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The prevalence of clinical diabetic polyneuropathy in Spain: a study in primary care and hospital clinic groups

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Summary A multiregional cross-sectional study of clinical diabetic polyneuropathy (DPN) was carried out among Spanish diabetes patients using a standard system for scoring symptoms and signs of polyneuropathy. The main patient sample comprised 2 644 patients (54.7 % women) aged 15–74 years (mean 57.2 ± 0.3 years), 86.9 % of whom had Type II (non-insulin-dependent) diabetes mellitus and 29.4 % were attending hospital clinics. Mean duration of diabetes since diagnosis was 10.2 ± 0.2 years. The prevalence of DPN was 22.7 % (95 % confidence interval 21.2–24.3 %) in the whole sample, 12.9 % (9.4–16.5 %) among patients with Type I (insulin-dependent) diabetes mellitus and 24.1 % (22.4–25.9 %) among patients with Type II diabetes; there was no significant difference in prevalence between men and women. Prevalence increased with age (from < 5 % in the 15- to 19-year-old age group to 29.5 % in the 70- to 74-year-old group) and with duration of diabetes since diagnosis (from 14.2 % among those with duration < 5 years to 44.2 % among those with duration > 30 years). In a supplementary sample of 161 diabetic patients aged 75 to 79 years (excluded from the main sample to prevent confusion between diabetes-induced and ageing-induced neuropathies), prevalence was 37.8 %. Ninety-three patients (3.3 %) had or had had foot ulcers and 21 of these 93 (0.7 %) had undergone amputation; 90.8 % of ulcerated patients had Type II diabetes, and 54 % had DPN (in most cases with loss of perception of vibration), as against a prevalence of DPN of 19.9 % among patients without ulcers. We conclude that nearly a quarter of Spanish diabetic patients have DPN; that over 90 % of DPN patients have Type II diabetes; that the prevalence of DPN increases with age and with the duration of the disease, and that the risk of foot ulcers among DPN patients is about three times the risk among diabetic patients without DPN. We accordingly emphasize the responsibility of primary care physicians to try to prevent diabetic foot lesions by early diagnosis of DPN. [Diabetologia (1998) 41: 1263–1269]

Keywords Diabetes, polyneuropathy, epidemiology, Type I, Type II, foot ulcers

In Spain, as in other industrialised nations, diabetes, with an estimated prevalence of 3.7 % [1, 2], constitutes a major cause of suffering and a major burden on the health system. In both cases, it is the specific complications of diabetes that are chiefly to blame. As an aid to managing health resources, we have therefore studied the prevalence of diabetic polyneuropathy among Spanish diabetic patients.

Previous studies of the prevalence of diabetic polyneuropathy [3–14] had widely differing results. This was attributable to differences in the kind of patient sample (most samples were recruited in specialised centres); to whether or not the neurological effects of ageing were taken into account; and to study or diagnostic methods and criteria or both (studies differed as to whether they included neurophysiological tests in the diagnostic protocol; target-

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Abbreviations: DPN, Diabetic polyneuropathy; NDS, neuropathy disability score; NSS, neuropathy symptom score

Table 1. Sample characteristics and prevalence of polyneuropathy

Sample	*n*	%	Age (years)	Duration of diabetes (years)	prevalence %
Whole sample	2644	100	57.2 ± 0.3	10.2 ± 0.2	22.7 (21.2–24.3)
Diabetes					
Type I	348	13.2	30.5 ± 0.6[a]	13.8 ± 0.5[a]	12.9 (9.4–16.5)[a]
Type II	2296	86.9	61.3 ± 0.2	9.7 ± 0.2	24.1 (22.4–25.9)
Sex					
Men	1197	45.3	56.3 ± 0.4[b]	9.8 ± 0.2[b]	22.0 (19.6–24.3)[c]
Women	1447	54.7	57.9 ± 0.4	10.6 ± 0.2	23.2 (21.0–25.4)
Origin					
Hospital	778	29.4	49.3 ± 0.6[a]	12.4 ± 0.3[a]	26.7 (23.6–29.8)[b]
Primary health care centre	1866	70.6	60.5 ± 0.3	9.3 ± 0.2	21.0 (19.1–22.8)

