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ORIGINAL ARTICLE

Correlation Between Diabetic Retinopathy Severity and HbA1c Levels

MUHAMMAD ABBAS[1], AJMAL KHAN[2], MUJAHID IQBAL[3], MUSHTAQ MUHAMMAD[4]
[1]*Associate Professor Medicine, Medical B Unit, BKMC / MMC Mardan.*
[2]*Senior Medical Officer, Family Physician, Mardan Medical Complex, Mardan*
[3]*Senior Registrar, POF Hospital, Wah Cantt*
[4]*Assistant Professor, Medical Specialist, DHQ Hospital Charsadda / Jinnah Medical College, Peshawar*
Correspondence to: Ajmal Khan, Email: dr.ajmalkhan@ymail.com

ABSTRACT

Background: Diabetic retinopathy is a leading microvascular complication of diabetes, and hyperglycemia over a long period of time is an important modifiable risk factor for its onset and progression. The study aimed to assess the association of HbA1c with the severity of DR.

Material and Methods: A cross-sectional analytical study was carried out with 77 diabetes mellitus (DM) adult patients attending medical outpatient department of Mardan Medical Complex, Mardan from December 2022 to May 2023. All participants had standardized ophthalmic examination and HbA1c testing. Diabetic retinopathy was classified as none or proliferative diabetic disease. The correlation between HbA1C and severity of retinopathy was evaluated using Spearman's correlation.

Results: The mean age was 58.7 ± 9.8 years, and 55.8% were male. Diabetic retinopathy was present in 47 (61.0%) participants. The mean HbA1c was significantly higher in participants with PR (11.1 ± 0.9%) than those without retinopathy (6.9 ± 0.8%). HbA1c showed a strong positive correlation with the severity of retinopathy (ρ=0.69, $p<0.001$). There was also a moderate positive correlation between Diabetes duration and severity (ρ=0.46, $p<0.001$). The prevalence of diabetic macular edema, vitreous hemorrhage, and retinal neovascularization was all significantly associated with higher HbA1c.

Conclusion: There was a strong association between increasing HbA1c concentrations and increasing severity of diabetic retinopathy and advanced ophthalmic complications.

Keywords: Diabetic retinopathy; HbA1c; Glycemic control; Retinopathy severity; Diabetes mellitus

INTRODUCTION

Diabetes mellitus is a significant global health problem[1] It is one of the most prevalent causes of preventable morbidity and is a significant contributor to long-term disability due to microvascular complications[2] Diabetic retinopathy (DR), a progressive neurovascular disorder of the retina, is one of the most significant causes of vision loss and visual impairment among working-age adults and is one of the complications[3]

DR is the result of a complex interaction of chronic hyperglycemia, oxidative stress, inflammation, endothelial dysfunction, capillary occlusion, and disruption of the blood-retinal barrier[4] The clinical course of the disease ranges from mild NPDR (lysis of the retinal blood vessels, usually with just microaneurysms) to moderate and severe NPDR (with more retinal blood vessel damage, including hemorrhages and blood vessel changes) to PDR (where the blood vessels in the back of the retina grow new blood vessels)[5] DME may develop at various times and can cause substantial loss of vision on its own[6] Factors that contribute to the development and progression of DR include the length of time a person has had type 1 or type 2 diabetes as well as the extent of chronic hyperglycemia; hypertension, dyslipidemia, and DKD further increase the risk of developing and progressing DR[7]

Glycated hemoglobin (HbA1c) is a blood test that is a reliable indicator of average glycemic exposure in the last 2–3 months and is commonly used as a measure of control over diabetes[8] Sustained hyperglycemia is indicated by an elevated HbA1c level, which can lead to advanced glycation, oxidative and inflammatory pathways, vascular endothelial damage, and microvascular dysfunction of the retina[9] Current diabetes management guidelines focus on achieving glycemic control to minimize DR progression and its risk of development after DR diagnosis[10] Critically, there is also some evidence that glycemic control is associated with the presence or absence of DR, and not simply with the presence or absence of the disease[11] This means that HbA1c could be related to the severity of retinal disease, beyond just the presence or absence of DR[12]

