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VITAMIN D STATUS AND COVID 19 CLINICAL OUTCOMES WITH VARIOUS LABORATORY PARAMETERS: A RETROSPECTIVE STUDY AT TERTIARY CARE COVID HOSPITAL, AHMEDABAD.

Pathology

Dr. Hinal K. Gajjar Assistant Professor, Department of Pathology, Smt. NHL Municipal Medical College Ahmedabad,

Dr. Divya D. Patel* 3rd Year Resident, Department of Pathology, Smt. NHL Municipal Medical College Ahmedabad *Corresponding Author

Dr. Minesh B. Gandhi Associate Professor, Department of Pathology, Smt. NHL Municipal Medical College Ahmedabad

ABSTRACT

A novel coronavirus named 'COVID-19' by WHO that began at the starting of December 2019 in Wuhan City, China. The present review aimed to summarize the association between vitamin D levels and risk of covid 19 infection and relation between vitamin D levels and CRP and D-Dimer. **Methods:** A retrospective observational study was conducted on the RT-PCR positive patients from April 2020 to December 2020.Total 450 patients were included and divided into four groups according to their vitamin D levels: Group I (0-10 ng/ml), Group II (10-20 ng/ml), Group III (20-30 ng/ml), and Group IV (vitamin D > 30 ng/ml).The aim of this study was to know the relation between covid 19 morbidity and mortality and vitamin D levels **Result:** Out of 450 patients,396 patients were recovered and 54 patients were expired. Male to female death ratio was 10: 1. The number of patients with increased CRP and D-DIMER were 83.77% and 73.33% respectively. As mentioned above, the patients were divided in to four groups according to their vitamin-D level: Group I: 51 patients (11.33%), Group II : 216 patients (48%), Group III : 82 patients (18.22%)and Group IV : 101 patients (22.44%). which means 349 patients were having low Vitamin-D level and rest (101) having normal vitamin-D level. **Conclusion:** Vitamin D supplementation has been shown to have protective effects against covid 19 infection. It is observed that vitamin D deficiency is associated with higher morbidity and mortality of covid 19 and longer hospital stay.

KEYWORDS

COVID-19, Vitamin D, Immunity, Mortality, Hospital stay.

INTRODUCTION:

A novel coronavirus (CoV) named '2019-nCoV' or '2019 novel coronavirus' or 'COVID-19' by the World Health Organization (WHO) that began at the Starting of December 2019 near in Wuhan City, Hubei Province, China [1–4]. Clinical or demographic risk factors for severe disease include older age, male sex, and chronic health conditions, like diabetes mellitus and cardiovascular disease. Recognizing markers of disease severity may thus profoundly help to detect at-risk patients. Some studies have reported that C-reactive protein (CRP) levels, D-Dimer levels and other laboratory parameters can be used in the early diagnosis [5]. The outbreak of COVID-19 has created a global public health crisis. Little is known about the protective factors of this infection. Therefore, preventive health measures that can reduce the risk of infection, progression and severity are desperately needed. [3,4]In the past decade, several studies demonstrated a potential link between vitamin D deficiency and various diseases, including systemic infection [6], [7], [8]. Vitamin D insufficiency affects the immune functions as vitamin D exerts an immunomodulation role [9], increasing innate immunity by secretion of antiviral peptides [10], [11], which improves mucosal defenses. Low vitamin D levels have been associated with an increase in inflammatory cytokines and a significantly increased risk of pneumonia and viral upper respiratory tract infections. Existing data suggest that the severity of the disease caused by SARS-CoV-2 largely depends on an individual's immune response, which can be significantly impaired by the comorbidities [12]. Vitamin D deficiency has been found to occur more frequently in patients with obesity and diabetes. These conditions are reported to carry a higher mortality in COVID-19.[13,14]The primary role of vitamin D is to boost the immunity and ease inflammation and this is probably why there are suggestions on increasing vitamin D intake to prevent COVID-19.[13] A weak innate immune response can lead to an increased SARS-CoV-2 viral load, resulting in an over-activation of the adaptive immune system and a massive production of pro-inflammatory cytokines such as IL (interleukin)-2, IL-6, IL-17, IL-21, IL-23 and IL-10 as well as an increase C-reactive protein (CRP) and d-dimer levels [15] So, early and effective predictors of clinical outcomes are urgently needed to improve management of covid-19 positive patients. This review has discussed the possible roles of vitamin D in reducing the risk of COVID-19 infections and severity.

