Prevalence and risk factors for diabetic retinopathy among Omani diabetics

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Abstract

***Aims*—To study the prevalence of diabetic retinopathy in a population of patients attending a diabetic clinic and to evaluate the medical risk factors underlying its development.**

***Methods*—500 randomly selected diabetic patients attending the diabetes clinic in Al Buraimi hospital were referred to the ophthalmology department where they were fully evaluated for the absence or presence of retinopathy. Any retinopathy present was graded as mild non-proliferative retinopathy (NPR), moderate-severe NPR, and proliferative retinopathy. Several risk factors were then evaluated in order to delineate those related to occurrence of retinopathy in general as well as to the different grades of retinopathy in particular.**

***Results*—Diabetic retinopathy was detected in 212 patients (42.4%), with mild NPR present in 128 patient (25.6% of the total population), moderate-severe NPR in 20 patients (4%), and proliferative diabetic retinopathy present in 64 patients (12.8%). Factors significantly related to occurrence of retinopathy were age of the patient, duration of diabetes, presence of ischaemic heart disease, presence of hypertension, a high fasting capillary glucose level as well as elevated serum levels of urea, creatinine, cholesterol, and triglycerides. After adjustment for covariates, it was found that duration of diabetes was the only risk factor associated with mild NPR, while high diastolic blood pressure and high levels of serum creatinine, cholesterol, and triglycerides were significantly associated with the occurrence of proliferative retinopathy.**

***Conclusions*—In addition to glycaemic control, lowering of blood lipids as well as diastolic blood pressure (in hypertensive patients) may be effective in lowering the incidence of retinopathy in compromised patients.**

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Retinopathy is the most common complication in patients with diabetes mellitus especially the insulin dependent type (IDDM) and is a major cause of blindness in the population of working age.[1]

A number of studies have shown marked difference in the prevalence of diabetic retinopathy whether in IDDM[2–4] or in the non-insulin dependent type (NIDDM).[5–9] The causes of such morphological changes in the diabetic could be grouped into three categories—biochemical, haemodynamic, and humoral.[10] Of these, the biochemical changes related to prolonged hyperglycaemia (as evidenced by increased levels of glycosylated haemoglobin) are important and studies have confirmed the association between prolonged hyperglycaemia and diabetic retinopathy.[11–13] Other factors which were also implicated in the occurrence of diabetic retinopathy include duration of diabetes,[14] type of treatment,[15] hypertension,[16–18] proteinuria,[19] serum creatinine levels,[20] serum cholesterol, and triglycerides.[21 22]

With the advance in the healthcare facilities in the Sultanate of Oman, the problem of diabetes mellitus has become one of the challenges that faces the health institutes and although various reports have been issued on the degree of the problem in general, none has dealt with the eye complications of diabetes mellitus and especially that of diabetic retinopathy. In this study, we attempted to quantify the degree of the problem of diabetic retinopathy in Omani diabetics and to underline the risk factors related to this problem in particular in this rapidly developing community.

Patients and methods

Five hundred randomly selected diabetic patients who attended the diabetes clinic in Al Buraimi hospital, between September 1996 and July 1997, were examined in the ophthalmology department for the presence or absence of diabetic retinopathy, after being thoroughly examined and investigated in the medical department. Randomisation was done using conventional randomisation tables with replacement of any dropout case (owing to difficulty in grading the retinopathy level as a result of concomitant corneal or lenticular opacities).

A full medical history was taken from each patient including age of the patient, age of onset of the diabetic status, duration of diabetes, type of diabetes (which included either IDDM or NIDDM according to the classification laid down by the WHO)[23] history of hypertension, and ischaemic heart disease. History of alcohol consumption was not included in the questionnaire owing to the rarity of such practice in the Omani community.

The capillary glucose level of each patient was examined after an overnight fast using a calibrated one touch blood glucose meter (Lifescan); care was taken to warm the patient's finger tip before making a prick and not to squeeze the finger to avoid ooze of serum in the sample which may give a wrong

Table 1 Criteria for the grading of diabetic retinopathy

Grade	*Severity*	*Definition*
0	No retinopathy	Diabetic retinopathy absent
1	Mild DR	HMA ⩽50% in 2 or more fields HMA >50% in one field HE in any field and to any extent
2	Moderate-severe DR	The presence of all the following in 2 out of 4 non-overlapping fields or 2 of them + severe HMA (>75%) in one standard field: Cotton wool spots Venous beading IRMA
3	Proliferative DR	NVE ⩾0.5 DD NVD 0.25–0.33 DD and/or VH or preretinal haemorrhage

