronic Glomerulonephritis	74 (11.7%)
Ophthalmic observations	Lens Opacities	379 (60.1%)
	Vitreous Opacities	430 (68.1%)
	Macular Edema	35 (5.5%)
	Retinal Hemorrhage	201 (31.9%)
	Retinal Exudates	175 (27.7%)
		Mean±SD
Demographics	Age	55.03 ± 16.05
Biometrics	Urinary Microalbumin	1334.16 ± 1487.94
	Urinary Protein	2.68 ± 3.17
	Urinary NAG	13.16 ± 21.42
	Urinary Beta2-Microglobulin	3.23 ± 6.56
	Blood Urea Nitrogen	16.51 ± 23.48
	eGFR	35.20 ± 33.73

Table_2.Association Between Declining eGFR and Odds Ratios for Ocular Symptoms

		Lens Opacity (n=380)		Vitreous Opacities (n=434)		Macular Edema (n=35)		Retinal Hemorrhage (n=203)		Retinal Exudates (n=175)	
eGFR ml/(min 1.73 m²)	Count	OR (95%CI)	p	OR (95%CI)	p	OR (95%CI)	p	OR (95%CI)	p	OR (95%CI)	p
>90	58	Ref.	-	Ref.	-	Ref.	-	Ref.	-	Ref.	-
60~90	84	1.34 (0.61, 2.97)	0.469	1.17 (0.57, 2.41)	0.666	inf*	-	3.24 (1.01, 10.40)	0.048	1.92 (0.74, 4.98)	0.179
<60	496	0.91 (0.48, 1.72)	0.768	1.31 (0.73, 2.33)	0.365	inf*	-	8.78 (3.11, 24.80)	<0.001	3.06 (1.35, 6.94)	<0.05
35.1 ± 32.2	638	0.91 (0.76, 1.09)	0.317	1.02 (0.87, 1.21)	0.779	1.84 (1.15, 2.94)	<0.05	2.16 (1.73, 2.70)	<0.001	1.44 (1.18, 1.76)	<0.001

*Odds ratios could not be estimated (denoted by inf) due to zero events observed in a comparison group

