



Vitamin D, A Predictor of Outcome in COVID-19 Patients

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Hypovitaminosis D is a commonly associated with increased prevalence of pulmonary infections. High mortality rate of COVID 19 infections is associated with immune dysfunction like cytokine storm. Many studies show important function of vitamin D in proper functioning of immune system. Very few studies are available to associate vitamin D level and severity of Covid infection, Hence this study was undertaken to find a relation of vitamin D levels and outcome of COVID-19.

Methods: Study design is retrospective observational analytical case control. A study population was hospital base cases and medical examination with clear definition of cases, medical examination, inclusion/ exclusion criteria, outcome and exposure. The Statistical analysis was done to measure the association of outcome (the death or severe disease risk) with exposure (low vitamin D) and that was determined by measuring Odds ratio.

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Results: Most of the patients (45%) were in an age ranging from 40 to 59 years . Maximum number of the patients (68%) have one comorbidity. Diabetes mellitus and hypertension , both present in 28 % and other co morbidity in 40 % of patients and 32% of patient reported to have no comorbidities. Present study reveals vitamin D deficiency in around for 74% of patients. Most of the patients were managed without supplementation of oxygen, but few needed high flow oxygen and even invasive ventilation. However prognosis was good. COVID-19 deaths occurred only in 2% of the cases. All dead patients and patients with a severe disease had vitamin D deficiency. This association of hypovitaminosis D was more significant than other co morbidities including hypertension and diabetes mellitus.

Conclusions: Our study concluded that, two third of patients were having vitamin D deficiency. Study clearly depicts severe vitamin D deficiency is associated with fatal cases, therefore vitamin D level can be used as a predictor of mortality.

Keywords: Poor prognosis; pandemic; respiratory disease; cytokine storm.

1. INTRODUCTION

Disorders due to low vitamin D level are very common, affecting paediatric and geriatric population. Several investigators are agreed upon the association between vitamin D deficiency and disturbed immune system predisposing to severe respiratory tract infections. It was observed further that there is an association between critically serious patients and vitamin D deficiency with bad outcomes like death [1]. Vitamin D is not found in a human dietary source. It is synthesized by human skin and liver in a presence of sunlight. Along with its important role in bone health, as increasing intestinal assimilation of calcium and phosphorus, it has very important action to boost human immune system [2].

Coronavirus disease 19 (COVID-19) is primarily attacks a respiratory tract, with mild to severe clinical presentation including even death. The pathophysiology of this exorbitant fluctuation in clinical presentation is exactly correlated with the cytokine storm. This abnormal cytokine storm is due to underline deficient immune system. Some studies have highlighted role of vitamin D as immune booster [3,4].

Many researches proved positive association of vitamin D and COVID-19 outcomes, while other studies did not prove it [5,6]. For example, Ali et al [7] suggested not sufficient proof on the correlation between vitamin D levels and COVID-19 severity and deaths. Furthermore, there is less evidence on the correlation between vitamin D levels and COVID-19 deaths. In this situation of grave COVID-19 pandemic, studies on vitamin D for COVID-19 are needed. Therefore, this study was undertaken to evaluate the possible correlation between vitamin D levels

and disease severity including mortality in COVID 19 patients.

2. MATERIALS AND METHODS

2.1 Study Design

It is a case control study, Retrospective observational analytical study.

2.2 Study Population

Inclusion criteria include Cases and control as per standard definitions given below, selected from patients admitted in Acharya Vinoba Bhave rural hospital (AVBRH) Wardha from September 2020 up to October, 2020. We included incident cases means newly occurring cases to reduce bias. Hospital based cases and control were selected with anticipating error of getting more severe cases than population. While Exclusion criteria include Previously known and treated patients of Vitamin D deficiency, Prevalent cases to reduce bias

2.3 Definition of Cases and Controls

In the present study patients with a severe disease with or without death are considered as cases and patient with mild disease or without symptoms considered as controls. Patients needing oxygen supplement or ventilatory support or with circulatory events were categorized as severe disease. Patients being managed without oxygen or without circulatory events were considered as mild disease.

Identification of COVID-19 cases was as per guidelines of World Health Organisation(WHO) [1], with a positive result on real-time reverse transcriptase-polymerase P chain reaction (RT-

PCR) assay from nasal and pharyngeal swab specimens.

