ORIGINAL ARTICLE

Association of HbA_1C with Grades of Retinopathy in Type 2 Diabetic Patients

MUHAMMAD UTHMAN[1], SYED NAEEMULLAH[2], FARHAN FATEH JANG[3], AMNA MALIK[4]
[1]*Associate Professor of Medicine, Shaikh Zayed Hospital, Lahore*
[2]*Consultant Neurologist, Department of Neurology, Shaikh Zayed Hospital, Lahore*
[3]*Associate Professor of Neurosurgery, Sharif Medical and Dental College, Lahore*
[4]*Assistant Professor of Neurology, Sharif Medical and Dental College, Lahore*
Correspondence to Dr. Muhammad Uthman, Email:medicalspecialist71@yahoo.com, Mob: 0300-4312499,

ABSTRACT

Aim: To study the association of retinopathy with level of HbA_1C in T2 DM patients.
Study design: Cross-sectional study.
Place and duration of study: This study is a 3 days study, conducted on 100 patients, who visited on 3 consecutive diabetic days of year 2012-2014 at Endocrine Clinic Shaikh Zayed Hospital, Lahore.
Methodology: One hundred adult type II diabetic patients of both genders were studied to see association of HbA1C (%) & age with the grades of retinopathy. Patients were divided into 3 categories based on HbA_1C levels viz. 7-7.5%, 7.6-9% and 9.1-11%. On the basis of fundoscopy, patients were grouped into 3 categories, group 1: No Diabetic Retinopathy (NDR), group 2: Non-Proliferative Diabetic Retinopathy (NPDR, includes background & pre-proliferative) and group 3: Proliferative Diabetic Retinopathy (PDR).
Results: Out of total 100 diabetic patients, 56% were males and 44% were females with a mean age was 40-58 years (50.55+5.17). Mean HbA1C was 7.1-11% (9.16+1.16). 8% patients showed no evidence of retinopathy with age range of 44-58 years (50.89+5.03), 37% had Non Proliferative Diabetic Retinopathy (NDPR) with age range of40-58 years (49.92+5.4). & 55% had Proliferative Retinopathy (PDR) with age range of 42-58 years (50.93+5.06). Mean HbA_1C was 7.2-9% (7.96+0.67); 7.1-11% (8.85+1.17); 7.6-11% (9.55+1.03), in all 3 groups i.e. No Retinopathy, Non Proliferative Retinopathy & Proliferative Retinopathy respectively.
Conclusion: This study has suggested that variation in HbA_1C is directly related to the visual symptom stages and progression of diabetic retinopathy. Periodic screening with HbA_1C is a cost effective, diagnostic and prognostic tool for the prevention of sight loss, or sight related complications in all diabetics.
Keywords: Retinopathy Grades, HbA_1C, Fundoscopy, T2DM

INTRODUCTION

Diabetes is a major metabolic disorder affecting each ethnic population and each age group. It can present with protean manifestations and some people present with lifelong complications at the first presentation. The WHO estimates that diabetes resulted in 1.5 million deaths in 2012, making it the 8th leading cause of death[1-5].

Diabetes prevalence is increasing rapidly. Data of 2017 estimates that almost 425 million people worldwide are living with diabetes.[2] This number is expected to increase to 200% by 2030.[1] Type 2 diabetes makes up about 85-90% of all cases.[3] People living in Asia and Africa, though are low to middle-income countries have greatest increase in prevalence of T2DM[5]. The reason is multifactorial and include (many if not all): urbanization, sedentary lifestyles, less physical exertion and intake of high energy-dense but nutrient-poor diet. In these geographical areas most patients will probably be diabetic by 2030[6].

Retinopathy is one of the major microvascular complications and the main cause of blindness in diabetics. Diabetes Control and Complication Trial (DCCT), total glycemic exposure is the main factor responsible for the occurrence & progression of diabetic eye disease.[7] Retinopathy is also linked with duration as well as age of onset of diabetes. Young-onset diabetic patients (diagnosed before their 30th year) had almost no pathognomoic retinal changes till 5 years past diabetes, a rapid increase in retinopathy upto 97% by after 15-20 years of the disease[8,9].

Vigorous monitoring of blood sugar level and HbA1c and modification in the treatment regimens accordingly decreases the morbidity, macro & microvascular complications including retinopathy and diabetes related mortality. HbA1C is a reliable indicator of chronic glycemia during the previous 2-3 months and precludes long-term diabetic related micro & macrovascular complications. HbA_1C is also aprognostic factor for the development & progression of retinopathy; higher A1C values associated with high prevalence and more severe retinopathy. The HbA1cis a good prognostic factor for insulin resistance too. It is considered as standard of care and is to be done thrice a year to monitor the average blood sugar control.[10-13,14] The average glucose (mg/dl) can be assessed from HbA1c% value and vice versa through a formula[15,16].

