Vitamin D , a predictor of outcome in COVID-19 patients

Abstract

Introduction:

Low **levels of** vitamin D are ~~is a~~ very commonly associated with increased ~~more~~ probability of pulmonary infections. Present days, are the days ~~of pandemic~~ of the Coronavirus 19 (COVID 19) pandemic. Mortality rate ~~Fatality~~ associated with this disease is because of some sort of immune dysfunction like a cytokine storm (Consider rewriting the sentence. "some sort of…." is not an appropriate expression for a scientific article). Many studies proved the role of vitamin D in the proper functioning of the immune system. Yet ~~But other~~ others did not have any correlation with the disease severity caused by ~~due to~~ COVID 19, (Add . without space after COVID-19) In this situation of ~~grave~~ serious COVID-19 pandemic , (delete space) studies on vitamin D for COVID-19 are immensely needed as there is no specific antiviral available for COVID-19 at present. (Reformulate this part. One suggestion could be adding "there is" before "no specific antiviral") Hence this study was undertaken to find a ~~out~~ relation of vitamin D levels and outcome of ~~due to~~ COVID-19.

Methods:

This is a single centre case control study. There are 250 study participants included in the study suffering from COVID-19, treated in Acharya Vinobha Bhave rural hospital (AVBRH), a tertiary care centre. It was a case control study at Acharya vinoba bhave rural hospital of central India, a tertiary care centre. The study design was **of the type** retrospective observational analytical case control. (Reformulate the Methods part. There are more than on sentence expressing the same idea, but with other words. Check the General Guidelines for Authors. It should be mentioned the

duration of the study) The Study population was hospital base cases and **medical examination** ~~controls~~ with clear definition of cases, **medical examination** ~~controls,~~ inclusion/ exlusion criteria, outcome and exposure. **The** Statistical analysis was performed ~~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. (Methodology not clear. Too many details. "Definition of cases, controls etc" should be mentioned only in Materials and Methods) ~~The study was approved by the Institutional ethics committee of university~~.

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 co morbidity (Reformulate these sentences. Not clear. Check grammar and punctuation (without space before a word and comma or point)). Present study reveals vitamin D deficiency ~~in 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. ~~Fortunately~~ (is not scientific register) over all prognosis was good. Death was in only 2% of cases (Reformulate. One suggestion might be "COVID-19 deaths occurred only in 2% of the cases"). All dead patients and patients with a severe disease had vitamin D deficiency (Start the sentence with a capitalized letter. Reformulate. An example could be "Vitamin D deficiency was observed at patients with a severe disease and the patients who died."). This association of hypovitaminosis D was more significant than other co morbidities including hypertension and diabetes mellitus.

Conclusions

In around (Check the grammar) two third of patients were having vitamin D deficiency. Study clearly depicts severe vitamin D deficiency is associated with deaths. Hence (Use synonyms: For this reason) it can be used as a predictor of mortality.

It is recommended to rephrase this paragraph in a proper scientific register.

Keywords – Poor prognosis, pandemic, respiratory disease, cytokine storm *(inclined, 10 font, justified)*

Introduction

Disorders due to low vitamin D level are also a pandemic, affecting paediatric and geriatric population (It is recommended to add a reference). Several investigators (Reference) are agreed (review tense) upon the connection between ~~connection in between~~ vitamin D deficiency and disturbed immune system predisposing to severe respiratory tract infections. It was observed further that there is an association ~~in~~ between critically serious patients and vitamin D deficiency with bad outcomes like ~~even~~ death[1] (Citations should be indicated by the reference number in brackets [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 , (without space) it has very important action to boost human immune system[2].

Coronavirus disease 19 (COVID-19) is primarily attacks a respiratory tract (Check tense (attacks the 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 ~~Number of~~ studies have highlighted role of vitamin D as immune booster[3,4].