2.4 Definition of Outcome

Severe disease (as per definition mention above) with or without death considered as outcome.

2.5 Definition of Exposure

Serum vitamin D levels more than 30ng/ml considered as normal and less than 30ng/ml as deficiency (further categorized into mild, moderate and severe 20–29, 10–19, and <10 ng/mL, respectively)¹.

2.6 Sample Size

250.

2.7 Data Collection

A patient both cases and control selected were having positive result on real-time reverse transcriptase-polymerase P chain reaction (RT-PCR) assay for COVID 19 from nasal and pharyngeal swab specimens. Cases and controls selected independent of vitamin D status that is a exposure in this study, Data was retrieved from the medical records of 250 admitted patients in Acharya Vinoba Bhave rural hospital (AVBRH) Wardha from September 2020 up to October, 2020 and it was collected by first Author.

Sample size- 250 Participants included

2.8 Statistical Analysis

Data entry mode was manual. Analysis of data was calculated to measure the association of

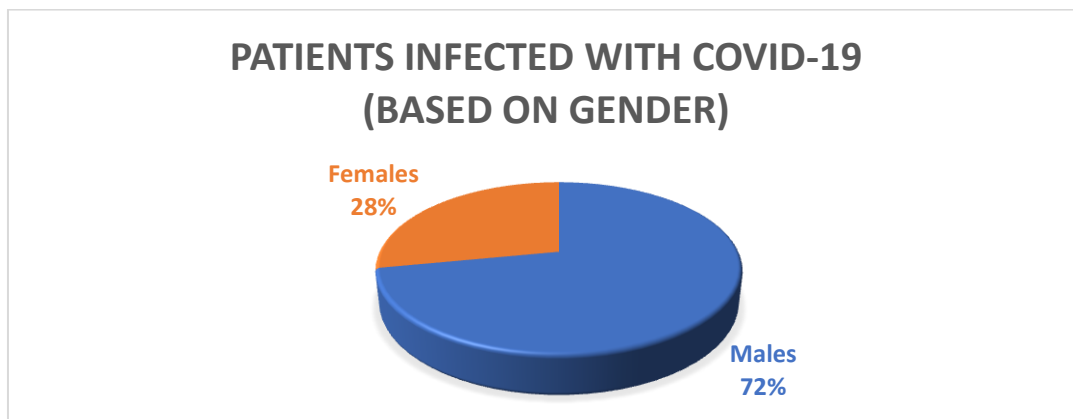
outcome (the death or severe disease risk) with exposure (low vitamin D) and that was determined by measuring Odds ratio (The punctuation should be checked, without space between point/comma and word).

