RELATION BETWEEN VITAMIN D AND THE SEVERITY OF COVID-19

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Abstract:

Acute respiratory disorders which caused by infection with COVID-19 resulted in problems in societies health care system in worldwide. Deficiency of vitamin D correlated with COVID-19 risk and vitamin D providing reduced respiratory infections. Vitamin D considered as essential modulator for innate and adaptive immunity. In current study ,sixty patients attended private clinics in Diwaniyah city are involved, according to the severity of disease patients divided into three groups.Vitamin D concenterations were estimated in blood for patients and healthy persons (as control group) .Results showed significant decrease in vitamin D concenterations in patients compared to control group.regarding the relation between concenteration of vitamin D and disease severity ,results recorded significant decrease in vitamin D concenteration in moderate and severe infection with COVID-19 in comparison with mild infection while non significant difference between moderate and severe infection . It is concluded the important relation between disease severity and vitamin D concenterations.

Keywords: *Vitamin D,COVID-19,Immunity,Cytokines.*

Introduction:

Vitamin D has essential role in calcium homeostasis and immune system,also has anti- inflammatory,immunomodulatory,antioxidant and antifibrotic effect(1) . Receptors of vitamin D VDR are found in skeletal muscles and the deficiency of vitamin D may cause muscle fibers degeneration (2).Vitamin D regulates calcium-phosphate homeostasis,therefore deficiency of vitamin D led to bone density reduction and may increase bone fractures(3). Presence of VDR in cardiomyctes and smooth muscles cells in blood vessels indicates the crucial role of vitamin D in vascular functions (4) .Low vitamin D levels promote the of multiple cancers development and the administration of vitamin D inhibits angiogenesis (5).

Vitamin D has important role in inflammation by increasing IL-10 cytokine and lowering cytokines TNF-α and IFN-γ (6). Vitamin D binding with receptors of vitamin D VDR stimulating several genes related to innate immunity (7) . VDR modulates immunity process such as stimulation of T-cell tolerance and anti-microbial activity .Vitamin D signaling can activates many genes which are targeted by vitamin D in immune cells (8).It is reported that vitamin D activates the expression of cathelicidin as antimicrobial protein, and thus enhanced autophagy , in addition to that vitamin D synthesis by macrophages and dendritic cells suppressed Th1 and Th17 cells (9) . VDR associated with B cell activity stimulation, decreases their proliferation rate and promoting IL-10 secretion,therefore activation of Th1 suppressed and lowered inflammation(10) . Vitamin D lowers harmful effects of viral pneumonia that caused by viruses such as SARS,MERS and influenza A(11) , also it noticed that high IL-6 and D-dimer levels related to deficiency of vitamin D and these factors resulted in poorer clinical outcomes in hospitalized patients(12). Vitamin D increase cytokines production,it was found that vitamin D directly stimulated IL-13 transcription,also vitamin D augmented the secretion of chemokines CCL3,CCL4 and CCL8(13).Monocyte activity enhanced by vitamin D ,also the ampilification of CYP27B1 activity stimulated ,and promoted the process of gene expression in monocytes(14).

Vitamin D and COVID-19:

Vitamin D plays significant role in the prevention of viral infection and inflammmation due to its immunoregulatory function by receptors of vitamin D,on the other hand, certain immune cells can manufacture vitamin D(15) . Researchers reported that vitamin D lowered the production of cytokines interleukin-2 and interferon gamma,also vitamin D acted as anti-inflammatory and immunomodulatory factor,in addition viral respiratory infections decreased after vitamin D treatment(16) .Vitamin D concenteration may related to some factors such as skin colour ,it was found that low vitamin D present at high rates among persons with dark skin , also persons living in high altitudes and health care workers(17).It was reported that deficiency of vitamin D correlated to the severity and mortality of the disease(18),and it was found that low levels of vitamin D have negative correlation with

COVID-19 severity in Europe (19). It was noticed that SARS-CoV2 caused severe lower respiratory symptoms (20) and more hospitalized patients have vitamin D deficiency(21). Deficiency of vitamin D may resulted in high mortality in patients. Providing Vitamin D to the patients may lower symptoms. Calcitriol has inhibitory effect against SARS-CoV2(21,22).

