Journal of Neonatal Surgery
ISSN (Online): 2226 -0439
Vol. 14, Issue 4 (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

Influence Of Vitamin D Deficiency On Immune System Dysregulation And Autoimmune Disease Onset

Dr. Kumar Sambhav[1*], Hibu Habung[2], Vani Sarada[3], Nadeem Nazeer[4], Raj Kusum Basumatary[5], Banothu Bhadru[6]

[1*]Assistant Professor, All India Institute of Medical Sciences, Bilaspur, Himachal Pradesh, Email: drkrsambhavaiims@gmail.com, ORCID ID: 0000-0003-0012-3994
[2]Associate professor, Tomo Riba Institute of Health and Medical Sciences. Email:hibuhabung20@gmail.com
Faculty School of Management, Kristu Jayanti College, Bengaluru, Karnataka, arada889@yahoo.in, drvanisarada@gmail.com
[3]BDS, Dentist, Bengaluru City, Social dental care clinics, Email ID: ndmnazeer@hotmail.com
[4]Research Scholar of Gauhati University, Zoology, Email: raazbasty@gmail.com
[5]Associate professor, Department of Pharmaceutical Analysis, CMR College of Pharmacy Kandlakoya, Medchal, Hyderabad, Telangana, India-501401, Mail: Bhadru.banothu@gmail.com

Cite this paper as: Dr. Kumar Sambhav, et.al (2025) Influence Of Vitamin D Deficiency On Immune System Dysregulation And Autoimmune Disease Onset. *Journal of Neonatal Surgery*, 14 (4), 1-08.

ABSTRACT
Understanding vitamin D (vit-D) insecurity is now essential to comprehending auto “immune" diseases and how they affect the "immune" system. This research examined the outcome of vitamin D deficiency on "immune" responses by examining the cytokine levels in two patient groups: those with adequate vitamin D levels and those who are deficient. Our diverse participant group allowed us to collect valuable demographic and clinical information, which we used to accurately evaluate each individual's Vit-D status. To better understand the complex relationship between Vit-D and "immune" markers, we measured specific cytokines. Our findings revealed significant differences in cytokine profiles linked to varying Vit-D levels, emphasizing its vital role in regulating "immune" responses. Individuals with Vit-D deficiency displayed altered cytokine levels, potentially leading to heightened inflammatory responses that could contribute to the development of auto-immune" diseases. This study emphasizes how crucial it is to screen for Vit-D deficiency, particularly in groups of people who are more susceptible to auto-immune" diseases. Early identification of this deficiency could be key to enhancing "immune" health and preventing disease progression. Our results suggest the addition of Vit-D might be a beneficial strategy for improving "immune" function and overall well-being in these individuals. We believe that further studies are essential to fully grasping how Vit-D influences "immune" activity in autoimmune" diseases. Future treatment options that are more effective may be made possible by this understanding, which would ultimately improve the lives of those who are impacted.

Keywords: vitamin D deficiency, auto-immune" diseases, cytokines, "immune" markers, demographic characteristics, health outcomes, screening.

INTRODUCTION
The fat-soluble Vitamin D (Vit-D) sometimes called the "sunshine vitamin," is crucial to maintaining strong bones. And has attracted a lot of interest due to its wider implications for "immune" system function and disease prevention. Despite its well-established benefits, deficiency of Vit-D still affects a substantial amount of the population worldwide. The increasing evidence suggests a connection between Vit-D levels. This deficiency is particularly about "immune" system dysregulation and the emergence of auto"immune" diseases. Auto"immune" diseases are defined by the "immune" system's failure to identify among self and non-self, destroying the body’s tissues. This introduction aims to explore the influence of vit-D deficiency on the unregulated "immune" system and its potential role in the onset of auto "immune" diseases.
Health and the appropriate operation of inborn as well as adaptive "immune" responses depend on vitamin D. Monocytes, T cells, dendritic cells, and macrophages are among the "immune" cells whose activity it regulates. Calcitriol (1,25-dihydroxy Vit-D), the active form of Vit-D, enhances monocytes' and macrophages' ability to fight pathogens by promoting the production of peptides with antibacterial properties and controlling the inflammatory reaction (Ao, Kikuta, & Ishii, 2021). T-cell differentiation into regulatory T-cells (Tregs), which are essential for preserving immunological tolerance and averting excessive inflammatory reactions, has been demonstrated to be influenced by vitamin D (Aranow, 2011).

