Screening For Peripheral Sensory Neuropathy In a Tunisian Population of Patients With Diabetes

Jemai Chaima C., El Frigui Sinène P.M.R., Ben Mami Faika C.

Abstract — Aims: Diabetes is a public health problem in the world. Its prevalence as well as that of degenerative complications, such as peripheral sensory neuropathy (PSN), are high. Our study was aimed at determining the prevalence of peripheral sensory neuropathy in a Tunisian population of patients with diabetes and at identifying its associated risk factors.

Methods: It was a descriptive prospective study conducted in department C of Diabetology and Nutrition of the National Institute of Nutrition of Tunis (September 2019). 100 patients with diabetes have been enrolled. PSN was screened by the 10 g monofilament test.

Results: The mean age was 54 ± 12.9 years. The sex ratio was 0.78. Active smoking was 35% common. Diabetes was type 2 in the majority of cases (78%). The average duration of diabetes was 13.62 ± 6.29 years. 78% of the population has been unbalanced. The prevalence of peripheral sensory neuropathy was 41%. It was significantly associated with diabetes duration ($p < 10^{-3}$), smoking ($p = 0.007$) and diabetic retinopathy ($p = 0.032$). Unbalanced diabetes was not significantly associated with PSN ($p = 0.09$).

Conclusion: Screening for peripheral sensory neuropathy is compulsory given it can be asymptomatic and only revealed at the stage of complications. Risk factors should be known and screened. This contribute in optimizing patients managing.

Index Terms — Diabetes, Diabetic retinopathy, Peripheral sensory neuropathy, Smoking, 10 g monofilament test.

I. INTRODUCTION

Diabetes is a chronic metabolic disease and a public health problem worldwide [1], [2]. Its prevalence has continued to rise worldwide due to the improvement in life expectancy, the increased prevalence of overweight and obesity and the sedentary lifestyle [3], [4]. The chronic glycemic imbalance exposes to degenerative complications of diabetes, particularly peripheral sensitive neuropathy (PSN). This complication is defined by the presence of signs of peripheral sensitive nerve damage caused by diabetes. It alters the quality of life of patients and exposes them to foot ulcers and Charcot's neuroarthropathy, implying the functional prognosis of the affected limb. The literature reports many factors that can precipitate the onset of PSN.

In this context, we conducted this study whose objectives were to determine the prevalence of PSN and to identify its associated risk factors.

II. PATIENTS AND METHODS

A. Definitions

The glycemic goal was defined by referring to the American Diabetes Association (ADA) recommendations of 2019 [5], by an $HbA1C \leq 7\%$. The glycemic target has been widened to 8% in patients having recurrent severe hypoglycemia, having advanced degenerative complications (chronic renal failure (stages 3 to 5), ischemic heart disease) or having a limited life expectancy.

-The elderly subject was defined according to the World Health Organisation (WHO) (age ≥ 65 years).

- We considered diabetes as old when it evolve for more than 15 years.

-The 10 g monofilament test was used and interpreted according to the International Consensus on the Diabetic Foot recommendations [6].

-Creatinine clearance was estimated using The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula.

B. Description of the study

This is a prospective cross-sectional descriptive study, about 100 patients with diabetes followed up in the department C of the National Institute of Nutrition of Tunis (INNTA), carried out in September 2019.

C. Study protocol

We included diabetic patients aged over 18 years. We did not include patients with type 1 diabetes evolving for less than 5 years, pregnant women, and patients with neuropathies related to other etiologies than diabetes.

A file has been pre-established to record the clinical and biological data of the patients.

We collected the socio-demographic characteristics of the population (age, gender, level of education, smoking) and the diabetes characteristics (type, duration, glycemic control, treatment, degenerative complications, associated cardio-metabolic comorbidities (Hypertension and diabetes)).

Screening for peripheral sensory neuropathy was done by the same clinician for all the patients, using the 10 g monofilament test.

We studied the association of PSN with the following factors: Smoking, diabetes duration, body mass index (BMI), glycemic control and diabetic retinopathy. Then, in multivariate analysis, we studied factors found significantly associated with PSN in univariate analysis.

Published on July 31, 2020.

