

## Risk factors of retinopathy in type 2 diabetes mellitus at a tertiary care hospital, Bahawalpur Pakistan.

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### ABSTRACT

**Objectives:** To find out the risk factors of diabetic retinopathy in type 2 diabetes mellitus.

**Methodology:** It was a cross-sectional study involving 300 patients of type 2 diabetes. Clinical history, relevant examination including fundoscopy and lab investigations were done. Data was analysed with SPSS 17.0. T-test and chi square/Fischer exact were applied to determine significance.

**Results:** Mean age of the patients was  $49.04 \pm 0.69$  years with slight female predominance with male to female ratio of 3:4. Average duration of disease was  $7.17 \pm 0.38$  years. Diabetic retinopathy was diagnosed in (74, 23.9%). Mean HbA1c was 8.15% in patients with retinopathy and 8.884% in those who had no retinopathy ( $p=0.08$ ). However, duration of DM, age of patients, male gender, high total cholesterol, high LDL and microalbuminuria were significantly associated with the development of retinopathy.

**Conclusions:** Diabetic retinopathy was found in 23.9% of type 2 diabetics. It was associated with duration of disease, age at presentation, male gender, high total cholesterol, high LDL and microalbuminuria. A single high level of HbA1c was not associated with retinopathy.

**KEY WORDS:** Type 2 diabetes mellitus, Diabetic retinopathy, HbA1c, Cholesterol, Microalbuminuria.

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### INTRODUCTION

Type 2 diabetes mellitus (DM) is a group of disorders characterized by hyperglycemia and associated micro vascular (retinal, renal, possibly

neuropathic), macro vascular (coronary, peripheral vascular), and neuropathic (autonomic, peripheral) complications. Unlike Type 1 diabetics, patients are not absolutely dependent upon insulin for life, even though many of these patients are ultimately treated with insulin.<sup>1</sup>

Prevalence of type 2 diabetes and diabetic Retinopathy in Pakistan is 10% and 27% respectively.<sup>2,3</sup> A spectrum of retinal changes accompanying long-standing diabetes may advance to cause the abnormal retinal neovascularization, which may lead to severe visual loss and even blindness. Diabetic retinopathy is a leading cause of visual impairment among diabetic patients.

There are many reports from various countries about incidence and prevalence of diabetic retinopathy and the risk factors associated with this condition. Limited studies are available on risk factors associated with diabetic retinopathy in Pakistan. Stratton et al reported that older age, male gender, hyperglycemia (persistently raised HbA1c), hypertension and smoking were significantly

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associated with the incidence and progression of retinopathy in type 2 diabetic patients.<sup>4</sup> Chatziralli IP et al found duration of diabetes, hypertension, poor glycemic control and male gender as strong independent risk factors of retinopathy and they reported that the age was a confounding factor.<sup>5</sup> A study on large number of diabetics having retinopathy (n=7577) from Asia found duration of disease, elevated blood glucose levels and high blood pressure as independent risk factors.<sup>6</sup>

In the blood stream are the red blood cells, which contain a molecule called hemoglobin. Glucose sticks to the hemoglobin to make a 'glycosylated hemoglobin' molecule, known as HbA1c. More the glucose and more HbA1C will be present in the blood. Red cells remain alive for 8-12 weeks before they are replaced. By measuring the HbA1c, how high blood glucose has been on average over the last 8-12 weeks can be assessed. A normal non-diabetic HbA1C is 3.5-5.5%. The HbA1c test is currently one of the best ways to check the control of diabetes. Persistent elevation in serum glucose (HbA<sub>1c</sub>) increases the risk for the long-term vascular complications of diabetes such as retinopathy.<sup>7,8</sup>

High levels of hemoglobin A1c (HbA1c) for long duration are important risk factor for progression to high risk proliferative diabetic retinopathy and decreased visual acuity. Intensive glycemic control for long duration (HbA1c levels normal or near normal) reduces the risk of retinopathy significantly. Intensive therapy is most effective when initiated early in the course of the diabetes, demonstrating a beneficial effect over the course and progression of retinopathy.<sup>9,10</sup>

Our objective was to find out various risk factors associated with retinopathy in type 2 diabetes mellitus.

