ORIGINAL ARTICLE

CORRELATION OF HBA1C LEVEL WITH DIABETIC RETINOPATHY

Kainaat Talat[1]✉, Shahid Hamid Mahmud[1], Muhammad Fahad Ikram[2], Shehar Bano[1], Tariq Munawar[1], Abdul Rafeh[3]

[1]CMH, Kharian-Pakistan, [2]WAPDA Hospital, Mangla-Pakistan, [3]Avicenna Medical College, Lahore-Pakistan

Background: Diabetes mellitus (DM) is considered to be a significant universal public health issue. According to the American Society of Retina Specialists, diabetic retinopathy (DR) is a complication of diabetes that damages retinal blood vessels. A Japanese study showed that HbA1C values can be considered as predictors for the development of DR. Thus, this study aimed to determine the correlation between HbA1c level and Diabetic Retinopathy. **Methods:** A descriptive cross-sectional study was conducted at the Department of Ophthalmology, Combined Military Hospital Kharian, from February 2024 to July 2024. Patients of either gender between 40 to 80 years of age with type 2 diabetes mellitus were included in this study. Complete ophthalmic examination was carried out of each patient. HbA1c was measured by standardized assay using high performance liquid chromatography. The data was analyzed using Statistical Package for Social Sciences (SPSS) version 26. **Results:** Out of 246 patients, 42.7% were male and 57.3% female, with a mean age of 49.26±11.47 years and a mean HbA1c of 9.11±2.54. The overall prevalence of diabetic retinopathy (DR) was 57.7%, with 52.8% having NPDR and 49% PDR. DR prevalence increased with diabetes duration and was significantly higher in those with HbA1c levels between 7–9.9%(p=0.000). The logistic regression identified age, duration of diabetes, and HbA1c levels as critical factors associated with the risk of DR. The odds ratio for HbA1c indicates higher levels are associated with increased DR risk (p<0.005). **Conclusion:** This study concluded that duration of diabetes and HbA1c level are important risk factors for onset or progression of Diabetic retinopathy in type 2 Diabetes and the patients with poor glycaemic control had severe diabetic retinopathy as compared to the patients with good diabetic control. There is a direct relation between HbA1c level and the severity of diabetic retinopathy.

Keywords: HbA1c; Diabetic Retinopathy; Proliferative Diabetic retinopathy; Non-Proliferative Diabetic Retinopathy; Vitreous Haemorrhage

Citation: Talat K, Mahmud SH, Ikram MF, Bano S, Munawar T, Rafeh A. Correlation of HBA1C level with diabetic retinopathy. J Ayub Med Coll Abbottabad 2025;37(1):144–8.

DOI: 10.55519/JAMC-01-13925

INTRODUCTION

Type-2 diabetes mellitus consists of a range of dysfunctions characterized by increased blood glucose levels, resulting from the combined effect of insulin resistance, inadequate insulin secretion, and excessive or inappropriate glucagon secretion.[1] According to WHO, Diabetes Mellitus is a group of metabolic disorders characterized by hyperglycaemia resulting from defective insulin secretion, insulin resistance or both together. If a person has more than two readings of fasting blood glucose of ≥126 mg/dl or glycated haemoglobin (HbA1c) >6.5% or 2-hour post-prandial glucose level of >200 mg/dl, he is diagnosed as a case of Diabetes Mellitus.[2] Data shows that in 2017, 451 million people were having diabetes mellitus and by 2045, the cases are expected to be as high as 693 million due to the increasing trend towards sedentary lifestyle. This makes diabetes as one of the largest health issues of 21st century worldwide.[3] Inadequate glycaemic control and duration of diabetes are the most important risk factors among others for diabetic retinopathy. Other risk factors include obesity, hypertension, socioeconomic status, proteinuria, dyslipidaemia, and pregnancy.[4] Elevated HbA1c levels, which reflect the average blood glucose concentration over the past 2–3 months, have been consistently associated with an increased risk of diabetic retinopathy[5] and is considered an independent risk factor for diabetes complications.[6,7] Hyperglycaemia induces a series of inflammatory and ischemic changes include increased basement membrane thickness, neovascularization of retina, leukostasis and generation of fibrovascular tissue at the vitreoretinal interface leading to diabetic retinopathy.[8] Diabetic retinopathy (DR), including diabetic maculopathy, is a microvascular complication of DM and the leading cause of visual disability in adults of working age in developed countries.[9] Proliferative diabetic retinopathy affects 5–10% of diabetic patients.[10]

