Dijlah Journal of Medical Sciences (DJMS) Vol. 1, No. 3, May, 2025, pp. 77-83
P-ISSN: 3078-3178, E-ISSN: 3078-8625, paper ID: 10

Association of Vitamin D and IL-7 Levels in Severity of COVID-19

Inas Sattar Abd*
Al-Karkh University of Science, Baghdad, Iraq

Article Info

Article history:

Received November, 25, 2024
Revised January, 10, 2025
Accepted February, 28, 2025

Keywords:

Severity,
COVID-19,
IL-7,
Vitamin D

ABSTRACT

Association among Vitamin D and IL-7 levels in severity of COVID-19 has harvested attention due to their roles in immune response modulation. Understanding these relations may provide insights into potential therapeutic strategies for managing COVID-19. Vitamin D is critical for both innate and adaptive immune responses; augmenting function of immune cells for instance T cells and macrophages. It has anti-inflammatory effects, potentially reducing the severity of cytokine storms attendant with severe COVID-19. IL-7 is vital for T and B cell development and survival with increased levels perceived in severe COVID-19 cases .It supports in recovery of lymphocyte populations that may be depleted through viral infections.

Aim of study to investigate association of vitamin D and IL-7 in severity of COVID-19

Corresponding Author:

* Inas sattar Abd
Al-Karkh University of Science, Baghdad, Iraq
Inasabd4@gmail.com

INTRODUCTION

Vitamin D has imperative associations with adaptive and innate immune systems. Numerous mechanisms have been proposed for serotype distribution and pathway of SARS-CoV-2 virus (1,2).

One of these mechanisms was an effort to describe predilection of virus for vitamin D-deficient societies (3).

IL-7 is a member of secreted protein group that belongs to four-alpha-helices bundle cytokines. It is a master regulator of both tasks and activities of innate and adaptive immune systems (4,5).

Since IL-7 is a vital player in the immune system, particularly in both T and B cell machinery, theoretical work has just been published on regulation of IL-7R pathway in the treatment of COVID-19 conditions. (6,7).

Although these cytokines have been defined as significant markers and tools for understanding the SARS-CoV-2 reproductive mechanism in state of pandemic, mechanism of these cytokines in protection of COVID-19 is still not well defined (8,9).

Aim of study to investigate association of vitamin D and IL-7 in severity of COVID-19.

Background

Vitamin D is metabolized to active hormone calcitriol, whose receptor is found in multiple immune cells. Its main role is to reduce foreign pathogens through secretion of cytokines, and it has been revealed to have antiviral properties (10,11).

IL-7 is cytokine, which vital for T lymphocyte improvement and functions. It is opposed to vitamin D, and existence of one lessens presence of other. Both IL-7 and vitamin D do in tandem to retain a healthy immune system (12).
It is well known which a low concentration of IL-7 is related with a serious condition (13,14).

Vitamin D has anti-inflammatory and immunomodulatory characteristics. It is a main inducer of cathelicidin production in host cells, which limit pathogen invasion. Vitamin D causes an antiviral state by averting development of RANTES (15, 16).

Deficiency of vitamin D linked with higher occurrence of infections of the upper respiratory system, particularly those occurring during the wintertime. It has been linked to increased HIV susceptibility, concurrently lowering the antiretroviral treatment efficacy in the background of TB scourge (17, 18).

Several studies suggest which a copiousness of biological pathways, for instance pro-inflammatory chemokines and cytokines that triggered in an exaggerated manner in response to this coronavirus that extensively damages the tissue (19, 20).

The Role vitamin D in immunity

Vitamin D plays major immunological role in humans. It is an important immunomodulatory ingredient. Furthermore, it also has a vital function in activation of immune cells. Vitamin D is crucial for both innate and adaptive immune system (21, 22).

Vitamin D can affect activation and expression of T cells, but it also has an influence on additional immune cells like B cells, monocytes, and macrophage. Vitamin D deficiency makes persons much more predisposed to infections (23).

Primary receptor of vitamin D is on surface of macrophages, and vitamin D increases expression of cathelicidin and LL-37. Moreover, vitamin D increases expression of antimicrobial peptides and enhances autophagy. Clinical studies have exposed correspondence among vitamin D and respiratory infections (18).

Nevertheless, little information is accessible on link between vitamin D and coronaviruses. This is vital because coronaviruses mostly effect on respiratory system (24).