Values of age and duration are mean ± SEM. For prevalence the 95 % confidence interval is given in parenthesis. Differences of values between rows are as follows: [a] $p < 0.001$, [b] $p < 0.05$, [c] p : NS

ed somatic or autonomic neuropathy; or distinguished between clinical diabetic polyneuropathy and mononeuropathy, multineuropathy, polyneuropathy of non-diabetic origin and subclinical forms of diabetic polyneuropathy). In our study, the prevalence of clinical diabetic polyneuropathy (DPN) was defined as „symmetrical sensorymotor polyneuropathy predominantly affecting the distal aspects of the lower limbs and due to diabetes mellitus. Sensory symptoms and deficits, a variable degree of autonomic dysfunction, and infrequent muscle weakness are characteristics" [15]. We determined such prevalence among diabetic patients attending both hospital and primary care clinics, in relation to patient age and sex, diabetes type and the duration of diabetes since diagnosis.

Subjects, materials and methods

Subjects. A main sample consisting of 2644 diabetic patients aged 15 to 74 years was studied; younger patients were excluded to avoid comprehension difficulties and older patients to avoid interference from the effects of ageing on the nervous system. In addition, 161 diabetic patients aged 75 to 79 years were examined. Neither sample contained patients who drank more than 15 units of alcohol a week or patients judged to have non-diabetic polyneuropathy using the criteria specified below. Both samples were proportionally distributed among the Spanish Autonomous Communities. In order to sample the whole diabetic population rather than just those patients attending hospital clinics, 70–75 % of the subsample corresponding to each Autonomous Community was taken from primary care centres (this figure is an estimate that roughly corresponds to the percentage of diabetic patients attending primary care centres). Within each centre, every third or fourth patient was included in the sample until the quota for the centre was completed. Data were collected between April 1996 and September 1997. The chief characteristics of the sample are listed in Table 1.

Methods. A standard data sheet (with slight modifications) was used to record the symptoms and signs used for neuropathy symptom score (NSS) and neuropathy disability score (NDS) [10]. For the NDS, the ankle reflex and perceptions of pinprick, cold and vibration were evaluated bilaterally. Pinprick perception was evaluated at the root of the great toe nail, cold perception by placing a cold tuning fork on the back of the foot and vibration perception by placing the vibrating 128 Hz tuning fork against the apex of the great toe. In patients aged over 64 years, percussion of the sole was used to elicit the ankle reflex if the usual stimuli had proved unsuccessful. On either side, the ankle reflex scored 0 if present and normal and 2 if absent, and the three perceptions scored 0 if present and normal and 1 if absent, reduced or uncertain, although following previous indications [16]. All participating physicians attended at least one training session before collecting data.

The criteria for diagnosis of DPN were an NDS score of at least 6, regardless of NSS score, or an NDS score of 3–5 in conjunction with an NSS score of at least 5. These criteria were fixed at the start of the study by the study coordinator but were not disclosed to other participants until the study had been concluded.

Statistical analysis. Patient subgroups were compared for prevalence of DPN by means of chi-square tests and the Mann-Whitney U test was used to estimate the significance of differences in the means of other variables between the groups. Pearson correlations between age or duration since diagnosis and prevalence in age/duration groups were calculated. Multivariate logistic regression analysis was carried out to identify risk factors associated with DPN. All statistical analyses were done using SPSS for Windows.

Results

Table 1 shows the general characteristics of the sample and the prevalence of DPN in the whole sample of 15- to 74-year-old subjects and in various subsets. Overall prevalence in this main sample was 22.7 %. There was no difference in prevalence between the sexes, but there was a great difference between insulin-dependent and non-insulin-dependent diabetic patients, 12.9 % as against 24.1 % ($p < 0.001$).