The relationship between HbA1c and the severity of DR is well known, but the strength of this association and its effect on the severity of DR may be different across different populations. This separation is of clinical relevance because a higher HbA1c would mean a greater risk of having more severe retinal disease and make it more likely that a patient would be monitored for retinal disease by an ophthalmologist and have more intensive diabetes management. In Pakistan, this association has also been shown to be positive, and the HbA1c level has been found to be a predictor of the severity of DR, which further underscores the importance of this relationship in the local population. Clinically, however, it is important that the association be investigated in other clinical settings, as local factors, diabetes duration, treatment regimen, and screening availability can affect the observed association. Therefore, a measurement of HbA1c, as a marker of diabetes control, may serve as a clinically relevant link between metabolic control and ophthalmic risk assessment, and this may be useful when considering the entire range of retinal disease. Thus, the present study was designed to evaluate the association between HbA1c and severity of DR in diabetic patients, and to find out if higher HbA1c levels are correlated with more severe DR.

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MATERIAL AND METHODS

A cross-sectional analytical study was conducted at medical outpatient department of Mardan Medical Complex, Mardan from December 2022 to May 2023.

The sample size was calculated using OpenEpi version 3.01 for a correlation-based analytical study. The calculation was based on a mean correlation coefficient of r=0.31 between HbA1c level and severity of diabetic retinopathy, reported in previous literature, with a 95% confidence level and 80% statistical power. The previous studies had already shown a significant positive correlation between HbA1c and severity of DR, which accounted for the use of a correlation coefficient in the estimation of sample size.[13] The minimum sample size calculated was 77 participants.

A non-probability consecutive sampling technique was used. Patients aged 18 years or older with a recorded diagnosis of diabetes mellitus who were willing to have an ophthalmic examination and be tested for HbA1c were included. Patients with detectable diabetic retinopathy (DR) of any severity as well as patients without retinopathy were eligible to participate so that the relationship between glycemic control and the entire range of diabetic retinopathy could be assessed. Informed consent was obtained, and the patient population was selected.

Patients with known non-diabetic retinal diseases that could affect the evaluation of DR were excluded. Patients with retinal vascular occlusion, age-related macular degeneration, marked ocular trauma, active ocular infection/inflammation, advanced media opacity that did not permit adequate fundus visualization, and other major ocular diseases that were detrimental to retinal assessment were excluded. Also excluded were patients who had incomplete medical records and patients who did not have a result for their HbA1c.

After approval from the institutional ethical review committee, eligible patients were approached, and the study objectives and procedures were explained. Written informed consent was obtained before enrollment. Data collection was done on a structured proforma, which included demographic and clinical data such as age, sex, type and duration of diabetes mellitus, relevant comorbidities, and the current antidiabetic treatment.

All participants were screened by a standardized eye exam. Best corrected visual acuity (BCVA) was examined with a Snellen visual acuity chart; anterior segment examination (ASE) was performed using slit-lamp biomicroscopy, and intraocular pressure (IOP) was measured as needed. After proper dilation of the pupils, the fundus was tested by an ophthalmologist with indirect ophthalmoscopy using the proper lens. The severity of DR was recorded based on the clinical DR grading system accepted by the ophthalmology department, which categorizes DR as none, NPDR, and PDR. Macular edema and other retinal changes were also charted where clinically appropriate.

Each participant had a venous blood sample taken for measurement of HbA1c. HbA1c was determined by the hospital laboratory using a standard technique and expressed as a percentage. The last HbA1C value recorded at or closest to the time of ophthalmic evaluation was used for analysis. The majority of the higher HbA1c levels were considered indicative of sub-optimal long-term glucose control.

