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Research Article

**THE ASSOCIATION BETWEEN SEVERE VITAMIN D
DEFICIENCY AND MORTALITY IN PATIENTS WITH
COVID-19****Dr. Mohudisah Ahmed¹, Dr. Rameeha Rauf², Dr Faiz Alam³**
^{1,2}Rawalpindi Medical University, ³Ayub Medical College, Abbotabad**Article Received:** November 2020 **Accepted:** December 2020 **Published:** January 2021**Abstract:**

Aim: The objective of this is to determine the association between severe vitamin D deficiency and mortality in patients presented with covid-19.

Study Design: Prospective/Observational

Place and Duration: The study was conducted at Benazir Bhutto Hospital, Rawalpindi for duration of three months from 1st July to 30th September, 2020.

Materials & Methods: In our study, total 140 patients of both genders who were diagnosed with covid-19 were enrolled. Patients ages were ranging from 15 years to 75 years. Detailed demographics including age, sex, and body mass index (BMI) were recorded after taking written consent. 5 ml blood sample was taken from all the patients to examine the vitamin D level. Severe Vitamin D deficiency was defined as 25(OH)D < 25 nmol/L (10 ng/dL). Association between mortality and severe vitamin D deficiency was examined. Data was analyzed by SPSS 24.0.

Results: Out of 140 patients, 82 (58.57%) were males while 58 (41.43%) were females with mean age 42.46±14.73 years. Severe vitamin D deficiency was observed in 60 (42.86%) patients. Mortality found in 22 (15.71%) patients. Patients with severe vitamin D deficiency had high rate of mortality 16 (26.67%) as compared to patients with no vitamin D deficiency 6 (7.5%), a significant association was observed between severe vitamin D deficiency and mortality in patients with covid-19 disease with p-value <0.05.

Conclusion: It is concluded that there was strong relationship between severe vitamin-D deficiency and mortality in patients with covid-19 disease.

Keywords: Covid-19, Vitamin D Deficiency, Mortality

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INTRODUCTION:

Coronavirus disease 2019 (COVID-19), which is caused by serious acute respiratory syndrome 2 (SARS-CoV-2) and has also caused more than 745 000 deaths worldwide, is often extreme lower respiratory symptoms [1]. The lack of evidence to show successful pharmacology strategies in order to avoid COVID-19 is a challenge to stop this pandemic. Treatment with vitamin D was described as a possible COVID 19 preventive or treatment strategy[2]. Other viral respiratory infections, particularly in people with deficiency in vitamin D, were found to decrease in vitamin D treatment [3]. Vitamin D deficiency among persons with darker skin or sun-residues, including those living in higher latitudes in the winter, nursing homes and health care workers[4], is widespread in almost half of the US population. COVID-19 has become more prevalent among people living in African American states[5], in the late winter, in north towns[6] old adults,[7] nurses and medical staff,9 populations all of which are at elevated risk of vitamin D deficiency[8].

As the main target cells, the virus infects pneumocytes of type II and enterocytes [9]. Spike viral proteins promote viral entry into target cells by linking to enzyme-converting angiotensin 2 (ACE-2) on cell surface[10]. ACE 2 is a reinforced renin-angiotensin system regulating organism in a wide variety of body tissues that may explain multi-organ failure in susceptible patients, including lung , kidney, gastrointestinal (GI) and cardiovascular systems [11].

Vitamin D has been proposed to defend against COVID-19. Immunomodulatory activity in vitamin D has been shown. Vitamin D, interacting in immune cells with the vitamins' receptor (VDR), modulates the immune systems that are born and acquires in response to bacterial and viral invasions, which is the product of an immune mechanism that is intrinsic in

the immune system. [12]. [12]. It also functions as a renin-angiotensin modulator and ACE-2 down-regulators[13]. Vitamin D therefore can help prevent cytokine storm and subsequent ARDS, commonly the causes of death, in the treatment of COVID-19. [14].

We conducted present study to find out the association between severe vitamin D deficiency and mortality in patients diagnosed to have severe Covid-19 disease.

MATERIALS AND METHODS:

This prospective/observational study was conducted at Benazir Bhutto Hospital, Rawalpindi for duration of three months from 1st July to 30th September, 2020. Total 140 patients of both genders diagnosed to have severe covid-19 were enrolled in this study. Patients ages were ranging from 15 years to 75 years. Detailed demographics including age, sex, and body mass index (BMI) were recorded after taking written consent. Patients on vitamin D supplementation and those with no consent were excluded.

