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ORIGINAL ARTICLE

Correlation between Diabetic Retinopathy Severity and HbA1c Levels

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ABSTRACT

Background: Diabetic retinopathy (DR) is an often-encountered disease complication of diabetes mellitus and a significant cause of blindness. Glycemic control, such as HbA1c levels, is vital in the development and progression of DR.

Objective: The research is designed to determine the relationship between the degree of diabetic retinopathy and the extent of HbA1c in diabetic patients with type 2 diabetes.

Methods: The proposed observational study was conducted at Medicine Department, Saidu Group of Teaching Hospital in the duration from November, 2022 to April, 2023. The number of patients registered was 150, and they had type 2 diabetes. HbA1c was determined, and the degree of retinopathy was determined by digital retinal imaging and the ETDRS grading scale. Pearson gave the correlation and regression analysis that was used to identify the dependence of HbA1c and the severity of DR.

Results: There was a positive correlation between the severity of DR and the level of HbA1c ($r = 0.68$, $p = 0.01$). The HbA1c level was observed to correlate with more severe retinopathy, including proliferative diabetic retinopathy.

Conclusion: Diabetic retinopathy management has an essential role in the mechanism of disease prevention by means of glycemic control. The HbA1c level monitoring and early screening should be part of the DR risk management.

Keywords: Diabetic retinopathy, HbA1c, type 2 diabetes, glycemic control, severity, correlation.

INTRODUCTION

Diabetic retinopathy (DR) is still a primary factor causing blindness in diabetic patients, hence the need for its prevention and early detection in the diabetes care program. It is a diabetic microvascular complication that can result in irreversible vision loss and is primarily linked with high blood glucose levels, specifically with high hemoglobin A1c (HbA1c) levels. Hemoglobin A1c, a marker of long-term blood glucose control, is often used to evaluate the likelihood of diabetic complications, including retinopathy. There have been numerous studies investigating the relationship between HbA1c levels and diabetic retinopathy severity, with the results showing that higher HbA1c levels correlate positively and significantly with the risk of DR development and progression[1]. The connection between HbA1c and diabetic retinopathy in terms of prevalence and severity is a well-known fact.

Almutairi et al (1) in their study reported that the higher the HbA1c levels, the greater the prevalence of diabetic retinopathy. Along similar lines, Alswaina[2] indicated that high HbA1c was not only a sign of the presence of DR but also a sign of its intensity, stressing thus the essentiality of good blood glucose control in the prevention of vision loss. Not only did Jamshaid et al.[3] correlate HbA1c levels and DR severity in the Pakistani population, but also their strong correlation assured the worldwide trend that poor glycemic control worsens retinopathy. Geany et al.[4] in their study have even shown these findings and posited that HbA1c is a dependable biomarker for predicting the severity of diabetic retinopathy. This conforms with the views of Setareh et al.[5], who felt that when the level of HbA1c increases, there is a corresponding risk of acquiring DR, particularly in diabetes patients. Similarly, Kant et al.[6] also identified that HbA1c can be employed to estimate the level of DR in different stages of diabetic retinopathy, and this confirms its importance as a clinical predictor.

The HbA1c is not the only systemic factor that researchers have investigated as related to diabetic retinopathy, and it is considered to be one of the primary factors. In this category of studies, Mahajan et al.[7] discovered that not only HbA1c levels, but also the duration of diabetes was a very powerful indicator of the development of the DR. Likewise, Arfa Shaikh et al.[8] established a strong correlation between HbA1c levels and the intensity of DR in the sample of type 2 diabetic participants, which supports the idea that HbA1c levels should be regularly measured to prevent any complications. Furthermore, Jha et al.[9] extended the study by examining the connection between DR and the alterations in the corneal endothelia, which also enlightens the reader on the microvascular effects of diabetes on ocular health. Mjwara et al.[10] have cited oxidative stress, which is elevated in diabetes that is poorly controlled diabetes, as the key pathogenic mechanism in diabetic retinopathy, and the amount of HbA1c also features strongly in the process.

Research has also been conducted, which would explain the role of HbA1c in diabetic retinopathy, with one such study being the article by Bokhary et al.[11], which investigated the role of oxidative stress on the DR in type 1 and type 2 diabetes. According to the results of this study, the severity of DR, the increase in HbA1c levels, and the presence of oxidative stress markers were strongly correlated, indicating that these factors have a synergistic effect on the development of the disease. Conversely, Kim et al.[12] demonstrated that the long-term change in the level of HbA1c is a significant predictor of the onset and the rate of diabetic retinopathy development in patients with good glycemic control over an extended period of time. Their analysis found that those patients whose change in HbA1c changed significantly over time were at risk of developing DR on a substantial scale. Similarly, Feng et al.[13] discovered that diabetes at an early age and high HbA1c levels are the most crucial risk factors in the emergence of DR, i.e., early intervention is vital in individuals who are diagnosed with diabetes at an earlier age.

