



# Burden of Diabetic Peripheral Neuropathy in Pima Indians With Type 2 Diabetes

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Diabetic peripheral neuropathy (DPN) and diabetic nephropathy (DN) share common pathological mechanisms and are favorably impacted by intensive glycemic control. American Indians have disproportionately higher rates of type 2 diabetes (T2D), younger age of diabetes onset, and earlier development of long-term complications than other ethnic groups (1). Diabetes as an underlying cause of death is 2.5–3.5 times higher among American Indians than whites, yet the DPN burden among American Indians has not been systematically evaluated. We assessed DPN prevalence in Pima Indians and evaluated the relationship between DPN and DN.

A total of 79 Pima Indians with T2D (age  $53 \pm 11$  years, diabetes duration  $25 \pm 6$  years, 73% female, and mean  $HbA_{1c}$   $9.5 \pm 1.9\%$  [ $80 \pm 7$  mmol/mol]) from the Gila River community were enrolled. DPN status was ascertained using the Michigan Neuropathy Screening Instrument (MNSI) (2) and defined by an MNSI exam (MNSIE) score  $\geq 2.5$ . Renal function was assessed by estimated glomerular filtration rate (eGFR), the urinary clearance of iothalamate (measured GFR), and albumin-to-creatinine ratio (ACR).

Of the 79 subjects, 70 (89%) had DPN. Subjects with and without DPN had poor glycemic control and similar age and sex distribution and total cholesterol. Subjects with DPN were more obese than subjects without DPN (BMI  $36 \pm 9$  vs.  $32 \pm 5$  kg/m<sup>2</sup>,  $P = 0.027$ ). Nine subjects with DPN and one without DPN had a lower-extremity amputation. Urine albumin excretion was higher in subjects with DPN (median ACR 50.3 [interquartile range 17.7, 502.5] vs. 11.5 [7.8, 73.8],  $P = 0.0004$ ). Measured GFR was similar in both groups. Higher MNSIE scores were associated with elevated ACR ( $r = 0.35$ ,  $P = 0.0013$ ) (Fig. 1A) and lower eGFR ( $r = -0.28$ ,  $P = 0.010$ ) (Fig. 1B), but not with measured GFR ( $r = -0.085$ ,  $P = 0.47$ ).

The high DPN rates in our cohort exceed those that were reported among Canadian (46%) (3) and Australian aboriginals (28%) (4). In the Sandy Lake Diabetes Complications Study (3), 189 Aboriginal Canadians were evaluated for DPN using the MNSIE. Subjects were younger ( $46 \pm 13$  years) and had shorter diabetes duration (9 years) than our study participants but had poor glycemic control (two-thirds had  $HbA_{1c} > 7\%$ ). In a small ( $N = 43$ )

study of Australian aboriginals (4) (age 50 years, duration 0–15 years,  $HbA_{1c}$   $8.5 \pm 2.9\%$ , and 60% albuminuria [microalbuminuria 38%, macroalbuminuria 22%]), 28% had DPN, defined by at least one sign (Semmes-Weinstein monofilament test, ankle reflex test, pain and temperature sensation, or vibration perception). Finally, the longitudinal population-based Strong Heart Study (SHS) (5) assessing 2,051 American Indians identified regional differences in sensory neuropathy prevalence using the Semmes-Weinstein monofilament test, with 22% of American Indians in Arizona, 8% in Oklahoma, and 9% in North and South Dakota exhibiting sensory neuropathy. Relative to these subjects, our population was younger (53 vs. 59 years) and had a longer diabetes duration (25 vs. 15 years), albeit similar poor glycemic control ( $HbA_{1c}$  9.5 vs. 9%).

The alarmingly high prevalence of DPN and its most adverse outcomes (amputation and DN) among American Indians in our study is a stark reminder that there is an urgent need to develop and implement treatment strategies to improve diabetes management in American Indian populations and enhance prevention efforts.

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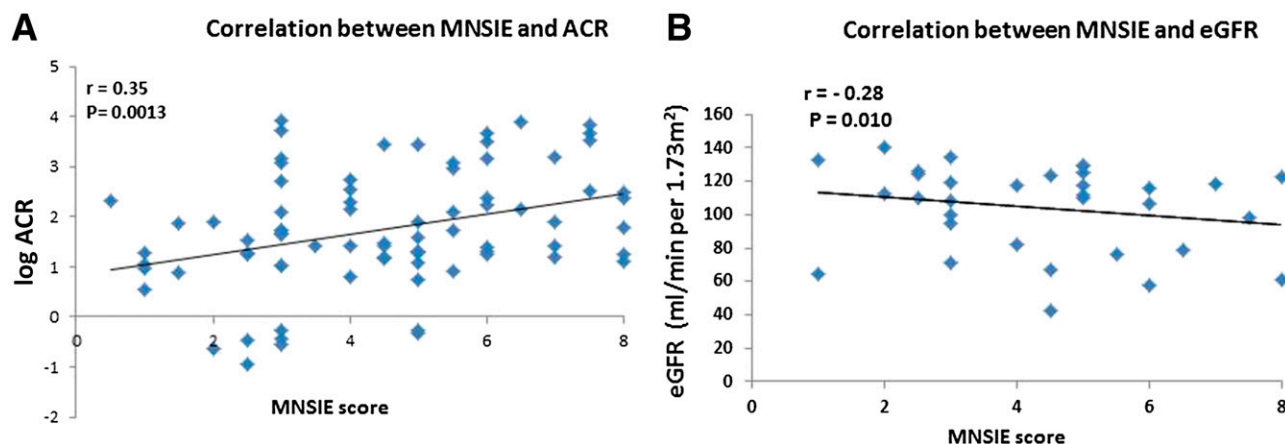
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**Figure 1**—Correlation between the MNSIE score and ACR (A) or eGFR (B).

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R.P.-B., R.G.N., and E.L.F. reviewed and edited the manuscript and provided feedback. E.L.F. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

#### References

1. Cho P, Geiss LS, Burrows NR, Roberts DL, Bullock AK, Toedt ME. Diabetes-related mortality among American Indians and Alaska Natives, 1990-2009. *Am J Public Health* 2014;104(Suppl. 3):S496–S503
2. Feldman EL, Stevens MJ, Thomas PK, Brown MB, Canal N, Greene DA. A practical two-step quantitative clinical and electrophysiological

assessment for the diagnosis and staging of diabetic neuropathy. *Diabetes Care* 1994;17:1281–1289

3. Hanley AJ, Harris SB, Mamakeesick M, et al. Complications of type 2 diabetes among Aboriginal Canadians: prevalence and associated risk factors. *Diabetes Care* 2005;28:2054–2057

4. Maple-Brown LJ, Brimblecombe J, Chisholm D, O’Dea K. Diabetes care and complications in a remote primary health care setting. *Diab Res Clin Pract* 2004 64:77–83

5. Sosenko JM, Sparling YH, Hu D, et al. Use of the Semmes-Weinstein monofilament in the Strong Heart Study. Risk factors for clinical neuropathy. *Diabetes Care* 1999;22:1715–1721