Research Article *Cuestiones de Fisioterapia* *Medicine*

Association Between Glycaemic Control (HbA1c) and Severity of Diabetic Retinopathy: A Hospital-Based Observational Study

Dr. Banker Mahima Suhas*

Associate Professor, Department of Ophthalmology, Indira Medical College & Hospital, Thiruvallur Taluk & Dist. Tamilnadu, India

Abstract

Background: Diabetic retinopathy (DR) is a leading cause of preventable visual impairment among working-age adults worldwide and an increasing burden in India. Glycated haemoglobin (HbA1c) reflects integrated glycaemic control over the preceding two to three months and is a plausible determinant of both the development and the progression of DR. We examined the association between HbA1c and the presence and severity of DR in a South Indian hospital population.

Methods: This hospital-based observational cross-sectional comparative study enrolled 200 patients with diabetes mellitus attending a tertiary care teaching hospital in South India. HbA1c was measured for all participants, and DR was graded on dilated fundus examination into No DR, Mild non-proliferative DR (NPDR), Moderate NPDR, Severe NPDR, and proliferative DR (PDR). HbA1c was categorised as good (<7%), fair (7-9%), and poor (>9%). Associations were assessed using the independent t-test, one-way analysis of variance (ANOVA), the chi-square test, and Pearson correlation, with $p<0.05$ considered significant.

Results: The mean age was 56.8 (SD 13.3) years and 105 (52.5%) were female. DR was present in 142 (71.0%; 95% CI 64.7-77.3%). Mean HbA1c was higher in patients with DR than without (8.70% vs 7.35%; $t=9.33$, $p<0.001$) and rose stepwise across DR severity (No DR 7.35%, Mild NPDR 8.48%, Moderate NPDR 8.48%, Severe NPDR 9.13%, PDR 10.29%; $F=35.08$, $p<0.001$). DR prevalence increased across HbA1c categories (23.8%, 67.5%, 96.4%; chi-square=41.04, $p<0.001$). Diabetes duration was longer in those with DR (16.5 vs 7.5 years; $t=9.00$, $p<0.001$). DR did not differ by hypertension status ($p=0.84$).

Conclusion: Poorer glycaemic control showed a strong, graded association with both the presence and severity of DR, supporting tight glycaemic control and regular retinal screening.

Keywords: *diabetic retinopathy; glycated haemoglobin; HbA1c; glycaemic control; diabetes mellitus; South India.*

Introduction

Diabetes mellitus has emerged as one of the foremost public health challenges of the twenty-first century, and India bears a disproportionate share of the global burden. Among the chronic microvascular complications of diabetes, diabetic retinopathy (DR) is of particular concern because it is the leading cause of preventable visual impairment and blindness among working-age adults. The condition develops insidiously, often remaining asymptomatic until vision-threatening stages such as macular oedema or proliferative disease

have supervened, and its consequences impose substantial individual, familial, and societal costs. As the prevalence of diabetes continues to rise in India, the absolute number of individuals at risk of sight-threatening retinopathy is expected to grow correspondingly, making the identification of modifiable determinants a clinical and public health priority [1].

The pathogenesis of DR is driven principally by chronic hyperglycaemia, which initiates a cascade of biochemical and vascular derangements within the retinal microcirculation. Sustained elevation of blood glucose promotes the formation of advanced glycation end-products, activation of the polyol and protein kinase C pathways, increased oxidative stress, and a low-grade inflammatory state. These processes culminate in pericyte loss, basement membrane thickening, breakdown of the blood-retinal barrier, capillary non-perfusion, and ultimately retinal ischaemia that stimulates pathological neovascularisation. Because these injurious mechanisms are fundamentally a function of cumulative glycaemic exposure, the degree of long-term glycaemic control is mechanistically central to whether, and how rapidly, retinopathy develops and progresses [3].