This study aims to assess the relationship between HbA1c levels and diabetic retinopathy in type 2 diabetes mellitus.

MATERIAL AND METHODS

After approval from institutional review board, written informed consent with demographic variables was collected from every patient. The study was conducted in a total of 246 patients between 40–80 years of age with type-II diabetes were included in this study, irrespective of their gender. The sample size was calculated by WHO criteria, keeping prevalence of 0.8%, 95% confidence interval and 5% of margin of error and 75% of response rate from our target population. Our inclusion criteria for the classification and diagnosis of DM were the new set criteria for diabetes adapted by American Diabetes Association (ADA) by in 1997 (1). Patients with secondary diabetes (acromegaly, Cushing's syndrome etc.) were not included in this study.

A descriptive cross-sectional study was conducted at the Department of Ophthalmology, Combined Military Hospital Kharian, from February to July 2024. Complete ocular examination including best corrected visual acuity, slit lamp biomicroscope, Goldmann Applanation tonometry and direct and indirect ophthalmoscopy of all the included patients was done by single classified eye specialist. Based on their fundoscopic findings they were classified into three groups as follow:

Group 1: No Diabetic Changes / DR (Normal fundus)
Group 2: NPDR
Group 3: PDR

HbA1c levels were classified in 4 groups as follow;

Group I: <6
Group II: 6.1–6.9
Group III: 7–9.9
Group IV: >10

According to the duration of diabetes the patients were divided into three groups. First group consisted of patients who were diabetic for

Group1: <5 years
Group 2: 6–10 years
Group 3: >10 years

Data was collected on specially designed Performa and analyzed using SPSS version 26. Frequency and percentages were used for categorical data while mean±SD was determined for numerical data. Chi-square test was used to compare categorical variables between groups of subjects. Logistic Regression analysis was performed to find out effective factors for the relationship between DR and, HbA1c and duration of diabetes with a p-value<0.05 considered to be statistically significant.

RESULTS

The demographic / clinical characteristics of the patients are presented in Table-1, out of 246 patients, 105(42.7%) are males and 141(57.3%) females. The mean age of patients is 49.26±11.47 years and mean HbA1c levels are 9.11±2.54. Out of 246 Diabetic patients, 3 groups are formed according to duration as 102 patients (41.55%) with <5 years, 79 patients (32.1%) with 6 and 10 years and 65 patients (26.4%) with >10 years. 21 patients (8.5%) had an HbA1c level of <6%, 8 (3.3%) between 6.1 and 6.9%, 150 (61%) between 7.0% and 7.9% and 67 (27.2%) >10%. In this study the overall frequency of Diabetic Retinopathy (DR) was 57.7% (52.8% have NPDR and 49% have PDR) whereas, (42.3%) have no DR.

In Table-2, DR observed higher trend in females as compared to males. Females have reported higher cases of NPDR 75(53.2%) and PDR 11(7.8%) than males (NPDR 55(52.8%) and PDR 1(0.9%).

When diabetic patients were grouped according to the duration of diabetes, those with diabetes for less than 5 years had the lowest number of NPDR cases, with 30 cases (29.4%). For patients with diabetes lasting between 6 and 10 years, 52 cases (65.8%) of NPDR were reported. The highest number of NPDR cases was observed in patients with diabetes for more than 10 years, with 48 cases (73.8%). A statistically significant difference of NPDR cases was found more in those patients who have diabetes for more than 10 years (p=0.000).