DR = diabetic retinopathy; HMA = haemorrhage and microaneurysmal formations; HE = hard exudates; IRMA = intraretinal microvascular anomalies; NVE = neovascularisation elsewhere; DD = disc diameter; NVD = neovascularisation on or within 1 DD from the optic disc; VH = vitreous haemorrhage.

reading. Diabetic control was diagnosed as good, fair, or poor when the fasting capillary glucose level was 6.6 mmol/l (120 mg/dl or less), 6.7–7.8 mmol/l (121–140 mg/dl), and more than 7. 8 mmol/l (140 mg/dl) respectively. No glycosylated haemoglobin assay was carried on in this study. Tight control of blood glucose level was aimed at in all patients especially those with IDDM as recommended by the Diabetes Control and Complication Trial (DCCT).[13] Ischaemic heart disease (IHD) was diagnosed by history and electrocardiographic abnormalities as designated by the Minnesota code.[24]

Seated blood pressure was measured in the right arm to the nearest 2 mm Hg with a random zero sphygmomanometer and the mean of two readings (for both systolic blood pressure (SBP), and the diastolic blood pressure (DBP)) was recorded. Hypertension was deemed to be present when the SBP was >140 mm Hg or when the DBP was >90 mm Hg.

The patients' characteristics described above and which included age of the patient, sex, duration of the diabetic status, type of diabetes, history of IHD, or hypertension as well as blood pressure and capillary glucose levels were related to the absence of retinopathy and the presence of any retinopathy as shown in Table 3.

A fasting serum sample was examined for the levels of urea, creatinine, cholesterol, and triglycerides using the end point technique of the BM 911 Hitachi machine.

The pupil of each eye was then dilated using tropicamide 1% and phenylephrine 10% followed by detailed fundus examination, using the Goldmann three mirror lens with the assessment carried on in seven fields,[25] and the different findings carefully recorded. The fundus findings were graded as shown in Table 1, with examination aimed at assessing the retinopathy status in an up to down direction—that is, trying not to overlook cases of proliferative diabetic retinopathy in favour of NPR findings.

Diabetic patients were classified according to the grading in the worse eye. Patients with photocoagulation scars were assigned to the proliferative group and all patients with at least two gradable fields were included in the study. Any patient with corneal opacity or lenticular opacities which precluded proper fundus examination was rejected from the study.

As regards diabetic maculopathy, only eyes with clinically significant macular oedema were recorded; however, no further discussion of such patients was undertaken in the current study.

STATISTICAL ANALYSES

The different variables chosen as risk factors for the occurrence of diabetic retinopathy in general were tested against the absence or presence of any retinopathy using a Mantel–Haensel χ^2 test. Categorial variables were entered as present or absent, while quantitative variables were transformed into binomial variables which indicated either the presence of a risk factor when it was more than the normal values for the variable (these normal values being the reference values for laboratory tests, 40 years or more for age, 10 years or less for duration of diabetes, 140 mm Hg or less for SBP, and 90 mm Hg or less for DBP) or its absence. The relative risk (RR) as well as the confidence interval (CI) were also calculated and cited whenever applicable and, for a continuous risk factor, was the risk for retinopathy associated with an increase in 1 SD of the risk factor while for a binary risk factor this was the risk of retinopathy associated with a change from 0 to 1.

After identifying the risk factors, a backward stepwise logistic regression was performed with the statistically significant variables tested against the absence of retinopathy or the presence of any retinopathy. The regression model removed variables if they were non-significant ($p > 0.05$), after which all the significant variables in the logistic model were tested against each type of retinopathy as dependent variables separately to identify the significantly effective risk factors for each grade of diabetic retinopathy.

Because the values of blood tests for urea, creatinine, cholesterol, and triglycerides were highly skewed, these variables were log transformed.

