FACTORS ASSOCIATED WITH PROGRESSION OF DIABETIC RETINOPATHY, A MULTI-CENTRIC STUDY IN KUWAIT

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ABSTRACT

Background: *Diabetic retinopathy (DR) is a progressive sight threatening diabetic complication. The prognosis seems to be related to largely modifiable risk factors.*

Objectives: *The aim of the study was to identify factors that could be associated with progression of DR. among adult diabetic patients attending primary health care centers in Kuwait.*

Methods: *The current study is a part of a larger multi-centric one that included 704 diabetic patients. A nested case-control study was used whereas all patients with proliferative diabetic retinopathy (PDR) (case group, n = 33) were compared with all other diabetic patients with non-proliferative diabetic retinopathy (NPDR) (control group, n = 183) to determine the associated factors with cases. A pre-designed questionnaire included socio-demographic, clinical data, laboratory investigations, in addition to health care characteristics and personal practice. Basically univariate analyses were followed by multiple logistic regression analysis.*

Results: *Out of 704 diabetic patients participated in the study 216 were diagnosed as having DR with an overall 30.7% prevalence rate. Among 216 patients with DR, 33 were diagnosed as PDR (4.7%) and 183 were diagnosed as NPDR (26.0%). Of the personal factors examined, nationality was the only significant determinant of PDR (OR = 0.8, 95% CI: 0.71 – 0.9). Among clinical factors, patients with type 2 – insulin treated diabetes were more prone to have PDR as compared to type 1 (OR = 1.2, 95% CI: 1.1 – 1.4). Duration of diabetes $\geq$ 20 years was a significant predictor of PDR (OR = 1.3, 95% CI: 1.1 – 1.5).*

Also, poor hyperglycemia and hypertension were significantly modifiable risk factors (OR = 1.2, 95% CI: 1.1 – 1.3) and (OR = 1.2, 95% CI: 1.1 – 1.4) respectively. Ex-smoking was significantly associated with PDR (OR = 8.3, 95% CI: 3.3 – 23.8).

Conclusion: *Hyperglycemia and hypertension are the strongest modifiable risk factor for PDR. Patients with longer duration of diabetes particularly those with type 2-insulin treated diabetes were more prone for PDR and should be regularly screened for DR.*

Keywords: *Diabetic retinopathy - progression - associated factors*

INTRODUCTION

Diabetes mellitus (DM) has long been recognized as a major health problem, not only for its adverse health impact on individuals, but also for its economic burden on health care system and society at large. A substantial proportion of patients with diabetes develop long - term complications.(1) Diabetic retinopathy (DR) is one of the commonest micro-vascular complications of DM. It is among the leading causes of blindness in people of working age. It is a progressive sight threatening disease that affects retinal vasculatures.(2,3)

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One of the widely accepted classifications of DR is the American Academy of Ophthalmology's classification.(2) According to this classification DR is classified as non-proliferative (NPDR) and proliferative (PDR). NPDR is the earliest stage of DR whereas retinal vasculatures are characterized by microaneurysm, intraretinal hemorrhage and cotton weed spots. NPDR is further classified as mild (Grade I), moderate (Grade II), and severe (Grade III) according the degree of Severity. PDR is the advanced stage of DR which is characterized by the formation of new vessels at the optic disc or new vessels elsewhere in the retina. (Grade IV) PDR progresses to the highest stage of severity and severe visual loss due to vitreous hemorrhage, progressive fibrovascular proliferation, retinal detachment, and neovascular glaucoma (Grade V) (Table 1).(2, 4, 5)

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Table I: International clinical diabetic retinopathy disease severity scale

Disease severity level	Findings observable upon dilated ophthalmoscopy
No apparent retinopathy	No abnormalities
Mild NPDR	Microaneurysms only
Moderate NPDR	More than just microaneurysms but less than severe NPDR
Severe NPDR	Any of the following – More than 20 intraretinal hemorrhages in each of four quadrants – Define venous beading in two or more quadrants – Prominent intraretinal microvascular abnormalities in one or more quadrants And no signs of proliferative retinopathy
PDR	One or both of the following – Neovascularization – Vitreous/preretinal hemorrhage

