D.2.1.7 Macaya 2020

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Bibliographic Reference	Macaya, Fernando; Espejo Paeres, Carolina; Valls, Adrian; Fernandez-Ortiz, Antonio; Gonzalez Del Castillo, Juan; Martin-Sanchez, F Javier; Runkle, Isabelle; Rubio Herrera, Miguel Angel; Interaction between age and vitamin D deficiency in severe COVID-19 infection.; Nutricion hospitalaria; 2020; vol. 37 (no. 5); 1039-1042

Study details

Study design	Case series
Trial registration (if reported)	Not reported.
Aim of the study	The aim of this study was to explore the association between vitamin D deficiency and the development of severe COVID-19.
County/ Geographical location	Madrid, Spain.
Study setting	Emergency department of a tertiary hospital.
Population description	A cohort of consecutive patients admitted with COVID-19 between 3rd March and 31st March 2020.
Inclusion criteria	1) a positive reverse-transcriptase polymerase chain reaction for SARS-CoV-2, and 2) an available measurement of serum 25-hydroxyvitamin D (25(OH)D) (chemiluminescent immunoassay, Abbott Diagnostics) at admission or within the 3 previous months.
Exclusion criteria	None reported.
Vitamin D status measurements	Described in the inclusion criteria.
Methods used to confirm COVID-19 infection	Described in the inclusion criteria.
Intervention	Not applicable.
Comparator (where applicable)	Not applicable.
Methods for population selection/allocation	Described above.

Methods for case-matching with control	Not applicable.
Methods of data analysis	For continuous variables, a univariate analysis with a t-test or rank-sum test was conducted. For categorical variables, a chi-square test or Fisher's exact test was used. The association between the composite COVID-19 outcome (death, admission to the intensive care unit, and/or need for higher oxygen flow than provided by a nasal cannula) and 25(OH)D level was conducted by multivariable logistic regression adjusting for obesity, sex, age and advanced kidney disease. Age group-specific analyses defined by percentile 50, were conducted. All analyses were conducted using Stata 13.
Attrition/loss to follow-up	11/91 had not completed follow-up by the time statistical analyses were conducted. The study did not explain how it dealt with attrition, but based on the percentages, it appears they only includes people who completed follow-up (n=80).
Source of funding	The Fundación interhospitalaria para la Investigación Cardiovascular covered the publication charge for this study.
Study limitations (Author)	Small sample size. More likely to have vitamin D measurements for the elderly, in patients with comorbidities, renal disease and obesity.
Study limitations (reviewer)	Retrospective study. Did not account for attrition statistically, only excluded participants from all analyses. Did not describe how many vitamin D measurements were up to 3 months old or taken on admission. As patients were admitted in March, measurements from 3 months previously would have been taken in mid-winter where vitamin D levels are lower. There could be differences in the clinical decisions made before hospitalisation and ICU admission due to this study not being in the UK and changes over the course of the pandemic

Study arms

Non-severe COVID-19 (N = 49)
Severe COVID-19 (N = 31) Defined by the composite endpoint: death, admission to the intensive care unit, and/or need for higher oxygen flow than that provided by a nasal cannula.

Characteristics

Arm-level characteristics

	Non-severe COVID-19 (N = 49)	Severe COVID-19 (N = 31)
Age		
MedianIQR	63 (50 to 72)	75 (66 to 84)
Under 67 years (n=40) Non-severe, n=30; Severe, n=10		
MedianIQR	51.5 (44 to 63)	54.5 (45 to 66)
Gender Male		
Sample Size	n = 14 ; % = 29	n = 21 ; % = 68
Under 67 years (n=40) Non-severe, n=30; Severe, n=10		
Sample Size	n = 6 ; % = 20	n = 8 ; % = 80
Ethnicity		
Custom value	NA	NA
Comorbidities		
BMI Number of people ≥ 30 kg/m2		
Sample Size	n = 12 ; % = 24	n = 14 ; % = 45
Under 67 years (n=40) Non-severe, n=30; Severe, n=10		
Sample Size	n = 5 ; % = 17	n = 5 ; % = 50
Use of immune suppressing treatments		
Custom value	NA	NA
Socioeconomic status		
Custom value	NA	NA
Previous history of COVID-19		
Custom value	NA	NA
Other supplement use		
Custom value	NA	NA
Timing of vitamin D measurements		