The frequency of DR varied according to HbA1c levels:

- In patients with an HbA1c of <6.0%, 11% (7 out of 142) had DR.
- In those with an HbA1c between 6.1% and 6.9%, 1.4% (2 out of 142) had DR.
- In patients with an HbA1c between 7% and 9.9%, 59.2% (84 out of 142) had DR.
- In patients with an HbA1c >10%, 31.7% (45 out of 142) had DR.

A statistically significant difference in DR frequency was found, with a higher prevalence of DR in patients with HbA1c levels between 7% and 9.9% (p=0.000).

The results of the logistic regression analysis indicated that the overall model goodness-of-fit was significant, with a p-value of 0.005.

- Age: Significant predictor with a chi-square value of 80.7, p< 0.000.
- Duration of Diabetes: Strongly predictive with a chi-square value of 62.4, p<0.000.
- HbA1c Levels: Significant predictor with a chi-square value of 24.1, p=0.005.
- Gender: Lesser influence with an odds ratio of 1.36 (95% CI:0.820–2.282), indicating no statistical significance.

The odds ratio for gender of 1.36 suggests a positive association between being female and having DR, but the wide confidence interval (0.820–2.282) means that this result is not statistically significant. The effect could be small or could be due to random variability in the sample data. The odds ratio for the duration of

diabetes group with a 95% CI is 0.056 (-3.692–1.663), and the odds ratio for HbA1c levels with a 95% CI is 0.186 (0.014–0.233).

The logistic regression identified age, duration of diabetes, and HbA1c levels as critical factors associated with the risk of DR. The odds ratio for HbA1c indicates higher levels are associated with increased DR risk.

Table-4 shows sensitivity and specificity for Diabetic Retinopathy (DR) at different HbA1c cutoffs. The area under the curve (AUC) is 0.554 which is not acceptable & represents a model with low sensitivity and low specificity shown in Fig-1.

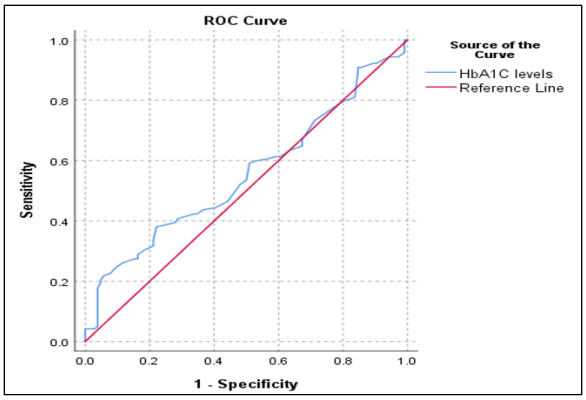

Figure-1: ROC curve of Sensitivity & Specificity of HbA1c levels

Table-1: Demographic variables

Characteristics	No. of Patients (%)
Gender	
Male	105 (42.7%)
Female	141 (57.3%)
Age (in years)	49.26±11.47
HbA1c levels	9.11±2.54
Diabetes Groups	
<5 years	102 (41.5%)
6 to 10 years	79 (32.1%)
>10 years	65 (26.4%)
HbA1c levels Grouping	
Group I	21 (8.5%)
Group II	8 (3.3%)
Group III	150 (61%)
Group IV	67 (27.2%)
Diabetic Retinopathy (DR)	
No DR	104 (42.3%)
DR	142 (57.7%)
DR Stages	
No DR	104 (42.3%)
NPDR	130 (52.8%)
PDR	12 (4.9%)

Table-2: Relationship between Clinical characteristics and Diabetic Retinopathy (DR)

