Regarding the presentation - Influence of Vitamin-D on Covid-19

First of all, Dr. Joji Abraham is a Scientist with two Master's degrees and a Ph.D. from the Federation University Australia, plus around 20 years of international research and consulting experience, including with the United Nations.

According to him

There are several published evidence linking vitamin D status and Acute respiratory tract infections and acute respiratory distress syndrome (ARDS), which are the main cause of death in Covid-19 patients.

It is reported that SARS-CoV-2 binds to angiotensin converting enzyme 2 (ACE2) receptors in the respiratory tracts of infected patients to enter the host cells. At the early stages of the infection, protective immune response is necessary for eliminating the virus and, therefore, strategies to improve immune responses are of significance. As disease progresses, lung inflammation and fibrosis occur due to the release of pro-inflammatory cytokines, namely interleukin (IL)-1B and IL-18 by activated macrophages and type 1 T helper (Th1) immune cells. Older patients and those that are immunocompromised are at the higher risk category. Unfortunately, current knowledge gap on human immune response to SARS-CoV-2 is a critical barrier for treating the disease; however, potential immunomodulators may help alleviate severity and improve outcomes. Here is the role of Vitamin-D

Vitamin-D is a prohormone synthesised in the human body when UV-B radiation from the solar rays falls on the skin. Vitamin-D is modulating the functioning of the immune system by stimulating macrophages and dendritic cells. It is proven that Vitamin-D is required for the maturation of immune cells, those have the vitamin-D receptors, including B cells, T cells, macrophages, and dendritic cells. It is also clinically proven that Vitamin-D has a particular role in inhibiting the cytokine inflammatory response. Inducing cathelicidins and defensins can lower the viral replications rates and can reduce the concentration of pro-inflammatory cytokines that injure the lining of the lungs leading to ARDS and can increase the concentrations of anti-inflammatory cytokines. Evidence supporting the role of Vitamin-D include:

- Outbreak became severe in countries (Europe, USA, Iran, Turkey) where there were winter, where Vitamin-D level (25(OH)D) was lower
- The number of cases in the southern hemisphere was low – near the end of summer with high hydroxy vitamin D levels
- More than 70% of death in USA is people with Asian/African origin as their vitamin-D levels are very low in winter
- Low population mortality from COVID-19 in countries south of latitude 35 °N supports vitamin D as a factor determining severity

Vitamin-D can reduce T helper cell inflammation, tumor necrosis factor $\dot{\alpha}$ and interferon-γ

Recently a significant correlation has been observed between low serum vitamin-D levels and Covid-19 mortality (specifically related to latitude).

European countries highlighted low serum vitamin-D levels corresponds with high mortality rate and high levels of vitamin-D with low mortality rate with the p-value 0.046 (>95.4% CI)

Recently Irish Medical Journal also highlighted that – optimising Vitamin-D status certainly have high potential benefits from Covid-19

Recently French National Academy of Science highlighted the significance of Vitamin-d among Covid-19 patients

The physicians from the Asian countries, who working in UK recently highlighted their concern regarding the Vitamin-D and asked the members to test Vitamin-D and keep it normal

Innate arm of the immunity is handling the virus around 7 to 10 days until adaptive immunity takes charge and it is found that in the deficiency of vitamin-D, the innate arm can't work properly, which causes the increase in viral load and cytokine storms and hospitalisation.

Vitamin-D levels and C reactive protein (CRP) correlate, in the sense, CRP can act as a representative for Vitamin-D. Recently CRP has been assessed from the hospitalised patients and found a strong correlation between reduced vitamin-D levels and increased risk of mortality. Recently Dhanasekhara and Agarwal (2020) analysed the possible role of Vitamin-D in suppressing the cytokine storms and associated mortality among Covid-19 patients using CRP as a representative of Vitamin-D

I requested you to kindly refer the following scientific articles to get deep into the subject. Including the ABC Radio podcast below

https://www.abc.net.au/radionational/programs/healthreport/is-there-a-link-between-vitamin-d-and-coronavirus/12566324

References

Merzon, E., Tworowski, D., Gorohovski, A., Vinker, S., Golan Cohen, A., Green, I., & Frenkel Morgenstern, M. (2020). Low plasma 25 (OH) vitamin D level is associated with increased risk of COVID-19 infection: an Israeli population-based study. *The FEBS journal*.

Bergman, P. (2020). The link between Vitamin D and Covid-19: distinguishing facts from fiction. *Journal of internal medicine*.

Martineau, A. R., & Forouhi, N. G. (2020). Vitamin D for COVID-19: a case to answer?. *The Lancet. Diabetes & Endocrinology*.

Panagiotou, G., Tee, S. A., Ihsan, Y., Athar, W., Marchitelli, G., Kelly, D., ... & Burns, G. (2020). Low serum 25-hydroxyvitamin D (25 [OH] D) levels in patients hospitalised with COVID-19 are associated with greater disease severity. *Clinical endocrinology*.

Grant, W. B., Lahore, H., McDonnell, S. L., Baggerly, C. A., French, C. B., Aliano, J. L., & Bhattoa, H. P. (2020). Evidence that vitamin D supplementation could reduce risk of influenza and COVID-19 infections and deaths. *Nutrients*, *12*(4), 988.

Lanham-New, S. A., Webb, A. R., Cashman, K. D., Buttriss, J. L., Fallowfield, J. L., Masud, T., ... & Ward, K. A. (2020). Vitamin D and SARS-CoV-2 virus/COVID-19 disease. *BMJ Nutrition, Prevention & Health*.

