Original Article

Duration of Diabetes as a Significant Factor for Retinopathy

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Purpose: To determine the frequency and risk factors for severity of retinopathy in diabetic patients referred to a tertiary level military hospital.

Material and Methods: Diabetic patients referred for suspected diabetic retinopathy on fundoscopy from medical outpatient clinic of Military Hospital Rawalpindi were randomly included in the study. Retinopathy was assessed with slit lamp biomicroscope using fundus lens or indirect ophthalmoscope, and graded into absent, non-proliferative or proliferative retinopathy. ANOVA test was used to perform univariate analysis, and to evaluate the simultaneous effect of significant risk factors on the different stages of retinopathy, multivariate regression analysis was done.

Results: Out of four hundred and eighty patients, retinopathy was confirmed in 38% cases with advanced retinopathy in 16%. In univariate analysis, duration of diabetes, fasting blood glucose and glyscosylated haemoglobin test were significantly associated with retinopathy ($P<0.005$). On multivariate analysis, however, only duration of diabetes proved to be an independent risk factor for both type and progression of retinopathy (Odds Ratio 5.7 for 5 to 10 years and 32.3 for more than 10 years in cases of non-proliferative retinopathy).

Conclusion. The frequency of retinopathy observed was high with strong association to duration of diabetes. This emphasizes the need for regular screening of diabetic individuals to detect retinopathy in the early stages and increasing public awareness.

Diabetes mellitus is one of the most common non communicable diseases with an increasing incidence worldwide. While most individuals affected with Diabetes in developed countries are elderly, it occurs at a much younger age in Asian countries[1]. According to the latest World Health Organization report, Pakistan has 5.2 million diabetic subjects, and the number is expected to increase to a staggering 13.9 million making it the 5th highest in the world by 2030[2]. Retinopathy is the most frequent microvascular complication of diabetes mellitus, causing blindness in over 10,000 people every year and is the leading cause of legal blindness[3]. According to Pakistan national blindness survey the prevalence of blindness in adults older than 30 years of age is 2.7%, out of these, 15.3% have diabetic retinopathy[4].

The role of various risk factors for development and progression of Diabetes has been demonstrated by several epidemiologic studies of western countries. These factors include type and duration of diabetes, age, gender, glycemic control, hypertension, body mass index, smoking, serum lipids and presence of microalbuminuria[5,6]. However, there is a paucity of data on the prevalence of diabetes-related eye diseases and the role of various risk factors in developing countries such as Pakistan[7].

The aim of this study was to determine the frequency of diabetic retinopathy and associated risk factors in a tertiary care setup receiving referrals of military personnel and their dependents with clinical suspicion of diabetic retinopathy.

MATERIALS AND METHODS

This was a cross sectional study conducted on diabetic patients with clinical suspicion of diabetic retinopathy based on direct Ophthalmoscopy carried out in diabetic outdoor clinic of Military Hospital Rawalpindi and referred to our institute for confirmation or otherwise, from March 2008 to February 2010. Only those cases were randomly included in the study who had not received any previous intervention for diabetic retinopathy. Any patient with corneal opacity or lenticular opacities which precluded proper fundus examination was excluded from the study. The cases were given a questionnaire that included information on patient's age, gender, weight, height, type and duration of diabetes. Laboratory evaluations consisted of measuring blood HbA1C test, and fasting blood glucose. HbA1C test was measured by high performance liquid chromatography system (reference range 4.7-6.0%; Merck-Hitachi 9100, Merck, Darmstadt, Germany). Fasting plasma glucose was measured by the glucose-peroxidase colorimetric enzymatic method (Biodiagnostics). Serum total cholesterol was measured by enzymatic-colorimetric methods (Merck Diagnostics, Germany). The Hospital Ethics Committees approved the study protocol and an informed consent was obtained from all patients.

Ophthalmoscopy was done after pupillary dilatation by 1% tropicamide and 10% phenylephrine eye drops. Classification of retinopathy was based on the findings in the worst eye. The binocular indirect ophthalmoscope (Keeler Instruments Inc. PA, USA) and slit lamp biomicroscope (Magnon SL-450, Japan) with fundus lens were used to examine the fundus. Diabetic retinopathy was clinically graded by an experienced retinal specialist as per the norms of the International Clinical Diabetic Retinopathy guidelines[10]. The cases were divided then as having no retinopathy, non-proliferative retinopathy, and proliferative retinopathy[15]. The presence of clinically significant macular oedema was also noted for future study.