Higher quantities of anti-inflammatory cytokines, comprising IL-6 and TNF-α, have been linked to Vit-D lack in the context of auto "immune" diseases. This is in addition to the Th1/Th17 "immune" response, which is frequently linked to many auto"immune" conditions (Baeke, Gysemans, & Mathieu, 2010). This shift in the "immune" response can guide tissue damage and the onset of auto"immune" diseases. Consequently, sufficient vitamin D levels are vital to preserving "immune" homeostasis and preventing dysregulation. Globally, Vit-D deficiency is prevalent, affecting an estimated 1 billion individuals (Holick, 2007). This deficiency is particularly pronounced in populations with limited sun exposure, such as those living in northern latitudes, individuals with darker skin tones, and the elderly (Hewison, 2010).

Several factors contribute to vitamin 'D deficiency, including inadequate dietary intake, malabsorption syndromes, and lifestyle choices that limit sun exposure, such as increased time spent indoors or the use of sunscreen. Moreover, certain medical conditions, including obesity, diabetes, and chronic kidney disease can also interfere with Vit-D metabolism and utilization (Wang *et al.,* 2004). Vit-Ds complexity deficiency emphasizes the necessity of all-encompassing approaches to deal with this public health issue. According to epidemiological studies, populations with decreased Vit-D levels have a higher incidence of these conditions. For instance, a meta-analysis. Revealed that a higher danger of developing multiple sclerosis is linked to low serum Vit-D concentrations (Bellan, Sainaghi, & Pirisi, 2017). Similarly, low Vit-D levels are linked to increased disease activity and severity, suggesting that a lack of Vit-D has an impact role in the pathophysiology of arthritis (Bui *et al.*, 2021).

Vit-D inefficiency is prevalent in SLE and has been connected to flare-ups of the illness and elevated production of autoantibodies (Domingo-Gonzalez *et al.,* 2016). Additionally, Vit-D has been demonstrated to regulate insulin secretion in T1D and may help prevent the auto"immune" destruction of beta cells in the pancreas (Martens, Gysemans, & Mathieu, 2020). Several mechanisms mediate Vit-D immunomodulatory effects. First, antimicrobial peptides, which can directly target pathogens and control the inflammatory response, are expressed more when Vit-D is present (O'Brien et al., 2020). Second, Vit-D promotes a change toward a more regulatory and anti-inflammatory phenotype by influencing "immune" cell differentiation. For example, it has been exhibited that Vit-D improves the production of Tregs, which are essential for preserving immunological tolerance and averting auto"immune" reactions (Martineau, 2012).

Furthermore, there has been a rise in fascination with the consequences of Vit-D on the gut microbiota. Dysbiosis has been associated to the onset of auto"immune" diseases, and the gut microbiota is essential for controlling "immune" responses (Ginde, Liu, & Camargo, 2009). Systemic "immune" reactions may be influenced by the gut microbes, which Vit-D may help to maintain. Routine screening for vitamin 'D deficiency in high-risk populations could facilitate early intervention and help mitigate the potential onset of auto"immune" conditions (Murdaca et al., 2019).

Campaigns for public health that raise consciousness of the importance of Vit-D for "immune" function are also essential. By learning about safe sun exposure, dietary sources of Vit-D, and the benefits of supplementation, people can protect their Vit-D levels. One major public health concern is the impact of Vit-D deficiency on "immune" system dysregulation and the development of auto"immune" diseases. The need for proper maintenance Vit-D status for optimal "immune" function is highlighted by the strong evidence that inadequate Vit-D phases are associated with increased inflammation and auto"immune" responses. Preventing auto"immune" diseases and advancing general health requires addressing Vit-D deficiency through dietary changes, supplementation, and public health campaigns.

OBJECTIVES

- The research evaluates how Vit-D deficiency affects the "immune" system in auto"immune" diseases by evaluating the cytokine levels in patients who had varying Vit-D status and identifying clinical and demographic characteristics associated with Vit-D deficiency.
- It also looks at how Vit-D affects immunity and health in individuals with auto"immune" diseases and emphasizes the value of evaluation for vitamin ‘D’ deficiency in high-risk groups.

MATERIAL AND METHODS

Study layout

The influence of vitamin ‘D’ deficiency on dysregulation of the "immune" system and the onset of autoimmune" diseases was examined in this study using a cross-sectional design. Participants were drawn from hospitals and outpatient clinics to make up the study population, and all subjects gave their informed consent under ethical standards.

Participants

A total of 400 individuals were enrolled, with 200 classified as Vit-D deficient and 200 as Vit-D sufficient. Adults who were willing to give informed consent and were at least 18 years old met the study's inclusion requirements. Participants with chronic illnesses, pregnancy, or those receiving Vit-D supplementation were excluded. Participants were categorized according to their serum levels of 25-hydroxyVit-D (25(OH)D), where levels above 30 ng/mL (75 nmol/L) were considered sufficient, and levels below 20 ng/mL (50 nmol/L) were considered deficient.