All the data collected were entered and analyzed in IBM SPSS Statistics version 26.0. Continuous variables like age, duration of diabetes, and HbA1c level were evaluated for distribution and were presented as mean ± standard deviation or median with interquartile range, whichever was appropriate. Categorical variables such as the type of diabetes, diabetic retinopathy severity categories, and sex were summarized as frequencies and percentages.

The main analysis compared the association of HbA1c level with severity of DR. The direction and strength of association between HbA1c and DR severity were determined by Spearman's rank correlation coefficient (ρ), as DR severity is an ordered clinical outcome. The one-way ANOVA was used to compare HbA1c levels between DR severity groups based on the distribution of the data and the assumptions of parametric testing. Chi-square and Fisher's exact test were used for associations between categorical variables and an independent t-test for continuous variables. A p-value of less than 0.05 was deemed to be statistically significant, and 95% confidence intervals were reported.

RESULTS

A total of 77 patients with diabetes mellitus were included. This resulted in a mean age of 58.7 ± 9.8 years and a male sex ratio of 55.8%. The majority of participants had type 2 diabetes (89.6%) and a mean diabetes duration of 9.6 ± 5.7 years. The prevalence of hypertension and dyslipidaemia was 53.2% and 37.7%, respectively. The mean HbA1c level was 8.4±1.9%. Almost half of the study population were on oral antidiabetic therapy, 32.5% on insulin therapy, and 18.2% on combined therapy. The average best-corrected visual acuity was 0.34 ± 0.29, and the average intraocular pressure was 15.8 ± 2.6 mmHg. (Table 1)

47 of the participants (61.0%) had diabetic retinopathy (DR), of which 31.2% had mild NPDR, 16.9% had moderate NPDR, 7.8% had severe NPDR, and 5.2% had PDR. Diabetic macular edema was found in 19.5% of the participants, vitreous hemorrhage in 5.2%, and retinal neovascularization in 5.2%. At least one cataract and at least one abnormal anterior segment were reported in 27.3% of each group, respectively. (Table 2)

DR group participants were older and had a longer duration of diabetes than those without DR. The use of insulin therapy was significantly higher in the DR group, and the HbA1c level was significantly higher in the DR group. There were no statistically significant differences between the sexes, diabetes types, hypertension, dyslipidemia, or diabetic nephropathy (Table 3).

The HbA1c level showed a significant progressive increase with severity of retinopathy from no DR to PDR. Overall difference in HbA1c level between retinopathy categories was statistically significant (p<0.001), indicating a clear gradient of poorer glycemic control, the higher the DR severity (Table 4).

Table 1: Demographic, clinical, and laboratory characteristics of study participants (n=77)

Variable	Mean ± SD / n (%)
Age (years)	58.7 ± 9.8
Male	43 (55.8)
Female	34 (44.2)
Type 1 diabetes mellitus	8 (10.4)
Type 2 diabetes mellitus	69 (89.6)
Duration of diabetes (years)	9.6 ± 5.7
Hypertension	41 (53.2)
Dyslipidemia	29 (37.7)
Diabetic nephropathy	12 (15.6)
Oral antidiabetic therapy	38 (49.4)
Insulin therapy	25 (32.5)
Combined oral agents + insulin	14 (18.2)
HbA1c (%)	8.4 ± 1.9
Best-corrected visual acuity	0.34 ± 0.29
Intraocular pressure (mmHg)	15.8 ± 2.6

Table 2: Distribution of diabetic retinopathy severity and associated ophthalmic findings (n=77)

Ophthalmic finding	n (%)
No diabetic retinopathy	30 (39.0)
Mild NPDR	24 (31.2)
Moderate NPDR	13 (16.9)
Severe NPDR	6 (7.8)
Proliferative diabetic retinopathy	4 (5.2)
Any diabetic retinopathy	47 (61.0)
Diabetic macular edema	15 (19.5)
Vitreous hemorrhage	4 (5.2)
Retinal neovascularization	4 (5.2)
Cataract	21 (27.3)
Abnormal anterior segment findings	21 (27.3)