Results

Diabetic retinopathy was detected in 212 (42.4%) of the 500 diabetic patients. Mild non-proliferative retinopathy (NPR) was present in

Table 2 Prevalence of diabetic retinopathy grades (0–3) in the whole population studied as well as by type of diabetes

	Grade 0		*Grade 1*		*Grade 2*		*Grade 3*		*Total*	
	No	*%*	*No*	*%*	*No*	*%*	*No*	*%*	*No*	*%*
NIDDM	228	45.6	116	23.2	16	3.2	44	08.8	404	80.8
IDDM	60	12.0	12	02.4	4	0.8	20	04.0	96	19.2
Total	288	57.6	128	25.6	20	4.0	64	12.8	500	100.0

Table 3 Medical risk factors v absence of retinopathy or presence of any retinopathy†*

	No retinopathy	*Any retinopathy*	*RR*	*CI*	*p Value*
Age (years)	40.2 (14.3)	36.9 (11.8)	1.6	1.1, 2.2	0.006
Sex (No)					
Male	158	130	1.3	1, 3	0.149
Female	130	82			
Duration (years)	6.7 (3.5)	11.8 (5.4)	8.7	6.2, 14.3	<0.0001
Type of DM (No)					
IDDM	60	36	1.3	1.0, 2.1	0.335
NIDDM	228	176			
IHD (present)	16	28	2.6	1.3, 5.1	0.005
SBP (mm Hg)	125 (12.2)	150 (15.6)	3.7	2.1, 7.1	<0.0001
DBP (mm Hg)	70.6 (7.2)	84.3 (9.9)	3.6	2.2, 6.4	<0.0001
FCG (mmol/l)	8.56 (1.4)	9.8 (3.6)	1.8	1.3, 3.2	0.002

*Mean (SD) for quantitative risk factors.
†Mantel–Haensel test.

Table 4 Values (mean/SD)) of urea, creatinine, cholesterol, and triglycerides in patients with and without retinopathy

	No retinopathy	*Any retinopathy*	*RR*	*CI*	*p Value*
Urea	3.8/2.7	7.2/3.1	2.4	1.9, 4.2	*
Creatinine	67.2/18.1	91.2/14.8	2.3	2.0, 4.2	*
Cholesterol	3.3/1.6	5.6/1.1	4.8	3.5, 8.2	*
Triglycerides	1.8/0.4	2.5/0.7	6.9	5.4, 11.1	*

*All values significant at p<0.0001.

25.6% of the total population studied (60.4% of patients with any form of diabetic retinopathy), moderate to severe NPR in 4%, and proliferative retinopathy in 12.8%. Overall, retinopathy was more prevalent in patients with NIDDM compared with those with IDDM (23.2% *v* 2.4% for mild NPR, 3.2% *v* 0.8% for moderate-severe NPR, and 8.8% *v* 4% for proliferative retinopathy respectively) (Table 2).

One hundred and thirty of the patients examined were males and 83% of the 212 patients had NIDDM. The mean duration of diabetes was 6.7 years in patients without retinopathy in comparison with 11.8 years in patients with any type of retinopathy. Ischaemic heart disease (IHD) was found in 16 patients with no retinopathy, the SBP had a mean of 150 mm Hg in patients with retinopathy, and fasting capillary glucose (FCG) level had a mean of 9.8 mmol/l in patients with retinopathy (Table 3).

Thirty six patients were rejected from the current study owing to lenticular and/or corneal opacities and were substituted with an equivalent number using a randomised process.

The various risk factors studied in relation to the occurrence of diabetic retinopathy are listed in Table 3 together with the relative risk of each factor as related to the development of any type of retinopathy, its confidence interval, and significance level.

The mean age of the patients with no retinopathy was not much different from that of patients with retinopathy (40.2 years *v* 36.9 years). Yet when patients were segregated into two categories, one including those less than 40 years (high risk group) and the other those patients 40 years or older, it was found that the risk for retinopathy in the first category was more than the second. Such risk increased 1.6 times for every standard deviation decrease in the age of patients less than 40 years of age; this risk was significant at p = 0.006.

The same finding was observed regarding duration of diabetes. The highest risk for the development of retinopathy (8.7) was in those patients having diabetes mellitus for more than 10 years, regardless of whether the patient was on insulin therapy or on oral treatment (p = 0.335). The presence of IHD, an SBP of more than 140 mm Hg, a DBP more than 90 mm Hg, and a FCG level more than 6.6 mmol/l (120 mg/dl) all carried a significantly increased risk for developing any form of diabetic retinopathy (RR = 2.6, 3.7, 3.6, 1.8 respectively and p values equal to 0.005, <0.0001, <0.0001, and 0.002 respectively). On the other hand, there was no relation between sex and the development of diabetic retinopathy in any patients studied (p = 0.149).

Blood urea, creatinine cholesterol, and triglycerides were all significantly related to the development of retinopathy (Table 4) and the maximum risk was with triglycerides which carried a relative risk of 6.9 and a confidence interval of 5.4 to 11.1.

