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Association of Baseline Serum Vitamins A and C with Disease Severity in COVID-19 Patients

Rehman Ullah[1], Najeeb Ul Haq[1], Nauman Iqbal[1], Najam Masood[2], Ali Yar Khan[1]✉

[1]Department of Medicine, Rehman Medical Institute, Peshawar - Pakistan [2]Department of Medicine, Khyber Teaching Hospital, Peshawar - Pakistan

Corresponding Author:
Ali Yar Khan
Department of Medicine,
Khyber Teaching Hospital,
Peshawar - Pakistan
Email: aliyarkn2014@gmail.com

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ABSTRACT

Background: Vitamin C and vitamin A are essential micronutrients in modulating the immune system and antioxidant defense. Lack of these micronutrients may contribute to adverse effects of viral infections, including COVID-19.

Objective: To identify baseline serum concentrations of vitamin C and vitamin A and their correlation with disease severity in COVID-19 patients.

Methodology: For the current study, 120 patients with confirmed COVID-19 were included and classified into mild (n = 34), moderate (n = 38), severe (n = 30), and critical (n = 18) groups based on WHO criteria. Demographic and clinical data at baseline were recorded. Serum vitamin A and C concentrations at admission were measured. Deficiency was defined as <0.70 μmol/L for vitamin A and <11 μmol/L for vitamin C.

Results: Mean vitamin A and C levels gradually reduced with increasing disease severity ($p < 0.001$). Vitamin A deficiency was found in 8.8% of mild and 50.0% of critical patients, and vitamin C deficiency increased from 2.9% in mild to 38.9% in critical patients. Logistic regression proved that higher vitamin A (adjusted OR: 0.75 per 0.1 μmol/L, $p = 0.002$) and vitamin C (adjusted OR: 0.82 per 5 μmol/L, $p = 0.004$) levels were independently protective against severe/critical illness, in addition to age and diabetes as risk factors.

Conclusion: Lower baseline serum levels of vitamin A and vitamin C show a high correlation with severity of COVID-19. Micronutrient deficiency may enhance inflammation, oxidative stress, and disease severity.

Keywords: COVID-19; Vitamin A; Vitamin C; Micronutrients; Inflammation

Introduction

Coronavirus disease 2019 (COVID-19), is the most critical global health crisis of the twenty-first century, caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). Internationally, COVID-19 has led to serious morbidity, mortality, and economic disruption since its declaration as a pandemic in March 2020.1 COVID-19 may manifest with a broad spectrum of clinical symptoms ranging from minimal flu-like symptoms or no symptoms at all to severe pneumonia, acute respiratory distress syndrome (ARDS), multi-organ failure, and even death. A variety of risk factors for serious illness have been noted, including comorbidities like diabetes mellitus, cardiovascular disease, and chronic respiratory issues, together with older age, male sex, and obesity. The relevance of host nutritional status and micronutrient deficiencies in affecting immunological response, clinical outcomes, and susceptibility to disease, however, has gained greater interest in recent years.[2]

Since they are essential micronutrients, vitamins play a significant role in maintaining immunologic function and reducing oxidative stress in case of an infection. Vitamins A and C are highlighted among the others due to their proven antioxidant and immunomodulatory effects. Both innate and adaptive immunity are closely controlled by vitamin A. It enhances antibody-mediated immune responses, maintains mucosal integrity, and affects epithelial cell differentiation and function. In measles and pneumonia, vitamin A deficiency has been found to impair prognosis and enhance susceptibility to respiratory infections.[3]

Similarly, vitamin C, a water-soluble antioxidant, is commonly believed to combat free radicals, reduce inflammation, and enhance the function of various immune cells, including phagocytes, lymphocytes, and neutrophils. Plasma vitamin C levels tend to decline during acute infections due to augmented metabolic need and utilization to combat oxidative stress. Lower immunity and susceptibility to severe respiratory infections have been linked to vitamin C deficiency. The role of vitamin C is particularly significant in the context of COVID-19, where oxidative stress, endothelial dysfunction, and cytokine storm are significant pathogenic mechanisms.[4]

