Original article

Systemic association of newly diagnosed proliferative diabetic retinopathy among type 2 diabetes patients presented at a tertiary eye hospital of Nepal

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Abstract

Introduction: Proliferative diabetic retinopathy (PDR) is the leading cause of blindness among the diabetics. **Objective:** to study the systemic association of proliferative diabetic retinopathy. **Materials and methods:** A prospective, case-series study was conducted among the newly diagnosed proliferative diabetic retinopathy cases presenting at the Tilganga Institute of Ophthalmology (TIO) from January 2012 to January 2013. Diabetic retinopathy was classified using the Early Treatment Diabetic Retinopathy Study criteria. Blood pressure, fasting and postprandial blood sugar, glycosylated hemoglobin, lipid profile, urine for microalbumin, urea, and creatinine were evaluated at the time of diagnosis. **Results:** A total of 104 type 2 diabetic patients with newly diagnosed PDR presented during the study period. Concurrent macular edema was present in 93 cases (89.42 %). The mean age was 56.96 ± 9.394 (range 32 - 78) years. Males and females comprised of 75.7 % and 24.3 % respectively. The majority (37.5 %) were involved in business, followed by government service (17.30 %), and housewives (16.34 %). Mean duration of diabetes was 11.42 ± 5.356 years (range 1 month - 26 years). Concurrent hypertension was found in 55.76 %, uncontrolled fasting and or postprandial blood sugar in 72.54 %, poor glycemic control (HbA1C > 7 %) in 73.97 %, abnormal lipid profile in 52.56 %, microalbuminuria in 67.85 %, and positive urine albumin in 50 % of the cases. **Conclusion:** Despite the short duration of diabetes, the concurrent hypertension, poor glycemic control, proteinuria and dyslipidemia were the main systemic associations for PDR at our clinical set-up. Awareness, identification and management of these systemic problems could reduce the rapid progression to PDR.

Keywords: Proliferative diabetic retinopathy, microalbuminuria, lipid profile, hypertension, proteinuria

Introduction

The recent rise of diabetes mellitus as epidemics in the majority of developing countries, especially in urban areas, has been one of the major public health issues (Chan et al, 2009; Editorial JNMA 2003; Singh et al, 2003; Wild et al, 2004). Diabetic retinopathy, the commonest complication of diabetes, is the fifth leading

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cause of blindness worldwide, contributing to 4.8 % of global blindness (WHO, 2005). Proliferative diabetic retinopathy (PDR) and diabetic macular edema (DME) are the main causes of visual impairment and blindness among the diabetics. Despite these being two preventable causes of blindness, a significant number of people from developing countries having PDR and DME develop irreversible blindness. The major cause for this has been the lack of awareness of the disease sequelae that has been compounded by its asymptomatic course until the advanced sight-threatening stage (Thapa et al, 2012). Besides the duration of diabetes, poor glycemic control, concurrent hypertension, uncontrolled lipid profile, and nephropathy are the important risk factors for the rapid progression of diabetic retinopathy. Pan-retinal photocoagulation (PRP) and grid focal lasers are the mainstay of treatment to prevent further deterioration of vision both from PDR and clinically significant macular edema (Early Treatment Diabetic Retinopathy Study Research Group, 1981; The Diabetic Retinopathy Study Research Group, 1985). It is equally important to control the blood glucose level and other concurrent systemic risk factors (Higgins et al, 2007). Although there are few studies regarding the risk factors for diabetic retinopathy (Shrestha et al, 2007; Paudel et al, 2008), systemic association of PDR with factors like proteinuria, hyperlipidemia and poor glycemic control are still poorly understood in our diabetic population. This study is expected to explore the concurrent systemic factors among the newly diagnosed PDR cases of type 2 diabetes mellitus at a tertiary eye-care hospital setting of Nepal.

Materials and methods

A hospital-based, prospective and descriptive study was conducted at the Tilganga Institute of Ophthalmology (TIO) from January 2012 to January 2013. All newly diagnosed proliferative diabetic retinopathy cases presenting during the study period and without prior laser pan retinal photocoagulation were enrolled in the study. Ethical approval was obtained from the Institutional Review Committee of the TIO. Informed consent was obtained from the patients before enrollment in the study. Detailed demographic and systemic history, like the duration of diabetes, history of concurrent hypertension, hyperlipidemia, and kidney problems, were taken. Patients were subjected to visual acuity and anterior segment examination and detailed posterior segment evaluation under mydriasis. Proliferative diabetic retinopathy and clinically significant macular edema (CSME) were classified using the Early Treatment Diabetic Retinopathy Study (ETDRS) criteria (Early Treatment Diabetic Retinopathy Study Research Group, 1981). Fundus fluorescein angiography was performed where possible and optical coherence tomography of the macula was done as needed. In brief, the PDR was categorized by the presence of combination of three of the four retinopathy risk factors: presence of vitreous or pre-retinal hemorrhage, presence of new vessels, location of new vessels on or near the optic disc and moderate to severe extent of new vessels. CSME was defined as the presence of any of the following criteria: retinal edema located at or within 500 μm of the center of the macula, hard exudates at or within 500 μm of the center if associated with thickening of the adjacent retina or a zone of thickening larger than 1 disc area if located within 1 disc diameter of the center of the macula. Patients were also subjected to fasting and postprandial blood sugar, glycosylated hemoglobin, lipid panel (total cholesterol, triglyceride, high-density lipoprotein and low-density lipoprotein), urea, creatinine, and routine urine examination including urine for microalbumin. The blood pressure was recorded. Patients with a blood pressure of more than 140/90 mm Hg and/ or those under antihypertensive medications