In both types of diabetes prevalence rose continuously with age with a correlation of 0.96 between prevalence and age ($p < 0.001$). Above age 74 years, the prevalence of DPN rose sharply, with a value of

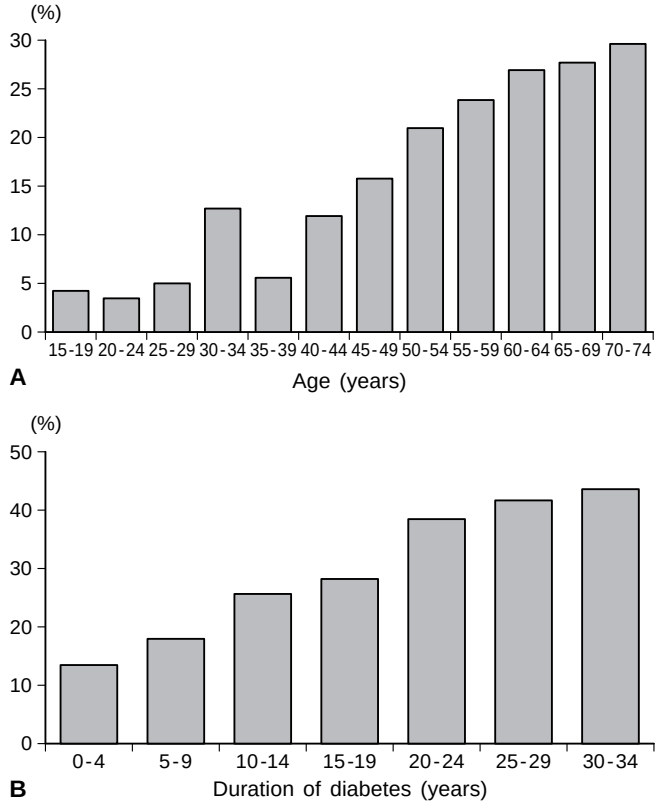

Fig. 1 A, B. Prevalence of clincical diabetic neuropathy among Spanish diabetic patients, by patient age (**A**) and duration of diabetes (**B**)

37.8 % in the sample of 74- to 79-year-olds as against 29.5 % in the 70- to 74-year group (Fig. 1, 2).

In both groups, prevalence increased fairly steadily with the duration of diabetes since diagnosis. Overall, there was a correlation of 0.98 between prevalence and duration of diabetes since diagnosis ($p < 0.001$). The duration of Type II diabetes prior to diagnosis was estimated as 12.5 years by extrapolating the prevalence-duration regression line for this group back to zero prevalence (Fig. 3).

Among patients attending primary care centres the prevalence of DPN was less than among hospital clinic patients, 21.0 % as against 26.7 % ($p < 0.05$). There was no significant correlation between prevalence and smoking (grouping patients as non-smokers, or smokers of < 10, 10–20 and > 20 cigarettes a day) or alcohol consumption (alcohol consumption was limited by the criteria for inclusion in the study but within this limit we looked for differences in prevalence among non-drinkers, occasional drinkers or habitual drinkers).

Multiple logistic regression analysis of the dependence of DPN prevalence on sex, age, duration of diabetes and origin of patients was done for the Type I and Type II subsamples separately because of the differences in age and duration of diabetes between both groups (Table 2). In the Type I group only duration of diabetes showed an association with DPN prevalence ($p < 0.05$) but in the Type II group both age and duration of diabetes were associated with DPN prevalence ($p < 0.001$). Another model including the origin of patients as a variable showed an

