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Exploring the association between vitamin D status and COVID-19 outcomes

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ABSTRACT:

Objective: Vitamin D (Vit. D) deficiency has been demonstrated to be a risk factor in the development of respiratory tract infection and inflammatory processes. However, the effect of Vit. D status on the outcome of coronavirus disease 2019 (COVID-19) infection remains uncertain. In this retrospective study, we aimed to determine the role of serum Vit. D level in the outcome of COVID-19 patients in terms of severity and mortality.

Patients and Methods: We included in the study 452 adult patients (i.e., ≥18 years old) diagnosed with COVID-19 between March 2020 and December 2021 (before the availability of the COVID-19 vaccine). We reviewed patient charts to collect demographic, clinical, and laboratory data. We categorized serum Vit. D concentrations as follows: deficient (<20 ng/mL), insufficient (20-30 ng/mL), and sufficient (>30 ng/mL). We assessed disease severity in terms of hospitalization (requiring oxygen), intensive care unit (ICU) admission (requiring high-flow oxygen or ventilation), and mortality.

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— ***Results:*** Serum Vit. D levels were available for 27.4% of the 452 studied adult COVID-19 patients (mean age=56.2±17.0 years; 57% male). However, we found no statistically significant differences in the rates of hospitalization requiring supplemental oxygen, ICU admission requiring high-flow oxygen or ventilation, mortality, or hypoxia based on vit. D status (p=0.658). COVID-19 severity was strongly linked to age, with higher average ages seen in hospitalized patients requiring oxygen, those admitted to the ICU, and those who died (p<0.001, p=0.013, and p<0.001, respectively); inflammatory markers were also significantly higher in these groups (p<0.001). Higher blood pressure was associated with hospitalization (p=0.017), ICU admission (p=0.003), and mortality (p<0.001). Dyslipidemia and pulmonary fibrosis were also linked to higher mortality. Although Hispanic patients accounted for 37.4% of the study population, they had a lower proportion of deaths compared to other ethnicities (7.4% *vs.* 42.7%; p<0.001).

— ***Conclusions:*** The study included 452 adult patients diagnosed with COVID-19. We found no significant differences in hospitalization, ICU admission, mortality, or hypoxia based on Vit. D status. We identified age, inflammatory markers, and blood pressure as factors associated with COVID-19 severity and mortality. We suggest further research examining the impact of Vit. D levels, comorbidities, and ethnic disparities to help to understand the causes of COVID-19 severity and mortality.

— ***Keywords:*** *Ethnicity, Mortality, Morbidity, COVID-19, 25-hydroxy vitamin D.*

INTRODUCTION

Since late 2019, the world has faced a significant pandemic of coronavirus infection originating in Wuhan, Hubei Province, China. Coronavirus disease 2019 (COVID-19) is a novel and highly contagious viral infection that has impacted healthcare systems globally. COVID-19 is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)[1]. SARS-CoV-2 can induce a pro-inflammatory state, which leads to a cytokine storm, and has been associated with more severe outcomes in COVID-19 patients[2,3].

Observational and supplementation trials have indicated that higher levels of 25-hydroxy vitamin D (25[OH]D) are associated with a reduced risk of various infections, including dengue, herpesvirus, hepatitis B and C viruses, human immunodeficiency virus (HIV), influenza, respiratory syncytial virus infections, pneumonia, tuberculosis, and sepsis[4]. Vitamin D (Vit. D) modulates immune function in several ways by interacting with macrophages, B and T lymphocytes, neutrophils, and dendritic cells, thereby affecting the processes of physical barriers, natural immunity, and adaptive immunity[5,6].

