



The Role of Vitamin D in Multidrug-Resistant Tuberculosis: Shedding Light on Potential Therapeutic Advancements

Zafar Iqbal¹, Mazhar Ali Khan^{2✉}

¹Pulmonology Department, Lady Reading Hospital, Peshawar-Pakistan ²Programmatic Management of Drug Resistant TB Unit, Lady Reading Hospital, Peshawar-Pakistan

Corresponding Author

Mazhar Ali Khan

Programmatic Management of drug Resistant TB Unit, Lady Reading Hospital, Peshawar-Pakistan
E-mail: mali_smile2005@yahoo.com

Article History

Received: Jan 24, 2023
Accepted: Feb 28, 2023
Available Online: Mar 02, 2023

Declaration of conflicting interests

The authors declare that there is no conflict to interest.

How to cite this editorial:

Iqbal Z, Khan MA. The Role of Vitamin D in Multidrug-Resistant Tuberculosis: Shedding Light on Potential Therapeutic Advancements, Pak J Chest Med 2023;29 (1): 01-3

Introduction

Multidrug-resistant tuberculosis (MDR-TB) remains a significant global health threat, with increasing incidence and limited treatment options. MDR-TB is characterized by resistance to the two most potent first-line anti-TB drugs, isoniazid and rifampicin. The emergence of MDR-TB has challenged the medical community, demanding innovative approaches to combat this formidable adversary.^{1,2} In recent years, researchers have turned their attention to the potential role of vitamin D as an adjunctive therapy for MDR-TB. This editorial explores the evolving evidence surrounding the role of vitamin D in MDR-TB treatment and its implications for the medical community.

Vitamin D, commonly known for its role in calcium homeostasis and bone health, is a potent immunomodulator. Its active form, calcitriol, interacts with the vitamin D receptor (VDR) expressed on various immune cells, including macrophages. Through this interaction, vitamin D regulates both innate and adaptive immunity, promoting antimicrobial defense mechanisms. Several studies have suggested that vitamin D deficiency might be associated with an increased risk of developing tuberculosis (TB) and potentially lead to poorer treatment outcomes, particularly in MDR-TB cases.

Vitamin D and TB: A Plethora of Evidence:

Over the past decade, numerous preclinical and clinical studies have explored the relationship between vitamin D and TB, particularly in the context of MDR-TB. In vitro studies have shown that vitamin D can enhance the antimicrobial capacity of macrophages by stimulating autophagy, promoting the fusion of phagosomes with lysosomes, and increasing the production of antimicrobial peptides like cathelicidin and defensins. These findings provide a compelling rationale for investigating the potential adjunctive role of vitamin D in MDR-TB treatment.³

Clinical studies examining the impact of vitamin D supplementation in TB patients, including those with MDR-TB, have yielded varying results. Some studies have reported favorable outcomes, such as reduced bacterial loads and shorter time to sputum conversion in MDR-TB patients supplemented with vitamin D. However, others have failed to demonstrate significant clinical benefits, leading to conflicting

interpretations and raising questions about the optimal dosing, duration, and patient selection.

The role of vitamin D in tuberculosis (TB) has been extensively studied, but the results have been somewhat conflicting. In recent years, several clinical trials have been conducted to investigate the use of vitamin D as an adjunctive treatment for TB. Some of these studies have reported that vitamin D has a significant positive effect, while others have found no significant results. A meta-analysis, for instance, found that vitamin D had no impact on the time it took for sputum cultures to convert to negative, although there was a positive influence observed in drug-resistant TB patients with regard to sputum culture conversion time.³ Observational studies conducted over the last 5 to 10 years have strongly suggested a relationship between profound vitamin D deficiency and susceptibility to TB, as well as an influence of vitamin D levels on sputum smear and culture conversion times.^{4,5} On the contrary, a systematic review conducted in 2018 did not support the idea that vitamin D supplementation had a significant effect on pulmonary TB patients. Despite the fact that vitamin D does possess antibacterial properties against *Mycobacterium* (the bacteria that causes TB), most clinical trials have yielded negative results after vitamin D supplementation.^{6,7} Another meta-analysis also reported similar findings, with no significant effect of vitamin D on sputum smear or sputum culture conversion times after supplementation. However, it did suggest that higher levels of vitamin D were associated with an increased proportion of sputum conversion.⁸

In the present issue, a study conducted by Basit et al. also suggested a strong association between vitamin D and the treatment outcome of multidrug-resistant TB (MDR-TB). This study aimed to determine the levels of vitamin D in MDR-TB patients compared to normal individuals in a control group. While the association was not found to be statistically significant, the results did indicate a potential connection between vitamin D levels and the occurrence of the disease.