2.9 Project Implementation Plan (Quality Assurances)

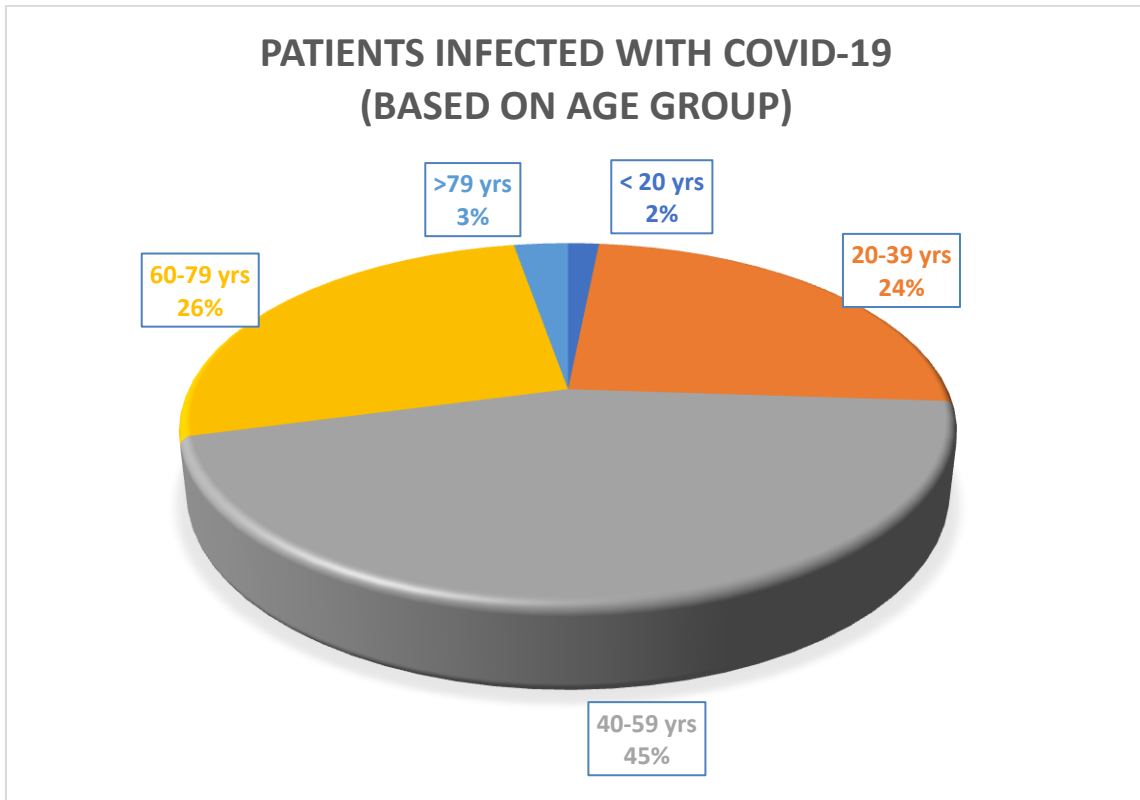
Data was collected objectively assuring reproducibility, accuracy and precision in exposure measurement, as it was from standard laboratory and performed by principal investigator .

3. RESULTS

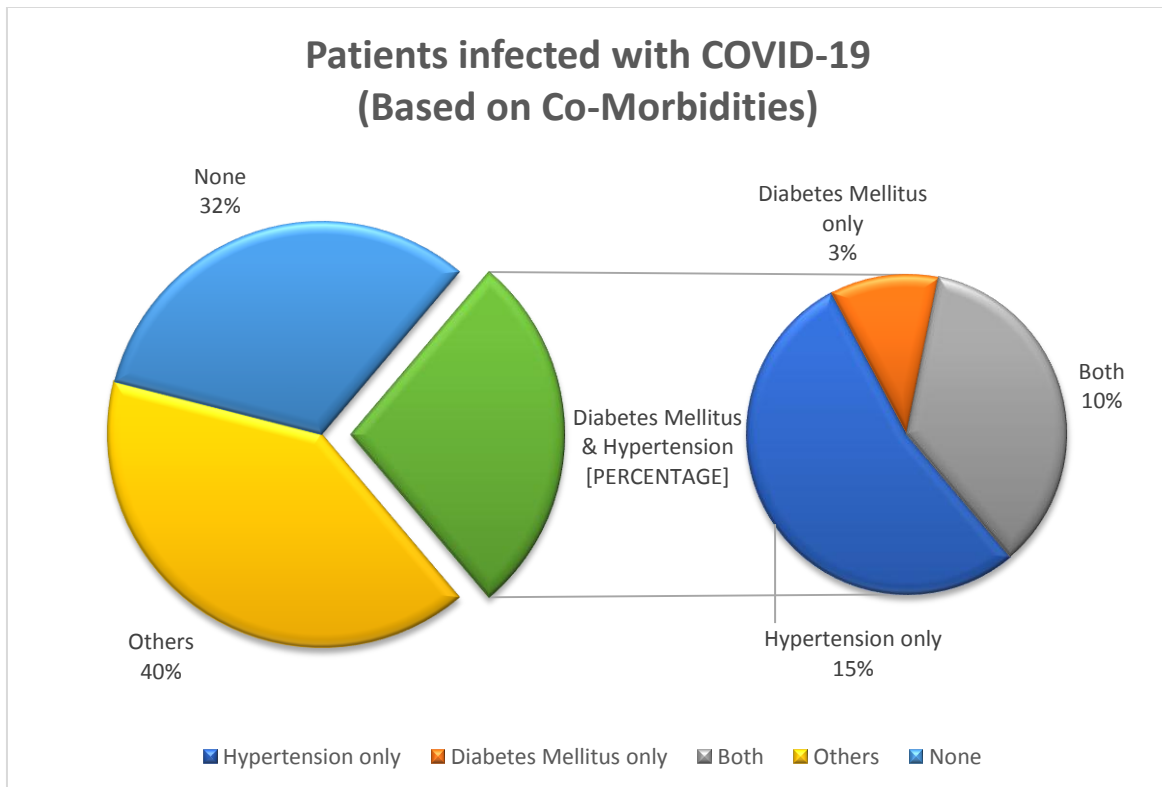
250 patients included in study. Males were outnumbered than women (72% vs 28%) Most of the patients (45%) were in a 40-59 years age range and least in age less than 20., (68%) participants have single associated disease as a comorbidity. 32% of patients reported to have no co morbidity. As per CT severity index 34 percent have severe disease,27% have moderate disease and 39% have mild disease. Around two-thirds of patients had vitamin D deficiency (74%). 10% had severe deficiency and mild and moderate deficiency in 32% each, 21% showed normal levels, while the remaining showed hypervitaminosis D. As per CT severity index 34 percent have severe disease,27% have moderate disease and 39% have mild disease. Above figure shows that all dead patients have severe vitamin D deficiency and age more than 40 years and this association of hypovitaminosis D was more significant than other co morbidities including hypertension and diabetes mellitus. As odds ratio is more than 1 hence hypovitaminosis D is positively associated with death.



