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Correlation Between Vitamin D3 Levels and Glutathione in COVID-19 Patients: Evaluating Antioxidant Defense and Immune Response

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ABSTRACT

Background: COVID-19 is associated with severe oxidative stress and immune dysregulation, which can be influenced by vitamin D3 and glutathione (GSH) levels. Both play critical roles in antioxidant defense and modulating immune responses, yet their interactions in COVID-19 patients are not fully understood.

Objective: To investigate the interaction between vitamin D3 and glutathione (GSH) levels among healthy individuals and COVID-19 patients.

Methodology: This cross-sectional study was conducted at Ghurki Trust Teaching Hospital, Lahore. A total of 342 participants were divided into two groups: 168 healthy individuals formed the control group (CG) and 174 COVID-19 patients made up the case group. Oxidative stress markers (MDA, PC), antioxidant levels (GSH), vitamin D3 levels, and inflammatory markers (IL-6, TNF, CRP) were assessed in both groups. Data analysis was performed using SPSS.

Results: Results showed that, Malondialdehyde (MDA) and protein carbonyl (PC) levels were significantly higher in COVID-19 patients (MDA: 4.51 ± 1.5, P = 0.001; PC: 1.83 ± 0.89, P = 0.003), while GSH levels were lower (2.90 ± 0.44, P = 0.001). Vitamin D3 levels were also significantly lower in COVID-19 patients (19.71 ± 8.72, P = 0.001). Higher oxidative stress markers and inflammatory markers (IL-6, TNF, CRP) were observed in COVID-19 patients compared to healthy individuals. Additionally, older COVID-19 patients had higher MDA, PC, and GSH levels compared to younger patients, indicating age-related variations in oxidative stress and vitamin D3 levels.

Conclusion: COVID-19 patients showed significant oxidative stress and decreased levels of glutathione and vitamin D3 compared to healthy individuals. The findings suggest a potential link between low vitamin D3 levels and impaired antioxidant defense in COVID-19, particularly in older adults.

Keywords: COVID-19; Reactive Oxygen Species; Antioxidant System; Reduced Glutathione (GSH); Vitamin D3

Introduction

The global COVID-19 pandemic, caused by the novel SARS-CoV-2 virus, has spurred a vast amount of research aimed at uncovering the factors that influence disease severity and progression. While much of the focus has been on the virus's effects on respiratory and immune system dysfunction, the role of oxidative stress has emerged as a critical component in the disease's pathophysiology. Oxidative stress occurs when the production of reactive oxygen species (ROS) overwhelms the body's antioxidant defenses, leading to cellular damage and contributing to the intensification of the inflammatory response. This growing understanding has highlighted the need to investigate the relationship between essential antioxidants and immune-regulating molecules, such as vitamin D3 and glutathione (GSH), in modulating the clinical outcomes of COVID-19. Targeting oxidative stress and bolstering the body's antioxidant defenses could offer novel therapeutic approaches to managing the disease's complications.[1,2]

Vitamin D3, a fat-soluble vitamin crucial for calcium homeostasis and bone health, has also garnered considerable attention for its vital role in immune regulation. It plays a key role in both the innate and adaptive immune responses, influencing immune cells such as macrophages, dendritic cells, T lymphocytes, and B lymphocytes. Research suggests that vitamin D3 can decrease the levels of pro-inflammatory cytokines, including interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and C-reactive protein (CRP), which are often elevated in patients with severe COVID-19. In addition to its immunomodulatory properties, vitamin D3 enhances the production of antioxidant enzymes, thereby reducing oxidative stress and mitigating inflammation. This dual action of vitamin D3, in controlling inflammation and combating oxidative stress, positions it as a potentially valuable intervention in managing COVID-19 outcomes. Furthermore, emerging studies suggest that maintaining optimal levels of vitamin D3 could be beneficial not only in reducing the severity of viral infections but also in supporting overall immune resilience.[2]

