DOI: https://doi.org/10.53350/pjmhs22164788

ORIGINAL ARTICLE

Co-Relation of HBA1C Level with Diabetic Retinopathy on Fundoscopy in Patients Suffering from Type-II DM for more than 10 years Duration

SYED ANEES AHMED GARDEZI[1], NAJMUSAQIB KHAN NIAZI[1], SYED HAIDER TIRMIZI[1], IFFAT RAFIQUE[1], RABIA SADIQ[1], MUNEEB UR REHMAN[1], TALHA LAIQUE[2]
[1]*Department of Medicine, Combined Military Hospital, Kharian- Pakistan*
[2]*Department of Pharmacology, Allama Iqbal Medical College, Lahore-Pakistan*
Correspondence to: Talha Laique, Email: talhalaique51@gmail.com, Cell:+92-331-0346682

ABSTRACT

Defects in insulin secretion or its metabolic functionality results in increased levels of glucose causing metabolic disorders.
Aims: To check the Co- relation of HbA1c level with diabetic retinopathy on fundoscopy in patients suffering from Type II DM for more than 10 years duration.
Study Design: Cross sectional study.
Methodology: Patients (n=61) who were diagnosed cases of diabetes mellitus type II according to American diabetes association guidelines for the past 10 years were included into the study. HbA1c was assessed on autoanalyzer from Roche and NGSP certified using turbidimetric inhibition immunoassay (TINIA) method of hemolyzed blood samples. Eye examination of patients were carried out by expert ophthalmologist after proper pupillary dialatation was carried out. After proper fundoscopy patients were classified into four stages of diabetic retinopathy based on ETDRS levels.
Statistical analysis: Data was analyzed using SPSS version 26. Results were presented as frequency and percentage. Age was presented as mean± SD.
Results: Out of 61 patients 38 (62.3%) were male and 23 (37.7%) were female. HbA1c levels and diabetic retinopathy showed a statistically significant association when assessed using chi square test (p=0.001). Comparison of HbA1c levels among various groups based on diabetic retinopathy grading revealed a statistically significant difference (p=0.001).
Conclusion: It was concluded that HbA1c levels and diabetic retinopathy were significantly associated. Higher levels of HbA1c which reflected the poor glycemic control that can be used as a predictor for the severity of developing retinopathy.
Keywords: Diabetes Mellitus, Diabetic Retinopathy, Fundoscopy, Microvascular Complication and Type-II Diabetes Mellitus

INTRODUCTION

Defects in insulin secretion or its metabolic functionality results in increased levels of glucose causing a group of metabolic disorders termed as diabetes mellitus. It is one of the wide spread chronic problem affecting all age groups, all areas whether urban or rural. The prevalence of type II diabetes is as high as 11.7% in Pakistan[1]. It is more prevalent in males as compared to females. Area wise distribution suggests a common occurance in urban areas as compared to rural areas. Many health care programs have been developed to decrease the global burden of this disease[2].

Type II diabetes mellitus is usually diagnosed with HbA1c levels which is basically the levels of glycated haemoglobin[3]. It reveals the average blood sugar levels for past two to three months. Diabetes mellitus constitutes a myriad of complications which occur solely or in combination with other systemic disorders. These complications include cardiovascular problems neuropathy, hearing impairment and many microvascular complications such as retinopathy and nephropathy[4]. The most commonly occurring microvascular complication among all these is the diabetic retinopathy.

Diabetic retinopathy is caused by an underlying increased levels of blood glucose for prolonged duration causing a damage to the retina. If left untreated it may lead to blindness[5]. Retinal images obtained on fundoscopy mainly aid in diagnosing this condition. For disease staging and categorization colour fundus photography is used. For treatment planning and to visualize the extent of disease fluorescein angiography is utilized[6]. As the burden of diabetes is increasing with time so are the complications associated with it as many of them remain undiagnosed and present later with greater severity[7]. Due to its increasing prevalence and debilitating effect on the quality of life of the patients, we designed this study. Thus it will help the clinicians to categorize the patients who are more prone to developing this complication based on the levels of HbA1c and it can also be used as a tool for risk assessment.

