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ORIGINAL RESEARCH ARTICLE

EVALUATION OF VITAMIN D STATUS IN PATIENTS WITH COVID-19 AND PREDICTION OF OUTCOME

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ABSTRACT

Background: COVID-19 is the pandemic disease declared by World Health Organization (WHO) on 11th March 2020. Growing body of evidence suggests that a vitamin D deficiency could be linked with developing a more severe case of COVID-19. The possible correlation between Vitamin D insufficiency and worse outcome has been postulated to be associated with metabolic, procoagulant and inflammatory events and is not independently related to COVID-19. **Objectives:** To evaluate the vitamin D status in patients with COVID-19 and prediction of outcome. **Method:** This prospective study was conducted at Armed Forces Institute of Pathology (AFIP) and Combined Military Hospital, Dhaka Cantonment from April 2020 to August 2020. One hundred COVID-19 positive cases admitted in CMH, Dhaka were enrolled. Detail socio-demographic data were collected from the informant and recorded in structured questionnaire. Clinical examination and relevant investigations were done. All collected data were analysed under SPSS-21 version. **Result:** Out of 100 cases in this study, maximum patients (43.0%) were in age group 41- 50 years, mean age of the patient was 42.35 ± 11.7 years. Male to female ratio was 3.54:1, 78% were male and 22% were female. Vitamin D deficiency was found in 15.0% cases and vitamin D insufficiency was found in 28.0% cases. On evaluation of outcome, 65.0%patients were recovered completely, complications were developed among 27.0% patients (17.0% cases required noninvasive ventilation and 10% cases required invasive ventilation) and 8.0% were died. Among the expired 8 patients, 7(87.5%) had deficient and 1(12.5%) had insufficient vitamin D. Among the recovered patients, maximum 54(83.0%)had normal vitamin D level. In this study high prevalence of hypovitaminosis D was found among patients not recovered and expired. **Conclusion:** Present study concluded that vitamin D can predict the outcome of COVID 19 patients.

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) is caused by SARS-CoV-2, a recently emergent coronavirus that was first identified in Wuhan, China, in December 2019. According to genetic sequencing, it is a β coronavirus closely related to the SARS virus.[1] According to the World Health Statistics printed in 2020, the COVID-19 pandemic is responsible for loss of significant number of life and bedeviling livelihoods. To prevent transmission and provide appropriate care in time, early recognition speedy identification and rapid diagnosis are essential. Evaluation ought to be done according to pneumonia severity indexes and sepsis guidelines (if sepsis is suspected) in all patients with severe illness.

Symptomatic transmission refers to transmission of SARS-CoV-2 from persons with symptoms. Medical and virologic studies recommend that transmission principally happens from symptomatic people to others by close contact through respiratory droplets by direct contact with infected persons or by contact with contaminated objects and surfaces. Clinical and virologic studies that have collected repeated biological samples from confirmed patients exhibit that aberration of SARS- CoV-2 is highest in the upper respiratory tract (nose and throat) early in the course of the disease, within the first 3 days from onset of symptoms. The incubation period for COVID-19, which is the time between becoming infected and symptom monsetison average 5–6d ays, but can be upto14 days.[2-4]

The risk factors of in-hospital death were studied in previous epidemiological studies. Older age, higher Sequential Organ failure assessment (SOFA) score and d-dimer >1µg/mL on admission were shown to be risk factors. In addition, the presence of coronary artery disease, diabetes and hypertension was also considered to be risk factors.[5] A study revealed that vitamin D can be an important predictor of hospital outcome. Hypovitaminosis D is associated with hospital outcome increased risk of respiratory tract infections.[6] In a study, it was reported that low 25-hydroxyvitamin D has been associated with inflammation, human immunodeficiency virus (HIV) disease progression, and death.[7]

METHODS

This study was conducted at Armed Forces Institute of Pathology (AFIP) and Combined Military Hospital, Dhaka Cantonment, Dhaka from April 2020 to August 2020 over a period of six months. One hundred diagnosed case of COVID-19 by RT-PCR of any sexes and age more than 30 were included in this study. Patients with mal-absorption syndrome, inflammatory bowel disease, history of malignancy, immunosuppressive condition, abnormal liver or renal function, thyroid or parathyroid disease, sarcoidosis, tuberculosis, rickets type I, II, III, hypophosphatemic rickets, nephrotic syndrome, autoimmune disease were excluded from this study. Serum 25(OH)D concentration was measured by immunoassay method, using a Roche Cobas 6000 kit. Patient outcome was assessed during their hospital stay. All the information was recorded in data collection sheet. Data were processed with the help of Microsoft excel. Quantitative data were expressed as mean with standard deviation and qualitative data as frequency with percentage.

Sample size is calculated by using following equation:

$$n = \frac{z^2 pq}{d^2}$$

n= the desired sample size.
z = Standard normal deviate usually set at 1.96.
p = Proportion in the population.
Previous study reported that prevalence of hypovitaminosis D was found in 81% of patients in COVID 19. SO, 'p' value considered as 81% or 0.81.
q= (1-p)or 0.19.
d= Degree of accuracy which is considered as 10% of value p or 0.081.