Micronutrient deficiencies, and especially those of antioxidant vitamins, could be linked with poorer outcomes in COVID-19, suggests new research. Serum concentrations of vitamins A, C, D, and E are decreased in patients with COVID-19 compared with healthy controls, based on various observational studies deficiencies are markedly evident in critically ill patients.[5,6] While there has been extensive research into vitamin D, there remains scarce inconclusive data for vitamins A and C, particularly from populations in middle- and low-income countries where nutritional deficiencies are prevalent. A baseline measurement of serum levels of vitamins A and C in COVID-19 patients is important for a number of reasons. First, in reflecting the immunological and nutritional status of the patient, these vitamins could serve as markers of disease severity. Second, identifying deficiencies could help inform nutritional therapy as adjunctive therapy designed to augment clinical outcomes. Third, an understanding of these associations would facilitate the creation of more inclusive pandemic readiness plans that emphasize how important nutrition is in mitigating infectious disease burden.

This research is planned because vitamins A and C have critical roles in maintaining epithelial barrier integrity, regulating immune cell function, and countering oxidative stress, all of which are central to the host response to SARS-CoV-2. Considering that an imbalanced immune response is a characteristic of life-threatening COVID-19, there lies a remarkable interest in examining whether deficiencies in these immunomodulatory micronutrients before infection are linked to worse clinical outcomes. Thus, this study seeks to establish the baseline serum concentration of vitamins A and C in COVID-19 patients and assess their correlation with disease severity, potentially uncovering simple, low-cost prognostic biomarkers that may facilitate early risk stratification and inform focused nutritional therapy.

Objective

To determine the baseline levels of serum vitamin A and vitamin C in patients with COVID-19 and analyze their association with the severity of the disease.

Methodology

This prospective observational cohort study was conducted at Rehman Medical Institute, Peshawar. 120 consecutive adult patients with laboratory-confirmed SARS-CoV-2 infection entering the emergency room or being admitted to COVID-19 isolation units and medical wards were enrolled in the study. For observational studies, the study protocol followed the STROBE guidelines. The study protocol was approved by the Institutional Review Board/Ethics Committee (RMI:118/2021/RA). Written informed consent was obtained from all participants or their legally authorized representatives prior to enrollment. For this research, 120 patients were chosen by feasibility as sample size and to have adequate power to detect moderate correlations between baseline serum vitamin concentrations and disease severity. With an assumed effect size (Cohen's d) of ~0.5 between severe and non-severe disease, two-tailed $\alpha=0.05$ and power $(1-\beta)=0.80$, approximately 100–120 patients were required. Criteria for inclusion were Age ≥18 years.

Laboratory-confirmed SARS-CoV-2 infection using RT-

PCR on nasopharyngeal swab and presentation within 7 days of the onset of the symptoms or within 24 hours of admission for transfer from other centers. Exclusion criteria included history of current or recent (within the last 30 days) high-dose vitamin A or vitamin C supplementation (>1,000 IU/day for vitamin A equivalents or >500 mg/day for vitamin C). Chronic liver illness or end-stage renal illness on dialysis (diseases with a significant impact on vitamin metabolism) and unwillingness to provide consent. Demographic and clinical data were collected at baseline with a standardized case report form: age, sex, weight, height (calculated body mass index), smoking status, comorbidities (hypertension, diabetes mellitus, chronic respiratory disease, cardiovascular disease), medication history, date of symptom onset, and time from symptom onset to presentation.

Adequate vital signs (temperature, respiratory rate, heart rate, blood pressure, SpO_2 on room air) and significant laboratory data (complete blood count, C-reactive protein, D-dimer, serum creatinine, liver enzymes) were collected from the admission notes. Continuous variables were given as mean ± standard deviation (SD) or median with interquartile range (IQR) according to distribution; categorical variables were given as number and percentage.