Table 3: Comparison of demographic, clinical, and laboratory characteristics according to presence of diabetic retinopathy

Variable	No DR (n=30)	Any DR (n=47)	p-value
Age (years)	55.9 ± 9.7	60.5 ± 9.3	0.047
Male	15 (50.0)	28 (59.6)	0.412
Type 1 diabetes mellitus	4 (13.3)	4 (8.5)	0.705
Type 2 diabetes mellitus	26 (86.7)	43 (91.5)	0.705
Diabetes duration (years)	6.9 ± 4.2	11.3 ± 5.8	0.001
Hypertension	12 (40.0)	29 (61.7)	0.065
Dyslipidemia	8 (26.7)	21 (44.7)	0.116
Diabetic nephropathy	2 (6.7)	10 (21.3)	0.094
Insulin therapy	7 (23.3)	32 (68.1)	<0.001
HbA1c (%)	6.9 ± 0.8	9.3 ± 1.6	<0.001

Table 4: HbA1c levels according to diabetic retinopathy severity

Diabetic retinopathy severity	n	HbA1c (%), mean ± SD
No DR	30	6.9 ± 0.8
Mild NPDR	24	8.0 ± 1.1
Moderate NPDR	13	9.0 ± 1.2
Severe NPDR	6	10.2 ± 1.0
Proliferative DR	4	11.1 ± 0.9
Overall	77	8.4 ± 1.9
ANOVA, p<0.001		

Table 5: Correlation of HbA1c and other clinical variables with diabetic retinopathy severity

Variable	Spearman's correlation coefficient (ρ)	p-value	Interpretation
HbA1c (%)	0.69	<0.001	Strong positive correlation
Duration of Diabetes	0.46	<0.001	Moderate positive correlation
Age	0.23	0.040	Weak positive correlation
Visual Acuity Impairment	0.38	0.001	Moderate positive correlation

Table 6: Association between HbA1c categories and diabetic retinopathy severity

HbA1c category	No DR n (%)	Mild NPDR n (%)	Moderate NPDR n (%)	Severe NPDR n (%)	PDR n (%)	p-value
<7.0%	18 (60.0)	4 (16.7)	0 (0)	0 (0)	0 (0)	
7.0–8.9%	11 (36.7)	15 (62.5)	5 (38.5)	1 (16.7)	0 (0)	
≥9.0%	1 (3.3)	5 (20.8)	8 (61.5)	5 (83.3)	4 (100)	<0.001

Table 7: Association of advanced ophthalmic findings with HbA1c

Ophthalmic finding	Present, HbA1c mean ± SD	Absent, HbA1c mean ± SD	p-value
Diabetic macular edema	10.0 ± 1.5	8.0 ± 1.7	<0.001
Vitreous hemorrhage	10.9 ± 0.8	8.3 ± 1.9	0.012
Retinal neovascularization	11.0 ± 0.9	8.3 ± 1.9	0.009

Spearman correlation analysis showed a significant and positive correlation between HbA1c and severity of DR. There was a moderate positive correlation between duration of diabetes and severity, and a weak but significant correlation with age. A moderately positive correlation was found between visual acuity impairment and severity of DR. (Table 5).

Significant differences were found according to the severity of retinopathy in each category of HbA1c (p<0.001). Participants who had an HbA1c level below 7.0% tended to have no DR, and the percentage of moderate and severe NPDR increased with HbA1c ≥9.0%. Poor glycemic control was highly associated with advanced retinopathy (HbA1c ≥9.0%) in all participants with PDR (Table 6).