Several risk factors for progression of retinopathy in diabetic patients have been considered. So far, the type of diabetes, duration of diabetes, hyperglycemia, hypertension, and hyperlipidemia have been shown to be the most powerful predictor of progression DR.[6-10]

Few studies have been carried in Kuwait on DR. However, none of these studies considered progression of DR, has been conducted on both types of DM, or in a multi-centric population. Also, these studies considered Kuwaiti population only and did not consider the control for possible confounding effect of the variables.[11-13]

In a country with a high prevalence of DM, like Kuwait, revealing the extent and factors associated with progression of DR is a high public health priority. The aim of the present study is to determine the prevalence of PDR among adult diabetic patients attending primary health care centers in Kuwait and to identify factors that could be associated with PDR especially those factors that can be considered avoidable.

METHODS

Setting and design:

This study was carried out in five primary health care centers representing the five health regions in Kuwait. The field duration of the study covered 5 months starting from June to October 2006. The current study is a part of a larger multi-centric descriptive one. The details of the methodology can be found elsewhere.[14] In brief, all diabetic patients attending to the selected centers were sequentially recruited. Two index days were randomly defined for each of the selected centers for collection of data. Newly discovered cases were excluded from the study. The sampling unit was diabetic patient who had been diabetic for at least 2 years. Also, they should be fully examined by an ophthalmologist with an ophthalmic report in their medical records. Selection criteria included age $\geq$ 18 years. All eligible subjects were asked to participate in the study. The final studied sample size was 704 adult diabetic patients.

The present study could be differentiated into two phases. The first one was a cross sectional study to determine the prevalence of different grades of DR among adult diabetic patients attending the selected centers. The second one was a nested case-control study, whereas all patients with PDR (case group, n = 33) were compared with all other diabetic patients with NPDR (control group, n = 183) to determine the associated factors with cases. Patients were considered eligible as cases if they had type 1 or type 2 diabetes for at least 2 years and PDR (grades IV or V) had been diagnosed by an ophthalmologist in one or both eyes. Patients were considered eligible as control if they had type 1 or type 2 diabetes for at least 2 years and NPDR (grades I, II, or III) had been diagnosed by an ophthalmologist in one or both eyes.

Verbal consent was obtained from all the subjects, after explanation of the purpose and importance of the research, prior to conducting the survey.

Study questionnaires

The structured interview method has been adopted to collect data for this study with a specially designed questionnaire. It was derived from other published studies dealing with the same topic as well as from our own experience. It included socio-demographic characteristics (age, gender, nationality, education, occupation, and marital status) and clinical data (type of DM, duration since diagnosis, treatment, glycemic state, presence of hypertension, co-morbid conditions, obesity and chronic diabetic complications), in addition to pattern of care and patient' practice (need of help to reach health care center, regular follow-up, compliance with diet recommendations, regular use of drug, regular check of urine glucose, regular check of blood glucose, smoking, physical activity). Biochemical investigations included fasting blood glucose, Hb_{A1c}, total cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL), triglycerides and micro-albuminuria.

Measurements:

Trained physicians in the chosen centers collected data by interviewing patients and reviewing their medical records. In order to ensure uniformity of data measuring methods that relied on clinical judgment, all participating physicians were trained on data collection and the questionnaire was thoroughly tested for clarity before it was accepted.

