ORIGINAL ARTICLE

Association of HBA1C Value With The Severity of Diabetic Retinopathy in Type 2 Diabetic Patients

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Abstract:

Objective: To determine association between $HbA_{1}c$ levels and severity of diabetic retinopathy (DR) in type 2 diabetes mellitus (DM) of a tertiary care setting.

Methods: A cross-sectional study was commenced in type II diabetes patients of a tertiary eye hospital using non-probability sequential sampling technique. The degree of DR was assessed by thorough ocular examinations and classified as mild, moderate, severe non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR). We assessed $HbA_{1}c$ levels and examined the relationship between $HbA_{1}c$ levels and DR severity using statistical package for social sciences (SPSS) version 19.

Results: A total 253 patients were involved in the study. Most of the subjects (61.3%) were men. Average age was 49.7 ± 7.3 years. According to DR classification, 35.6% had Mild NPDR, 56.9% had moderate NPDR, 5.5% had severe NPDR and 2% had PDR. Significant association was found between $HbA_{1}c$ levels and DR severity ($p < 0.001$).

Conclusion: Our study showed significant association between DR severity and higher $HbA_{1}c$ levels. Early screening and timely management can minimize the threat of DR. *Al-Shifa Journal of Ophthalmology 2025; 21(3): 208-214. © Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan.*

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Introduction:

Diabetes is a major global health issue. About 463 million people worldwide currently have diabetes and it is predicted to increase about 700 million by 2045. Of these, one-third may have some kind of retinopathy.[1,2] DR is one of the most prevalent microvascular complications which is associated with diabetes mellitus and leading cause of vision loss among people of working age worldwide. Depending on the population under study, the incidence of DR might vary significantly; higher rates are seen in those with a longer history of diabetes and poor glycemic management. [1,2]

The processes of DR are primarily connected to chronic hyperglycemia, which begins a sequence of biochemical and structural abnormalities in the retinal microvasculature. Hyperglycemia produces oxidative stress and inflammation combined with endothelium dysfunction leading to the basement membrane thickness, loss of pericytes, and increased

vascular permeability.[1] All of these changes progress in various stages of DR, in which there is neovascularization and the presence of increased risk of complications such as vitreous hemorrhage and retinal detachment. [1]

Glycated hemoglobin (HbA1c) is a measure of long-term glycemic management, suggesting an average blood glucose level over the preceding 2–3 months. Many studies have shown strong association between levels of HbA1c and the severity of DR.[7, 8] The United Kingdom Prospective Diabetes Study (UKPDS) showed that patients with type 2 diabetes who maintain strict glycemic control have a significantly lower risk of developing diabetic retinopathy (DR). In particular, a 31% reduction in the risk of retinopathy was linked to a 1% decline in HbA1c levels.[1] Nonetheless, glycemic control deficiencies remain widespread in underdeveloped countries, contributing to the growing prevalence of DM and associated aftereffects.[2]

The length of diabetes, dyslipidemia, and hypertension are additional risk factors. Even yet, hyperglycemia continues to be a hallmark of the onset and course of DR.[2] Therefore, glycemic control remains the cornerstone of prevention and treatment of DR. Detection of DR at its earliest stage with regular screening and early intervention is a strategy of reducing visual loss.

Thus, the aim of the study is to see relationship between HbA1c concentration levels and the degree of DR severity among patients with Type II DM, with a focus on our local community. This research aims to determine if proper glycemic treatment may slow down the DR, given the high prevalence of diabetes in the country and our hospital's central location as one of the best eye care facilities with a great patient flow.

Methodology:

The LRBT Tertiary Teaching Eye Hospital in Karachi served as the site of this prospective cross-sectional study from Mar 2023-Sep 2023. Sample size was calculated by using OpenEpi calculator. Keeping 95% confidence level and 5% desired precision. All eligible patients who met the inclusion criteria and visited the retina clinic throughout the study period were invited to participate using a non-probability sequential sampling technique.

