E-ISSN 2250-0944
ISSN 2250-1150
doi: 10.31838/ijprt/16.02.118

Research Article

ASSOCIATION OF DIABETIC RETINOPATHY SEVERITY WITH FASTING BLOOD GLUCOSE, POSTPRANDIAL BLOOD GLUCOSE AND GLYCATED HAEMOGLOBIN (HBA1C): A HOSPITAL-BASED CROSS-SECTIONAL STUDY

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Received date: 20-07-2026, Date of acceptance: 23-07-2026**, date of publication: 24-07-2026.**

Abstract

Background: Diabetic retinopathy (DR) is a leading microvascular complication of diabetes mellitus and a major cause of preventable blindness. Chronic hyperglycaemia drives its progression, but which routinely available glycaemic index best reflects DR severity is uncertain.

Objectives: To examine the association of fasting blood glucose (FBG), postprandial blood glucose (PPBG), HbA1c and diabetes duration with the severity of DR.

Methods: In this hospital-based cross-sectional study, 130 adults with diabetes mellitus and established DR were enrolled at a tertiary-care centre (2017–2019). DR was graded by fundoscopy per the Early Treatment Diabetic Retinopathy Study (ETDRS) scale as mild, moderate or severe non-proliferative DR. Glycaemic control was categorised per ICMR 2018 criteria. Associations were tested with the chi-square test and one-way ANOVA, with multivariable analysis; $p<0.05$ was significant.

Results: Mean age was 58.3 ± 10.6 years; 52.3% were men. DR was moderate in 59.2%, mild in 35.4% and severe in 5.4%. Diabetes duration >5 years (76.2%) was significantly associated with

greater DR severity (p=0.002). Uncontrolled HbA1c (94.6%) was significantly associated with DR severity (p<0.001); every patient with severe DR had HbA1c >10%. In contrast, uncontrolled FBG (70.8%; p=0.114) and PPBG (78.5%; p=0.354) were not. On multivariable analysis, only diabetes duration (p=0.002) and HbA1c (p=0.017) remained independently associated.

Conclusion: Among patients with DR, HbA1c and diabetes duration—but not single fasting or postprandial glucose measurements—correlate with retinopathy severity. HbA1c is the more informative marker for microvascular risk stratification.

Keywords: Diabetic retinopathy; HbA1c; Glycaemic control; Diabetes mellitus; Microvascular complications.

INTRODUCTION

India is experiencing a rapidly expanding epidemic of diabetes mellitus and has one of the largest diabetic populations in the world.[1] As the prevalence and duration of diabetes increase, so does the burden of chronic microvascular complications. Diabetic retinopathy is the commonest microvascular complication of diabetes and a leading cause of preventable blindness among working-age adults.[2] Reported prevalence in Indian studies ranges widely (approximately 10–26%) depending on population and method of ascertainment.[3],[4],[5]

A chronically elevated blood glucose level is the single most important modifiable factor driving the development and progression of DR, acting through non-enzymatic glycation, oxidative stress, accelerated retinal microvascular cell death, pericyte loss and breakdown of the blood–retina barrier.[6],[7],[8] Glycaemic status can be assessed by several routinely available measures. Fasting and postprandial blood glucose are single-point measurements subject to short-term fluctuation, whereas HbA1c reflects average glycaemia over the preceding two to three months and therefore approximates cumulative glycaemic exposure.[9]

Landmark trials established tight glycaemic control as protective against retinopathy,[10],[11] but in routine practice it is not clear which of these indices best mirrors the severity of established DR. We therefore examined the association of FBG, PPBG, HbA1c and diabetes duration with DR severity in patients with established retinopathy.

MATERIAL AND METHODS

Study design, setting and participants

This hospital-based cross-sectional descriptive study was conducted in the Department of Medicine of a tertiary-care teaching hospital between 2017 and 2019. Adults (≥18 years) with type 1 or type 2 diabetes mellitus diagnosed per American Diabetes Association criteria and with fundoscopically confirmed diabetic retinopathy were eligible.[12] Patients were excluded if they had retinopathy attributable to another cause, pre-existing non-diabetic maculopathy, prior laser

photocoagulation, or declined participation. Because the study enrolled only patients with established DR, the analyses examine the association of glycaemic and clinical variables with the severity of retinopathy rather than with its presence.