Figures

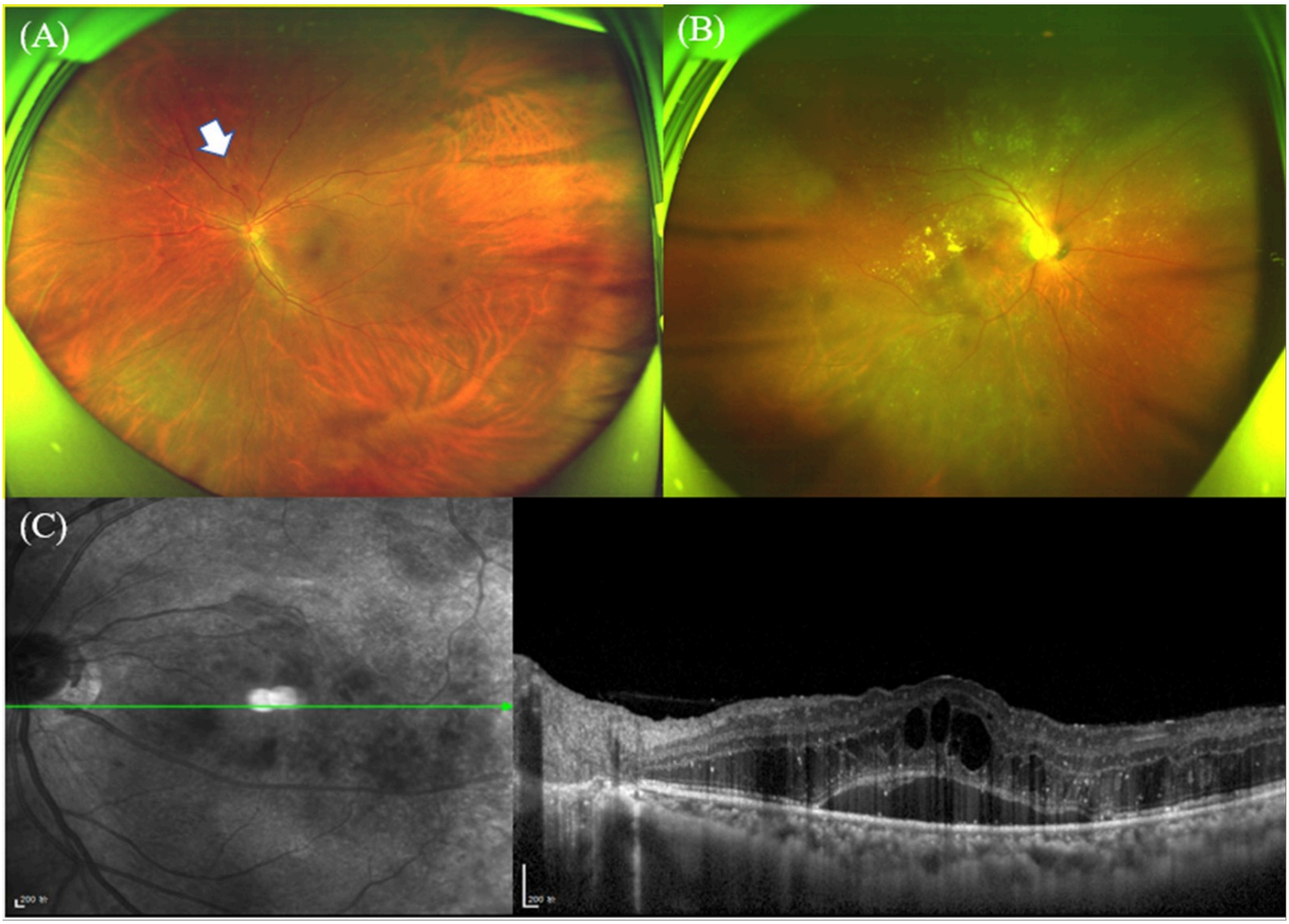


Figure 1

Signs of fundus damage: A: SLO shows retinal hemorrhage; B: SLO shows retinal exudation; C: OCT shows macular edema.