Advanced ophthalmic complications were also significantly related to higher HbA1c. The mean HbA1c was significantly higher in participants with diabetic macular edema as compared to those who were not, <0.001 (Table 7), and was significantly higher in participants with vitreous hemorrhage as compared to those who were not, 0.012 (Table 7), and was significantly higher in participants with retinal neovascularization as compared to those who were not, 0.009 (Table 7).

DISCUSSION

The present study showed a high positive correlation between the severity of diabetic retinopathy and glycemic status. HbA1c was found to have a Spearman correlation coefficient of 0.69 with severity of DR (p<0.001), and was found to be higher as DR severity became greater, from 6.9 ± 0.8% in participants without DR to 11.1 ± 0.9% in participants with proliferative DR. This observation aligns with the idea that chronic hyperglycemia is tightly coupled, not just to the onset, but also to the progression of DR to more severe stages. The observed trend was clinically significant, with all PDR patients having an HbA1C ≥9.0%. This association is strong, which means that HbA1c could be a valuable tool in determining patients who require more intensive monitoring of the retina.

The results obtained were similar to that of Chaudhary et al (2018), who studied 75 patients with diabetes in Lahore and found that all patients with retinal abnormalities had HbA1c >6.0%, with high HbA1c showing positive predictive value for retinal disease. Their findings endorse the clinical relevance of an elevated HbA1c as a cue to consider an eye examination. Although their study did not measure a correlation with severity in a graded fashion, our results confirm this finding, showing that higher levels of HbA1c were correlated with more severe DR[14]

Likewise, Koçak Altıntaş et al. (2018) analysed 68 patients with mild or moderate NPDR and explored changes in HbA1c levels with retinal structural parameters. They found that metabolic parameters such as HbA1c were important for changes in retinas in their study, which included patients with established NPDR, and that these parameters were relevant to their follow-up period. Central macular thickness was not a key endpoint in their study, but results of this study add biological evidence for chronic glycemic exposure and retinal structural abnormalities. In contrast, our study assessed the entire clinical range from no DR to PDR and so reflected the association at increasingly advanced DR stages[15]

The results also align with a study of 151 type 1 diabetes patients in 2019, who received intensified insulin therapy, showing that cumulative glycemic exposure measured as “HbA1c years” had the strongest correlation with DR severity (p<0.001). This correlation was also not as strong as the one found in our population (ρ=0.69), which may be due to differences in type of diabetes, duration of diabetes, glycemic exposure, and HbA1c quantification. However, both studies confirm that higher or duration of glycemic exposure is linked to increased severity of retinal disease. Importantly, earlier studies have shown that HbA1c exposure can be cumulative, thereby implying that one HbA1c measurement may not be sufficient to fully represent the total lifetime metabolic burden associated with disease progression of DR[16]

A 2019 study of quantitative ultra-widefield angiography also determined that HbA1c was significantly associated with DR severity (p=0.001), and that the burden of retinal leakage, retinal ischemia, and microaneurysms grew significantly as severity increased. These findings are consistent with our observation that increased HbA1c was linked to more severe clinical markers of DM, such as diabetic macular edema, vitreous hemorrhage, and retinal neovascularization. This clinical-conventional/biological correlation of the extent of microvascular leakage and ischemia with the extent of glycemic exposure further supports the biological plausibility of our results and indicates that greater glycemic exposure can be associated with increasing microvascular leakage and ischemia[17]

The findings of the present work are also corroborated by Liu et al. (2020), who conducted a study based on evidence from five large randomized clinical trials and concluded that intensive glycemic control offered retinal benefits, especially in DR subjects without severe lesions, such as moderate NPDR. They said effective benefits were linked with having an HbA1c drop of at least 0.8% or the ability to attain an HbA1c level below 7%, and that benefits took place only with continued therapy. This is a further confirmation of our cross-sectional results; that is, the majority of those with HbA1c < 7% did not have DR, while those with HbA1c ≥9% did have the more advanced forms of DR (NPDR and PDR). Our study does not prove that better glycemic control will prevent the progression of retinopathy, but both studies highlight the need to have good glycemic control before the disease is advanced[18]