Real time PCR was done to all the patients to diagnose covid-19 disease. 5 ml blood sample was taken from all the patients to examine the vitamin D level. Severe Vitamin D deficiency was defined as 25(OH)D < 25 nmol/L (10 ng/dL). Association between mortality and severe vitamin D deficiency was examined. All the data was analyzed by SPSS 24.0. Frequencies and percentages were recorded in tabulation form. Chi-square test was done to examine the association between severe vitamin D deficiency and mortality. P-value <0.05 was taken as significant.

RESULTS:

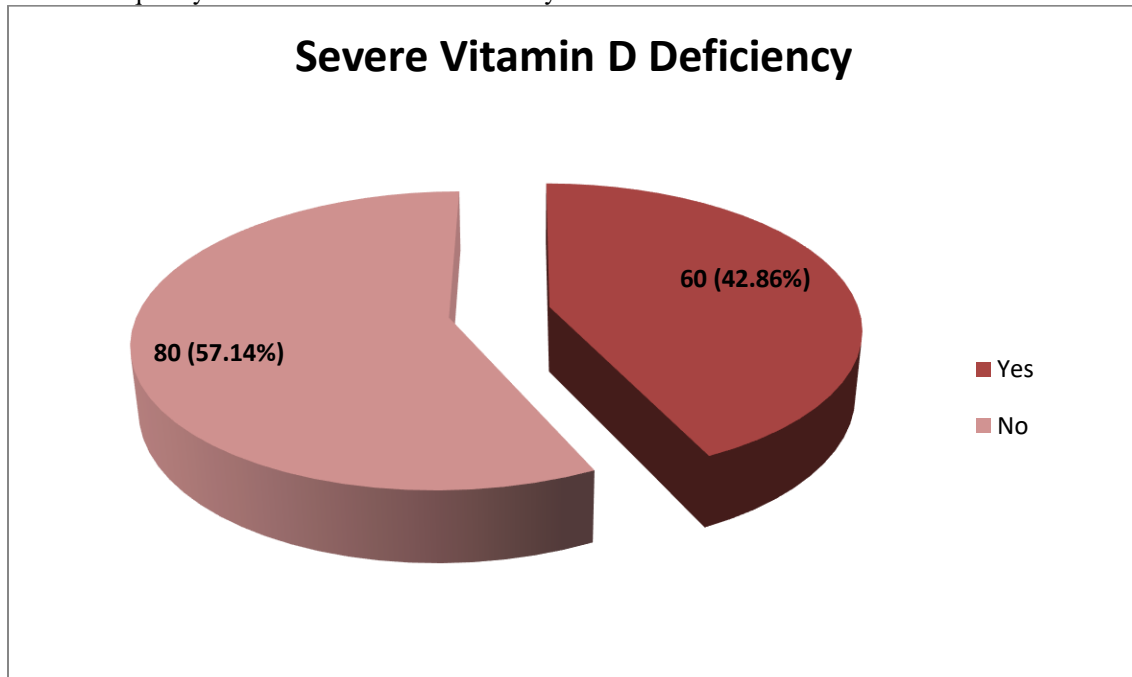
Out of 140 patients, 82 (58.57%) were males while 58 (41.43%) were females with mean age 42.46±14.73 years. Mean BMI of patients was 23.48±3.62 kg/m². (Table 1)

Table No 1: Demographics of all the patients

Variables	Frequency No.	%age
Mean Age (Years)	42.46±14.73	
Mean BMI (kg/m)	23.48±3.62	
Gender		
Male	82	58.57
Female	58	41.43

60 (42.86%) patients had vitamin D level <25 nmol/L and 80 (57.14%) patients had vitamin D level >25 nmol/L. (Figure 1)

Figure No 1: Frequency of Severe Vitamin D Deficiency



Mortality found in 22 (15.71%) patients. Patients with severe vitamin D deficiency had high rate of mortality 16 (26.67%) as compared to patients with no vitamin D deficiency 6 (7.5%), a significant association was observed between severe vitamin D deficiency and mortality in patients with covid-19 disease with p-value <0.05. (Table 2)

Table No 2: Association between mortality and severe vitamin D deficiency

Variables	Severe Vitamin D Deficiency		P-value
	Yes (n=60)	No(n=80)	
Mortality			0.02
Yes	16 (26.67%)	6 (7.5%)	
No	44 (73.33%)	74 (92.5%)	

DISCUSSION:

In December 2019 in Wuhan, China, the first case of corona virus was found and this life-threatening disease spread rapidly around the world. More than three hundred thousand people in Pakistan have been affected by corona virus and over six thousand deaths have already been registered [15]. Pakistan is one country where the spread of corona-virus is too high and because of unheavy human behaviour and the SOPs for life-threatening diseases are not followed. A worldwide epidemic, not only in the North, but increasingly also in the South, is the vitamin D deficiency. For instance, whereas in Europe, deficits in all age groups (< 30 nmol) range from 20% to 60%, in Asia childhood figures range to 61% (Pakistan, India) and 86% (Iran) [16-17]. Studies demonstrated that patients with history of severe vitamin D deficiency were on high risk to develop coronavirus disease [18]. We conducted present study

to examine the association between severe vitamin D deficiency and mortality among patients with severe covid-19 disease. In this regard 140 patients were enrolled. Majority 58.57% patients were males and maximum number of patients were ages between 30 years to 50 years. These results showed similarity to many of previous studies in which male patients were predominant 60% and majority of patients were ages above 40 years [18, 19].

In present study severe vitamin D deficiency was found in 60 (42.86%) patients while 80 (57.14%) patients had vitamin D level >25 nmol/L. A study conducted in Iran by Maghbooli Z et al [20] reported that severe covid-19 was found in 74% patients and among them severe vitamin D deficiency was observed in 32.8% patients. Another study by G. E. Carpagnano et al [21] reported that out of 42 covid-

19 patients, severe vitamin D deficiency was found in 81% patients.

In our study, mortality was found in 22 (15.71%) patients. Patients with severe vitamin D deficiency had high rate of mortality 16 (26.67%) as compared to patients with no vitamin D deficiency 6 (7.5%), a significant association was observed between severe vitamin D deficiency and mortality in patients with covid-19 disease with p-value <0.05. A study by Baktash V et al [22] demonstrated that severe vitamin D deficiency had a significant association with adverse outcomes in patients with covid-19 disease.

Alipio (2020) and D'Avolio and their colleagues [23] provide evidence of a correlation between the vitamin D deficiency and the adverse COVID-19 outcome. For patients with Vitamin D deficiency the earlier study (pre-print) showed that the disease incidence is increased and for patients with COVID-19 positive and negative vitamin D serum concentration has decreased. These two cohort studies were retrospective, covering a sample size of 212 and 120.

In order to research vitamin D interaction and COVID-19 morbidity and mortality in twenty European countries, Iliia and colleagues [24] carried out a meta-analysis and suggested possible associations between vitamin D levels, SARS-CoV-2 infections, and mortality. Hastie and colleagues [25] have used data from 449 biobank persons with reported SARS-CoV-2-infections and have found no correlation to serum levels of 25(OH)D.

CONCLUSION:

Vitamin D plays an important role in the prevention of any severe illness. We concluded that severe vitamin D deficiency was found in 42.86% patients. Also vitamin D deficiency had a strong association between with increase rate of mortality. Patients with severe Vitamin D deficiency had high rate of mortality as compared to patients with vitamin D level >25nmol/L.

REFERENCES:

1. COVID-19 corona virus pandemic. Worldometer. Updated August 12, 2020. Accessed August 12, 2020. <https://www.worldometers.info/coronavirus>
2. Grant WB, Lahore H, McDonnell SL, et al. Evidence that vitamin D supplementation could reduce risk of influenza and COVID-19 infections and deaths. *Nutrients*. 2020;12(4):988. doi:10.3390/nu12040988.
3. Martineau AR, Jolliffe DA, Hooper RL, et al. Vitamin D supplementation to prevent acute