Sample size

The sample size was estimated as $n = Z^2pq/e^2$, with $Z = 1.96$, $p = 8.4\%$ (regional DR prevalence), $q = 1 - p$ and allowable error $e = 5\%$, plus 10% for non-response, yielding approximately 130 participants.

Assessments and definitions

All participants underwent a detailed history, general and systemic examination, and routine investigations including complete blood count, renal and liver function tests, fasting and postprandial blood glucose and HbA1c (measured in a NABL-accredited laboratory). Glycaemic parameters were categorised per ICMR 2018 guidelines; fasting glucose >125 mg/dL, 2-hour postprandial glucose >180 mg/dL and HbA1c ≥7% were regarded as uncontrolled.[13] Fundus examination was performed by the investigator and confirmed by an ophthalmologist, and retinopathy was graded per the ETDRS scale as mild, moderate or severe non-proliferative DR.[14]

Statistical analysis

Data were analysed with SPSS version 20. Categorical variables were expressed as frequencies and percentages and continuous variables as mean ± standard deviation. Associations between glycaemic/clinical variables and DR severity were tested with the chi-square test for categorical data and one-way ANOVA for continuous data, with multivariable analysis to identify independently associated factors. A $p<0.05$ was considered statistically significant.

Ethics

The study was approved by the Institutional Ethics Committee, and written informed consent was obtained from every participant.

RESULTS

A total of 130 patients with diabetes mellitus and established DR were studied. The mean age was 58.3 ± 10.6 years; 44.6% were aged over 61 years. There were 68 men (52.3%) and 62 women (47.7%). Diabetes duration exceeded five years in 99 patients (76.2%). Most were on insulin (72.3%). Hypertension was the commonest comorbidity (54.6%), followed by obesity (28.5%), ischaemic heart disease (16.2%) and cerebrovascular disease (11.5%). Baseline characteristics are shown in Table 1.

Retinopathy was moderate in 77 patients (59.2%), mild in 46 (35.4%) and severe in 7 (5.4%) (Figure 1). Diabetes duration was significantly associated with DR severity: among the 99

patients with duration >5 years, 67 (51.5%) had moderate and 4 had severe DR (chi-square 12.31, p=0.002).

The three glycaemic indices behaved very differently (Table 2). Although uncontrolled fasting glucose (70.8%) and uncontrolled postprandial glucose (78.5%) were common, neither was significantly associated with DR severity (p=0.114 and p=0.354, respectively). In contrast, HbA1c showed a strong association: 94.6% had an uncontrolled HbA1c, and its distribution differed significantly across severity grades (chi-square 52.4; one-way ANOVA F = 23.08; p<0.001). Notably, all 7 patients with severe DR had an HbA1c above 10%, whereas patients with well-controlled HbA1c were concentrated in the mild and moderate grades (Figure 2).

Body-mass index (mean 28.2 kg/m²) and the presence of comorbidities or specific diabetes treatments were not significantly associated with DR severity. On multivariable analysis, only diabetes duration (p=0.002) and HbA1c (p=0.017) remained independently associated with DR severity (Table 3).

