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RELATIONSHIP BETWEEN VITAMIN D SERUM [25(OH)D] AND MORBUS HANSEN: A SYSTEMATIC REVIEW

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Abstract

Morbus Hansen (MH) is a chronic granulomatous infection caused by Mycobacterium leprae, characterized by anesthesia, peripheral nerve thickening, and the presence of acid-fast bacilli (AFB) on bacteriological examination. Vitamin D is known to play an important immunomodulatory role in the immune response to mycobacterial infections. This study aims to review existing research on the relationship between serum levels of 25-hydroxyvitamin D [25(OH)D] and Morbus Hansen. A critical analysis was performed on scientific articles retrieved from PubMed, Google Scholar, and ScienceDirect databases, covering publications from the past 10 years that discussed vitamin D levels in patients with Morbus Hansen. Five articles meeting the inclusion criteria for this study. Serum vitamin D levels in Morbus Hansen patients were lower compared to healthy controls and showed a significant association with the clinical type of MH. Patients with the paucibacillary type had higher vitamin D levels than those with the multibacillary type. Vitamin D plays a role in the immune response against Mycobacterium leprae, and vitamin D deficiency may increase the risk and severity of the disease

Keywords: *Morbus Hansen, Vitamin D, 25(OH)D, Outcome*

INTRODUCTION

Hansen's disease (MH) or known as leprosy or leprosy , is disease infection granulomatous chronic leprosy caused by Mycobacterium leprae. The bacteria This attack skin, nerves edges and mucosa channel breathing above, with manifestation clinical in the form of anesthesia thickening nerve peripheral, as well as lesions skin that can accompanied by disability permanent . Based on classification clinical from *World Health Organization* (WHO), MH is distinguished become two type main, namely paucibacillary (PB) And multibacillary (MB) which is determined based on amount lesions skin and results index bacteria (IB) from inspection microscopic. Classification This important in determining therapy strategies and assessment disease progression.

Although globally the number case new tend decreased, MH still become problem health communities in developing countries. Indonesia occupies ranking third case leprosy the largest in the world after India and Brazil . Based on data from the Indonesian Ministry of Health (2023), the prevalence of leprosy in Indonesia reached 0.55 per 10,000 population, increasing compared to recorded in 2021 of 0.5 per 10,000 population. The high number case new show that transmission active Still happened, so that needed greater understanding deep about factors that influence progressiveness this disease.

Vitamin D has Lots proven play a role in journey a number of diseases , including MH. In addition functioning in metabolism calcium and mineralization bones, vitamin D is also

known own role important as immunomodulator. 25-hydroxyvitamin D [25(OH)D] is form the main vitamin D in circulation blood and used in a way wide as indicator of the body's vitamin D status . Although No active in a way directly, 25(OH)D plays a role as precursor for synthesis of 1,25-dihydroxyvitamin D [$1,25(OH)_2D_3$], form active vitamin D produced in the kidneys and tissues. Adequate levels of 25-hydroxyvitamin D [25(OH)D] play a role important in allows activation local vitamin D in various cell immune , including macrophages and T lymphocytes . Activation This contribute to various mechanism immunological, such as induction synthesis peptide antimicrobial like cathelicidin and β-defensin which play a role in defense immunity default, as well as arrangement response immune adaptive through modulation activity effector T cells and regulatory T cells . Therefore that is , optimal vitamin D status, as reflected from 25(OH)D levels , seen play a role important in support function immune For hinder replication bacteria and suppress disease progression. Review systematic aim For evaluate and synthesize evidence scientific related connection between 25(OH)D levels with Morbus Hansen.