Normality was tested through Shapiro–Wilk test and histogram check. Comparative tests between vitamin levels in groups of severity utilized one-way ANOVA for normally distributed data or Kruskal–Wallis tests with non-normal distributions. Multiple testing adjustment was performed for post-hoc pairwise comparisons (Bonferroni or Dunn's test as appropriate). Correlations between vitamin levels and continuous markers of disease severity (e.g., oxygen saturation, CRP) were evaluated by Pearson or Spearman correlation coefficients.

Logistic regression analyses were used to evaluate the association of baseline vitamin levels (continuous and dichotomous) with the risk of severe/critical disease. Multivariate models adjusted for pre-specified potential confounders: age, sex, body mass index, diabetes, hypertension, smoking status, and time from symptom onset to sampling. Results. were reported as adjusted odds ratios (aOR) with 95% confidence intervals (CI). Statistical tests were two-tailed and a p-value of <0.05 was considered statistically significant. Statistical analysis was performed on SPSS version 26.

Results

120 patients with laboratory-confirmed COVID-19 were included in the final analysis.According to WHO criteria, 34 patients (28.3%) had mild disease, 38 (31.7%) had moderate disease, 30 (25.0%) had severe disease, and 18 (15.0%) were critical. The mean age of participants was 52.4 ± 14.8 years, with a progressive increase across severity groups, from 45.2 years in mild cases to 61.7 years in critical cases ($p < 0.01$). Males comprised 55% of the study population, with no statistically significant difference in distribution by disease severity ($p = 0.18$). The average BMI was 27.6 ± 4.3 kg/m², and in those with severe and critical illness, it was higher than in mild illness ($p = 0.04$). There was a rise in comorbidities according to severity such as hypertension occurring in 36.7% overall but increasing to 61.1% in the critical group ($p = 0.01$), and diabetes in 33.3% overall and occurring most commonly in the critical cases (61.1%, $p = 0.01$). Smoking history was more prevalent among severe and critical patients (23.3% and 33.3%, respectively), although the difference

Table 1. Baseline demographic and clinical characteristics of COVID-19 patients (N = 120)

Characteristic	Total (N=120)	Mild (n=34)	Moderate (n=38)	Severe (n=30)	Critical (n=18)	p-value
Age, years (mean ± SD)	52.4 ± 14.8	45.2 ± 12.1	50.6 ± 13.8	56.8 ± 15.1	61.7 ± 14.6	<0.01
Male sex, n (%)	66 (55.0)	16 (47.1)	18 (47.4)	20 (66.7)	12 (66.7)	0.18
BMI, kg/m² (mean ± SD)	27.6 ± 4.3	25.9 ± 3.8	27.4 ± 4.1	28.7 ± 4.2	29.3 ± 4.5	0.04
Hypertension, n (%)	44 (36.7)	7 (20.6)	11 (28.9)	15 (50.0)	11 (61.1)	0.01
Diabetes, n (%)	40 (33.3)	6 (17.6)	10 (26.3)	13 (43.3)	11 (61.1)	0.01
Smoking history, n (%)	22 (18.3)	4 (11.8)	5 (13.2)	7 (23.3)	6 (33.3)	0.09

Table 2. Baseline serum vitamin A and vitamin C levels by disease severity

Severity group	Vitamin A (μmol/L, mean ± SD)	Vitamin C (μmol/L, mean ± SD)
Mild (n=34)	1.15 ± 0.32	45.8 ± 12.6
Moderate (n=38)	1.01 ± 0.29	38.4 ± 11.8
Severe (n=30)	0.82 ± 0.25	27.6 ± 10.1
Critical (n=18)	0.66 ± 0.21	20.3 ± 8.9
p-value	<0.001	<0.001

was not statistically significant ($p = 0.09$) (Table 1).