Glycated haemoglobin (HbA1c) is the most widely accepted laboratory index of integrated glycaemic control, reflecting average glycaemia over the preceding two to three months. Unlike a single fasting or random glucose value, HbA1c is relatively unaffected by short-term fluctuations and provides a stable, reproducible measure of the metabolic milieu to which the retinal vasculature is exposed. Landmark interventional trials and subsequent observational studies have consistently demonstrated that improved glycaemic control, as reflected by lower HbA1c, reduces the incidence and slows the progression of microvascular complications, including retinopathy. A graded, or dose-response, relationship between HbA1c and retinopathy risk has been described in several populations, lending biological coherence to the notion that glycaemic exposure is causally implicated [3].

In the Indian context, large epidemiological investigations have characterised the burden and correlates of DR in considerable detail. The Chennai Urban Rural Epidemiology Study (CURES) and the Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetics Study (SN-DREAMS) have each contributed substantially to the understanding of DR prevalence and its risk factors in southern India, identifying duration of diabetes, glycaemic control, and other systemic factors as important determinants [1,2]. These studies have also drawn attention to the relationship between the age of onset of diabetes and retinopathy, and to additional systemic correlates such as anaemia [2,4]. Despite this body of evidence, the relationship between glycaemic control and DR severity continues to merit examination in distinct hospital-based populations, where the clinical spectrum and case mix may differ from community-based samples.

Hospital-based data remain valuable because they reflect the population that clinicians actually encounter in routine practice and because they can directly inform decisions regarding glycaemic targets and the intensity of retinal screening. There is a continuing need for contemporary, setting-specific evidence quantifying how strongly HbA1c tracks with not merely the presence of DR but with its graded severity across the recognised clinical stages. The present study was undertaken to address this gap. Specifically, we sought to determine the prevalence and severity distribution of DR in a South Indian tertiary care hospital population, and to examine the association of HbA1c with both the presence and the severity of DR, while also describing the contribution of diabetes duration and hypertension. We hypothesised that higher

HbA1c would be associated with a greater prevalence and severity of DR in a graded

manner.

Materials and Methods

Study design and setting

This was a hospital-based observational study of cross-sectional, comparative design conducted at tertiary care teaching hospital in South India, over the period of six months.

Study population

Patients with an established diagnosis of diabetes mellitus attending the hospital during the study period were eligible for inclusion. A total of 200 patients were enrolled.

Inclusion criteria: Adult patients with a confirmed diagnosis of diabetes mellitus who were able to undergo HbA1c measurement and dilated fundus examination and who provided informed consent.

Exclusion criteria: Patients with media opacities or other ocular conditions precluding adequate fundus visualisation and grading, and those who declined participation or in whom HbA1c could not be reliably measured.

Sample size

A sample of 200 consecutive eligible patients with diabetes mellitus was studied. This sample size was considered adequate to estimate the prevalence of diabetic retinopathy with acceptable precision and to detect clinically meaningful differences in mean HbA1c between patients with and without retinopathy and across severity grades.

Data collection and clinical assessment

For each participant, demographic details, type and duration of diabetes, and the presence of systemic hypertension were recorded. HbA1c was measured for all participants as the index of glycaemic control. For analysis, HbA1c was categorised as good control (<7%), fair control (7-9%), and poor control (>9%).

Grading of diabetic retinopathy

All participants underwent dilated fundus examination. Diabetic retinopathy was graded according to standard clinical criteria based on the Early Treatment Diabetic Retinopathy Study (ETDRS) framework and Klein-based non-proliferative and proliferative categories into the following mutually exclusive groups: No DR, Mild non-proliferative diabetic retinopathy (NPDR), Moderate NPDR, Severe NPDR, and proliferative diabetic retinopathy (PDR). For analyses comparing patients with and without disease, any grade of NPDR or PDR was classified as "DR present."

Statistical analysis

Data were analysed using descriptive and inferential statistics. Continuous variables were summarised as means with standard deviations (SD) and categorical variables as frequencies and percentages. The prevalence of DR was reported with a 95% confidence interval (CI). Differences in mean HbA1c between patients with and without DR, and in diabetes duration, were assessed using the independent samples t-test. Differences in mean HbA1c across the five DR severity grades were assessed using one-way analysis of variance (ANOVA). Associations between categorical variables, including DR prevalence across HbA1c categories and the association of DR with hypertension, were assessed using the chi-square test. The relationship between HbA1c and duration of diabetes was examined using the Pearson correlation coefficient. A two-sided p value of less than 0.05 was considered statistically significant.

