RESEARCH PAPER

Discordance Between Disease Severity and Patient Awareness in Diabetic Retinopathy

Dr. China[1], Dr. Mohan Lal Pandey[2], Dr. Lalit Gupta[3], Dr. Disha Garg[4]

[1]Junior Resident, Department of Ophthalmology, Maharishi Markandeshwar Institute of Medical Sciences, Mullana, Ambala. Email: chinasingla53@gmail.com (Corresponding Author)

[2]Professor and Head, Department of Ophthalmology, Maharishi Markandeshwar Institute of Medical Sciences, Mullana, Ambala. Email: Mlpandey23@gmail.com

[3]Professor, Department of Ophthalmology, Maharishi Markandeshwar Institute of Medical Sciences, Mullana, Ambala. Email: glalit7@gmail.com

[4]PG 3rd Year, Department of Ophthalmology, Government Medical College, Bakshi Nagar, Jammu. Email: gargdisha225@gmail.com

***Corresponding author: Dr. China, Junior Resident, Department of Ophthalmology, Maharishi Markandeshwar Institute of Medical Sciences, Mullana, Ambala**

Email: chinasingla53@gmail.com

Received: 25th May, 2026; **Revised:** 6th June, 2026; **Accepted:** 8th June, 2026; **Available Online:** 17th June, 2026

ABSTRACT

Background

Diabetic retinopathy (DR) and diabetic nephropathy (DN) are major microvascular complications of type 2 diabetes mellitus (T2DM) that share common pathogenic mechanisms. However, progression of retinal and renal disease may not always occur in parallel, creating discordance between disease severity and clinical manifestations. This study evaluated the association between DR and DN and identified systemic risk factors associated with proliferative diabetic retinopathy (PDR) and end-stage renal disease (ESRD).

Materials and Methods

This retrospective case–control study included 200 patients with T2DM, categorized into mild nephropathy (n=100) and ESRD (n=100) groups. Comprehensive ophthalmic examination was performed to classify retinopathy as mild non-proliferative diabetic retinopathy (NPDR) or PDR. Clinical, biochemical, and renal parameters were recorded. Univariate and multivariate logistic regression analyses were used to identify predictors of PDR and ESRD.

Results

Patients with ESRD had significantly longer diabetes duration, higher systolic blood pressure, elevated serum creatinine levels, lower estimated glomerular filtration rate (eGFR), and lower hemoglobin levels compared with patients with mild nephropathy ($p<0.05$). Patients with PDR were younger and demonstrated significantly higher blood pressure, serum creatinine, and urine albumin-to-creatinine ratio, along with lower eGFR values ($p<0.001$). Multivariate analysis identified younger age (OR=0.96, p=0.004), higher systolic blood pressure (OR=1.03, p=0.013), elevated serum creatinine (OR=1.28, $p<0.001$), albuminuria (OR=4.12, $p<0.001$), and Hispanic ethnicity (OR=3.08, p=0.002) as independent predictors of PDR. For ESRD, lower HbA1c (OR=0.58, p=0.012) and higher serum creatinine (OR=198.46, $p<0.001$) were significant independent predictors.

Conclusion

Diabetic retinopathy and diabetic nephropathy demonstrated a strong association, with renal dysfunction and albuminuria significantly contributing to the risk of proliferative retinopathy. Serum creatinine emerged as the strongest predictor of ESRD. These findings support integrated retinal and renal surveillance in patients with long-standing T2DM to facilitate early detection and management of advanced microvascular complications.

Keywords: Diabetic retinopathy, diabetic nephropathy, proliferative diabetic retinopathy.

How to cite this article: China, Pandey ML, Gupta L, Garg D. Discordance Between Disease Severity and Patient Awareness in Diabetic Retinopathy. Int J Drug Deliv Technol. 2026;16(61s): 65-69. DOI: 10.25258/ijddt.16.61s.9

Source of support: Nil.

Conflict of interest: None.