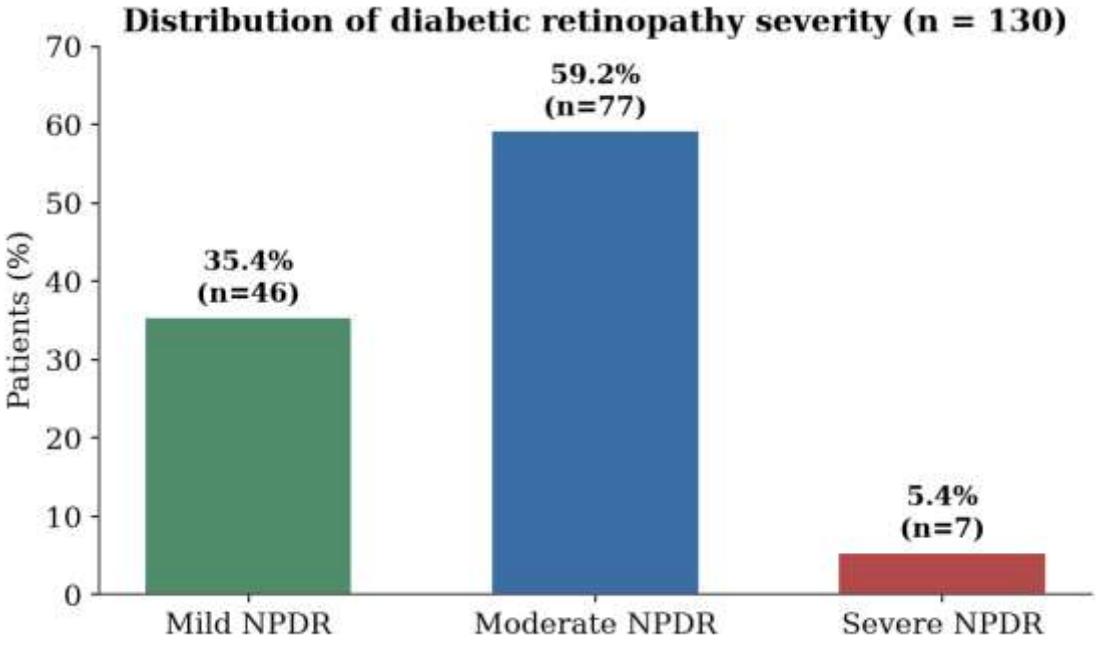

Figure 1. Distribution of diabetic retinopathy severity among the 130 study patients. Moderate non-proliferative DR predominated.

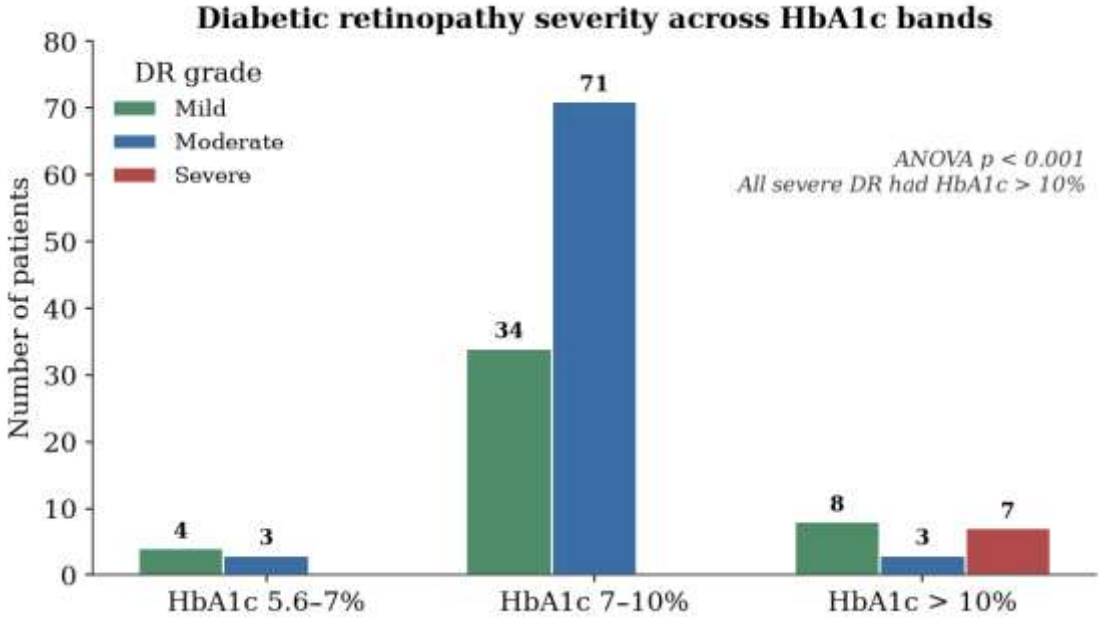

Figure 2. Diabetic retinopathy severity across HbA1c bands. DR severity increased with rising HbA1c (ANOVA p<0.001); all patients with severe DR had an HbA1c >10%.

Table 1. Demographic and clinical characteristics of the study population (n = 130)

Variable	Category	n (%)
Age (years)	Mean ± SD	58.3 ± 10.6
Sex	Male / Female	68 (52.3) / 62 (47.7)
Diabetes duration	>5 years	99 (76.2)
Treatment	Insulin	94 (72.3)
	Oral agents	25 (19.2)
	Both	11 (8.5)
Body-mass index (kg/m²)	Mean	28.2
Hypertension	Present	71 (54.6)
Obesity	Present	37 (28.5)
Ischaemic heart disease	Present	21 (16.2)
Cerebrovascular disease	Present	15 (11.5)
DR severity	Mild	46 (35.4)
	Moderate	77 (59.2)
	Severe	7 (5.4)

SD, standard deviation; DR, diabetic retinopathy.