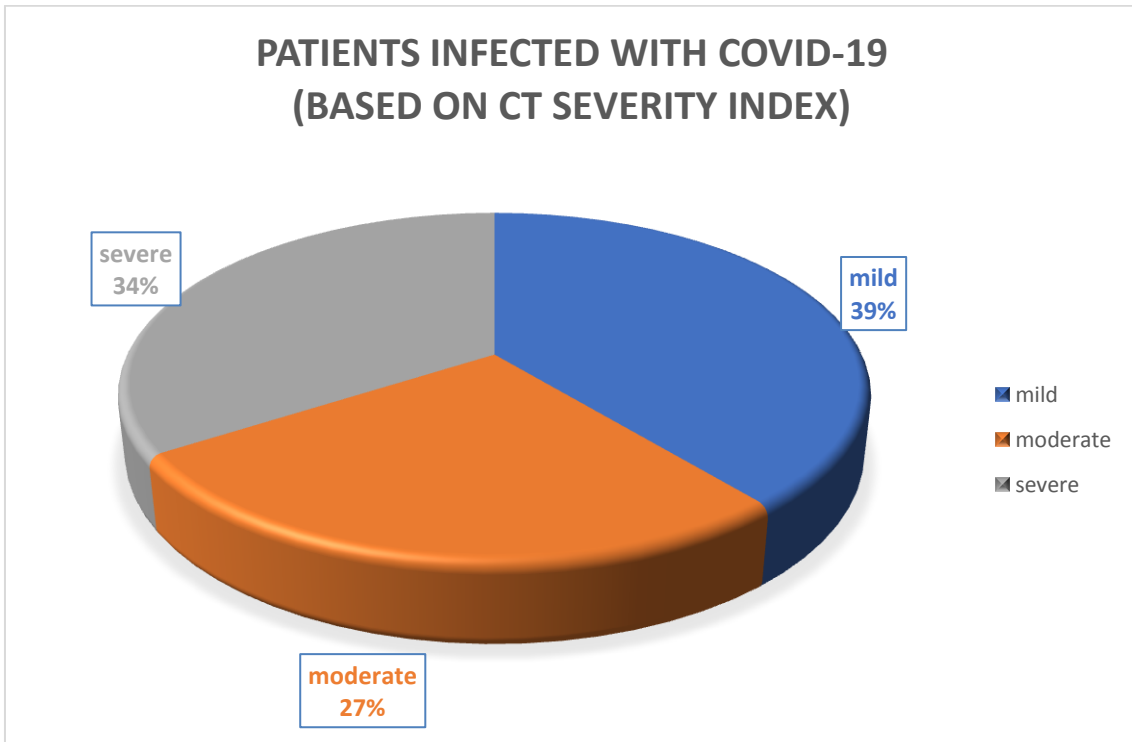
Graph 1. Gender distribution



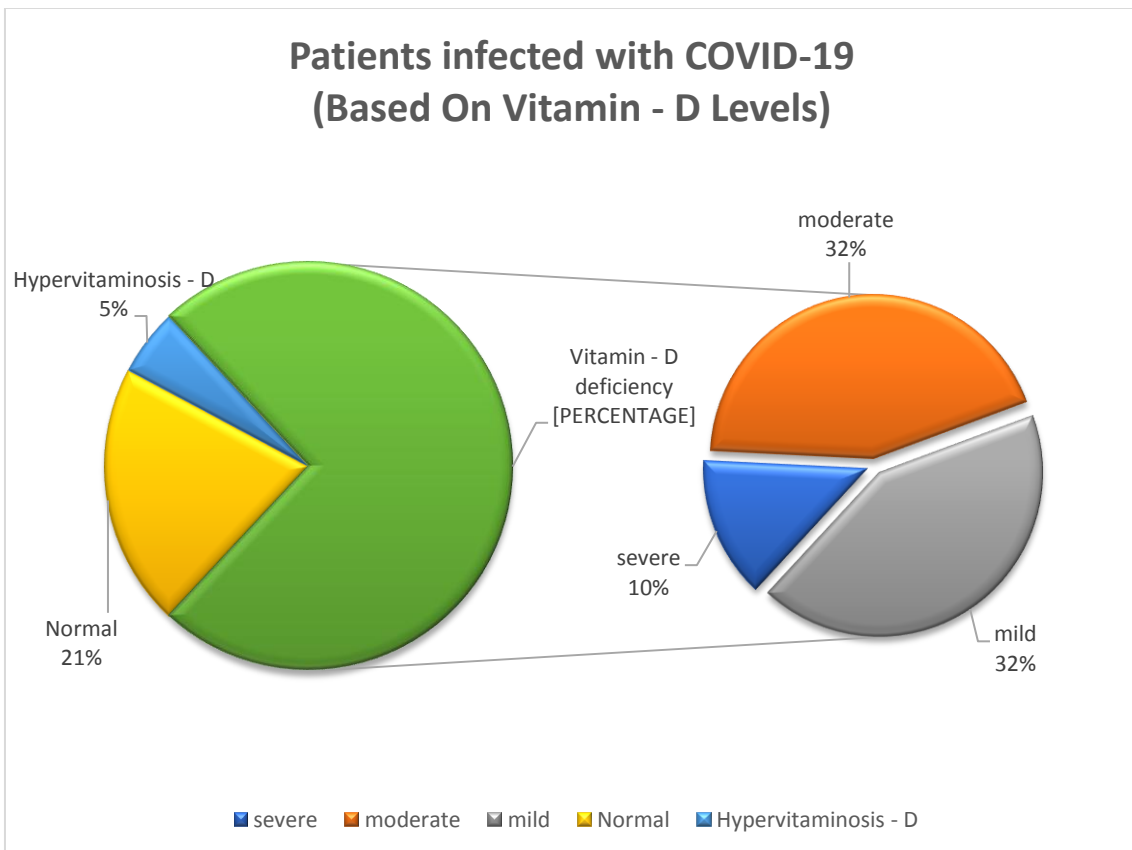
Graph 2. Age distribution



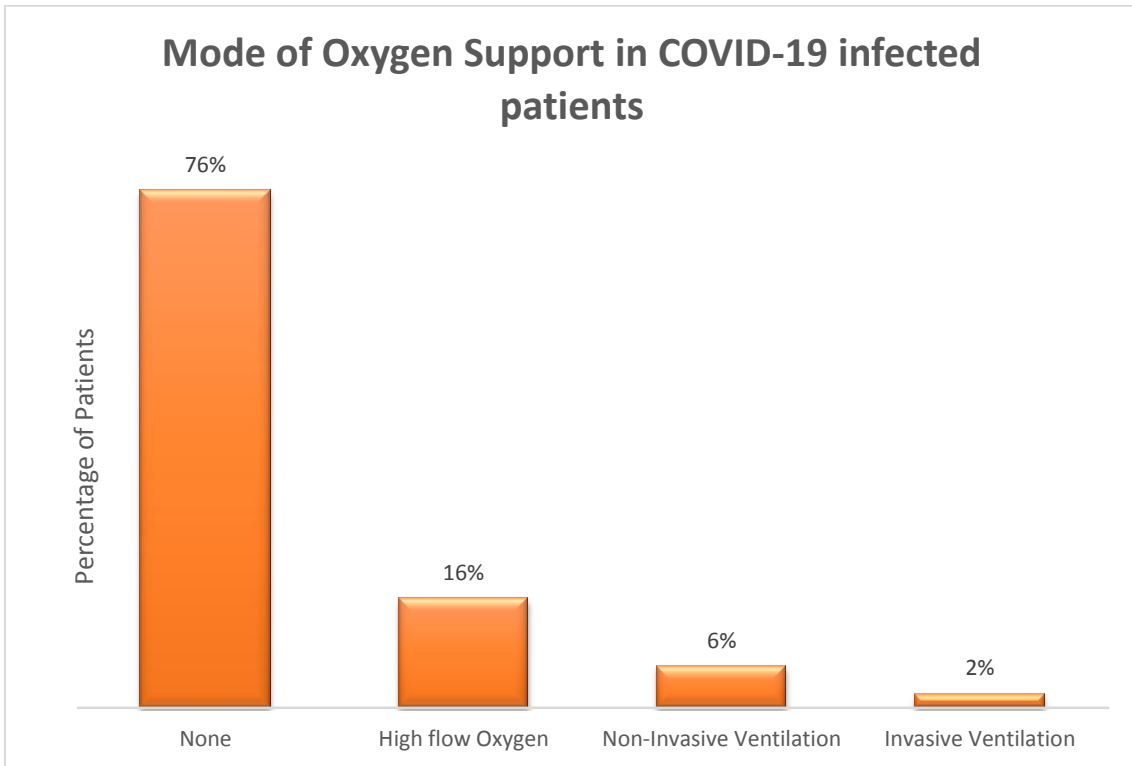
Graph 3. Co-morbidities' distribution



Graph 4. Computerized tomography (CT) severity index