#### **Operational Definitions:**

**Diabetic retinopathy** A diagnosis of diabetic retinopathy will be established if the subject has a minimum of one micro aneurysm in any field, or showing hemorrhages (dot & blot, or flame shaped), or maculopathy (with or without clinically significant edema).

**High glycosylated hemoglobin (HbA1c)** Value of glycosylated hemoglobin more than 7% will be taken as high.

**Poor:** A person who earn less than 2\$ per day.

## METHODOLOGY

Patients of type 2 diabetes mellitus (DM) of both genders irrespective of duration of diabetes, more

than 30 years of age attending Bahawal Victoria Hospital, Bahawalpur were included in this cross sectional descriptive study. It was conducted at Department of Pathology, Department of Ophthalmology Bahawal Victoria Hospital/ Quaid-e-Azam Medical College Bahawalpur between July 2011 to June 2012. Patients of type I DM, Known cases of retinopathy which may be due to causes other than DM and value of HbA1c less than 7% were excluded.

**Sample size:** Sample size was 299, rounding off the nearest whole number 300. The prevalence of retinopathy in type2 DM was 27%. Purposive Sampling technique was used for this study. The study was approved by the local ethical committee. After taking written and verbal consent from the patients, a structured proforma containing demographic features, duration of DM, oral or insulin therapy was filled. Blood samples were collected for analysis of HbA1c, serum total cholesterol and LDL cholesterol. HbA1c was measured by Boronate affinity chromatography (Clover A1c). Total and LDL cholesterol were measured by automated chemistry analyzer. A detailed fundus examination was performed by slit lamp bio microscopy.

**Data analysis:** Data was analyzed using SPSS version 17. The results were evaluated using frequencies, proportions and group means. The frequencies and percentages were calculated for all the qualitative data including gender, age group, and diabetic retinopathy.

## RESULTS

Mean age of the patients was  $49.04 \pm 0.69$  years. Females were slightly predominant (n=174, 56.1%) as compared to males (M:F ratio 3:4). All patients were type 2 diabetics with average duration of disease of  $7.17 \pm 0.38$  years. Diabetic retinopathy was diagnosed in about 1/4<sup>th</sup> patients (n=74, 23.9%). Mean HbA1c was  $8.71 \pm 0.08$  percent. A majority of patients was literate (n=198, 63.9%) as compared to illiterate (n=112, 36.1%), similarly 187 patients (60.3%) had good socioeconomic status as compared to poor patients (n=123, 39.7%). It was found that patients (n=105, 33.9%) were counseled by the

Table-I: Comparison of HbA1c in diabetic patients having retinopathy.

	Retinopathy	N	Mean	Std. Deviation	Std. Error Mean
HbA1c	Yes	74	8.154%	1.1169	0.1298
	No	236	8.884%	1.4488	0.0943

Table-II: Association of duration of diabetes with development of retinopathy.

	N	Mean duration in years	Std. Deviation	Std. Error Mean
Retinopathy	74	16.05	7.767	0.903
No Retinopathy	236	4.39	3.029	0.197

treating doctor about compliance to medication and complications of diabetes mellitus if poorly controlled, as compared to 205 (66.1%) patients who were just prescribed treatment without counseling. Family cooperation was noted in 227 (73.2%) patients. History of Hakeem medication was found in 119 (38.4%) patients. As shown in Table-I, there was no statistical difference of mean HbA1c among the patients who had diabetic retinopathy or not ( $p = 0.080$ ).

Mean duration of diabetes mellitus who had developed retinopathy was  $16.05 \pm 0.903$  years as compared to  $4.39 \pm 0.197$  years who had not developed retinopathy yet. Independent Samples t Test was applied and a statistically significant difference (0.0001) was calculated as shown in Table-II.