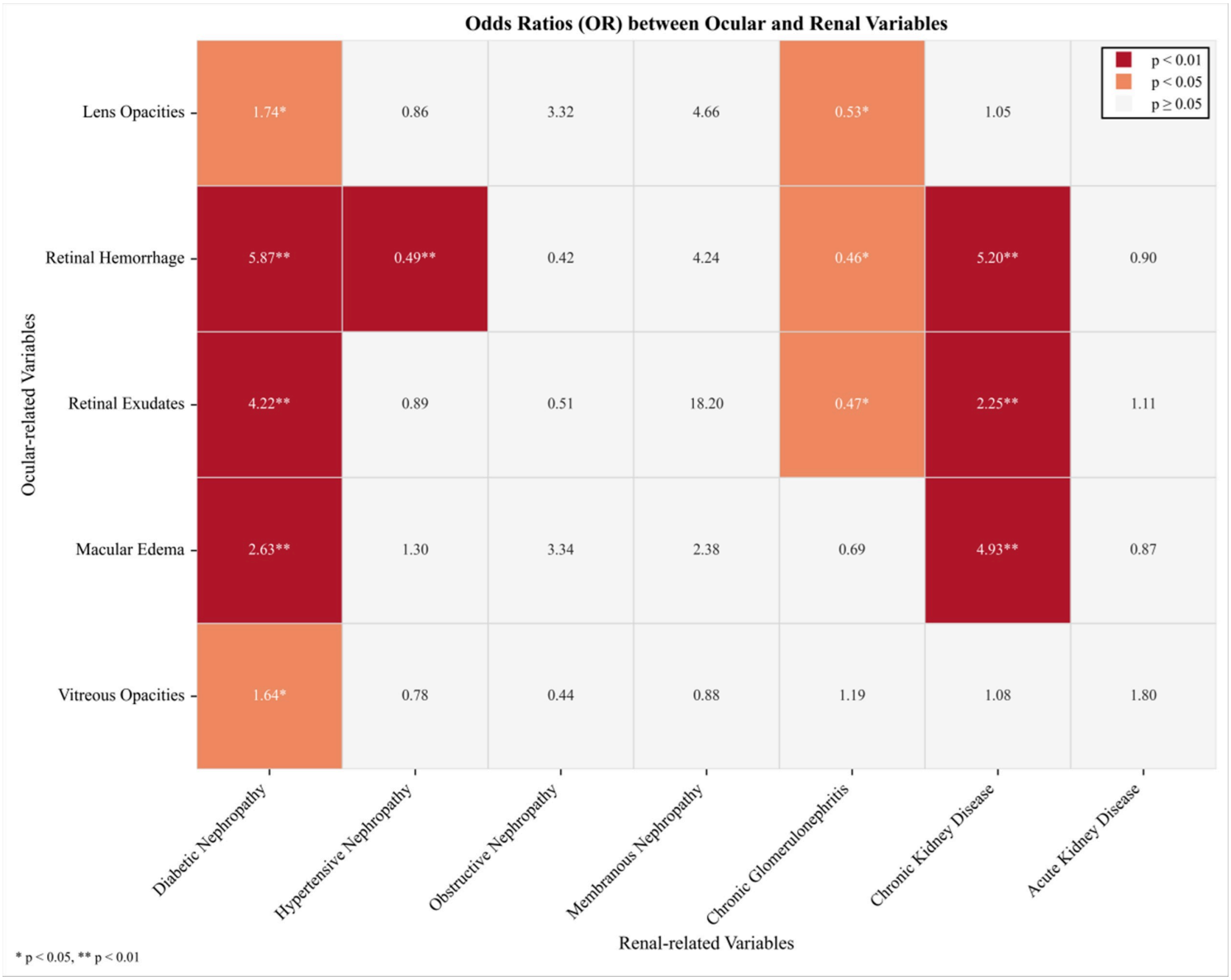


Figure 2

Odds ratios for associations between different types of kidney disease and ocular manifestations.