Table 2. Glycaemic control and diabetes duration by diabetic retinopathy severity

Parameter	Mild (n=46)	Moderate (n=77)	Severe (n=7)	Test	p
Duration >5 years	28	67	4	χ^2=12.3	0.002*
FBG >125 mg/dL	34	51	7	χ^2=3.88	0.114
PPBG >180 mg/dL	36	59	7	χ^2=2.08	0.354
HbA1c ≥7%	42	74	7	χ^2=52.4	<0.001*
HbA1c >10%	8	3	7	F=23.1	<0.001*

*Values are counts of patients within each severity grade. FBG, fasting blood glucose; PPBG, postprandial blood glucose. *Statistically significant (p<0.05). χ^2, chi-square; F, one-way ANOVA F-statistic.*

Table 3. Multivariable analysis of factors associated with diabetic retinopathy severity

Factor	Association	p value
Diabetes duration (>5 years)	Independent	0.002*
HbA1c	Independent	0.017*
Fasting blood glucose	Not significant	NS
Postprandial blood glucose	Not significant	NS
Body-mass index	Not significant	NS
Comorbidities	Not significant	NS

**Statistically significant (p<0.05). NS, not significant.*

DISCUSSION

In this cross-sectional study of 130 patients with established diabetic retinopathy, HbA1c and diabetes duration were significantly associated with retinopathy severity, whereas single fasting and postprandial glucose measurements were not. The gradient was striking for HbA1c: every patient with severe DR had an HbA1c above 10%. On multivariable analysis, only diabetes duration and HbA1c remained independently associated with severity.

These findings are biologically coherent. HbA1c integrates glycaemia over the preceding two to three months and therefore approximates the cumulative glycaemic burden that drives microvascular injury through advanced glycation and oxidative stress.[6,9] Single fasting or postprandial glucose values are labile snapshots influenced by the timing of the last meal, intercurrent illness and same-day treatment, and are consequently weaker correlates of a chronic structural complication. The dominant contribution of diabetes duration is consistent with it

being the most reproducible risk factor for DR across epidemiological studies, including the Wisconsin Epidemiologic Study of Diabetic Retinopathy.[15],[16]

Our results align with the DCCT and UKPDS, which demonstrated that sustained reductions in HbA1c reduce the incidence and progression of retinopathy,[10],[11] and with Indian and international studies linking higher HbA1c to more advanced DR.[17],[18],[19],[20] Henricsson et al. observed that the frequency and severity of retinopathy relate to HbA1c values after, but not at, the diagnosis of type 2 diabetes, underscoring the role of cumulative exposure.[21] Some authors have reported postprandial hyperglycaemia to be a stronger short-term predictor of progression than HbA1c, and the relative contributions of fasting versus postprandial glycaemia to vascular complications remain debated;[22],[23] our data, using single spot measurements, favour the integrated index. The practical implication is that HbA1c, rather than isolated blood glucose readings, should anchor microvascular risk assessment: patients with long-standing diabetes and persistently elevated HbA1c warrant closer retinal surveillance and earlier intensification of therapy.[25],[26]

Limitations

First, the study enrolled only patients who already had DR; it therefore characterises correlates of DR severity and cannot estimate the association of glycaemic indices with the presence versus absence of retinopathy, as no non-DR comparison group was included. Second, the cross-sectional design precludes causal inference. Third, the number of patients with severe DR was small (n=7), so severity-stratified estimates are imprecise; associations were nonetheless confirmed using both categorical and analysis-of-variance approaches. Fourth, retinopathy was graded by fundoscopy without optical coherence tomography or fundus fluorescein angiography, and a lipid profile—another recognised contributor to retinopathy—was not analysed.[24] Finally, this was a single-centre study using convenience sampling. Prospective, multicentre studies with a non-DR comparison group and objective retinal imaging would strengthen these findings.

CONCLUSION

Among patients with diabetic retinopathy, HbA1c and diabetes duration are significantly and independently associated with retinopathy severity, whereas single fasting and postprandial glucose measurements are not. HbA1c, which reflects cumulative glycaemic exposure, is the more informative marker for microvascular risk stratification. Regular HbA1c monitoring and sustained glycaemic control, particularly in patients with long-standing diabetes, should be prioritised to limit progression of diabetic retinopathy.

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