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ORIGINAL ARTICLE

Retinopathy and Microalbuminuria in Type 2 Diabetic Patients

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The aim of this study was to identify risk factors for the development of retinopathy and microalbuminuria and their relation in type 2 diabetic patients.

Materials and Methods: In this cross-sectional study, 590 patients suffering from type 2 diabetes were examined. Fundoscopy was performed by an ophthalmologist. The ratio of urinary albumin to creatinine was assessed by clinitek 100 (Bayer corporation–USA). HbA1C, height and weight also were measured.

Results: The overall prevalence of retinopathy was 39.3% (232 patients), 5.4% of which proved to be proliferative diabetic retinopathy (PDR). The diabetic retinopathy had a significant inverse relationship with body mass index (BMI) (P=0.02). HbA1C was higher in patients with PDR (mean=10.5%) than in patients with no signs of retinopathy (mean=9.5%), (P=0.001). The prevalence of microalbuminuria was 25.9% while 14.5% of the patients were seen to have macroalbuminuria. As expected, diabetic retinopathy and renal involvement were highly positively related. (P=0.001).

Conclusion: Microalbuminuria is associated with diabetic retinopathy in type 2 diabetic patients and is a reliable marker of retinopathy.

Key Words: Retinopathy, Microalbuminuria, Diabetes type 2

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Introduction

Diabetes mellitus is one of the most common metabolic diseases in which either the hormone insulin is lacking or the body's cells are insensitive to insulin effects.The multisystem complications of diabetes such as retinopathy, nephropathy, neuropathy and cardiovascular diseases are considered important, impinging on public health.

Diabetic retinopathy is one of the leading causes of blindness world wide; individuals with this condition run a 25 time higher risk of loosing the sight than do normal individuals.[1] Using new surgical and medical techniques, the incidence of blindness can be reduced by 90%.[2] Decrease in visual acuity in diabetic retinopathy is either associated with maculopathy or its proliferative complications. Many studies have been undergtaken to determine the precipitation factors of retinopathy such as duration and type of diabetes, hyperglycemia, pregnancy, change in hormonal levels, genetics and microalbuminuria.

The occurrence of microalbuminuria in type 1 diabetes is highly predictive of renal and cardiovascular diseases whereas in diabetes, type 2, lesser association is observed.[3]

The purpose of this study is to evaluate the prevalence of microalbuminuria and macro-

albuminuria and their relation to diabetic retinopathy and other risk factors such as hyperglycemia, hypertension in diabetes type 2.

Materials and Methods

This cross sectional study was carried out on the patients with type 2 diabetes who referred to Yazd Diabetes Research Center between the years 2000 to 2001.

The diagnosis of diabetes mellitus was performed according to World Health Organization (WHO) criteria, reported by the WHO study group (1985).

Subsequent to completing preliminary questionnaires that covered personal data, the patients' ophthalmologic examination and laboratory tests were also carried out.

The Clinitek 100 (Bayer Corporation, Elkhart, IN 46515, USA) was used to measure microalbuminuria. Three urine samples were taken during three to six months and if two samples were positive, microalbuminuria was confirmed; the device shows the ratio of albumin to creatinine in mg/g. If the ratio was less than 30, the patient was normoalbuminuric. Ratios between 30-300mg/g were indicative of microalbuminuria and above 300mg/g revealed macroalbuminuria.

Detailed assessment was caaried out to exclude other possible causes of microalbuminuria. Ophthalmologic examination including visual acuity (by means of snellen charts), intraocular pressure (using Applanation Tonometry), fundoscopy (utilizing slit lamp and contact lenses) and indirect ophthalmoscopy. If required, fluoresceine angiography was requested. All the relevant examinations were completed by an ophthalmologist and the patients were categorized according to the degree of their retinopathy. ie: No retinopathy; Mild nonproliferative diabetic retinopathy (NPDR); Moderate NPDR; Severe NPDR; Proliferative diabetic retinopathy (PDR). Five minutes after resting in the sitting position, the patient's blood pressure was measured using a mercury Sphygmomanometer and BP$\geq$ 135/80 mmHg was considered abnormal. Patient's medications, including hypertensive drugs, were also recorded. Body Mass Index (BMI) was also documented. HbA1c was measured and all data were analyzed by chi-square and Fischer exact tests. P values less than 0.05 were considered significant.

Results

A total of 590 patients (346 females and 244 males) were included in this study. The existing methods of treatment at the first visit focused on dietary habits alone for 56 patients, oral agents for 453 patients, insulin for 61 patients and insulin plus oral agents for 7 patients. The mean age of patients was 54.9±10.2 and the durations of diabetes ranged between 1 to 32 years (Mean = 10.2±6.6). Duration of diabetes was less than 5 years in 30% of the patients, between 6-10 years in 30% and over 10 years in 40% of them. Duration of diabetes was a strong predictor of severity of retinopathy (p=0.001) (Table 1). Of the patients 39.3% had some degree of retinopathy; 19.2% had mild NPDR, 12% moderate NPDR, 2.7% severe NPDR and 5.4% had PDR. Fifty-two patients (13.3%) had Clinically Significant Macular Edema (CSME). Two hundred patients had BP $\geq$ 135/80 mmHg, 173 of whom were under treatment with antihypertensive drugs. There was no significant relationship (p=0.37) between high blood pressure and different degrees of retinopathy. Gender also had no significant relationship with severity of retinopathy (p=0.31).