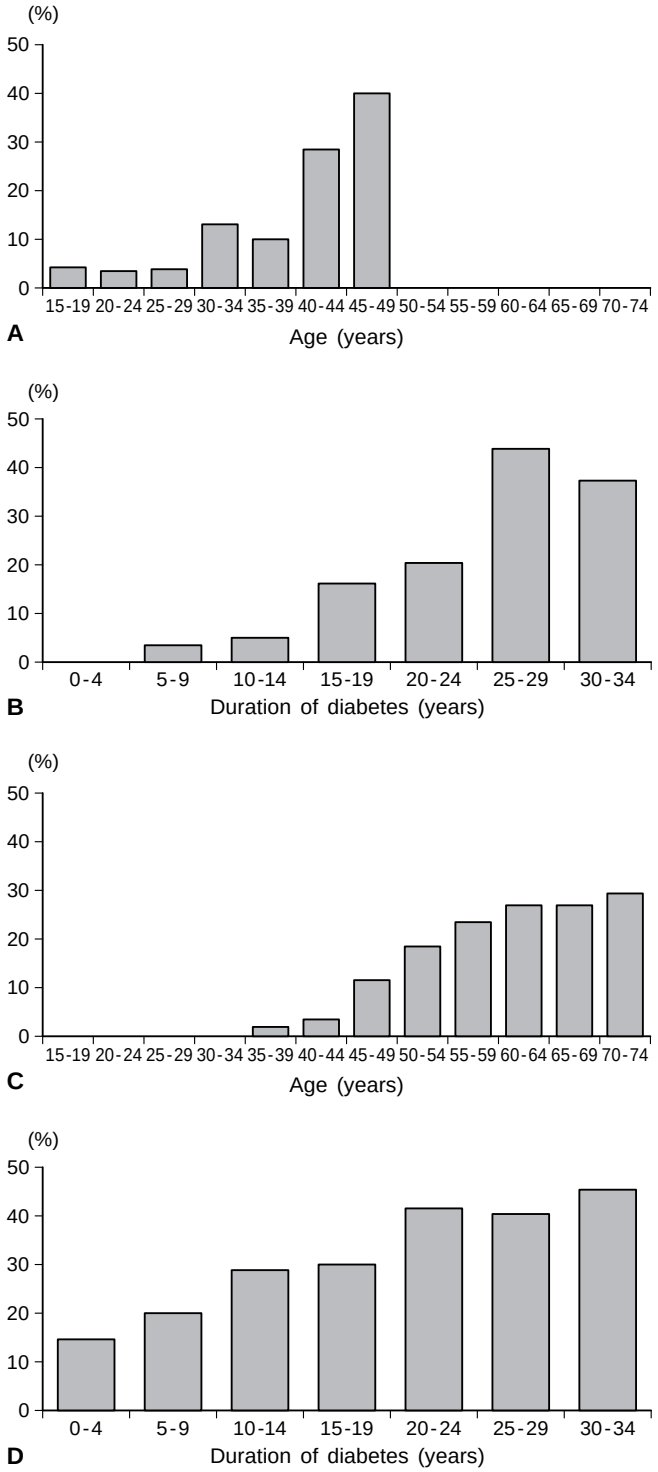

Fig. 2. Prevalence of clinical diabetic neuropathy among spanish diabetic patients of Type I (**A** and **B**) and in Type II (**C** and **D**) increases with age (**A** and **C**) and duration of diabetes since diagnosis (**B** and **D**)

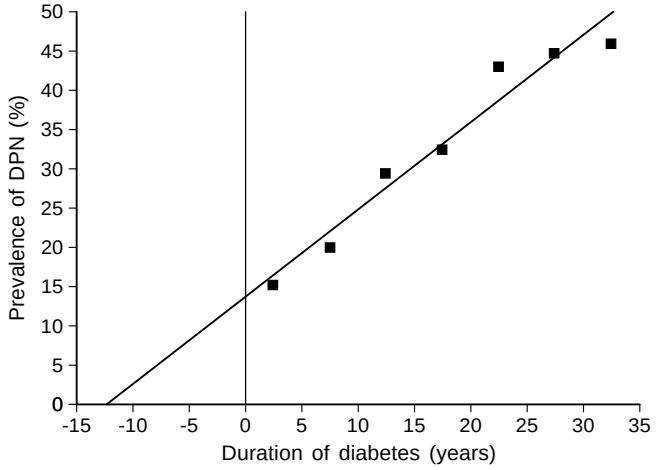

Fig. 3. Linear regression of the prevalence of clinical diabetic polyneuropathy on duration of diabetes since diagnosis. Extrapolation to zero prevalence estimates the onset of polyneuropathy as 12.5 years prior to diagnosis of diabetes

association only in the Type II group; age, duration of diabetes and origin of patients was associated with DPN prevalence ($p < 0.001$). Sex was not significantly associated with prevalence in any model or group.

In the pooled 15- to 74-year-old and 75- to 79-year-old samples, 93 patients (3.3%) had or had had foot ulcers and 21 of these 93 (0.7% of the total) had undergone amputation; 90.8% of the patients with ulcers had Type II diabetes. Table 3 shows the association between ulceration and the absence of ankle reflex or vibration perception in the 2805-member group and its Type I and Type II diabetic subgroups.