Mean serum vitamin A concentrations progressively declined from 1.15 ± 0.32 μmol/L in mild cases to 0.66 ± 0.21 μmol/L in critically ill patients ($p < 0.001$). A similar trend was observed for vitamin C, with levels decreasing from 45.8 ± 12.6 μmol/L in the mild group to 20.3 ± 8.9 μmol/L among critical cases ($p < 0.001$). (Table 2)

Overall, 23.3% of patients had vitamin A deficiency and 16.7% had vitamin C deficiency. Both deficiencies were significantly more common among patients with severe and critical illness compared to those with mild or moderate disease (p for trend <0.001). Specifically, vitamin A deficiency was present in only 8.8% of mild cases but increased to 50% among critical patients. Similarly, vitamin C deficiency was observed in 2.9% of mild cases, rising sharply to 38.9% in the critical group (Table 3).

Both vitamin A and vitamin C levels showed a significant positive correlation with oxygen saturation ($r = 0.42$ and $r = 0.46$, respectively; $p < 0.001$), indicating that higher vitamin concentrations were associated with better oxygenation. Conversely, negative correlations were observed with inflammatory and prognostic markers. Vitamin A ($r = –0.38$, $p < 0.001$) and vitamin C ($r = –0.41$, $p < 0.001$) were inversely related to C-reactive protein levels, suggesting a link between lower vitamin status and systemic inflammation. Similarly, both vitamins showed modest but significant negative correlations with D-dimer concentrations and length of hospital stay, implying that deficiencies may contribute to hypercoagulability and prolonged recovery (Table 4).

Results showed that both vitamins demonstrated independent protective effects. Each 0.1 μmol/L increase in serum vitamin A was associated with a 25% reduction in the odds of severe/critical disease after adjustment for confounders (adjusted OR = 0.75, 95% CI: 0.62–0.90, $p = 0.002$). Similarly, each 5 μmol/L increase in vitamin C was linked to an 18% reduction in risk (adjusted OR = 0.82, 95% CI: 0.71–0.94, $p = 0.004$). Among covariates, older age (per 10-year increase) significantly increased disease severity (adjusted OR = 1.28, $p = 0.01$), while diabetes nearly doubled the risk (adjusted OR = 1.95, $p = 0.04$). Hypertension showed a non-significant trend toward higher severity ($p = 0.09$). These findings indicate that both vitamin A and vitamin C are independent predictors of less severe disease, even after controlling for age and comorbidities (Table 5).

Discussion

The current research examined the baseline serum levels of vitamin A and vitamin C and how they correlate with

Table 3. Prevalence of vitamin A and C deficiency by disease severity

Severity group	Vitamin A deficiency (<0.70 μmol/L), n (%)	Vitamin C deficiency (<11 μmol/L), n (%)
Mild (n=34)	3 (8.8)	1 (2.9)
Moderate (n=38)	6 (15.8)	3 (7.9)
Severe (n=30)	10 (33.3)	8 (26.7)
Critical (n=18)	9 (50.0)	7 (38.9)
p-value (trend)	<0.001	<0.001

Table 4. Correlation of serum vitamin levels with markers of disease severity

Variable	Vitamin A (r)	p-value	Vitamin C (r)	p-value
Oxygen saturation (SpO_2, %)	+0.42	<0.001	+0.46	<0.001
C-reactive protein (mg/L)	-0.38	<0.001	-0.41	<0.001
D-dimer (ng/mL)	-0.29	0.002	-0.33	0.001
Length of hospital stay (days)	-0.25	0.007	-0.28	0.004

disease severity in COVID-19 patients. Our data shows that the two vitamins were considerably lower among patients with severe and critical conditions than among those with mild or moderate disease. In addition, the prevalence of vitamin A and vitamin C deficiencies was higher in those with poorer outcomes, and both micronutrients independently were related to lower odds of severe or critical COVID-19 after controlling age and comorbidities. These findings indicate a potential protective effect of optimal vitamin A and C status on countering disease progression and emphasize the significance of dietary components in pathophysiology of COVID-19. Mean age rose stepwise over strata of severity (45.2 years in mild → 61.7 years in critical, $p < 0.01$).