Patients were considered as having type 1 diabetes if their age at diagnosis was < 30 years and

insulin was used continuously from the time of diagnosis. They were considered as having type 2 diabetes if their age at time of diagnosis was ≥ 30 years. Three blood pressure measurements were obtained by trained physicians using a standardized sphygmomanometer after a 5-minute sitting rest. Hypertension was considered on the basis of clinical judgment and confirmed by history of receiving anti-hypertensive drugs and/or the presence of systolic blood pressure value > 140 mmHg and/or diastolic pressure > 90 mmHg.[15]

Patients were classified as having diabetic neuropathy or cardiovascular complication on the basis of the presence of clinical symptoms and signs and confirmed by medical reports in their records. Nephropathy was considered if patient had microalbuminuria (albumin excretion < 30 mg per 24 hours), clinical proteinuria, or subjected to dialysis. The glycemic state of patient referred to the last value of Hb_{A1c} and it was considered adequate if < 7%. Normal levels for blood lipids were identified as 5.6 mmol/L for total cholesterol, 2.1 mmol/l for triglycerides, 3.4 mmol/L for LDL, and 0.91 mmol/L for HDL. Major limb complications included foot ulcer, claudication, gangrene, persistent ischemic pain or amputation. Co-morbidity included conditions that had been already present prior to the diagnosis of DM (angina pectoris, hypertension, renal disease, endocrine dysfunction, dyslipidemia and liver diseases).

Physical activity was considered if it was practiced for 30 minutes at least 3-4 times a week. For height and weight measurement, we used the Detecto-Scale Instrument, which was calibrated once a day before use. Body mass index was calculated as weight in kg / height in square meters.

Statistical analysis:

Analysis was initially carried out based on a series of univariate comparisons. In order to control simultaneously for possible confounding effect of the variables, multiple logistic regression was used for the final analysis. In the univariate analysis Chi-square test was used to detect the association between PDR and explanatory variables. In multiple logistic regression analysis, the association between exposure and outcome was expressed in terms of odds ration (OR) together with their 95% confidence intervals (95% CI).

All the explanatory variables included in the logistic model were categorized into two or more levels (R = reference category): gender: male^R, female; age (years): < 40^R, 40 – 59, ≥ 60; nationality: Kuwaiti^R, non-Kuwaiti; education: primary or less^R, intermediate / secondary, university or higher; occupation: unemployed^R, worker, clerk, professional; marital state: married^R, unmarried; type of diabetes: type 1^R, type 2, type 2 – insulin treated; duration of diabetes (years): < 10^R, 10 – 19, ≥ 20; treatment: oral^R, insulin, oral + insulin; glycemic state: good control^R, poor control; hypertension: no^R, yes; co-morbid conditions: no^R, yes; obesity: no^R, overweight, obese, severely obese; cardio-vascular complications: no^R, yes; nephropathy: no^R, yes; neuropathy: no^R, yes; diabetic foot: no^R, yes; need of help to reach health care center: no^R, yes; regular follow-up visits: no^R, yes; compliance with diet recommendations: no^R, yes; regular check of urine glucose: no^R, yes; regular check of blood glucose: no^R, yes; smoking: no^R, yes, Ex-smoking; physical activity: no^R, yes. Analysis was performed using SPSS package.

RESULTS

Out of 704 diabetic patients participated in the study 216 were diagnosed as having DR with an overall 30.7% prevalence rate. Among 216 patients with diabetic retinopathy, eye complications were classified as grade I (40.7%), grade II (26.4%), grade III (17.6%), grade IV (9.3%), and grade V (6.0%). (Figure 1)

A total of 33 (4.7%) diabetic patients with PDR or SVA were compared with 183 (26.0%) patients with NPDR.

The socio-demographic, clinical, health care related characteristics and personal factors together with the results of unvariate analyses were presented in tables II – IV. The results of the final analysis using multiple logistic regression were summarized in table V. No significant association between PDR and socio-demographic factors was detected except for nationality. Non-Kuwaiti patients had 20% lower risk of PDR than Kuwaiti patients (OR = 0.8, 95% CI: 0.71 – 0.9).

Among clinical factors, type of diabetes was significantly associated with PDR. Patients with type 2 -insulin treated diabetes had an increased risk of PDR as compared with type 1 (OR = 1.2, 95% CI: 1.1 – 1.4). Longer duration of diabetes seamed to increase the risk PDR. Patients who had diabetes for ≥ 20 years had 30% more risk as compared with those who had diabetes for less than ten years (OR = 1.3, 95% CI: 1.1 – 1.5). Poor glycemic state and hypertension were significantly associated factors with PDR (OR = 1.2, 95% CI: 1.1 – 1.3) and (OR = 1.2, 95% CI: 1.1 – 1.4) respectively. Ex-smoking was significantly associated with PDR as compared with non smoking (OR = 8.3, 95% CI: 3.3 – 23.8).

