Association of Severity of Diabetic Retinopathy with HbA1c Level.



License.

Muhammad Asif¹, Fazal Noman², Samina Karim³, Javed Rasul³ Pak International Medical College, Peshawar.^{1,2,4} Hyatabad Medical Complex, Peshawar.³

ABSTRACT

Purpose: To compare the association of the severity of Diabetic Retinopathy with the level of HbA1c.

Methodology: This cross-sectional study was conducted at Pak International Medical College and Hospital Peshawar from March, 2019 to June, 2019 after approval of ethical review board. Using consecutive sampling technique, total of 106 patients with Diabetic Mellitus type -2 were enrolled in the study who presented to out patient department of ophthalmology, Pak International Medical College and Hospital, Peshawar. Non diabetic patients and those who did not give consent to participate were excluded. After informed consent, full ophthalmologic examination was carried out for each patient. Diabetic retinopathy was graded as 0-5. No diabetic changes were labeled as Grade-0, and mild to moderate NPDR were included in Grade-1, CSME with NPDR as Grade 2, PDR as Grade 3, Advanced DR (VIT HE+ RD) was labeled as Grade 4, and nerve Palsy, CRAO, CRVO was labeled as Grade-5. Frequency and percentages were calculated for categorical data while mean, maximum, minimum, and standard deviation for continuous data via SPSS version- 27. One way ANOVA was applied to check for significance. P value less than 0.05 was considered significant.

Results: Out of the 106 participants, 44 were male (41.50%) and 62 were female (58.50%). Among participants, Grade -2 (HbA1c range 8-12) comprised the highest percentage of patients at 44.3%, followed by Grade-1 (HbA1c range 5-8) with 35.8%, and Grade -3 (HbA1c range 12-15) with 19.8%. This suggests that as HbA1c values increase, the severity of DMR tends to escalate, emphasizing the critical role of glycemic control in managing diabetic complications affecting the retina.

Conclusion: As the HbA1c level increases the severity of diabetic retinopathy increases.

Keywords: Diabetic Retinopathy, Glycated Hemoglobin, Diabetes.

How to Cite this Article: Asif M, Noman F, Karim S, Rasul J. Association of Severity of Diabetic Retinopathy with HbA1c Level. Ophthalmol Pak. 2024;14(3):79-83. DOI: https://doi.org/10.62276/OphthalmolPak.14.03.158

INTRODUCTION

Diabetic mellitus (DM) is a metabolic syndrome in which insulin resistance is absolute or is of relative lack. It can damage every organ and system of our body resulting in impaired quality of life and leading to community burden and economics to the society.¹ Global statistics show that about 451 million people suffered from DM in 2017 and was expected that this figure may increase to 693 million in 2045.²

Correspondence: Samina Karim Hyatabad Medical Complex, Peshawar. **Email:** drsaminakarim@yahoo.com

Received: 29-05-2024 **Accepted:** 24-06-2024 Diabetes Mellitus is a big health problem worldwide, affecting millions of people and putting a burden on both individuals and healthcare systems. The global prevalence of diabetes went up from 108 million in 1980 to 422 million by 2014.

The prevalence rate of diabetes is notable as it has been rising at a quicker rate in low- and middleincome nations compared to high-income countries. It is also noted that between 2000 and 2019, there was a 3% increase in diabetes mortality rates by age.³ Universally, diabetes is viewed as a risk, with an expected 463 million individuals living with the sickness. In 2019, it was the 10th major reason for death, representing an expected of 1.5 million. Regarding the present status of diabetes prevalence of the diabetes may be increased to 700 million by the year 2045 in low-income countries.⁴

Diabetic retinopathy (DR) is a common complication of DM that leads to blindness. Diabetic retinopathy, which happens when the blood vessels in the eyes get damaged, is still one of the main reasons why adults lose their ability to see well.⁵ DMR usually causes blindness in the age group of 20-65 years.⁶ DMR is present in 45% of people with both Type 1 Diabetic myelitis (T1DM) and Type 2 Diabetic mellitus (T2DM). People with T1DM are affected more than T2DM with diabetic retinopathy.⁷ Proliferative diabetic retinopathy affects about 5%-10% of all diabetic patients. The severity of DMR depends upon many factors which include: the onset of DM, glycemic control, cataract surgeries, hypertension, and smoking.^{8,9} Another important factor that may contribute to DMR is microalbuminuria. A high grade of microalbuminuria is a key risk factor for the development and severity of DR.¹⁰

This study was conducted to assess the association between the severity of retinopathies and HbA1c status in patients with diabetic mellitus.