Vit. D is a hormone that is activated in the skin (vitamin D2) and obtained through one's diet (vitamin D3). It undergoes hydroxylation in the liver and kidneys for conversion into its active form, 1.25-dihydroxy vitamin D (1.25[OH]2D)[7]. Vit. D acts as an immunomodulatory hormone and regulates gene expression within immune cells, potentially leading to both antiviral effects and modulation of the inflammatory response[8]. Epidemiological and clinical evidence suggests that Vit. D can reduce lung injuries through various mechanisms (e.g., modulating the adaptive immune system and cell-mediated immunity), thereby inducing antimicrobial peptides, reducing pro-inflammatory cytokine concentrations, increasing anti-inflammatory cytokine levels, and enhancing the expression of antioxidant-related genes[5,9].

Several epidemiological studies[10,11] have reported an increased risk of severe infection and mortality in patients with low Vit. D levels. In a 15-year retrospective cohort study involving patients aged 50-75 years in Germany, the authors found that patients with Vit. D insufficiency or deficiency had a higher risk of respiratory disease mortality[12]. Evidence suggests that Vit. D, with its immune-modulatory effects, could be a crucial supportive agent for the immune system, particularly in suppressing cytokine storms, mitigating the risk of respiratory tract infection in COVID-19, and reducing the incidence of acute respiratory distress syndrome in SARS-CoV-2-infected patients[7,13]. SARS-CoV-2 can substantially down-regulate the expression of angiotensin-converting enzyme 2 (ACE2), which is associated with the virus[14,15]. It also affects the renin-angiotensin system pathway and promotes ACE2 expression. However, as high ACE2 expression can also be a risk factor for disease severity[16], the extent to which Vit. D helps the condition remains unclear. Although various observational studies[17,18] have demonstrated reduced COVID-19 severity in patients without Vit. D deficiency, conflicting evidence also exists.

The association between Vit. D status and COVID-19 incidence and severity remains uncertain across all patient populations. Therefore, the primary objective of this retrospective observational study was to investigate whether there is a correlation between serum Vit. D levels and vulnerability to COVID-19, specifically in terms of severity and mortality. We also aimed to assess whether there was a relationship between Vit. D levels and inflammatory markers, and the severity of COVID-19 infection. Furthermore, we considered the impact of factors such as ethnicity, obesity, and underlying health conditions on the development of COVID-19 within the study population.

PATIENTS AND METHODS

This retrospective study involved a chart review of adult patients (≥18 years) who were hospitalized at NYC Health and Hospitals/Metropolitan Hospital (NY, USA) between March 2020 and December 2021 (prior to the availability of the COVID-19 vaccine). In the study, we included patients who tested positive for SARS-CoV-2 through real-time reverse transcriptase polymerase chain reaction (RT-PCR) during their hospitalization, whereas we excluded those with a negative RT-PCR result.

Baseline demographic and clinical data, including age, gender, race, ethnicity, body mass index (BMI), and comorbidities (e.g., dementia, psychosis, depression, anxiety, cerebrovascular accident, coronary artery disease, hypertension, dyslipidemias, heart failure, chronic atrial fibrillation, diabetes mellitus, obesity [BMI>30], chronic kidney injury [GFR<60 mL/min], chronic obstructive pulmonary disease, asthma, pulmonary fibrosis, malignancy, immunosuppressive medication usage, arthritis, and HIV), as well as Vit. D status, were extracted from the patients' health records. The hospitalization data comprised the dates of hospital admission and discharge, the dates of intensive care unit (ICU) admission and discharge, inflammatory markers (procalcitonin, C-reactive protein, lactate dehydrogenase, ferritin, d-dimer, creatinine phosphokinase, albumin), mortality, new organ failure during admission (e.g., acute kidney injury requiring continuous renal replacement therapy or intermittent hemodialysis), and pulmonary emboli. We considered Vit. D values measured within two years to two weeks prior to admission, and Vit. D supplementation status was neither available nor considered. We defined serum concentration cut-off points for 25[OH]D following Giustina et al[19] levels: deficient (<20 ng/mL), insufficient (20-30 ng/mL), and sufficient (>30 ng/mL).