The LRBT Eye Hospital Ethics Committee, LRBT/TTEH/ERC/4503/11, approved this research with the Declaration of Helsinki's ethical guidelines. Patients who had been diagnosed with Type 2 diabetes for five to ten years and for whom HbA1c testing had been recommended as a standard measure to assess long-term glycemic control were included in the study. Individuals having recent intraocular surgery, other retinal conditions, or inadequate medical data were excluded. Slit-lamp biomicroscopy, indirect ophthalmoscopy, fundoscopy, and best-corrected visual acuity were used in thorough ophthalmologic evaluations. The early treatment diabetic retinopathy study (ETDRS) severity scale was used to classify the degree of retinopathy into four categories: mild, moderate, severe, and PDR. Without being aware of the HbA1c readings, two skilled ophthalmologists separately inspected the fundus. If they disagreed, they came to an agreement.

Age, gender, years of illness, and family history were among the demographic and clinical data collected using structured questionnaires and patient files. Excellent-Performance Liquid Chromatography (HPLC), the gold standard technique for glycated hemoglobin testing because of its excellent accuracy and repeatability, was used to analyze biochemical profiles, including HbA1c. This technique offers accurate measurement of long-term glycemic control throughout the two to three months beforehand.

The Global Physical Activity Questionnaire (GPAQ), developed by the World Health Organization (WHO), was

used to grade lifestyle data about physical activity levels into sedentary, mild, moderate, and vigorous categories.[1] Physical activity categories were assigned to the following using Metabolic Equivalent of Task (MET) values:

- Sedentary activity: Less than 1.5 METs
- Light activity: 1.5–3.0 METs
- Moderate activity: 3.0–6.0 METs
- Vigorous activity: Greater than 6.0 METs

The statistical software SPSS version 19.0 was used for all analyses. Continuous data were presented as mean ± standard deviation (SD). Whereas categorical variables were presented as frequencies and percentages. The correlation between HbA1c levels and DR severity along with relationships between family history of diabetes and DR severity, were evaluated using chi-square testing. A p-value <0.05 was considered statistically significant.

Results:

The investigation comprised 253 individuals with Type 2 diabetes, with a female-to-male ratio of 38.7% to 61.3%. Mean age was 49.66 ± 7.27 years (Range: 37-69 years). 52.6% of the patients did not have a family history of diabetes, while 47.4% of the patients did. HbA1c was 7.57 ± 1.15% on average.

The distribution of diabetic retinopathy severity among participants is shown in Table 1. Most patients were classified with moderate nonproliferative diabetic retinopathy (mod) 56.9%, (n = 144), followed by mild NPDR (mild) 35.6%, (n = 90). Cases of severe NPDR and PDR were observed in 5.5% (n = 14) and 2.0% (n = 5) respectively.

Table 1. The distribution of diabetic retinopathy severity among participants

Severity Level	Percentage	Number of Participants
Mild NPDR	35.60%	90
Moderate NPDR	56.90%	144
Severe NPDR	5.50%	14
PDR	2.00%	5

Higher HbA1c levels are linked to more severe retinopathy. A Chi-square test was used and significant association was found between HbA1c levels and retinal severity ($p < 0.001$). Significant differences were found in HbA1c levels across the four severity groups, ($p < 0.001$). PDR had significantly higher HbA1c levels than people with mild or moderate NPDR as shown in Table 2.

Table 2. Relationship between HbA1c Levels and Severity of Diabetic Retinopathy

HBA1C	Mild (n)	Moderate (n)	Severe (n)	PDR (n)	Total (n)	Chi-square	Df	p-value
5	3	5	0	0	8	42.3	6	0.001
6	16	15	0	0	31			
7	29	65	0	0	94			
8	30	38	2	0	70			
9	14	18	2	5	39			
10	2	3	2	4	11			
Total	94	144	6	9	253			

The Chi-square test of independence was used for analysis of lifestyle factors which reveal an insignificant association with diabetic retinopathy severity. Sedentary,

mild, moderate, and vigorous levels of physical activity did not significantly correlate with the severity of retinopathy (p = 0.900), as shown in Table 3.

Table 3. Association between Lifestyle Factors and Diabetic Retinopathy

Severity of Retinopathy	Light activity (n)	Moderate activity (n)	Sedentary (n)	Vigorous (n)	Total (n)	Chi-square	Df	P-value
Mild	36	6	44	5	91	1.234	18	0.900
Moderate	57	9	66	10	142			
Severe	8	0	7	0	15			
PDR	3	0	2	0	5			
Total	104	15	119	15	253			

The relationship between the severity of retinopathy and family history of diabetes was also determined using chi-square and no significant association was found (p = 0.467) as seen in table 4.