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METHOD

Study This is studies review library systematic and purposeful For evaluate connection between serum 25(OH)D levels by type clinical and index bacteria in MH patients . Writing review systematic This based on PRISMA (*Preferred Reporting Items for Systematic reviews and Meta-Analyses*) guidelines are shown in Figure 1. Search literature done through three main databases, namely *PubMed , Google Scholar* , and *ScienceDirect* , with a range time publication 10 years last . Keywords used among others: *"vitamin D"* , *"25-hydroxyvitamin D"* , *"Hansen's Disease"* , *"leprosy"* , *"bacterial index"* , and *"immune response"* . The use of Boolean operators such as AND And OR implemented For expand results search criteria inclusion in review This is article study original containing results 25(OH)D levels in Hansen's Morbus patients , using method inspection valid laboratory , as well as report relationship with index bacteria . Articles in English English and Indonesian available in access full *(full text)* participate included . While that , article *review* , study animals , reports cases , and publications that are not relevant to the focus study issued from analysis . After stage filtering , articles that meet the requirements condition analyzed in a way qualitative For evaluate design research , characteristics sample , method vitamin D measurements , and results main reported related connection vitamin D levels in MH cases .

RESULT AND DISCUSSION

From the results search literature , a total of 127 relevant articles were obtained . After through the selection process based on title , abstract , and criteria inclusion-exclusion , as many as 5 articles study fulfil conditions and analyzed more carry on in review this . Most of studies use ELISA method for measure serum 25(OH)D levels , and involves patients with MH-PB and MH-MB classification based on WHO criteria . Serum 25(OH)D levels in patients with Hansen's Morbus (MH) are significant more low compared to the group control healthy . No there is correlation between 25(OH)D levels with bacteria index (BI). Vitamin D levels are related significantly with the MH type , where patients with this type paucibacillary (PB) has higher vitamin D levels tall compared to type multibacillary (MB). Vitamin D levels are also

higher high in patients men and at the age of 36–45 years . In addition That is , low vitamin D levels increase risk infected with MH significant . Research results shown in table 1.