Mitchell, F. (2020). Vitamin-D and COVID-19: do deficient risk a poorer outcome?. *The Lancet. Diabetes & Endocrinology*.

Rhodes, J. M., Subramanian, S., Laird, E., Griffin, G., & Kenny, R. A. (2020). Perspective: Vitamin D deficiency and COVID-19 severity–plausibly linked by latitude, ethnicity, impacts on cytokines, ACE2, and thrombosis (R1). *Journal of internal medicine*.

Panfili, F. M., Roversi, M., D'Argenio, P., Rossi, P., Cappa, M., & Fintini, D. (2020). Possible role of vitamin D in Covid-19 infection in pediatric population. *Journal of Endocrinological Investigation*, 1-9.

McCartney, D. M., & Byrne, D. G. (2020). Optimisation of vitamin D status for enhanced Immuno-protection against Covid-19. *Ir Med J*, *113*(4), 58.

Laird, E., Rhodes, J., & Kenny, R. A. (2020). Vitamin D and inflammation: potential implications for severity of COVID-19. *Irish med J*, *113*(5), P81.

Rhodes, J. M., Subramanian, S., Laird, E., & Kenny, R. A. (2020). low population mortality from COVID-19 in countries south of latitude 35 degrees North supports vitamin D as a factor determining severity. *Alimentary pharmacology & therapeutics*, *51*(12), 1434-1437.

Silberstein, M. (2020). Vitamin D: A simpler alternative to tocilizumab for trial in COVID-19?. *Medical Hypotheses*, 109767.

Carter, S. J., Baranauskas, M. N., & Fly, A. D. (2020). Considerations for Obesity, Vitamin D, and Physical Activity Amid the COVID-19 Pandemic. *Obesity*.

Lau, F. H., Majumder, R., Torabi, R., Saeg, F., Hoffman, R., Cirillo, J. D., & Greiffenstein, P. (2020). Vitamin D insufficiency is prevalent in severe COVID-19. *medRxiv*.

Kow, C. S., Hadi, M. A., & Hasan, S. S. (2020). Vitamin D Supplementation in Influenza and COVID-19 Infections Comment on:"Evidence that Vitamin D Supplementation Could Reduce Risk of Influenza and COVID-19 Infections and Deaths" Nutrients 2020, 12 (4), 988. *Nutrients*, *12*(6), 1626.

Ebadi, M., & Montano-Loza, A. J. (2020). Perspective: improving vitamin D status in the management of COVID-19. *European Journal of Clinical Nutrition*, 1-4.

Panarese, A., & Shahini, E. (2020). Covid-19, and vitamin D. *Alimentary Pharmacology & Therapeutics*, *51*(10), 993.

Arboleda, J. F., & Urcuqui-Inchima, S. (2020). Vitamin D Supplementation: A Potential Approach for Coronavirus/COVID-19 Therapeutics?. *Frontiers in Immunology*, *11*.

Bertoldi, G., Gianesello, L., & Calò, L. A. (2020). ACE2, Rho kinase inhibition and the potential role of vitamin D against COVID-19. *Alimentary Pharmacology & Therapeutics*, *52*(3), 577.

Muscogiuri, G., Barrea, L., Savastano, S., & Colao, A. (2020). Nutritional recommendations for CoVID-19 quarantine. *European Journal of Clinical Nutrition*, 1-2.

Molloy, E. J., & Murphy, N. (2020). Vitamin D, Covid-19 and Children. *Ir. Med. J*, *113*, 64.

Kara, M., Ekiz, T., Ricci, V., Kara, Ö., Chang, K. V., & Özçakar, L. (2020). 'Scientific Strabismus' or Two Related Pandemics: COVID-19 & Vitamin D Deficiency. *British Journal of Nutrition*, 1-20.

Jakovac, H. (2020). COVID-19 and vitamin D—Is there a link and an opportunity for intervention?. *American Journal of Physiology-Endocrinology and Metabolism*, *318*(5), E589-E589.

Ilie, P. C., Stefanescu, S., & Smith, L. (2020). The role of vitamin D in the prevention of coronavirus disease 2019 infection and mortality. *Aging Clinical and Experimental Research*, 1-4.

Kumar, D., Gupta, P., & Banerjee, D. (2020). does vitamin D have a potential role against COVID-19?. *Alimentary Pharmacology & Therapeutics*.

Zwart, S. R., & Smith, S. M. (2020). Vitamin D and COVID-19: Lessons from Spaceflight Analogs. *The Journal of Nutrition*.

Grant, W. B., Lahore, H., McDonnell, S. L., Baggerly, C. A., French, C. B., Aliano, J. L., & Bhattoa, H. P. (2020). Vitamin D supplementation could prevent and treat influenza, coronavirus, and pneumonia infections.

Torjesen, I. (2020). Covid-19: Public health agencies review whether vitamin D supplements could reduce risk.

Whittemore, P. B. (2020). COVID-19 fatalities, latitude, sunlight, and vitamin D. *American Journal of Infection Control*.

Braiman, M. (2020). Latitude Dependence of the COVID-19 Mortality Rate—A Possible Relationship to Vitamin D Deficiency?. *Available at SSRN 3561958*.

Hadizadeh, F. (2020). Supplementation with vitamin D in the COVID-19 pandemic?. *Nutrition Reviews*.

Trovas, G., Tournis, S. Vitamin D and COVID-19. *Hormones* (2020). https://doi.org/10.1007/s42000-020-00231-9