

Subclinical diabetic neuropathy

A common complication in Saudi diabetics

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ABSTRACT

Objective: To determine the prevalence of sub clinical diabetic neuropathy in Saudi diabetics and the risk factors associated with symptomatic diabetic neuropathy.

Methods: A prospective study of Saudi diabetics attending King Abdulaziz University Hospital out patient clinic from January 1998 until April 1999. Detailed information of each patients' age, sex, body mass index, type and duration of diabetes mellitus, mode of treatment, degree of blood glucose control, presence of hypertension, hyperlipidemia, smoking, family history of diabetes mellitus and hypertension were recorded. Patients were assessed for diabetic neuropathy using the Michigan Neuropathy Program. Patients who were asymptomatic and scored less than 2 on simple clinical examination were referred to a neurologist for a complete neurological examination and nerve conduction studies.

Results: A total of 237 patients were studied with a mean age of 54.19 years and mean duration of diabetes 10.6 years. Symptomatic diabetic neuropathy was present

in 132 (56%) patients while subclinical neuropathy was present in 58 (57%) of asymptomatic patients. Old age, type II diabetes with long duration, poor control and smoking were risk factors associated with symptomatic diabetic neuropathy ($p < 0.001$, $p = 0.09$, $p < 0.001$, $p = 0.04$, $p = 0.08$).

Conclusion: Subclinical diabetic neuropathy is common. Early diagnosis is important for possible prevention of late neuropathic complications (foot ulcers and infections). Prolonged poorly controlled diabetes mellitus, old age and smoking are risk factors for symptomatic diabetic neuropathy. Meticulous blood glucose control is important for nerve function protection. Researches are urgently needed for satisfactory therapy.

Keywords: Diabetic neuropathy, subclinical, symptomatic, risk factors.

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Diabetic Neuropathy (DN) is a common complication of diabetes mellitus (DM) and it is encountered in more than one-third of diabetic patients.¹ Prospective examination of over 4,400 patients in an out-patient diabetes clinic revealed that 10% of patients had diabetic neuropathy at the time of diagnosis of diabetes and after 25 years of diabetes >50% of patients had DN.² Diabetic neuropathy leads to substantial morbidity and unhappiness³ and is associated with increased mortality in relation to its severity⁴ and complications such as foot ulcers.⁵

The diabetes control and complications trials provided the evidence that nerve function is protected by meticulous blood glucose control, both in term of symptomatology and in minimizing the degree of nerve conduction deterioration^{6,7} so early diagnosis of subclinical DN is of great value as tight blood glucose control can protect nerve function. The aim of our study is to determine the prevalence of subclinical DN in Saudi diabetics and the risk factors associated with symptomatic DN.

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Methods. King Abdulaziz University Hospital (KAUH) is a teaching hospital in Jeddah, Saudi Arabia, with a catchment area of around one million. We prospectively studied Saudi diabetic patients being followed in the medical out-patient clinic from January 1998 until April 1999. All patients studied had established diabetes mellitus (DM) using World Health Organisation (WHO) criteria and classified as either type I or type II by WHO criteria.⁸ At the initial visit, patients' age and sex were recorded, as well as their body mass index (BMI) (weight in kilogram divided by square height in meters), duration of DM, type and duration of treatment (diet, oral hypoglycemic agents (OHG), insulin or combined), presence or absence of hypertension and hyperlipidemia, history of smoking, family history of DM and hypertension. Hypertension was diagnosed if blood pressure was >140/90mmHg. Plasma lipids usually performed after 12-14 hours fasting. It was determined using the enzymatic colorimetric method and LDL (low density lipoprotein) was determined using the homogeneous turbidimetric test. Patients were considered hyperlipidemic if total serum cholesterol >5.2mmol/l or LDL >2.6mmol/l. Poorly controlled patients were diagnosed by their compliance to diet and medications, symptoms of hyperglycemia and a level of HbA1c more than 7%. Neuropathy was diagnosed using the Michigan Neuropathy Program⁹ which is a two- step program, Diabetic Neuropathy Index (DNI) and Diabetic