Discussion

The results show an overall prevalence of DPN of 22.7% in the 15- to 74-year-old sample. The discrepancy with respect to the 28.5% for the United Kingdom [10] is doubtless due to the restriction to patients attending hospital clinics, whereas 70.6% of our patients attended primary care centres: patients with complications tend to be monitored at hospital clinics rather than primary care centres. The prevalence of DPN among hospital patients in our study, 26.7%, is similar to that reported by the British study.

Our results agree with those of other studies that have examined Type I diabetic patients [6, 13, 17–20], Type II diabetic patients [4, 5, 7, 8, 11, 12] or both Type I and Type II patients [3, 9, 10, 14] in finding higher prevalence of DPN in Type II diabetes. Our 35.4% prevalence for Type II diabetic hospital patients is similar to the 32.1% for the British study [10]. That for Type I diabetic hospital patients there *is* a difference from that study (13.2% as against 22.7%; $p < 0.001$) is probably due to the median age of our Type I diabetic hospital patients having been 28 years as against 45 years in the British study (Type II diabetic hospital patients had a median age of 63 years in both studies).

Table 2. Results of logistic regression analysis of DPN status on: age, diabetes duration, sex and origin of patients. Analysis is performed separately for Type I and Type II. In parenthesis are given the 95% confidence intervals for the odds ratios

Variable	Parameter estimate	Standard error	p-value	Odds ratio
Type I				
Age	0.0434	0.0257	NS	1.04 (0.99–1.10)
Duration	0.0880	0.0287	< 0.05	1.09 (1.03–1.15)
Sex	– 0.3621	0.3662	NS	0.99 (0.34–1.43)
Origin	0.5651	0.4466	NS	1.76 (0.73–4.22)
Constant	– 4.5561	0.6537		
Type II				
Age	0.0380	0.0063	< 0.001	1.04 (1.03–1.05)
Duration	0.0469	0.0062	< 0.001	1.05 (1.03–1.07)
Sex	– 0.0145	0.1009	NS	0.99 (0.83–1.24)
Origin	0.6293	0.1140	< 0.001	1.88 (1.50–2.35)
Constant	– 4.1692	0.4000		

Model: log (P/1-P) = constant + β_1 age + β_2 duration + β_3 sex + β_4 origin, where P is the probability of having neuropathy. Sex code: male = 0, female = 1. Origin code: hospital: 1, primary care centre: 0

Table 3. Prevalence of neurological signs in groups defined by presence of foot ulcer and diabetes type

	Absent ankle reflex			Absent vibratory perception		
	Overall	Type I	Type II	Overall	Type I	Type II
Foot ulcer	44.8%	37.5%	45.6%	47.1%	37.5%	48.1%
No foot ulcer	26.0%	19.1%	27.1%	18.6%	10.0%	19.9%

Differences of prevalence of absence of ankle reflex and vibratory perception between patients with and patients without foot ulcers are significant on the whole sample and in the Type II group ($p < 0.001$)

To prevent the sample from being contaminated by patients with mononeuropathy, multineuropathy or non-diabetic polyneuropathy, which has an estimated prevalence of 6–10% [21], some rigorous exclusion criteria were used including alcohol intake more than 15 units a week. This resulted in an homogeneous sample in which there were no differences in DPN prevalence between non-drinkers, occasional drinkers or habitual drinkers.

The diagnostic procedures used in studies of DPN have included assessment of symptoms alone [8] or signs alone [22], quantitative sensory tests [23], and various combinations of these methods: symptoms and signs [6, 9, 10]; signs and electrophysiological tests [14]; symptoms, signs and electrophysiological test [11, 13]; and symptoms, signs, electrophysiological tests and quantitative sensory tests [24, 25]. This variety of methods has contributed to discrepancies among the results. To enhance the meaningfulness of direct comparison of our results with those of the British study [10] which is the largest European study of the prevalence of DPN among both Type I and Type II patients, we used (with two exceptions) the same diagnostic methods and criteria as in that study.