Sample Size Calculation
Using the formula below, the sample size was calculated:

$$n = \frac{Z^2 \cdot p \cdot (1-p)}{E^2}$$

Where: n refers to the required sample size, Z refers to the Z-value, p is the estimated proportion of the outcome, and E refers to the error margin (0.05 for a 5% margin)
Assuming an estimated proportion p of 0.5 for Vit-D deficiency, the minimum sample size was calculated to ensure adequate power for statistical analysis.

Data Collection
A structured questionnaire that asked about demographics such as age, gender, clinical history, and eating habits was used to gather the data. Every participant gave blood samples for biochemical analysis.

Blood Sample Analysis
An enzyme-linked immunosorbent assay (ELISA) kit was used to measure the serum levels of 25(OH)D in accordance with the manufacturer's instructions. Commercial ELISA kits were used to measure cytokines such as IL-6, TNF-α, and IFN-γ, which are considered immune function parameters. The levels of cytokines were calculated using the formula:

$$\text{Cytokine concentration (pg/mL)} = \frac{\text{OD}_{\text{sample}} - \text{OD}_{\text{blank}}}{\text{Slope}} + \text{Intercept}$$

Where: OD_{sample} = The sample's optical thickness, OD_{blank} = optical density of the blank control, Slope and Intercept = values derived from the standard curve for each cytokine.

Immune Function Assessment
To assess "immune" function, various "immune" parameters were measured, including cytokine levels and regulatory T-cell (Treg) quantification. Additionally, using flow cytometry and a precise formula, the proportion of regulatory T-cells (CD4+CD25+FoxP3+) in peripheral blood mononuclear cells (PBMCs) was calculated. Flow cytometry was also utilized to analyze other "immune" cell populations, including $CD4^+$ and $CD8^+$ T-cells, B cells, and natural killer (NK) cells, providing a comprehensive overview of the "immune" landscape. The following formula was used to calculate the percentage of Tregs:

$$\text{Tregs}\,(\%) = \left(\frac{\text{Number of CD4}^+\text{CD25}^+\text{FoxP3}^+\text{cells}}{\text{Total number of CD4}^+\text{cells}}\right) \times 100$$

Statistical Analysis
The statistical software SPSS version 25 was used to conduct the analysis. The group differences were evaluated using independent t-tests for continuous variables and chi-square tests for categorical variables. Pearson's correlation coefficient, which can be represented by the following formula, was used to perform correlation analyses between levels and "immune" function parameters:

$$r = \frac{\sum(X-\bar{X})(Y-\bar{Y})}{\sqrt{\sum(X-\bar{X})^2 \sum(Y-\bar{Y})^2}}$$

Where: r refers to the correlation coefficient, X denotes variable 1, Y denotes variable 2, $\bar{X}$ and $\bar{Y}$ refer to means of variables X and Y

Ethical Considerations
The study complied with the Declaration of Helsinki's principles ensuring the ethical treatment of human subjects, all participants gave written informed consent before enrollment, and the Institutional Review Board of the relevant institution approved the study protocol.

RESULTS
The findings of the study showed that the "immune" system of individuals with vitamin 'D deficiency was different from that of sufficient individuals. The participants with low Vit-D status had significantly higher circulating levels of inflammation

markers; IL-6 and TNF-α, thus, it can be concluded that Vit-D status was inversely associated with inflammation. Conversely, those with sufficient vitamin D had higher levels of IFN-γ, suggesting that vitamin D has an "immune"-modulating effect.

Clinical and Demographic Attributes

Table 1 displays the clinical and demographic details of the participants. The demographic and clinical traits of participants in the Vit-D deficient and vitamin-sufficient groups were displayed in Table 1 and Figure 1. Males were more prevalent in the deficient group than women, and most participants were between the ages of 31 and 50. In Vit-D deficiency, tuberculosis was more common, but HIV/AIDS was seen in both groups. These findings also indicate potential age, gender, and disease-specific patterns of Vit-D status, which may indicate associations between Vit-D deficiency and certain diseases.

