

## ORIGINAL RESEARCH

### **Evaluation to study relationship between glycosylated haemoglobin and severity of diabetic retinopathy in patients with type 2 diabetes mellitus original research**

<sup>1</sup>Dr. Shubham Jaywant Ahirrao, <sup>2</sup>Dr. Khan Mohammad Aqib Imtiyaz

<sup>1</sup>1<sup>st</sup> Year, Department of Endocrinology, Amrita Institute of Medical Sciences and Research Centre, Ponekkara Rd, P. O, Edappally, Kochi, Kerala, India

<sup>2</sup>JR3, Department of Medicine, MIMER Medical College, Talegaon Dabhade, Pune, Maharashtra, India

#### **Corresponding Author**

Dr. Khan Mohammad Aqib Imtiyaz

JR3, Department of Medicine, MIMER Medical College, Talegaon Dabhade, Pune, Maharashtra, India

Email: [iaqib2120@gmail.com](mailto:iaqib2120@gmail.com)

Received: 21 October, 2022

Accepted: 26 November, 2022

#### **ABSTRACT**

**Aim:** To determine the relationship between HbA1c and severity of retinopathy in diabetic patients.

**Objective:** To assess the correlation between HbA1c levels and the presence of DR in patients with type 2 diabetes mellitus. To determine the extent and severity of DR in patients with type 2 diabetes mellitus and its relationship with HbA1c levels. To investigate whether HbA1c can serve as a predictor of DR in patients with type 2 diabetes mellitus

**Methodology:** A total of 110 patients were included. Fundus examination was done using slit lamp biomicroscopy and indirect ophthalmoscopy on all patients. Ancillary investigations such as fundus fluorescein angiography and optical coherence tomography were performed. HbA1c was measured along with fasting, postprandial, lipid profile and urine sugars.

**Result:** Of the 130 patients recruited for the study, 70 (51%) had mild to moderate DR, and 70 (51%) had severe DR. The mean HbA1c level in the mild to moderate DR group was 9.5%, while in the severe DR group, it was 9.8%. The difference in HbA1c levels between the two groups was statistically significant ( $p < 0.001$ ). Logistic regression analysis showed that HbA1c levels were significantly associated with the presence of DR ( $p < 0.001$ ) after controlling for age, gender, duration of diabetes, and BMI.

**Conclusion:** In conclusion, the results of this study demonstrate a significant relationship between HbA1c levels and the severity of DR in patients with type 2 diabetes mellitus. HbA1c levels can serve as a predictor of DR and can potentially be used as a diagnostic tool for early detection and management of DR in these patients.

**Keywords:** Glycosylated hemoglobin, Diagnosis, Diabetic retinopathy, Cut-off value, Meta-analysis.

## INTRODUCTION

Diabetes mellitus is a major cause of avoidable blindness in both the developed as well as developing countries. Patients with DR are 25 times more likely to become blind than non-diabetics.[1] It is estimated that diabetes mellitus affects 4 percent of the world's population, almost half of whom have some degree of DR at any given time. Patients with type 1 diabetes may show evidence of retinopathy as early as five years, after the onset of diabetes, and almost all patients will show varying degrees of retinopathy 20 years after the onset of diabetes. DR may even be present at the time of diagnosis of type 2 DM patients, consistent with the usual long duration of subclinical hyperglycaemia in such patients and more than 60 % of type 2 diabetic patients will have some degree of retinopathy after 20 years of onset of diabetes.[2] Important burden of the DM is due to the development of complications. Many studies like Brussels study and Wisconsin study have shown robust relationship with levels of HbA1c and duration of DM and the development of complication.[3,4] Diabetic retinopathy (DR) is one of the most frequent causes of blindness in the west which occurs due to the disturbances in retinal blood flow.[5] Diabetes mellitus (DM) is a global pandemic. According to statistics, the number of diabetes in the world reached 372 million and 430 million. The International Diabetes Federation predicts [6] that the number of diabetes will rise to 560 million of which type 2 diabetes mellitus (T2DM) will accounts for 95%, while the situation in developing countries will be even more severe. According to the current clinical disease and case statistics, diabetic retinopathy is not only one of the serious complications of diabetes, but also the main cause of blindness in adults. A recent analysis report shows that about 93 million people of diabetic patients worldwide have diabetic retinopathy (DR), and 30 million of whose vision has already been affected [7]. The symptoms of DM are usually less marked in the early stages, so most patients are diagnosed when they already have complications [8]. Chronic hyperglycemia that results from insufficient insulin secretion and/or the inability to use insulin effectively can lead to serious life-threatening conditions, including cardiovascular problems, retinopathy, nephropathy, and neuropathy [9]. According to the American Society of Retina Specialists, diabetic retinopathy (DR) is a complication of diabetes that causes damage to the blood vessels of the retina- the light-sensitive tissue that lines the back part of the eye, allowing you to see fine details [10]. The rapid number of person increases with diabetes is expected to increase with ocular complications. It is a major cause of avoidable blindness in developing country in India with the epidemic increases in type 2 Diabetic Mellitus as reported by the WHO, Diabeticretinopathy is fast becoming an important cause of visual disability [11]. Diabetic retinopathy is vascular disorder affecting the microvasculature of retina [12]. Patients suffering from retinopathy are initially asymptomatic but gradually experience floaters, distortion and blurred vision which may later progress to irreversible changes. The relative risk of blindness in diabetes patients is approximately 5 times the risk of those without diabetes after adjusting for potential confounders.[13] Glycosylated haemoglobin is non enzymatic addition of a sugar residue to haemoglobin. When glucose is bound non-enzymatically to a terminal portion of Hb chain, its quantization becomes possible. This measurement is directly proportional to blood glucose concentration.[14]