Objectives: To check the Co- relation of HbA1c level with diabetic retinopathy on fundoscopy in patients suffering from Type II DM for more than 10 years duration.

METHODOLOGY

Present study was a descriptive cross sectional study. Informed consent was taken from the patients or guardians prior to enrolling the patients into the study. A Sample size of 61 was calculated considering the correlation coefficient of 0.354 between mean HbA1c levels and development of retinopathy in children with type I diabetes taken from a study conducted by Rebecka et al[8].

Non-probability consecutive sampling technique was used. Patients who were diagnosed cases of diabetes mellitus type II according to American diabetes association guidelines (with fasting plasma glucose levels ≤126 mg/dl or random plasma glucose level ≤ 200mg/dl) for the past 10 years were included into the study. Patients with other associated comorbid conditions like renal failure (acute or chronic), secondary diabetes (due to cushing syndrome or acromegaly) and ocular disorders which would likely interfere with diagnosis of retinopathy like cataract were excluded from the study. Also patients with active signs of infection/ inflammation, hypertension, cardiac failure were also excluded in the study.

Patients whose samples were collected and analysed had an Informed consent signed prior to starting the study. 3-4 ml of venous sample was obtained in EDTA vials under aseptic conditions. HbA1c was assessed on autoanalyzer from Roche and NGSP certified using turbidimetric inhibition immunoassay (TINIA) method of hemolyzed blood samples. Patients were divided into three groups based on the HbA1c levels. Very good control group (HbA1c <7), good control group (HbA1c between 7-8) and poor control group (HbA1c >8).

Eye examination of patients were carried out by expert ophthalmologist after proper pupillary dialatation was carried out. After proper fundoscopy patients were classified into four stages of diabetic retinopathy based on ETDRS levels. Mild non proliferative diabetic retinopathy (NPDR), moderate NPDR, severe NPDR and proliferative diabetic retinopathy (PDR). BMI was also recorded.

Statistical Analysis: Data was analyzed using SPSS version 26.0. Mean and SD will be calculated for variables such as Age and HbA1c levels. Percentage and Frequency was calculated for variables (categorical) such as gender and patients falling in different categories of diabetic retinopathy and HbA1c levels. Data Normality was assessed using Shapiro wilk test, which showed a

parametric distribution of data. Chi square test was used for assessing association between HbA1c level and diabetic retinopathy. Pearson correlation was used for assessing correlation between HbA1c levels and BMI. Difference in HbA1c level and BMI between genders was assessed by independent samples T test. One way ANOVA was used to compare HbA1c levels among 4 groups based on diabetic retinopathy grading. p value of ≤0.05 was considered to be significant.

RESULTS

Out of 61 patients 38 (62.3%) were male and 23 (37.7%) were female. Mean age of patients was 65.7 years with a range of 47 to 84 years. Mean HbA1c levels were 7.46% with a range of 4.30-10.60%. BMI falls in the range of 23-39 kg/m^2 with a mean value of 29.21 kg/m^2. Patient distribution based on HbA1c levels and diabetic retinopathy grading was shown in figure-1 & 2.