PATIENTS AND METHODS

This study was conducted at Endocrine & Diabetic Clinic of Shaikh Zayed Hospital, Lahore during 3 consecutive yearly World Diabetic Days 2012, 2013 and 2014. Amongst patients attended the clinic at these 3 days, only those patients were included who had type 2 diabetes for at least 5 years.

All patients with co-existent hypertension, H/O Cerebrovascular Accidents (CVA), Ischemic heart disease (IHD), diabetic nephropathy or patients on dialysis, history of eye surgery, or retinal procedures were excluded. 100

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patients were included in the research who fulfilled the criteria. Patients 'demographics viz. gender, age and urban/rural residence were entered on a data collection form. There were 4 dichotomous categorical variables recorded as yes or no weight loss, weight gain, drug treatment, visual symptoms and nocturia. The following tests variables were performed in all participants.

(i) HbA1C% & (ii) Fundoscopyto grade the retinopathy

HbA1c was assessed in laboratory. Fundoscopy was performed by Opthalmologist/Neurologist and patients were grouped into 3 categories according to grades of retinopathy:

i) No Diabetic Retinopathy (NDR)
ii) Non Proliferative Diabetic Retinopathy (NPDR) &
iii) Proliferative Diabetic Retinopathy (PDR)

Categorical variables were recorded in percentages. Nominal data were expressed as mean+SD. Analysis of variance test was used to determine the relationship of grades of retinopathy with HbA1C and age of patients with T2 DM. Post HOC analysis was done to determine whether gender, visual symptoms, change in weight had significant association with stage of retinopathy.

RESULTS

Characteristics of the 100 studied participants in this cross-sectional study are presented in Table 1.

Distribution of HbA1C levels in three grades of retinopathy is presented in Figure 1: On post HOC analysis, Chi-square tests (Table 4) revealed change in vision had significant association ($p<0.000$) with stage of retinopathy while no such association was found with gender and weight change (tab 5)

Fig. 1: HbA1c levels in three grades of retinopathy

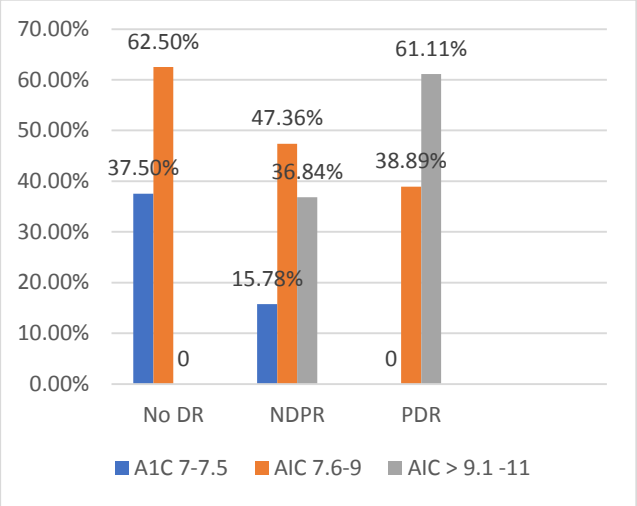

Table 1: Categorical variables of patients (n=100)

Gender		Residence		Weight change			Nocturia	Visual symptoms	On treatment
Male	Female	Urban	Rural	Loss	Gain	Neutral	Yes	Yes	Yes
56	44	46	54	77	6	17	89	84	97

Table 2: Age and HbA1C record of the 3 groups of patients

	No retinopathy	Non Proliferative retinopathy	Proliferative Retinopathy	Total
	8	37	55	
Age (years)				
Range	44-58	40-58	42-58	40-58
Mean+SD	50.89+5.03	49.92+5.4	50.93+5.06	50.55+5.17
HBA1C%				
Range	7.2-9	7.1-11	7.6-11	7.1-11
Mean+SD	7.96+0.67	8.85+1.17	9.55+1.03	9.16+1.16

Table 3: One way ANOVA

ANOVA		Sum of Squares	df	Mean Square	F	Sig.
HbA1C %	Between Groups	23.245	2	11.622	10.280	.000
	Within Groups	109.668	97	1.131		
	Total	132.913	99			
Age	Between Groups	23.409	2	11.705	.433	.650
	Within Groups	2619.341	97	27.004		
	Total	2642.750	99			