Jemai Chaima C., National Institute of Nutrition of Tunis, Tunisia.
(corresponding e-mail: jemaichaima87@yahoo.fr)

El Frigui Sinène P.M.R., Sahloul hospital of Sousse, Tunisia.

Ben Mami Faika C., National Institute of Nutrition of Tunis, Tunisia.

D. Statistical analysis

Data were analyzed using SPSS version 21.0 software. Simple frequencies were calculated for the qualitative variables, means, medians, and standard deviations and the extreme values for the quantitative variables.

Percentage comparisons on independent series were carried out by the Pearson Chi-square test, and in case of significance but invalidity of this test, by the Fisher bilateral test.

The significance level was set at 0.05. Multivariate analysis was performed using multinomial logistic regression.

III. RESULTS

A. Characteristics of the population

1. General characteristics of the population

The sample studied consisted of 44% men and 56% women, a sex ratio of 0.78. The mean age was 54 ± 12.9 years with extremes of 29 and 87 years. 27% (n = 27) were over the age of 65. 56% had a secondary or higher education level. 37% were smoking. Overweight and obesity were the main comorbidities associated with diabetes in our population with a frequency of 70%, followed by high blood pressure (44%) and dyslipidemia (38%).

2. Characteristics of diabetes

Diabetes was type 2 in the majority of cases (78%). Its average duration was 13.62 ± 6.29 years, with extremes of 2 and 32 years. Its duration was more than 15 years in 43% of the cases. 69% of the patients were on insulin therapy. The others were under oral anti-diabetics.

Fig. 1. Diabetes degenerative complications of the population.

3. Clinical and biological characteristics

The mean weight was 74.62 ± 12.65 kg. The mean height was 1.62 ± 0.05 m. The mean BMI was 28.36 ± 5.6 kg / m² with extremes of 19.36 and 43.7 kg / m². The mean HbA1C was $9.47 \pm 2.32\%$ with extremes of 5.3 and 14.9%. 78% of the population had unbalanced diabetes. The mean creatinine clearance was $105,16 \pm 21,46$ ml/mn.

4. Prevalence of peripheral sensory neuropathy and associated risk factors

The prevalence of PSN was 41%.

TABLE 1: ASSOCIATED RISK FACTORS WITH PERIPHERAL SENSITIVE NEUROPATHY IN UNIVARIATE ANALYSIS

Associated risk factors	Patients with PNS (n=41)	Patients without PNS (n=59)	p value	OR,95%CI
Smoking (n=32)	68.8% (n=22)	31.3% (n=10)	<10 ⁻³	5.67 [2.2;14.1]
No smoking (n=68)	27.9% (n=19)	72.1% (n=49)		
Diabetes duration ≥15 years (n=43)	67.4% (n=29)	32.6% (n=14)	<10 ⁻³	7.76 [3.1;19.1]
Diabetes duration <15 years (n=57)	21.1% (n=12)	78.9% (n=45)		
BMI ≥25 kg/m ² (n=70)	38.6% (n=27)	61.4% (n=43)	0.509	-
BMI <25 kg/m ² (n=30)	46.7% (n=14)	53.3% (n=16)		
Unbalanced diabetes (n=78)	47.7% (n=37)	52.6% (n=41)	0.015	4 [1.2;13]
Well balanced diabetes (n=22)	18.2% (n=4)	81.8% (n=18)		
Patients with diabetic retinopathy (n=30)	66.7% (n=20)	33.3% (n=10)	0.001	4.6 [1.8;11.6]
Patients without diabetic retinopathy (n=70)	30% (n=21)	70% (n=49)		

TABLE 2: ASSOCIATED RISK FACTORS WITH PSN IN MULTIVARIATE ANALYSIS

Associated risk factors with PSN	p value	OR, 95% CI
Diabetes duration ≥15 years	<10 ⁻³	7.25 [2.5; 21]
Smoking	0.007	4.9 [1.5; 15.4]
Diabetic retinopathy	0.032	3.5 [1.1; 11.1]
Unbalanced diabetes	0.09	3.3[0.8; 13.3]

IV. DISCUSSION

PSN is a degenerative complication of diabetes, precipitated by chronic glycemic imbalance. The implication of diabetes duration and hyperglycemia in the genesis of neuropathy has been established in several studies including the study The Diabetes Control and Complications Trial Research (DCCT) [7], [8].