Another comparison is given by Ng et al. (2020), who sought to determine the potential modifying role of HbA1c on genetic susceptibility to severe DR in patients with type 2 diabetes. Their work focused on the fact that HbA1c might influence underlying susceptibility in its role in severe retinal disease. This is important to our findings because although there is a strong overall association between hyperglycemia and the severity of DR, not all patients with elevated HbA1c will have advanced retinopathy. Therefore, along with duration of diabetes, blood pressure, renal disease, lipid abnormalities, and susceptibility, HbA1c should be viewed as an important modifiable determinant of the severity of the disease[19]

Similarly, Alharbi et al. (2021) conducted a study in Saudi Arabia on 130 diabetic patients and found that DR was present in 26.9% of the patients. HbA1c was significantly correlated with DR ($p=0.040$), and duration of diabetes was significantly correlated with retinopathy ($p=0.001$). In our study, both HBA1c and disease duration were found to be significant factors associated with disease severity, and disease duration was found to be moderately positively correlated with disease severity ($\rho=0.46$, $p<0.001$). This higher DR prevalence (61.0%) in our population may be due to variations in the selection of patients, referral system, duration of diabetes, glycemic control, and access to healthcare between the two populations studied. However, the uniformity in HbA1c and duration of diabetes supports the overall generalizability of these factors as important determinants of DR[20]

A study in Pakistan by Jamshed et al, (2021) comes closest to our results. In their cross-sectional study, patients with poor glycemic control had more severe DR, and patients with grade IV DR had an HbA1c level of about 11.5%. They concluded that HbA1c was directly related to retinopathy severity. In a similar fashion, our results showed a progressive rise in HbA1c levels from no DR to mild NPDR, moderate NPDR, severe NPDR, and PDR. The similarity in the consistency between two Pakistani ophthalmic populations indicates that the relation between glycemic control and the presence of advanced DR is relevant in the clinical context and is not limited to other ethnic and healthcare settings[21]

Likewise, Riaz et al. (2021) conducted a study in a trust hospital in Pakistan where 395 cases of type 2 diabetes were assessed, and only 31.4% had HbA1c levels within the normal range, whereas 14.4% were diagnosed with DR. They also found poor treatment adherence and socioeconomic factors as relevant factors for poor glycemic control. Their goal was different than ours, and they did not calculate a correlation coefficient between HbA1c and the severity of DR, but their results offer important context for our observation that the mean HbA1c is high, and the DR burden is considerable. Variations in the prevalence of DR found between the two studies could be explained by variations in the study populations and referral characteristics[22]

The outcomes of Geany et al. (2022) are very similar to the present findings. The mean HbA1c was 6.49% in individuals without DR, 8.17% in the NPDR group, and 8.47% in the PDR group in this study of 72 diabetic patients. A very strong and statistically significant correlation was observed between HbA1c and DR severity ($p<0.001$) by Spearman analysis. The strength of the correlation between HbA1c and a severity category was also demonstrated by Spearman analysis in our study ($\rho=0.69$, $p<0.001$), in addition to a larger HbA1c gradient for each severity category. The close agreement is even more significant due to the fact that both studies used ordered clinical classification and employed non-parametric correlation analysis, which lends strength to the relationship observed[22]

Lastly, Khan et al. (2022) found that in their cross-sectional study of 120 diabetic patients, poor glycemic control was associated with the worst diabetic retinopathy, with HbA1c levels of about 11.8% in patients with grade IV DR. Similarly, Gardezi et al. (2022) investigated patients with a diabetes duration of more than 1 decade, and reported a significant relationship between HbA1c and DR ($p=0.001$), and significant variations in HbA1c between DR grades. Our finding that advanced retinopathy occurred primarily in those with significantly elevated HbA1c is well supported by these studies. Our study also showed that HbA1C levels of 9.0% or higher were significantly enriched in moderate, severe NPDR and PDR categories, which gives an important clinically relevant severity gradient[23, 24]

