

Vitamin D deficiency is associated with nerve conduction deficit and symptoms of peripheral neuropathy in type 2 diabetes

Aims: To comprehensively assess the associations between vitamin D levels and diabetic peripheral neuropathy (DPN)-related symptoms, signs, and abnormal nerve conduction (EMG) parameters.

Methods: Data were retrospectively collected from a Chinese cohort and those patients were included who fulfilled the criteria having T2D and completed DPN screening. Patients with co-occurring conditions interfering with neuropathy assessment and those on vitamin D supplementation were excluded. The eligible patients (n=701) underwent EMG examination of the upper and lower limbs and measurement of serum 25-hydroxyvitamin D (25-OH-D). For reference, data of 119 healthy subjects with available 25-OH-D and EMG were included as well. Diabetic symptoms and signs were assessed, and Michigan Neuropathy Screening Instrument (MNSI) scored. As for EMG, action potential amplitudes, conduction velocities and distal latencies were determined.

Results: 25-OH-D levels were significantly lower in those with DPN compared to healthy controls ($p=0.004$) and among patients with DPN, vitamin D deficiency (<30 nmol/L, $n=66$) was more common (12.4% vs 3%). T2D patients with vitamin D deficiency tended to have more symptoms and signs of small- and large-fibre damage than those with sufficient vitamin D. Compared to insufficient (30-50 nmol/L, $n=164$) and sufficient (>50 nmol/L, $n=471$) levels, deficient vitamin D was associated with lower nerve conduction amplitudes and slower motor velocities as well as longer F-wave minimum latencies. There was a significant trend for better nerve conduction parameters according to vitamin D gradient. In multivariate regression analysis, there was a 17% increase in the odds of having DPN per 10-unit decrease in vitamin D and the risk of DPN was significant until it reached 30 nmol/L.

Conclusions: Vitamin D relates to most DPN-related symptoms/signs and vitamin D deficiency is associated with impaired nerve conduction abilities in patients with T2D.

Comments. Vitamin D deficiency is a proven risk marker for many conditions such as cardiovascular morbidity, malignancies, autoimmune diseases, etc. Patients with type 2 diabetes are a high-risk group for low vitamin D and data are accumulating on the association between DPN and vitamin D deficiency. The above study investigated the relationship between DPN and vitamin D levels thoroughly in a huge number of patients. Beyond sample size, further strengths of the study are using nerve conduction studies for DPN assessment, and that external validation of study findings was done against data of 3 other Chinese centres. The study did not only prove the association between vitamin D levels and DPN but it determined a 25-OH-D threshold for the risk of DPN around 30 nmol/L. The external validation of the study reaffirmed this threshold and the associations with MNSI score as well. Interestingly, this study could not prove any association between vitamin D deficiency and painful symptoms of neuropathy that is somewhat contrasting to previous findings (Alam U et al *Diabetes Metab Res Rev.* 2021;37:e3361). However, it can be a consequence of the heterogeneity of diabetic populations. Of note is that real vitamin D deficiency was quite uncommon in the study population ($n=66$) that limits the generalisability of statistical analysis and conclusions. Further important limitation is the retrospective design of the study. Confounders such as sunlight exposure, dietary factors were not investigated either.

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Reference. Pang C, Yu H, Cai Y, Song M, Feng F, Gao L, Li K, Chen Y, Xie J, Cheng Y, Lin E, Pan X, Zhang W, Deng B. Vitamin D and diabetic peripheral neuropathy: A multi-centre nerve conduction study among Chinese patients with type 2 diabetes. *Diabetes Metab Res Rev.* 2023 Oct;39(7):e3679.

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