Section: Ophthalmology

Original Research Article

SEVERITY PATTERNS OF DIABETIC RETINOPATHY IN RELATION TO GLYCEMIC CONTROL, DISEASE DURATION, AND HYPERTENSION

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Received *: 28/04/2026*
Received in revised form *: 20/06/2026*
Accepted *: 04/07/2026*

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DOI: 10.70034/ijmedph.2026.3.107

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2026; 16 (3); 649-653

ABSTRACT

Background: Diabetic retinopathy (DR) remains a leading cause of preventable blindness, with severity classically attributed to glycemic exposure, disease duration, and systemic hypertension. The relative and combined contribution of these three determinants remains insufficiently quantified in Indian tertiary care populations. The objective is to evaluate the severity of DR and its correlation with glycated hemoglobin (HbA1c), duration of diabetes, and systemic hypertension among patients attending a tertiary ophthalmology centre.

Materials and Methods: This cross-sectional study enrolled 370 consecutive patients with type 2 diabetes mellitus at the Department of Ophthalmology, Surabhi Institute of Medical Sciences, Siddipet, over an eleven-month period (October 2024–August 2025). DR severity was graded using the ETDRS classification. Associations between DR severity and HbA1c category, diabetes duration, and hypertension status were assessed using Kruskal–Wallis and Spearman correlation tests, with independent predictors identified through ordinal logistic regression.

Results: Mild non-proliferative DR was the most common finding (34.9%), followed by no DR (30.0%), moderate (20.0%), severe non-proliferative (8.1%), and proliferative DR (7.0%). Proliferative disease was entirely absent among well-controlled patients (HbA1c <7.0%) but present in 22.7% of poorly controlled patients (HbA1c ≥9.0%), and rose from 0% in patients with diabetes duration under five years to 19.0% beyond a decade. HbA1c category, diabetes duration, and hypertension each independently predicted higher DR severity on multivariable analysis (all p<0.001).

Conclusion: DR severity was driven cumulatively and independently by glycemic control, disease duration, and hypertension, supporting integrated, duration-aware screening strategies that extend beyond glycemic monitoring alone in similar tertiary care settings.

Keywords: Diabetic retinopathy, diabetic eye disease, glycemic control, comorbidities, hypertension.

INTRODUCTION

Diabetic retinopathy (DR) is the most prevalent microvascular complication of diabetes mellitus and a leading cause of preventable blindness in working-age adults worldwide. Global DR prevalence is estimated at 22.27% among individuals with diabetes, with vision-threatening stages affecting a further 6.17%; the absolute burden is projected to reach 160.5 million by 2045.[1]

DR is rooted in chronic hyperglycaemia-driven injury to the retinal microvasculature. The cardinal early histopathological event is selective pericyte loss — detectable in trypsin-digest preparations — which disrupts the blood–retina barrier, triggers capillary basement membrane thickening, and culminates in the formation of acellular, non-perfused capillary ghosts.[2] Resultant ischaemia drives uncontrolled upregulation of vascular endothelial growth factor (VEGF), the principal mediator of pathological neovascularisation. Activation of the polyol and

hexosamine pathways and accumulation of advanced glycation end-products (AGEs) amplify oxidative stress and sustain a pro-inflammatory milieu, accelerating endothelial dysfunction.[2] These cellular events map directly onto the ETDRS severity spectrum: mild non-proliferative DR (NPDR) reflects microaneurysm formation at sites of pericyte dropout; moderate NPDR signals expanding capillary non-perfusion with hard exudates and cotton-wool spots; severe NPDR (the "4-2-1" stage) is characterised by intraretinal microvascular abnormalities (IRMA) and venous beading indicating near-complete pre-proliferative ischaemia; and proliferative DR represents VEGF-driven neovascularisation, with fragile, pericyte-deficient new vessels prone to haemorrhage and fibrotic traction threatening irreversible visual loss.[2]

