

Vitamin D Deficiency and Systemic Lupus Erythematosus: Cause or Consequence?

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To the Editor,

We read with great interest the study by Attar et al. in which the authors report, in agreement with previous studies, that vitamin D deficiency is very common in systemic lupus erythematosus (SLE) patients with 87% of SLE patients observed to be deficient, and 48% of patients found to have serum 25-hydroxyvitamin D (25[OH]D) levels <25 nmol/L.¹ Whereas, the authors explore various plausible hypotheses likely to underlie the association between SLE and vitamin D through which SLE may lead to lower vitamin D levels, we believe that it is also important to consider the possibility that vitamin D deficiency may have a causative role in SLE etiology. This notion is currently accumulating a substantial evidence base with regard to a number of autoimmune diseases, most notably multiple sclerosis (MS) and type 1 diabetes (T1D) for which vitamin D deficiency is widely recognized as a risk factor of disease development.²

In the case of MS, a landmark study by Munger et al. measured serum vitamin D levels in individuals before MS onset in which they showed that individuals with high 25(OH)D levels (>100 nmol/L) have a 62% lower MS risk.³ In determining a potentially causal role for vitamin D in SLE, the establishment of a temporal relationship in which vitamin D deficiency precedes disease onset is necessary, but the current evidence in this regard is limited.

Hiraki et al. have recently reported that they did not observe any association between adolescent dietary vitamin D intake and SLE development in adulthood in a large cohort of American nurses.⁴ Instead, other time-points have been postulated as important in influencing SLE risk, including in utero. Disanto et al. observed a clear seasonal distribution of births for a number of immune-mediated diseases, including MS and SLE, in which there is thought to be a peak in April and a trough exactly six months later in October, thus implicating a varying seasonal factor such as UVB radiation and subsequent vitamin D synthesis in disease etiology.⁵ Further, genes associated with SLE, MS, and T1D have also been shown to be significantly enriched for vitamin D receptor binding sites, thus suggesting that vitamin D may potentially influence disease risk through regulation of SLE associated genes.⁶ Importantly, the finding by Attar et al. that the levels of 25(OH)D were significantly lower in patients with active SLE (n=41; 43%) compared to those with inactive disease (n=54; 57%; $p=0.04$) suggests that vitamin D may also be a useful therapeutic agent in reducing some disease activity, and such interventional measures may be the only way in

which to conclusively establish whether vitamin D is involved in SLE etiology and disease course.¹

In conclusion, it is well known that vitamin D has an immune modulating effect and thus it is plausible that vitamin D deficiency is a risk factor, rather than a consequence of SLE. However, the time-points at which vitamin D may influence disease risk are currently not determined and further longitudinal studies are critical in establishing whether the association between SLE and vitamin D truly represents an association, causative relationship, or both. The strength of current associations implicating vitamin D deficiency in the etiology of a number of autoimmune diseases makes further investigation an urgent public health issue as vitamin D supplementation may help to reduce the substantial burden of SLE and other autoimmune diseases.

Sincerely,

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