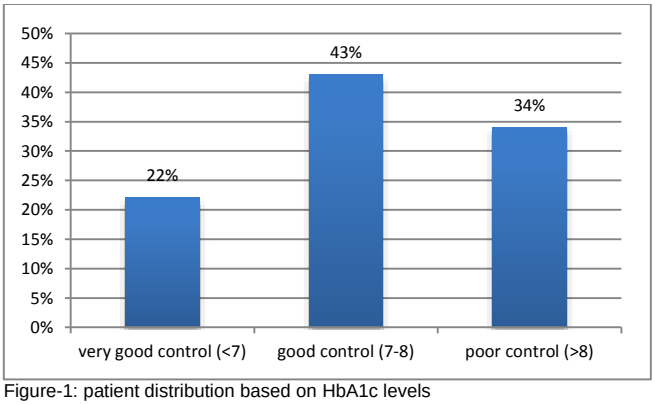

Figure-1: patient distribution based on HbA1c levels

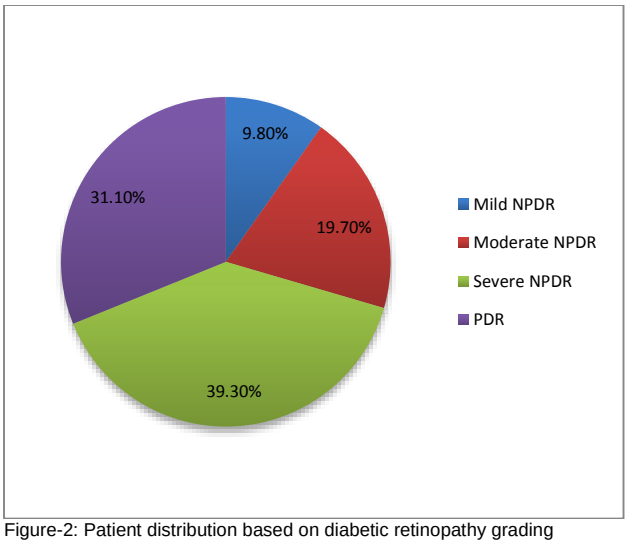

Figure-2: Patient distribution based on diabetic retinopathy grading

HbA1c levels and diabetic retinopathy showed a statistically significant association when assessed using chi square test (p=0.001) as shown in Table-1

Table-1: Association of Diabetic retinopathy and HbA1c levels.

		Diabetic retinopathy group					
	Groups	Mild NPDR	Moderate NPDR	Severe NPDR	PDR	Total	
HbA1c level	Very good control (<7)	6	8	0	0	14	P value
	Good control (7-8)	0	4	20	2	26	
	Poor control (>8)	0	0	4	17	21	0.001*
	Total	6	12	24	19	61	

*Statistically significant

When HbA1c levels and BMI were compared among male and female patients a statistically insignificant difference was observed in HbA1c levels among these two groups (p=0.7). BMI levels however showed statistically significant increase in female group as compared to male patients (p=0.005) as shown in Table-2.

Table-2: Comparison of BMI and HbA1c levels among male and female patients.

Parameter	Male (n=38)	Female (n=23)	p Value
HbA1c level (%)	7.19 ± 1.25	7.93 ± 1.48	0.7
BMI (kg/m^2)	28.3 ± 2.5	30.60 ± 4.03	0.005*

*Statistically significant

Comparison of HbA1c levels among various groups based on diabetic retinopathy grading revealed a statistically significant difference (p=0.001) as shown in Table-3.

Table-3: Comparison of HbA1c levels among various diabetic retinopathy grades.

Diabetic retinopathy group	HbA1c levels	p value
Mild NPDR (n=6)	4.73 ± 0.42	0.001*
Moderate NPDR (n=12)	6.37 ± 0.91	
Severe NPDR (n=24)	7.66 ± 0.35	
PDR (n=19)	8.79 ± 0.69	

*Statistically significant

DISCUSSION

Hyper glycemia in type II diabetic patients lead to dilatation of blood vessels and changes in the blood flow leading to a change in retinal metabolism. One of the hallmark of early establishment of Diabetic retinopathy is the loss of pericytes. These cells are important for providing structural support to the capillaries. Thus when they are destroyed the capillary wall outpouching starts leading to formation of microaneurysm[9].

Our study revealed that as the HbA1c levels increased the severity of diabetic retinopathy also increased as depicted by the results. As the control of diabetes became poor the severity of diabetic retinopathy progressed from non proliferative to the proliferative lesions. A study conducted on Japanese men suggested similar findings with higher levels of HbA1c correlating with increased prevalance of diabetic retinopathy[10]. They further suggested that in order to prevent diabetic retinopathy the HbA1c levels should remain in range which donot cause hyperglycemia. Another study conducted by Xin et al suggested that prevalence of diabetic retinopathy increased as the HbA1c levels increased from 6.4%[11].