It is important to maintain therapeutic levels of vitamin D to suppress pro-inflammatory responses and thus prevent complications. Across the globe, vitamin D deficiency has become an alarming issue in numerous countries. In this context, vitamin D supplementation should be tested to avoid a cytokine storm, given increasing prevalence of COVID-19 in numerous countries (25, 26).

Vitamin D may improve recovery of COVID-19 patients. Vitamin D also affects cell signaling by p38, ERK, and c-Jun phosphorylation, which are nuclear targets, affecting the inflammatory pathway by producing cytokine suppressors (27. 28).

Vitamin D increases E-cadherin expression of lung epithelial integrity. In fact, in the lung, the NF-κB pathway further diminishes intercellular contact molecule-1. (29, 30).

It also forestalls transforming growth factor-β-increased E-cadherin repressors to tighten intercellular connections in lung epithelium, increasing IL-10 expression, which is a vital anti-inflammatory cytokine for surviving ARDS patients (13).

Vitamin D inhibits IL-6 that rises immune response and is called the cytokine storm in severe case of COVID-19 (31).

Role of IL-7 in Immunity

IL-7 is a cytokine vital for T and B cell improvement and survival in two main types: from bone marrow to thymus (B cells) and from thymus to peripheral blood and lymphoid tissues (T cells). (7, 16).

Increased IL-7 production may be a critical response of immune system to loss of lymphocytes. IL-7 helps T cells to survive and proliferate and is a survival factor for naïve and memory T cell populations. (7, 16, 17).

Under conditions of poor antigenic stimulation, such as in malignancy or chronic infections causing gradual exhaustion of the immune system, IL-7 leads to lymphocyte expansion. After the immune cells are depleted by any stress condition, for instance myeloablative chemotherapy or viral infection, IL-7 is an essential cytokine for driving T and probably B cells into cell division, which is exactly what the immune system needs to recover (7,32).

It has long been considered an immune-enhancing factor and a potential growth factor for immune suppression-related lymphopenia. It can preserve T cell homeostasis in severe immune suppression, particularly in patients. (33).

Autoimmune diseases are chronic, catabolic, debilitating, and often result in early mortality. IL-7 antagonism may prove beneficial for adequately reducing immune cell populations in autoimmune diseases where they contribute to disease pathogenesis and modify normal homeostatic balances. (34, 35).

Given that administration of IL-7 is related with T cell expansion, IL-7 may have a therapeutic effect in infectious diseases, protection against T cell deprivation, and may improve secondary response to bacterial and viral vaccination by increasing number of memory T cell populations by one or two orders of magnitude. (7, 34).

Furthermore, a spiraling expansion in T cell population in secondary response to infection will attract dendritic cells and B cells to produce more antibodies. (7)

The role of IL-7 in viral infections has been demonstrated mainly in study of infections. In context of infection, IL-7 levels found to parallel biomarkers commonly related with disease severity, for instance low absolute lymphocyte count. Moreover, patients with severe cases of disease have increased levels of cytokines and chemokines, including IL-7, compared with patients with mild cases (36).

COVID-19 Disease Severity

COVID-19 has a varied symptom variety from mild disease to severe pneumonia comprising hypoxia, respiratory distress and septic shock ,acute respiratory distress syndrome (ARDS), sepsis besides extra-pulmonary organ dysfunction that can development to death (37,38).

Infected patients may existing with mild clinical symptoms comprising: fever, fatigue and dry cough, or progress to more serious pulmonary complications, for instance interstitial pneumonia with progressive, severe respiratory distress (39).

Mortality attributable to COVID-19 also diverse between infected patients with hypertension, cardiovascular disease, diabetes, chronic respiratory system issues and liver disease. Moreover, male gender and advanced age in patients are more probable to result in severe COVID-19 (40,41).

Host immune responses play essential role in shaping outcomes of individuals with COVID-19 infections. These immune response comprise cellular immunity, humoral immunity and microbiota that influenced by environmental factors, comprising age, gender, comorbidities, genetic predispositions and metabolic and nutritional status of the host (42, 43).

Multisystem complications have also been recognized probably due to an extreme host inflammatory response so called “cytokine storm.” Levels of some of circulating cytokines with pro-inflammatory properties containing IL-1, IL-2, IL-6, IL-7, IL-8, IL-17 and type II interferons are able to reflect severity of COVID-19 that regulated by vitamin D (44,45).

