·Clinical Research·

Neuropathy and retinopathy in diabetes: Is there any association?

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Abstract

• AIM: To evaluate correlation of retinopathy and diabetic peripheral neuropathy (DPN) as microvascular complications of diabetes and also to identify their risk factors in patients with type 2 diabetes.

• METHODS: We conducted a cross-sectional study in an outpatient diabetes clinic during an 18-month period. 100 patients (51 male and 49 female), all affected by non-insulin-dependent diabetes mellitus (NIDDM), were examined for the presence of diabetic neuropathy and diabetic retinopathy.

• RESULTS: 78.1% of patients with retinopathy had DPN; and 79.1% of patients with DPN had retinopathy. Analysis of the association between DPN and retinopathy showed no significant correlation between them. 90.9% of patients with proliferative diabetic retinopathy (PDR) had DPN; and 27.8 % of patients with DPN had PDR. Both the univariate analysis and multiple logistic regression analysis revealed significant correlation between them ($r = 0.42$, $P = 0.02$).

• CONCLUSION: A severe diabetic retinopathy is associated with diabetic neuropathy. Our study further supports that diabetic neuropathy might be used as a tell-tale sign of diabetic retinopathy, necessitating more intensive ophthalmic care, especially in long-lasting diabetes.

• KEYWORDS: diabetes mellitus; retinopathy; neuropathy

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INTRODUCTION

Diabetes mellitus is a major public health concern that has a significant socioeconomic impact. The prevalence of diabetes in the working population of some countries has doubled over the past 10 years [1,2]. Diabetes is a common endocrine disease with a prevalence of 2% -3% in Iran according to the Endocrine and Metabolism Research Center of Shariati Hospital[3]. The long-term systemic complications of diabetes are destructive. They are major causes of morbidity and mortality, significantly impairing the quality of life of patients and constituting a significant health cost in the society[2,4].

Retinopathy, the second cause of severe blindness in the world, has been a recent focus of attention because of its potential treatability with laser photocoagulation when detected early [5-9]. The incidence ranged from 22% to 79% and the rate of progression ranged from 29% to 69% [10,11]. Several studies have showed that neuropathy is more common than other diabetic microvascular complications. It has been reported that more than 8% of diabetic patients have diabetic peripheral neuropathy (DPN) at presentation [12]. It has also been shown that duration of diabetes, chronic hyperglycemia control, and types of diabetes are associated with severity of DPN. The presence of clinical neuropathy is also correlated with presence of retinopathy, arterial hypertension, microangiopathy in some other studies[13-17].

The exact pathophysiology of DPN has not been well understood but association with microvascular disease like retinopathy may be implicated in its cause. Finding such an association may also be helpful in earlier diagnosis of the devastating complications and prediction of severity of them [13]. We conduct a study to evaluate correlation of retinopathy and DPN as microvascular complications of diabetes and also to identify their risk factors in patients with type 2 diabetes.

MATERIALS AND METHODS

Subjects This analytical cross-sectional study involved random selection of 100 patients with type 2 diabetes who were referred to the Endocrine and Metabolism Research Center in Shariati Hospital, Tehran, from September 2002 to March 2004.

Methods Demographic data and clinical information for all patients were collected from the standardized referral forms, including age and sex of patient, duration of diabetes, type of diabetic treatment (diet control, oral hypoglycemic agent or

Table 1 Association of risk factors with retinopathy

Risk factor	Patient with no retinopathy	Patient with retinopathy	*P* value
No	27	73	
Mean age	55.3±9.1	59.7±8.5	0.18[1]
Sex (female/male)	62.6%/37.4%	45.6%/54.4%	0.14[2]
Mean duration of diabetes	8.5±5.0	14.3±6.9	<0.001[1]
Treatment type			
Diet	22.2%	12.3%	0.14[2]
Oral hypoglycaemic agent or Insulin	77.8%	87.7	
Fasting blood sugar(mmol/L)	7.76±2.56	10.58±4.04	0.001[1]
Mean glycated haemoglobin (%)	8.13±3.42	8.66±3.24	0.73[1]

[1]Student's *t* test; [2]Chi-square test

Table 2 Association of risk factors with distal peripheral neuropathy (DPN)

Risk factor	Patient with no DPN	Patient with DPN	*P* value
No	28	72	
Mean age	59.7±9.1	56.7±10.2	0.17[1]
Sex (female/male)	32.1%/67.9%	58.3%/41.7%	0.01[2]
Mean duration of diabetes	12.7±9.6	12.8±5.6	0.98[1]
Treatment type			
Diet	32.1%	13.8%	0.07[2]
Oral hypoglycaemic agent or Insulin	67.9%	86.2%	
Fasting blood sugar(mmol/L)	7.94±2.75	10.53±4.04	0.001[1]
Mean glycated haemoglobin (%)	8.15±3.80	8.61±3.18	0.72

[1]Student's *t* test; [2]Chi-square test

insulin), updated glycosylated hemoglobin (HbA1c) within 1 year, visual acuity by Snellen's chart, and presence of other ophthalmopathy such as cataract and previous eye laser treatment. Indirect ophthalmoscopy was performed for all the patients by an ophthalmologist after dilation of pupil. A neurologist examined all the patients and filled the neuropathy symptoms and change (NSC) questionnaires[12].

Statistical Analysis The explanatory variables included in the analysis were chosen on the basis of clinical relevance and previous literature findings [2]. These included age, sex, duration of diabetes, treatment type, and HbA1c.