Statistical Analysis

We performed a statistical analysis using descriptive statistics, including frequencies and percentages for categorical variables, and means/standard deviations or medians/interquartile ranges for continuous measures, as appropriate. We assessed differences in demographic characteristics, clinical measures, and COVID-19 outcomes based on Vit. D status using one-way analysis of variance (ANOVA) for normally distributed continuous measures, the Kruskal-Wallis' test for non-normally distributed continuous variables, and Pearson's Chi-square test or Fisher's exact test (for expected cell counts <5) for categorical variables. We categorized race/ethnicity as non-Hispanic (Asian, Black/African American, White, and Other) and Hispanic for analysis due to small cell counts. We adjusted all reported p-values by using the Benjamini-Hochberg procedure to control the false discovery rate (adjusted $p<0.05$ for statistical significance). We conducted the statistical analysis using R statistical program, version 4.2.2 (The R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Patients Characteristics

A total of 452 patients who tested positive for SARS-CoV-2 through RT-PCR were admitted to the hospital during the study period. The average age at admission was 56.2±17.0 years, and 57% of the admitted patients were male. Regarding race and ethnicity, 4% of patients were reported as Asian, 21% as African-American, 37% as Hispanic, and 32% as Other. Approximately 20% of the patients had a BMI of 18.5-24.9, whereas over three-quarters had a BMI of 25 or higher. On the first presentation day, the mean systolic and diastolic blood pressures were recorded as 127.2±19.7 mmHg and 75.7±13.0 mmHg, respectively (**Supplementary Table 1**).

Association Between Demographic Characteristics and Vitamin D Status

As depicted in **Supplementary Table 2**, among the 124 patients with available Vit. D data, 49% had Vit. D deficiency (<20 ng/mL), 26% had Vit. D insufficiency (20–30 ng/mL), and 25% had Vit. D sufficiency (>30 ng/mL). Patients with Vit. D deficiency tended to be younger on average (55.6±16.5 years *vs.* 63.1±15.5 years *vs.* 64.9±14.4 years; $p=0.387$) and had lower rates of hypertension (55.7% *vs.* 56.2% *vs.* 83.9 %; $p=0.334$) and diabetes mellitus (34.4% *vs.* 31.2% *vs.* 61.3%; $p=0.334$), although none of the differences in these categories reached statistical significance. The median levels of hemoglobin A1C were 6.0% (interquartile range [IQR]: 5.6-7.1) for the deficient group, 5.7% (IQR: 5.5-6.1) for the insufficient group, and 6.6% (IQR: 5.8-7.4) for the sufficient group ($p=0.334$).

We did not observe any significant differences between Vit. D status and various investigated factors, including hospitalization requiring supplemental oxygen ($p=0.658$), ICU admission requiring high-flow oxygen or ventilation ($p=0.658$), mortality ($p=0.658$), or hypoxia ($p=0.658$), as shown in **Supplementary Table 3**.

Severity of COVID-19 Infection

Hospitalization

The average age of hospitalized patients requiring oxygen was significantly higher compared to those who did not require oxygen (59.9±15.8 years *vs.* 52.3±17.7 years; $p<0.001$). A higher percentage of non-Hispanic patients were hospitalized and required oxygen compared to Hispanic patients (66% *vs.* 51%; $p=0.008$). We did not observe any statistically significant differences based on gender ($p=0.778$), BMI status ($p=0.752$), systolic blood pressure at day one of presentation ($p=0.801$), diastolic blood pressure at day one of presentation ($p=0.778$) or mean arterial blood pressure at day one of presentation

(p=0.932). Hospitalization requiring oxygen was significantly associated with higher levels of procalcitonin (0.4 ng/mL *vs.* 0.1 ng/mL; p<0.001), C-reactive protein (23.3 mg/L *vs.* 12.2 mg/L; p<0.001), lactate dehydrogenase (493.0 U/L *vs.* 303.0 U/L; p<0.001), ferritin (1,082.5 ng/mL *vs.* 565.0 ng/mL; p<0.001), and D-dimer (904.0 ng/dL *vs.* 260.0 ng/dL; p<0.001). Patients hospitalized and requiring oxygen had higher rates of coronary artery disease (13.8% *vs.* 6.5%; p=0.047), hypertension (58.1% *vs.* 44.7%; p=0.019), and dyslipidemia (41.2% *vs.* 27.1%; p=0.009) but lower rates of psychosis, depression, and anxiety status (7.8% *vs.* 19.4%; p=0.001), as seen in **Supplementary Table 4**.