Consequently, IL-6, IL-2, IL-1 and vitamin D are possible targets for intervention in COVID-19. Furthermore, dysregulation of ACE2, a functional receptor for S-protein of SARS-CoV-2 relates with severe disease (46, 47).

Besides, MERS-CoV likewise to SARS-CoV-2 has ability to induce inflammation resulting in accumulation of inflammatory cells and release of inflammatory cytokines. Dependably, in SARS-CoV-2-infected individual’s lungs, inflammatory cell infiltration, diffusion of exudate, and protein deposits in alveoli of left lung are noticeable by high-resolution computed tomography (48).

Systemic inflammation could reason for life threatening multiple organ impairment and coagulation system activation. Briefly, immune dysregulation associates with severe COVID-19 (49, 50).

CONCLUSION

The interaction between Vitamin D and IL-7 may affect COVID-19 severity, suggesting that further research could explore their therapeutic potential in managing the disease.

REFERENCES

[1] Roth, A., Lütke, S., Meinberger, D., Hermes, G., Sengle, G., Koch, et al. (2020). LL-37 fights SARS-CoV-2: The vitamin D-inducible peptide LL-37 inhibits binding of SARS-CoV-2 spike protein to its cellular receptor angiotensin-converting enzyme 2 in vitro. bioRxiv. https://doi.org/10.1101/2020.12

[2] Dong, W. (2021). Environmental and genetic factors affecting bone diseases and phenotypes in mouse models.

[3] Lélu, K., Dubois, C., Evlachev, A., Crausaz, M., Baldazza, M., Kehrer, N., et al. (2022). Viral delivery of IL-7 is a potent immunotherapy stimulating innate and adaptive immunity and confers survival in sepsis models. The Journal of Immunology, 209(1), 99–117. https://doi.org/10.4049/jimmunol.2100352

[4] Chen, D., Tang, T. X., Deng, H., Yang, X. P., & Tang, Z. H. (2021). Interleukin-7 biology and its effects on immune cells: Mediator of generation, differentiation, survival, and homeostasis. Frontiers in Immunology, 12, 747324. https://doi.org/10.3389/fimmu.2021.747324

[5] Que, Y., Hu, C., Wan, K., Hu, P., Wang, R., Luo, J., et al. (2022). Cytokine release syndrome in COVID-19: A major mechanism of morbidity and mortality. International Reviews of Immunology, 41(2), 217–230. https://doi.org/10.1080/08830185.2021.1943267

[6] Siddiqui, M., Manansala, J. S., Abdulrahman, H. A., Nasrallah, G. K., Smatti, M. K., Younes, N., et al. (2020). Immune modulatory effects of vitamin D on viral infections. Nutrients, 12(9), 2879. https://doi.org/10.3390/nu12092879

[7] Argano, C., Mallaci Bocchio, R., Lo Monaco, M., Scibetta, S., Natoli, G., Cavezzi, A., et al. (2022). An overview of systematic reviews of the role of vitamin D on inflammation in patients with diabetes and the potentiality of its application on diabetic patients with COVID-19. International Journal of Molecular Sciences, 23(5), 2873. https://doi.org/10.3390/ijms23052873

[8] Wang, G. L., Gao, H. X., Wang, Y. L., Wei, X., Liu, Y. Z., Lu, J. H., et al. (2021). Serum IP-10 and IL-7 levels are associated with disease severity of coronavirus disease 2019. Cytokine, 142, 155500. https://doi.org/10.1016/j.cyto.2020.155500

[9] Zhao, R., Zhang, W., Ma, C., Zhao, Y., Xiong, R., Wang, et al. (2021). Immunomodulatory function of vitamin D and its role in autoimmune thyroid disease. Frontiers in Immunology, 12, 574967. https://doi.org/10.3389/fimmu.2021.574967

[10] Oktaria, V., Danchin, M., Triasih, R., Soenarto, Y., Bines, J. E., Ponsonby, et al. (2021). The incidence of acute respiratory infection in Indonesian infants and association with vitamin D deficiency. PLoS ONE, 16(3), e0248722. https://doi.org/10.1371/journal.pone.0248722