Although there was slight female preponderance among type 2 diabetics however, males were found to have higher frequency of retinopathy ( $n=41/136$ , 30.15%) as compared to females ( $n=33/174$ , 18.96%). Similarly, high serum total cholesterol, high serum LDL-cholesterol, presence of albuminuria and insulin therapy were found to have significant associations with the development of diabetic retinopathy as shown in Table-III. Chi square was applied which revealed significant difference ( $p = 0.023$ ) between the two genders.

## DISCUSSION

Diabetes mellitus is a global problem and diabetic retinopathy is a common complication of this systemic disorder with its overall global prevalence of 34.6% (range = 17.99% – 51.2%).<sup>11</sup> However, the studies from within Pakistan show the prevalence of diabetic retinopathy ranging from 9.0% to 43.0%.<sup>12-15</sup> Insulin treatment, duration of diabetes, age at examination, HbA1c, systolic blood pressure, cholesterol, triglyceride and microalbumin were found to be significantly related to the development and the progression of retinopathy among type 2 diabetics from Kuwait by AlKharji et al.<sup>16</sup> However, a recent study by Chitrazalli and colleague documented that effect of age is a confounding factor but years since DM diagnosis, hypertension, serial high HbA1c levels and male sex were independent risk factors for the development of diabetic retinopathy.

Table-III: Association of various risk factors with diabetic retinopathy.

Risk factors	Retinopathy		p value
	Frequency	Percentage	
Gender			
- Male	41/136	30.15%	0.023
- Female	33/174	18.96%	
Age			
- ≤49 years	13/164	7.93%	0.0001
- >49 years	61/146	41.78%	
Total cholesterol			
- Normal	19/119	15.97%	0.010
- High	55/191	28.79%	
LDL cholesterol			
- Normal	33/198	16.67%	0.0001
- High	41/112	36.61%	
Albuminuria			
- Absent	14/193	7.25%	0.0001
- Present	60/117	51.28%	
Therapy			
- Insulin	49/74	66.22%	0.001
- Oral hypoglycemics	25/234	10.68%	

In our study there is no significant association of retinopathy with single high HbA1c level among patients of type 2 diabetes. It is common observation that most of the patients of type 2 diabetes have high HbA1c levels at the time of diagnosis of the disease but they have no retinopathy at that time. There are many studies conducted in various countries over the period of last decade or so which provide fair evidence of association of persistently high HbA1c with the development of various grades of retinopathy in type 2 diabetic patients.<sup>17-19</sup>

In our patients, the overall frequency of retinopathy was 23.9% whereas a study from Karachi involving large number of diabetic patients reported similar frequency of retinopathy (27.4%).<sup>20</sup> Another study conducted recently, showed higher frequency (34.5%),<sup>21</sup> however this difference may be attributed to patient selection in that study and/or other demographic variables.

Our study showed that the retinopathy was found in 74 patients whose average duration of type 2 diabetes was  $16.05 \pm 0.90$  years as compared to those who had no retinopathy. The latter group of patients had 236 patients with mean duration of disease of  $4.39 \pm 0.20$  years. Thus a strong correlation was found between the retinopathy and duration of diabetes. Many other studies have also identified the duration of diabetes as the major risk factor of the development of diabetic retinopathy.<sup>22</sup> Shaukat et al also showed positive correlation between

the duration of diabetes with the incidence of retinopathy as in current study.<sup>23</sup>

### CONCLUSIONS

Diabetic retinopathy was found in 23.9% of type 2 diabetics which was significantly associated with male gender, duration of diabetes, older age, high cholesterol, high LDL, albuminuria and insulin therapy. No association of high HbA1c levels for short duration (months not years) was found with diabetic retinopathy. Persistently raised HbA1c level may be associated with diabetic retinopathy.

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### Author's Contribution:

**SH and MRQ** formulated the study design and helped in the final drafting of the manuscript. **MAI and AA** critically revised the manuscript. **EU** has performed the data analysis, interpretation, drafted the manuscript, and substantially contributed to conception and design of the study.