A multiple logistic regression model was then developed to try to sort out the various risk factors as well as to identify which of the latter were related to each level of retinopathy. The results listed in Table 5 show that age of the patient, IHD, a high SBP, a high FCG, and a high urea level were no longer significant when adjusted for in the logistic model. On the other hand longer duration of diabetes, high levels of blood cholesterol, triglycerides, and creatinine and patients with high DBP were still at risk of developing any grade of diabetic retinopathy in decreasing frequency of significance.

When analysing these factors after considering mild NPR retinopathy, moderate-severe NPR, and proliferative retinopathy as separate

Table 5 Multiple logistic regression analysis of risk factors for any retinopathy as well as for different grades of retinopathy

		Grade 1	*Grade 2*	*Grade 3*
	DR/No DR	*RR (CI)/P*	*RR (CI)/P*	*RR (CI)/P*
Age (years)	0.008	1.1 (0.8, 1.9)/0.3	1 (0.2, 2)/0.3	1.6 (1.4, 3.1)/0.06
Duration (years)	<0.0001	4 (2, 6)/0.004	5 (2, 8)/0.003	1.1 (0.7, 2.1)/0.07
IHD	0.9			
SBP (mm Hg)	0.5			
DBP (mm Hg)	0.007	1.1 (0.5, 2.3)/0.06	5 (3, 8)/0.04	5 (2, 8)/0.002
FCG (mmol/l)	0.42			
Urea	0.5			
Creatinine	0.002	0.7 (0.5, 2.2)/0.23	4 (2, 7)/0.02	5 (3, 9)/0.01
Cholesterol	<0.0001	1.5 (.8, 2.7)/0.08	5 (3, 8)/0.05	5 (2, 7)/0.002
Triglycerides	<0.0001	2 (1, 3)/0.07	8 (5, 11)/0.02	11 (7, 13)/0.001
Goodness of model fit	74.2%	76.9%	78.7%	74.7%

dependent variables, it was found that as far as mild NPR retinopathy was concerned, only duration of diabetes was a statistically significant risk factor ($p = 0.004$) yet the relative risk for this factor decreased to 4 instead of 8.7. In the other two categories of retinopathy all the variables were significant risk factors (except for duration of diabetes in cases with proliferative retinopathy) with variable levels of significance, the highest being related to the level of blood triglycerides ($p = 0.001$) which showed a relative risk of 11 in eyes with proliferative diabetic retinopathy in comparison with 6.9 for the risk of any retinopathy. For the other risk factors, there was also a noticeable increase in risk for the different types of retinopathy in comparison with the occurrence of any retinopathy.

It should be noted that the logistic model was able to predict around 75% of the variables related to the occurrence of any retinopathy; the values for the different grades of retinopathy studied were 77%, 79%, and 75% respectively.

Discussion

With the marked improvement in the quality of health care in the various health institutes of the Sultanate of Oman in recent years, diabetes mellitus has emerged as one of the major health problems.

In a recent survey on this issue, Asfour *et al* [26] found a 10% overall diabetes rate, rising to over 30% in the elderly. Impaired glucose tolerance on the other hand was found in 13% of females and 8% of males. Alwan and King[27] suggest that these very high rates may be due to the thrifty genotype in action. They believe that the populations of the harsh desert environment of the Middle East have developed an unusually efficient metabolism favouring a hunter-gather way of life. Once westernisation occurs, however, with associated weight increase and exercise reduction, the former advantage becomes detrimental and diabetes occurs. Paralleling this high prevalence of diabetes was a concern that complications of diabetes, mainly diabetic retinopathy, in such subjects might also be high.

In the present study diabetic retinopathy was present in 42.4% of the 500 patients referred for evaluation. Mild NPR retinopathy was present in 25.6% of patients, moderate-severe NPR retinopathy in 4% of patients, and proliferative retinopathy in 12.8% of patients.

Various reports give different figures for the prevalence of diabetic retinopathy; however, they approximate to those found in the present study. This is evident in the study by Gonzalez *et al* [6] who cite a 50% prevalence of diabetic retinopathy in Mexico, as well as the study from Sri Lanka[7] where a prevalence rate of 31.3% was reported. A 50% prevalence was found in a study carried out in the UK[8] and a similar figure was also given from a study in Spain.[9] Prevalence rate as high as 60.5% was given in a study by Agardh *et al* [4] as well as in a study by Henricsson *et al*.[28] A relatively low prevalence of 26% was found in one study from Pakistan,[29] although both Oman and Pakistan are within the same geographic area. However, this was only a pilot study and the prevalence found does not duplicate the original situation and, in addition, the recording of fundus changes did not follow a standard pattern similar to other studies. It should also be remembered that it is more common to underestimate than to overestimate fundus changes related to diabetic retinopathy (as when confused with those changes due to hypertension).