[11] Zhou, Z., Ren, L., Zhang, L., Zhong, J., Xiao, Y., Jia, et al. (2020). Heightened innate immune responses in the respiratory tract of COVID-19 patients. Cell Host & Microbe, 27(6), 883–890. https://doi.org/10.1016/j.chom.2020.05.022

[12] Sîrbe, C., Rednic, S., Grama, A., & Pop, T. L. (2022). An update on the effects of vitamin D on the immune system and autoimmune diseases. International Journal of Molecular Sciences, 23(17), 9784. https://doi.org/10.3390/ijms23179784

[13] Ismailova, A., & White, J. H. (2022). Vitamin D, infections and immunity. Reviews in Endocrine and Metabolic Disorders. https://doi.org/10.1007/s11154-022-09720-8

[14] Jolliffe, D. A., Camargo, C. A., Sluyter, J. D., Aglipay, M., Aloia, J. F., Ganmaa, D., et al. (2021). Vitamin D supplementation to prevent acute respiratory infections: A systematic review and meta-analysis of aggregate data from randomised controlled trials. The Lancet Diabetes & Endocrinology, 9(5), 276–292. https://doi.org/10.1016/S2213-8587(21)00051-6

[15] Balla, M., Merugu, G. P., Konala, V. M., Sangani, V., Kondakindi, H., Pokal, M., et al. (2020). Back to basics: Review on vitamin D and respiratory viral infections including COVID-19. *Journal of Community Hospital Internal Medicine Perspectives, 10*(6), 529–536. https://doi.org/10.1080/20009666.2020.1840026

[16] El Hoss, K., Salla, M., Khaled, S., Krayem, M., Hassan, H., & El Khatib, S. (2023). Update on vitamin D deficiency and its impact on human health: Major challenges and technical approaches of food fortification. *Journal of Agriculture and Food Research, 12*, 100616. https://doi.org/10.1016/j.jafr.2023.100616

[17] Khalil, B., Sharif-Askari, N. S., Hafezi, S., Sharif-Askari, F. S., Al Anouti, F., Hamid, Q., & Halwani, R. (2024). Vitamin D regulates COVID-19-associated severity by suppressing the NLRP3 inflammasome pathway. *PLoS ONE, 19*(5), e0302818. https://doi.org/10.1371/journal.pone.0302818

[18] Gayan Ramirez, G., & Janssens, W. (2021). Vitamin D actions: The lung is a major target for vitamin D, FGF23, and Klotho. *Journal of Bone and Mineral Research Plus, 5*(12), e10569. https://doi.org/10.1002/jbm4.10569

[19] Fiorino, S., Gallo, C., Zippi, M., Sabbatani, S., Manfredi, R., Moretti, R., et al. (2020). Cytokine storm in aged people with CoV-2: Possible role of vitamins as therapy or preventive strategy. *Aging Clinical and Experimental Research, 32*, 2115–2131. https://doi.org/10.1007/s40520-020-01682-2

[20] Singh, M., Vaughn, C., Sasaninia, K., Yeh, C., Mehta, D., Khieran, I., & Venketaraman, V. (2020). Understanding the relationship between glutathione, TGF-β, and vitamin D in combating *Mycobacterium tuberculosis* infections. *Journal of Clinical Medicine, 9*(9), 2757. https://doi.org/10.3390/jcm9092757

[21] Barros, P. O., Berthoud, T. K., Aloufi, N., & Angel, J. B. (2021). Soluble IL-7Rα/sCD127 in health, disease, and its potential role as a therapeutic agent. *ImmunoTargets and Therapy, 10*, 47–62. https://doi.org/10.2147/ITT.S307796

[22] Coppola, C., Hopkins, B., Huhn, S., Du, Z., Huang, Z., & Kelly, W. J. (2020). Investigation of the impact of IL-2, IL-7, and IL-15 on the growth and signaling of activated CD4+ T cells. *International Journal of Molecular Sciences, 21*(21), 7814. https://doi.org/10.3390/ijms21217814

[23] Tsai, P. H., Lai, W. Y., Lin, Y. Y., Luo, Y. H., Lin, Y. T., Chen, H. K., et al. (2021). Clinical manifestation and disease progression in COVID-19 infection. *Journal of the Chinese Medical Association, 84*(1), 3–8. https://doi.org/10.1097/JCMA.0000000000000463