Among health care and patients' practice, need of help to reach health care center was the only factor that could be proved to be significantly associated with PDR (OR = 4.2, 95% CI: 1.8 – 9.5)

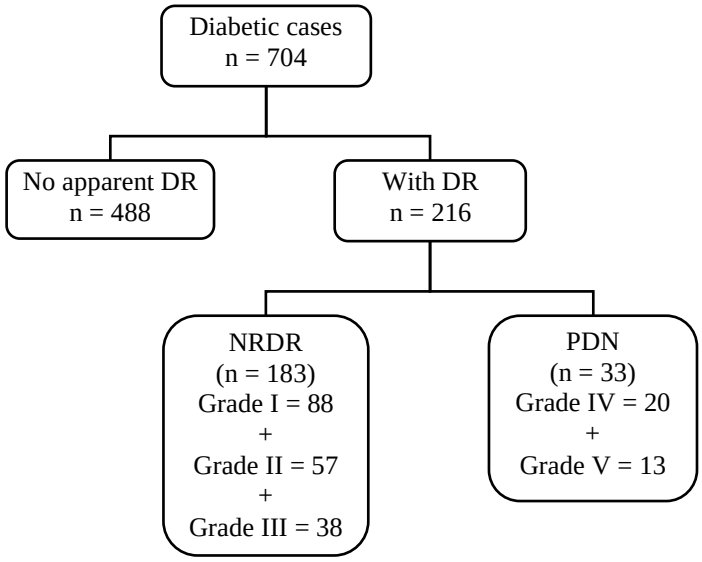

Fig 1. Scheme flowchart for classification of diabetic patients included in the study.

Table II: Socio-demographic characteristics of diabetic patients with proliferative and non-proliferative retinopathy

Variables	Retinopathy				Significance
	Non-proliferative (n=183)		Proliferative (n=33)		
	No.	%	No.	%	
Gender					
Male	81	*44.3*	16	*48.5*	X^2 = 0.20
Female	102	*55.7*	17	*51.5*	P = 0.65
Age (years)					
< 40	8	*4.4*	1	*3.0*	X^2 = 7.15
40 - 59	88	*48.1*	8	*24.2*	P = 0.03
≥ 60	87	*57.5*	24	*72.7*	
Nationality					
Kuwaiti	117	*63.9*	29	*87.9*	X^2 = 17.12
Non-Kuwaiti	66	*36.1*	4	*12.1*	P = 0.01
Education					
Primary or less	72	*39.3*	15	*45.5*	X^2 = 0.48
Intermediate / Secondary	71	*38.8*	11	*33.3*	P = 0.79
University or higher	40	*21.9*	7	*21.2*	
Occupation					
Unemployed	98	*53.6*	23	*69.7*	
Worker	57	*31.1*	4	*12.1*	X^2 = 8.07
Clerk	13	*7.1*	5	*15.2*	P = 0.05
Professional	15	*8.2*	1	*3.0*	
Marital state					
Married	138	*75.4*	22	*66.7*	X^2 = 1.11
Unmarried	45	*24.6*	11	*33.3*	P = 0.29

Table III: Clinical characteristics of diabetic patients with proliferative and non-proliferative retinopathy