Many researches proved positive association of vitamin D and COVID-19 outcomes (Put the references separately, after positive examples and negative ones), 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 (This sentence expresses the same idea from Ali et al article). In this situation of grave COVID-19 pandemic , studies on vitamin D for COVID-19 are immensely needed as no specific antiviral available for COVID-19 at present (Reformulate). Therefore, this study was undertaken to evaluate the possible correlation between vitamin D levels and disease severity including mortality in COVID 19 patients.

Materials and Methods (Reformulate this part. It seems like it is not completed)

Study design-

Case control study,

Retrospective observational analytical (Formulate a sentence, mentioning the information in just one place)

Study population –

Inclusion criteria

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.

Exclusion criteria

Previously known and treated patients of Vitamin D deficiency

Prevalent cases to reduce bias

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 ~~needed~~ 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 ~~were~~ 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.

Definition of outcome

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

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].

Sample size -250

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

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).

Project implementation plan (quality assurances)

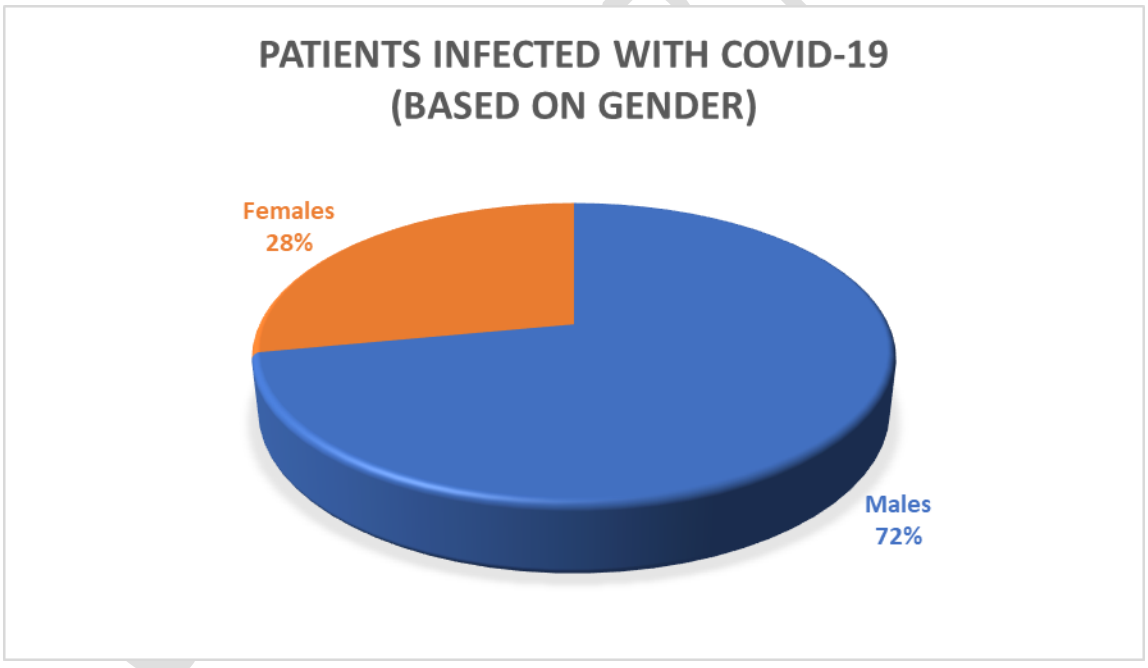
Data was collected objectively assuring reproducibility, accuracy and precision in exposure measurement, as it was from standard laboratory and performed by principal investigator .

