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Symptomatic diabetic autonomic neuropathy in type 1 diabetes: findings from the T1D exchange

Aim: This cross-sectional study aimed to determine the frequency and severity of diabetic autonomic neuropathy (DAN) symptoms, as defined by the Survey of Autonomic Symptoms (SAS) in adults in the T1D Exchange registry cohort, a large cohort with type 1 diabetes (T1D) managed in diverse settings across the US. Clinical characteristics and comorbidities were evaluated as potential risk factors for both the presence and severity of DAN symptoms.
Methods: DAN symptoms and severity were obtained through completion of SAS by 965 individuals (age 40±17 years, 64% female, 90% non-Hispanic White, and with 20 years median diabetes duration). Diabetes history, management, and monitoring; general health; lifestyle; family history; socioeconomic factors; medications; acute and chronic diabetic complications; other medical conditions; and laboratory results were also extracted.
Results: 17% of participants had symptomatic DAN (SAS score >3), of which 28% had mild, 27% moderate, 25% severe and 20% very severe symptoms. Participants with symptomatic DAN were more likely to be female (p=0.03) and smokers (P=0.002), with higher median HbA1c (p=0.03), a higher median duration of T1D (p=0.004) and lower annual income (P=0.03). Cardiovascular disease, gastroparesis, diabetic peripheral neuropathy, use of opioids, and anxiety and depression were reported as risk factors for symptomatic DAN. DAN symptom status or severity was not associated with lipid profile and management, BMI, pump use or CGM, hypertension, albuminuria, erectile dysfunction, and retinopathy.
Conclusions: Glycaemic exposure, duration of diabetes, vascular disease, lower socioeconomic status, and psychological comorbidities are associated with symptomatic DAN in T1D.

Comments. This study evaluates the prevalence of symptomatic DAN and associated risk factors in a large cohort of T1D. The authors suggested SAS as an appropriate tool to assess DAN in large cohort settings due to the ease of administration, low participant burden, high specificity, and lack of invasive procedure. However, the prevalence of symptomatic DAN reported in this study was lower than in previous cohorts such as DCCT/EDIC. The lower reported DAN prevalence is due to the use of a symptom-based assessment with 90% specificity but only 65% sensitivity in detecting DAN.
This study reported the expected glycaemic associations with the presence of DAN. Hba1c was significantly higher in patients with symptomatic DAN and progressively increased by increasing the severity of symptoms. Participants with symptomatic DAN were more likely to have had both severe hypoglycaemic and DKA events, which resulted in hospitalization, higher care costs and lower quality of life. The association between socioeconomic status and symptomatic DAN prevalence suggests poorer self-management and thus more diabetes complications. Another novel finding of this study was the association between symptomatic DAN and depression, anxiety, and opioid use. Depression and anxiety are common in T1DM and associated with corresponding worse glycaemic control and DKA events, highlighting the importance of addressing psychological comorbidities in T1D. The authors suggested that clinicians avoid using opioids to treat neuropathy-associated pain, which possibly causes worsening of gut motility, a marker of autonomic neuropathy. The authors acknowledged the limitations of their study, such as low sensitivity of SAS and sample selection bias which limits the generalizability of their findings.
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Reference. Mizokami-Stout K, Bailey R, Ang L, Aleppo G, Levy CJ, Rickels MR, Shah VN, Polsky S, Nelson B, Carlson AL, Vendrame F, Pop-Busui R; T1D Exchange Clinic Network. Symptomatic diabetic autonomic neuropathy in type 1 diabetes (T1D): Findings from the T1D exchange. J Diabetes Complications. 2022 May;36(5):108148. doi: 10.1016/j.jdiacomp.2022.108148.

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