Variables	Retinopathy				Significance
	Non-proliferative (n=183)		Proliferative (n=33)		
	No.	%	No.	%	
Type of diabetes					
Type 1	8	*4.4*	1	*3.0*	X^2 = 7.41
Type 2	115	*62.8*	13	*39.4*	P = 0.03
Type 2 – insulin treated	60	*32.8*	19	*57.6*	
Duration of diabetes (years)					
< 10	76	*41.5*	6	*18.2*	X^2 = 8.58
10 - 19	70	*38.3*	14	*42.4*	P = 0.01
≥ 20	37	*20.2*	13	*39.4*	
Treatment					
Oral	113	*61.7*	13	*39.4*	X^2 = 10.65
Insulin	38	*20.8*	6	*18.2*	P = 0.01
Oral + insulin	32	*17.5*	14	*42.4*	
Glycemic state					
Good control	46	*25.1*	3	*9.1*	X^2 = 4.10
Poor control	137	*74.9*	30	*90.9*	P = 0.04
Dyslipidemia					
No	132	*72.1*	28	*84.8*	X^2 = 2.36
Yes	51	*27.9*	5	*15.2*	P = 0.13
Hypertension					
No	108	*59.0*	13	*39.4*	X^2 = 4.37
Yes uncontrolled	75	*41.0*	20	*60.6*	P = 0.04
Co-morbid conditions					
No	93	*50.8*	16	*48.5*	X^2 = 0.06
Yes	90	*49.2*	8	*51.5*	P = 0.81
Obesity					
No	25	*13.7*	4	*12.1*	X^2 = 1.65
Overweight	68	*37.2*	9	*27.3*	P = 0.65
Obese	46	*25.1*	11	*33.3*	
Severely obese	44	*24.0*	9	*27.3*	
Cardio-vascular complications					
No	97	*53.0*	10	*30.3*	X^2 = 5.76
Yes	86	*47.0*	23	*69.7*	P = 0.02
Nephropathy					
No	142	*77.6*	21	*63.6*	X^2 = 2.94
Yes	41	*22.4*	12	*36.4*	P = 0.09
Neuropath					
No	79	*43.2*	6	*18.2*	X^2 = 7.31
Yes	104	*56.8*	27	*81.8*	P = 0.01
Diabetic foot					
No	51	*27.9*	3	*9.1*	X^2 = 5.26
Yes	132	*72.1*	30	*90.9*	P = 0.02

Table IV: Pattern of care and patients' practice of diabetic patients with proliferative and non-proliferative retinopathy

Variables	Retinopathy				Significance
	Non-proliferative (n=183)		Proliferative (n=33)		
	No.	%	No.	%	
Need of help to reach health care center					
No	133	*72.7*	13	*39.4*	X^2 = 14.14
Yes	50	*27.3*	20	*60.6*	P < 0.001
Regular follow-up visits					
No	67	*36.6*	14	*42.4*	X^2 = 48.63
Yes	116	*63.4*	19	*57.6*	P = 0.53
Compliance with diet recommendations					
No	117	*63.9*	24	*72.7*	X^2 = 0.95
Yes	66	*36.1*	9	*27.3*	P = 0.33
Regular use of drugs					
No	39	*21.3*	7	*21.2*	X^2 = 0.00
Yes	144	*78.7*	27	*78.8*	P = 1.00
Regular check of urine glucose					
No	180	*98.4*	32	*97.0*	Fisher Exact
Yes	3	*1.6*	1	*3.0*	P = 0.35
Regular check of blood glucose					
No	120	*65.6*	21	*63.6*	X^2 = 0.05
Yes	63	*34.4*	12	*36.4*	P = 0.83
Smoking					
No	148	*80.9*	22	*66.7*	X^2 = 2.81
Yes	31	*16.9*	9	*27.3*	P = 0.25
Ex- smoker	4	*2.2*	2	*6.1*	
Physical activity					
No	94	*51.4*	22	*66.7*	X^2 = 2.63
Yes	89	*48.6*	11	*33.3*	P = 0.10

Table V: Factors associated with progression of diabetic retinopathy, results of multivariate logistic regression analysis

