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The role of vitamin D in the association between tuberculosis and end-stage renal disease

To the Editor:

We read with great interest the study by Hu *et al.* [1] in which the authors report a significantly increased risk of tuberculosis (TB) within 2 years of onset of end-stage renal disease (ESRD) in their population-based cohort study. The authors suggested that this association is likely to be a consequence of an immunocompromised state and frequent hospital attendance of patients with ESRD. Indeed, whereas these factors plausibly contribute substantially to increased TB risk, vitamin D deficiency may also be an important factor contributing to the observed association between TB and ESRD.

The primary source of vitamin D in the body is endogenous synthesis following UVB exposure to the skin (with a small proportion of vitamin D intake obtained through diet) [2]. Upon UVB exposure, 7-dehydrocholesterol in the epidermal skin layer is converted to previtamin D_3 which rapidly undergoes a thermal reaction to produce cholecalciferol (an inactive form of vitamin D_3) [2]. Subsequently, cholecalciferol is hydroxylated in the liver by 25-hydroxylase to form 25-hydroxyvitamin D_3. This molecule is finally hydroxylated in the kidney by the enzyme 1-alpha-hydroxylase to form calcitriol (1,25-dihydroxyvitamin D_3), the active form of vitamin D [2]. Patients with chronic kidney disease including ESRD are thought to have a high incidence of vitamin D insufficiency and deficiency in part as a result of impaired renal function and reduced ability to generate the active form of vitamin D [3]. An American study of 825 consecutive patients on haemodialysis found that 78% of patients were vitamin D-deficient and 18% classified as severely deficient [4]. Low vitamin D levels in haemodialysis patients has also been associated with increased mortality [4, 5]. Further, a substantial evidence base of both basic science and clinical research has shown that vitamin D deficiency is significantly associated with active TB (odds ratio 2·9, 95% confidence interval 1·3–6·5) [6]. This is also supported, for example, by the historical use of phototherapy in the treatment of TB.

Vitamin D receptors are found on a variety of human cells including monocytes, macrophages and dendritic cells and both *in vivo* and *in vitro* studies have shown that vitamin D has an immune-modulatory role against *Mycobacterium tuberculosis* [7, 8]. Therefore, information on the use of vitamin D supplementation in the reported patients with ESRD would have been highly interesting, but we appreciate that this may not have been available to the authors. Nevertheless, a strong association between chronic kidney disease and vitamin D deficiency suggests that vitamin D supplementation, particularly in individuals with ESRD, may be important in reducing vitamin D-associated comorbidities, including TB. Given that Taiwan has the highest incidence and prevalence of ESRD in the world, this may potentially be an important public health issue for its population.

Declaration of Interest

None.

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