Calculation,

$$n = \frac{1.96^2 \times 0.81 \times 0.19}{0.081^2}$$

$$\text{Or, } n = \frac{0.59}{0.006}$$

According to this formula the targeted sample is 98.5. Therefore 100 samples were taken for analysis and statistical convenience. Sample was selected by purposive sampling technique. Inclusion criteria were diagnosed case of COVID 19 of both sexes and age more than 30 years. Patients giving informed consent took part in this study. Data were categorized and analyzed using IBMSPSS Statistics for windows version21.0. Mean age of the patient was 42.35 ±11.7 years. Maximum patients (43.0%) were in age group 41-50 years. Out of 100 cases 78% were male and 22% were female. Male and female ratio was 3.54:1.

RESULTS

Table 1. Demographic profile of the patients (n=100)

Age (years)	Frequency (n)	Percentage (%)	Mean ± SD
≤30	4	4.0	
31-40	24	24.0	
41-50	43	43.0	42.35 ± 11.7
51-60	18	18.0	
61-70	11	11.0	
Gender			
Male	78	78.0	
Female	22	22.0	

Mean age of the patient was 42.35 ±11.7 years. Maximum patients (43.0%) were in age group 41-50 years. Out of 100 cases 78% were male and 22% were female. Male and female ratio was 3.54:1.

Table 2. Assessment of serum Vitamin D level in the study population (n=100)

Serum Vitamin D		Frequency (n)		Percentage (%)
Deficient (<50.0 nmol/L)		15		15.0
Insufficient (50.0-75.0 nmol/L)		28		28.0
Sufficient (>75.0 nmol/L)		57		57.0

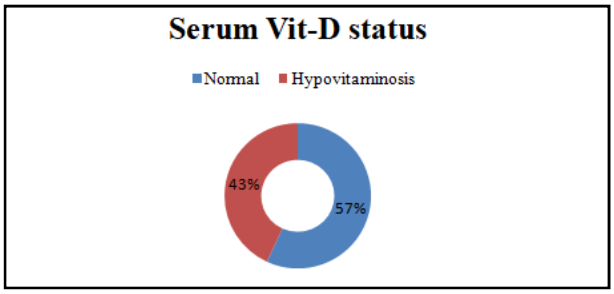

Fig-1:Prevalenceof hypovitaminosis D in COVID-19 patients(n=100)

In this study, 15.0% patients had deficient vitamin D, 28.0% had insufficient vitamin Dand 57.0% had sufficient vitamin D.

Table 3. Evaluation of the outcome of the patients (n=100)

Outcome	Frequency (n)	Percentage (%)
Recovery	65	65.0
Developed complication & needed Mechanical Ventilation	27	27.0
Expired	8	8.0

Hypovitaminosis D was significantly associated with significant mortality and morbidity of COVID-19 patients. Among the expired 8 patients, 7(87.5%) had deficient and 1 (12.5%) had insufficient vitamin D. Among the recovered patients, 54 (83.0%) had normalvitamin D level.

Table 4. Correlation of serum vitamin D with patients outcome (n=100)

Serum Vitamin D	Recovery (n=65)	Complication (n=27)	Death (n=8)	p-value
Deficient (<50.0 nmol/L)	0	8 (29.6)	7 (87.5)	<0.001
Insufficient (50.0-75.0 nmol/L)	11 (16.9)	16 (59.3)	1 (12.5)	
Sufficient (>75.0 nmol/L)	54 (83.1)	3 (11.1)	0	

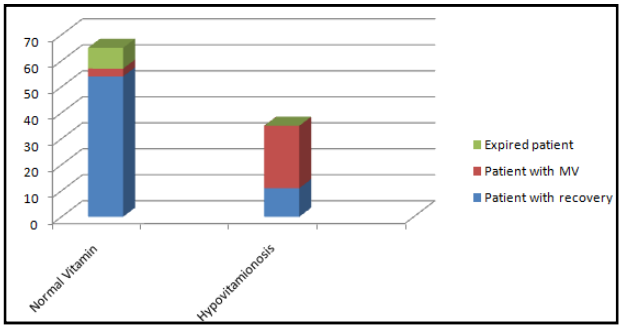

Fig 2. Prognostic value of vitamin D with patients outcome(n=100)