despite their normal blood pressure were categorized as hypertensive. The history and examination findings were documented in a specially-designed proforma and data was analyzed in the SPSS version 11.5 (SPSS Inc, Chicago,IL, USA).

Results

A total of 104 type2 diabetic patients with PDR presented during the study period. CSME was found in 93 cases (89.42 %). The mean age of patients was 56.96 ± 9.394 years and the age ranged from 32 to 78 years. Most of the patients were of 51 - 60 years of age (36.53 %), followed by 61 - 70 years (28.84 %) and 41 - 50 years (24.03 %). Almost one-fifth of the cases were below 50 years of age. Males and females comprised of 75.7 % and 24.3 % respectively. These details have been given in Table 1.

Table 1: Age distribution of the enrolled type 2 diabetic patients

Age groups	Number	Percent
< 40 years	3	2.88
41 - 50 years	25	24.03
51 - 60 years	38	36.53
61 - 70 years	30	28.84
71 - 80 years	8	7.69
Total	104	100

The majority of the patients had completed their primary education of class five. Fifteen percent of patients were illiterate whereas only 12.5 % of the patients had completed their higher education. Almost one-third of the study participants (37.5 %) were involved in business, followed by government service (17.30 %), and housewives (16.34 %). Other service holders comprised of retired service holders and other occupations. These details have been outlined in Table 2.

Table 2: Occupation and educational status of the diabetes patients

		Number	Percent
Education status	No education	16	15.38
	Primary school	35	33.65
	High school	24	23.07
	Intermediate	12	11.53
	Higher education	13	12.5
	Self education	1	0.96
	Adult education	3	2.88
Occupation	Government services	18	17.30
	Commercial/ business services	39	37.5
	Industry	2	1.9
	Farming	8	7.69
	Labour (non-agriculture)	1	0.96
	Labour (agriculture)	3	2.88
	Housewife	17	16.34
	Others	16	15.38

The mean duration of diabetes was 11.42 ± 5.356 years and the duration ranged from 1 month to 26 years. Almost half of the cases had PDR for less than 10 years.

Table 3: Duration of diabetes among the enrolled type 2 diabetes cases

Duration of diabetes	Frequency	Percent
< 5 years	16	15.38
6 - 10 years	38	36.53
11 - 15 years	27	25.96
16 - 20 years	18	17.30
21 - 25 years	4	3.84
>25 years	1	0.96

Concurrent hypertension was found in 58 cases (55.76 %). Fasting and or post prandial blood sugar was not under control in 74 cases (72.54 %). HbA1C of more than 7 % was found in 73.97 % cases, abnormal lipid panel in 52.56 % despite the positive history in only 4.8 % of cases, microalbuminuria in 67.85 % of cases, urine albumin positive in 50 % of cases, and 2.8 % of cases had a history of heart disease. These details have been shown in Table 4.

Table 4: Concurrent hypertension, poor glycemic control, and abnormal lipid panel among the PDR cases in type 2 diabetes patients

	Total number of diabetic patients undergoing examination	Frequency of abnormal cases	Percent (%)
History of Hypertension	104	58	55.76
Poor control of BP at presentation	104	27	25.96
Poor control of blood sugar (Fasting/ PP)	102	74	72.54
Poor control of blood sugar (HbA1C > 7)	73	54	73.97
Abnormal lipid panel	78	41	52.56
Mcroalbuminuria	56	38	67.85
Albuminuria	52	26	50
Elevated urea, creatinine	56	3	5.35
History of heart disease	104	3	2.88
History of deranged lipid panel	104	5	4.8

The most common dyslipidemia was elevated triglyceride level (46.34 %), followed by low HDL (31.7 %), combined elevated triglyceride and low HDL (7.31 %) as presented in Table 5.