Human subject protection

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

Results **(The results should be detailed)**

Graph 1 Gender distribution **(Fig. 1. Gender distribution)**

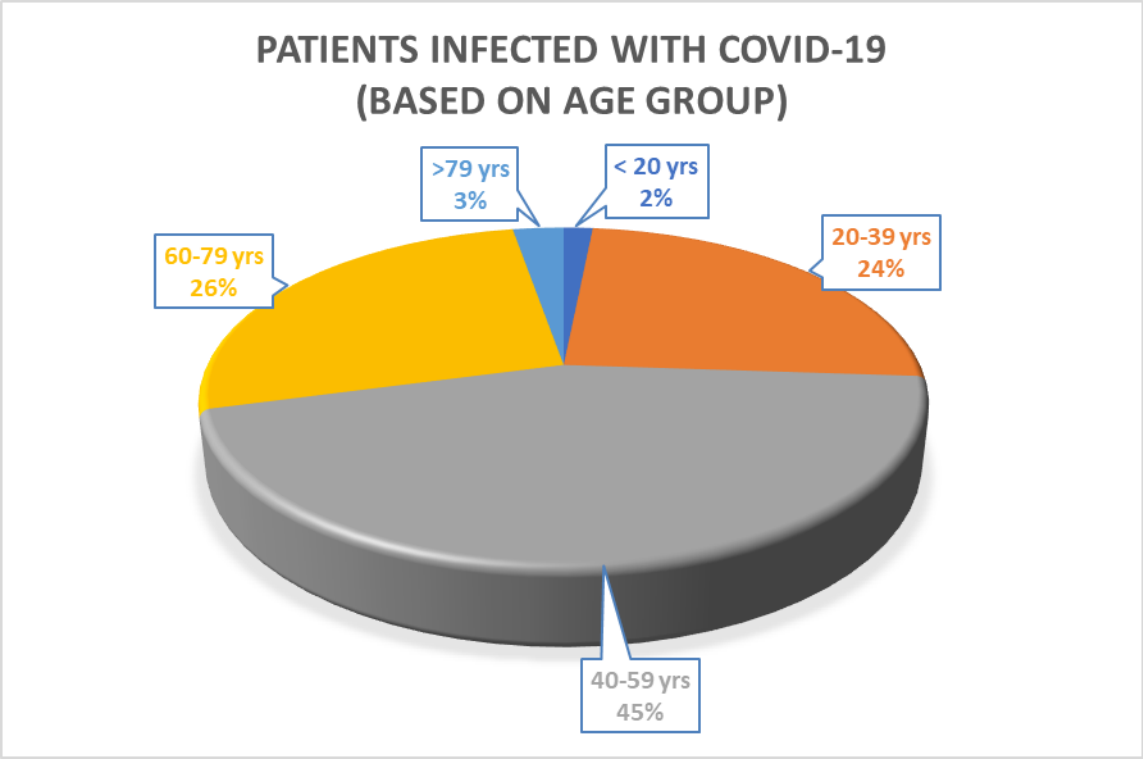


250 patients included in study. Males were outnumbered than women (72% vs 28%)

(Develop the sentences. It is suggested that the discussion about the figures should appear in the