MATERIAL AND METHODS:

A retrospective observational study from the laboratory and medical records was conducted on the patients who were RT-PCR Positive and were admitted from April 2020 to December 2020, during the first wave of the covid, at the tertiary care hospital. In this retrospective study total 450 patients were included. These covid patients were underwent testing of multiple laboratory parameters e.g, CBC, coagulation profile, D-Dimer, CRP, IL-6, Serum ferritin level, prolactin, fibrinogen level and vitamin D level.

Out of this we included CRP, D-Dimer, vitamin D in this study. Clinical or demographic risk factors for severe disease include older age, sex, ICU admissions, chronic health conditions especially diabetes mellitus, cardiovascular disease are also analysed and grouped. The days from which the patients were admitted till the time they were discharged following a negative RT PCR test was recorded as the duration of hospital stay. In this study, COVID-19 patients were divided into four groups according to their vitamin D levels: Group I: severe vitamin D deficiency (0-10 ng/ml), Group II : vitamin D insufficiency(10-20 ng/ml), Group III : vitamin D deficiency (20-30 ng/ml), and Group IV : normal vitamin D (vitamin D > 30 ng/ml). The cut off for C- reactive protein and D-Dimer is <0.6 mg/dl and 0.5 mcg/ml respectively.

RESULTS:

The total numbers of patients enrolled in the study was 450 patients of which 396 (88%) patients were recovered and 54 (12%) patients were expired.

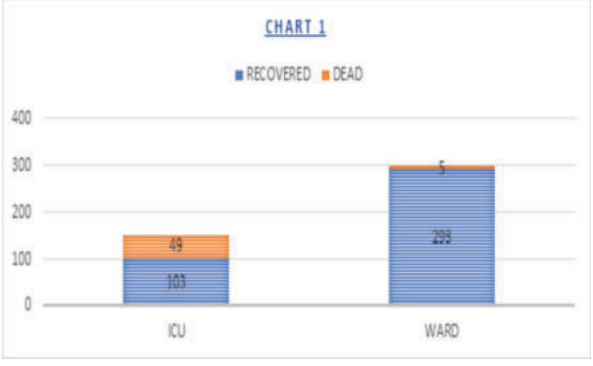
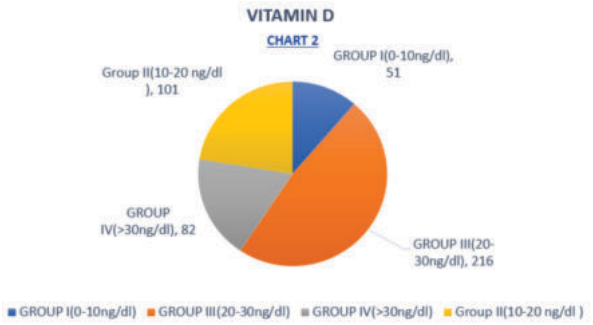
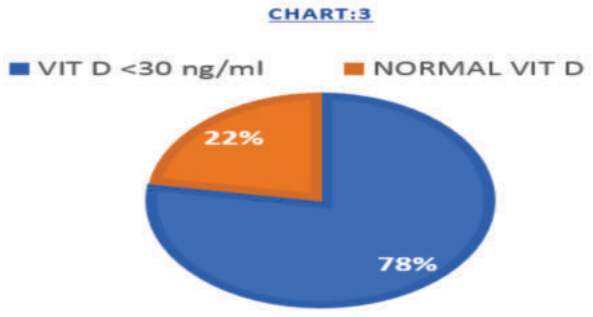
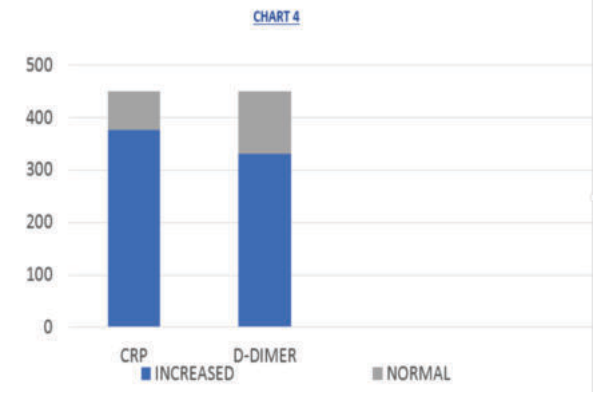


CHART 1 : Total 152(33.77%) patients were admitted in Intensive care unit(ICU)From them 49 patients were died And 298(66.33%) were admitted in ward out of them 5 patients were died. Male to female ratio observed was 2.5:1 and male to female death ratio was 10:1(out of total 54 dead patients 5 were female and 49 were male). Out of 450 patients 222(49.33%) were diabetic, 175 (38.88%) were hypertensive.





