

Letter:

Protective role of vitamin D as a cellular immuno-modulator in *Mycobacterium tuberculosis* infected health care workers

To the Editor: I would like to raise a concern about health care workers' (HCW) exposure to *Mycobacterium tuberculosis*. Tuberculosis (TB) is a significant occupational problem among HCW in low- and middle-income countries.¹ The greatest single risk factor for developing TB from infection is concurrent HIV infection.² In the period from 1994 to 2006, TB incidence increased 4.2 times in South Africa (SA) while it was halved in the United States of America (USA).³⁻⁴ The risk ratio, based on the ratio of the incidence of TB, is over 300 times higher for HCW in SA than in the USA in 2006 (1 133 vs 3.7 per 100 000).⁵⁻⁶

Table 1: Comparable table of incidence rate and ratio in South Africa vs the USA

Country	Year	General population (per 100 000)	Health care workers (per 100 000)
South Africa (SA)	1994	223 ³	---
	2000	576 ⁴	---
	2006	940 ⁴	1133 (in 2004/5) ⁵
USA	1994	9.2 ⁴	5.4 ⁶
	2000	5.78 ⁴	3.7 ⁶
	2006	4.6 ⁴	---
SA vs USA	2006	204	306

Epidemiological, clinical and histopathological evidence suggest that black people are susceptible to TB.⁷ 25(OH)D₃ deficiency is associated with active tuberculosis.⁸ Differences in the ability of human populations to produce vitamin D may contribute to susceptibility to microbial infection.⁹ Recent studies showed the importance of vitamin D use as an immuno-modulator in the treatment of TB.¹⁰⁻¹¹ I would like you to note that 25(OH)D₃ acts as a steroid hormone. The activated form of vitamin D₃ is an immunoregulatory hormone, which activates monocytes and stimulates cell-mediated immunity.¹² Vitamin D effects are exerted through interaction with the vitamin D receptor (VDR).¹² Vitamin D-mediated human antimicrobial activity against *M tuberculosis* is dependent on the induction of cathelicidin.¹³

Causes of ineffective vitamin 25(OH)D₃ mediated immunoregulation are:

1. Environmental:
 - Limited bioavailability: insufficient vitamin D₃ intake¹⁴
 - UV light effect: inadequate sunlight¹⁴
2. Host related:
 - "Mirror effect": high reflectiveness of melanin-rich skin types that lowers synthesis of D₃
 - VDR polymorphism
 - Variable effects of HIV infection on immunoregulation

Effective 25(OH)D₃ mediated immunoregulation requirements are:

1. 25(OH)D₃ serum level between 90–100 nmol/l¹⁵, which is achieved by
2. Vitamin D₃ intake of 1 000 IU per day,¹⁵ particularly in the absence of sun exposure, with
3. Risk of hypercalcaemia between 1 in 10 000 and 5 in 1 000 for vitamin D₃ intake of 2 000 IU per day.¹⁶

4. Pre- and on-treatment follow-ups of serum 25(OH)D₃ levels are recommended to keep it in therapeutic range.

South African national food fortification programme legislation has been operational since 2003. Vitamin D₃ is not listed in the programme as the required fortification nutrient. Based on the above information I would recommend the following:

1. When HCW work in high-risk environment and the usual protective measures are of limited value, then occupational prophylaxis with vitamin D₃ supplementation needs to be considered as an Adjuvant protective measure against *M tuberculosis*. Presently, no information is available that vitamin D₃ is less protective in MDR- and XDR-TB contained environments.
2. Vitamin D₃ supplementation by vitamin D₃-fortified food, drinks and vitamin supplements in the form of drops or tablets may limit the burden of the number one killer infection even in HIV co-infected patients whose immune deficiency is controlled with antiretroviral medication. It will be important to assess the current evidence and its impact on the future changes in legislation regarding vitamin D₃ supplementation.

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