In summary, the role of vitamin D in tuberculosis remains a topic of ongoing research, with some studies indicating a positive influence, especially in drug-resistant cases, while others have not found significant effects. Observational studies suggest a link between vitamin D deficiency and TB susceptibility, but the results from clinical trials have been mixed. Further research is needed to clarify the precise role of vitamin D in TB prevention and treatment.

Challenges and Considerations

While the potential benefits of vitamin D supplementation in MDR-TB are promising, several challenges and considerations must be addressed. Firstly, the optimal

dosing and duration of vitamin D supplementation need to be elucidated through well-designed clinical trials. Individual variations in vitamin D metabolism and genetic polymorphisms affecting VDR expression may also influence treatment responses.

Furthermore, we must emphasize that vitamin D supplementation should not replace standard anti-TB therapy but rather serve as an adjunctive therapy to enhance the immune response and possibly accelerate sputum conversion. The overall success of MDR-TB treatment requires a comprehensive approach that includes early and accurate diagnosis, appropriate drug regimens, infection control measures, and patient compliance.

Conclusion

The role of vitamin D in MDR-TB treatment remains an intriguing and evolving area of research. Although the evidence is promising, further well-designed clinical trials are warranted to determine the optimal dosing, duration, and patient selection criteria for vitamin D supplementation in MDR-TB cases. As the global health community continues to combat the challenges posed by MDR-TB, exploring innovative adjunctive therapies, such as vitamin D, is crucial in the pursuit of improved treatment outcomes. By shedding light on the potential role of vitamin D in MDR-TB, we take another step towards a brighter and healthier future for patients battling this relentless disease.

References

1. Iqbal Z, Khan MA, Aziz A, Nasir SM. Time for culture conversion and its associated factors in multidrug-resistant tuberculosis patients at a tertiary level hospital in Peshawar, Pakistan. *Pak J Med Sci.* 2022;38(4Part-II):1009.
2. Khan MA, Mehreen S, Basit A, Khan RA, Jan F, Ullah I, et al. Characteristics and treatment outcomes of patients with multi drug resistant tuberculosis at a tertiary care hospital in Peshawar, Pakistan. *Saudi Med J.* 2015;36(12):1463.
3. Martineau AR, Leandro AC, Anderson ST, Newton SM, Wilkinson KA, Nicol MP, et al. Association between Gc genotype and susceptibility to TB is dependent on vitamin D status. *Euro Resp J* 2010;35(5): 1106-12.
4. Jolliffe DA, Ganmaa D, Wejse C, Raqib R, Haq MA, Salahuddin N, et al. Adjunctive vitamin D in tuberculosis treatment: meta-analysis of individual participant data. *Euro Resp J* 2019;53(3).
5. Huang SJ, Wang XH, Liu ZD, Cao WL, Han Y, Ma AG, Xu SF. Vitamin D deficiency and the risk of

- tuberculosis: a meta-analysis. Drug design, development and therapy. 2016;91-102.
6. Junaid K, Rehman A, Jolliffe DA, Saeed T, Wood K, Martineau AR. Vitamin D deficiency associates with susceptibility to tuberculosis in Pakistan, but polymorphisms in VDR, DBP and CYP2R1 do not. BMC Pul Med. 2016;16(1):1-6.
 7. Wu HX, Xiong XF, Zhu M, Wei J, Zhuo KQ, Cheng DY. Effects of vitamin D supplementation on the outcomes of patients with pulmonary tuberculosis: a systematic review and meta-analysis. BMC Pul Med. 2018;18:1-2.
 8. Ji W, Malong F, Shidong Y, Jianfang Z, Xiaoqing LI. Efficacy and safety of vitamin D supplementation for pulmonary tuberculosis: a systematic review and meta-analysis. Iranian J Pub Health. 2018;47(4):466.