Table 4. Association between Family History and Diabetic Retinopathy

Severity of Retinopathy	Family History: No (n)	Family History: Yes (n)	Total (n)	Chi-Square	Df	p-value
Mild	47	45	92	2.541	8	0.467
Moderate	79	66	145			
Severe	11	11	22			
PDR	1	3	4			
Total	138	126	253			

Discussion:

DR is a major cause of blindness and visual impairment worldwide, particularly in those with inadequate glycemic control.[3] According to our research, increasing the level of HbA1c will be the risk of developing proliferative diabetic retinopathy (PDR) and other severe forms of DR. This emphasizes how important long-term hyperglycemia is for retinal damage.

Findings of our study are similar to the study of Wang et al., who discovered in a large population-based investigation that a higher HbA1c was a major predictor of DR development.[3] Stratton et al. explained that any increase of 1% in the level of HbA1c higher the threat of microvascular complications including diabetic retinopathy.[1] This shows that long-term glycemic control is key to reducing DR risk. Our one-way ANOVA showed a significant difference in mean HbA1c across retinopathy severity. Patients with PDR had the highest mean HbA1c, as found by Jamshed et al. who showed that patients with severe DR have poorer glycemic control compared to those with milder forms of the disease.[4]

In our study, at an HbA1c level of 5, only mild and moderate DR were observed, with 3 cases classified as mild and 4 as moderate, and no severe or proliferative cases. As HbA1c increased to 6, there were 16 and 15 cases of mild and moderate NPDR respectively, no proliferative diabetic retinopathy noted up to HbA1c levels of 8%. Increased numbers of proliferative diabetic retinopathy were seen with high HbA1c level.

According to a research by Alabdul wahhab et al., individuals with uncontrolled diabetes who had elevated HbA1c levels were 66.61% more likely to develop diabetic retinopathy.[2]

A thorough examination of our results indicates that the occurrence of eye problems is significantly impacted by elevated HbA1c levels. Additionally, the data show how severe the disease is in connection to additional elevations in HbA1c levels. According to a cross-sectional research, people with a HbA1c of > 7% are 17.5 times more likely to acquire DR than those with adequate control.[1] Within Pakistan, studies report DR prevalence ranging from 9.0% to 43.0% in Type 2 diabetics, with significantly higher mean HbA_1c values observed in affected patients compared to those without retinopathy.[6]

Furthermore, it was found in another research that risk of diabetic retinopathy is 1.9 times higher in patients with HbA1C ≥ 7% compared to patients with HbA1C < 7%.[1] This further establishes the requirement of proper monitoring of the levels of sugar among patients, especially those who have had uncontrolled diabetes. If the patient's blood sugar levels are consistently high, the retinal tissues may sustain more damage.

Physical activity and family history of diabetes was not associated with DR severity in our study but lifestyle modifications are still important in diabetes management. Previous studies have shown that regular physical activity and dietary interventions can improve glycemic control and potentially reduce DR progression but these were not assessed in the context of DR severity in our study.[7, 8] However, our study did not show significant relationship between family history of diabetes and DR but some studies have shown that genetic predisposition may affect DR through its effect on glycemic control and other metabolic parameters.[1] Further studies are needed to clarify this.

These similarities between our cohort's mean HbA_1c readings and global standards suggest that they are indicative of larger patterns. We suggest a tiered, HbA_1c-driven screening protocol in our area to put these insights into practice: biannual screenings for patients with $HbA_1c \geq 8.5\%$ due to their significantly elevated risk of severe DR, community-based HbA_1c monitoring with referral pathways to ophthalmology for high-risk individuals, and annual fundus examinations for patients with $HbA_1c \geq 7\%$ to detect early NPDR. By concentrating on individuals who are most likely to develop to vision-threatening phases, such focused screening might maximize scarce resources in underdeveloped settings.

The cross-sectional study ddesign makes it difficult to draw conclusions about causation, and it uses self-reported information on lifestyle variables, which might be skewed. To validate our results and assess the effect of short-term glycemic management strategies on DR-expressed outcomes, longitudinal research is necessary.

Conclusion:

Our findings underscore the significance of routine HbA1c monitoring to identify patients at risk for DR. The American Diabetes Association recommends a HbA1c below 7% to prevent or delay DR.[7] Regular ophthalmologic screening is crucial for early detection, especially in

patients with persistently elevated HbA1c levels, as timely interventions like intravitreal injections or laser therapy can prevent vision loss.[7]

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