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from impaired insulin secretion, insulin resistance, or both. The global prevalence of type 2 diabetes mellitus (T2DM) has increased substantially over recent decades, making it a major public health concern. Long-standing diabetes is associated with numerous microvascular complications, particularly

diabetic retinopathy (DR) and diabetic nephropathy (DN), which contribute significantly to morbidity, disability, and healthcare expenditure.[1, 2]

Diabetic retinopathy remains one of the leading causes of preventable blindness among working-age adults worldwide. The progression from mild non-proliferative diabetic retinopathy (NPDR) to proliferative diabetic retinopathy (PDR) reflects worsening microvascular damage caused by chronic hyperglycemia and associated metabolic abnormalities.[3] Several systemic factors, including hypertension, dyslipidemia, duration of diabetes, and renal dysfunction, have been implicated in the development and progression of diabetic retinopathy.[4]

Diabetic nephropathy represents one of the most serious complications of diabetes and is a major cause of chronic kidney disease (CKD) and end-stage renal disease (ESRD). The coexistence of diabetic retinopathy and nephropathy suggests shared pathogenic mechanisms involving endothelial dysfunction, inflammation, oxidative stress, and microvascular injury. Identification of factors associated with these complications may facilitate earlier intervention and improved patient outcomes.[5- 7]

Understanding the relationship between retinal and renal microvascular complications is clinically important because retinal examination may provide insight into systemic vascular damage.[6- 8] Therefore, this study was conducted to evaluate the association between diabetic retinopathy and diabetic nephropathy in patients with type 2 diabetes mellitus and to identify systemic risk factors associated with progression to proliferative diabetic retinopathy and end-stage renal disease.

MATERIALS AND METHODS

This retrospective case–control study was conducted using data obtained from the Cerner PowerChart electronic medical record system of a tertiary care academic health center. Patients diagnosed with type 2 diabetes mellitus and documented diabetic nephropathy and/or diabetic retinopathy were screened for eligibility. A total of 200 patients fulfilling the inclusion criteria were enrolled. Patients were categorized into two groups: those with end-stage renal disease (ESRD) and those with mild nephropathy. Retinopathy status was assessed through comprehensive ophthalmological evaluation, including visual acuity assessment, slit-lamp biomicroscopy, indirect ophthalmoscopy, fundus photography, and optical coherence tomography. Based on retinal findings, subjects were classified as having mild non-proliferative diabetic retinopathy (NPDR) or proliferative diabetic retinopathy (PDR). Clinical and laboratory parameters including age, sex, duration of diabetes, glycated hemoglobin (HbA1c), body mass index (BMI), blood pressure, lipid profile, serum creatinine, estimated glomerular filtration rate (eGFR), albuminuria, hemoglobin, and medication history were recorded. Statistical analysis was performed using SPSS software. Continuous variables were expressed as mean ± standard deviation and compared using Student's t-test, while categorical variables were analyzed using Chi-square tests. Logistic regression analyses were performed to identify independent predictors of PDR and ESRD. A p-value <0.05 was considered statistically significant.

RESULTS

The mean age was comparable between the two groups (59.3 vs. 61.8 years; p=0.48). Patients with ESRD demonstrated significantly lower HbA1c levels than those with mild nephropathy (7.12% vs. 8.96%; $p<0.001$). The duration of diabetes was significantly longer among ESRD patients (25.1 vs. 19.7 years; p=0.021). Systolic blood pressure was markedly elevated in the ESRD group (145.7 vs. 129.3 mmHg; $p<0.001$). Renal function parameters showed substantial differences, with significantly higher serum creatinine levels (5.8 vs. 1.1 mg/dL; $p<0.001$) and lower eGFR values (17.3 vs. 73.2 mL/min/1.73m²; $p<0.001$) among ESRD patients. Hemoglobin levels were significantly reduced in the ESRD group (11.2 vs. 13.9 g/dL; $p<0.001$), whereas BMI did not differ significantly between the groups (p=0.29). Patients with PDR were significantly younger than those with mild NPDR (60.5 vs. 66.2 years; p=0.001). Although HbA1c levels were slightly higher in the PDR group, the difference was not statistically significant (8.28% vs. 8.09%; p=0.36). Both systolic and diastolic blood pressures were significantly elevated among patients with PDR (140.9 vs. 133.5 mmHg and 73.1 vs. 69.8 mmHg, respectively). Markers of renal dysfunction were significantly worse in the PDR group, with higher serum creatinine levels (3.62 vs. 1.68 mg/dL; $p<0.001$), lower eGFR values (39.4 vs. 65.8 mL/min/1.73m²; $p<0.001$), and markedly increased urine albumin-to-creatinine ratios (1795 vs. 468 mg/g; $p<0.001$), indicating a strong association between advanced retinopathy and nephropathy severity. Longer duration of diabetes was associated with an increased likelihood of ESRD (OR=1.04, 95% CI: 1.01–1.08; p=0.021). Elevated systolic blood pressure (OR=1.05, $p<0.001$), higher serum creatinine levels (OR=18.92, $p<0.001$), increased urine protein excretion (OR=1.12, p=0.018), and elevated urine albumin-to-creatinine ratio (OR=1.31, $p<0.001$) were all significant risk factors for ESRD. In contrast, higher hemoglobin levels (OR=0.78, $p<0.001$) and hematocrit values (OR=0.94, p=0.009) were inversely associated with