Figure 1. PRISMA Method Flowchart

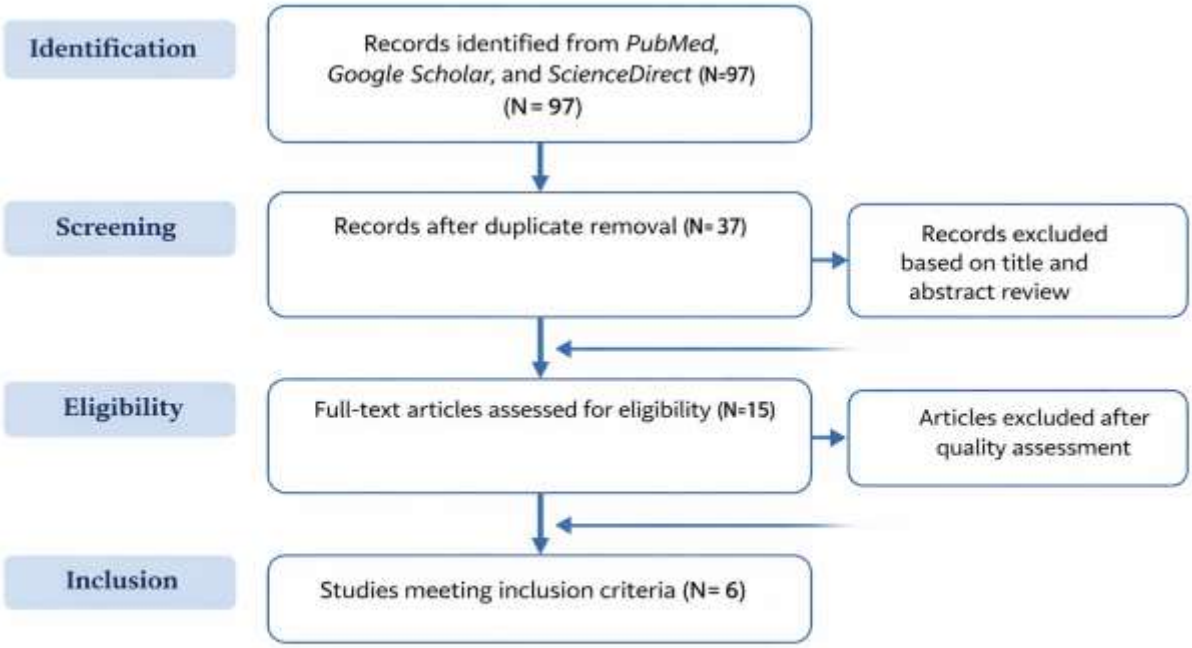

Table 1. Search Result Criteria Studies Literature

Researcher (year)	Type Study	Subject Study	Research result
Hilma et al., (2023) [5]	*Cross-sectional study*	28 MH patients	- The median serum 25(OH)D level was 12.68 ng/ mL. - No there is correlation between serum 25(OH)D and BI levels (r=0.033; p=0.869).
Theresia et al., (2021) [6]	Studies observational laboratory with design series case	33 MH patients - 22 PB people - 11 people MB	- There is significant relationship between 25(OH)D levels and patient MH type (OR = 9.643; p = 0.010). - There is correlation positive significant medium between 25(OH)D levels and MH type (r = 0.467; p = 0.006)
Garg et al., (2020) [7]	*Case control study*	- 60 MH patients (33 PB and 27 MB) - 28 control people	- Vitamin D levels in general significant more low in MH cases compared to the control group control healthy (P<0.05). - Case paucibacillary own significant vitamin D levels more high (P<0.05) compared multibacillary .
Darus et al., (2019) [8]	Studies observational analytics by design *cross-sectional*	- 20 patients case new MH - 20 control people	- Serum vitamin D levels in patients leprosy more low compared to controls (22.27 vs 33.00 ng/mL; p < 0.05). - Patient man own level more tall from women (23.69 vs 16.55 ng/mL), - Highest level found at the age of 36–45 years (25.31 ng/mL).
Rusyati , LMM et al. (2018) [9]	*Case control study*	50 MH patients - 25 PB people - 25 MH people	- There is difference significant serum vitamin D levels between PB type and MB type , where patients with PB type show higher levels high (p < 0.05). - Low serum vitamin D levels associated with increased risk infected with MH (OR = 12.667; CI 95%)

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Discussion

Mycobacterium leprae, the causative agent of leprosy, is an intracellular pathogen that primarily infects macrophages and Schwann cells. The immune response to M. leprae largely determines the clinical spectrum of the disease, ranging from tuberculoid (strong cellular immunity) to lepromatous (weak cellular immunity) forms. Host factors that regulate immunity, including micronutrients such as Vitamin D, play a crucial role in susceptibility, disease severity, and outcomes.

In the context of M. leprae, Vitamin D contributes to macrophage activation and enhances the killing of intracellular bacilli. Studies have shown that sufficient Vitamin D levels are associated with improved macrophage responsiveness, partly by promoting phagolysosomal fusion and restricting bacterial growth. Conversely, Vitamin D deficiency may impair these pathways, potentially predisposing individuals to lepromatous leprosy or more severe disease forms.

Vitamin D, beyond its classical role in calcium and bone homeostasis, has emerged as a significant immunomodulatory molecule. It influences both innate and adaptive immunity. Activated Vitamin D (1,25-dihydroxyvitamin D3) binds to the Vitamin D receptor (VDR) expressed in immune cells, leading to transcriptional changes that enhance antimicrobial pathways. This includes induction of antimicrobial peptides such as cathelicidin (LL-37) and defensins, which have direct activity against mycobacteria.

Vitamin D is one of the nutrition important that is not only play a role in regulations metabolism bones and calcium , but also has function key in modulation system immune. In system immune congenital, vitamin D plays a role in the process of differentiation monocytes become macrophages, cells very important phagocytes in defense body to infection. Activation macrophages influenced by vitamin D and its interaction with the vitamin D receptor (VDR), which is expressed in a way wide in various type cell immune, including CD4+ and CD8+ T cells, B cells , neutrophils , antigen presenting cells (APC), and dendritic cells.[4,9] This show that vitamin D affects response immune in a way comprehensive, both on the track immune default and adaptive.