Results

Patient characteristics

A total of 200 patients with diabetes mellitus were studied. The mean age was 56.8 (SD 13.3) years. There were 105 women (52.5%) and 95 men (47.5%). The mean duration of diabetes was 13.9 (SD 7.6) years. By recorded type, 114 patients were classified as type 1 and 86 as type 2 diabetes. Systemic hypertension was

present in 97 patients (48.5%). The mean HbA1c for the cohort was 8.31% (SD 1.12), with values ranging from 5.6% to 11.3%. Baseline characteristics are summarised in Table 1.

Table 1. Baseline characteristics of the study population (N=200)

Characteristic	Value
Age, mean (SD), years	56.8 (13.3)
Female, n (%)	105 (52.5)
Male, n (%)	95 (47.5)
Duration of diabetes, mean (SD), years	13.9 (7.6)
Diabetes type 1 (as recorded), n	114
Diabetes type 2 (as recorded), n	86
Hypertension present, n (%)	97 (48.5)
HbA1c, mean (SD), %	8.31 (1.12)
HbA1c range, %	5.6-11.3

Prevalence and severity of diabetic retinopathy

Diabetic retinopathy was present in 142 of the 200 patients, giving a prevalence of 71.0% (95% CI 64.7-77.3%). Among all participants, 58 (29.0%) had no retinopathy, 62 (31.0%) had mild NPDR, 44 (22.0%) had moderate NPDR, 29 (14.5%) had severe NPDR, and 7 (3.5%) had proliferative DR. The severity distribution is presented in Table 2.

Table 2. Prevalence and severity distribution of diabetic retinopathy (N=200)

DR category	n	%
No DR	58	29.0
Mild NPDR	62	31.0
Moderate NPDR	44	22.0
Severe NPDR	29	14.5
PDR	7	3.5
Any DR (DR present)	**142**	**71.0**

HbA1c and diabetic retinopathy

Mean HbA1c was significantly higher in patients with DR than in those without (8.70% vs 7.35%; independent t-test t=9.33, p<0.001). Across the five severity grades, mean HbA1c rose in a stepwise, graded manner from 7.35% in patients with no DR to 10.29% in those with PDR (one-way ANOVA F=35.08, p<0.001). This dose-response relationship between worsening glycaemic control and increasing DR severity was the principal finding of the study. The values are shown in Table 3.

Table 3. HbA1c by diabetic retinopathy status and across severity grades

Group	Mean HbA1c (%)	Statistical test
DR absent	7.35	t=9.33, p<0.001
DR present	8.70	(vs DR absent)
No DR	7.35	One-way ANOVA
Mild NPDR	8.48	F=35.08
Moderate NPDR	8.48	p<0.001
Severe NPDR	9.13	
PDR	10.29	

DR prevalence across HbA1c categories, duration, and hypertension

The prevalence of DR increased markedly across the three categories of glycaemic control. Among patients with good control (HbA1c <7%), DR was present in 23.8%; this rose to 67.5% among those with fair control (7-9%) and to 96.4% among those with poor control (>9%) (chi-square=41.04, p<0.001).

Duration of diabetes was substantially longer in patients with DR than in those without (16.5 vs 7.5 years; t=9.00, p<0.001), and HbA1c was modestly positively correlated with duration of diabetes (Pearson r=0.386, p<0.001). In contrast, the prevalence of DR did not differ significantly by hypertension status: 69.9% among patients without hypertension versus 72.2% among those with hypertension (chi-square=0.04, p=0.84). These findings are summarised in Table 4.