	Non-severe COVID-19 (N = 49)	Severe COVID-19 (N = 31)
Custom value	NA	NA
Shielding status		
Custom value	NA	NA
Living in care homes		
Custom value	NA	NA
Smoking history		
Sample Size	n = 6 ; % = 12	n = 7 ; % = 23
Under 67 years (n=40) Non-severe, n=30; Severe, n=10		
Sample Size	n = 4 ; % = 13	n = 1 ; % = 10
Hypertension		
Sample Size	n = 20 ; % = 57	n = 30 ; % = 67
Under 67 years (n=40) Non-severe, n=30; Severe, n=10		
Sample Size	n = 9 ; % = 30	n = 5 ; % = 50
Diabetes		
Sample Size	n = 20 ; % = 41	n = 12 ; % = 39
Under 67 years (n=40) Non-severe, n=30; Severe, n=10		
Sample Size	n = 8 ; % = 27	n = 2 ; % = 20
Cardiac disease		
Sample Size	n = 11 ; % = 22	n = 8 ; % = 26
Under 67 years (n=40) Non-severe, n=30; Severe, n=10		
Sample Size	n = 2 ; % = 7	n = 1 ; % = 10
Advanced chronic kidney disease CKD-EPI < 30 mL/min/m2		
Sample Size	n = 12 ; % = 24	n = 14 ; % = 45
Under 67 years (n=40) Non-severe, n=30; Severe, n=10		

	Non-severe COVID-19 (N = 49)	Severe COVID-19 (N = 31)
Sample Size	n = 5 ; % = 17	n = 5 ; % = 50
Chronic respiratory disease		
Sample Size	n = 8 ; % = 16	n = 5 ; % = 16
Under 67 years (n=40) Non-severe, n=30; Severe, n=10		
Sample Size	n = 1 ; % = 3	n = 0 ; % = 0
Vitamin D supplements Number of people who took vitamin D supplements		
Sample Size	n = 24 ; % = 49	n = 20 ; % = 65
Under 67 years (n=40) Non-severe, n=30; Severe, n=10		
Sample Size	n = 15 ; % = 50	n = 6 ; % = 60
serum 25(OH)D *(ng/mL)*		
MedianIQR	19 (9 to 30)	13 (8 to 25)
Under 67 years (n=40) Non-severe, n=30; Severe, n=10		
MedianIQR	22 (11 to 31)	11 (9 to 12)
Vitamin D deficiency 25(OH)D <20ng/mL		
Sample Size	n = 25 ; % = 51	n = 20 ; % = 65
Under 67 years (n=40) Non-severe, n=30; Severe, n=10		
Sample Size	n = 13 ; % = 43	n = 10 ; % = 100

Outcomes

Risk of reaching composite outcome

This model associated variables with the composite outcome in a multivariable regression model. The variables included in the model were obesity, cardiac disease, age, sex, advanced chronic kidney disease. The variables shown below are those reported in the study.

	Severe COVID-19 vs Non-severe COVID-19
	N1 = 31, N2 = 49
Vitamin D deficiency *Polarity: Not set*	
Odds ratio/95% CI	3.2 (0.9 to 11.4)
Over 75 years *Polarity: Not set*	
Odds ratio/95% CI	10.4 (2 to 54.8)
Gender Male *Polarity: Not set*	
Odds ratio/95% CI	6.2 (2 to 19.5)

Section	Question	Answer
Study participation	Summary Study participation	Moderate risk of bias *(Ethnicity, socioeconomic status, and use of immune suppressing treatments not included.)*
Study Attrition	Study Attrition Summary	High risk of bias *(No information for people who had dropped out or why they had dropped out.)*
Prognostic factor measurement	Prognostic factor Measurement Summary	Low risk of bias *(Appropriate methods for measuring vitamin D were used. The study reported that there was missing outcome data but not for vitamin D measurements. Missing outcome data is considered in other domains and has not been considered as a factor for this domain.)*
Outcome Measurement	Outcome Measurement Summary	High risk of bias *(Difficult to judge when follow-up was halted. The study only says "until data analysis was conducted". No detail on how outcomes were measured are reported.)*
Study Confounding	Study Confounding Summary	High risk of bias *(Ethnicity, socioeconomic status, and use of immune suppressing treatments not included.)*
Statistical Analysis and Reporting	Statistical Analysis and Presentation Summary	High risk of bias *(The results are not reported in full, only those that are critical to the paper or that are significant.)*

Section	Question	Answer
Overall risk of bias and directness	Risk of Bias	High *(No information for people who had dropped out or why they had dropped out. Ethnicity, socioeconomic status, and use of immune suppressing treatments not included. The results are not reported in full, only those that are critical to the paper or that are significant.)*
	Directness	Directly applicable *(There could be differences in the clinical decisions made before hospitalisation and ICU admission due to this study not being in the UK and changes over the course of the pandemic)*