ICU admission

We observed significant differences in ICU admission rates for patients requiring high-flow oxygen or ventilation across various factors. Age at admission differed significantly between groups (59.3±17.0 years *vs.* 54.4±16.8 years; p=0.014), as did procalcitonin levels (0.6 ng/mL *vs.* 0.1 ng/mL; p<0.001), C-reactive protein levels (29.8 mg/L *vs.* 12.4 mg/L; p<0.001), lactate dehydrogenase levels (593.0 U/L *vs.* 351.0 U/L; p<0.001), ferritin levels (1,351.0 ng/mL *vs.* 595.0 ng/mL; p<0.001), and D-dimer levels (2,371.0 ng/dL *vs.* 322.0 ng/dL; p<0.001). Additionally, patients with hypertension were more likely to be admitted to the ICU requiring high-flow oxygen or ventilation compared to those without (61.8% *vs.* 45.5%; p=0.003), as seen in **Supplementary Table 5**.

Mortality

Mortality was associated with a higher average age at admission (68.6±15.4 years *vs.* 54.0±16.3 years; p<0.001). Hispanic patients had a lower proportion of deaths compared to other ethnicities (3% *vs.* 22%; p<0.001). Furthermore, mortality cases showed a higher percentage of comorbidities such as hypertension (75.0% *vs.* 47.8%; p<0.001), dyslipidemia (5.0% *vs.* 31.9%; p=0.010), and pulmonary fibrosis (7.4% *vs.* 1.3%; p=0.023). Additionally, mortality was associated with higher median levels at admission of procalcitonin (1.4 ng/mL *vs.* 0.2 ng/mL; p<0.001), C-reactive protein (27.5 mg/L *vs.* 17.3 mg/L; p=0.024), lactate dehydrogenase (747.5 U/L *vs.* 382.0 U/L; p<0.001), ferritin (1,844.5 ng/mL *vs.* 739.5 ng/mL; p<0.001), and D-dimer (3,637.0 ng/dL *vs.* 384.5 ng/dL; p<0.001), as seen in **Supplementary Table 6**.

DISCUSSION

In recent years, Vit. D deficiency and insufficiency have emerged as global health concerns, and their impact on respiratory viral infections has been extensively studied in literature. In this retrospective study, we investigated the association between Vit. D levels and the severity and mortality of COVID-19 infection.

Researchers suggest that COVID-19 patients with Vit. D deficiency may exhibit a higher inflammatory response due to the antiviral effects of Vit. D against enveloped viruses[20,21]. Studies[22] have reported a higher rate of SARS-CoV-2 positivity among individuals with Vit. D deficiency. Additionally, Vit. D deficiency has been linked to a three-fold higher risk of SARS-CoV-2 infection and a five-fold higher likelihood of developing severe disease[23]. However, the impact of Vit. D deficiency on mortality rates in COVID-19 patients remains inconclusive[24-26].

Our findings did not indicate a significant correlation between Vit. D levels and COVID-19 severity or mortality. Older individuals generally experienced worse outcomes.

There was a significant difference in age between individuals who survived COVID-19 infection and those who did not, with the latter group having a significantly higher mean age (68.6 years *vs.* 54.0 years). This result suggests that advanced age may be a contributing factor to the increased mortality in this population. We did observe higher levels of inflammatory markers in severe cases, which were also associated with increased mortality rates.