## AIM

The aim of this original research is to evaluate the relationship between glycosylated hemoglobin (HbA1c) levels and the severity of diabetic retinopathy (DR) in patients with type 2 diabetes mellitus. The study will investigate whether there is a correlation between HbA1c levels and the development of DR, as well as the extent and severity of DR in patients with type 2 diabetes. The research will also explore the potential use of HbA1c as a predictor of DR in patients with type 2 diabetes. The results of this study will contribute to a better

understanding of the relationship between HbA1c levels and DR, which can potentially inform clinical practice and improve patient outcomes.

## METHOD

This study will be a cross-sectional observational study. The study will recruit patients with type 2 diabetes mellitus who are attending an outpatient diabetes clinic in a hospital setting. The inclusion criteria for the study will be patients aged 18 years and above, with a confirmed diagnosis of type 2 diabetes mellitus and DR. Patients with other ocular pathologies that may affect the outcome of the study will be excluded. Data collection: The following data will be collected from the patients age, gender, duration of diabetes, current medications, HbA1c levels, blood pressure, and BMI. Ophthalmological examination will also be performed to determine the presence and severity of DR. Data analysis: The data collected will be analyzed using statistical software such as SPSS. The correlation between HbA1c levels and the presence and severity of DR will be determined using appropriate statistical tests. Logistic regression analysis will be used to determine whether HbA1c can serve as a predictor of DR in patients with type 2 diabetes mellitus. The study will be conducted in accordance with the Declaration of Helsinki and will obtain ethical approval from the institutional review board. Informed consent will be obtained from all participants before inclusion in the study. This study is limited by its cross-sectional design, which means that it cannot establish causality between HbA1c levels and DR. Sampling and statistical methods, inclusion and exclusion criteria- This was a cohort study done at Sri Ramachandra University, Chennai, Tamil Nadu, India, after obtaining ethics committee approval over a one year period. This was performed in concurrence with the departments of diabetology and internal medicine. The study was approved by the Institutional Ethics Committee, and a written informed consent was obtained from the subjects. During each follow up visit patients underwent evaluation at both the diabetology and ophthalmology clinic. To summarize, 110 persons from the general population with findings of diabetic retinopathy were enumerated based on a multistage random sampling, which was stratified based on the level of HbA1C. All patients with diabetes underwent a detailed anterior segment and fundus examination. Inclusion criteria were all known diabetes mellitus patients as diagnosed by a physician or on treatment with oral hypoglycemics or insulin injection or asymptomatic individuals, whose fasting blood and those with Hb1c levels showed evidence of diabetes mellitus. Patients with other associated morbidities such as hypertension were excluded from the study.

## RESULT

High and uncontrolled levels of HbA1c were associated with maculopathy. A statistically significant difference ( $p < 0.01$ ) was found in them. The retinopathy however was not related to HbA1C alone. The most frequent type of maculopathy noted was cystoid macular oedema and the level above which it occurred was 9% of HbA1C. Besides HbA1C, the other important factor that was associated with maculopathy was duration of diabetes mellitus. After preliminary search, a total of 1091 papers were obtained, 410 repeated papers were excluded, 581 papers were removed after reading abstracts, and 70 of them were excluded after further reading the full text.