A pre-tested form was used to collect the information for this study. The data was entered in SPSS version 15 (SPSS Inc, Chicago, USA). It was checked for inconsistencies and duplications. For descriptive purposes, quantitative variables were presented as mean and standard deviation. Univariate analysis was carried out using Analysis of variance (ANOVA) for the comparison of quantitative variables between different stages of retinopathy. These variables were gender, type of diabetes, duration, fasting blood glucose, serum total cholesterol, and HbA1C. P-value of less than 0.05 was considered significant. To evaluate the simultaneous effect of significant risk factors on univariate analysis on the different stages of retinopathy (the response variable), multivariate regression model was used.

RESULTS

A total of four hundred and seventy patients were evaluated (65.7% males, 92.4% type II diabetics). Mean age was 56.23 $\pm$ 8.73 years (95% CI 55.47 to 57.78). Age distribution according to type of retinopathy is given in Table 1. Diabetic retinopathy was confirmed in 38% cases (n = 180). 104 patients (22%) had non proliferative retinopathy and 76 patients (16%) were diagnosed with proliferative retinopathy. The demographic and clinical characteristics of patients are shown in table 2. Overall, retinopathy was more prevalent in patients with type-2 Diabetes compared with those with type-1 (12.6% *vs.* 9.4% for non-proliferative, and 8.6 % *vs.* 6.2% for proliferative respectively). During univariate analysis, patients with retinopathy showed statistically significant difference in duration of diabetes, fasting blood glucose, HbA1c, compared to patients with no retinopathy ($p<0.001$). Insignificant differences were found in hyperliipidemia ($p=0.337$). A multiple logistic regression model was then developed to identify which of the latter were related to each level of retinopathy. The results listed in Table 3 show that HbA1C and high fasting blood glucose were no longer significant when adjusted for in the logistic model. On the other hand, longer duration of diabetes was still at risk of developing any grade of diabetic retinopathy (table-3). During calculating the odds ratio the reference category was taken as no retinopathy. Similarly for duration of diabetes and its effect on retinopathy, the first category (duration less than five years) was taken as reference.

DISCUSSION

Recent studies indicate that prevalence of diabetes in our country is around 9-10%. This increase has been attributed to the rapid economic, demographic, and nutritional transition experienced that has led to lifestyle changes resulting in increased prevalence of diabetes. Paralleling this high prevalence of diabetes is a concern that complications of diabetes, mainly diabetic retinopathy, in such subjects might also be high. However, few studies have attempted to assess

the prevalence of diabetic complications in Pakistan[4,7,12,13]. In this study, we report the prevalence of DR in subjects attending the diabetic clinic of a tertiary care military hospital. In the present study diabetic retinopathy was present in 38% of the 470 patients considered for evaluation. Various studies give different figures for the prevalence of diabetic retinopathy. High prevalence rates of 50-60% were found in UK, Australia[14] and other European nations[15]. Our figures for non-prolifeartive retinopathy coincide with those of other studies[16,17], with a slightly higher rate for proliferative retinopathy. This higher rate could be explained by the fact that the microvascular complications of DR are higher in the subcontinent due to poorer diabetic control.

In this study, a number of medical risk factors were assessed (Table-2), and the risk factors independently associated with any diabetic retinopathy, in order of importance, were, longer duration of diabetes, FBG, and HbA1C levels. Logistic regression analysis revealed longer duration of diabetes to be an independent risk factor associated with both the presence and severity of diabetic retinopathy.

Similar to regional studies[18,19], the type of diabetes mellitus did not seem to be associated with the occurrence of diabetic retinopathy. This may be because diabetic patients on Insulin were treated with the aim of tight glycaemic control so that they were now at a lower risk for such an occurrence.

Table 1: Age characteristics of study patients with retinopathy

Type of DR	No of Cases	Mean age ± SD	95% Confidence Interval
No DR	290	55.69± 9.40	53.97 to 57.06
Non prolife-rative DR	104	57.26± 8.74	56.19 to 59.07
Prolifera-tive DR	76	56.53± 8.90	55.27 to 57.89
Total	470	56.23 ± 8.73	55.47 to 57.78

P value of 0.684 using ANOVA test, DR= Diabetic retinopathy

Association of total cholesterol levels with retinopathy has been clearly demonstrated, especially in type 2 diabetes patients[12]. However, this was not observed in the present study for any type of retinopathy. This could be explained by low mean levels of total cholesterol (<200 mg/ dl) of our patients studied, and could reflect the major role of genetic factors in various stages of diabetic eye disease. However, the cross-sectional design adopted precludes confirmation of this hypothesis.