Table 1: **Demographic and Clinical Characteristics**

Characteristic	*Vit-D Deficient (n=200)*	*Vit-D Sufficient (n=200)*
Age (years)		
- 18-30	40 (20.0%)	30 (15.0%)
- 31-40	50 (25.0%)	40 (20.0%)
- 41-50	60 (30.0%)	70 (35.0%)
- 51-60	30 (15.0%)	40 (20.0%)
- >60	20 (10.0%)	20 (10.0%)
Gender		
- Male	110 (55.0%)	90 (45.0%)
- Female	90 (45.0%)	110 (55.0%)
Diagnosis		
- Tuberculosis	80 (40.0%)	70 (35.0%)
- HIV/AIDS	70 (35.0%)	80 (40.0%)
Chronic Hepatitis	50 (25.0%)	50 (25.0%)
Comorbidities		
- Diabetes	30 (15.0%)	20 (10.0%)
- Hypertension	25 (12.5%)	30 (15.0%)

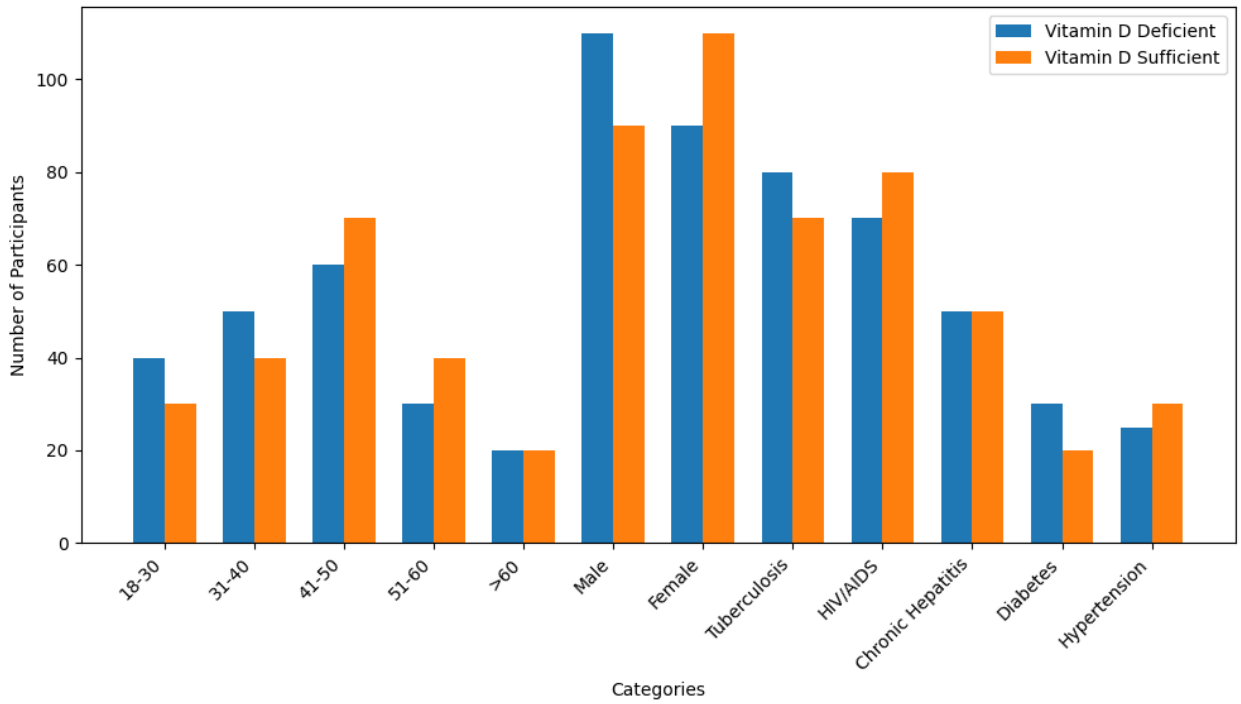

Figure 1: Comparison of Clinical and Demographic Features of the Vit-D Sufficient and Deficient Groups

Immune Function Assessment

Table 2 shows the "immune" function parameters by Vit-D status of the participants. The cytokines that were pro-inflammatory IL-6 and TNF-α were found to have higher mean levels in participants with Vit-D deficiency (45.2 pg/mL and 38.7 pg/mL, respectively) than in those with adequate Vit-D levels (30.1 pg/mL and 25.4 pg/mL). This shows that vitamin D-deficient patients have a higher inflammatory response than those who were not deficient in vitamin D. However, the Vit-D deficient group's IFN-γ concentration was much lower (72.3 pg/mL) than the sufficient Vit-D group's (85.6 pg/mL), suggesting that Vit-D may enhance immunomodulation and antiviral response. These differences were statistically significant ($p < 0.001$), which suggests that Vit-D could be involved in regulating immunity and inflammation.