Symmetric sensitive distal polyneuropathy is the most common form. Its prevalence varies widely depending on the used diagnostic criteria (clinical criteria, 10 g monofilament test, electroneuromyogram). It is estimated to be present in almost 50% of diabetics and that it requires treatment in 10 to 20% of patients [9], [10].

In our study, 41 % of the population had PSN. This high frequency could be related to the high prevalence of imbalanced diabetes in the population studied. However, this prevalence is probably underestimated since the diagnosis was based solely on the 10 g monofilament test. The use of other screening tools could reveal a higher prevalence. In this context, Reilhes et al concluded that the threshold of vibratory perception constitutes a more sensitive means of diagnosis [11].

On the other hand, more than half of the population does not have PSN despite the high prevalence of glycemic imbalance and regardless of the type of diabetes. Indeed, the time taken for the onset of neuropathy in patients with diabetes is unpredictable. Some authors have shown that it can even precede the diagnosis of diabetes [12]. Others have shown that a severe form can appear precociously [13]. Furthermore, in our study, multivariate analysis revealed that glycemic imbalance was not a factor

significantly associated with PSN.

All of these findings suggest the involvement of other factors in PSN development, such as genetic and nutritional factors. Indeed, patients with diabetes are often obese and they cumulate cardiovascular risk factors such as smoking and unhealthy eating carrying insufficient amounts of micronutrients and vitamins. Many nutritional deficiencies are known to be implicated in the neuropathy genesis.

Smoking ($p < 10^{-3}$, 5.67, 95% CI [2.2; 14.1]), diabetes duration ≥ 15 years ($p < 10^{-3}$, 7.76, 95% CI [3.1; 19.1]) and diabetic retinopathy ($p = 0.001$, 4.6, 95% CI [1.8; 11.6]) were the risk factors significantly associated with PSN in our study.

Thus, we join the results of the literature on risk factors associated with neuropathy for most of the factors studied. Indeed, as well as smoking [14], [15], [16], as long duration of diabetes [14], [17], and diabetic retinopathy [18], [19], have been reported as risk factors associated with PSN. Other factors have also been reported, including glycemic uncontrol [18], [19], and fasting hyperglycemia [20], [21]. However, this result could be a confounding factor given its association with the imbalance and long duration of diabetes. BMI was also found as an associated factor, by Al Mahroos as well as by Yang CP contrary to our study [14], [19]. Diastolic blood pressure [21], [22], as well as azotemia [21], [23], have also been described as associated factors in other studies.

Authors of a recent meta-analysis about 16 studies (2 cohorts and 14 cross-sectional studies) have shown that age, diabetes control, diabetes duration, and diabetic retinopathy were the factors most frequently significantly associated with diabetic neuropathy, unlike smoking, BMI, and total cholesterol and triglyceridemia [24].

Thus, not only screening for PSN is necessary, but also that of the associated risk factors. Diabetes Control and managing modifiable risk factors, such as smoking and nutritional deficiencies, effectively help prevent this dreaded complication.

V. CONCLUSION

PSN is a common complication of diabetes. It can occur even in recent well-balanced diabetes. This could be related to many other factors independent from diabetes control and duration.

Thus, identifying and managing these factors with simple measures such as stopping smoking and bringing needed micronutrients and vitamins, optimize medical care and avoid filling the prescription with drugs.

REFERENCES:

- [1] Bonita R, Winkelman R, Douglas KA, Courten M, McQueen DV, Puska P. The WHO stepwise approach to surveillance (STEPS) of non communicable disease risk factors. Behavioral Risk Factor Surveillance. New York: Kluwer academic/Plenum publishers.2003; 9-22.
- [2] Boutayeb A, Boutayeb S. The burden of non communicable diseases in developing countries. International Journal for Equity in Health. 2005; 4:2.
- [3] Fédération internationale de diabète. Atlas de diabète de l'IDF, Sixième édition, 2013.
- [4] Wild S. Global prevalence of diabetes-estimated for the year 2000 and projections for 2030. Diabetes care, 2007; 20: 1183-93.
- [5] 2-Bakris G, Blonde L, Boulton AJM, D'Alessio D, Greene EL, Hood KK et al. Diabetes care. 2019 ;42 (Suppl 1).
- [6] American Diabetes Association. Position Statement. Preventive foot care in diabetes. Diabetes Care. 2004; 27 (Suppl 1) :63-4.
- [7] -The diabetes control and complications trial research Group. N Engl J Med. 1993; 329-977.
- [8] -Martin CL, Albers JW, Pop-Busui R; DCCT/EDIC Research group. Neuropathy and related findings in the diabetes control and complications trial/epidemiology of diabetes interventions and complications study. Diabetes care. 2014; 37: 31-8.
- [9] Argoff CE, Cole BE, Fishbain DA, Irving GA. Diabetic peripheral neuropathic pain: clinical and quality-of-life issues. Mayo Clinic proceedings. 2006 ;81(Suppl 4) :3-11.
- [10] Iqbal Z, Azmi S, Yadav R, Ferdousi M, Kumar M, Cuthbertson DJ, et al. Diabetic Peripheral Neuropathy: Epidemiology, Diagnosis, and Pharmacotherapy. Clinical Therapeutics. 2018 ;40(6) :828-49.
- [11] Reilhers L, Buvry S, Goletto M, Schuldiner S, Richard JL. OP3 Dépistage du risque podologique: seuil de perception vibratoire ou monofilament?. Diabetes metab. 2011 ;38: 125.
- [12] Kamel M. Prévalence élevée de la neuropathie périphérique dès le stade de prédiabète. Médecine des maladies Métaboliques. 2016; 10.
- [13] Said G, Goulon-Goeau C, Slama G, Tchobroutsky G. Sever early-onset polyneuropathy in insulin-dependent diabetes mellitus. A clinical and pathologic study. N Engl J Med. 1992; 326: 1257-63.
- [14] Al-Mahroos F, Al-Roomi K. Diabetic neuropathy, foot ulceration, peripheral vascular disease and potential risk factors among patients with diabetes in Bahrain: a nationwide primary care diabetes clinic-based study. Annals of Saudi medicine. 2007 ;27(1) :25-31.
- [15] Tesfaye S, Stevens LK, Stephenson JM, Fuller JH, Plater M, Ionescu-Tirgoviste C, et al. Prevalence of diabetic peripheral neuropathy and its relation to glycaemic control and potential risk factors: the EURODIAB IDDM Complications Study. Diabetologia. 1996 ;39(11) :1377-84.
- [16] Maser RE, Steenkiste AR, Dorman JS, Nielsen VK, Bass EB, Manjoo Q, et al. Epidemiological correlates of diabetic neuropathy. Report from Pittsburgh Epidemiology of Diabetes Complications Study. Diabetes. 1989 ;38(11) :1456-61.
- [17] Kiani J, Moghimbeigi A, Azizkhani H, Kosarifar S. The prevalence and associated risk factors of peripheral diabetic neuropathy in Hamedan, Iran. Archives of Iranian medicine. 2013 ;16(1) :17-9.
- [18] Nie C, Bao HP. Analysis of the related risk factors of diabetic peripheral neuropathy. Chinese journal of experimental and clinical virology. 2012 ;26(6) :467-9.
- [19] Yang CP, Lin CC, Li CI, Liu CS, Lin WY, Hwang KL, et al. Cardiovascular Risk Factors Increase the Risks of Diabetic Peripheral Neuropathy in Patients With Type 2 Diabetes Mellitus: The Taiwan Diabetes Study. Medicine. 2015 ;94(42) :e1783 10.1097/MD.0000000000001783.
- [20] Chen L, Zheng F, Li H. A change of serum cystatin C in diabetic peripheral neuropathy in type 2 diabetic patients and its clinical significance. Chinese Journal of Diabetes. 2014 ;22(8) :700-3.
- [21] Wei W, Wang Z, Zhou I, Zhao S, Mao H. Risk factors analysis of diabetic peripheral neuropathy in patients with type 2 diabetes. Hainan Medical Journal. 2017 ;28(20) :3379-81.
- [22] Chen X, Bi Y, Hu Y, Tong G, Zhu D. Prevalence and risk factors of diabetic peripheral neuropathy. Journal of Medical Postgraduates. 2011 ;24(10) :1035-8.