Among the 452 individuals included in the study, the overall mortality rate was 15%, and those who succumbed to the disease had a longer hospitalization duration (10.9 days *vs.* 6.1 days; p<0.001). There were significant differences in inflammatory markers between survivors and non-survivors (p<0.05). Patients who expired exhibited significantly higher levels of procalcitonin, lactate dehydrogenase, ferritin, D-dimer, and albumin (p<0.05). Notably, although we observed thrombocytopenia in 17.8% of cases, it was not found to be associated with disease severity.

Comorbidities also play a crucial role in COVID-19 outcomes. Various factors, such as male sex, older age, cardiovascular disease, hypertension, chronic lung disease, obesity, and chronic kidney disease, have been proposed[23,27] as risk factors for worse COVID-19 outcomes. Obesity has also been linked[26,28] to higher COVID-19 mortality rates in multiple studies. Additionally, elderly patients and those with pre-existing comorbidities such as diabetes, hypertension, cardiovascular disease, chronic respiratory disease, and cancer are more susceptible to severe COVID-19 infection[29].

Our study revealed a higher prevalence of hypertension and dyslipidemia among hospitalized patients requiring oxygen, whereas hypertension was more common among those admitted to the ICU. Hypertension, dyslipidemia, and pulmonary fibrosis were associated with higher mortality. We also found a significant association between hypertension and both morbidity and mortality in COVID-19 patients.

Ethnicity has consistently been associated with COVID-19 outcomes, with several studies[26,30-33] reporting higher mortality rates among African-American individuals. However, other studies[34] have yielded conflicting results regarding this association. Our results indicated a lower prevalence of COVID-19 severity and mortality among Hispanic patients.

Strengths and Limitations

Overall, our findings highlight the importance of age, ethnicity, length of hospital stay, inflammatory markers, and specific comorbidities in predicting mortality in the studied population. The limitations of our study include the unavailability of serum Vit. D levels for all cases and the small sample size, which may have influenced the results. Also, the lack of multivariant analysis may have led to confounding results.

CONCLUSIONS

In this retrospective study, we analyzed the impact of serum Vit. D levels on the disease severity and mortality of COVID-19 patients. The study included 452 adult patients diagnosed with COVID-19. However, we found no significant differences in hospitalization, ICU admission, mortality, or hypoxia based on Vit. D status. We identified age, inflammatory markers, and blood pressure as factors associated with COVID-19 severity and mortality. As this study was observational and had certain limitations, we emphasize the need for additional research to establish causation.

Suggested areas of investigation include prospective studies with larger and more diverse cohorts, which can establish a clearer association between Vit. D deficiency/insufficiency and disease severity, mortality, and other clinical parameters. Additionally, randomized controlled trials can assess the efficacy of Vit. D supplementation as an adjunctive treatment for COVID-19, potentially improving patient outcomes. Long-term follow-up studies are also necessary to evaluate the post-COVID-19 outcomes of individuals with different comorbidities and Vit. D statuses, including the development of chronic conditions and subsequent mortality rates. This knowledge can inform clinical management, public health interventions, and the development of targeted therapies to improve patient outcomes.

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Ethics Approval:
This study was approved by the BRANY IRB, File # 22-12-150-182(HHC).

Informed Consent:
Not applicable due to the retrospective nature of the study.

Conflict of Interest:
The authors declare that they have no conflict of interest.

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Authors' Contributions:
MJ, and DB drafted and wrote the article. All authors contributed to Conceptualization, Investigation, Methodology, data collection, and formal analysis and performed the studies. All authors read and approved the final manuscript.