Table 2: Patients' characteristics according to different stages of diabetic retinopathy (n=470)

Risk Factors	No DR (n=290) n(%)	NPDR (n=104) n(%)	PDR (n=76) n(%)	P values
Type of Diabetes				
Type –I	36 (12.5)	47 (45.2)	31 (40.8)	0.368
Type –II	254 (87.5)	57 (54.8)	45 (59.2)	
Duration of Diabetes				
Less than 5yrs	186 (64.2)	19 (18.3)	12 (15.8)	<0.001
5- 10 years	82 (28.3)	32 (30.7)	25 (32.9)	
More than 10yr	22 (7.5)	53 (51.0)	39 (51.3)	
Fasting Blood Glucose				
Less than 100 mg/dl	146 (50.3)	22 (21.1)	16 (21.0)	<0.001
From 100-150 mg/dl	98 (33.8)	31 (29.8)	18 (23.6)	
More than 150 mg/dl	46 (15.9)	51 (49.1)	43 (56.4)	
Hyperlipidemia				
Total cholesterol more than 6.2 mmol/l	22 (7.5)	11 (10.5)	7(9.2)	0.431
Total cholesterol of less than 6.2 mmol/l	268 (92.5)	93 (89.5)	69 (90.8)	
Glycosylated haemoglobin (HbA1c)				
Less than 7%	135 (46.5)	38 (36.5)	19 (25.0)	<0.001
From 7 to 9%	112 (38.6)	29 (27.8)	30 (39.5)	
More than 9%	43 (14.9)	37 (35.7)	27 (35.5)	

Data expressed as number of cases (percentage), DR= diabetic retinopathy.

Table 3: Multivariate analysis of risk factors for mild to moderate and advanced diabetic retinopathy (n = 470)

Risk factor	Non proliferative retinopathy		Proliferative retinopathy	
	Odds Ratio	P value	Odds Ratio	P value
Duration of Diabetes 05 to 10 years	5.780	<0.001	2×10^{6}	<0.001
Duration of Diabetes more than 10 years	32.364	<0.001	2×10^{8}	<0.001

The duration of diabetes, however, remained the strongest predictor for any diabetic retinopathy as well as its severity. Patients with duration 5-10 years had 5 times more chances to have non proliferative retinopathy and 2×10^{6} times more chances for advance retinopathy than patients with duration less than 5 years and no retinopathy. Similarly patients with duration more than 10 years had 32 times more chances to have non proliferative retinopathy and 2×10^{8} times more chance to have proliferative retinopathy than patients with duration less than 5 years and no retinopathy (Table 3). Moreover, such an association has been observed by several other investigators as well[20], and it was probably related to the magnitude or prolonged exposure, or both, to hyperglycaemia coupled with other risk factors.

Reports in Asian developing countries have also observed an association of high levels of fasting plasma glucose and HbA1c with retinopathy[8,13,21]. Our study also showed these factors to be significant in univariate analysis.

Poor diabetic control could reflect a dearth of clinical, evidence-based-knowledge regarding diabetic medication amongst our physicians. In view of the global increase in diabetes, this is a major concern for healthcare and underscores the importance of routine retinal examination in all diabetic patients. In contrast with developed countries[22,23] most of the patients in our study had no regular follow up program for management of diabetes and the prevalence of retinopathy was found to be higher in these patients.

The limitation of the present study was the target population and so the possibility of a selection bias. Another limitation was that retinopathy grading was based on indirect ophthalmoscopy and not on fundus photography grading. This could have resulted in the underestimation of the prevalence of retinopathy.

CONCLUSION

In conclusion, the present study suggests that although the frequency of retinopathy is similar to that reported earlier, given the large number of diabetic subjects in the country, even with the lower prevalence rates, diabetic retinopathy still poses an enormous public health and economic burden for Pakistan. Those with a longer duration of diabetes, elevated fasting blood glucose and HbA1C levels, are at highest risk of complications. This emphasizes the need for regular screening of diabetic individuals to detect retinopathy in the early stages and increasing public awareness. This would minimize the occurrence of avoidable blindness in developing nations such as Pakistan.

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REFERENCE

1. World Health Organization: Guidelines for the prevention, management and care of diabetes mellitus. EMRO Technical publications series 32, Geneva 2006.
2. **Javadi MA, Katibeh M, Rafati N, et al.** Prevalence of diabetic retinopathy in Tehran province: a population-based study. BMC Ophthalmol. 2009; 16: 9-12.