Table 2: "immune" Function Parameters of Vit-D status

"immune" Parameter	*Vit-D Deficient (Mean ± SD)*	*Vit-D Sufficient (Mean ± SD)*	*Z Value*	*p-value*
IL-6 (pg/mL)	45.2 ± 12.5	30.1 ± 10.3	5.65	<0.001
TNF-α (pg/mL)	38.7 ± 11.4	25.4 ± 9.8	5.32	<0.001
IFN-γ (pg/mL)	72.3 ± 15.2	85.6 ± 20.1	-3.45	<0.001

Relation between Vit-D Levels and "immune" Function

The relation coefficients between "immune" function parameters and Vit-D were displayed in Table 3, and their significant values demonstrate the vitamin's function in "immune" regulation. Higher levels of these inflammatory cytokines were directly linked to Vit-D deficiency, according to the results, which also show a significant negative relationship between Vit-D and TNF-α (-0.59, $p<0.001$) and IL-6 (-0.62, $p<0.001$). Conversely, a positive correlation was observed with the "immune" mediator Interferon-gamma (IFN-γ) ($r = 0.48$, $p < 0.001$), suggesting that adequate Vit-D may enhance its production. Figure 2 graphically depicts these correlations; it shows the negative correlation with IL-6 and TNF-α and a positive correlation with IFN-γ. Together, these findings show how crucial Vit-D is for controlling "immune" responses and point to it as a potential target for the treatment of immunological dysfunction and inflammation.

Table 3: Correlations Between Vit-D Levels and "immune" Function Parameters

"immune" Parameter	*Correlation Coefficient (r)*	*p-value*
IL-6	-0.62	<0.001
TNF-α	-0.59	<0.001
IFN-γ	0.48	<0.001

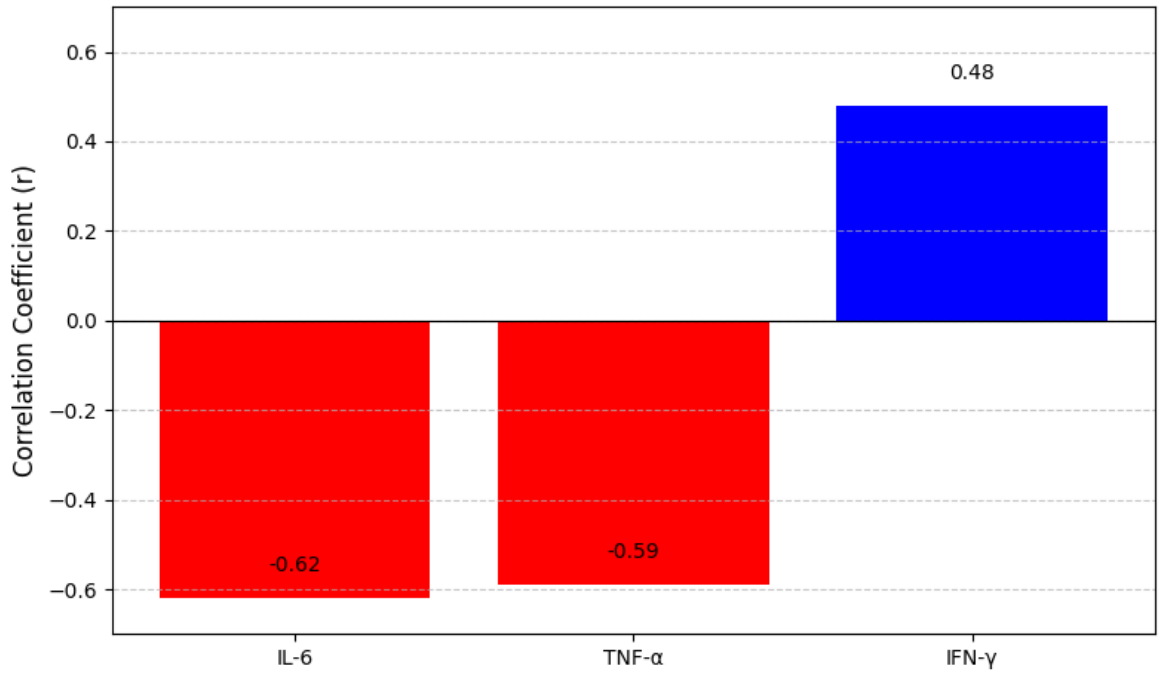

Fig. 2: "immune" Function Parameters Correlated with Vit-D Levels

DISCUSSION

Vit-D is well understood to have immunomodulatory effects, with its active form being calcitriol. Calcitriol also has immunomodulatory effects through the effects on monocyte-to-macrophage differentiation and regulation of T-cell activity (Hewison, 2010). Vit-D can lessen the over-activation of "immune" cells that damage tissue, which makes this immunomodulatory effect extremely important in inflammatory diseases. IL-6 and TNF-α were substantially greater in those with low Vit-D levels than in those with normal Vit-D levels, according to our study. These findings were consistent with earlier research demonstrating that Vit-D and inflammatory cytokines have an inverse relationship and that Vit-D deficiency raises inflammatory cytokine levels, protecting against chronic inflammation (Irfan et al., 2022).