Neuropathy Score (DNS). Patients were initially screened for DN using a 15 "Yes or No" questionnaire (Figure 1) and a simple clinical examination (which consist of foot inspection, an assessment of vibration sensation on the great toe and the presence of ankle reflex) known as DNI (Table 1). Patients who were asymptomatic and scored less than 2 on simple clinical examination were referred to a neurologist for the second component of the program which is the DNS. This component consist of a more complete neurological examination of sensation in the feet, distal strength, and reflexes followed by nerve conduction studies. Nerve conduction studies (NCS) (common peroneal, median motor and sensory conduction velocities) are performed with the temperature maintained at 22^o using standard protocols.¹⁰ A nerve is considered abnormal if the calculated conduction velocity is less than the average conduction velocity defined as values between the 1st and 99th percentile.¹⁰ Nerve conduction abnormalities were classified into normal and abnormal (mild, moderate, severe abnormalities) according to common peroneal nerve (CPN) and median nerve (MN) conduction. Normal > 44.4 m/s for CPN, mild 40-44.3 m/s, moderate 36-39.9 m/s, severe < 36 m/s, while for MN normal is > 52.8 m/s, mild 48-52.7 m/s, moderate 40-47.9 m/s, severe < 40 m/s.

Statistical analysis was carried out using the Statistical Package for Social Sciences (SPSS7.5). T-

Figure 1 - Neuropathy screening instruction questionnaire.

1. Are your legs and/or feet numb?	1. Yes	2. No
2. Do you ever have any burning pain in your legs and/or feet?	1. Yes	2. No
3. Are your feet too sensitive to touch?	1. Yes	2. No
4. Do you get muscle cramp in your legs and/or feet?	1. Yes	2. No
5. Do you ever have any pricking feeling in your legs and/or feet?	1. Yes	2. No
6. Does it hurt when the bed covers touch your skin?	1. Yes	2. No
7. When you get into the tub or shower, are you able to tell the hot water from the cold water?	1. Yes	2. No
8. Have you ever had an open sore on your foot?	1. Yes	2. No
9. Has your doctor ever told you that you have diabetic neuropathy?	1. Yes	2. No
10. Do you feel weak all over most of the time?	1. Yes	2. No
11. Are your symptoms worse at night?	1. Yes	2. No
12. Do your legs hurt when you walk?	1. Yes	2. No
13. Are you able to sense your feet when you walk?	1. Yes	2. No
14. Is the skin on your feet so dry that it cracks open?	1. Yes	2. No
15. Have you ever had an amputation?	1. Yes	2. No
Total:		/15points

Table 1 - Diabetic neuropathy index.

			Yes (0)	No (1)
Appearance of feet	Right	Normal	If no check all that apply	Deformed Dry skin Infection Ulceration (1)
	Left	Normal	If no check all that apply	Deformed Dry skin Infection Ulceration (1)
Ankle reflexes	Right	Present (0)	Present with reinforcement (0.5)	Absent (1)
	Left			
Vibration at great toe	Right			
	Left			
			Total:	/8points

test and Chi-square were used appropriately. Results were considered significant if the p value is less than 0.05.

Results. A total of 237 patients were studied with mean age of 54.19±12.79 years and a male:female of (97:140) 1:1.4. Thirty-seven of 237 (16%) patients were type I diabetics and 200 of 237 (84%) were type II diabetics with a mean diabetes duration of 10.6±6.56 years. The mean BMI was 28.79±5.1. Most of the patients were using OHG agents for blood sugar control 150 of 237 (63%), while 66 of 237 (28%) were on insulin, 11 of 237 (5%) on diet alone and the remaining 10 of 237 (4%) were using combined OHG agents and insulin. Poor glycemic control was found in 141 of 237 (59.5%) while the remaining 96 of 237 (40.5%) had good control. Neuropathy as assessed by the DNI was present in 132 of 237 (56%) patients and 105 of 237 (44%) did not have neuropathy. Four of those who did not have neuropathy when assessed by the DNI (4%) were discovered to have neurological abnormalities when assessed by the neurologist in the second component of the program (DNS) so, they were excluded and the remaining 101 of 237 (43%) underwent nerve conduction studies. Nerve conduction studies were normal in 43 of 101 (43%) and abnormal in 58 of 101 (57%). Degree of nerve conduction defects are