Table 4. DR prevalence across HbA1c categories and by duration and hypertension

Variable	DR prevalence / value	Statistical test
HbA1c <7% (good)	23.8%	chi-square=41.04, p<0.001
HbA1c 7-9% (fair)	67.5%	
HbA1c >9% (poor)	96.4%	
Duration, DR absent (mean)	7.5 years	t=9.00, p<0.001
Duration, DR present (mean)	16.5 years	
HbA1c vs duration correlation	r=0.386	p<0.001
DR with no hypertension	69.9%	chi-square=0.04, p=0.84
DR with hypertension	72.2%	

Discussion

In this hospital-based observational study of 200 patients with diabetes mellitus attending a tertiary care teaching hospital in South India, poorer glycaemic control was strongly associated with both the presence and the severity of diabetic retinopathy. The central finding was a clear dose-response relationship: mean HbA1c increased in a stepwise fashion across the recognised clinical stages of DR, from 7.35% in patients with no retinopathy to 10.29% in those with proliferative disease (F=35.08, p<0.001). In parallel, the prevalence of DR climbed steeply across categories of glycaemic control, from less than a quarter of patients with good control to almost all patients with poor control (chi-square=41.04, p<0.001). Together, these results provide internally consistent evidence that the burden and severity of retinopathy track closely with cumulative glycaemic exposure as captured by HbA1c.

The graded association observed here is biologically coherent and consistent with the established pathophysiology of DR, in which chronic hyperglycaemia drives the microvascular injury that underlies progressive retinopathy. The relationship between metabolic control and DR has been reviewed extensively, and the literature supports the view that better glycaemic control is associated with a lower risk and slower progression of retinopathy [3]. Our finding that the highest mean HbA1c values were observed in patients with the most advanced retinopathy reinforces the concept that glycaemic control is not merely a determinant of whether DR develops but also of how far it advances. The very high DR prevalence of 96.4% among patients with HbA1c above 9% underscores the clinical importance of avoiding sustained poor control.

The overall prevalence of DR in our cohort was 71.0%, which is higher than the prevalence typically reported in community-

based Indian studies. This is to be expected in a tertiary care hospital setting, where patients are likely to have longer-standing or more poorly controlled diabetes and where referral patterns enrich the sample for complications. Indian epidemiological work, including the Chennai Urban Rural Epidemiology Study (CURES) and the Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetics Study (SN-DREAMS), has documented the prevalence and risk factors of DR in southern India and has consistently identified longer duration of diabetes and poorer glycaemic control as key correlates of retinopathy [7]. Our results are concordant with this body of evidence in direction and emphasis, while the higher absolute prevalence reflects the hospital-based nature of the present sample.

Duration of diabetes was the second major correlate identified in our study. Patients with DR had been diabetic for substantially longer than those without (16.5 vs 7.5 years; $t=9.00$, $p<0.001$), in keeping with the cumulative nature of microvascular damage and with prior observations that the duration and age of onset of diabetes are important determinants of retinopathy [8]. We also observed a modest positive correlation between HbA1c and duration of diabetes ($r=0.386$, $p<0.001$), suggesting that longer disease duration and poorer control may, to some degree, co-occur and jointly contribute to the retinopathy burden. The modest magnitude of this correlation also indicates that HbA1c and duration capture partly distinct dimensions of risk, each contributing independently to the likelihood of retinopathy [9].

Notably, the prevalence of DR did not differ significantly by hypertension status in this sample (69.9% without versus 72.2% with hypertension; $p=0.84$). Although hypertension is a recognised systemic risk factor for DR in many studies, the absence of a significant association here may reflect the overwhelming influence of glycaemic control and disease duration in this particular hospital population, the cross-sectional design, or limited statistical power to detect a more modest effect against the high background prevalence of retinopathy. This observation should therefore be interpreted with caution rather than as evidence that blood pressure is unimportant in DR. The broader Indian literature has highlighted that several systemic factors beyond glycaemia, including anaemia, may be associated with retinopathy in type 2 diabetes [4], and the role of such covariates was not the focus of the present analysis[10.11].