Characteristics	No. of Patients (%)	No. of Patients with DR			*p*-value
Gender		No DR	NPDR	PDR	0.036*
Male	105 (42.6%)	49(46.6%)	55(52.3%)	1(0.95%)	
Female	141 (57.3%)	55(39%)	75(53.1%)	11(7.8%)	
Diabetes Groups					0.000*
<5 years	102 (41.4%)	71(69.6%)	30(29.4%)	1(0.98%)	
6–10 years	79 (32.1%)	27(34.1%)	52(65.8%)	0	
>10 years	65 (26.4%)	6(9.2%)	48(73.8%)	11(16.9%)	
HbA1c levels Groups					0.000*
Group I (<6)	21 (8.5%)	10(47.6%)	11(52.3%)	0	
Group II (6.1–6.9)	8 (3.2%)	6(75%)	2(25%)	0	
Group III (7–9.9)	150 (60.9%)	66(44%)	82(54.6%)	2(1.3%)	
Group IV (>10)	67 (27.2%)	22(32.8%)	35(52.2%)	10(14.9%)	

Table 3: Relationship between of HbA1c levels with Diabetic Retinopathy (DR)

Variables	No. of Patients (%)	No. of Patients with DR (%)	
HbA1c levels Groups		No DR	DR
Group I (<6 mmol/mol)	21(8.5%)	10(9.6%)	11(7.7%)
Group II (6.1 – 6.9 mmol/mol)	8(3.3%)	6(5.8%)	2(1.4%)
Group III (7 - 9.9 mmol/mol)	150(61%)	66(63.5%)	84(59.2%)
Group IV (>10 mmol/mol)	67(27.2%)	22(21.2%)	45(31.7%)
Total	246 (100%)	104(100%)	142(100%)

Table-4: Sensitivity & Specificity of HbA1c levels with Diabetic Retinopathy (DR)

Variables	No. of Patients (%)	No. of Patients with DR (%)		Sensitivity (%)	Specificity (%)
HbA1c levels		No DR	DR		
Group I (<6 mmol/mol)	21(8.5%)	10(9.6%)	11(7.7%)	97%	98%
Group II (6.1 – 6.9 mmol/mol)	8(3.3%)	6(5.8%)	2(1.4%)	92%	88%
Group III (7 - 9.9 mmol/mol)	150(61%)	66(63.5%)	84(59.2%)	57%	52%
Group IV (>10 mmol/mol)	67(27.2%)	22(21.2%)	45(31.7%)	16%	7%

DISCUSSION

DR is a specific microvascular complication of diabetes.[11,12] The type and duration of diabetes, hyperglycaemia, dyslipidaemia and increased blood pressure are well known associated risk factors for development and progression of DR. Diabetic retinopathy is the leading cause of blindness and early predictor of cascading complications.[13]

HbA1C measurement is regarded as the "gold standard" indicator for glycemic control in diabetic patients, reflecting glucose levels over a 2–3 months period.[14] At present, the target HbA1C level differs in various diabetes guidelines worldwide. According to guidelines of American diabetes association, the target HbA1C level should be <7.5% in children and <7% in adults.[15] Whereas in UK, recommended HbA1C level by National Institute for Health and Care Excellence is <6.5% for children and adults both.[16] The International Society for Paediatric and Adolescent Diabetes further reduces the target HbA1C level to <7%.[17]

In this study the frequency of diabetic retinopathy, both NPDR and PDR was higher (59.2%) in the group with HbA1C level of more than 7%, while in the group with HbA1C level less than 6.0%, the frequency was low (7.7%). Our findings were consistent with another cross-sectional study that found the potential to develop DR in patients with an HbA1c ≥7% was 17.5 times more than those with good control.[18] Another study reported that patients with an HbA1c ≥7% were 1.9 times more likely to have DR than those with an HbA1c <7%.[17] Our data demonstrate a correlation of lower HbA1C levels with a lower frequency of DR. By reducing the blood glucose or HbA1C concentrations in patients with diabetes reduces the rate of progression of microvascular complication such as DR, nephropathy and neuropathy.[19–21]

In our study, the frequency of DR was 57.7% (52.8% have NPDR and 4.9% have PDR). According to the IDF, China (140.9 million), India (74.2 million), Pakistan (33.0 million), and the USA (32.2 million) had the highest number of diabetics in 2021.[22] A systematic review and meta-analysis performed by Yang *et al*. in Asian patients with Type 2 Diabetes, determined a prevalence of DR of 28% of which 6% suffered from PDR and 27% were affected by NPDR, the prevalence of PDR and NPDR in patients already diagnosed with DR was 17% and 83%, respectively.[23] The most important risk factor for DR is the duration. [24] The Cox regression model relates the severity of retinopathy to longer duration, older age at examination, and higher levels of glycosylated haemoglobin for persons with diabetes of 10 years' duration or less.[5] Our study also indicates an association between longer duration of diabetes and increased frequency of retinopathy. More NPDR and DR frequency was found among those who have diabetes for more than ten years duration.

