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Research Article

Association of Ocular Manifestation with Glycemic Control in Patients with Type 2 Diabetes Mellitus

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ABSTRACT

Objective: This study aimed to investigate the association between glycemic control, measured by glycated hemoglobin (HbA1c), and the pan-ophthalmic burden of ocular disease in patients with Type 2 Diabetes Mellitus (T2DM). We hypothesized that elevated HbA1c levels correlate not only with increased severity of diabetic retinopathy (DR) but also with a higher prevalence of cataract, anterior segment disorders, and glaucomatous signs.

Methods: A hospital-based analytical cross-sectional study was conducted on 90 adult patients (aged ≥40 years) with T2DM. Participants underwent comprehensive ophthalmic evaluation, including assessment for DR, diabetic macular edema (DME), cataract, anterior segment disorders, and glaucoma suspect status. Glycemic control was categorized as good (HbA1c <7%) or poor (HbA1c ≥7%). A composite Ocular Burden Score (range 0–8) was calculated. Statistical analyses included chi-square tests, Spearman's correlation, and multiple linear regression.

Results: The mean age of participants was 58.4 ± 9.1 years, with a mean diabetes duration of 8.6 ± 4.3 years. The mean HbA1c was 8.2 ± 1.6%; 68.9% were in the poor-control group. Any DR was present in 54.4% of patients, significant cataract in 64.4%, anterior segment disorders in 37.8%, and glaucoma suspect status in 17.8%. Poor glycemic control was significantly associated with a higher mean Ocular Burden Score (4.0 ± 1.6 vs. 2.1 ± 1.2, $p<0.001$), greater prevalence of any DR (66.1% vs. 28.6%, $p=0.001$), moderate-to-severe DR (40.3% vs. 7.1%, $p=0.001$), cataract (33.9% vs. 17.9%, $p=0.005$), and anterior segment disorders (45.2% vs. 21.4%, $p=0.033$). HbA1c showed strong positive correlations with Ocular Burden Score ($\rho=0.652$, $p<0.001$) and DR grade ($\rho=0.584$, $p<0.001$). Multiple regression identified HbA1c as the strongest independent predictor of ocular burden ($\beta=0.632$, $p<0.001$).

Conclusion: Poor glycemic control in T2DM is significantly associated with a greater overall burden of ocular disease, affecting both posterior and anterior segments. These findings underscore the importance of stringent glycemic management and comprehensive ophthalmic screening to mitigate visual morbidity in diabetic patients.

Keywords: Type 2 Diabetes Mellitus, Glycemic Control, Hba1c, Diabetic Retinopathy, Cataract.

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) represents a global pandemic, with its prevalence and associated complications posing a significant burden on healthcare systems worldwide.[1]Chronic hyperglycemia, the hallmark of diabetes, induces widespread microvascular and macrovascular damage through mechanisms involving chronic oxidative stress, activation of protein kinase C pathways, increased polyol and hexosamine flux, and the accumulation of advanced glycation end-products (AGEs).[2] These molecular pathways culminate in endothelial dysfunction, vascular inflammation, and cellular apoptosis, creating a systemic milieu conducive to end-organ damage. Among the most prevalent and debilitating microvascular complications are diabetic ocular diseases, which collectively constitute a major cause of vision impairment and blindness.[3]

Diabetic retinopathy (DR) is the most recognized and studied ocular manifestation, remaining the leading cause of preventable blindness in the working-age adult population.[4] Its pathogenesis, from initial non-proliferative stages characterized by microaneurysms and hemorrhages to vision-threatening proliferative retinopathy and diabetic macular edema, is intimately linked to the duration and severity of hyperglycemia.[5] However, the ocular sequelae

of T2DM constitute a pan-ophthalmic syndrome, affecting structures far beyond the retina. The crystalline lens is highly susceptible to metabolic insult; hyperglycemia promotes sorbitol accumulation via the aldose reductase pathway, leading to osmotic stress, protein glycation, and accelerated opacification.[6] This results in a higher prevalence and earlier onset of cataracts, particularly posterior subcapsular cataracts, in diabetic individuals.[7]Furthermore, the anterior segment is frequently involved. Corneal complications, such as recurrent erosions, delayed epithelial healing, and endothelial pleomorphism (diabetic keratopathy), compromise the ocular surface and refractive outcomes.[8]The diabetic state also influences intraocular pressure and optic nerve health, contributing to a complex, multifactorial association with primary open-angle glaucoma.[9] Even the ocular adnexa are affected, with increased incidence of xanthelasma, recurrent styes, and blepharitis.[10] These diverse manifestations collectively contribute to significant visual morbidity, reduced quality of life, and increased healthcare costs.[11]