As mentioned above **[CHART: 2],** the patients were divided in to four groups according to their vitamin-D level: Group I: Had severe vit D deficiency (0 to 10 ng/ml) were 51 (11.33%), Group II: Had vitamin D insufficiency (10-20 ng/ml) were 216(48%), Group III : Had vitamin D deficiency (20-30 ng/ml)were 82 (18.22%)and Group IV : normal vit D (> 30 ng/ml) were 101(22.44%). which means 349 (77.55%) patients were having low Vitamin-D level and rest of having [101(22.44%)] normal vitamin-D level as shown in **CHART [2 & 3]**



The cut off for C- reactive protein and D-Dimer was <0.6 mg/dl and 0.5 mcg/ml respectively. The number of patients with increased CRP were 377(83.77%) and 73(16.22%) patients were having normal CRP levels. 330 (73.33%) patients were showing increased D-Dimer and 120 (26.66%) patients were having normal level**. [As shown in CHART 4]**

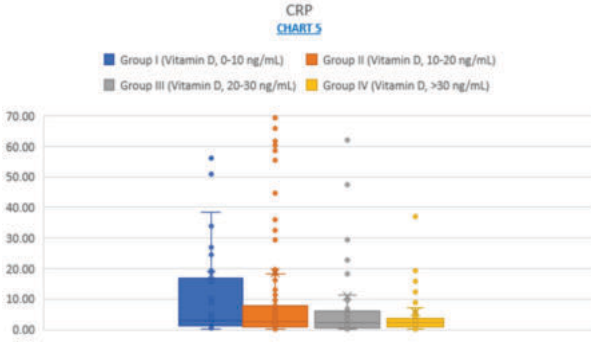


CHART:5 CRP Value of covid 19 positive patients. From this study we can observe a direct relationship between CRP with vitamin D level. As vitamin D level decreased, the level of CRP increased **(see above)**

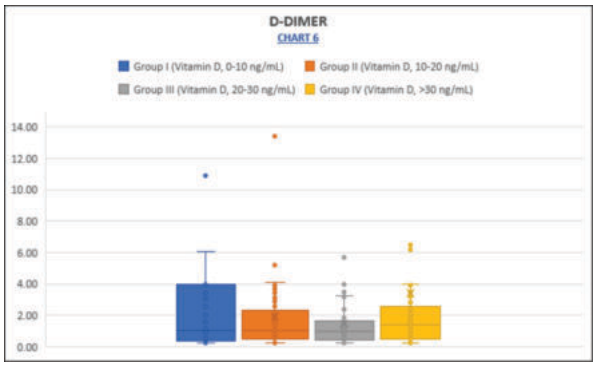
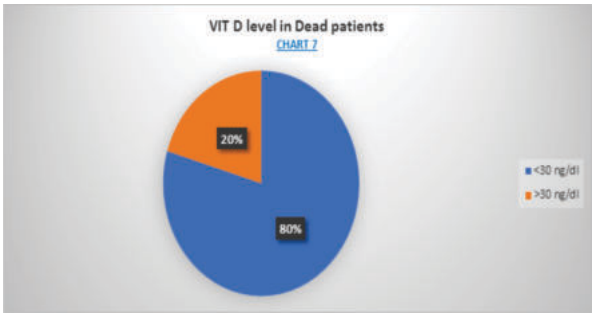
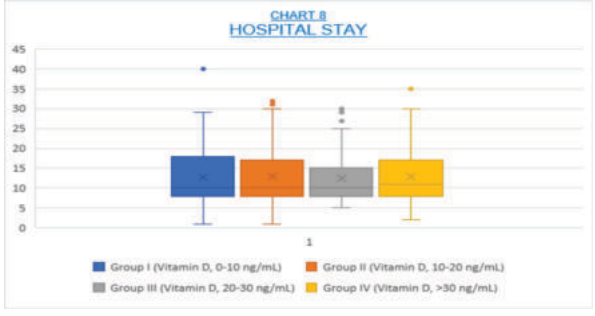