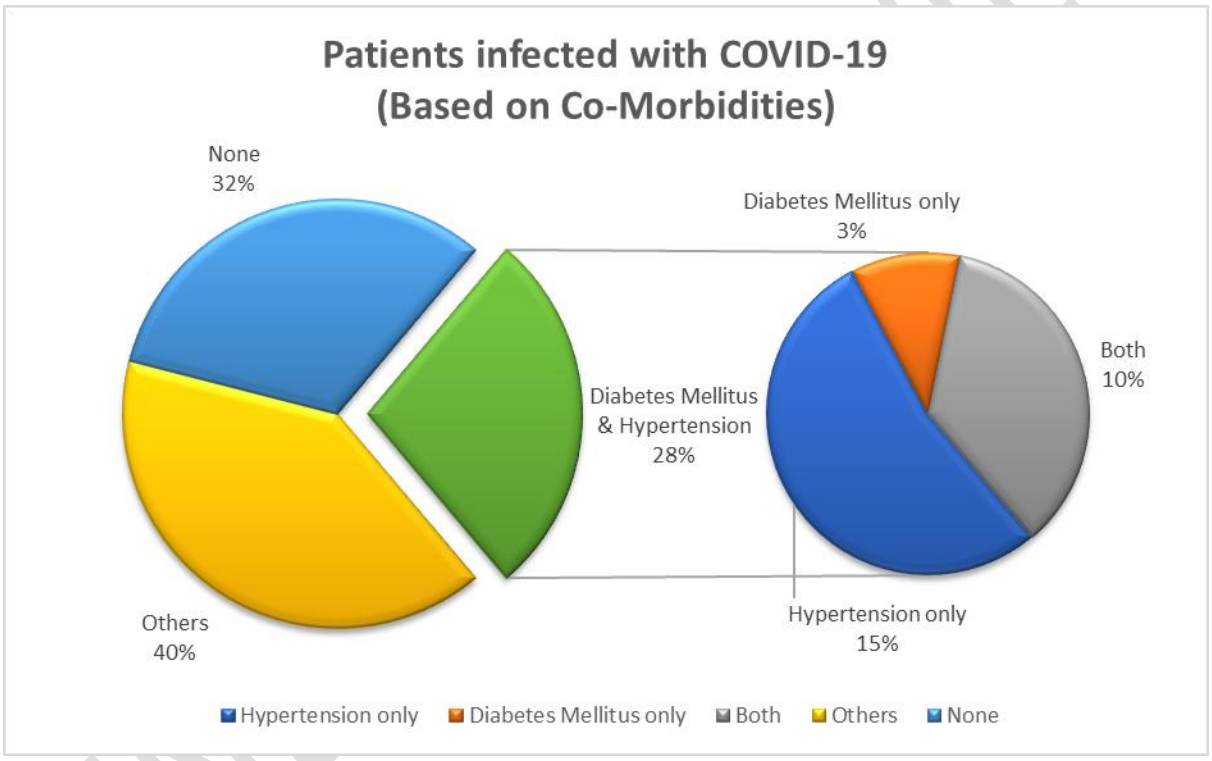
text before the appearance of the respective figures. Figures should be placed inside the text- (72 % vs 28%) (Figure 1)).

Graph 2 Age distribution



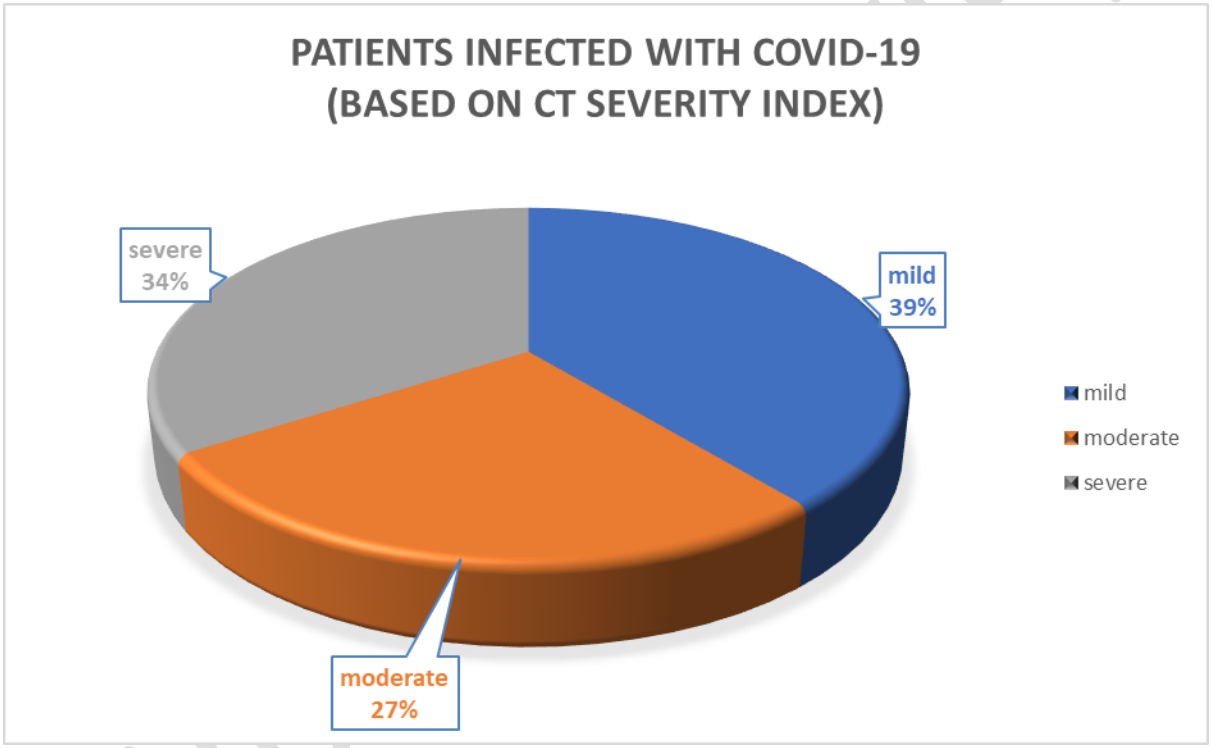
Most of the patients (45%) were in a 40-59 years age range and least in age less than 20.