Variables	Odds Ratio	95% CI
Nationality		
Kuwaiti [R]	1	
Non-Kuwaiti	0.8	(0.7 – 0.9)
Type of diabetes		
Type 1 [R]	1	
Type 2	1.0	(0.8 – 1.3)
Type 2 – insulin treated	1.2	(1.1 – 1.4)
Duration of diabetes (years)		
< 10 [R]	1	
10 - 19	1.1	(1.0 – 1.3)
≥ 20	1.3	(1.1 – 1.5)
Glycemic state		
Good control [R]	1	
Poor control	1.2	(1.1 – 1.3)
Hypertension		
No [R]	1	
Yes	1.2	(1.1 – 1.4)
Smoking		
No [R]	1	
Yes	1.0	(0.9 – 1.2)
Ex-smoking	8.3	(3.3 – 23.8)
Need of help to reach health care center		
No [R]	1	
Yes	4.2	(1.8 – 9.5)

[R] = Reference category, OR = Odds ratio, CI = Confidence interval

DISCUSSION

To our knowledge, the present study, aimed at identifying factors associated with the progression of DR, is one the largest studies conducted in Kuwait. It was designed to investigate importance of both clinical and care-related factors affecting progression of diabetic eye complications. The focus on the problem of avoidability, and thus on the quality of care-related issues required the involvement of a large number of patients. Furthermore, patients were enrolled from all health regions in Kuwait, making the results mare generalized.

The overall prevalence of DR in the present study was 30.7%. PDR constituted 4.7% (2.8% with grade IV and 1.9% with grade V) as compared with 26.0% for NPDR (12.5% with grade I, 8.10% with grade II, and 5.4% with grade III). The prevalence of PDR reported in the present study was relatively lower than that reported in many previous studies that showed a wide range of rates of progression of DR due to differences in duration of diabetes, type of diabetes and baseline glycemic state.[16-18] Recent changes in rates of progression and improvement of DR would be expected with the more widespread use of intensive glycemic and blood pressure control.[19-21]

In his study, Shah found that the overall incidence of PDR and SVL observed in studies after 1985 (e.g., 2.6% for PDR and 3.2% for SVL at 4 years) were substantially lower than rates observed before 1985 (19.5% for PDR and 9.7% for SVL at 4 years).[16] These finding may reflect improved patient and physician awareness, screening and prevention, as well as better management of diabetes and associated risk factors.[17,22]

Once the patient is diagnosed with DR the goal is to slow down the progression of the disease and prevent the development of sight-threatening retinopathy that eventually will lead to partial visual loss or blindness. Many risk factors are believed to play an important role in this process. While some of them can be modified others cannot. Maintaining modifiable risk factors within normal ranges such as blood pressure and glycosylated hemoglobin (HbA1c) has shown to reduce the progression of DR.[18] Various studies have shown that chronic hyperglycemia, hypertension and hyperlipidemia

contribute to the pathogenesis of DR and its progression.

In the present study, among modifiable factors, hyperglycemia and hypertension, but not hyperlipidemia, were proved to be significant risk factors for PDR. This goes in accordance with previous preliminary observational studies,[23,24] as well as large randomized controlled trials in which effective glycemic control has been demonstrated to reduce both the incidence and progression of DR. In both types 1 and 2 DM, improved glycemic control (measured by HbA1c), reduces the progression of DR. The advantages of improved glycemic control apply to all ages and both genders. The Diabetes Control and Complications Trial (DCCT) randomized patients with type 1 diabetes to receive intensive glycemic or conventional therapy with the objective to investigate whether this would prevent or delay the progression of early pre-proliferative retinopathy. Results of over 6.5 years of follow-up showed that, progression of DR reduced by 54% in the intensive treatment group.[25] The results of DCCT were further confirmed by the UK Prospective Diabetes Study (UKPDS). The UKPDS randomized patients of type 2 diabetes to either conventional therapy or an intensive treatment.[10] Over 10 years' follow-up, reductions of HbA1c by 11%, microvascular end points by 25%, and laser photocoagulation by 29% in the intensive therapy group.[4]