While the figure for mild retinopathy seems to agree with other studies,[3 6 21] the present study showed a higher prevalence of proliferative diabetic retinopathy which contrasted with most other reports which gave a maximum of 10% of prevalence of such a condition and a minimum of 3.3%.[11] However, in the study by Jerneld and Algvere[30] and that of the EURODIAB IDDM[21] the prevalence rate was similar to our study.

In this study, a number of medical risk factors were investigated and it was found that many were significantly related to retinopathy. These included age of the patient, duration of diabetes, presence of ischaemic heart disease, a high systolic blood pressure, a high diastolic blood pressure, and an increased level of fasting capillary glucose level. Laboratory tests showing high levels of urea, creatinine, cholesterol, and triglycerides were also associated with an increased risk for any grade of diabetic retinopathy.

Duration of diabetes and occurrence of retinopathy are closely associated and this has been proved in a number of previous studies.[2 31] In the present study the risk for diabetic retinopathy after 10 years of onset of diabetes was increased 8.7-fold compared with patients with duration of diabetes less than or equal to 10 years and the risk would increase with the same amplitude for approximately every 5 years of duration afterwards. Duration of diabetes was still significant in the multiple logistic model for the occurrence of any retinopathy as well as the occurrence of mild and moderate-severe NPR but was not significant for the occurrence of proliferative retinopathy. This may be caused by a bias in estimating the real duration of diabetes in such patients, especially as about 70% were non-insulin dependent and so the discovery of diabetes could have been delayed.

Age of the patient was also related to the occurrence of retinopathy; however, in the logistic model presented it lost its significance after adjusting for the duration of diabetes and it seems that it is coupled to the duration of diabetes and cannot be regarded as an independent risk factor.

Ischaemic heart disease was also associated with retinopathy yet this also lost its significance when adjusting for confounders, a finding similar to that of Muh *et al*,[22] and probably the small number of such patients (44/500) could explain such an event; further studies are needed to clarify the strength of such an association.

Hypertension was significantly related to any retinopathy and both systolic and diastolic blood pressures were deemed to have an association; however, DBP was found to be the variable consistent with the development of moderate-severe NPR as well as proliferative retinopathy in the logistic model with a higher risk than if any retinopathy was considered (5 *v* 3.6). A similar finding has been reported in the EURODIAB IDDM Complications Study[21] although a number of studies[12 16 32] suggested that diastolic blood pressure was related more to the progression rather than to the occurrence of retinopathy.

High blood pressure may be related to diabetic nephropathy and our study showed that elevated urea and creatinine were associated with the occurrence of any retinopathy yet only creatinine levels was considered as significant after adjusting for confounders and were specifically related to the more severe type of NPR as well as to proliferative retinopathy. Such association was also cited by Muh *et al* [22] and by Jensen and Deckert.[33]

Surprisingly, the degree of glycaemic control, although proved to be a significant risk factor when tested alone against the occurrence of retinopathy, failed to retain this significance in the final model and although hyperglycaemia was found to be a profound risk factor for diabetic retinopathy[34–36] others failed to show such association.[22] Failure to show this association in the present study may be because we did not check the glycosylated haemoglobin levels, which would have better illustrated the control of the diabetic status.

Cholesterol and triglycerides blood levels were significantly associated with both the occurrence of any retinopathy as well as the occurrence of moderate-severe NPR and proliferative retinopathy, with increased levels of blood triglycerides having a higher risk for development of the various grades of retinopathy especially proliferative diabetic retinopathy (RR = 11). This is in accordance with the study by Mouton and Gill.[37] However, in the EURODIAB IDDM Complications Study[21] study as well as that by Weber *et al*,[38] triglycerides were only related to severe forms of retinopathy and not cholesterol; one explanation would be that raised triglycerides and not cholesterol is associated with insulin resistance.[39]

Similar to[26 39] or in contrast with,[40] the type of diabetes mellitus did not seem to be associated with the occurrence of diabetic retinopathy. This may be because patients were treated with the aim of tight glycaemic control, especially in IDDM patients, so that such patients, who used to have a higher prevalence of retinopathy, were now at a lower risk for such an occurrence.

More effort should be given to determine more risk factors for the occurrence of diabetic retinopathy in patients with diabetes mellitus, and although the present study was able to define around 75% of these factors much still needs to be done.

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