Graph 3 Co-morbidities' distribution



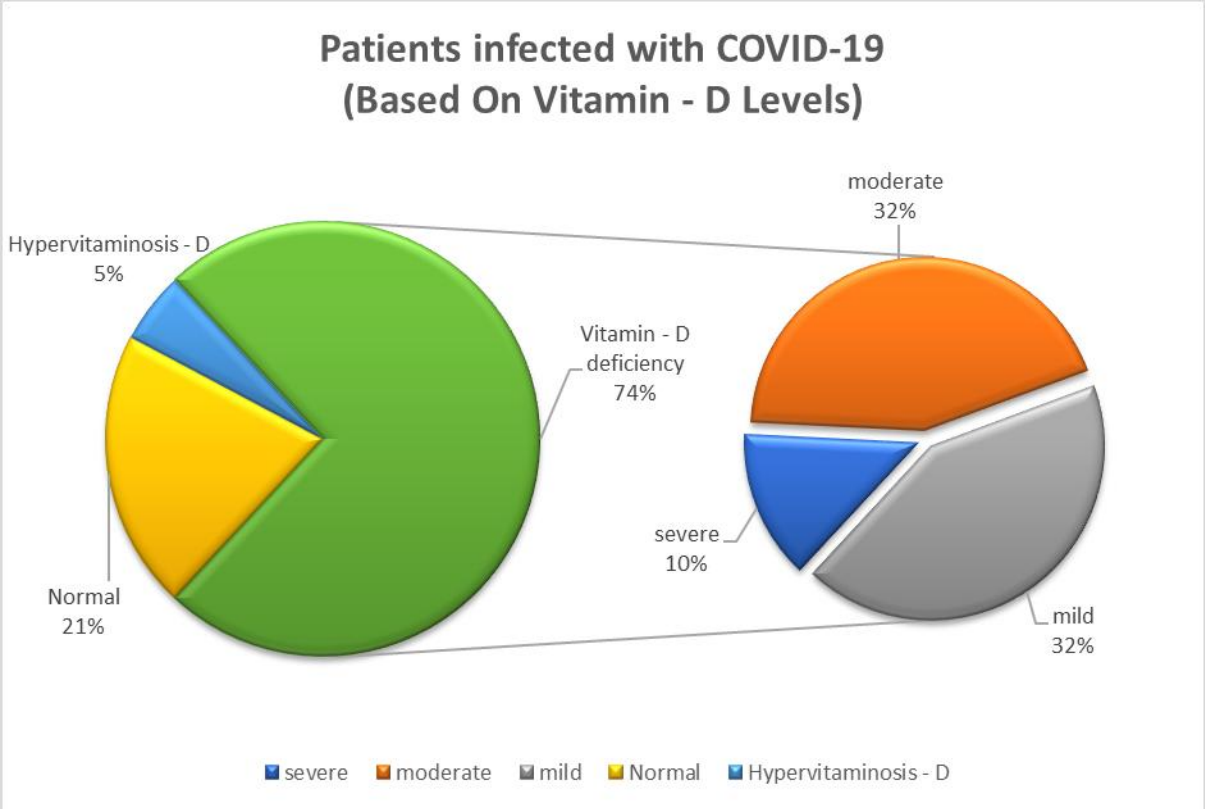
(68%) participants have single associated disease as a comorbidity. 32% of patients reported to have no co morbidity (Reformulare. Leave 68% without ()).