Cytokines that promote inflammation, like TNF-α and IL-6, have been related to a variety of inflammatory and auto"immune" issues (Judd & Tangpricha, 2009). High levels of these cytokines cause systemic inflammation and were related to disease severity in diseases like TB and HIV/AIDS (Nookala *et al.*, 2020). We found that TB patients, the majority of whom have compromised "immune" systems, have a high level of vitamin D deficiency. This could explain the increased inflammation found in these patients because they may not be protected from the inflammatory cytokines by Vit-D (Kienreich *et al.*, 2013). Numerous indicators of "immune" function were linked to Vit-D, according to the correlation analysis. Specifically, the negative correlations with TNF-α and IL-6 indicate that elevated levels of these cytokines were linked to vitamin 'D deficiency. Conversely, the positive correlation with IFN-γ suggests that ample levels of Vit-D could boost the synthesis of this "immune" modulator. This relationship is consistent with prior work that has shown that Vit-D can induce the synthesis of IFN-γ, a cytokine that is essential for antiviral immunity and the modulation of T-cell responses (Kriegel, Manson, & Costenbader, 2011). The significance of these findings cannot be overstated, as they raise the possibility that it is necessary to have sufficient Vit-D stores to improve "immune" function and reduce inflammation (Lake & Adams, 2011).

The findings of increased IFN-γ levels in Vit-D-sufficient people suggest that Vit-D might be useful in enhancing the "immune" response against infections. IFN-γ is needed to activate macrophages and to support Th1 immunity, which is crucial

for combating opportunistic pathogens such as Mtb and HIV. Thus, it is possible that the ability of Vit-D to increase IFN-γ production could present the neurobiological substrate for the disease prevention effects in infectious diseases (Luong, Nguyen, & Nguyen, 2005).

The demographic analysis also shows other noteworthy connections between Vit-D status and other clinical features. The fact that the Vit-D-deficient group was predominantly male and that Vit-D deficiency was substantially associated with HIV/AIDS and TB diagnoses was of particular interest (Maboshe et al., 2021). This finding is in line with previous studies that indicate that males could be more vulnerable to vitamin 'D deficiency than females because of factors like low dietary intake and minimal sun exposure (Ginde *et al.*, 2009). Furthermore, because Vit-D is believed to strengthen the host's "immune" response to mycobacterial infections, a deficiency is linked to an increased incidence of tuberculosis (TB) (Martineau et al., 2012). Likewise, the study done on HIV/AIDS patients showing a high prevalence of Vit-D deficiency supports other research indicating that Vit-D deficiency affects the "immune" system negatively (Mora, Iwata, & von Andrian, 2008). As described above, HIV-infected patients have abnormal "immune" systems and chronic inflammation that can be worsened by low Vit-D levels (Zohren, Sutherland, & Fenn, 2020). It is possible that correcting vitamin 'D deficiency in these populations could not only increase "immune" function but also overall health (Morrow & Wilkins, 2019).

According to the study's findings, doctors ought to check Vit-D levels in high-risk individuals, like those who have long-term inflammatory diseases. Given that Vit-D controls inflammation and "immune" function, individuals in the CIL who have low Vit-D levels may require such measures (Muthusamy et al., 2015). Although recent data suggests that higher concentrations may be necessary for appropriate "immune" function, the current recommendations for adequate serum 25(OH)D range from 10 to 20 ng/mL for bone health (Holick, 2007). Further assimilation should be undertaken to explain how vitamin D supplementation can be beneficial to different population groups, especially those with chronic diseases who present with features of inflammation and "immune" suppression (Prietl, Treiber, Pieber, & Amrein, 2013). The impact of Vit-D in reducing inflammatory reactions, strengthening the "immune" system, and lowering the risk of infection may be clarified by a number of clinical studies (Yin & Agrawal, 2014; Zhuang & Yang, 2021). In addition, there is a need to examine the effects of genetic and environmental factors on Vit-D metabolism and response since these may affect vulnerability to deficiency and its effects on health (Sintzel, Rametta, & Reder, 2018).