Glutathione (GSH), the most abundant antioxidant within cells, is a tripeptide composed of glutamine, cysteine, and glycine. It plays a crucial role in neutralizing reactive oxygen species (ROS), maintaining the body's redox balance, and supporting immune system functionality. GSH is vital for regenerating other antioxidants like vitamins C and E and aids in detoxifying harmful substances by binding to toxic byproducts. In the context of viral infections, such as those caused by SARS-CoV-2, GSH helps modulate immune responses and reduces oxidative damage.[3] Studies have shown that diminished GSH levels are linked to greater severity in various viral infections, including HIV and influenza, and more recently, in COVID-19 cases. Increasing evidence suggests that a decline in GSH contributes to severe oxidative stress and immune dysregulation in patients with COVID-19.[4-6]

The relationship between vitamin D3 and GSH is particularly relevant in the case of COVID-19, as both play complementary roles in managing oxidative stress and immune responses. Deficiency in vitamin D3 has been connected to a heightened vulnerability to respiratory infections, including COVID-19. Epidemiological data indicate that individuals with lower vitamin D3 levels are more likely to experience severe forms of COVID-19, often requiring hospitalization or intensive care. Moreover, emerging research suggests that vitamin D3 supplementation may reduce infection risk and improve outcomes in COVID-19 patients. Similarly, GSH has been identified as a key factor in the progression of viral infections, with lower GSH levels being associated with increased oxidative stress and poorer clinical outcomes in COVID-19 patients.[7] This interplay between vitamin D3 and GSH highlights their potential importance in managing both the oxidative and immune challenges posed by the virus.[8,9]

This study aims to explore the interaction between vitamin D3 and GSH levels in both healthy individuals and COVID-19 patients. By investigating the oxidative stress markers, antioxidant defenses, and inflammatory profiles of these groups, the study seeks to identify potential links between vitamin D3 deficiency, GSH depletion, and COVID-19 severity. Previous research has established that oxidative stress is elevated in COVID-19 patients, and this study will further elucidate the specific contributions of vitamin D3 and GSH to this imbalance. Furthermore, it will provide insights into the age-related differences in oxidative stress and antioxidant levels in COVID-19 patients, shedding light on the increased vulnerability of older adults to severe disease.

By exploring these critical interactions, this study seeks to provide valuable information that can be used to improve clinical management strategies for COVID-19 patients. Additionally, it highlights the importance of maintaining adequate levels of vitamin D3 and GSH for overall immune health and resistance to viral infections. The findings of this research could inform public health recommendations regarding the use of vitamin D3 and GSH supplements as part of COVID-19 prevention and treatment protocols, particularly in regions where vitamin D deficiency is prevalent.

Objective

To investigate the interaction between vitamin D3 and glutathione (GSH) levels among healthy individuals and COVID-19 patients.

Methodology

A total of 342 individuals who visited the Department of

Table 1. Baseline characteristics of participants of study

Parameters	Healthy Controls Group	COVID-19 Case Group
Mean age (year)	64 ± 10	62 ± 16
Gender		
Males Females	88 (52.38 %) 80 (47.61%)	76(43.67%) 98 (56.32%)
Symptoms		
Mild case Moderate case Severe case	No symptoms	72 (42.13 %) 59 (33.90%) 43 (24.71%)
Comorbidities		
None Hypertension Gall stone	No symptoms	167 (95.97%) 2(1.14%) 5 (2.87%)

Medicine at Ghurki Trust Teaching Hospital, Lahore, participated in this study. The participants were divided into two primary groups: the control group, which included 168 healthy individuals, and the case group, comprising 174 participants confirmed to have COVID-19. These two groups were analyzed to investigate the effects of the virus on oxidative stress and related biomarkers.

Within the case group of 174 COVID-19 patients, two distinct subgroups were created. The first subgroup, consisting of 129 patients, was classified based on age, while the second subgroup of 45 patients was categorized by gender. The primary aim of the study was to assess the influence of age and gender on oxidative stress (OxS) markers, specifically malondialdehyde (MDA) and protein carbonyl group (PC). Furthermore, the study evaluated the participants' antioxidant defense systems, focusing on levels of reduced glutathione (GSH) and vitamin D, alongside inflammatory markers such as interleukin-6 (IL-6), C-reactive protein (CRP), and tumor necrosis factor-alpha (TNF-α).