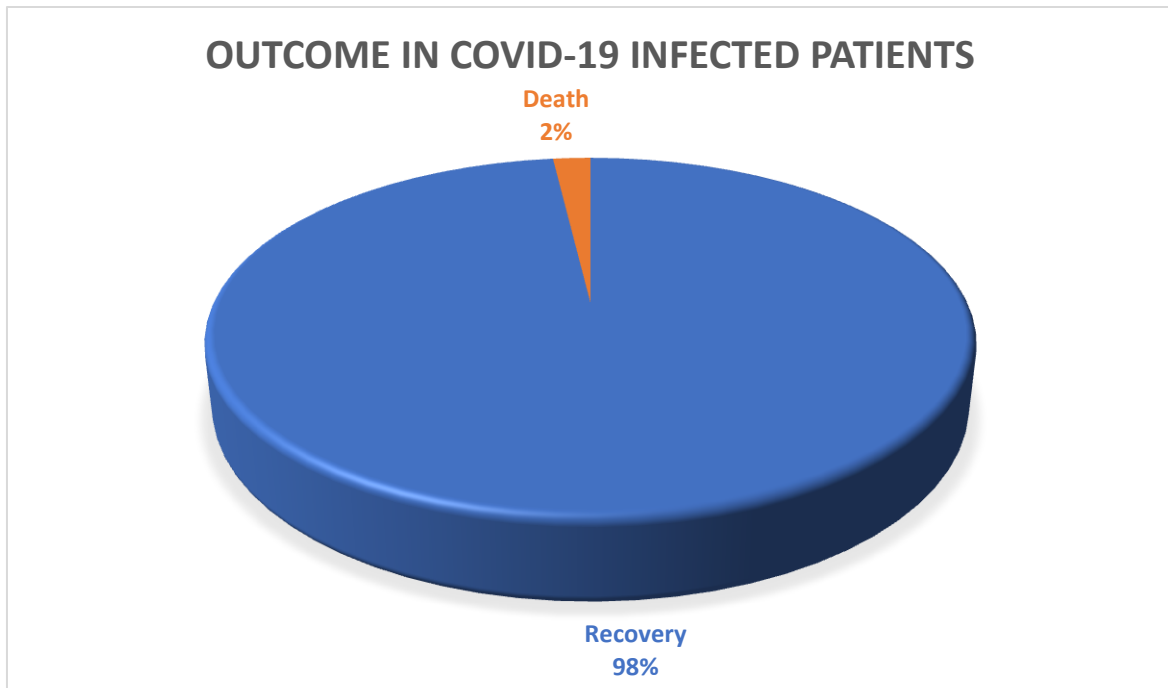


Graph 5. Patients infected with COVID-19 based on vitamin D levels



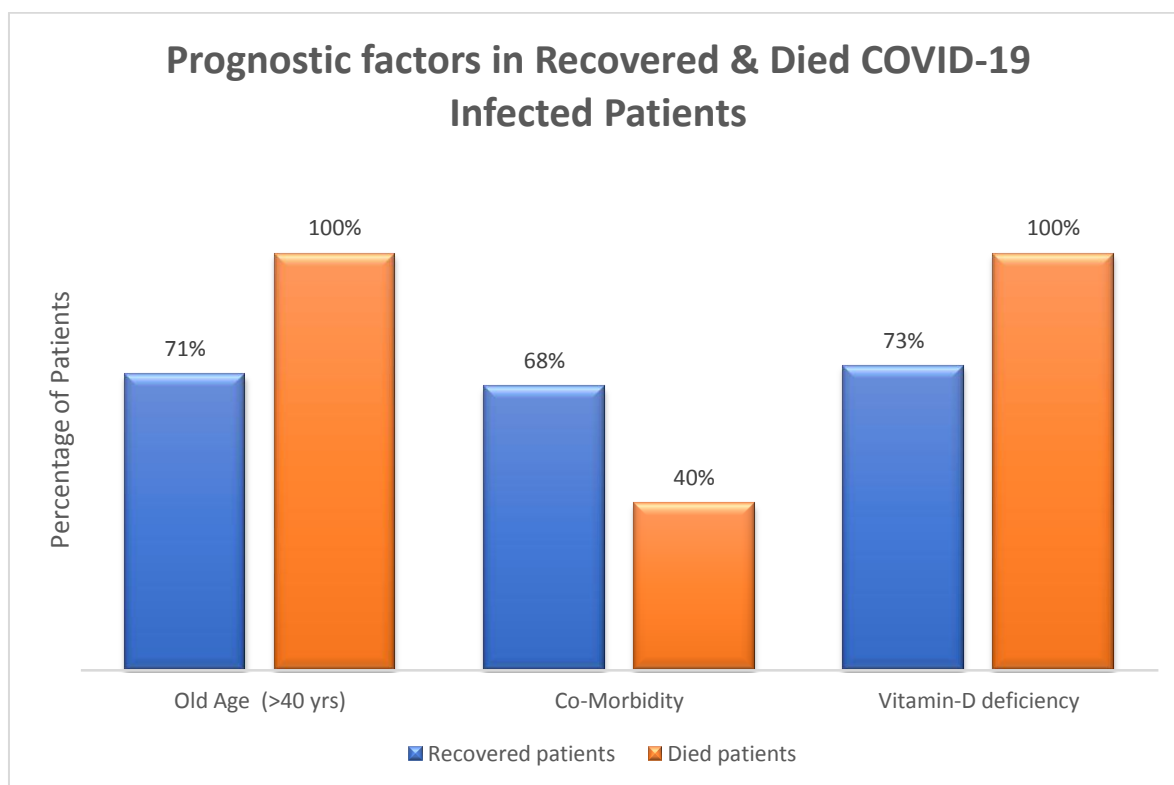
Graph 6. Mode of oxygen requirements in a treatment of COVID-19 patients

Most of the patients (76%) were managed without supplementation of oxygen, 16% patients required high flow oxygen, 6% needed non-invasive ventilation and 2% patients have invasive ventilation.



Graph 7. outcome in COVID-19 patients

Above graph depicts that 98% patients recovered fully, death was in only 2% of cases.