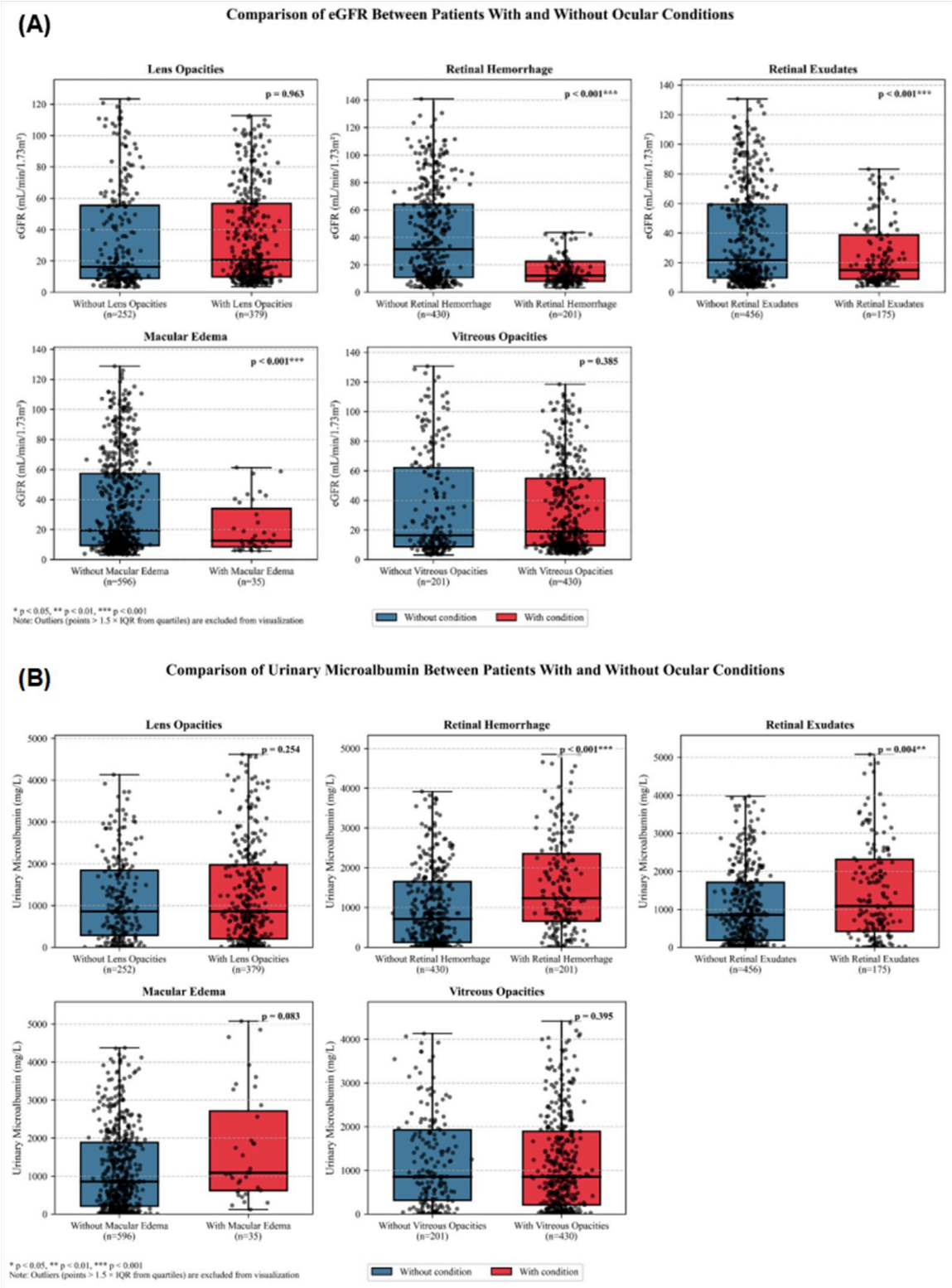


Figure 3

Boxplots of eGFR (A) and urinary microalbumin (B) distribution in various ocular diseases.

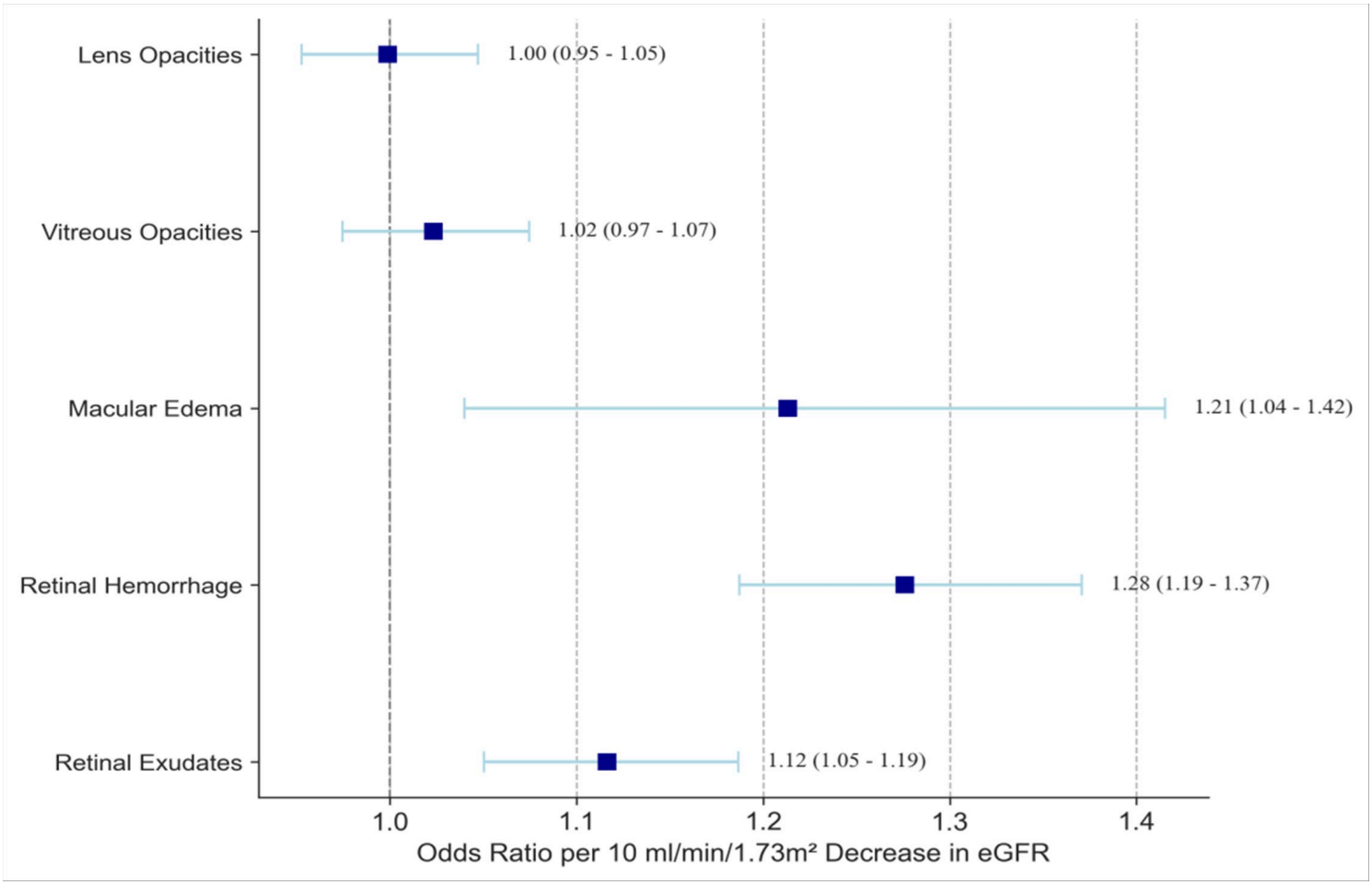


Figure 4

Odds ratios for ocular symptoms associated with declining eGFR.