This study comprising of 105 (42.6%) males and 141 (57.3%) females. We found that the female patients in our study were more likely to have diabetic retinopathy than males. However, there was no statistically significant association between DR and gender (OR: 1.36, 95% CI: 0.820-2.282, p= 0.0036), aligning with previous studies by Valizadeh *et al.* [26], and Badawi *et al.*[18], showing inconclusive evidence of gender's role in DR development.

CONCLUSION

This study stated that the frequency of DR was 57.7% (52.8% have NPDR and 4.9% have PDR). There was a strong relationship between duration of diabetes and DR (p=0.000) and a similar relationship between HbA1C and DR (p=0.000). Our findings contribute that by reducing the HbA1C levels or achieving ADA criteria can prevent or delay the onset / or progression of microvascular complications such as diabetic retinopathy. Regular screening for diabetic retinopathy and tighter glycaemic control could reduce the frequency of vision-threating retinopathy.

Limitation of Study

The study sample was small to extrapolate to regional and national trends. Treatment modalities and their cost implications were not discussed. Long term follow up and outcome of the treatment modalities was not discussed.

Conflict of Interest

There was no conflict of interest among the authors.

AUTHORS' CONTRIBUTION

KT, MFI, SB: Obtained the literature search, conceptualization of the study design, data collection, analysis, interpretation and write-up. SHM, TM, AR: Contributed to conceptualization of the study design, data analysis, write-up and proof reading.