3. WHO-Magnitude and causes of Visual impairment. Available from: http://www.who.int/mediacentre/factsheets/fs282/en/ November 2004.
4. **Shaikh A, Shaikh F, Shaikh ZA, et al.** Prevalence of Diabetic retinopathy and influence factors among newly diagnosed Diabetics in Rural and Urban Areas of Pakistan: Data analysis from the Pakistan National Blindness & Visual Impairment Survey 2003. Pak J Med Sci. 2008; 24: 774-79.
5. **Klein R, Sharrett AR, Klein BE, et al.** ARIC Group The association of atherosclerosis, vascular risk factors, and retinopathy in adults with diabetes: the atherosclerosis risk in communities study. Ophthalmology. 2002; 109: 1225-34.
6. **Cai XL, Wang F, Ji LN.** Risk Factors of Diabetic retinopathy in type 2 diabetic patients. Chin Med J (Engl). 2006; 119: 822-6.
7. **Amin SS, Mukhtar MA.** Diabetic Retinopathy - Recent Developments and Challenges. Pak Armed Forces Med J. 2006; 56: 182-8.
8. **Mohan V, Shanthirani CS, Deepa R.** Glucose intolerance (diabetes and IGT) in a selected South Indian population with special reference to family history, obesity and life style factors: The Chennai Urban Population Study (CUPS 14). J Assoc Physicians India. 2003; 51: 771–7.
9. **Rani PK, Raman R, Chandrakantan A, et al.** Risk factors for diabetic retinopathy in self-reported rural population with diabetes.
10. Grading diabetic retinopathy from stereoscopic color fundus photographs an extension of the modified airle house classification. ETDRS report number 10. Early treatment Diabetic Retinopathy Study Research Group. Ophthalmology. 1991; 98: 786-806.
11. **Wilkinson CP, Ferris FL 3rd, Klein RE, et al.** Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales. Ophthalmology. 2003; 110: 1677-82.
12. **Basit A, Hydrie MZ, Hakeem R, et al.** Glycemic control, hypertension and chronic complications in type 2 diabetic subjects attending a tertiary care center. J Ayub Med Coll Abottabad. 2005; 17: 63-8.
13. **Wahab S, Mahmood N, Shaikh Z, et al.** Frequency of retinopathy in newly diagnosed type 2 diabetes patients. J Pak Med Assoc. 2008; 58: 557-61.
14. **Smith TS, JSzetu J, Bourne RA.** The prevalence and severity of diabetic retinopathy, associated risk factors and vision loss in patients registered with type 2 diabetes in Luganville, Vanuatu. Br J Ophthalmol. 2007; 91: 415-9.
15. **Henricsson M, Nilsson A, Groop L, et al.** Prevalence of diabetic retinopathy in relation to age at onset of the diabetes, treatment, duration and glycemic control. Acta Ophthalmol Scand. 1996; 74: 523–7.
16. **Lim MC, Lee SY, Cheng BC, et al.** Diabetic Retinopathy in Diabetics Referred to a Tertiary Centre from a Nationwide Screening Programme. Ann Acad Med Singapore. 2008; 37: 753-9.
17. The EURODIAB IDDM Complications Study. Retinopathy and vision loss on insulin-dependent diabetes in Europe. Ophthalmology. 1997; 104: 252–60.
18. **El-Haddad OA, Saad MK.** Prevalence and risk factors for diabetic retinopathy among Omani diabetics. Br J Ophthalmol. 1998; 82: 901-6.
19. **Asfour MG, Lambourne A, Soliman A.** High prevalence of diabetes mellitus and impaired glucose tolerance in the Sultanate of Oman:results of the 1991 National Survey. Diabetes Med. 1995; 12: 1122–5.
20. **Pradeepa R, Anitha B, Mohan V, et al.** Risk factors for diabetic retinopathy in a South Indian Type 2 diabetic population--the Chennai Urban Rural Epidemiology Study (CURES) Eye Study 4. Diabetes Med. 2008; 25: 536-42.
21. **Abdollahi A, Malekmadani MH, Mansoori MR, et al.** Prevalence of diabetic retinopathy in patients with newly diagnosed type II diabetes mellitus. Acta Medica Iranica. 2006; 44: 415-9.
22. **Sundling V, Gulbrandsen P, Jervell J, et al.** Care of vision and ocular health in diabetic members of a national diabetes organization: a cross-sectional study. BMC Health Serv Res 2008, 8: 159.
23. **Wong TY, Cheung N, Tay WT, et al.** Prevalence and Risk Factors for Diabetic Retinopathy the Singapore Malay Eye Study. Ophthalmology. 2008, 115: 1869-75.

R N F L Analysis

Quantitative retinal nerve fiber layer analysis at present is still a research tool but is likely to become a useful clinical tool in future.

Prof. M. Lateef Chaudhry
Editor in Chief