Data analysis was performed with SPSS software (version 10.0). Descriptive information for each of the explanatory variables was derived. Univariate association of the variables with retinopathy and neuropathy was assessed through using the Mann-Whitney test for continuous variables and Chi-square test for categorical variables. Correlation of retinopathy and neuropathy was also assessed by univariate analysis. Logistic regression with explanatory variables selected by the forward conditional method was applied to adjust confounding factors. A P value of less than 0.05 was considered significant.

RESULTS

A total of 100 patients with a mean age of 58.1±8.5 (range 40-78) years were included in the study. There were slightly more female subjects (51.0%) than male (49.0%). Mean duration of diabetes was 12.8±8.5 (range 1 to 35) years, and the mean level of HbA1c was 8.40%±3.46%. Three quarters of patients required oral hypoglycemic medication.

Retinopathy 73% of our patients had diabetic retinopathy. Proliferative diabetic retinopathy (PDR) was present in 22 (22.0%) patients. Univariate analysis for the association of risk factors with retinopathy revealed that subjects with retinopathy had a longer history of diabetes (P<0.001), and elevated level of fasting blood sugar (FBS). Sex, age and HbA1c were not significantly associated with retinopathy (Table 1). After the confounding effects between variables in the logistic regression model were adjusted, the duration of diabetes and poor glycemic control were the only risk factors significantly associated with retinopathy (P<0.001).

DPN Both the univariate analysis and multiple logistic regression analysis revealed consistent results. FBS was positively associated with the DPN (P<0.001). There was no significant relationship between progression of neuropathy and duration of diabetes (P=0.98), HbA1c level (P=0.72), and age (P=0.17). Female subjects were more likely to have neuropathy (P=0.01) (Table 2).

Correlations 78.1% of patients with retinopathy had DPN; and 79.1% of patients with DPN had retinopathy. Univariate analysis of the association between DPN and retinopathy showed no significant correlation between them. After the confounding effects between variables in the logistic regression model were adjusted, the result was the same (r=0.59, P=0.61).

90.9% of patients with PDR had DPN; and 27.8 % of patients with DPN had PDR. Both the univariate analysis and multiple logistic regression analysis revealed significant correlation between them (r=0.42, P=0.02). Odd ratio of having PDR in patients with DPN was 5.89 (P=0.01). 12.0% of patients had neither retinopathy nor neuropathy, and 57.0% of them had both of them.

DISCUSSION

Diabetic retinopathy is one of the major causes of severe blindness in the world. It affects 75% of diabetic patients after 15 years[18,19]. Early detection of the condition and timely intervention are the keys to successful management. Screening has been recommended worldwide as a standard procedure to decrease the threat of blindness[20-22]. In our study also 73.0% of patients had diabetic retinopathy with a mean duration of 12.8 years. DPN have shown to be one of the most common diabetic microvascular complications. It has been reported that more than 8% of diabetic patients have DPN at presentation[12]. Based on epidemiological studies and controlled clinical trials, total hyperglycemia exposure has been shown to be an important risk factor for occurrence of DPN [13,23]. Apart from chronic hyperglycemia, there is only weak and inconsistent evidence implicating other risk factors such as older age, height, male sex, smoking and lipoprotein concentration[13-17]. We used NSC for detection and scoring of DPN. The prevalence of DPN was 72.0% in our study and was comparable with other reports in Japan (84.4%) and Germany (66.0%)[12,24].

Retinopathy Both the univariate analysis and multiple logistic regression analysis revealed consistent results. FBS and duration of diabetes was positively associated with the retinopathy. This result was compatible with the reports of previous studies[23,25,26] but interestingly, we could not find any correlation between age, glycosylated hemoglobin and retinopathy.

Neuropathy Likewise, FBS and duration of diabetes was statistically associated with DPN. Previous reports [14,26] also showed these factors as risk factors for development of DPN. Moreover, we found that female sex might have positive correlation with DPN. It was also compatible with the previous reports. Unlike Dyck's study [13], we didn't find any association between age, glycosylated hemoglobin and neuropathy. Although FBS is not a longitudinal marker of blood glucose control, it may be an indicator of bad glucose control especially in patients who used oral hypoglycemic agents. In our study retinopathy and neuropathy were not correlated, but the most important finding was that there was significant correlation between DPN and PDR.

What are the likely reasons that our models didn't show correlation between retinopathy and neuropathy? One reason may be that we did not assess severity of DPN. The second reason might be that we did not consider all the risk factors, such as smoking, height, weight, serum creatinine and cholesterol. The third reason might be that risk factors might not have been considered at right time or for sufficiently long time. The exact pathophysiology of DPN has not been well understood but association with microvascular diseases like retinopathy may be implicated in its cause [13,23]. Significant correlation between DPN and PDR in our study might be another reason for pathogenesis of DPN, i.e. microvascular abnormality, as neuropathy was correlated with more advanced stage of microvascular abnormality.

As expected by other major studies [13,24], a severe retinopathy is associated with neuropathy. It is suggested that patients with PDR referred to neurologist should have complete neurologic examination to exclude DPN. Appropriate screening program and more intensive diabetic control may reduce DPN. Also our study further supports that diabetic neuropathy might be used as a tell-tale sign of diabetic retinopathy, necessitating more intensive ophthalmic care, especially in long-lasting diabetes.

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