The two points in which our method differed were that we excluded patients older than 74 years from the main study and, for patients older than 64 years, percussion of the sole was used to elicit the ankle reflex if the usual, less powerful, stimuli had proved unsuccessful. Both measures were adopted to prevent contamination of the sample by patients with polyneuropathy due to normal ageing rather than to the diabetes. The prevalence of signs and symptoms of polyneuropathy (paraesthesia, numbness, and reduction or absence of ankle reflex, positional awareness and perception of vibration, pinprick or pressure or both), though much less among normal subjects than among diabetic patients of the same age and sex, has been found not to be negligible among normal subjects aged more than 70 years [26]. Similarly, symptoms and signs compatible with a diagnosis of polyneuropathy have been found in 2.9% of 480 non-diabetic subjects [9], and in 2.1% of control subjects [11]. Our results suggest that the two measures taken to exclude ageing-induced polyneuropathy were largely successful, since prevalence rose quite smoothly with age to 29.5% in the 70- to 74-year-old age group but then jumped sharply to 37.8% among 75- to 79-year-olds. In the British study, prevalence was about 44% at age 74 years and 55% at age 85 years [10].

Like that study, we found no difference in DPN rate between the sexes. This contrasts with the results of other studies [3, 8], which found greater prevalence among men than among women. Neither of these studies is, however, properly comparable with ours or the British study: the first did not use symptoms for diagnosis and did not distinguish between polyneuropathy and mononeuropathy or multineuropathy; and the second only comprised Type II diabetic patients.

Like autonomic neuropathy [27], DPN is more prevalent among Type II than among Type I diabetic patients [10, this study]. This could be due to the period of occult hyperglycaemia preceding diagnosis being longer in Type II than in Type I diabetes but it has also been suggested that Type II, but not Type I, diabetes involves the action of neurotoxic agents other than glucose [28]. This hypothesis has been supported by pointing to the contrast between the rate of increase in prevalence among Type I diabetic patients estimated in a longitudinal study as 2.5% per year of duration [20] and the rate we estimated from reported data for Type II diabetic patients [11] as 3.6% per year of duration. It is possible, however, that this data was an overestimate: arrived at by comparing the prevalence of about 8% in newly diagnosed Type II diabetic patients found in that [11] and other studies [3, 7] with the percentage obtained from the 10-year follow-up in that study. It implies on average DPN develops for about 2 years before diagnosis, a much shorter time than the 12.5 years we found in this study or the 4–7 years estimated in a study of retinopathy among Australian and USA Type II diabetic patients [29]. In view of these longer estimates of pre-diagnosis duration of polyneuropathy, and of the new criteria proposed for diagnosis of diabetes [30], we believe it likely that the only causes of the greater prevalence among Type II diabetic patients are the duration of the disease and the older age of Type II diabetic patients, which probably acts via effects on microcirculation and the ensuing ischaemia [31].

For a variety of reasons, diabetic patients with DPN are liable to develop foot ulcers or require amputation [32–35]. In this study, 93 patients (3.3% of the whole sample) had or had had foot ulcers and 21 of these 93 (0.7% of the total) had undergone amputation; 91.4% of the patients with ulcers had Type II diabetes. That DPN was diagnosed in 57.0% of the 93 (on the basis of signs including zero perception of vibrations in 45 patients), as against only 19.9% of DPN patients without ulcers, confirms that DPN in general, and reduced perception of vibration in particular [32], are major risk factors for neuropathic foot ulcers in diabetes.

In conclusion, in this study of a total of 2805 diabetic patients recruited from primary health care centres and hospital clinics in 14 of the 17 Spanish Autonomous Communities we found that nearly a quarter had DPN (over 90% of them were Type II diabetic patients) and that prevalence increased with age and the duration of the disease. Although the prevalence of DPN was naturally greater among hospital patients than among those attending primary centres, the number of cases detected in the second was

almost twice the number detected at hospitals. Since patients in whom DPN had been diagnosed were about three times more likely to develop foot ulcers or require amputation than patients without DPN, the major role that primary care physicians play in the prevention of diabetic foot lesions becomes obvious.

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