The risk of DR development and progression is closely associated with glycaemic control, disease duration, and blood pressure. Glycated haemoglobin (HbA1c) — the established index of cumulative glycaemic exposure — is the most rigorously validated predictor of retinopathy severity; the Diabetes Control and Complications Trial (DCCT) demonstrated that every 10% proportional reduction in HbA1c conferred approximately a 43–45% lower risk of progression, without a discernible safe threshold.[3] Disease duration is an equally important determinant: subclinical macular vascular changes accumulate progressively before ophthalmoscopic retinopathy is evident, confirming that structural injury antedates clinical detection.[4] Systemic hypertension, which coexists with diabetes in approximately half of South Asian patients, exerts an independent and synergistic damaging effect on the retinal microvasculature; the UKPDS demonstrated that tight blood pressure control reduced retinopathy progression by 34% and the risk of significant visual deterioration by 47%.[5,6]

Despite this evidence base, data precisely characterising the relative and combined contributions of HbA1c, disease duration, and hypertension to DR severity in Indian tertiary care populations remain limited, with existing South Indian studies reporting prevalence ranging from 18% to 31%.[7,8] The present study was therefore undertaken to evaluate DR severity and its correlation with these three determinants in a consecutive tertiary care cohort, with a view to informing locally applicable screening and risk stratification strategies.

MATERIALS AND METHODS

Study Design and Setting: This was a hospital-based, observational cross-sectional study conducted in the Department of Ophthalmology, Surabhi Institute of Medical Sciences, Siddipet, Telangana, India, over a 11-month period from October 2024 to August 2025. The study was designed to evaluate the severity of diabetic retinopathy (DR) and its correlation with glycated hemoglobin (HbA1c), duration of diabetes mellitus, and systemic hypertension in a consecutive tertiary care cohort.

Sample Size: Sample size was calculated using the formula $n = Z^2pq/d^2$, where $Z = 1.96$ (95% confidence interval), $p = 0.2227$ (global DR prevalence among diabetics),[1] $q = 1 - p$, and $d = 0.05$ (margin of error), yielding a minimum of 268 participants. Accounting for a 10% non-response rate and to optimize statistical power for multivariate subgroup analyses, the final target was set at 370 participants. Consecutive sampling was employed.

Eligibility Criteria

Patients aged 18 years and above with a confirmed diagnosis of type 2 diabetes mellitus, established per World Health Organization criteria (fasting plasma glucose ≥7.0 mmol/L, or HbA1c ≥6.5% on two separate occasions),[10] and attending the ophthalmology outpatient clinic during the study period were eligible for inclusion. Minimum diabetes duration of one year was required to ensure adequate exposure for retinal evaluation. Patients were excluded if they had: type 1 diabetes mellitus; pre-existing non-diabetic retinal pathology (age-related macular degeneration, retinal vein occlusion, glaucomatous optic neuropathy, or inherited retinal dystrophies); media opacity precluding adequate fundal visualization (dense cataract, vitreous hemorrhage, or corneal opacity); prior intraocular surgery or laser photocoagulation; current or prior intravitreal anti-vascular endothelial growth factor therapy; pregnancy or lactation; or a diagnosis of hemoglobinopathy that could confound HbA1c interpretation.

Data Collection

All participants underwent a standardized, structured clinical assessment. Demographic data (age, sex, body mass index) and disease history (duration of diabetes, antidiabetic medication, antihypertensive therapy) were recorded from medical records and direct patient interview using a predesigned proforma. Systemic hypertension was defined as a resting blood pressure ≥140/90 mmHg on at least two separate readings taken on the same visit, or a documented history of antihypertensive drug use, in accordance with JNC 8 criteria.[11]

HbA1c was measured from venous blood samples using high-performance liquid chromatography (HPLC) and was categorized as: well-controlled (<7.0%), sub optimally controlled (7.0–8.9%), and poorly controlled (≥9.0%). Fasting lipid profile, fasting plasma glucose, serum creatinine, and urine albumin: creatinine ratio was additionally recorded to characterize the metabolic phenotype.