ESRD, suggesting a protective effect. Additionally, ACE inhibitor use was associated with a significantly lower risk of ESRD (OR=0.42, p=0.001). For PDR, increasing age was found to be protective (OR=0.96, 95% CI: 0.93–0.99; p=0.004), while higher systolic blood pressure (OR=1.03, p=0.013), elevated serum creatinine levels (OR=1.28, p<0.001), and the presence of albuminuria (OR=4.12, p<0.001) significantly increased the risk of developing PDR. Hispanic ethnicity was also independently associated with a higher likelihood of PDR (OR=3.08, p=0.002). For ESRD, lower HbA1c levels were independently associated with disease status (OR=0.58, p=0.012), whereas serum creatinine emerged as the strongest predictor of ESRD, demonstrating an exceptionally high odds ratio (OR=198.46, 95% CI: 24.85–>999; p<0.001). These findings highlight the significant contribution of renal dysfunction and albuminuria to the progression of diabetic microvascular complications.

Table 1. Baseline Characteristics of Mild Nephropathy and ESRD Patients (n=200)

Variable	Mild Nephropathy (n=100)	ESRD (n=100)	P-value
Age (years)	59.3	61.8	0.48
HbA1c (%)	8.96	7.12	<0.001*
Duration of Diabetes (years)	19.7	25.1	0.021*
BMI (kg/m²)	31.3	30.1	0.29
SBP (mmHg)	129.3	145.7	<0.001*
Serum Creatinine (mg/dL)	1.1	5.8	<0.001*
eGFR (mL/min/1.73 m²)	73.2	17.3	<0.001*
Hemoglobin (g/dL)	13.9	11.2	<0.001*

*: Significant

Table 2. Comparison of Retinopathy Severity in ESRD and Mild Nephropathy Cohorts (n=200)

Variable	Mild NPDR (n=78)	PDR (n=122)	P-value
Age (years)	66.2	60.5	0.001*
HbA1c (%)	8.09	8.28	0.36
SBP (mmHg)	133.5	140.9	<0.001*
DBP (mmHg)	69.8	73.1	0.002*
Serum Creatinine (mg/dL)	1.68	3.62	<0.001*
eGFR (mL/min/1.73m²)	65.8	39.4	<0.001*
Urine Albumin/Creatinine Ratio (mg/g)	468	1795	<0.001*

Table 3. Significant Factors Associated with ESRD on Univariate Analysis

Variable	Odds Ratio (OR)	95% CI	P-value
Duration of Diabetes	1.04	1.01–1.08	0.021*
Systolic Blood Pressure	1.05	1.03–1.08	<0.001*
Serum Creatinine	18.92	9.65–37.10	<0.001*
Urine Protein	1.12	1.02–1.24	0.018*
Urine Albumin/Creatinine Ratio	1.31	1.18–1.47	<0.001*
Hemoglobin	0.78	0.69–0.88	<0.001*
Hematocrit	0.94	0.90–0.98	0.009*
ACE Inhibitor Use	0.42	0.24–0.72	0.001*

*: Significant

Table 4. Multivariate Logistic Regression Analysis

Variable	Odds Ratio (OR)	95% CI	P-value
Predictors of PDR			
Age (years)	0.96	0.93–0.99	0.004*
SBP (mmHg)	1.03	1.01–1.05	0.013*
Serum Creatinine (mg/dL)	1.28	1.12–1.46	<0.001*
Albuminuria	4.12	1.96–8.66	<0.001*
Hispanic Ethnicity	3.08	1.52–6.22	0.002*
Predictors of ESRD			
HbA1c (%)	0.58	0.38–0.89	0.012*
Serum Creatinine (mg/dL)	198.46	24.85–>999	<0.001*