Graph 8. Assessment of prognostic factors

Table 1. Shows association vitamin D deficiency and mortality

	Death	Survived	Total
Hypovitaminosis D	5 (a)	180 (b)	185(a+b)
Normal or hypervitaminosis	0 (c)	65 (d)	65 (c+d)
	(a+c)	(b+d)	(a+b+c+d) 250

odds ratio =1.8

Table 2. Shows association vitamin D deficiency and disease severity

	Severe disease plus death	Asymptomatic or mild disease
Hypovitaminosis D	49	136
Normal or hypervitaminosis	11	54

Odds ratio =1.76

4. DISCUSSION

This was an analytical single centre case control study. It comments on the link in between vitamin D serum level and fatality of COVID19. Males were outnumbered than women (72% vs 28%). (see Graph 1) Most of the patients (45%) were in an age group of 40-59 years followed by the age group of 60-79 years of around 26%. (see Graph 2)

Most of the patients (68%) presented at least one comorbidity. hypertension and Diabetes mellitus

both present in 28 % and other co morbidity in 40 % of patients and 32% of patient reported to have no co morbidity. (see Graph 3) As per CT severity index 34 percent have severe disease, 27% have moderate disease and 39% have mild disease. (see Graph 4)

In around two third of patients were having vitamin D deficiency (74%). 10% had severe deficiency and mild and moderate deficiency in 32% each, 21% shows normal levels and 5% subjects shows hypervitaminosis D. (see Graph 5) Most of the patients (76%) were managed

without supplementation of oxygen, 16% patients required high flow oxygen, 6 % needed non-invasive ventilation and 2% patients have invasive ventilation. (see Graph 6) Fortunately over all prognosis was good.98% patients recovered fully, death was in only 2% of cases. (see Graph 7) all died patient have severe vitamin D deficiency and age more than 40 years and this association of hypovitaminosis D was more significant than other co morbidities including hypertension and diabetes mellitus. (see Graph 8) After calculating Odds ratio it was concluded that hypovitaminosis D was associated with bad prognosis in COVID 19 patients like mortality and severe disease. (see Table 1 and 2)

Giovanna Elisiana Carpagnano et al [1] conducted similar study and obtained results depending on vitamin D serum levels one fifth of patients had normal vitamin D levels, one fourth had mild deficiency, rest have moderate and severe deficiency, Giovanna Elisiana Carpagnano et al¹ also suggested similar findings in their study and proves a strong association of vit D deficiency and bad prognosis in COVID 19 patients. results are comparable to present study.

Dancer RC et al [3] conducted study reveals that vitamin D deficiency association is present who develop acute respiratory distress syndrome (ARDS). This hypovitaminosis supposed to help in creating body environment possibly because of deficient immunity susceptible to ARDS.

Grant WB et al [4], his article explains that prescription of vitamin D can lower the chance of pulmonary infections and subsequent consequences like ARDS and even deaths in COVID 19 patients.

Petre Cristian Ilie et al [5] suggested that severe low vitamin D level is responsible for mortality in aging population of European countries. Lehouck et al [6] also explained the effect of administering high doses of vitamin D to decrease the disease severity and prognosis of chronic obstructive pulmonary disease (COPD). Also, the research indicate that the severe vitamin D deficiency can alter the prognosis.

Although Ali et al [7] suggested no correlation between vitamin D levels and COVID-19 severity and deaths, but they put forth evidence showing protective effect of vitamin D supplementation against pulmonary infections.

Xu Y et al [8] advocated to administer vitamin D to halt disease progression of COVID-19 patients by boosting immunity.

Whittemore PB et al [9] suggested in his research that deaths due to COVID 19 in a country located near to the equator are less than those being far away from it. He postulated it is probably an effect of sunlight ultraviolet radiation , being nearest the equator, which increases vitamin D deficiency. Hence obviously farther places from equator have vitamin D deficiency. More COVID-19 death may be due to less sun exposure.

5. CONCLUSIONS

In around two third of patients were having vitamin D deficiency. Study indicates that vitamin D deficiency is associated with deaths and severe disease manifestations. Therefore it can be used as a predictor of mortality.

6. RECOMMENDATIONS

A universal guideline should be developed to treat vitamin D deficiency in patients with COVID 19.

7. LIMITATIONS

As the sample size is small hence it is recommended to conduct a large multicentred randomised controlled trial including large sample size.

CONSENT

As per international standard or university standard, patient's consent has been collected and preserved by the authors. Confidentiality of data was maintained.

ETHICAL APPROVAL

The study was approved by the Institutional ethics committee of university. (Ethical Committee number: DMIMS (DU)/IEC/2020-21/9128).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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