Graph 4 Computerized tomography (CT) severity index (It should be mentioned in Material and Methods)



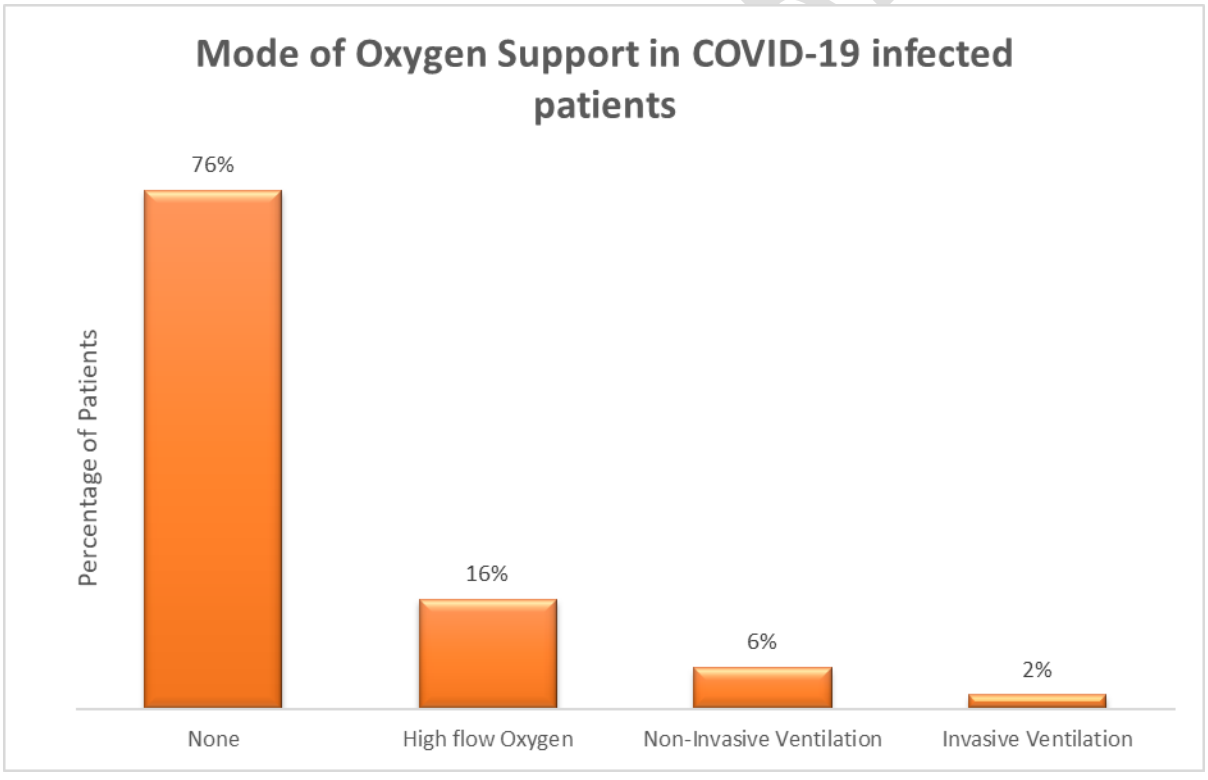
As per CT severity index 34 percent have severe disease,27% have moderate disease and 39% have mild disease.