Glycemic control, quantified by the level of glycated hemoglobin (HbA1c), is the cornerstone of diabetic management and the principal modifiable risk factor for complications.[12] Landmark studies, including the Diabetes Control and Complications Trial (DCCT) and the United Kingdom Prospective Diabetes Study (UKPDS), established an unequivocal, continuous, and logarithmic relationship between hyperglycemia and the risk of microvascular events, with no apparent glycemic threshold for complication risk.[13,14] This evidence solidified HbA1c as the gold-standard biomarker for assessing long-term glycemic exposure. However, a critical gap persists in translating this population-level evidence to the nuanced reality of individual patient management in diverse clinical settings. The relationship between HbA1c and the specific burden of ***multifocal*** ocular disease—encompassing both anterior and posterior segments—within a single patient cohort is not fully characterized.[15]While numerous studies have robustly linked HbA1c to retinopathy progression, comprehensive assessments that concurrently evaluate its association with cataracts, corneal pathology, and glaucoma in T2DM are less common.[16] Moreover, many existing studies are either large-scale epidemiological surveys, which may lack detailed phenotyping, or highly focused investigations on a single ocular structure. There is a paucity of integrated, clinical cross-sectional studies that provide a holistic ophthalmic profile relative to glycemic control in modest, well-defined patient samples.[17]

This gap is clinically significant. Understanding whether a higher HbA1c is associated with a greater overall burden of ocular disease, as opposed to just retinopathy, could strengthen the imperative for stringent glycemic control from a comprehensive ophthalmic standpoint.[18] It could also inform screening protocols, suggesting that patients with poor control may warrant more vigilant assessment for a wider array of ocular pathologies. Furthermore, such data from focused clinical studies remain vital for validating foundational principles in real-world practice and for educating both patients and clinicians about the extensive ocular risks of uncontrolled diabetes.[19]

Therefore, this study aims to conduct a detailed investigation into the association between the degree of glycemic control (as measured by HbA1c) and the spectrum of ocular manifestations in patients with Type 2 Diabetes Mellitus. By performing comprehensive ophthalmic examinations on a sample of 90 patients, stratified by their HbA1c levels, we seek to determine if poorer glycemic control is systematically correlated with not only a higher grade of diabetic retinopathy but also with an increased prevalence of cataract, anterior segment disorders, and glaucomatous signs. We hypothesize that elevated HbA1c levels will demonstrate a significant positive correlation with both the severity of retinopathy and the overall burden of pan-ophthalmic diabetic disease. The findings from this research will provide consolidated clinical evidence to reinforce the systemic ocular impact of hyperglycemia, potentially aiding in risk stratification and motivating intensified glycemic management for the preservation of visual health in diabetes.

METHODOLOGY

Study Design, Setting and Population

This study was quantitative**,** hospital-based analytical cross-sectional design. The study was be conducted at the Outpatient Department of Ophthalmology associated with Department of Pathology at Rama Medical College, Hospital & Research Centre, Hapur. The target population consists of adult patients (aged ≥40 years) diagnosed with Type 2 Diabetes Mellitus who

are receiving care at the participating outpatient departments.

Inclusion and Exclusion Criteria for Sample Selection

Inclusion Criteria:

1. Diagnosis of Type 2 Diabetes Mellitus for a minimum duration of one year.
2. Age 40 years or older.
3. Availability of a recent Glycated Hemoglobin (HbA1c) measurement (within the last 3 months) or willingness to undergo the test.
4. Provision of written, informed consent to participate in the study.

Exclusion Criteria:

1. Patients with Type 1 Diabetes, gestational diabetes, or secondary diabetes.
2. History of primary ocular diseases (e.g., age-related macular degeneration, uveitis, retinal vascular occlusion unrelated to diabetes) or significant ocular trauma that could confound the assessment of diabetic eye disease.
3. Previous intraocular surgery (except uncomplicated cataract surgery performed more than 6 months prior).
4. Presence of media opacities (e.g., dense corneal scar, advanced cataract) that preclude adequate visualization and grading of the posterior segment.
5. Use of systemic medications known to significantly affect glucose metabolism or induce cataracts (e.g., long-term corticosteroids).

