

# Vitamin D: The Unsought Solution to the TB Pandemic

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Tuberculosis has been known to mankind since ancient times. Despite Tuberculosis (TB) having been a major killer from antique time to date and the improvement in diagnostic tools, its eradication still remains a pipedream. An everlasting solution to TB control/eradication keeps eluding us.<sup>1</sup>

TB control requires multiple interventions to score the desired eradication. Vitamin D plays a pivotal role in maintaining the integrity of the innate immunity and has been used as an adjuvant therapy even prior to the first antimycobacterial clinical trials in the 1950s. Despite this historical background, there are still mixed views about the use of Vitamin D as an adjuvant therapy in TB treatment and thus its supplementation is not part of international guidelines on TB management. This may be due in part selection bias of studies in previous meta-analysis of Vitamin D supplementation in TB treatment. Therefore, it was not surprising to find an equivocal benefit of its supplementation. This led to dearth of specific studies investigating the use of Vitamin D supplementation in TB treatment.

In over 50 years there have only been two new drugs licensed, Bedaquiline and Delamanid. A downcast to the new drug development is the findings for the recent phase III trial the efficacy of delamanid is not indistinct. The first TB drug to be developed are streptomycin and paraminosalicylic acid, of which their role in TB treatment is currently insignificant, only used as add-on or peripheral drugs in drug resistant TB. In the 70 years of drug development our arsenal still remains limited and is further

compromised by development of drug resistance. Alternatives or adjuvant therapies need to be explored to increase our armaments against the scourge of TB.

Vitamin D is one of the natural hormones generated by the body through exposure to ultraviolet B radiation in sunlight and acquired from certain foodstuffs like cod liver, sardines, milk, eggs, fruits and vegetables. Vitamin D plays a vital role in the immune response against TB. Before the discovery of anti-tuberculous drugs TB was treated by exposing patients to sunshine, so that they are exposed to the natural ultraviolet B radiation for the formation of vitamin D as well as directly killing the mycobacteria.

Numerous studies have demonstrated the relationship between vitamin D deficiency and TB. Reactivation tends to occur with decreased levels of Vitamin D. This comes about as a result of the impaired function of macrophages in the absence of Vitamin D. Macrophages and monocytes require 1, 25-dihydroxycholecalciferol which is the active metabolite of Vitamin D to activate the phagolysosome cascade and autophagy. The immune modulation by Vitamin D is through the stimulation of Beta-defensins and cathelicidin of which both lead to the production of antimicrobial peptides which kill the Mycobacterium Tuberculosis.

Vitamin D deficiency arises, as a result, of reduced exposure to sunlight. This may be due to daytime somnolence or working indoors during the daytime.

During winter time serum Vitamin D level are at their lowest, this is attributed to the shield of ultraviolet radiation by the cloud cover. Strict vegan diet, a diet without milk, fruits, sardines, liver oils.

Skin pigmentation does predispose one to vitamin D deficiency, individuals with Fitzpatrick score of IV to VI (darker skin pigmentation) take a longer time to make an equivalent amount of Vitamin D compared to individuals with Fitzpatrick score of I (white caucasians).

Studies have revealed that Vitamin D deficiency is highly prevalent among blacks especially those with poor social economic status. In the USA vitamin D deficiency is high among blacks followed by Hispanics, the two ethnic groups that habitually live under poor social economic status.'

Globally vitamin D deficiency is most prevalent in south-east Asia countries, despite their proximity to the equator.

There is a direct correlation between prevalence of Vitamin D deficiency and the burden of TB, countries like Cambodia, China and India have high rates of vitamin D deficiency and happen to be among countries with the highest burden of TB in the world.' This adds to the correlation of Vitamin D deficiency and TB.

Given its important role in restoring immune response against TB (both historically and present day associations), Vitamin D supplementation has been established to be beneficial. Studies have shown that supplementation of Vitamin D improves clinical and radiological recovery. A metanalysis analysis review of 8 studies done, two of the studies showed improved microbiological clearance with vitamin D supplementation. The studies above had marked differences in multiple characteristics including the baseline serum vitamin D levels."

Emerging evidence is in favour of vitamin D supplementation which shows that MTB is eliminated more efficiently with vitamin D supplementation. A study by Lopez et al in diabetes

types 2 with low Vitamin D receptor expression level and infected with TB, when supplemented with vitamin D it was noted that there was an increased clearance of MTB in the arm with vitamin D supplementation.

Management of Tuberculosis over the years has become more complex in establishing the diagnosis and treatment. This can be attributed to HIV which leads to paucibacillary rendering microbiological diagnosis less likely. Poor adherence to the chemotherapy as a consequence of inadequate community funding has contributed to the development of drug resistance. This further complicates the treatment of the resultant complex diseases forms such as Multidrug-resistant and Extensively drug resistant TB (require longer treatment duration and the multiple drugs with increased toxicity). Cost implications of these complex treatment regimens add to the economic burden of the already impoverished developing countries.

It is evident a long lasting solution is needed to TB. The correlation of the high prevalence rates of vitamin D deficiency with the soaring burden of TB as well as the beneficial effects of Vitamin D on TB clearance, vitamin D supplementation/ fortification should be sought in high TB regions as an adjuvant therapy and perhaps prophylactic treatment against TB. For speedy implementation, prudent studies are urgently needed to evaluate the use of vitamin D as prophylaxis and adjuvant treatment for TB in the subsaharan Africa.

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