Ophthalmic assessment included best-corrected visual acuity (BCVA), intraocular pressure (applanation tonometry), slit-lamp anterior segment examination, and detailed dilated fundus evaluation using a 90-dioptre non-contact lens on a slit lamp and indirect ophthalmoscopy with a 20-dioptre lens. DR severity was graded bilaterally by a trained vitreoretinal surgeon, masked to the clinical records, using the Early Treatment Diabetic Retinopathy

Study (ETDRS) classification into: no DR; mild, moderate, and severe non-proliferative diabetic retinopathy (NPDR); and proliferative diabetic retinopathy (PDR).[12] For analyses, the more severely affected eye was used. Clinically significant diabetic macular oedema (CSME) was identified using stereoscopic slit-lamp biomicroscopy and confirmed on spectral-domain optical coherence tomography (SD-OCT).

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using SPSS version 26.0 (IBM Corp., Armonk, NY). Continuous variables were tested for normality using the Shapiro–Wilk test; normally distributed variables are expressed as mean ± standard deviation, and non-normally distributed variables as median (interquartile range). Categorical variables are presented as frequencies and proportions. Differences in DR severity across HbA1c categories, diabetes duration groups (<5, 5–10, >10 years), and hypertension status were assessed using the Kruskal–Wallis test with Dunn's post-hoc correction for non-parametric data, and one-way ANOVA for parametric comparisons. Spearman's rank-order correlation was used to examine ordinal associations between DR severity and continuous clinical variables. Factors independently associated with higher DR severity were identified through ordinal logistic regression, with DR severity grade as the dependent variable and HbA1c category, diabetes duration, hypertension status, age, sex, and BMI as covariates. Odds ratios with 95% confidence intervals are reported; a two-tailed p-value of <0.05 was considered statistically significant.

Ethical Considerations

Ethical approval was obtained from the Institutional Ethics Committee of Surabhi Institute of Medical Sciences, Siddipet, prior to study commencement. Written informed consent was obtained from all participants prior to enrolment. Patient confidentiality was maintained throughout; all data were anonymized and stored securely. Participation was voluntary, with the right to withdraw at any time without consequence to clinical care.

RESULTS

Participant characteristics and DR severity distribution

All 370 consecutively enrolled patients were analyzed. The mean age was 53.1 years (SD 11.8 years) and 202 (54.6 %) were women (data not shown). Hypertension was present in 202 patients (54.6 %). HbA1c was < 7.0 % in 136 patients (36.8 %), 7.0–8.9 % in 146 (39.5 %) and ≥ 9.0 % in 88 (23.8 %). Diabetes duration was < 5 years in 117 (31.6 %), 5–10 years in 127 (34.3 %) and > 10 years in 126 (34.1 %).

Distribution of DR severity: Mild NPDR was the most frequent stage, affecting 129 patients (34.9 %). No DR was documented in 111 (30.0 %), moderate NPDR in 74 (20.0 %), severe NPDR in 30 (8.1 %) and PDR in 26 (7.0 %).

Correlation of HbA1c with DR severity

Among patients with HbA1c < 7.0 %, 71 (52.2 %) had no DR and none developed PDR. In the 7.0–8.9 % group, mild NPDR occurred in 38.4 % and PDR in 4.1 %. Poor glycemic control (HbA1c ≥ 9.0 %) was associated with higher severity: 24 (27.3 %) had moderate NPDR, 16 (18.2 %) severe NPDR and 20 (22.7 %) PDR. The proportion of PDR rose from 0 % in well controlled diabetes to 22.7 % in poorly controlled patients.

Duration of diabetes and DR severity

Patients with disease duration < 5 years had mostly no DR (63.2 %) or mild NPDR (32.5 %), and none developed PDR. In the 5–10-year group, mild NPDR remained common (39.4 %), while severe NPDR and PDR occurred in 7.9 % and 1.6 % respectively. Longer disease duration (> 10 years) markedly increased severity: moderate NPDR occurred in 29.4 %, severe NPDR in 15.9 % and PDR in 19.0 % of patients. Thus, PDR prevalence increased from 0 % in < 5 years to 19.0 % when diabetes exceeded a decade.

Systemic hypertension and DR severity

Among normotensive participants, 60 (35.7 %) had no DR, 61 (36.3 %) mild NPDR, 31 (18.5 %) moderate NPDR, 10 (6.0 %) severe NPDR and 6 (3.6 %) PDR. Hypertensive patients had a higher prevalence of severe stages: severe NPDR was found in 20 (9.9 %) and PDR in 20 (9.9 %), compared with 5.9 % and 3.6 % among normotensive patients. Overall, 19.8 % of hypertensive patients had severe NPDR or PDR versus 15.9 % of normotensive patients.