When we compared the HbA1c levels among various diabetic retinopathy grades, it was revealed that as the HbA1c levels increased grade of retinopathy also increased. The highest HbA1c levels were observed in proliferative retinopathy group. Similar findings were documented by Song et al in their sudy. Mean level of HbA1c was higher in the patients with progressive diabetic retinopathy (7.30 ± 1.05) as compared to those in which the disease was controlled and did not progress (7.52 ± 1.03)[12]. Patients with poor glycemic control had greater incidence of severe

NPDR and PDR. Similar results were revealed by Long et al. He concluded that diabetes of greater duration and with poor glycemic control attributed to higher HbA1c levels were positively associated with greater severity in the retinopathy grading and progression (Odds ratio=3.522, P=2.00E-5)[13].

The underlying cellular as well as molecular processes are effected by the poor glycemic control reflected by increased HbA1c levels, this can inturn cause vascular complications including ischemic episodes, changes in level of vascular endothelial growth factor and inflammatory changes. A study conducted by Hammes et al suggested that HbA1c levels >8%, BMI>35 kg/m^2 and male gender were significantly associated with development of diabetic retinopathy[14]. Univariate analysis in a study conducted by Chatziralli et al revealed a positive association between diabetic retinopathy and HbA1c levels (rho=0.6315, p<0.001)[15]. Garg et al gave similar results, in his study that patients having very good glycemic control with HbA1c levels <7.0% had lower prevalence of diabetic retinopathy as compared to those with good control (HbA1c lvels 7-8%) and poor control (HbA1c levels >8%). In the poor glycemic control group the most prevalent retinopathy was the proliferative diabetic retinopathy which has the poorest prognosis of all[16].

Manaviat et al concluded in his study BMI and diabetic retinopathy had an inverse correlation with diabetic retinopathy and Patients with Proliferative diabetic retinopathy presented with increased HbA1c levels as compared to those with no retinopathy[17]. Bagzai et al in their study supported the findings of our study and revealed a significant association between HbA1c levels and severity of retinopathy. Also the prevalence of DR is lesser (23.5%) in cases with good glycemic control as compared to those having fair (79.04%) or poor control(98.6%)[18].

The most frequently encountered cause of blindness in patients before the age of 50 years is the development of diabetic retinopathy. To decrease the visual disabilities occurring because of diabetic retinopathy it is prudent to identify the disease at earliest stage and intervene accordingly. Ideally retinal examination of patients who have greater risk factors like greater duration of diabetes, increasing BMI and poor glycemic control should be done regularly in order to avoid vascular complications and permanent eye damage[19]. Many treatment modalities have been established for the treatment of diabetic retinopathy however pharmacotherapy remains the primary treatment modality. Trends of Laser therapy has been increasing in the past decade with promising results[20].

Limitations: Our study had limitations like financial constraints, lack of resources, genetic workup and short duration of study.

CONCLUSION

It was concluded that HbA1c levels and diabetic retinopathy were significantly associated. Higher levels of HbA1c which reflected the poor glycemic control can be used as a predictor for the severity of developing retinopathy.

Authors' Contribution:

SAAG&NKN: Conceptualized the study, analyzed the data, and formulated the initial draft.

SHT&IR: Contributed to the proof reading.

RS,MUR & TL: Collected data.

Acknowledgements: I am thankful to Allah and all my colleagues for their help.