CHART:6 D-DIMER Value of covid 19 positive patients. From this study we can observe a direct relationship between D-DIMER with vitamin D levels. As vitamin D level decreased, the level of D-DIMER increased. **(see above)**



Vitamin D level in dead patients :80% (43) of dead patients were having low Vitamin D levels. Only 20% (11) of them having normal Vitamin D level(**as shown in chart 7**). Vitamin D deficiency has been suggested to favour a poorer outcome of covid-19



From **CHART:8 [see above]** It is observed that patients with vitamin D deficiency exhibit a longer hospital stay

DISCUSSION:

The outbreak of coronavirus disease.2019 (COVID.19) is a leading cause of death worldwide. Severe patients with COVID.19 are generally treated in the intensive care unit, while mild or non.severe patients treated in the usual isolation ward of the hospital. Clinical studies demonstrated that altered levels of some blood markers might be linked with the degree of severity and mortality of patients with COVID.19. [16,17] Of these clinical parameter, serum C.reactive protein (CRP) has been found as an important marker that changes significantly in severe patients with COVID.19. [18,19,20] From this study we observed a direct relationship between CRP and Vitamin D status that low vitamin D status exacerbates inflammation, as measured by markers of inflammation such as CRP. Altered level of CRP and D-DIMER were associated with high mortality, morbidity and longer hospital stay. The severity of coronavirus 2019 infection (COVID-19) is determined by the presence of pneumonia, severe acute respiratory distress syndrome (SARS-CoV-2), myocarditis, microvascular thrombosis and/or cytokine storms, all of which involve underlying inflammation. A principal defence against uncontrolled inflammation, and against viral infection in general, is provided by T regulatory lymphocytes (Tregs). Treg levels have been reported to be low in many COVID-19 patients and can be increased by vitamin D supplementation. Low vitamin D levels have been associated with an increase in inflammatory cytokines and a significantly increased risk

of pneumonia and viral upper respiratory tract infections.[21] Vitamin D deficiency is associated with an increase in thrombotic episodes, which are frequently observed in COVID-19. Vitamin D deficiency has been found to occur more frequently in patients with obesity and diabetes. These conditions are reported to carry a higher mortality in COVID-19. The anti-thrombotic effects of vitamin D on these thrombogenic and anti-thrombogenic components of the coagulation system have been very well documented [22,23,24]. A recent study demonstrated the association of low vitamin D levels with the development of deep venous thromboembolic (DVT) events in patients with ischemic stroke [22].

Table 1

Parameters	COVID-19	Vitamin D deficiency
IL-6	Increased	Increased
TNF-α	Increased	Increased
IFNγ	Increased (late in course)	Increased
C-reactive protein	Increased	Increased
D-dimer	Increased	Increased
Innate immune response	Decreased	Decreased
Th1 adaptive immune response	Increased (late in course)	Increased
Cytokine storm	Increased	Increased
ACE2 expression	Decreased	Decreased
Coagulability	Increased	Increased

Table 1: Biochemical correlations between COVID-19 and vitamin D deficiency. Data composed from [25], [26], [27], [28], [29], [30], [31], [32], [33].

CONCLUSION:

Prevention and early diagnosis of Covid 19 is seriously needed to reduce mortality and morbidity of patients affected worldwide. It is important to understand the reason behind severity and fatality of covid 19, therefore improvement of immunity through better nutrition might be a considerable factor. Vitamin D supplementation has been shown to have protective effects against respiratory tract infections; therefore, people who are having vitamin D deficiency are at the higher risk of developing covid-19 and its complications during this global health crisis. People with vitamin D deficiency during this global pandemic should consider taking vitamin D supplements to maintain the circulating 25(OH)D3(25-hydroxyvitamin D3) in the optimal levels (75–125 nmol/L). From this study we can also conclude that vitamin D deficiency is associated with higher risk of COVID-19 hospitalization and longer duration of hospital stay.

Abbreviations:

SARS-CoV-2: Severe acute respiratory syndrome corona virus 2
IL: Interleukin
CRP:C-Reactive protein
Tregs: Regulatory T cell
TNF-α: Tumor necrosis factor α
IFNγ: Interferon γ

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