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



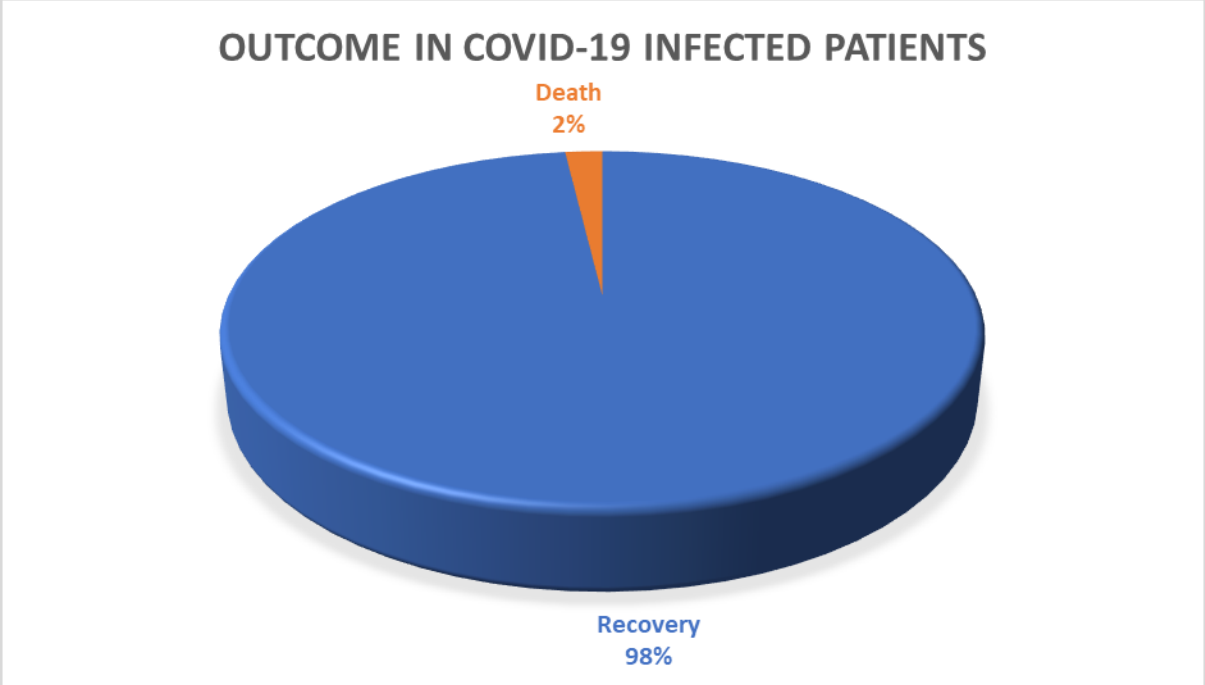
~~In~ Around two-thirds of patients ~~were~~ had vitamin D deficiency (74%). 10% had severe deficiency and mild and moderate deficiency in 32% each, 21% showed ~~shows~~ normal levels, while the remaining ~~and~~ 5% of subjects showed ~~shows~~ hypervitaminosis D.

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.