Table 5: Pattern of dyslipidemia among PDR cases in type 2 diabetes patients

Pattern of dyslipidemia	Frequency	Percent
High Triglyceride	19	46.34
Low HDL	13	31.7
High Triglyceride + Low HDL	3	7.31
High Cholesterol + Triglyceride	2	4.87
High Cholesterol	1	2.43
Low HDL+ high LDL	1	2.43
High Cholesterol + LDL + Triglyceride	1	2.43
High Triglyceride + LDL	1	2.43
Total	41	

Discussion

Diabetic retinopathy is the leading cause of new-onset blindness among the working age population in the western world (Klaver et al. 1998; The eye disease prevalence research group, 2004). The changing lifestyle led to the increased number of type 2 diabetics in the early age groups in developing countries like Nepal (Chan et al. 2009; Wild S et al, 2004). Nearly two-thirds of cases in our series belonged to the age group of below 60 years of age. The lower mean age of PDR cases (56.96 ± 9.394 years) in this series indicates an early onset and a rapid progression to sight-threatening retinopathy, a serious public health concern. As in similar studies from Nepal, the low number of patients with a higher education reflects the limited access to higher education in the country. The majority of patients from occupations like business, service holders and housewives reflect the sedentary nature of their work. The demographic profile of the educational status and occupation of the patients was similar to that of other similar studies in Nepal (Shrestha et al, 2007; Thapa et al, 2012).

The duration of diabetes is the most important risk factor for development of diabetic retinopathy. At 20 years of duration, almost 60 % of type 2 diabetes has some form of DR according to the Wisconsin epidemiological study of diabetic retinopathy (Davis et al, 1998; Klein et al, 1984; Katulanda et al, 2014). In our series, the mean duration of diabetes was 11.42 ± 5.356 years and half of the cases had diabetes

for up to 10 years. The practice of consultation with a physician only for the symptomatic systemic problems and the lack of regular blood sugar tests may have contributed to this situation of late presentation as the majority of type 2 diabetics are asymptomatic till the advanced stage of systemic involvement.

More than half of our patients had concurrent hypertension, which is higher than found in a previous series that included all diabetic cases irrespective of their diabetic retinopathy (Thapa et al, 2012; Shrestha et al, 2007; Rahman et al, 2011). This could be one of the causes for rapid deterioration of diabetic retinopathy despite the short duration of diabetes.

In our series, almost four-fifths of the patients had abnormal fasting and/ or postprandial blood sugar and 73 % have poor glycemic control (HbA1C > 7.0 %), which reflects the poor compliance of the patients for sugar control. The high number of PDR and CSME even in patients with a short duration of diabetes could be largely due to this poor glycemic control, like in other studies (Klein et al, 1984; Pradeepa et al, 2008), where both poor glycemic control and abnormal fasting and post prandial sugar levels were the significant risk factors for diabetic retinopathy. So, besides adequate laser therapy, counseling regarding the importance of glycemic control is very important while managing such cases.

Almost two-thirds of our cases had dyslipidemia despite the fact that only three cases were aware of their underlying lipid panel abnormality. This could be either due to a lack of routine blood examination for lipid panel or a low level of counseling for such concurrent systemic conditions. Among the lipid panel abnormality, the most common dyslipidemia observed was a high level of triglyceride, and it was followed by a low HDL level (a protective lipid) and a combined high triglyceride and low HDL. As in the series of Larsson et al. 1999, we found low level of HDL though triglyceride was not a risk factor in multivariate analysis in their series and lipid panel abnormality was correlated with severity of diabetic retinopathy. Likewise, total cholesterol and LDL were the independent risk factors for DR in the series by Sachdev et al. 2010. The higher number of concurrent CSME along with PDR in our series could be due to concurrent dyslipidemia as in other series (Chetin et al, 2013; Ozer et al, 2009).

More than two-thirds of our cases having coexisting microalbuminuria, half of the cases with proteinuria on routine urine examination and three cases having abnormal urea, creatinine (elevated when significant renal damage) reflects the deranged kidney function that is considered to be an important risk factor for rapid progression of DR that was present in a large number of our cases as in some other series (Cruickshanks et al, 1993; Reddy et al, 2013; Padmaja et al, 2011).

Though the large sample size of our PDR case series, the limitation of the study is a lack of control group for specific risk factors at our diabetic population. With the large number of PDR cases having concurrent systemic problems, we recommend further studies involving different control groups.

Conclusion

Systemic hypertension, poor glycemic control, proteinuria and dyslipidemia were found in majority of cases as important risk factors for the early onset and rapid progression to proliferative diabetic retinopathy and macular edema despite short duration of diabetes among our diabetic patients. Diabetics with such concurrent systemic problems should undergo prompt evaluation for diabetic retinopathy. Timely identification and proper control of these systemic conditions could help in reducing visual impairment and blindness among the diabetics.

Acknowledgements
The authors acknowledge the Fred Hollows Foundation, Australia for the financial support for this study.

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Source of support: acknowledged. Conflict of interest: none