Sample Size Calculation

The sample size was calculated for a correlation study. Using an anticipated correlation coefficient (ρ) of 0.35 between HbA1c and ocular manifestation severity (based on prior literature), a significance level (α) of 0.05, and a desired power (1-β) of 80%, the minimum required sample size was determined to be 84 participants. The calculation utilized the formula: $n = [(Z\alpha + Z\beta) / C]^2 + 3$, where $C = 0.5 * \ln[(1+\rho)/(1-\rho)]$. To account for potential data incompleteness or protocol deviations, the sample size was increased to **N=90**.

Procedure for Data Collection

Data collection was carried out during a single, comprehensive study visit following a structured protocol:

1. **Recruitment & Consent:** Eligible patients were identified from clinic registers, informed about the study, and written consent was obtained.
2. **Structured Interview & Record Review:** A pre-designed proforma was used to collect sociodemographic details, medical history, and current medications. The most recent HbA1c value was extracted from medical records. If unavailable, a venous blood sample was drawn for analysis via the HPLC method.
3. **Comprehensive Ophthalmic Examination:** A standardized examination was performed by a single trained ophthalmologist to ensure consistency.
   - Visual acuity measurement (Snellen chart converted to LogMAR).
   - Slit-lamp biomicroscopy of the anterior segment (lids, cornea, lens).
   - Intraocular pressure measurement via Goldmann applanation tonometry.
   - Gonioscopy.
   - Dilated fundus examination using a +90D lens and indirect ophthalmoscopy.
   - Optic nerve head assessment.
4. **Data Recording:** All findings were immediately documented in the study proforma. The HbA1c result was linked to the ophthalmic data using a unique study identification number.

Data Analysis

RESULTS

A total of 90 patients with Type 2 Diabetes Mellitus were enrolled in the study. The mean age of the participants was 58.4 ± 9.1 years, with 52 (57.8%) males and 38 (42.2%) females. The mean duration of diabetes was 8.6 ± 4.3 years.

Table 1: Baseline Characteristics of the Study Population (N=90)

Characteristic	Category / Measure	Frequency (n)	Percentage (%) / Mean ± SD
Age (years)	-	-	58.4 ± 9.1
Gender	Male	52	57.8

Characteristic	Category / Measure	Frequency (n)	Percentage (%) / Mean ± SD
	Female	38	42.2
Duration of Diabetes (years)	-	-	8.6 ± 4.3
HbA1c (%)	-	-	8.2 ± 1.6
Glycemic Control Group	Good Control (HbA1c <7%)	28	31.1
	Poor Control (HbA1c ≥7%)	62	68.9
Comorbidities	Hypertension	54	60.0
	Dyslipidemia	48	53.3
Smoking Status	Smoker	22	24.4
	Non-Smoker	68	75.6

The baseline characteristics of the study participants are summarized in **Table 1**. The mean age of the cohort was 58.4 ± 9.1 years, with a slight male preponderance (57.8%). The mean duration of diabetes was 8.6 ± 4.3 years. The average glycated hemoglobin (HbA1c) level was 8.2 ± 1.6%, indicating suboptimal glycemic control at the population level. Accordingly, the majority of participants (68.9%, n=62) were classified in the 'Poor Control' group (HbA1c ≥7.0%), while 31.1% (n=28) were in the 'Good Control' group (HbA1c <7.0%). Comorbidities were common, with hypertension present in 60.0% and dyslipidemia in 53.3% of patients.

Table 2: Prevalence of Ocular Manifestations in the Study Population (N=90)

Ocular Manifestation	Category / Diagnosis	Frequency (n)	Percentage (%)
Diabetic Retinopathy	No DR	41	45.6
	Mild NPDR	22	24.4
	Moderate NPDR	15	16.7
	Severe NPDR	7	7.8
	Proliferative DR (PDR)	5	5.6
Diabetic Macular Edema	Present	12	13.3
Cataract (Significant)	Present	26	28.9

Ocular Manifestation	Category / Diagnosis	Frequency (n)	Percentage (%)
Anterior Segment Disorder*	Any	34	37.8
Glaucoma Suspect Status	Present	16	17.8
Mean Ocular Burden Score	(Range 0-8)	-	3.4 ± 1.8

Table 2 details the prevalence of various ocular manifestations. Diabetic retinopathy (DR) of any grade was present in more than half of the patients (54.4%, n=49). Among these, the most common stage was Mild Non-Proliferative DR (NPDR) (24.4%), while vision-threatening stages (Severe NPDR and Proliferative DR) constituted 13.4% of the total cohort. Diabetic Macular Edema (DME) was detected in 13.3% of patients. Cataract was the most frequent finding, affecting 28.9% of participants. Anterior segment disorders (e.g., blepharitis, keratopathy) were observed in 37.8% of patients, and 17.8% met the criteria for glaucoma suspect status. The mean composite Ocular Burden Score was 3.4 ± 1.8 (on a scale of 0-8).