DISCUSSION

Diabetic retinopathy (DR) is one of the most common microvascular complications of diabetes mellitus and a leading cause of preventable visual impairment worldwide. Despite advances in screening and treatment, many patients remain unaware of the presence and severity of their retinal disease. A significant discordance often exists between the clinical severity of diabetic retinopathy and patients' perception of their ocular health. Individuals with advanced retinal changes may remain asymptomatic until vision-threatening complications develop. This lack of awareness can delay timely ophthalmic evaluation and intervention, resulting in poorer visual outcomes. Understanding the gap between disease severity and patient awareness is essential for improving screening adherence, patient education, and early detection strategies in diabetic retinopathy.[8- 10]

In the present study, among 200 patients, age and BMI were comparable between the mild nephropathy and ESRD groups. ESRD patients had significantly lower HbA1c levels, longer diabetes duration, higher systolic blood pressure, elevated serum creatinine, lower eGFR, and reduced hemoglobin levels compared with those with mild nephropathy (all $p<0.05$). Patients with PDR were significantly younger and had higher systolic and diastolic blood pressures than those with mild NPDR. They also exhibited significantly worse renal function, characterized by higher serum creatinine levels, lower eGFR, and markedly elevated urine albumin-to-creatinine ratios (all $p<0.001$), whereas HbA1c levels were comparable between groups. Fitzgerald et al. conducted a case–control study to evaluate the concordance between diabetic retinopathy (DR) and diabetic nephropathy (DN) severity in patients with type 2 diabetes. The study included 164 patients with end-stage renal disease (ESRD) and 165 patients with mild nephropathy. Retinopathy status was assessed by dilated fundus examination, and systemic parameters were obtained from medical records. The prevalence of proliferative diabetic retinopathy (PDR) was higher in the ESRD group (65%) than in the mild DN group (38%). ESRD was significantly associated with lower HbA1c levels and higher systolic blood pressure. Within the ESRD cohort, PDR was linked to younger age, increased blood pressure, higher LDL levels, elevated serum creatinine, and albuminuria, whereas HbA1c showed no significant association. PDR demonstrated limited utility as a screening marker for chronic kidney disease.[11] Perais et al. conducted a systematic review and meta-analysis of 59 longitudinal studies involving patients with type 1 and type 2 diabetes to identify prognostic factors associated with progression to proliferative diabetic retinopathy (PDR). Markers of renal dysfunction, including nephropathy and elevated serum creatinine, were also associated with an increased risk of disease progression. Additional risk factors included younger age at diabetes diagnosis, higher triglyceride levels, and larger retinal venular diameters, particularly among patients with type 1 diabetes. In contrast, diabetes duration, blood pressure, lipid fractions, gender, ethnicity, body mass index, socioeconomic status, and tobacco or alcohol use showed no consistent association with PDR development. The authors concluded that poor glycemic control, advanced retinopathy, and renal impairment are key predictors of progression to PDR, emphasizing the importance of early detection and optimal metabolic control to reduce the risk of vision-threatening complications.[12]

In the present study, on univariate analysis, longer diabetes duration, elevated systolic blood pressure, increased serum creatinine, urine protein, and urine albumin-to-creatinine ratio were significantly associated with ESRD, while higher hemoglobin, hematocrit, and ACE inhibitor use were protective factors. Multivariate analysis identified younger age, higher systolic blood pressure, elevated serum creatinine, albuminuria, and Hispanic ethnicity as independent predictors of PDR. For ESRD, lower HbA1c and higher serum creatinine remained independent predictors, with serum creatinine demonstrating the strongest association with disease progression. Song et al. conducted a 3-year retrospective cohort study involving 604 patients with type 2 diabetes mellitus to evaluate differences in risk factors associated with the progression of diabetic retinopathy (DR) and diabetic nephropathy (DN). During follow-up, 67 patients showed DR progression and 34 demonstrated DN progression. Patients with DR progression had significantly higher mean HbA1c levels, and average glycemic control emerged as an independent predictor of worsening retinopathy. In contrast, patients with DN progression exhibited greater HbA1c variability, higher baseline urine albumin-to-creatinine ratios, and elevated triglyceride-to-HDL cholesterol ratios. Glycemic variability and dyslipidemia were identified as independent predictors of nephropathy progression. The authors concluded that the determinants of DR and DN progression differ, with sustained hyperglycemia being more strongly associated with retinopathy progression, whereas glycemic fluctuations and lipid abnormalities play a greater role in nephropathy progression, highlighting a discordance in the mechanisms underlying these diabetic microvascular complications.[13]