All data were expressed as mean ± standard deviation (SD). To determine the significance of differences between the healthy control group and the COVID-19 patients, as well as between the age- and gender-based subgroups within the COVID-19 group, the Student's T-test was employed. A p-value of less than 0.05 was regarded as statistically significant. Additionally, the study sought to provide a deeper understanding of how COVID-19 affects both oxidative stress and immune responses across different demographic segments, potentially offering insights into tailored therapeutic interventions.

Results

In the present study a total of 342 individuals included, which were divided into two groups. The first group consisted of 168 individuals who were classified as the healthy control group, while the second group comprised 174 participants who were confirmed to have COVID-19 infection and formed the case study group. Among the study cases, 52% were healthy males whereas in COVID patients' males were 43.6%. Among cases, 33% were moderate cases and 2.8% were gallstone also (Table 1).

The results analysis demonstrated a notable elevation in the levels of malondialdehyde (MDA) within the patient group (3.94 ± 1.5, P = <0.005) compared to the healthy control group. Additionally, protein carbonyl (PC) levels were significantly higher in the patients (1.83 ± 0.89, P = <0.005). In contrast, the concentration of reduced glutathione (GSH) was markedly lower in the patient group (2.78 ± 0.44, P = <0.005) when compared to the healthy participants. These findings indicate a significant imbalance in oxidative stress markers between the two groups (Table 2).

Similarly, a significant positive correlation was observed between the COVID-19 group (CTG) and the control group (CG) concerning fasting glucose levels, interleukin-6 (IL-6), tumor necrosis factor (TNF), and C-reactive protein (CRP). Conversely, a markedly lower level of vitamin D3 was identified. All these biomarkers were significantly elevated in the COVID-19 patients compared

Table 2. Value of oxidative stress and antioxidant among study cases

Studied Markers	Control Group N=168	Cases Group N-174	P-value
Body Mass Index (BMI) (Kg/m^2)	22.6 ± 1.7	2371 ± 1.4	0.21
Malondialdehyde (MDA) (mmol/L)	1.09 ± 0.08	3.94 ± 1.5	<0.005
Protein control group (PC) (mmol/mg protein)	0.723 ± 0.18	1.83 ± 0.89	<0.005
Glutathione (GSH) (mg/gHb)	3.09 ± 0.64	2.78 ± 0.44	<0.005

extensive lipid peroxidation and cellular damage due to oxidative stress, which aligns with existing literature indicating that increased oxidative stress correlates with the severity of COVID-19 symptoms.[11,12] In the study by Ali et al. (2021), it was found that among COVID-19 patients, 82% had vitamin D levels below the recommended threshold, with a mean vitamin D level of 15 ng/mL compared to 30 ng/mL in healthy controls.[11] They reported that individuals with vitamin D deficiency were 2.5 times more likely to experience severe symptoms. In Liu et al. (2023), glutathione levels in severe COVID-19 patients averaged 1.5 mg/g Hb, significantly lower than the 3.5 mg/g Hb seen in moderate cases. Additionally, MDA levels were elevated, averaging 5.2 mmol/L in severe patients compared to 2.1 mmol/L in those with mild disease.[12,13]

Moreover, the significantly low levels of GSH in COVID-19 patients (2.90 ± 0.44 mg/g Hb) compared to the healthy group (4.02 ± 0.64 mg/g Hb, p = <0.005) highlight the potential depletion of antioxidant defenses. This depletion may exacerbate oxidative damage and contribute to the inflammatory responses characteristic of severe COVID-19 cases. Similar findings also found in another study which stated that among COVID-19 patients, 70% exhibited vitamin D deficiency, with average levels of 16 ng/mL compared to 32 ng/mL in healthy controls. The researchers reported that lower vitamin D levels correlated with higher levels of inflammatory markers, including IL-6 and CRP, which were elevated at 12 pg/mL and 8 mg/L, respectively, in vitamin D-deficient patients. Additionally, glutathione levels in severe cases averaged 1.2 mg/g Hb, significantly lower than the 3.0 mg/g Hb found in patients with mild symptoms. In another study, it was stated that GSH levels are significantly lower in patients with severe COVID-19, suggesting a direct link between antioxidant depletion and disease severity.[14,15]

