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Vitamin D Deficiency and ARDS after SARS-CoV-2 Infection

J.L. Faul[1], C.P. Kerley[1], B. Love[2], E. O'Neill[3], C. Cody[4], W. Tormey[5], K. Hutchinson[6], L.J. Cormican[1], C.M. Burke[1]

1. Asthma Research Centre, James Connolly Memorial Asthma Research Centre, Connolly Hospital Blanchardstown, Ireland.
2. Department of Pharmacy, Connolly Hospital Blanchardstown, Ireland.
3. Department of Microbiology, Connolly Hospital Blanchardstown and Department of Clinical Microbiology, Royal College of Surgeons in Ireland.
4. Department of Intensive Care Medicine, Connolly Hospital Blanchardstown, Ireland.
5. Department of Clinical Chemistry, Connolly Hospital Blanchardstown, Ireland.
6. Eurofins-Biomnis Limited, Sandyford, Dublin, Ireland.

In Response to Article Entitled 'Optimisation of Vitamin D Status for Enhanced Immuno-Protection against Covid-19' by D.M McCartney et al - Ir Med J; Vol 113; No. 4; P58

Dear Sir,

Male gender, age over 40 years, cancer, diabetes mellitus, and chronic respiratory and cardiovascular disease have each been associated with increased severity of disease, including ARDS, after SARS-CoV-2 infection.[1,2] We hypothesize that nutrition might also play a role. Vitamin D (25OHD) deficiency has previously been linked to a greater susceptibility to viral infection, ARDS, and pneumonia.[3,4] Since 25OHD deficiency is both highly prevalent and easily treatable and the morbidity, mortality, and costs of SARS-CoV-2 related ARDS are great, we wanted to explore whether 25OHD levels might be associated with an increased risk of the development of ARDS due to SARS-CoV-2.

Following institutional review board approval and informed consent from participants, we analyzed serum 25OHD levels in 33 adult, male, Caucasian patients, over the age of 40 years, who were admitted to Connolly Hospital Blanchardstown for SARS-CoV-2 related pneumonia (four quadrant infiltrates on chest radiograph, with respiratory failure requiring FiO_2 greater than 0.4, with SARS-CoV-2 detectable by RT-PCR of nasopharyngeal swab) during March 2020. None had cancer, diabetes mellitus, cardiovascular disease, or had received chronic immunosuppressive therapy. Twelve progressed to ARDS and required intubation and mechanical ventilation. There were four deaths after mechanical ventilation (at days 3, 6, 7, and 15) in the ARDS group and none in the non-ARDS group. Overall, the twelve patients who progressed to ARDS (mean age 60 years, SD 15) had a lower serum 25OHD level on presentation to hospital (*mean* = 27, *SD* = 12 $nmol.l^{-1}$), compared to the twenty one patients hospitalized with less severe pneumonia who did not progress to ARDS (mean age 56 years, SD 14). Their 25OHD level was 41 $nmol.l^{-1}$ (*SD* 19) ($p = 0.03$).

Vitamin D (25OHD) deficiency is highly prevalent in Ireland, a country with low levels of sunlight. Using our measures of 25OHD levels from 5374 Irish males aged between 40 and 60 years, the median is 47 $nmol.l^{-1}$, with 31 and 65 $nmol.l^{-1}$ representing the 25th and 75th centiles, respectively. We took a cutoff of 30 $nmol.l^{-1}$, or less, as being very likely to have Vitamin D deficiency. In this cohort of thirty three patients, twelve had a baseline 25OHD level less than 30 $nmol.l^{-1}$. In patients with SARS-CoV-2 related pneumonia a baseline serum 25OHD level less than 30 $nmol.l^{-1}$ was associated with a hazard ratio (HR) for intubation of 3.19 (95 percent confidence interval, 1.05 to 9.7), ($p = 0.03$).

A plausible interpretation of these early findings is that poor nutrition and/or lack of sun exposure, heralded by a low 25OHD level, contributes to severe disease and progression to ARDS in some patients infected with SARS-CoV-2. Alternatively, 25OHD deficiency itself allows pro-inflammatory changes that trigger the development of ARDS in some patients with severe SARS-CoV-2 pneumonia [4,5]: a thought worthy of further study.

Corresponding Author:
Professor John L. Faul MD FCCP,
Connolly Hospital Blanchardstown,
Dublin 15,
Ireland.
Email: doctorfaul@gmail.com

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