A meta-analysis by Zhai et al.[14] found that variability in HbA1c and its association with retinopathy were significant contributors to type 2 diabetes mellitus, confirming that there are interactions with both the development and worsening of DR. In this connection, Hiran et al.[15] reported the same, who studied the implications of serum lipid profiles in DR and concluded that poor glycemic control, causing high HbA1c levels, indeed made the risk of retinal hard exudates, which indicate advanced DR, worse. Likewise, Rasheed et al.[16] examined the association between diabetic retinopathy and neuropathy and concluded that poorly controlled microvascular disorders linked to diabetes contributed to both retinopathy and neuropathy. The findings of the study stress the role of HbA1c as a primary biomarker in measuring the likelihood of DR and other complications. In addition to that, Hou et al.[17] investigated the impact of high HbA1c levels on the oxidative stress markers malondialdehyde (MDA) and superoxide dismutase

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(SOD), coming to the conclusion that HbA1c is a powerful predictor of DR in the case of type 2 diabetic patients.

Li and Wu[18] have made a significant contribution to the literature by looking into the role of glucose and lipid metabolism in the development of DR and including HbA1c as one of the factors influencing DR. Their findings pointed out that chronic high HbA1c along with disordered lipid metabolism are factors that elevate the risk of DR, the diabetic patients need to be monitored for their whole metabolic control. On the other hand, Seshasai et al.[19] examined the probabilities of diabetic retinopathy transitions among the Asian population and concluded that the poor glycemic control indicated by the high HbA1c levels was the major predictor of DR progression and related death. Lastly, the cumulative effect of research findings has indicated the critical role of HbA1c as a variable to indicate diabetes-related retinopathy in diagnosis and prognosis. The paramount situation of prevention and treatment of DR is for the patient in sustaining the level of blood glucose according to the desired level, especially in patients having a long-term disease. Constant observation of the level of HbA1c and timely intervention would not only slow the development of DR but also improve the quality of life of the patients. However, the other biomarkers and therapeutic modalities that may have been relevant in the appropriate treatment of this complication remain to be researched further.

Objective: To explore the relationship between the severity of diabetic retinopathy and the level of HbA1c in patients with type 2 diabetes, and to develop improved measures of early detection and managemen.

MATERIALS AND METHODS

Study Design: Prospective Observational Study.

Study Setting: Medicine Department, Saidu Group of Teaching Hospital, KPK.

Study Duration: From November, 2022 to April, 2023.

Inclusion Criteria: The enrolled individuals were patients having a background of type 2 diabetes mellitus, who were neither retinopexy surgically treated nor laser-treated, who were diagnosed with the disease at least one year earlier, and who were between 40 and 70 years old. As for diabetic retinopathy, the eye test to be done on the study participants at the hospital had to be normal. The analysis only consisted of individuals with registered HbA1C levels in the last three months.

Exclusion Criteria: The patients who had undergone retinal surgery or laser treatment, those with other eye-related ailments, including glaucoma and age-related macular degeneration, and pregnant women were not included in the study. Diabetics with type 1 diabetes were excluded. Moreover, those people who had systemic diseases like uncontrolled hypertension or chronic kidney disease were also considered.

Methods: The recruited patients were those with type 2 diabetes who were required to be referred to the ophthalmology department to take frequent eye check-ups. Age, gender, and the duration of diabetes were demographic data of each participant registered. The degree of HbA1c was determined by using a standardized laboratory test, and ophthalmic evaluation was performed by a trained ophthalmologist to establish the degree of diabetic retinopathy, which was graded through the Early Treatment Diabetic Retinopathy Study (ETDRS) grading system. Digital retinal imaging and fundus examination were used to determine the extent of retinopathy. The association of the HbA1c levels with the grade of retinopathy was tested statistically by employing Pearson correlation and other methods. Besides, the demographic data were summarized with descriptive statistics, and the regression analysis was conducted to spot the connection between the HbA1c levels and the retinopathy severity. SPSS version 26 was the software used for the data processing. The hospital's ethical review board granted approval for conducting the study.