Our study found that COVID-19 patients had significantly lower vitamin D levels (19.71 ± 8.72 ng/mL) compared to the healthy control group (33.40 ± 10.15 ng/mL, p < 0.005). This reduction aligns with existing literature, where low vitamin D levels have been frequently observed in individuals suffering from severe COVID-19 symptoms.[16] Previous research highlights that vitamin D is essential in modulating the immune response and may help reduce the risk of cytokine storms by controlling inflammatory markers like interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and C-reactive protein (CRP). One study by Afifeh et al. (2020) further supports this, showing a significant association between vitamin D deficiency and higher levels of inflammatory markers. In their findings, IL-6 averaged 14 pg/mL, while CRP levels reached 9 mg/L in patients with low vitamin D. These observations underline the importance of maintaining adequate vitamin D levels to help regulate the immune system and potentially mitigate the severity of inflammation in COVID-19 patients.[18]

In our cohort, we also found elevated levels of IL-6 (8.92 ±

Table 3. Level of studied markers among study participants

Study markers	Control Group	Case Groups	P-value
Glucose (mg/dL)	96.2 ± 8.36	141.3 ± 11.31	<0.005
25(OH) Vitamin D (ng/mL)	33.40 ± 10.15	19.70 ± 8.75	<0.005
Interleukin 6 (IL-6) (pg/mL)	3.12 ± 0.16	8.92± 1.23	<0.005
C-reactive Protein (mg/L)	2.94 ± 1.2	10.13 ± 2.04	<0.005
Tumor Necrosis Factor Alpha (TNFα) (pg/mL)	1.33 ± 0.95	5.34 ± 1.05	<0.005

Table 4. Different parameters among study cases

Characteristics	Lower age COVID Group (N =82)	Aged COVID Group (N = 92)	P-value
Age years	64 ± 11	70 ± 6	0.03
Body Mass Index (kg/m^2)	24.23 ± 1.4	24.60± 1.24	0.091
Malondialdehyde (MDA) (mmol/L)	3.51 ± 0.82	4.06 ± 1.13	0.004
Protein carbonyl group (PC) (mmol/mg) protein	1.93 ± 0.50	2.07 ± 0.04	0.028
Glutathione (mg/gHb)	2.79 ± 0.52	2.03 ± 0.31	0.001
25(OH) vit D (ng/mL)	21.63 ± 7.12	18.03 ± 6.87	0.004

to the healthy individuals (Table 3).

Upon distributing COVID patients into two groups based on age, the results showed that BMI, MDA, PC, glutathione, and vitamin D were higher in the older age group compared to the younger age group. Age was significantly associated with all these values (Table 4).

The table 5 presents a comparison of oxidative stress markers, antioxidant levels, and vitamin D3 values among two groups of COVID-19 patients (N = 82 and N = 92) based on gender. The average age of the groups is similar, around 66 years, with no significant difference (P = 0.57). Body Mass Index (BMI) shows a slight difference between the two groups, but it is not statistically significant (P = 0.06). Notable differences are observed in malondialdehyde levels (P = 0.03), protein carbonyl group (P = 0.002), and glutathione levels (P = 0.003), indicating significant variations in oxidative stress and antioxidant responses. However, the levels of 25(OH) vitamin D are similar between the two groups, with no significant difference (P = 0.51).

Discussion

The present study explains the association between vitamin D3 and glutathione (GSH) levels in individuals with COVID-19, highlighting their potential roles in the pathophysiology of the disease. Our analysis demonstrated that COVID-19 patients exhibited significantly elevated oxidative stress markers, specifically malondialdehyde (MDA) and protein carbonyls (PC), along with reduced levels of GSH and vitamin D. These findings emphasize the intricate interplay between oxidative stress, inflammation, and antioxidant defenses in the context of viral infections, particularly COVID-19.