Occurance of viral disease such as influenza,hepatitis and COVID-19 were related to the deficiency of vitamin D,it was discovered the benifitial effect of vitamin D supply to individuals suffered from vitamin D deficiency in addition to infectious disease (14).

It was recorded in survey 2001-2006, that 25-hydroxyvitamin D has negative impact on respiratory infection (22).Vitamin D decreased effects of renin-angiotensin pathway,thereby lowering acute lung damage(23).Vitamin D treatment lowers the severity of respiratory tract infection and individuals with vitamin D insufficiency have been recorded this fact (24)

Subjects and methods:

Sixty patients aged (20-66) years were involved in current study and ten of healthy persons considered as a control group .In the present study, patients were attended the private clinics from December 2021 to March 2022 in Diwaniyah city .Information about patients was obtained by questionnaire form which included age,treatment and severity of diseases.Patients were divided into three groups (mild,moderate and severe)according to the severity of the infectin with disease.

Measurement of vitamin D:

An enzyme- linked immunosorbent assay, ElISA kit was used to detect vitamin D levels.Vitamin D was measured after two weeks from the infection

Statistical analysis: Statistical package for social sciences SPSS version 22 was used to analyze current results ,t-test was performed to compare means between two groups,while one way ANOVA was used to compare means among more than two groups . A probability level (P≤ 0.05) was adopted to find out the significant differences between the groups.

Results:

In current study, significant decrease (P≤ 0.05) was showed in vitamin D   concenterations in patients in comparison with healthy or control group(Fig 1) .Regarding relation between severity of disease and concenteration of vitamin D, significant decrease (P≤ 0.05) in vitamin D concenteration in moderate and severe infection in comparison with mild infection ,in addition its was found non significant difference between moderate and severe infection with SARS-CoV2 (Fig 2)
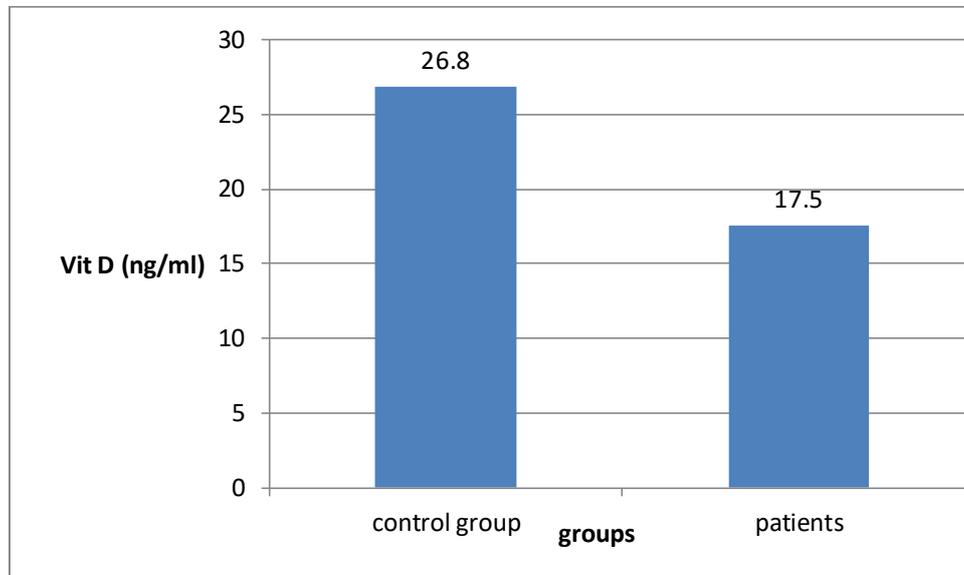
Fig(1): Vitamin D Concenteration in contorl and patients . * Significant increase
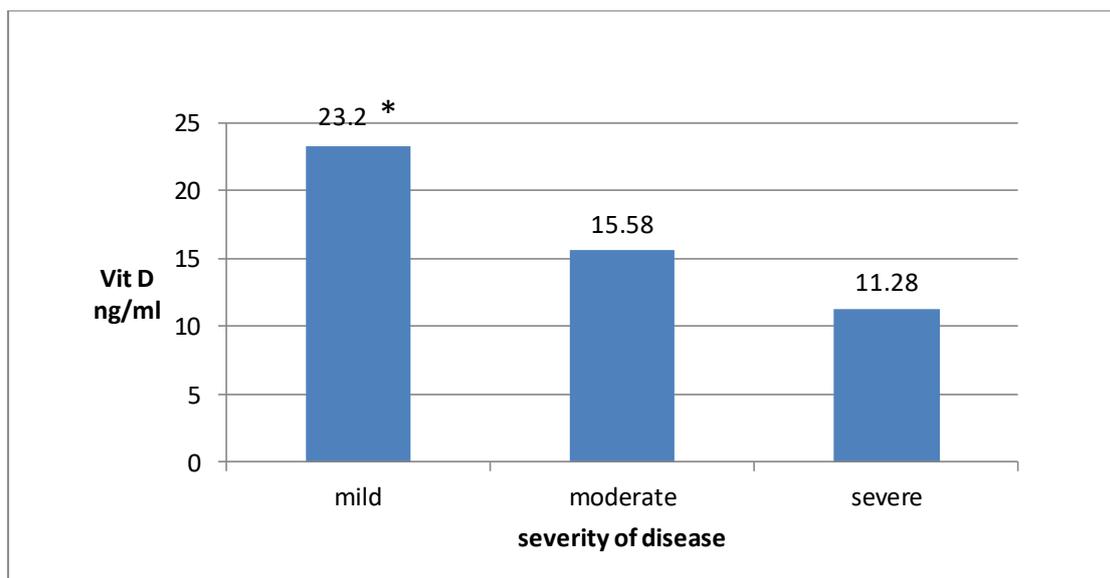
Fig(2): Vitamin D concenteration in mild ,moderate and severe infection with SARS-CoV2 * Significant increase.

Discussion:

Results showed significant decrease in vitamin D concenteration in patients compared to control group. It is reported that positive patients for COVID-19 have low vitamin D compared with negative patients (25) , also the mortality rates where high in patients with chronic disease and in older adults with low serum vitamin D levels,also it has been recorded the correlation between exposure to sunlight and mortality rates in COVID-19 infections (26)The current findings resulted from the effect of vitamin D in immune cells,it was found   high levels of cytokines and C- reactive protein associated with the disease (27). Vitamin D has significant role on patients by reducing the risk of cytokines and chemokines storm (28).Vitamin D decreases TNF, IL-6 and IFN-γ in mononuclear cells in addition,vitamin D raises levels of IL-10 (29). When vitamin D sufficient in patients the rate of mortality is low , that may resulting from low pro-inflammatory factors and high anti-inflammatory factors in monocytes and macrophages (30), on the other hand,vitamin D can modulates neutrophil activity and therefore,lowering the recruitment of neutrophil into lung,thus reducing the alveolar damage in patients (31). One of the mechanisms in which vitamin D lower viral infection,vitamin D promote induction of cathelicidin an anti-microbial peptide against bacteria and viruses (25) SARS-COV-2 may affects vitamin D action,the enterance of virus resulted in endothelial dysfunction that in turn,reduced vitamin D binding to VDR,causing further increasing in inflammation and the virus severity (32).Low vitamin D may explained the significant difference in immune response among groups depending on the severity of disease.

Conclusion:

Its concluded that increase the severity of COVID1-19 may resulted from high inflammation and low vitamin level.

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