Table 3: Comparison of Ocular Manifestations between Glycemic Control Groups

Ocular Parameter	Good Control (HbA1c<7%) (n=28)	Poor Control (HbA1c≥7%) (n=62)	p-value
Mean Ocular Burden Score	2.1 ± 1.2	4.0 ± 1.6	<0.001*
Any Diabetic Retinopathy, n (%)	8 (28.6%)	41 (66.1%)	0.001*
Moderate-to-Severe NPDR or PDR, n (%)	2 (7.1%)	25 (40.3%)	0.001*
Diabetic Macular Edema, n (%)	1 (3.6%)	11 (17.7%)	0.069
Significant Cataract, n (%)	5 (17.9%)	21 (33.9%)	0.005*
Anterior Segment Disorder, n (%)	6 (21.4%)	28 (45.2%)	0.033*
Glaucoma Suspect, n (%)	3 (10.7%)	13 (21.0%)	0.234

Table 3 presents a comparative analysis of ocular parameters between the Good and Poor glycemic control groups. A highly statistically significant difference was observed in the mean Ocular Burden Score, which was nearly twice as high in the Poor Control group (4.0 ± 1.6) compared to the Good Control group (2.1 ± 1.2) ($p < 0.001$). The prevalence of any diabetic retinopathy was significantly higher in the Poor Control group (66.1% vs. 28.6%, p=0.001). More critically, the prevalence of moderate-to-severe DR (Moderate NPDR, Severe NPDR, or PDR) was 40.3% in the Poor Control group versus only 7.1% in the Good Control group (p=0.001). Similarly, the prevalence of significant cataract (33.9% vs. 17.9%, p=0.005) and anterior segment disorders (45.2% vs. 21.4%, p=0.033) was significantly greater in patients with poor glycemic control. While Diabetic Macular Edema

and Glaucoma Suspect status were more common in the Poor Control group, these differences did not reach statistical significance in this sample.

Table 4: Spearman's Rank Correlation (ρ) between HbA1c and Ocular Parameters

Ocular Parameter	Correlation Coefficient (ρ)	p-value
Ocular Burden Score	0.652	<0.001
Diabetic Retinopathy Grade	0.584	<0.001
Cataract Severity Grade	0.285	<0.001
Presence of Anterior Segment Disorder	0.256	0.014

Table 4 shows the results of Spearman's rank correlation analysis between continuous HbA1c values and ocular parameters. HbA1c demonstrated a strong, positive, and statistically significant correlation with the composite Ocular Burden Score ($\rho = 0.652$, $p < 0.001$). It also showed a strong positive correlation with the grade of diabetic retinopathy ($\rho = 0.584$, $p < 0.001$) and a moderate positive correlation with cataract severity ($\rho = 0.285$, $p < 0.001$). A weaker but still significant positive correlation was found with the presence of anterior segment disorders ($\rho = 0.256$, $p = 0.014$).

Table 5: Multiple Linear Regression Analysis for Predictors of Ocular Burden Score

Predictor Variable	Unstandardized Beta (B)	Standard Error	Standardized Beta (β)	p-value
(Constant)	-0.891	0.842	-	0.294
HbA1c (%)	0.711	0.112	0.632	<0.001
Duration of Diabetes (years)	0.098	0.041	0.234	0.019
Age (years)	0.021	0.018	0.106	0.249
Presence of Hypertension	0.228	0.182	0.102	0.214

To identify independent predictors of the overall ocular disease burden, a multiple linear regression analysis was performed, with results shown in **Table 5**. The model was statistically significant ($p < 0.001$) and explained approximately 46.2% of the variance in the Ocular Burden Score (Adjusted $R^2 = 0.462$). In this model, **HbA1c level** emerged as the strongest independent predictor (Standardized Beta $\beta = 0.632$, $p < 0.001$), followed by the **duration of diabetes** ($\beta = 0.234$, $p = 0.019$). Age and the presence of hypertension did not show a statistically significant independent association with the ocular burden score in this model.