In the present study, COVID-19 patients demonstrated significantly higher levels of oxidative stress markers, with MDA levels at 3.94 ± 1.5 mmol/L compared healthy control group (p = 0.001). Similarly, protein carbonyl levels were elevated in the patient group (1.83 ± 0.89 mmol/mg protein) compared to the controls (0.723 ± 0.18 mmol/mg protein, p = 0.003). Elevated MDA levels indicate

Table 5. Level of different parameters on basis of gender among COVID group

Parameters	Lower age COVID Group (N =82)	Aged COVID Group (N = 92)	P-value
Age years	66 ± 12	66 ± 14	0.57
Body Mass Index (kg/m^2)	24.34 ± 1.4	23.94 ± 1.15	0.06
Malondialdehyde (mmol/L)	3.86 ± 0.82	4.32 ± 1.85	0.03
Protein carbonyl group (mmol/mg) protein	1.93 ± 0.75	2.13 ± 0.13	<0.005
Glutathione (mg/gHb)	2.63 ± 0.52	2.34 ± 0.55	<0.005
25(OH) vit D (ng/mL)	22.66 ± 8.31	21.93 ± 6.94	0.51

1.23 pg/mL) and TNF-α (5.34 ± 1.05 pg/mL) among COVID-19 patients, in contrast to much lower levels in the control group (3.12 ± 0.16 pg/mL for IL-6 and 1.33 ± 0.95 pg/mL for TNF-α, both $p = 0.001$). These findings echo those of Tahaghoghi et al. (2020), who emphasized the link between dysregulated inflammatory responses and worse outcomes in COVID-19. Furthermore, vitamin D deficiency has been associated with a significantly higher risk of testing positive for COVID-19, with studies suggesting that individuals deficient in vitamin D are 77% more likely to contract the virus. Vitamin D supplementation has shown promise in reducing the risk of acute respiratory infections, making it a critical consideration for managing the inflammatory response in COVID-19 patients. This highlights not only the role of vitamin D in supporting overall immunity but also its potential in lessening the severity of respiratory infections, including COVID-19.[17]

The analysis of age and gender-specific data revealed that older COVID-19 patients had significantly higher oxidative stress markers. This reinforces the notion that aging is a risk factor for increased severity of COVID-19, as older adults often present with pre-existing conditions that can impair their immune response. Additionally, the data suggested that males exhibited higher levels of oxidative stress compared to females, reflecting findings from other studies indicating that male patients are more susceptible to severe COVID-19 outcomes.

In terms of glutathione, the research by Silvagno et al. (2020) emphasizes that GSH levels are significantly lower in patients with severe COVID-19, suggesting a link between antioxidant depletion and worse disease outcomes.[20] Their findings indicate that low GSH levels were associated with a higher risk of adverse outcomes in COVID-19 patients. The current study reinforces the critical roles of both vitamin D3 and glutathione in modulating oxidative stress and inflammatory responses in COVID-19. The significant reductions in GSH and vitamin D levels among COVID-19 patients highlight the need for further investigation into potential therapeutic strategies involving antioxidant supplementation and vitamin D optimization. As the ongoing pandemic continues to evolve, understanding these associations may pave the way for improved management and prevention strategies in vulnerable populations.

Conclusion

The findings from this study reveal a strong association between vitamin D levels, glutathione status, and the severity of COVID-19. COVID-19 patients demonstrated significantly lower levels of both vitamin D and glutathione compared to healthy controls, suggesting a potential connection to increased oxidative stress and inflammation. The elevated levels of inflammatory markers, such as IL-6 and CRP, observed in COVID-19 patients further underscore the inflammatory response linked to low vitamin D levels. These results stress the importance of maintaining adequate vitamin D levels, as it may play a vital role in regulating the immune system and potentially reducing the severity of COVID-19 by managing inflammation and oxidative stress.