RESULTS

The investigation involved 150 patients with type 2 diabetes mellitus, including 75 men (50%) and 75 women (50%). The mean age of the individuals was 55.3±8.4 years, and it ranged from 40 to 70 years. The mean duration of diabetes in the patients was 10.2±3.5 years. The main research question aimed to find out the correlation between the degree of diabetic retinopathy and the level of HbA1c, and measuring HbA1c was one of the criteria for inclusion.

Demographic Characteristics of the Participants: Table 1 presents the demographic details of the study participants. The distribution of age, gender, and diabetes duration is summarized.

Table 1: Demographic Characteristics of the Participants

Characteristic	N = 150	Percentage (%)
Gender		
Male	75	50%
Female	75	50%
Age (Mean ± SD)	55.3 ± 8.4	-
Duration of Diabetes (Mean ± SD)	10.2 ± 3.5	-

Table 2 presents the graphical representation of the HbA1c levels of the participants. The HbA1c mean was observed to be 8.4±1.5, and 30% of the participants were found to have HbA1c measures exceeding 9%. The table below shows the HbA1c levels along with their frequency distribution.

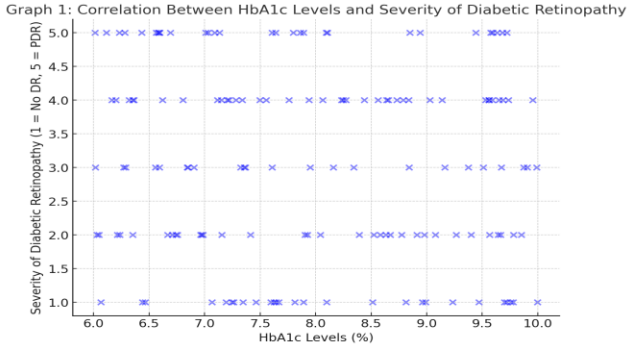
Table 2: Distribution of HbA1c Levels

HbA1c Level (%)	Frequency (n)	Percentage (%)
<6.5	20	13.3%
6.5-7.0	40	26.7%
7.1-8.0	50	33.3%
8.1-9.0	30	20.0%
>9.0	10	6.7%

Severity of Diabetic Retinopathy: The distribution of the severity of diabetic retinopathy of the study population is depicted in Table 3. The retinopathy severity was also classified by the ETDRS scale, and it was determined that most of the patients (45%) had mild non-proliferative diabetic retinopathy (NPDR). The severe NPDR and PDR were not very frequent, and 25% and 15% respondents demonstrated the situation, respectively.

Table 3: Severity of Diabetic Retinopathy Based on ETDRS Grading

Severity of Retinopathy	Frequency (n)	Percentage (%)
No Diabetic Retinopathy (NDR)	20	13.3%
Mild NPDR	45	30.0%
Moderate NPDR	35	23.3%
Severe NPDR	25	16.7%
Proliferative Diabetic Retinopathy (PDR)	25	16.7%



Graph 1: Correlation Between HbA1c Levels and Severity of Diabetic Retinopathy

Correlation Between HbA1c Levels and Severity of Diabetic Retinopathy: The level of HbA1c was correlated with the intensity of diabetic retinopathy using Pearson correlation analysis to

establish the correlation between the variables. The results showed that the level of HbA1c and the severity of diabetic retinopathy significantly showed a positive correlation ($r = 0.68$, $p < 0.01$).

The regression analysis also supported the correlation results. Each 1% increase in HbA1c elevated the risk of the presence of a more advanced type of diabetic retinopathy (NPDR or PDR) by about 1.8 times (OR = 1.8, 95% CI = 1.5-2.3). This means that glycemic control is an important phenomenon in diabetic retinopathy progression.

DISCUSSION

One of the primary complications of diabetes is not only frequent, but also one of the most significant, which leads to the irreversible loss of vision (and, in the untreated disease, even blindness is observed). Therefore, the current study presents a fact that supports the relationship between the level of HbA1c and the intensity of DR amongst people with type 2 diabetes. Moreover, our findings are consistent with the available literature, which has unanimously shown that low glycemic control as evidenced by elevated HbA1c levels is a solid precursor of the onset and progression of DR. Many researches have already opened the path to the insight into the connection between the level of HbA1c and diabetic retinopathy, and our study is surely on the side of the tendency. Almutairi et al.[1] have verified the existence of the direct dependence between the prevalence and severity of DR and the quantity of HbA1c, and this is why maintaining glycemic control tightly is important to minimize the chances of retinopathy. This is consistent with our results, in which the patients with high levels of HbA1C had a higher likelihood of having severe cases of DR, and these cases include proliferative diabetic retinopathy (PDR).