Table 4: Chi-Square

	Value	df	P value
Pearson Chi-Square	18.291[a]	2	.000
Likelihood Ratio	15.430	2	.000
Linear-by-Linear Association	16.319	1	.000
N of Valid Cases	100		

Table 5: Gender has no significant effect on the occurrence or progression of retinopathy Chi-Square Tests

Value	df	Asymptotic Significance (2-sided)
1.684[a]	2	.431
1.686	2	.431
1.330	1	.249
100		

DISCUSSION

Chronic hyperglycemia is considered an important risk factor for the development of diabetes related complications including diabetic retinopathy. HbA1c is a reliable indicator of diabetic control, it is now recommended a test of choice for testing and monitoring of diabetes.[8] Elevated HbA_1c, is thought to be a significant risk for the development and progression of diabetes related complications including retinopathy. Our study has made significant weight age to this observation of previous researchers. The mean of HbA1c in No DR was 7.79, in NPDR 8.7 and 8.4 in PDR group. Prevalence of diabetic retinopathy was upto 40% if HbA_1C is upto 9%.

Our findings are similar with those quoted in international literature. Similar study was published in 2018 by Sewak et al. shows a significant difference between HbA1c values of NPDR, PDR compared to control group. The elevated HbA1c was associated with severity of diabetic retinopathy.[17] Also prevalence of retinopathy was higher in NPDR (43.75%) group than PDR (37.54%).[17] Our study revealed a significant association of visual symptoms with grades of retinopthy & HbA_1C, but no significant association of age and gender with retinopathy was observed. These findings are synonymous with those narrated in international literature. Micky et al done a prevalences tudy in Australia. >4500 diabetics patients were evaluated for diabetic retinopathy which was present in 29%. While 2.8% had visual problems there was significant positive relation ($p<0.01$) of retinopathy with the chronicity of diabetes. On the other hand, retinopathy had poor association with patient related factors i.e. age, race, body weight, glaucoma, near sightedness, alcohol abuse, smoking , or salicylic acid intake (all $p >0.05$)[18].

In contrast to this study the higher prevalence of retinopathy in our study may be attributed to longer duration of diagnosis of diabetes, longer duration of dysglycemia & poor compliance to the health advicein our set up. In a study done by Xie et al in 4000 Chinese population, the risk factors for the occurrence of diabetic retinopathy (37%) were age >40 years, rural residence ($p=0.004$), chronicity of diabetes ($p=0.009$), poor compliance to treatment ($p=0.02$) and low academic background ($p=0.003$).[19] But almost 15% of these subjects were having symptoms related to sight. This study contradicts our observations. The difference may be attributed to variation in genetics, ethnicity, food preferences.

Elevated HbA_1C in patients with proliferative DR in our study is consistent with few quoted in international literature. In Wisconsin study.[8,9] the patients were divided into groups according to HbA_1C. The early-age onset diabetics had 45%-80% incidence of retinopathy. In the later-age-onset diabetics on insulin had 40-50% incidence of retinal eye disease[8,9].

Our study indirectly highlights the importance of regular follow ups and screening of all diabetics for the onset & deterioration of retinal eye disease. This is in accordance with the international research found in the world literature. In a study published in 2017, Scanlon et al concluded that people with no retinal eye disease at first visit have low risk of vision-threatening retinopathy over next 2-years follow up[20].

In English National Screening Programme (2003-20016), 2.14 million diabetics were screened for diabetic retinopathy. By virtue of this screening & the social efforts as a result of this programme, diabetic maculopathy is no longer the leading cause of blindness in England[21]. Despite being statistically significant, however there are a few limitations to our study. It's a single centered study and only small no of patients presenting on the world diabetic days were included. If the study would have been multi-centered & on a larger scale with a control group for comparison, the results would have been more inferential. Also the minimal difference in mean HbA_1C, in NPDR 8.7 and 8.4 in PDR group reflects either or all: the more diversity of HbA_1C values in PDR group versus NPDR, diverse age groups, poor socio economic status, poor compliance, and drugs.

CONCLUSION

HbA_1C is a trustworthy, easily manageable and cost effective tool to monitor adequate control of diabetes especially in countries with limited resources like Pakistan. Timely screening of all the diabetics (i.e. fundoscopy) should be emphasized for the development and progression of diabetic retinopathy to diagnose & prevent progression of stage of retinopathy.

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