- respiratory tract infections: systematic review and meta-analysis of individual participant data. *BMJ*. 2017;356:i6583. doi:10.1136/bmj.i6583.
4. Forrest KY, Stuhldreher WL. Prevalence and correlates of vitamin D deficiency in US adults. *Nutr Res*. 2011;31(1):48-54. doi:10.1016/j.nutres.2010.12.001.
5. Garg S, Kim L, Whitaker M, et al. Hospitalization rates and characteristics of patients hospitalized with laboratory-confirmed coronavirus disease 2019: COVID-NET, 14 States, March 1–30, 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(15):458-464. doi:10.15585/mmwr.mm6915e3.
6. Umhau JC. Casting sunlight on an epidemic: is vitamin D a critical host factor to prevent COVID-19? *MedPage Today*. Published March 25, 2020. Accessed April 13, 2020.
7. Huotari A, Herzig KH. Vitamin D and living in northern latitudes—an endemic risk area for vitamin D deficiency. *Int J Circumpolar Health*. 2008;67(2-3):164-178.
8. owah D, Fan X, Dennett L, Hagtvedt R, Straube S. Vitamin D levels and deficiency with different occupations: a systematic review. *BMC Public Health*. 2017;17(1):519.
9. Lamers MM, Beumer J, van der Vaart J, Knoops K, Puschhof J, Breugem TI, et al. SARS-CoV-2 productively infects human gut enterocytes. *Science*. 2020:eabc1669. pmid:32358202.
10. Ortega JT, Serrano ML, Pujol FH, Rangel HR. Role of changes in SARS-CoV-2 spike protein in the interaction with the human ACE2 receptor: An in silico analysis. *EXCLI journal*. 2020;19:410. pmid:32210742
11. Gheblawi M, Wang K, Viveiros A, Nguyen Q, Zhong J-C, Turner AJ, et al. Angiotensin-Converting Enzyme 2: SARSCoV-2 Receptor and Regulator of the Renin-Angiotensin System: Celebrating the 20th Anniversary of the Discovery of ACE2. *Circulation research*. 2020;126(10):1456–74. pmid:32264791.
12. Gruber-Bzura BM. Vitamin D and Influenza-Prevention or Therapy? *International journal of molecular sciences*. 2018;19(8). Epub 2018/08/18. pmid:30115864.
13. Xu J, Yang J, Chen J, Luo Q, Zhang Q, Zhang H. Vitamin D alleviates lipopolysaccharide-induced acute lung injury via regulation of the renin-angiotensin system. *Molecular medicine reports*. 2017;16(5):7432–8. Epub 2017/09/26. pmid:28944831.
14. Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C, et al. Pathological findings of COVID-19 associated with acute respiratory distress

- syndrome. *The Lancet respiratory medicine*. 2020;8(4):420–2. pmid:32085846.
15. Cucinotta D, Vanelli M. WHO Declares COVID-19 a Pandemic. *Acta bio-medica: Atenei Parmensis*. 2020;91(1):157–60. Epub 2020/03/20. pmid:32191675.
 16. Asghar, Muhammad Sohaib & Kazmi, Syed Jawad & Ahmed, Noman & Akram, Mohammed & Khan, Salman & Rasheed, Uzma & Hassan, Maira & Memon, Gul. (2020). Clinical Profiles, Characteristics, and Outcomes of the First 100 Admitted COVID-19 Patients in Pakistan: A Single-Center Retrospective Study in a Tertiary Care Hospital of Karachi. 12. e8712. 10.7759/cureus.8712.
 17. John Hopkins University of Medicine Coronavirus Resource Center. Data retrieved on 05/18/2020. <https://coronavirus.jhu.edu>
 18. Panarese A , Shahini E . COVID-19, and vitamin D. *Aliment Pharm Ther* 2020;51:993. doi: 10.1111/apt.15752.
 19. Biesalski, Hans. (2020). Vitamin D deficiency and comorbidities in COVID-19 patients – A fatal relationship?. *NFS Journal*.
 20. 10.1016/j.nfs.2020.06.001. 20. Maghbooli Z, Sahraian MA, Ebrahimi M, Pazoki M, Kafan S, Tabriz HM, et al. (2020) Vitamin D sufficiency, a serum 25-hydroxyvitamin D at least 30 ng/mL reduced risk for adverse clinical outcomes in patients with COVID-19 infection. *PLoS ONE* 15(9): e0239799. <https://doi.org/10.1371/journal.pone.0239799>.
 21. Carpagnano, G.E., Di Lecce, V., Quaranta, V.N. et al. Vitamin D deficiency as a predictor of poor prognosis in patients with acute respiratory failure due to COVID-19. *J Endocrinol Invest* (2020). <https://doi.org/10.1007/s40618-020-01370-x>.
 22. Baktash V, Hosack T, Patel N, et al. Vitamin D status and outcomes for hospitalised older patients with COVID-19. *Postgraduate Medical Journal* Published Online First: 27 August 2020. doi: 10.1136/postgradmedj-2020-138712
 23. D’Avolio A , Avataneo V , Manca A , et al. 25-hydroxyvitamin D concentrations are lower in patients with positive PCR for SARS-CoV-2. *Nutrients* 2020;12:1359. doi: 10.3390/nu12051359.
 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;32:1195–8. doi: 10.1007/s40520-020-01570-8.
 25. Hastie CE , Mackay DF , Ho F , et al. Vitamin D concentrations and COVID-19 infection in UK Biobank. *Diabetes Metab Syndr* 2020;14:561–5. doi: 10.1016/j.dsx.2020.04.050.