The relationship between different types of retinopathy and risk factors such as HbA1C, FBS, BMI and age were found to be significant (Table 2).

Table 1. Relationship between duration of diabetes and different types of retinopathy

Duration of retinopathy (years)	Total	Grade of retinopathy				
		Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
1-5	174	157 (90.2%)	10 (5.7%)	6 (3.4%)	0 (.0%)	1 (.6%)
6-10	176	122 (69.3%)	36 (20.5%)	13 (7.4%)	1 (.6%)	4 (2.3%)
11-15	106	52 (49.1%)	29 (27.4%)	17 (16.0%)	5 (4.7%)	3 (2.8%)
16-32	129	22 (17.1%)	38 (29.5%)	35 (27.1%)	10 (7.8%)	24 (18.6%)
Total	585	353 (60.3%	113 (19.3%)	71 (12.1%)	16 (2.7%)	32 (5.5%)

Table 2. The relationship between retinopathy and its risk factors

Risk factors	p
HbA1c (%)	0.001
Fasting blood sugar (mg/dL)	0.001
Body mass index (kg/m²)	0.028
Age (years)	0.014

Examination of urine samples in 330 subjects (59.5%) showed normal range of albumin excretion (normoalbuminuria). 25.9% of the patients, were microalbuminuric and 14.5% had macroalbuminuria. Table 3 show the significant relationship between different grades of retinopathy and albuminuria (p=0.001).

Table 3. Relationship between different types of retinopathy and albuminuria

Albuminuria		Grade of retinopathy				
		Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Normoalbuminuria	330	239 (72.4%)	57 (17.3%)	26 (7.9%)	1 (0.3%)	7 (2.1%)
Microalbuminuria	143	81 (56.6%)	27 (18.9%)	24 (16.8%)	4 (2.8%)	7 (4.9%)
Macroalbuminuria	80	17 (21.3%)	21 (26.3%)	19 (23.8%)	9 (11.3%)	14 (17.5%)
Total	553	337 (60.9%)	105 (19.0%)	69 (12.5%)	14 (2.5%)	28 (5.1%)

Discussion

Numerous studies carried out to determine the prevalence of retinopathy and albuminuria in patients with type 2 diabetes, have yielded different rates, between 16 to 53.4%, for retinopathy.[4-9] Our study showed a prevalence rate of 39.3% which is somewhere in between. The variation in rates could be as a result of the different methods used in those studies, the population and or the races involved, or variations in controlling blood sugar levels. The prevalences of microalbuminuria and macroalbuminuria in our study were 25.9% and 14.5% respectively. Parving et al reported a prevalence rate of 22% for microalbuminuria in diabetes type 2[10] whereas Lunetta reported a prevalence rate of 15%.[4] The above-mentioned studies show that there is a significant relationship between the degree of retinopathy and albuminuria. However there are few studies contradicting such a relationship. Erasmus et al showed that in 113 patients suffering from NIDDM, the prevalence rate of microalbuminuria was as high as 54% among males and 59% among females. Prevalence of retinopathy and hypertention was 16% and 41% respectively. They concluded that microalbuminuria may not predict retinopathy and occurs independently of both glycaemic control or elevated blood pressure levels.[8] The population chosen for the study influences the different incidences achieved in various studies. For example, 5-6% of normal nondiabetic individuals in the United Kingdom and the United States of America have microalbuminuria whereas in South Korea this value is 12.2% and in Finland 30-35%.[11]

Our study showed that in addition to HbA1c, BMI, and length of illness, microalbuminuria is a contributing factor to the degree of retinopathy (p=0.001) and this association can be explained by the common mechanisms involved in tissue damage by all those factors. In addition to blood sugar level and blood pressure, there are also other factors which damage vessels in the retina and kidney. For example, Klein et al showed that microalbuminuria could be seen in 29.2% of insulin taking patients and 22% of non-insulin dependent patients. Therefore, insulin can also have a role in nephropathy.[12]

In a study on 497 normal nondiabetic cases who were above 40 years in Seoul, Kim et al, after regression analysis, reported that fasting plasma level of insulin and systolic blood pressure have independent correlation with micoralbuminuria.[11] Besides common mechanisms, renal damage may accelerate retinopathy which is associated with increased blood pressure and serum levels of fibrinogen and lipoproteins.

Also microalbuminuria has a positive relation with incidence of coronary heart disease.[4,13] Albuminuria also has been considered as a predictor of diabetic retinopathy and coronary heart disease. Thus excretion of albumin in urine can be regarded as a sign of kidney involvement and can reflect generalized vessel damage throughout the body. Further prospective studies should be carried out to evaluate the effect of lowering albumin excretion on the reduction of blood vessel damage.

Conclusion

Microalbuminuria is associated cross sectionally with the presence of retinopathy in persons with type 2 diabetes. These data suggest that microalbuminuria may be a marker for the risk of proliferative retinopathy development. If longitudinal studies confirm these findings, diabetic patients who have microalbuminuria may benefit from close ophthalmologic follow up.

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