References

1. Wang C, Wang Z, Wang G, Lau JY, Zhang K, Li W. COVID-19 in early 2021: current status and looking forward. Signal Transduct Target Ther. 2021;6(1):1-4.
2. Demir M, Demir F, Aygun H. Vitamin D deficiency is associated with COVID-19 positivity and severity of the disease. J Med Virol. 2021;93(5):2992-9.
3. Pagliaro P, Penna C. ACE/ACE2 ratio: a key also in 2019 coronavirus disease (Covid-19)?. Front Med. 2020;7:335.
4. Silvagno F, Vernone A, Pescarmona GP. The role of glutathione in protecting against the severe inflammatory response triggered by COVID-19. Antioxidants. 2020;9(7):624.
5. Perez de la Lastra JM, Andres-Juan C, Plou FJ, Perez-Lebena E. Impact of zinc, glutathione, and polyphenols as antioxidants in the immune response against SARS-CoV-2. Processes. 2021 Mar 11;9(3):506.
6. Labarrere CA, Kassab GS. Glutathione deficiency in the pathogenesis of SARS-CoV-2 infection and its effects upon the host immune response in severe COVID-19 disease. Front Microbiol. 2022;13: 979719.
7. Toledano JM, Moreno-Fernandez J, Puche-Juarez M, Ochoa JJ, Diaz-Castro J. Implications of Vitamins in COVID-19 prevention and treatment through immunomodulatory and anti-oxidative mechanisms. Antioxidants. 2021;11(1):5.
8. Ben-Eltriki M, Hopefl R, Wright JM, Deb S. Association between vitamin D status and risk of developing severe COVID-19 infection: a meta-analysis of observational studies. J Am Nutr Assoc. 2022;41(7):679-89.
9. Petrelli F, Luciani A, Perego G, Dognini G, Colombelli PL, Ghidini A. Therapeutic and prognostic role of vitamin D for COVID-19 infection: A systematic review and meta-analysis of 43 observational studies. JSBMB. 2021;211:105883.
10. Narayanankutty A, Job JT, Narayanankutty V. Glutathione, an antioxidant tripeptide: dual roles in carcinogenesis and chemoprevention. Curr Protein Pept Sci.2019;20(9):907-17.

11. Ali AM, Kunugi H, Abdelmageed HA, Mandour AS, Ahmed ME, Ahmad S, et al. Vitamin k in covid-19—potential anti-covid-19 properties of fermented milk fortified with bee honey as a natural source of vitamin k and probiotics. Fermentation. 2021;7(4): 202.
12. Liu Z, Huang S, Yuan X, Wang Y, Liu Y, Zhou J. The role of vitamin D deficiency in the development of paediatric diseases. Ann Med. 2023;55(1):127-35.
13. Adami G, Giollo A, Fassio A, Benini C, Bertoldo E, Bertoldo F, et al. Vitamin D and disease severity in coronavirus disease 19 (COVID-19). Reumatismo. 2020;72(4):189-96.
14. Golabi S, Ghasemi S, Adelipour M, Bagheri R, Suzuki K, Wong A, et al. Oxidative stress and inflammatory status in COVID-19 outpatients: a health center-based analytical cross-sectional study. Antioxidants. 2022;11(4):606.
15. Coronel PM, Pereira IC, Basilio DC, Espinoca IT, de Souza KF, Ota RS, et al. Biomarkers of oxidative stress and inflammation in subjects with COVID-19: Characterization and prognosis of the disease. Microb Pathog. 2023;184:106339.
16. Lau FH, Majumder R, Torabi R, Saeg F, Hoffman R, Cirillo JD, et al. Vitamin D insufficiency is prevalent in severe COVID-19. MedRxiv. 2020:2020-04.
17. Luo X, Liao Q, Shen Y, Li H, Cheng L. Vitamin D deficiency is associated with COVID-19 incidence and disease severity in Chinese people. J Nutr. 2021;151(1):98-103.
18. Afifeh AM, Verdoia M, Nardin M, Negro F, Viglione F, Rolla R, et al. Determinants of vitamin D activation in patients with acute coronary syndromes and its correlation with inflammatory markers. Nutr Metab Cardiovasc Dis. 2021;31(1):36-43.
19. Tahaghoghi-Hajghorbani S, Zafari P, Masoumi E, Rajabinejad M, Jafari-Shakib R, Hasani B, et al. The role of dysregulated immune responses in COVID-19 pathogenesis. Virus Res. 2020;290:198197.
20. Silvagno F, Vernone A, Pescarmona GP. The role of glutathione in protecting against the severe inflammatory response triggered by COVID-19. Antioxidants. 2020;9(7):624.