METHODOLOGY

This cross-sectional study was conducted at Pak International Medical College and Hospital Peshawar from March, 2019 to June, 2019 after approval of ethical review board. Using consecutive sampling technique, total of 106 patients with Diabetic Mellitus type -2 were enrolled in the study who presented to out patient department of ophthalmology, Pak International Medical College and Hospital, Peshawar. Non diabetic patients and those who did not give consent to participate were excluded. After informed consent, full ophthalmologic examination was carried out for each patient. Diabetic retinopathy was graded as 0-5. No diabetic changes were labeled as Grade-0, and mild to moderate NPDR were included in Grade-1, CSME with NPDR as Grade 2, PDR as Grade 3, Advanced DR (VIT HE+ RD) was labeled as Grade 4, and nerve Palsy, CRAO, CRVO was labeled as Grade-5. Frequency and percentages were calculated for categorical data while mean, maximum, minimum, and standard deviation for continuous data via SPSS version-27. One way ANOVA was applied to check for significance. P value less than 0.05 was considered significant.

RESULTS

Out of the 106 participants, 44 were male (41.50%) and 62 were female (58.50%). The participants' ages ranged from 30 to 75 years, with a mean age of 52.45 years and a standard deviation of 11.04 years. Table 1 showed the HbA1c level and severity of DR was given in table 1. The patients were categorized into Grade-1 (HbA1c range 5-8), Grade -2 (HbA1c range 8-12), and Grade -3 (HbA1c range 12-15). Among these, Grade -2 (HbA1c range 8-12) comprises the highest percentage of patients at 44.3%, followed by Grade-1 (HbA1c range 5-8) with 35.8%, and Grade -3 (HbA1c range 12-15) with 19.8%. This suggests that as HbA1c values increase, the severity of DMR tends to escalate, emphasizing the critical role of glycemic control in managing diabetic complications affecting the retina. Table 2 showed mean differences between and within groups for a variable. Between-group comparisons show a significant difference (p =0.032) with a mean difference of 0.03. Withingroup differences vary: Group 1, Group 2 and Group 3 has a non-significant mean difference of 0.170, P=0.067.

Sr #	HbA1c Grading	No of Patients		Dmr Severity Level		
		Freqency	% age		Freqency	% age
(1)	Grade -1 (5 - 8)	38	35.8%	Grade -0	0	0%
				Grade -1	14	13.2%
				Grade -2	4	3.7%
				Grade -3	8	7.5%
				Grade -4	7	6.6%
				Grade -5		4.7%
(2)	Grade -2 (8 - 12)	47	44.3%	Grade -0	9	8.4%
				Grade -1	7	6.6%
				Grade -2	12	11.3%
				Grade -3	14	13.9%
				Grade -4	4	3.7%
				Grade -5	1	0.9%
(3)	Grade -3 (12 - 15)	21	19.8%	Grade -0	0	0%
				Grade -1	5	4.7%
				Grade -2	4	3.7%
				Grade -3	3	2.8%
				Grade -4	6	5.6%
				Grade -5	3	2.8%

 Table -1: Descriptive statistics of HbA1c level

 with Severity of DR level

Table -2: One Way Anova

Variables	Mean	Confidenc	P- Value					
variables	Difference	Lower Case	Upper Case	0.032				
Between the Group	0.03	0.0678	0.0987	0.032				
Within the Group								
Group 1 VS Group 2	0.170	0.313	3.337					
Group 1 VS Group 3	0.267	0.390	2.920	0.067				
Group 2 VS Group 3	0.097	0.314	2.802					

DISCUSSION

Diabetic retinopathies are one of the critical and most important factors that lead to blindness. It puts a heavy burden on the ophthalmic community.¹¹It is important to identify these risk factors that increase the progression of DR. In this study, we found the HbA1c level status with the severity of diabetic retinopathy. HbA1c level shows the glycemic control in diabetic patients which is thought to be a grave factor in the development of diabetic retinopathy.