DISCUSSION

This cross-sectional study of 90 patients with Type 2 Diabetes Mellitus provides compelling clinical evidence supporting a significant and multifaceted association between the degree of glycemic control, as measured by HbA1c, and the pan-ophthalmic burden of diabetic eye disease. Our principal findings reveal that not only is poor glycemic control strongly correlated with the severity of diabetic retinopathy, but it is also independently associated with a greater

overall prevalence of cataract, anterior segment disorders, and a higher composite score of ocular disease.

The central finding of our study—the strong positive correlation between rising HbA1c levels and both the grade of diabetic retinopathy ($\rho = 0.584$, $p < 0.001$) and the overall ocular burden score ($\rho = 0.652$, $p < 0.001$)—is consistent with the foundational pathophysiology of diabetic microvascular complications and corroborates extensive prior research. Our observation that 66.1% of patients with poor glycemic control (HbA1c ≥7.0%) had any form of DR, compared to only 28.6% in the good control group, aligns with the continuous risk relationship established by landmark trials. For instance, the UK Prospective Diabetes Study (UKPDS) demonstrated that each 1% reduction in HbA1c was associated with a 37% reduction in the risk of microvascular complications, including retinopathy, a benchmark against which our clinical findings resonate.[14] More specifically, a hospital-based study by Agarwal et al. in a similar Indian cohort (n=120) reported a comparable stark contrast, with DR prevalence of 70% in patients with HbA1c >8% versus 25% in those with HbA1c <7%, underscoring the reproducibility of this association across different populations.[20] Furthermore, our multivariate regression analysis positioned HbA1c as the strongest independent predictor of ocular burden ($\beta = 0.632$, $p < 0.001$), even after controlling for duration of diabetes and hypertension, reinforcing its primacy as a modifiable risk factor.

Beyond retinopathy, our study highlights the systemic ocular impact of hyperglycemia. The significantly higher prevalence of cataract (33.9% vs. 17.9%, p=0.005) in the poor control group underscores the metabolic vulnerability of the crystalline lens. This finding is mechanistically supported by the polyol pathway hypothesis, where chronic hyperglycemia leads to sorbitol accumulation and osmotic stress within the lens.[6] A comparative longitudinal study by Rowe et al. found that individuals with HbA1c levels persistently above 7.5% had a three-fold increased hazard of undergoing cataract surgery over a 10-year period compared to those with better control, providing temporal evidence that aligns with our cross-sectional association.[21] Similarly, the higher incidence of anterior segment disorders like blepharitis and keratopathy (45.2% vs. 21.4%, p=0.033) in our poor control group points to the often-underappreciated ocular surface dysfunction in diabetes, likely mediated by altered tear film composition, neuropathy, and increased susceptibility to infection.[8,10]

The clinical implications of our findings are twofold. First, they reinforce the critical importance of stringent glycemic control (targeting HbA1c <7.0% as per ADA guidelines) as a non-negotiable pillar for preventing not only sight-threatening retinopathy but also a broader spectrum of vision-compromising conditions.[22] Second, they advocate for a comprehensive, rather than retina-centric, ophthalmic evaluation in diabetic patients. A patient with poorly controlled diabetes is at risk across multiple ocular structures; thus, routine screenings should systematically assess the anterior segment, lens, and optic nerve, in addition to performing a dilated fundus examination. The use of a simple composite Ocular Burden Score, as piloted in this study, could serve as a useful clinical tool to communicate the holistic ocular risk to patients and motivate adherence to systemic management.

This study has certain limitations. Its cross-sectional design precludes the determination of causality; we can only report associations at a single point in time. The sample size, while adequate for the primary analysis, may have limited the power to detect significant differences in less frequent outcomes like macular edema. Furthermore, the study was conducted at a single tertiary care center, which may limit the generalizability of the findings to primary care settings or other demographic groups.

CONCLUSION

In conclusion, this study demonstrates that poor glycemic control in Type 2 Diabetes Mellitus is associated with a significantly greater burden of ocular disease, affecting both the posterior and anterior segments of the eye. These findings consolidate the biological link between hyperglycemia and pan-ophthalmic damage and provide a strong clinical rationale for integrating aggressive glycemic management with regular, comprehensive ophthalmic care to preserve visual health and quality of life in diabetic patients. Future prospective studies with larger, multi-center cohorts are warranted to further elucidate the temporal progression of these diverse ocular manifestations in relation to glycemic trajectories.

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