shown in Table 2. The total number of patients who have neuropathy diagnosed clinically (as assessed by DNI and complete neurological examination) were 136 of 237 (57%) and those diagnosed electroneurographically (who were clinically asymptomatic) were 58 of 237 (24.5%). History of hypertension, hyperlipidemia and smoking was found in 73, (31%), 43 (28%) and 66 (18%) of 327 patients. Family history of diabetes was present in 61 of 237 (26%), hypertension in 11 of 237 (5%) and both diabetes and hypertension in 38 of 237 (16%). As

Table 2 - Degree of nerve conduction defects according to nerve conduction studies.

Degree of conduction defects	Number of patients (%)
Mild	16 (28)
Moderate	21 (36)
Severe	21 (36)
Total	58

Table 3 - Relation of symptomatic peripheral neuropathy to some variables.

Variable	Symptomatic PN N (%) Total = 132	Asymptomatic PN N (%) Total = 105	P Value
Age (years)	57	50	S
Sex (M:F)	1:1.5	1:1.3	NS
BMI	28.5	29	NS
Type II diabetes	116 (88)	84 (80)	S
Duration of diabetes (years)	13	8	S
Poor glycemc control	86 (65)	55 (52)	S
Hypertension	45 (34)	28 (27)	NS
Hyperlipidemia	36 (27)	30 (28)	NS
Smoking	29 (22)	14 (13)	S

PN = peripheral neuropathy
 BMI = body mass index
 S = significant (<0.05)
 NS = not significant (>0.05)
 M:F = male:female

shown in Table 3, symptomatic peripheral neuropathy was significantly related to old age, type II diabetes, long duration of DM, poor glycemc control and smoking, while no significant relation was found to sex, BMI, presence of hypertension or hyperlipidemia.

Discussion. Diabetic neuropathy is a common complication of DM and it represents a major health problem.¹¹⁻¹⁴ Its prevalence varies widely between 23%-85%.¹⁵⁻¹⁹ The prevalence of DN in our study as assessed by symptoms, complete neurological examination and nerve conduction studies (for asymptomatic patients) is 82%. Most of our patients were type II poorly controlled diabetics with 10 years mean duration of DM, which could contribute to this high prevalence. Electrophysiological studies are more sensitive than clinical examination and the least available non-invasive measure of neuropathy. Nerve conduction velocity (NCV) alteration may not be concordant with signs-symptoms of DN. Up to 75% of asymptomatic patients with normal or abnormal clinical examination may have nerve conduction abnormalities that are typical of neuropathy.²⁰⁻²² Sub clinical neuropathy was found in 57% a finding comparable to that reported by Bertora et al.²³ This means that we have to look for subclinical DN for possible prevention of late neuropathic complications such as foot ulcers and infections. Presence of DN is significantly associated with old age, prolonged uncontrolled DM and smoking^{16-18,24,25} we also found that development of symptomatic DN is significantly

associated with these risk factors. No significant association was found between symptomatic DN and sex, BMI, presence of hypertension or hyperlipidemia which is in agreement with what has been reported by Hillson et al²⁶ and Maser et al.²⁷ Neuropathic damage (painful sensory symptoms and the anesthetic foot) contributes significantly to morbid foot problem and unhappiness in diabetes.²⁸⁻³¹ Provision of foot care services has been shown to reduce occurrence of ulceration and amputation and simple screening procedures produce great reduction in the amputation rate.³²⁻³³

In conclusion, it is clear that as yet a satisfactory and fundamental therapy is not available for DN and it is therefore of great importance to educate our professionals who care for the diabetic patients to do regular screening of the feet and strenuous control of blood glucose as this would be saving our patients from the complications of DN and discomfort. It is also obvious that further researches are needed especially into possible pathogenic mechanisms of DN in order that a more satisfactory treatment is achieved.

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