REFERENCES

1. Aamir AH, Ul-Haq Z, Mahar SA, Qureshi FM, Ahmad I et al. Diabetes Prevalence Survey of Pakistan (DPS-PAK): prevalence of type 2 diabetes mellitus and prediabetes using HbA1c: a population-based survey from Pakistan. BMJ open. 2019; 9(2):e025300
2. Khan MA, Hashim MJ, King JK, Govender RD, Mustafa H, Al Kaabi J. Epidemiology of type 2 diabetes–global burden of disease and forecasted trends. J Epidemiol Glob Health. 2020. 10(1):107.
3. Chatterjee S, Khunti K, Davies MJ. Type 2 diabetes. Lancet. 2017. 389(10085):2239-51
4. Cole JB, Florez JC. Genetics of diabetes mellitus and diabetes complications. Nat Rev Nephrol. 2020. 16(7):377-90.
5. Sabanayagam C, Banu R, Chee ML, Lee R, Wang YX, Tan G, Jonas JB, Lamoureux EL, Cheng CY, Klein BE, Mitchell P. Incidence and progression of diabetic retinopathy: a systematic review. Lancet Diab Endocrinol. 2019. 7(2):140-9.
6. Qummar S, Khan FG, Shah S, Khan A, Shamshirband S, Rehman ZU, Khan IA, Jadoon W. A deep learning ensemble approach for diabetic retinopathy detection. IEEE Access. 2019. 15(7):150530-9.
7. Cheloni R, Gandolfi SA, Signorelli C, Odone A. Global prevalence of diabetic retinopathy: protocol for a systematic review and meta-analysis. BMJ open. 2019. 9(3):e022188
8. Andreasson R, Ekelund C, Landin-Olsson M, Nilsson C. HbA1c levels in children with type 1 diabetes and correlation to diabetic retinopathy. J Pediatr Endocrinol Metabol. 2018. 31(4):369-74
9. Wang W, Lo AC. Diabetic retinopathy: pathophysiology and treatments. Int J Mol Sci. 2018. 19(6):1816.
10. Matsushita Y, Takeda N, Nakamura Y, Yoshida-Hata N, Yamamoto S, Noda M, Yokoyama T, Mizoue T, Nakagawa T. A Comparison of the Association of Fasting Plasma Glucose and HbA1c Levels with Diabetic Retinopathy in Japanese Men. J Diab Res. 2020. 2020(1);1-6
11. Xin Z, Yuan MX, Li HX, Hua L, Feng JP, Shi J, Zhu XR, Cao X, Yang JK. Evaluation for fasting and 2-hour glucose and HbA1c for diagnosing diabetes based on prevalence of retinopathy in a Chinese population. PloS one. 2012. 7(7):e40610.
12. Song KH, Jeong JS, Kim MK, Kwon HS, Baek KH, Ko SH, Ahn YB. Discordance in risk factors for the progression of diabetic retinopathy and diabetic nephropathy in patients with type 2 diabetes mellitus. J Diabetes Investig. 2019. 10(3):745-52
13. Long M, Wang C, Liu D. Glycated hemoglobin A1C and vitamin D and their association with diabetic retinopathy severity. Nutr Diabetes. 2017. 7(6):e281
14. Hammes HP, Welp R, Kempe HP, Wagner C, Siegel E, Holl RW, DPV Initiative—German BMBF Competence Network Diabetes Mellitus. Risk factors for retinopathy and DME in type 2 diabetes—results from the German/Austrian DPV database. PloS one. 2015. 10(7):e013249
15. Chatziralli IP, Sergentanis TN, Keryttopoulos P, Vatkalis N, Agorastos A, Papazisis L. Risk factors associated with diabetic retinopathy in patients with diabetes mellitus type 2. BMC Res Notes. 2010;3(1):1-4
16. Garg P, Misra S, Yadav S, Singh L. Correlative study of diabetic retinopathy with HbA1c and microalbuminuria. Int J Ophthal Res. 2018. 4(2):282-6.
17. Manaviat MR, Afkhami M, Shoja MR. Retinopathy and microalbuminuria in type II diabetic patients. BMC Ophthalmol. 2004 Dec;4(1):1-4.
18. Bagzai DS, Bagzai A. Correlation between Severity of Diabetic Retinopathy with HbA1c in Type II Diabetic Patients.J Med Sci Clin Res. 2019 7(3);310-13
19. Song P, Yu J, Chan KY, Theodoratou E, Rudan I. Prevalence, risk factors and burden of diabetic retinopathy in China: a systematic review and meta-analysis. J Glob Health. 2018. 8(1).
20. Mansour SE, Browning DJ, Wong K, Flynn Jr HW, Bhavsar AR. The evolving treatment of diabetic retinopathy. Clin Ophthalmol . 2020;14:653