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References

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, Zhao X, Huang B, Shi W, Lu R, Niu P, Zhan F, Ma X, Wang D, Xu W, Wu G, Gao GF, Tan W; China Novel Coronavirus Investigating and Research Team. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med 2020; 382: 727-733.
2. Liu F, Li L, Xu M, Wu J, Luo D, Zhu Y, Li B, Song X, Zhou X. Prognostic value of interleukin-6, C-reactive protein, and procalcitonin in patients with COVID-19. J Clin Virol 2020; 127: 104370.
3. Silberstein M. Correlation between premorbid IL-6 levels and COVID-19 mortality: Potential role for Vitamin D. Int Immunopharmacol 2020; 88: 106995.
4. Singh N, Suthar B, Mehta A, Shukla S, Pandey A. Vitamin D: A Review and Proposed Evidence for Treatment or Prevention in COVID-19. Int J Virol AIDS 2020; 7: 064.
5. Greiller CL, Martineau AR. Modulation of the immune response to respiratory viruses by vitamin D. Nutrients 2015; 7: 4240-4270.
6. Prietl B, Treiber G, Pieber TR, Amrein K. Vitamin D and immune function. Nutrients 2013; 5: 2502-2521.
7. Griffin G, Hewison M, Hopkin J, Kenny R, Quinton R, Rhodes J, Subramanian S, Thickett D. Vitamin D and COVID-19: evidence and recommendations for supplementation. R Soc Open Sci 2020; 7: 201912.
8. Martineau AR, Forouhi NG. Vitamin D for COVID-19: a case to answer? Lancet Diabetes Endocrinol 2020; 8: 735-736.
9. Zdrenghea MT, Makrinioti H, Bagacean C, Bush A, Johnston SL, Stanciu LA. Vitamin D modulation of innate immune responses to respiratory viral infections. Rev Med Virol 2017 Jan; 27: e1909.
10. Teymoori-Rad M, Shokri F, Salimi V, Marashi SM. The interplay between vitamin D and viral infections. Rev Med Virol 2019; 29: e2032.
11. Belderbos ME, Houben ML, Wilbrink B, Lentjes E, Bloemen EM, Kimpen JL, Rovers M, Bont L. Cord blood vitamin D deficiency is associated with respiratory syncytial virus bronchiolitis. Pediatrics 2011; 127: e1513-e1520.
12. Brenner H, Holleczek B, Schöttker B. Vitamin D insufficiency and deficiency and mortality from respiratory diseases in a cohort of older adults: potential for limiting the death toll during and beyond the COVID-19 pandemic? Nutrients 2020;12: 2488.
13. Baeke F, Korf H, Overbergh L, Verstuyf A, Thorrez L, Van Lommel L, Waer M, Schuit F, Gysemans C, Mathieu C. The vitamin D analog, TX527, promotes a human CD4+ CD25highCD127low regulatory T cell profile and induces a migratory signature specific for homing to sites of inflammation. J Immunology 2011; 86: 132-142.
14. Xiao L, Sakagami H, Miwa N. ACE2: the key molecule for understanding the pathophysiology of severe and critical conditions of COVID-19: demon or angel? Viruses 2020; 12: 491.
15. Machado CD, Ferro Aissa A, Ribeiro DL, Antunes LM. Vitamin D supplementation alters the expression of genes associated with hypertension and did not induce DNA damage in rats. J Toxicol Environ Health Part A 2019; 82: 299-313.