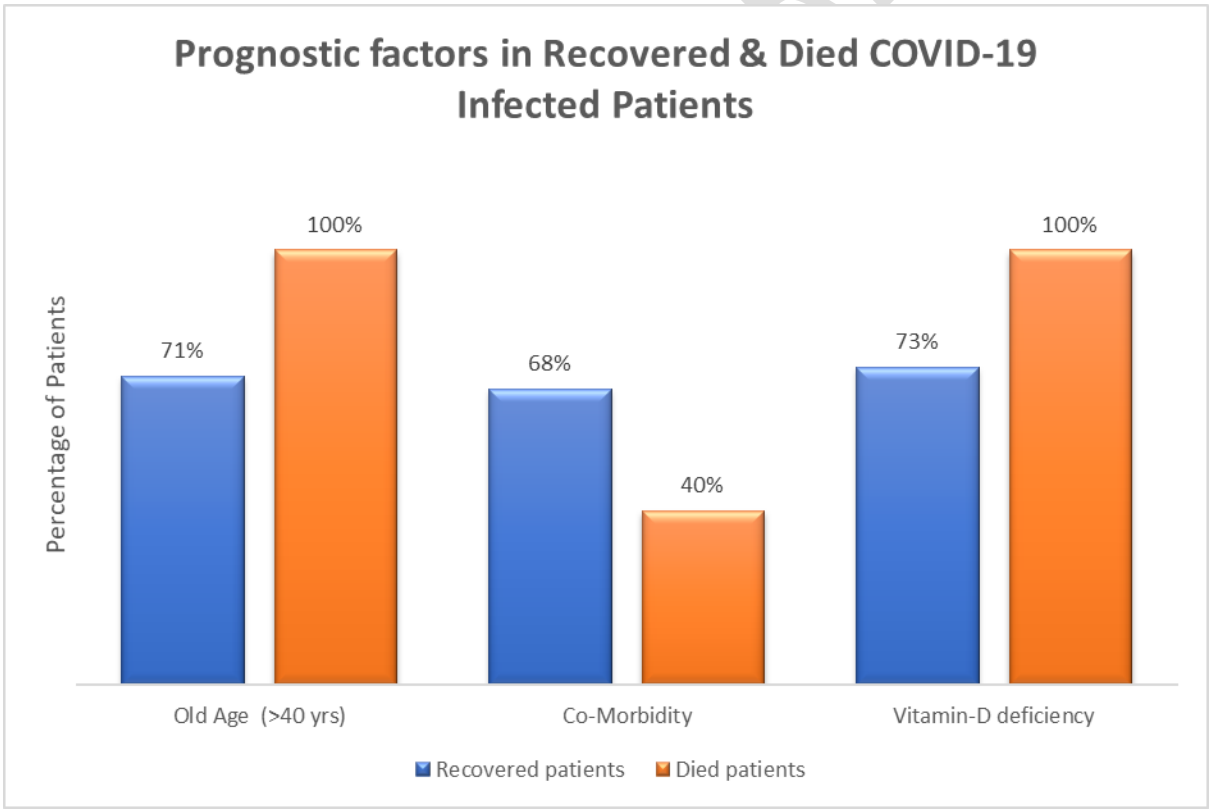
Graph 7 outcome in COVID-19 patients



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

All five ~~5~~ fatalities (It is not clear which are the five fatalities) had ~~were having~~ severe vitamin deficiency with ~~having~~ levels of vitamin D less than 10 ng/ml.

Graph 8 Assessment of prognostic factors



Above figure shows that all dead patients ~~in 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.

Table 1 shows association vitamin D deficiency and mortality (It is not clear if the sentence is the title of the table or is part of the results. No tables should be given without discussion or reference inside the text. Discussion about the tables should appear in the text before the appearance of the respective tables)

	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 =1.80

as odds ratio is more than 1 hence hypovitaminosis is positively associated with death (Explain and reformulate. Not clear).

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

as odds ratio is more than 1 hence hypovitaminosis is positively associated with severe disease or death.

Discussion (Reformulate. The discussion should not repeat the results, but provide detailed interpretation of data)

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 al[1] 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 (Not clear. Verify punctuation, use capitalized letters to begin a sentence).

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 ~~administration of~~ high doses of vitamin D to decrease the ~~in decreasing~~ disease severity and prognosis of chronic obstructive pulmonary disease (COPD). Also, the research indicate ~~depicts~~ 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 ~~outcome of~~ research that deaths due to COVID 19 in a country located near to the equator are less than those being far ~~that~~ away from it. He postulated it is probably an effect of sunlight ultraviolet radiation ~~of sunlight~~, being ~~is~~ nearest ~~more near~~ 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.

Conclusions (Reformulate)

In around two third of patients were having vitamin D deficiency. The Study ~~clearly~~ ~~depicts~~ indicates that vitamin D deficiency is associated with deaths and severe disease manifestations. Hence (Use synonyms like Therefore) it can be used as a predictor of mortality.

Recommendations

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

Limitations

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

References

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