Ordinal logistic regression

After adjusting for age, sex and BMI (covariate data not shown), each one level increase in HbA1c category (e.g., from < 7.0 % to 7.0–8.9 %) was associated with a 35.97-fold increase in the odds of more severe DR (95 % CI 19.54–62.20, p < 0.001). Similarly, each category increase in diabetes duration conferred an OR of 41.20 (95 % CI 23.74–71.64, p < 0.001). Hypertension independently increased the odds of more severe DR by 23.77 times (95 % CI 12.64–44.72, p < 0.001). These findings indicate strong, independent associations of poor glycemic control, longer disease duration and hypertension with DR severity.

Table 1: Distribution of diabetic retinopathy severity (n = 370)

DR severity	Frequency	Percentage
No DR	111	30.0 %
Mild NPDR	129	34.9 %
Moderate NPDR	74	20.0 %
Severe NPDR	30	8.1 %
PDR	26	7.0 %

Table 2: DR severity by HbA1c category (n)

HbA1c category	No DR	Mild NPDR	Moderate NPDR	Severe NPDR	PDR	Total
< 7.0 %	71	49	16	0	0	136
7.0–8.9 %	36	56	34	14	6	146
≥ 9.0 %	4	24	24	16	20	88

Table 3: DR severity by duration of diabetes (n)

Duration	No DR	Mild NPDR	Moderate NPDR	Severe NPDR	PDR	Total
< 5 years	74	38	5	0	0	117
5–10 years	33	50	32	10	2	127
> 10 years	4	41	37	20	24	126

Table 4: DR severity by hypertension status (n)

Hypertension	No DR	Mild NPDR	Moderate NPDR	Severe NPDR	PDR	Total
No	60	61	31	10	6	168
Yes	51	68	43	20	20	202

Table 5: Multivariable ordinal logistic regression predicting higher DR severity

Predictor (per category increase)	Coefficient	Odds ratio	95 % CI	p-value
HbA1c category (< 7.0 %, 7.0–8.9 %, ≥ 9.0 %)	3.58	35.97	19.54–62.20	< 0.001
Duration of diabetes (< 5, 5–10, > 10 years)	3.72	41.20	23.74–71.64	< 0.001
Hypertension (No → Yes)	3.17	23.77	12.64–44.72	< 0.001

[Figure 1] visualizes the distribution of DR stages across HbA1c categories. The stacked bar chart illustrates the absence of PDR in the well-controlled group and the progressive increase in moderate, severe and proliferative stages with rising HbA1c. Figure 2 depicts odds ratios from the ordinal logistic model, with log scaled estimates and 95 % CIs.

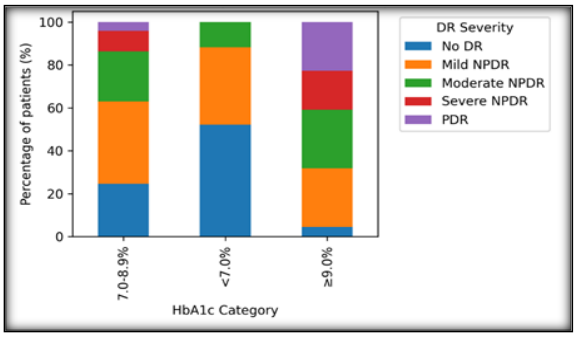

Figure 1: Distribution of DR severity across HbA1c categorie

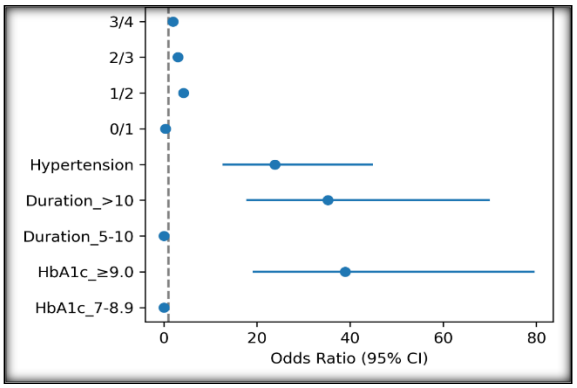

Figure 2: Odds ratios from ordinal logistic regression with 95 % confidence intervals