The other discovery of the current study was that higher levels of HbA1c were related to diabetic macular edema, vitreous hemorrhage, and retinal neovascularization. Those who presented with these complications also had significantly higher HbA1c levels compared to those who did not present with the respective finding. This is clinically significant as these complications are more advanced or vision-threatening complications of diabetic retinal disease. This is consistent with data demonstrating that as retinopathy severity increases, so do retinal vascular leakage and ischemia. Therefore, in our study, the association of HbA1c with DR was not only limited to categorising retinopathy stages but also to clinically relevant complications that relate to visual impairment[17]

However, the relationship between diabetes duration and severity of DR in our study should also be considered. There was a moderate positive correlation between duration of diabetes and severity, and duration of diabetes was significantly longer in patients with DR compared with patients without DR. This is consistent with the Saudi Arabian study, which showed that diabetes duration was an independent factor affecting the presence of DR, and with Pakistani literature, which has focussed on the duration of diabetes as an important factor determining retinal disease. The biological explanation is reasonable, in that the more prolonged hyperglycemia there is, the more time there will be to allow for the cumulative damage to the endothelial cells, for capillary closure, for retinal ischemia, and for the resulting neovascularization[20, 22]

The present study also revealed that DR patients were significantly more likely to be on insulin treatment. This association should be interpreted with caution as there may be a tendency towards increased severity of diabetes, duration of disease, or baseline glycemia, which may explain why a higher number of insulin users may have retinopathy. This association between insulin therapy and DR may therefore be a confounder due to disease severity. Likewise, hypertension, dyslipidaemia and DR nephropathy were more common in participants with DR; however, there were no significant differences, possibly due to the small sample size. The independent contribution of these factors would be better determined with larger studies accounting for more variables.

The results of the present study are in full agreement with the findings reported from 2018 to 2022 in Pakistani, Middle Eastern, Asian, and international populations. Most studies have shown an association of higher HbA1c and the presence or severity of DR and some studies conducted with more detailed retinal measurements have shown associations between glycemic exposure and retinal vascular abnormalities. As demonstrated in our study ($\rho=0.69$) and seen as HbA1c levels continue to rise with each stage of retinopathy, it is crucial to incorporate metabolic and ophthalmic assessment. However, the present study lacked the time sequence for establishing causality and progression, and hence it was cross-sectional. Additional studies that adjust for diabetes duration and systemic risk factors, and that use cumulative exposure to HbA1c, standardized ETDRS grading, and a longitudinal design to assess the association between HbA1c trajectory and subsequent DR progression would strengthen the evidence on whether HbA1c trajectories predict subsequent DR progression.

Limitations: There were some limitations to the study. This was because of the cross-sectional design that did not allow for a causal relationship or a temporal progression of DR to be determined. The small number of participants (n=77) and the use of consecutive sampling may have restricted the statistical power and generalizability of the study. The study was performed in one center and may have contained referral and selection bias. The

HbA1c was measured only once and only reflected glycemic exposure over the current period. Multivariable analysis was not performed to assess potential confounding factors, such as blood pressure, lipid profile, renal function, diabetes treatment adherence, and socioeconomic characteristics. Retinopathy grading was also not based on standardized photographic grading as in the ETDRS classification.

CONCLUSION

An increase in HbA1c was robustly correlated with increased severity of DR. HbA1c was found to be higher at each stage of retinopathy, with higher levels seen in more severe NPDR and PDR. More advanced disease was also related to longer duration of diabetes. These results reinforce the need for good glycemic control and frequent eye examinations, especially for those with longstanding diabetes and/or elevated HbA1c. Longitudinal multicenter studies are suggested to investigate whether HbA1c levels can accurately predict the risk of developing SRDR.

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