In pathogenesis of Hansen's disease (MH) caused by bacteria *Mycobacterium leprae*, role macrophages are very important. The mechanism beginning invasion *Mycobacterium leprae* happen through activity immune congenital. Bacteria pathogen This phagocytosis by cells monocytes. After phagocytosis, bacteria develop breed in a way intracellular, which threatens cell host. However, the cells This have pathogen sensors such as TLR2/1 which increases expression CYP27B1 enzyme. The CYP27B1 enzyme converts form of vitamin D, namely converts 25(OH)D to 1,25(OH)$_2$D. Molecule active 1,25(OH) $_2$D Then binds to the vitamin D receptor (VDR) and induces antimicrobial protein expression like cathelicidin and defensin-2, which function as peptide antimicrobial (AMP).Vitamin D promotes production cathelicidin , an antibacterial protein , through activation by the CYP27B1 enzyme . The availability of 25(OH)D in serum greatly influences activity enzyme. In patients with this type paucibacillary (MH-PB), many dead bacteria or phagocytosed, while in this type multibacillary (MH-MB), only A little dead bacteria or happen phagolysosome formation.

Study show that serum 25(OH)D levels in patients leprosy in a way significant more low compared to the group healthy control. Decline vitamin D levels in patients , can indicates disturbance function potential immunity lower ability body in oppose infection. This is according to the findings that low vitamin D levels associated with risk more tall infected with Morbus Hansen This is support hypothesis that vitamin D deficiency is factor significant risk in development MH disease. In addition that, there is significant relationship between vitamin D levels by type clinical Hansen's Morbus. Patients with this type

paucibacillary (PB) has higher levels of vitamin D tall compared to type multibacillary (MB). This important Because MB type shows index more bacteria height and more disease heavy. Thus , higher levels of vitamin D low in MB type contributes to improvement severity disease and ability decreased macrophages in control bacteria . One of them study show difference vitamin D levels based on type gender and group age . Patient man own higher serum vitamin D levels tall compared to women. Difference This can influenced by hormonal factors, patterns live, and level exposure ray different sun between men and women. Age also plays a role, with the highest vitamin D levels found in the group age 36–45 years. Age This Possible is a time when activities physical and exposure ray sun more optimal than age carry on or young, so that better vitamin D levels.

Genetic variations in the Vitamin D receptor (VDR) have also been implicated in leprosy susceptibility. Certain VDR polymorphisms are linked to altered immune responses against M. leprae, affecting cytokine production and bacterial clearance. These findings highlight a complex interplay between host genetics, Vitamin D status, and pathogen virulence, shaping the clinical presentation of leprosy.

In a way overall, results study This confirm the importance of vitamin D in modulation immunity and its effects to Morbus Hansen's disease. Sufficient vitamin D levels can help increase response immune through improvement activity macrophages and expression peptide antimicrobial, so that lower burden bacteria and severity disease. Therefore that , monitoring vitamin D levels and potential vitamin D supplementation in patients leprosy worthy considered as part from management strategy disease this . Research more carry on required For understand mechanism more molecular deep as well as effectiveness vitamin D intervention in treatment leprosy. Besides that, other factors such as nutritional status , conditions health general , and exposure ray the sun is also necessary taken into account in studies advanced For get a clearer picture comprehensive.

CONCLUSION

In Finally, Vitamin D serves as an important immunomodulatory factor in host defense against M. leprae. Adequate Vitamin D levels enhance innate antimicrobial mechanisms, while deficiencies or genetic variations in its pathway may contribute to increased susceptibility and disease progression. This suggests that monitoring and correcting Vitamin D status in endemic populations could be a potential adjunct strategy in leprosy control and management, alongside established multidrug therapy.

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