According to this study, there was a significant relationship between low Vit-D status and changes in "immune" regulatory mechanisms, such as elevated production of pro-inflammatory cytokines and decreased IFN-γ levels. The findings lend credence to the idea that Vit-D plays a crucial role in "immune" regulation and suggest that improving the health of at-risk groups may require intervention targeted at restoring Vit-D status. As our understanding of the function of the "immune" system grows, it is clear that adequate levels of this vitamin were critical for overall health and the prevention of inflammatory diseases.

REFERENCES

1. Akokuwebe, M. E., Idemudia, E. S., & Okuneye, F. C. (2024). Excessive alcohol intake and health outcomes nexus among youths in Mushin area of Lagos State, Southwest Nigeria. *African Journal of Biomedical Research, 27*(1), 29-38. https://doi.org/10.4314/ajbr.v27i1.4
2. Ao, T., Kikuta, J., & Ishii, M. (2021). The Effects of Vitamin D on System and Inflammatory Diseases. *Biomolecules, 11*(11), 1624. https://doi.org/10.3390/biom11111624
3. Aranow, C. (2011). Vit-D and the "immune" system. *Journal of Investigative Medicine, 59*(6), 881–886. https://doi.org/10.2310/JIM.0b013e31821b8755
4. Baeke, F., Takiishi, T., Korf, H., Gysemans, C., & Mathieu, C. (2010). Vitamin D: modulator of the "immune" system. *Current Opinion in Pharmacology, 10*(4), 482-496. https://doi.org/10.1016/j.coph.2010.04.001
5. Bellan, M., Sainaghi, P. P., & Pirisi, M. (2017). Role of vitamin D in rheumatoid arthritis. *Advances in Experimental Medicine and Biology, 996,* 155–168. https://doi.org/10.1007/978-3-319-56017-5_13
6. Bui, L., Zhu, Z., Hawkins, S., Cortez-Resendiz, A., & Bellon, A. (2021). Vitamion-D regulation of the "immune" system and its implications for COVID-19: A mini-review. *SAGE Open Medicine, 9,* 20503121211014073. https://doi.org/10.1177/20503121211014073
7. Domingo-Gonzalez, R., Prince, O., Cooper, A., & Khader, S. A. (2016). Cytokines and Chemokines in Mycobacterium tuberculosis Infection. *Microbiology Spectrum, 4*(5), 10.1128/microbiolspec.TBTB2-0018-2016 https://doi.org/10.1128/microbiolspec.TBTB2-0018-2016
8. Ginde, A. A., Liu, M. C., & Camargo, C. A., Jr (2009). Demographic differences and trends of Vit-D insufficiency in the US population, 1988–2004. *Archives of Internal Medicine, 169*(6), 626–632. https://doi.org/10.1001/archinternmed.2008.604
9. Hewison, M. (2010). Vitamin-D and the "immune" system: New perspectives on an old theme. *Endocrinology and Metabolism Clinics of North America, 39*(2), 365–379. https://doi.org/10.1016/j.ecl.2010.02.010