In this study, the subject's ages ranged from 30 to 75 years, with an average age of 52.45 years and a standard deviation of 11.04 years. A study in Pakistan, Punjab by Khan RM et al also stated similar findings.¹² We found that 44 were male

(41.50%) and 62 were female (58.50%). A similar comparable analysis was reported in India showed that males (69%) were high in comparison to females (31%). This may occur due to gender bias.¹³ We found that most of the subjects in our study 44% had grade 2 diabetic retinopathy as compared to grade 1. Similar findings were also reported from a study conducted in Pakistan, Punjab by Khan RM et al.^{13,14} In our study 13.2% of the subjects were NPDR and about 14% had PDR. These values are similar to Khan RM et al and Sewak et al while assessing and relating the HbA1c level with the severity of diabetic retinopathies.^{12,15}

Only 8.4% of the patients had no diabetic changes in our study population. Relating to this, a study conducted in South Korea also reported that only 4.1% mean 5 out of 120 patients have no diabetic changes.¹⁶ This small portion of bad indicator of the DMR was associated with poor glycemic control. We also found that Grade-1 (HbA1c range 5-8) with 35.8% has NPDR in our total study sample. Similarly, Grade -2 (HbA1c range 8-12) comprises the highest percentage of patients at 44.3%, and Grade -3 (HbA1c range 12-15) with 19.8% in our total study population. In contrast, some of the findings also reported in some studies showed that most of the NPDR has only (15) cases had grade 1 and 2 with HbA1c at Grade 2 (8-12). However, their Grade III HbA1c (12-15) was seen among patients with Grade-V diabetic retinopathy was 19-20 of the subjects. Prasad et al. also recorded, that their mean levels of HbA1c as 9.30 +1.60 in their study and showed an accumulative slope in the diabetic retinopathy with the severity of DR as HbA1clevels increased.^{17,18}

A comparable study conducted in Sadie Arabia also reported that uncontrolled diabetes and HbA1c level have a 67% of risk developing diabetic retinopathy.¹⁹ A study conducted in Sweden by Rebecca Andreasson et al also supported the same findings in type 1 diabetes.²⁰ As the level of HbA1c increases the severity of the diabetic retinopathy may increase. A similar statement was also reported in a study conducted in China by Valencia Foo et al that an increase in HbA1c level and systolic blood pressure has a direct impact on diabetic retinopathy.²¹ Sample size was very small in our study when seen in context of magnitude of disease. Moreover, it was collected from a single centre. Multicaentre data may put forth a more conclusive evidence regarding this issue.

CONCLUSION

As the HbA1c level increases the severity of diabetic retinopathy increases. We also noted that diabetes has a direct relation with diabetic retinopathy.

Conflict of Interest: None to declare

Ethical Approval: The study was approved by the Institutional Review Board / Ethical Review Board Vide No.02/19/DMR/PIMC.

Author Contributions: Muhammad Asif: Concept, Design, Data Collection.

Fazal Noman: Data Collection, Literature Review.

Samina Karim: Data Analysis, Article Draft.

Javed Rasul: Critical Review.

REFERENCES

- 1. Alrashedi M, Alshaban J, Alshamdin T, Alharbi M, Morsi O, Alharby M. The incidence of Diabetic Retinopathy in Diabetic patients attending the ophthalmic clinic in Khayber General Hospital, Medinah region. Intern J Med.2019;3(3):289-293.doi:10.24911/IJMD C. 51-1544991756.
- Roglic G. WHO Global report on diabetes: A summary. Int J Noncommun Dis. 2016;1(1):3-8. DOI: 10.4103/2468-8827.184853.
- Jamshed S, Hanif A, Malik IQ, Zahid N, Imtiaz HS. Relationship between HbA1c Levels and Severity of Diabetic Retinopathy. Pak J Ophthalmol. 2021;37(4):352-355. Doi:10.363 51/pjo.v37i4.1210.
- 4. Kehlenbrink S, Smith J, Ansbro É, Fuhr DC, Cheung A, Ratnayake R, et al. The burden of diabetes and use of diabetes care in humanitarian crises in low-income and middleincome countries. Diabet & Endocrinol.

2019;7(8):638-47. doi:10.1016/S2213-8587 (19)30082-8.