DISCUSSION

This cross-sectional analysis of 370 patients demonstrated a strong, graded relationship between diabetic retinopathy (DR) severity and each of the three exposures studied, with all three retaining independent significance after multivariable adjustment. PDR was absent among well-controlled patients (HbA1c <7.0%) but present in 22.7% of those with HbA1c ≥9.0%, while severe disease rose from 0% in patients with diabetes under five years to nearly one-fifth of those with disease exceeding a decade. Hypertensive patients carried a near two-fold excess of severe NPDR and PDR compared with normotensive patients. These findings align closely with regional Indian literature. Shrote et al, similarly found that duration since diagnosis (p=0.0006) and hypertension (p=0.045) were significantly associated with DR presence, and that duration of diabetes independently predicted severity (p=0.04) — a pattern that mirrors our duration-stratified findings closely.[13] The proportionate relationship we observed between worsening HbA1c and rising DR severity is also consistent with the broader Indian evidence base linking glycemic control to retinopathy grade in tertiary care populations.[14] The dose-dependent glycemic gradient observed here is consistent with the foundational evidence from the Diabetes Control and Complications Trial, in which mean HbA1c was the dominant predictor of retinopathy progression across the entire observed range, without a discernible safe threshold.[3] This pattern is further corroborated by Yau et al., whose pooled global analysis of 35 population-based studies identified longer diabetes duration and higher HbA1c as the two most consistent risk factors for DR worldwide.[15] Outside India, Li et al., in a twelve-province Chinese cohort of 12,766 patients with type

2 diabetes, confirmed that both hypertension (OR 1.215, 95% CI 1.120–1.318) and diabetes duration (OR 1.069 per year, 95% CI 1.062–1.075) were independent predictors of DR after multivariable adjustment, lending cross-population support to the independent contributions we observed for these two variables.[16]. Similarly, Xiao et al., screening 2,677 patients with diabetes in southern China, reported that HbA1c above 6.5% independently increased DR risk (OR 1.58, p<0.01), alongside insulin use and longer disease duration, reinforcing glycemic control and duration as reproducible determinants across diverse populations.[17] The hypertension-driven excess in severity we observed corroborates the UKPDS finding that tight blood pressure control reduces both retinopathy progression and visual deterioration,[7] A relationship mechanistically explored by Stratton et al. in their analysis of risk factors for retinopathy incidence and progression over six years of follow-up in the UKPDS cohort, which identified systolic blood pressure as an independent predictor of retinopathy progression alongside HbA1c.[18] The unusually large odds ratios obtained in our ordinal model — particularly for HbA1c category and duration — most likely reflect the quasi-complete separation evident in Tables 2 and 3, where PDR was entirely absent in the lowest exposure strata. This pattern of inflated point estimates with correspondingly wide confidence intervals is a recognised feature of regression models applied to strongly skewed categorical exposures, and should be interpreted as confirmatory of a strong gradient rather than a precise multiplicative risk. Taken together, our results reinforce that HbA1c, diabetes duration, and hypertension act as compounding, largely independent drivers of retinopathy severity, and that none of the three can be safely deprioritized in screening or management protocols for this population.

CONCLUSION

ODiabetic retinopathy severity in this tertiary care cohort was driven independently and cumulatively by poor glycemic control, longer disease duration, and systemic hypertension, underscoring that effective retinal protection requires simultaneous, sustained control of all three risk dimensions rather than glycemic management alone. These findings support integrating routine blood pressure optimization and duration-based risk stratification into existing diabetic eye screening protocols, particularly for patients nearing or exceeding a decade of disease, to enable earlier referral and reduce the burden of vision-threatening retinopathy in similar South Asian tertiary care settings.

Acknowledgements: The author would like to extend his gratitude for the support provided by the staff at the institutional department.

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