DISCUSSION

This prospective study reports that data about the association between serum vitamin D level and disease outcome and prognosis in patients affected by COVID-19. Present study demonstrates that maximum patients (43.0%) were in age group 41-50 years, mean age of the patient was 42.35 ± 11.7 years. Out of 100 cases 78% were male and 22% were female, male to female ratiowas3.54:1. Findings consistent with result of other study. In a study by Carpagnano *et al*, the mean age was 65±13 year and Sex (M/F, n, %) was (30/12, 71, 29%)[6]. In our study hypovitaminosis was observed in 43.0% cases, at deficient level in 15.0% cases and at insufficient level in 28.0% cases. Normal or sufficient vitamin D was found in 57.0% of the patients (Table-2).Similar study also found high prevalence of hypovitaminosis D (81%). Twenty-four percent of patients had severe deficiency.[6]Another study showed that vitamin D deficiency is common in Western, Southern and Eastern Europe (30–60%) and in Middle East countries (>80%) and severe deficiency is found in more than 10% of Europeans. In addition to lack of sun exposure and less dietary intake, age over 70 years and institutionalization are presented as the main risk factors for impaired vitamin D status.[8] Following evaluation of outcome, 65 patients recovered completely and 27 patients developed different complications (17 cases required noninvasive ventilation and 10 cases required invasive ventilation). In this study mortality rate was 8.0% of COVID-19 patients. Present study shows that hypovitaminosis D was significantly associated with mortality and morbidity of COVID-19 patients. Among the expired 8 patients, 7(87.5%) had deficient and 1 (12.5%) had insufficient vitamin D. None of the cases with fatal outcome were detected for normal vitamin D status; whereas, those patients recovered, maximum 54(83.0%) had normal vitamin D level. Previous study of Carpagnano *et al*. also reported that patients with severe vitamin D deficiency had a significantly higher mortality risk. Based on vitamin D serum levels, 20% of patients had no hypovitaminosis D, 25% had insufficiency, 30% had moderate deficiency, and 25% had severe deficiency. IL-6 levels are found higher in patients with severe vitamin Ddeficiency but this data is statistically insignificant. By contrast, a survival analysis reported that, after 10 days of hospitalization, patients with severe vitamin D deficiency had a considerably higher mortality risk than the others.[6] This finding may recommend a possible role for the vitamin D supplementation in the supportive treatment of COVID-19patients.In our study high prevalence of hypovitaminosis D was found in patients not recovered (or those developed complications) and in patients, those expired. So it may be concluded that vitamin D can predict the outcome of COVID 19 patients. These data are consistent with results of a study conducted by Ilie *et al*.[9] They aimed on mean vitamin D levels in European countries (severely low in aging population especially in Italy, Spain and Switzerland) and found a negative correlation between vitamin D levels and COVID-19 cases and mortality in the population of those countries. Accordingly, in a recent review, it was reported that Vitamin D may decrease the risk of influenza and Covid-19.The outbreak happened in winter, when vitamin D concentrations are lowest; on the other hand, the number of cases in the Southern Hemisphere near the end of summer is low. Vitamin D deficiency has been reported to contribute to ARDS; case-fatality rates increase with age and with chronic disease co-morbidity, both of which are related with lower 25(OH)D concentration.[6]In addition, in a recent study, Panfili and colleagues reported some evidence of the role of vitamin D in preventing pulmonary fibrosis, which has been described as a common complication of ARDS and that could be a long-term issue in these patients. This antifibrotic role may be an additional element that supports the use of vitamin D supplements before and after COVID-19 infection. However, this hypothesis will be supported by research with long follow-up onsurvivors.[10]

The association between hypovitaminosis D, airways inflammation and increased risk of respiratory infections began before the COVID-19 era when a large portion of the studiese valuated the effectiveness of vitamin D supplements as adjunctive treatment of patients with respiratory diseases. In a study Lehouck *et al*. showed that the supplementation of high doses of vitamin D helps in reducing the incidence of COPD exacerbations.[11] Furthermore, a meta-analysis conducted by Martineau *et al*. on 25 Randomized Controls Trials (RCTs) reported that the supplementation of vitamin D reduced the risk of acute respiratory infections and that the protective effects of vitamin D were more pronounced in those individuals with 25(OH)D baseline concentrations below 25 nmol/L at baseline.[12]By contrast, a survival analysis showed that, after 10 days of hospitalization, patients with severe vitamin D deficiency had a chance of 50% mortality, while those with vitamin D≥10 nmol/L had a chance of 5% mortality.[13]

Recommendation

- Vitamin D can be used as prognostic marker in high risk COVID-19patients.
- Supplementation of vitamin D can be justified both in terms of efficacy and health economics in high risk patients.

Limitations of the study

- Small sample size.
- Single center study; only patients admitted in CMH Dhaka were taken for the study. So this will not reflect the overall picture of the country. A large scale study needs to be conducted to reach to a definitive conclusion.
- Sample were taken by purposive method in which question of personal biasness might arise.

Conclusions

In our study, a higher mortality risk was related to lower 25(OH)D levels. Present study concluded that patients with vitamin D deficiency had a significantly higher mortality and morbidity risk. Therefore, vitamin D deficiency can be used as a marker of poor prognosis in COVID 19 patients. This suggests that vitamin D supplementation may protect against the fatal consequences of COVID-19 infections, reduce the severity of the disease and consequently reduce the risk of death.

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