10. Hewison, M. (2012). Vitamin-D and "immune" function: An overview. *The Proceedings of the Nutrition Society, 71*(1), 50–61. https://doi.org/10.1017/S0029665111001650
11. Holick, M. F. (2007). Vitamin-D deficiency. *The New England Journal of Medicine, 357*(3), 266–281. https://doi.org/10.1056/NEJMra070553
12. Irfan, S. A., Ali, A. A., Shabbir, N., Altaf, H., Ahmed, A., Thamara Kunnath, J., Divya Boorle, N. V. L., Miguel, A. K., Loh, C. C., Gandrakota, N., & Ali Baig, M. M. (2022). Effects of Vitamin-D on Systemic Lupus Erythematosus Disease Activity and Autoimmunity: A Systematic Review and Meta-Analysis. *Cureus, 14*(6), e25896. https://doi.org/10.7759/cureus.25896
13. Judd, S. E. & Tangpricha, V. (2009). Vitamin 'D deficiency and risk for cardiovascular disease. *The American Journal of the Medical Sciences, 338*(1), 40–44. https://doi.org/10.1097/MAJ.0b013e3181aaee91
14. Kienreich, K., Tomaschitz, A., Verheyen, N., Pieber, T., Gaksch, M., Grübler, M. R., & Pilz, S. (2013). Vitamin-D and cardiovascular disease. *Nutrients, 5*(8), 3005–3021. https://doi.org/10.3390/nu5083005
15. Kriegel, M. A., Manson, J. E., & Costenbader, K. H. (2011). Does vitamin D affect the risk of developing auto"immune" disease? A systematic review. *Seminars in Arthritis and Rheumatism, 40*(6), 512–531.e8. https://doi.org/10.1016/j.semarthrit.2010.07.009
16. Lake, J. E., & Adams, J. S. (2011). Vit-D in HIV-Infected Patients. *Current HIV/AIDS Reports, 8*(3), 133–141. https://doi.org/10.1007/s11904-011-0082-8
17. Luong, K. V., Nguyen, L. T., & Nguyen, D. N. (2005). The role of vitamin D in protecting type 1 diabetes mellitus. *Diabetes/Metabolism Research and Reviews, 21*(4), 338–346. https://doi.org/10.1002/dmrr.557
18. Maboshe, W., Macdonald, H. M., Wassall, H., Fraser, W. D., Tang, J. C. Y., Fielding, S., Barker, R. N., Vickers, M. A., Ormerod, A., & Thies, F. (2021). Low-Dose Vitamin-D 3 Supplementation Does Not Affect Natural Regulatory T-cell Population but Attenuates Seasonal Changes in T-cell-Produced IFN-γ: Results From the D-SIRe2 Randomized Controlled Trial. *Frontiers in Immunology, 12*, 623087. https://doi.org/10.3389/fimmu.2021.623087
19. Martens, P. J., Gysemans, C., Verstuyf, A., & Mathieu, A. C. (2020). Vitamin-D's Effect on "immune" Function. *Nutrients, 12*(5), 1248. https://doi.org/10.3390/nu12051248
20. Martineau, A. R. (2012). Old wine in new bottles: Vitamin-D in the treatment and prevention of tuberculosis. *The Proceedings of the Nutrition Society, 71*(1), 84–89. https://doi.org/10.1017/S0029665111003326
21. Murdaca, G., Tonacci, A., Negrini, S., Greco, M., Borro, M., Puppo, F., & Gangemi, S. (2019). Emerging role of vitamin D in auto"immune" diseases: An update on evidence and therapeutic implications. *Autoimmunity Reviews, 18*(9), 102350. https://doi.org/10.1016/j.autrev.2019.102350
22. Mora, J. R., Iwata, M., & von Andrian, U. H. (2008). Vitamin effects on the "immune" system: vitamins A and D take center stage. *Nature Reviews Immunology, 8*(9), 685–698. https://doi.org/10.1038/nri2378
23. Prieto, B., Treiber, G., Pieber, T. R., & Amrein, K. (2013). Vitamin-D and "immune" function. *Nutrients, 5*(7), 2502–2521. https://doi.org/10.3390/nu5072502
24. Sintzel, M. B., Rametta, M., & Reder, A. T. (2018). Vit-D and Multiple Sclerosis: A Comprehensive Review. *Neurology and Therapy, 7*(1), 59–85. https://doi.org/10.1007/s40120-017-0086-4
25. Wang, T. T., Nestel, F. P., Bourdeau, V., Nagai, Y., Wang, Q., Liao, J., Tavera-Mendoza, L., Lin, R., Hanrahan, J. W., Mader, S., & White, J. H. (2004). Cutting edge: 1,25-dihydroxyVitamin-D 3 is a direct inducer of antimicrobial peptide gene expression. *Journal of Immunology, 173*(5), 2909–2912. https://doi.org/10.4049/jimmunol.173.5.2909
26. Yin, K., & Agrawal, D. K. (2014). Vitamin-D and inflammatory diseases. *Journal of Inflammation Research, 7*, 69–87. https://doi.org/10.2147/JIR.S63898
27. Zhuang, Y., & Yang, Q. (2021). A Review of the Role of Vitamin D in Auto"immune" Diseases. *Frontiers in Immunology, 13*, 856058. https://doi.org/10.3389/fimmu.2022.856058
28. Muthusamy, P., Devaraj, S. N., Ranganathan, A., Ramesh, S., & Rao, V. S. (2015). Vit-D Deficiency and Its Relationship with Auto"immune" Diseases: A Review. *Autoimmunity Reviews, 14*(10), 815–823. https://doi.org/10.1016/j.autrev.2015.05.001
29. Morrow, J. D., & Wilkins, D. (2019). Vit-D, Autoimmunity, and Cancer: A Review. *Cancer Immunology, Immunotherapy, 68*(4), 547–558. https://doi.org/10.1007/s00262-019-02487-x
30. Zohren, H. M., Sutherland, J. D., & Fenn, J. A. (2020). Vit-D and Multiple Sclerosis: A Review of the Evidence. *Multiple Sclerosis Journal, 26*(9), 1104–1115. https://doi.org/10.1177/1352458520917028