REFERENCES

1. Medscape. Diabetic Retinopathy Overview [Internet]. [cited 2025 Jan 21]. Available from: https://emedicine.medscape.com/article/117853-overview?form=fpf
2. Powers A, Niswender K, Molina C. Diabetes mellitus: diagnosis, classification, and pathophysiology. In: Kasper DL, Fauci AS, Hauser SL, Longo DL, Jameson JL, Loscalzo J, editors. Harrison's principles of internal medicine. 20th ed. New York: McGraw-Hill Medical. 2020; p.2580–8.
3. 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. Diabetes Res Clin Pract 2018;138:271–81.
4. Fong DS, Aiello L, Gardner TW, King GL, Blankenship G, Cavallerano JD, *et al*. Retinopathy in diabetes. Diabetes Care 2004;27(Suppl 1):S84–7.
5. Klein R, Klein BE, Moss SE, Davis MD, DeMets DL. The Wisconsin epidemiologic study of diabetic retinopathy. II. Prevalence and risk of diabetic retinopathy when age at diagnosis is less than 30 years. Arch Ophthalmol 1984;102(4):520–6.
6. Wang SY, Andrews CA, Herman WH, Gardner TW, Stein JD. Incidence and risk factors for developing diabetic retinopathy among youths with type 1 or type 2 diabetes throughout the United States. Ophthalmology 2017;124(4):424–30.
7. Nordwall M, Abrahamsson M, Dhir M, Fredrikson M. Impact of HbA1c, followed from onset of type 1 diabetes, on the development of severe retinopathy and nephropathy: the VISS Study (Vascular Diabetic Complications in Southeast Sweden). Diabetes Care 2015;38(2):308–15.
8. ValdezGuerrero AS, Quintana-Pérez JC, Arellano-Mendoza MG, Castañeda-Ibarra FJ, Tamay-Cach F, Alemán-González-Duhart D. Diabetic retinopathy: important biochemical alterations and the main treatment strategies. Can J Diabetes 2021;45(6):504–11.
9. Mohamed Q, Gillies MC, Wong TY. Management of diabetic retinopathy: a systematic review. JAMA 2007;298(8):902–16.
10. Rawat D. Retinopathy and its associated factors in type 2 diabetes mellitus in rural population of central India. J Med Sci Clin Res 2019;7(6):e69.
11. Kohner EM, Aldington SJ, Stratton IM, Manley SE, Holman RR, Turner RC. United Kingdom Prospective Diabetes Study, 30: diabetic retinopathy at diagnosis of non-insulin-dependent diabetes mellitus and associated risk factors. Arch Ophthalmol 1998;116:297–303.
12. Bate KL, Jerums G. Preventing complications of diabetes. Med J Aust 2003;179(9):498–503.
13. Kropp M, Golubnitschaja O, Mazurakova A, Koklesova L, Sargheini N, Vo T-TK S, *et al*. Diabetic retinopathy: molecular mechanisms, potential therapeutic targets, and experimental strategies. Front Mol Biosci 2023;10:1082061.
14. Khaw KT, Wareham N, Luben R, Bingham S, Oakes S, Welch A, *et al*. Glycated haemoglobin, diabetes, and mortality in men in the Norfolk cohort of the European Prospective Investigation of Cancer and Nutrition (EPIC-Norfolk). BMJ 2003;322(7277):15–8.
15. American Diabetes Association. 6. Glycemic targets: standards of medical care in diabetes-2018. Diabetes Care 2018;41(Suppl 1):S55–64.
16. National Institute for Health and Care Excellence. Type 1 diabetes in adults: diagnosis and management. NICE guideline; 26 August 2015. [Internet]. [cited 2019 Jul 9]. Available from: https://www.nice.org.uk/guidance/ng17
17. DiMeglio LA, Acerini CL, Codner E, Craig ME, Hofer SE, Pillay K, *et al*. ISPAD Clinical Practice Consensus Guidelines 2018: glycemic control targets and glucose monitoring for children, adolescents, and young adults with diabetes. Pediatr Diabetes 2018;19(Suppl 27):105–14.
18. Badawi AH, Al-barry M, Abusayf M, Rashwan M, Alghamdi A, Alsebaee A. Prevalence and risk factors of diabetic retinopathy: a clinical-based cross-sectional study in Madinah's Tertiary Diabetic Center, Saudi Arabia. Int J Sci Res 2016;5:587–90.
19. American Diabetes Association. Standards of medical care in diabetes. Diabetes Care 2004;27(Suppl 1):S15–35.
20. Fong DS, Aiello LP, Ferris FL, Klein R. Diabetic retinopathy. Diabetes Care 2004;27(10):2540–53.
21. International Diabetes Federation. IDF Diabetes Atlas. 10th ed. Brussels: International Diabetes Federation; 2021.
22. Yang QH, Zhang Y, Zhang XM, Li XR. Prevalence of diabetic retinopathy, proliferative diabetic retinopathy and non-proliferative diabetic retinopathy in Asian T2DM patients: a systematic review and Meta-analysis. Int J Ophthalmol 2019;12(2):302–11.
23. Vinker S, Shpiz M, Elhayany A, Nakar S. Improvement of early detection of diabetic retinopathy—a primary care intervention study. Harefuah 2003;142(12):826–8.
24. Valizadeh R, Moosazadeh M, Bahaadini K, Vali L, Lashkari T, Amiresmaili M. Determining the prevalence of retinopathy and its related factors among patients with type 2 diabetes in Kerman, Iran. Osong Public Health Res Perspect 2016;7(5):296–300.

Submitted: October 11, 2024	*Revised: January 21, 2025*	*Accepted: February 3, 2025*

Address for Correspondence:

Dr. Kainaat Talat, House No. 1/786, MP Checkpost Housing Society Mangla Cantt, District Jhelum-Pakistan
Cell: +92 305 862 2894/ +92 332 972 2267
Email: kainaat.talat@gmail.com