- Ting, D. S. W., Cheung, G. C. M., Wong, T. Y. Diabetic retinopathy: Global prevalence, major risk factors, screening practices, and public health challenges: A review. Clin & Exp Ophthalmol. 2017;46(2):160-171. doi: 10.1111 /ceo.12696.
- Cho N, Shaw J, Karuranga S, Huang Y, da Rocha Fernandes J, Ohlrogge A, et al. IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. Diab Res Clin Pract. 2018; 138: 271-281. doi: 10.1016/j.diabres.2018.02.023.
- Nojomi M. Study of diabetic retinopathy and its risk factors in diabetic patients, Ahvaz, Iran. J Diab Metab. 2016; 07(09):20. http://dx.doi. org/10.4172/2155-6156.C1.053.
- Shrote A. Clinical Evaluation of Correlation between Diabetic Retinopathy with Modifiable, Non-Modifiable, and Other Independent Risk Factors in Tertiary Set-up in Central Rural India. J Clin Diag Res. 2015; 9 (10): 10-14. doi: 10.7860/JCDR/2015/12785.6689.
- 9. Niveditha H, Yogitha C, Liji P, Sundeep Shetty, N.V.V. Himamshu, Vinutha BV, et al. Clinical correlation of hba1c and diabetic nephropathy with diabetic retinopathy. J Evol Med Dent Sci. 2013; 2 (49): 9430-9435.
- Zhang X, Lim SC, Tavintharan S, Yeoh LY, Sum CF, Ang K, et al. Association of central arterial stiffness with the presence and severity of diabetic retinopathy in Asians with type 2 diabetes. Diabet & Vas Dis Res. 2019;16(6):49 8-505. doi:10.1177/1479164119845904.
- Khan RM, Saleem H, Bhatti SA, Sadiq MU, Sadiq MI. Association of Severity of Diabetic Retinopathy with Levels of HbA1c. Pak J Med & Health Sci. 2022; 16(07):790-. DOI: https:// doi.org/10.53350/pjmhs22167790.
- 12. Melo LG, Morales PH, Drummond KR, Santos DC, Pizarro MH, Barros BS, et al. Current epidemiology of diabetic retinopathy in patients with type diabetes: a national multicenter study

in Brazil. BMC Pub Health. 2018; 18(1):1-9. doi:10.1186/s12889-018-5859-x.

- 13. Matsushita Y, Takeda N, Nakamura Y, Yoshida-Hata N, Yamamoto S, Noda M, et al. A Comparison of the Association of Fasting Plasma Glucose and HbA1c Levels with Diabetic Retinopathy in Japanese Men. J Diabet Res.2020;2020.3214676.doi:10.1155/2020/ 3214676.
- 14. Mathala N, Akula A, Hegde S, Bitra R, Sachedev V. Assessment of circulating biomarkers in relation to various stages of diabetic retinopathy in type 2 diabetic patients-a cross sectional study. Curr Diabet Rev. 2020; 16(4):402-9.doi:10.2174/1573399815666190 823155534.
- Andreasson R, Ekelund C, Landin-Olsson M, Nilsson C. HbA1c levels in children with type 1 diabetes and correlation to diabetic retinopathy. J Pediatric Endocrinol & Metabol. 2018; 31(4):369-74. doi: 10.1515/jpem-2017-0417.
- 16. Dhoot DS, Baker K, Saroj N, Vitti R, Berliner AJ, Metzig C, et al. Baseline factors affecting changes in diabetic retinopathy severity scale score after intravitreal aflibercept or laser for diabetic macular edema: post hoc analyses from VISTA and VIVID. Ophthalmology.2018; 125(1):51-6. doi:10.1016/j.ophtha.2017.06.0 29.

- Liu Y, Song Y, Tao L, Qiu W, Lv H, Jiang X, et al. Prevalence of diabetic retinopathy among 13473 patients with diabetes mellitus in China: a cross-sectional epidemiological survey in six provinces. BMJ open.2017;7(1):e013199. https ://doi.org/10.1136/bmjopen-2016-013199.
- Pereira DM, Shah A, D'Souza M, Simon P, George T, D'Souza N, et al. Quality of life in people with diabetic retinopathy: Indian study. J Clin & Diagn Res. 2017; 11(4):NC01-NC06. doi:10.7860/JCDR/2017/24496.9686.
- Song SJ, Han K, Lee SS, Park JB. Association between the number of natural teeth and diabetic retinopathy among type 2 diabetes mellitus: The Korea national health and nutrition examination survey. Medicine. 2017; 96(47):e8694. DOI: 10.1097/MD.000000000 008694.
- 20. López M, Cos FX, Álvarez-Guisasola F, Fuster E. Prevalence of diabetic retinopathy and its relationship with glomerular filtration rate and other risk factors in patients with type 2 diabetes mellitus in Spain. DM2 HOPE study. J Clin & Translat Endocrinol. 2017;29:9:61-65. doi:10. 1016/j.jcte.2017.07.004.
- 21. Foo V, Quah J, Cheung G, Tan NC, Ma Zar KL, Chan CM, et al. HbA1c, systolic blood pressure variability and diabetic retinopathy in Asian type 2 diabetics. J Diabetes. 2017;9(2):200-207. doi: 10.1111/1753-0407.12403.