[24] Badraoui, R., Alrashedi, M. M., El-May, M. V., & Bardakci, F. (2021). Acute respiratory distress syndrome: A life-threatening associated complication of SARS-CoV-2 infection inducing COVID-19. *Journal of Biomolecular Structure and Dynamics, 39*(17), 6842–6851. https://doi.org/10.1080/07391102.2020.1791721

[25] Statsenko, Y., Al Zahmi, F., Habuza, T., Almansoori, T. M., Smetanina, D., Simiyu, G. L., et al. (2022). Impact of age and sex on COVID-19 severity assessed from radiologic and clinical findings. *Frontiers in Cellular and Infection Microbiology, 11*, 777070. https://doi.org/10.3389/fcimb.2021.777070

[26] Bajaj, V., Gadi, N., Spihlman, A. P., Wu, S. C., Choi, C. H., & Moulton, V. R. (2021). Aging, immunity, and COVID-19: How age influences the host immune response to coronavirus infections. *Frontiers in Physiology, 11*, 571416. https://doi.org/10.3389/fphys.2020.571416

[27] Kumar, S., Nyodu, R., Maurya, V. K., & Saxena, S. K. (2020). Host immune response and immunobiology of human SARS-CoV-2 infection. In S. K. Saxena (Ed.), *Coronavirus Disease 2019 (COVID-19): Epidemiology, Pathogenesis, Diagnosis, and Therapeutics* (pp. 43–53). Springer. https://doi.org/10.1007/978-981-15-4814-7_5

[28] Balzanelli, M. G., Distratis, P., Lazzaro, R., Cefalo, A., Catucci, O., Aityan, S. K., et al. (2021). The vitamin D, IL-6, and eGFR markers: A possible way to elucidate the lung–heart–kidney cross-talk in COVID-19 disease: A foregone conclusion. *Microorganisms, 9*(9), 1903. https://doi.org/10.3390/microorganisms9091903

[29] Conti, P., Caraffa, A., Gallenga, C. E., Ross, R., Kritas, S. K., & Frydas, I. (2020). Coronavirus-19 (SARS-CoV-2) induces acute severe lung inflammation via IL-1 causing cytokine storm in COVID-19: A promising inhibitory strategy. *Journal of Biological Regulators and Homeostatic Agents, 34*(6), 1971–1975. https://doi.org/10.23812/20-2EDIT_1-5

[30] Giamarellos-Bourboulis, E. J., Netea, M. G., Rovina, N., Akinosoglou, K., Antoniadou, A., Antonakos, N., et al. (2020). Complex immune dysregulation in COVID-19 patients with severe respiratory failure. *Cell Host & Microbe, 27*(6), 992–1000. https://doi.org/10.1016/j.chom.2020.04.009

Dijlah Journal of Medical Sciences (DJMS) Vol. 1, No. 3, May, 2025, pp. 77-83
P-ISSN: 3078-3178, E-ISSN: 3078-8625, paper ID: 10

العلاقة بين مستويات فيتامين د وإنترلوكين -٧ في شدة كوفيد - ١٩

الخلاصة

لقد حظي الارتباط بين مستويات فيتامين د وإنترلوكين - 7 في شدة فيروس كورونا (COVID-19) بالاهتمام بسبب دورهما في تعديل الاستجابة المناعية. وقد يوفر فهم هذه العلاقات نظرة ثاقبة للاستراتيجيات العلاجية المحتملة لإدارة كوفيد – 19.

فيتامين -د أمر بالغ الأهمية لكل من الاستجابات المناعية الفطرية والتكيفية؛ زيادة وظيفة الخلايا المناعية على سبيل المثال الخلايا التائية والبلاعم. وله تأثيرات مضادة للالتهابات، مما قد يقلل من شدة عواصف السيتوكين المصاحبة لحالات كوفيد - 19 الشديدة. يعد إنترلوكين - 7 أمراً حيوياً لنمو الخلايا التائية والبائية والبقاء على قيد الحياة مع زيادة مستوياته في حالات كوفيد - 19 الشديدة. وهو يدعم تعافي مجموعات الخلايا الليمفاوية التي قد يتم استنفاده منها خلال الالتهابات الفيروسية.

الهدف من الدراسة هو دراسة العلاقة بين فيتامين د وإنترلوكين - 7 في شدة الإصابة بكوفيد – 19.