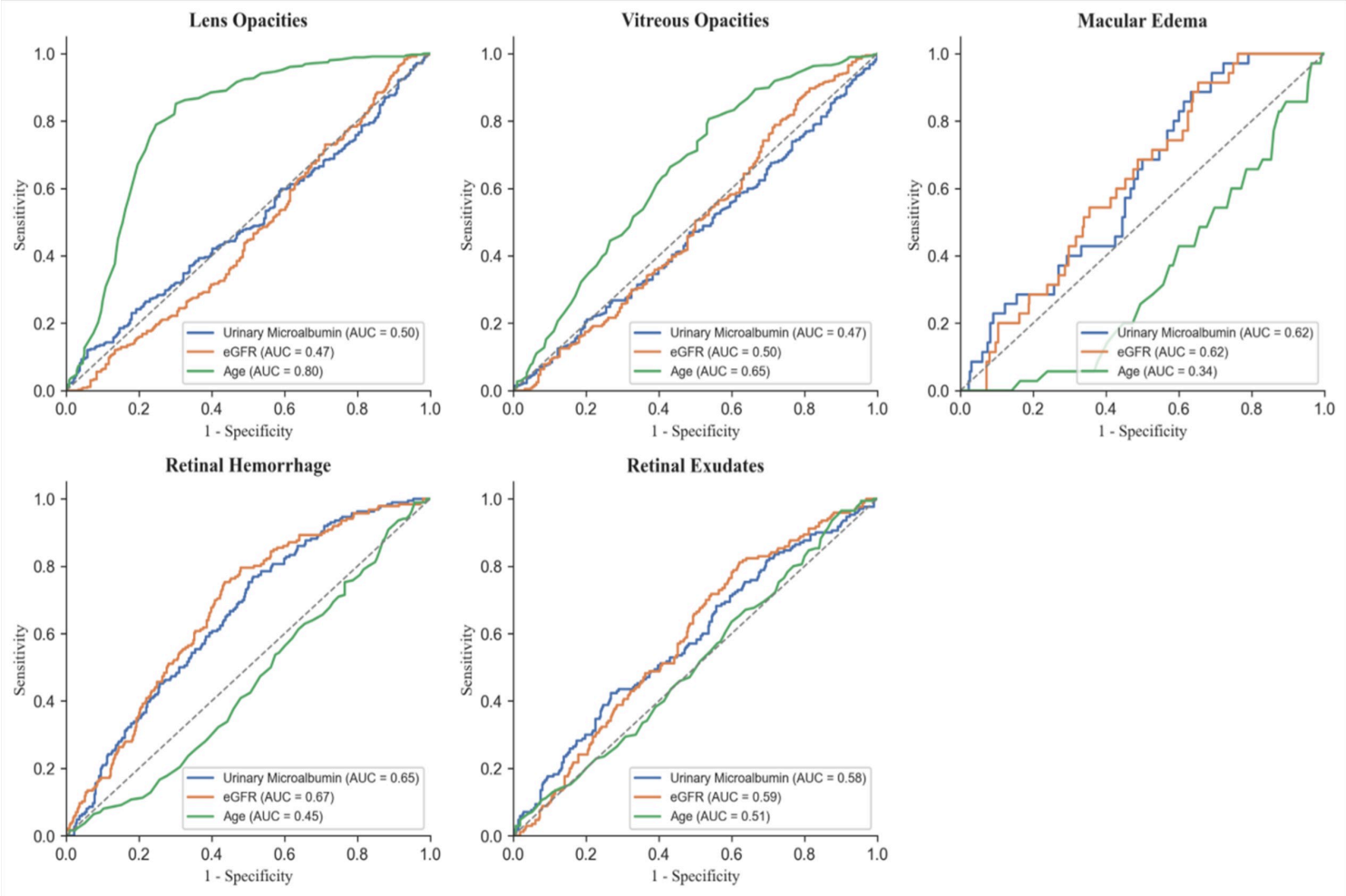


Figure 5

Diagnostic performance (ROC Curve) of urinary microalbumin, eGFR, and age in predicting ocular signs.