Hypertension is one of the important and modifiable risk factors for worsening of DR.[26] Results of randomized control trials have demonstrated that hypertension is detrimental to each stage of DR and a tight BP control strategy can reduce the risk of progression of eye complications from diabetes.[27-30] In type 1 DM patients, treatment of hypertension resulted in a 23% reduction in the progression of DR. In addition, in type 2 DM patients, the analyses of the UKPDS trial showed that control of blood pressure reduces the progression of DR and visual acuity deterioration by 34% and 47% with tight control of blood pressure.[27,31] The results from this study and other studies suggested that the beneficial effect of anti-hypertensive treatment and the deleterious effect of increased blood pressure are immediate and require regular measurement of blood pressure.(prog6) As opposed to UKPDS, the findings of Appropriate Blood Pressure Control in Diabetes Trial however found no difference in DR progression between the groups assigned to a policy of tight BP control versus less tight BP control over a period of 5.3 years.[28]

In the present study, hyperlipimia was not a significant determinant of PDR. This goes in accordance with previous studies. Although reduction in low-density lipoprotein cholesterol is associated with decreased macrovascular complications of diabetes, the role of lipid lowering therapy for DR prevention remains inconclusive.[32] In addition, no randomized control trial has shown any benefit of lowering cholesterol blood level in terms of retinopathy risk reduction.[18] However, many other studies reported a positive correlation between dyslipidemia and progression of retinopathy or macular edema. Dyslipidemia leads to development of hard exudates, that in turn interfere with vision in DR. [33] A study of type 1 diabetic patients' cohort from the DCCT studies further confirmed this correlation and showed that severity of retinopathy was positively associated with triglycerides and negatively associated with HDL cholesterol levels.[34] The impact of long-term lipid lowering therapy on progression of retinopathy and the need for laser treatment in patients with type 2 diabetes has been assessed in the Fenofibrate Intervention and Event Lowering in Diabetes study. In this study, it was found that the progression of retinopathy did not differ significantly after lipid lowering therapy.[35]

In the present study, within the non-avoidable factors, duration and type of diabetes were associated significantly with NPR. Patients with longer duration, and those with type 2-insulin treated diabetes were more liable for PDR. Patient with type 1 diabetes may show evidence of retinopathy as early as 5 years after the onset of diabetes, and almost all patients will show varying degrees of retinopathy 20 years after the onset of diabetes. Background retinopathy may even be present at time of diagnosis of type 2 diabetic patients, consistent with the usually long duration of subclinical hyperglycemia in such patients, and more than 60% of type 2 diabetic patients will have some degree of retinopathy after 20 years of onset of diabetes.[32] Type 2 insulin treated patients are usually older in age, with uncontrolled hyperglycemia and with many other complications. All of which are themselves risk factors for development and progression of DR.

In the present study Ex smoking and need of help to reach health care facilities were positively associated with PDR. However, this could be an association rather than causation, as patients with severe diabetic complications are usually advised to discontinue smoking. Also, patients with severe eye complication are, of course, in need of someone to accompany them everywhere and not for clinical examination only. The same result has been found by Prog6 who reported that discontinuation of smoking is recommended for reducing the development of other complications of diabetes, however, it appears that cigarette smoking is not a risk factor for the progression of DR.[18]

Kuwaiti patients have been proved to be at higher

risk of PDR than non-Kuwait patients. This could be attributed to the fact that non-Kuwaiti patients are usually healthy persons that come to Kuwait for work opportunities. Also they stay in Kuwait for limited periods, hence they would leave Kuwait before the progression of DR if they had.

We acknowledge some limitations in our study. As we relied upon patient interview and record study, the data obtained might be, to certain extent, affected by the quality of recording. Also, as in any case control study, the design of the study is by definition retrospective and is subjected to recall bias. Also, the baseline figures of patients at the onset of diabetes could not be studied due to the nature of the study. There is a limitation with accuracy of the duration of diabetes as it was based on self reports from diabetic patients. Nevertheless, the results are consistent with those coming from cohort studies.

Conclusion:

Also, diabetic patients without evidence of retinopathy should undergo eye examinations periodically to detect its emergence and to detect early treatable stages of DR which are frequently asymptomatic. For patients with moderate-to-severe pre-proliferative disease, more frequent eye examinations are necessary to determine when to initiate therapy. More aggressive management of hyperglycemia and hypertension could reduce the prevalence of PDR.

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