The clinical implications of these findings are straightforward and actionable. The strong, graded association between HbA1c and DR severity reinforces the value of tight glycaemic control as a means of reducing both the incidence and the progression of retinopathy, and supports the use of individualised glycaemic targets in routine diabetes care. Equally, the high prevalence of DR even among patients with fair control, and the very high prevalence among those with poor control, argue for systematic, regular retinal screening of all patients with diabetes, with particular vigilance in those with elevated HbA1c and longer disease duration. Integrating HbA1c assessment with structured fundus screening offers a practical pathway to identify high-risk patients and to intervene before sight-threatening complications develop. These priorities are consistent with the longstanding recognition of DR as a leading, yet largely preventable, cause of blindness in the Indian context [12].

Limitations

Several limitations should be acknowledged. First, the cross-sectional, observational design precludes any inference regarding causation or temporality; although the associations observed are strong and graded, they cannot establish that poor glycaemic control caused the retinopathy. Second, the study was conducted at a single tertiary care centre, which limits generalisability and likely inflates the

absolute prevalence of DR relative to community settings owing to referral bias. Third, no adjustment was made for lipid profile or other potential covariates, so residual confounding cannot be excluded. Fourth, glycaemic control was assessed using a single HbA1c measurement, which captures only recent glycaemia and may not reflect long-term control over the entire duration of diabetes. These limitations should be considered when interpreting and applying the findings.

Conclusion

In this hospital-based observational study from South India, poorer glycaemic control, as reflected by higher HbA1c, was strongly associated with both the presence and the severity of diabetic retinopathy, with a clear dose-response gradient across severity grades and across categories of glycaemic control. Longer duration of diabetes was also associated with retinopathy, whereas hypertension was not significantly associated in this sample. These findings support the importance of tight glycaemic control and regular, structured retinal screening for the prevention and timely management of diabetic retinopathy.

References

1. Rema M, Pradeepa R. Diabetic retinopathy: an Indian perspective. Indian J Med Res. 2007;125(3):297-310. PMID: 17496357.
2. Raman R, Vaitheeswaran K, Vinita K, Sharma T. Is prevalence of retinopathy related to the age of onset of diabetes? Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetic Report No. 5. Ophthalmic Res. 2010;45(1):36-41. doi: 10.1159/000314720
3. Rodriguez-Fontal M, Kerrison JB, Alfaro DV, Jablon EP. Metabolic control and diabetic retinopathy. Curr Diabetes Rev. 2009;5(1):3-7. doi: 10.2174/157339909787314176
4. Ranil PK, Raman R, Rachepalli SR, Pal SS, Kulothungan V, Lakshmipathy P, et al. Anemia and diabetic retinopathy in type 2 diabetes mellitus. J Assoc Physicians India. 2010;58:91-4. PMID: 20653149.
5. Patel A, MacMahon S, Chalmers J, et al.; ADVANCE Collaborative Group. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. N Engl J Med. 2008;358(24):2560-2572.
6. Mohamed Q, Gillies MC, Wong TY. Management of diabetic retinopathy: a systematic review. JAMA. 2007;298(8):902-916.
7. Klein BEK, Myers CE, Howard KP, Klein R. Serum glucose and hemoglobin A1c in relation to retinal disease and retinopathy. Arch Ophthalmol. 2010;128(5):645-651.
8. Raman R, Rani PK, Reddi Rachepalle S, et al. Prevalence of diabetic retinopathy in India: Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetics Study (SN-DREAMS). Ophthalmology. 2009;116(2):311-318.
9. Wong TY, Klein R, Islam FMA, Cotch MF, Folsom AR, Klein BEK, et al. Diabetic retinopathy in a multi-ethnic cohort in the United States. Am J Ophthalmol. 2006;141(3):446-455.
10. Cheung N, Mitchell P, Wong TY. Diabetic retinopathy. Lancet. 2010;376(9735):124-136.
11. Yau JWY, Rogers SL, Kawasaki R, et al. Global prevalence and major risk factors of diabetic retinopathy. Diabetes Care. 2012;35(3):556-564.
12. Stratton IM, Adler AI, Neil HAW, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. BMJ. 2000;321(7258):405-412.