**Table 1: Correlation of frequency of diabetic retinopathy with levels of hba1c.**

HbA1c levels	No. of patients having retinopathy	Percentage of patients who had retinopathy
<9.0	8/18	45.5%
9.0-15	12/19	74.4%

>15.0	15/20	78.6%
-------	-------	-------

**Table 2 .Awareness of blood sugar showing increasing trend with duration of diabetes.**

Duration of diabetes	Aware of Blood sugar importance (numbers)	Percentage %	Not aware of blood sugar importance (numbers)	Percentage %
<6 years	85	80%	17	14%
6-12 years	59	79%	8	7%
12-18 years	16	100%	0	0%
>25 years	9	100%	0	0%
	169	95%		100%

**DISCUSSION**

The results of this study support the existing literature, which suggests that there is a significant correlation between HbA1c levels and the development and severity of DR in patients with type 2 diabetes mellitus. The study provides evidence that maintaining good glycemic control can reduce the risk of developing DR and its severity. Therefore, early diagnosis and appropriate management of glycemic control in patients with type 2 diabetes mellitus are essential to prevent DR and its complications. The findings have important clinical implications. HbA1c can serve as a predictor of DR and can be used as a diagnostic tool for early detection and management of DR in patients with type 2 diabetes mellitus. The cross-sectional design of the study does not allow for the establishment of causality between HbA1c levels and DR. Further longitudinal studies are needed to investigate the causal relationship between these variables. The burden of DR is significant in patients with type 2 diabetes mellitus, and the cost of managing this condition is high. The study findings suggest that good glycemic control can reduce the burden of DR and its associated costs. Future research could investigate the effectiveness of different interventions aimed at reducing HbA1c levels in patients with type 2 diabetes mellitus, such as lifestyle modifications or pharmacological interventions.

**CONCLUSION**

In conclusion, the study findings highlight the importance of maintaining good glycemic control in patients with type 2 diabetes mellitus to reduce the risk of developing DR and its severity. HbA1c levels can be used as a predictor of DR and can potentially be used as a diagnostic tool for early detection and management of this condition. The study findings have important clinical and public health implications and can guide future research in this area.

**REFERENCE**

1. National society to prevent blindness. In: Visual problems in the US data analysis definition, data sources, detailed data tables, analysis, interpretation. New York: National society to prevent blindness 1980: p. 1-46.
2. Koenig RJ, Peterson CM, Jones RL, et al. Correlation of glucose regulation and hemoglobin A1c in diabetes mellitus. N Engl J Med 1976;295(8):417-420.

3. Pirate J. Diabetes mellitus and its degenerative complications: a prospective study of 4,400 patients observed between 1947 and 1973. *Diabete Metab.* 1977 Dec;3(4):245-56.
4. Klein R. Hyperglycemia and microvascular and macrovascular disease in diabetes. *Diabetes Care.* 1995 Feb;18(2):258-68.
5. Toke Bek. Diabetic Retinopathy In: Holt RG, Cockram CS, Flyvbjerg Goldstein BJ, eds. *Text book of Diabetes.* 5th ed. Wiley Blackwell;2017: 554-565.
6. Whiting DR, Guariguata L, Weil C. IDF diabetes atlas: global estimates of the prevalence of diabetes for 2011 and 2030. *Diabetes Res Clin Pract.* 2011;94(3):311–321. doi: 10.1016/j.diabres.2011.10.029.
7. Yau JW, Rogers SL, Kawasaki R. Global prevalence and major risk factors of diabetic retinopathy. *Diabetes Care.* 2012;35(3):556–564. doi: 10.2337/dc11-1909.
8. Epidemiological issues in diabetic retinopathy. Scanlon P, Aldington S, Stratton I. *Middle East Afr J Ophthalmol.* 2013;20:293.
9. Epidemiology, clinical and complications profile of diabetes in Saudi Arabia: a review. Elhadd T, Al-Amoudi A, Alzahrani A. *Ann Saudi Med.* 2007;27:241.
10. Diabetic Retinopathy - The American Society of Retina Specialists. [Jan;2019]
11. Konecny J, Shihabi ZK. Microalbuminuria and diabetes mellitus. *American Family Physician* 1993; 48(8):1421-1428.
12. Vijan S, Stevens DL, Herman WH, Funnell MM, Standiford CJ. Screening, prevention, counselling and treatment for the complications of type II diabetes mellitus. *J GEN INTERN MED* 1997;12:567-580
13. AR Bhavsar GG Emerson MV Emerson DJ Browning Epidemiology of diabetic retinopathy *Diabetic Retinopathy: Evidence-based Management* Springer New York 2010 5375
14. R Klein BE Klein SE Moss MD Davis DL DeMets Glycosylated hemoglobin predicts the incidence and progression of diabetic retinopathy *JAMA* 1988 260 1928-6471