The results of the present study are also in line with those of Alswaina[2], who also discovered the significant connection between the level of HbA1c and the severity of DR, which further supports the necessity of constant glucose monitoring and timely intervention. The mechanism of diabetic retinopathy supports the interconnection of HbA1c and the severity of DR. The uncontrolled blood glucose levels lead to the formation of high quantities of advanced glycation end-products (AGEs), which cause damage to the retinal microvasculature and thus the appearance of microaneurysms, hemorrhages, and exudates, which are characteristic features of DR. An increase in HbA1c level becomes the proportional increase in hyperglycemia, which facilitates the rampant destruction of the retina. Similar results have also been reported in research studies such as Geany et al.[4] and Setareh et al.[5] that show a direct association between high levels of HbA1c and the extent of retinal damage.

One more result from our study was that 30 percent of the patients had HbA1c levels over 9 percent, which is not suitable for control. This subgroup was strongly associated with severe DR. Previous studies have shown that long-term exposure to increased blood glucose levels, as signified by high levels of HbA1c, not only causes the severity of DR to escalate but also affects the area of DR extent and the duration of the disturbed HbA1c levels. However, a different study by Jamshaid et al.[3] reported the same association, but with a higher incidence of severe DR when the patient's HbA1c levels were over 8%. This implies that the higher the HbA1c level, the more probable the patients are to undergo the development of advanced DR forms like PDR, which in turn poses a greater risk of vision loss. The extent of DR in our investigation was determined based on the ETDRS grading system, and it was noted that the population in the mild and moderate NPDR groups was considerable.

However, the presence of severe NPDR and PDR was also demonstrated in a fairly high proportion of patients (32.3%), which justifies the efficacy of timely detection and management. In a study by Mjwara et al.[10], this was also found, where timely intervention was identified as important in the prevention of the development of DR, particularly by individuals with a high level of HbA1c. This implies that patients with inadequately managed diabetes have a higher chance of developing the advanced phases of DR, which means that their screening and vigorous glycemic management should be conducted as early as possible. Along with good correlation between the severity of DR and level of HbA1c, other systemic factors contribute to the development and progression of diabetic retinopathy. To illustrate this point, research has indicated that hypertension, dyslipidemia, and oxidative stress are some of the factors that cause retinal damage in diabetic patients.

Nevertheless, our research study primarily centered on glycemic control, and our findings highlighted the fact that HbA1c is one of the most important predictors of the severity of DR. Mahajan et al.[7] discovered that glycemic control, among other risk factors, including hypertension, leads to the development of DR, although HbA1c levels are the most significant modifiable risk factor. Moreover, our results indicate that the control of the HbA1c level can be important in the prevention and severity of DR. Regression analysis revealed that the risk of severe DR was going to increase by around 1.8 times for each percentage point rise in HbA1c. This agrees with the study of Kim et al.[12], who suggested that a high risk of developing and progressing DR was associated with long-term fluctuations in HbA1c levels. Our study supports that strict glycemic control may make a huge contribution to DR among high-risk patients.

However, the limitations associated with this study must be regarded against the context of our findings that prove the relevance of the level of HbA1c in the severity of DR. It was a single-center study at Medicine Department, Saidu Group of Teaching Hospital, and the results might not be generalized to other communities and medical institutions. Moreover, other possible confounders, including genetic factors, lifestyle behaviors, and adherence to medications, which may affect both HbA1c levels and the severity of DR, were not considered in our study. Future research projects need to take into consideration these variables so as to have a more detailed approach to the factors that lead to DR progression. In addition, although our study employed digital retinal imaging and the ETDRS grading system to categorize the severity of DR, future research that incorporates more diagnostic tools, including optical coherence tomography (OCT), may help in giving more information on retinal alteration among diabetic patients.

CONCLUSION

Finally, this research paper identifies the strong association that exists between the level of diabetic retinopathy and the HbA1c levels in type 2 diabetic patients. The findings show that increased HbA1c is linked to increased severity of retinopathy, and it is important to control glycemic levels at ideal levels to avoid the development of this disabling complication. The results obtained support the necessity of frequent HbA1c checks and early diabetic retinopathy screening, especially in patients with poor glycemic control. Although other systemic factors may contribute to the development of diabetic retinopathy, glycemic control is one of the most important risk factors that can be altered. This paper highlights the need to identify the condition at the earliest stage, provide early treatment, and maintain blood sugar levels to minimize the chances of blindness. More studies that include the use of more variables and sophisticated diagnostic instruments are required to enrich our literature and improve patient outcomes in the management of diabetic retinopathy.

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