CONCLUSION

Diabetic nephropathy and diabetic retinopathy demonstrated a strong clinical association, with

albuminuria, elevated serum creatinine, and higher systolic blood pressure emerging as significant predictors of proliferative diabetic retinopathy. Serum creatinine was the strongest independent predictor of end-stage renal disease, highlighting the importance of integrated retinal and renal assessment in patients with long-standing type 2 diabetes mellitus.

REFERENCES

1. Fang J, Luo C, Zhang D, He Q, Liu L. Correlation between diabetic retinopathy and diabetic nephropathy: a two-sample Mendelian randomization study. Front Endocrinol (Lausanne). (2023) 14:1265711.
2. Penno G, Solini A, Zoppini G, Orsi E, Zerbini G, Trevisan R, et al. Rate and determinants of association between advanced retinopathy and chronic kidney disease in patients with type 2 diabetes: the Renal Insufficiency And Cardiovascular Events (RIACE) Italian multicenter study. Diabetes Care. (2012) 35:2317–23.
3. Wong CW, Wong TY, Cheng CY, Sabanayagam C. Kidney and eye diseases: common risk factors, etiological mechanisms, and pathways. Kidney International 2014;85(6):1290-302.
4. Wong TY, Sun J, Kawasaki R, Ruamviboonsuk P, Gupta N, Lansingh VC, et al. Guidelines on diabetic eye care: the international council of ophthalmology recommendations for screening, follow-up, referral, and treatment based on resource settings. Ophthalmology 2018;125(10):1608-22.
5. Wubben TJ, Johnson MW, Sohn EH, Peairs JJ, Kay CN, Kim SJ, et al. Anti–vascular endothelial growth factor therapy for diabetic retinopathy: consequences of inadvertent treatment interruptions. American Journal of Ophthalmology 2019;204:13-8.
6. Yau JW, Rogers SL, Kawasaki R, Lamoureux EL, Kowalski JW, Bek T, et al. Global prevalence and major risk factors of diabetic retinopathy. Diabetes Care 2012;35(3):556-64.
7. Wang E, Feng B, Chen S, Su Z, Chakrabarti S. Differential microvascular endothelial cell responses in the retina in diabetes compared to the heart and kidneys, a spatial transcriptomic analysis. PloS One. (2024) 19:e0310949.
8. Christensen PK, Larsen S, Horn T, Olsen S, Parving HH. Causes of albuminuria in patients with type 2 diabetes without diabetic retinopathy. Kidney Int. (2000) 58:1719–31.
9. Hong D, Zheng T, Jia-qing S, et al. Nodular glomerular lesion: a later stage of diabetic nephropathy? Diabetes Res Clin Pract. 2007;78:189–195.
10. Mason RM, Wahab NA.. Extracellular matrix metabolism in diabetic nephropathy. J Am Soc Nephrol. 2003;14:1358–1373.
11. Fitzgerald A, Das R, Moezzi CJ, Salazar SR, Mankad R, Qualls CR, Cabrera A, Kathuria A, Monickaraj F, Tzamaloukas A, Das A. Discordance of diabetic retinopathy severity in a cohort of diabetic nephropathy patients: a cross-sectional case–control study in a new Mexican population of type 2 diabetes. Front Endocrinol (Lausanne). 2025 Aug 1;16:1638415.
12. Perais J, Agarwal R, Evans JR, Loveman E, Colquitt JL, Owens D, Hogg RE, Lawrenson JG, Takwoingi Y, Lois N. Prognostic factors for the development and progression of proliferative diabetic retinopathy in people with diabetic retinopathy. Cochrane Database Syst Rev. 2023 Feb 22;2(2):CD013775.
13. Song KH, Jeong JS, Kim MK, Kwon HS, Baek KH, Ko SH, Ahn YB. Discordance in risk factors for the progression of diabetic retinopathy and diabetic nephropathy in patients with type 2 diabetes mellitus. J Diabetes Investig. 2019 May;10(3):745-752.