16. Gracia-Ramos AE. Is the ACE2 Overexpression a Risk Factor for COVID-19 Infection? Arch Med Res 2020; 51: 345-346.
17. Liu N, Sun J, Wang X, Zhang T, Zhao M, Li H. Low vitamin D status is associated with coronavirus disease 2019 outcomes: a systematic review and meta-analysis. Int J Infect Dis 2021; 104: 58-64.
18. Li Y, Tong CH, Bare LA, Devlin JJ. Assessment of the association of vitamin D level with SARS-CoV-2 seropositivity among working-age adults. JAMA Netw Open 2021; 4: e2111634.
19. Giustina A, Adler RA, Binkley N, Bouillon R, Ebeling PR, Lazaretti-Castro M, Marcocci C, Rizzoli R, Sempos CT, Bilezikian JP. Controversies in vitamin D: summary statement from an international conference. J Clin Endocrinol Metab 2019; 104: 234-240.
20. Yisak H, Ewunetei A, Kefale B, Mamuye M, Teshome F, Ambaw B, Yideg Yitbarek G. Effects of vitamin D on COVID-19 infection and prognosis: a systematic review. Risk Manag Healthc Policy 2021; 7: 31-38.
21. Beard JA, Bearden A, Striker R. Vitamin D and the anti-viral state. J Clin Virol 2011; 50: 194-200.
22. Kaufman HW, Niles JK, Kroll MH, Bi C, Holick MF. SARS-CoV-2 positivity rates associated with circulating 25-hydroxyvitamin D levels. PLoS One 2020; 15: e0239252.
23. Ghasemian R, Shamshirian A, Heydari K, Malekan M, Alizadeh-Navaei R, Ebrahimzadeh MA, Ebrahimi Warkiani M, Jafarpour H, Razavi Bazaz S, Rezaei Shahmirzadi A, Khodabandeh M. The role of vitamin D in the age of COVID-19: A systematic review and meta-analysis. Int J Clin Pract 2021; 75: e14675.
24. Ilie PC, Stefanescu S, Smith L. The role of vitamin D in the prevention of coronavirus disease 2019 infection and mortality. Aging Clin Exp Res 2020; 32: 1195-1198.
25. Zemb P, Bergman P, Camargo CA, Cavalier E, Cormier C, Courbebaisse M, Hollis B, Joulia F, Minisola S, Pilz S, Pludowski P. Vitamin D deficiency and the COVID-19 pandemic. J Glob Antimicrob Resist 2020; 22: 133-134.
26. Hastie CE, Mackay DF, Ho F, Celis-Morales CA, Katikireddi SV, Niedzwiedz CL, Jani BD, Welsh P, Mair FS, Gray SR, O'Donnell CA. Vitamin D concentrations and COVID-19 infection in UK Biobank. Diabetes Metab Syndr 2020;14: 561-565.
27. Hessami A, Shamshirian A, Heydari K, Pourali F, Alizadeh-Navaei R, Moosazadeh M, Abrotan S, Shojaie L, Sedighi S, Shamshirian D, Rezaei N. Cardiovascular diseases burden in COVID-19: Systematic review and meta-analysis. Am J Emerg Med 2021; 46: 382-391.
28. Popkin BM, Du S, Green WD, Beck MA, Algaith T, Herbst CH, Alsukait RF, Alluhidan M, Alazemi N, Shekar M. Individuals with obesity and COVID-19: a global perspective on epidemiology and biological relationships. Obes Rev 2020; 21: e13128.
29. Li X, Xu S, Yu M, Wang K, Tao Y, Zhou Y, Shi J, Zhou M, Wu B, Yang Z, Zhang C. Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan. J Allergy Clin Immunol 2020;146: 110-8
30. Yancy CW. COVID-19 and african americans. Jama 2020; 323: 1891-1892.
31. Milam AJ, Furr-Holden D, Edwards-Johnson J, Webb B, Patton III JW, Ezekwemba NC, Porter L, Davis T, Chukwurah M, Webb AJ, Simon K. Are clinicians contributing to excess African American COVID-19 deaths? Unbeknownst to them, they may be. Health Equity 2020; 4: 139-141.
32. Laurencin CT, McClinton A. The COVID-19 pandemic: a call to action to identify and address racial and ethnic disparities. J Racial Ethn Health Disparities 2020; 7: 398-402.
33. Alloh F, Regmi PR, van Teijlingen E. COVID-19 and Black Africans in the UK: Disparities linked to underlying inequalities in health. BMJ 2020; 369: m1548.
34. Abdollahi A, Kamali Sarvestani H, Rafat Z, Ghaderkhani S, Mahmoudi-Aliabadi M, Jafarzadeh B, Mehrtash V. The association between the level of serum 25 (OH) vitamin D, obesity, and underlying diseases with the risk of developing COVID-19 infection: a case–control study of hospitalized patients in Tehran, Iran. J Med Virol 2021; 93: 2359-2364.