This age gradient reflects previous and large cohorts in Wuhan and worldwide that had recognized older age as the major risk factor for ICU admission and death.[7] Older age is mechanistically plausible as a risk factor due to immunosenescence, increased burden of comorbidities, and decreased physiological reserve, and has been persistently controlled for as a major confounder in prognostic analyses.[8] While males made up 55% of our cohort and were proportionally more common among severe/critical cases, the distribution did not achieve statistical significance ($p = 0.18$). Larger registry studies proved a strong association between male sex and adverse outcomes of COVID-19 (e.g., increased risk of COVID-19 death in OpenSAFELY), which implies that our nonsignificant finding most probably represents restricted sample size and regional case-mix rather than sex effect absence. Explanations for male susceptibility at a biological level encompass sex disparity in innate and adaptive immunity, comorbidity profiles, as well as behavioral risk factors.[9] Mean BMI increased through severity groups (25.9 29.3 kg/m^2; $p = 0.04$), consistent with international analyses demonstrating obesity elevates the risk for hospitalization, ICU admission, and mortality. A systematic meta-analysis and pooled analyses reported significantly increased odds of severe outcomes and mortality in individuals with obesity. Contributing pathophysiologic factors are impaired respiratory mechanics, chronic pro-inflammatory condition, and metabolic derangement. These associations facilitate routine adjustment for BMI in models analyzing biomarkers (e.g., vitamin status) and outcomes.[10] The rising rates of hypertension (20.6% in mild 61.1% in critical) and diabetes (17.6% in mild 61.1% in critical) in our cohort replicate trends in large series from New York, Lombardy, and multi-center registries, where cardiometabolic comorbidities were the most frequent conditions in hospitalized and critically ill patients. Both diseases are credibly associated with poorer outcomes through endothelial dysfunction, increased baseline inflammation, and decreased homeostatic reserve; diabetes specifically depresses innate immune function and has been consistently linked with increased risk of severe disease and death.[11] In our sample, smoking history trended upward in severe/critical groups (11.8% 33.3%) but was not statistically significant ($p = 0.09$). Early reports indicated heterogeneous results for smoking such that some small studies paradoxically indicated reduced prevalence of current smokers among hospitalized cases (presumably biased), whereas larger and better-controlled estimates demonstrate increased current and ex-smoking predisposing to severe COVID-19. Our nonsignificant trend, considering possible under-reporting and the modest sample size in this study, is consistent with the general body of evidence. [12] Table 2 shows an unmistakable inverse correlation between vitamin concentrations in the serum and the severity of COVID-19. Progressively lower mean vitamin A levels decreased from 1.15 μmol/L in mild illness to 0.66 μmol/L in critical disease ($p < 0.001$). Correspondingly, vitamin C concentrations dropped from 45.8 μmol/L in mild disease to 20.3 μmol/L in critical disease ($p < 0.001$). These observations point to a possible contribution of antioxidant micronutrient deficiency to the pathophysiology of COVID-19. Vitamin A deficiency has been shown to impair epithelial integrity, mucosal immunity, and immune response, making one more susceptible to respiratory infections. Our observation of increasingly lower vitamin A with increasing severity is in agreement with Jovic et al. (2020),[13] who reported lower serum retinol levels in more severe cases of COVID-19 compared to milder disease. Analogously, Trasino (2020)[14] described the possible role of vitamin A deficiency in dysregulated immune response

Table 5. Logistic regression: association between vitamin levels and severe/critical disease

Predictor	Crude OR (95% CI)	Adjusted OR (95% CI)	p-value
Vitamin A (per 0.1 μmol/L increase)	0.72 (0.60–0.86)	0.75 (0.62–0.90)	0.002
Vitamin C (per 5 μmol/L increase)	0.80 (0.70–0.91)	0.82 (0.71–0.94)	0.004
Age (per 10 years)	—	1.28 (1.05–1.56)	0.01
Diabetes	—	1.95 (1.03–3.68)	0.04
Hypertension	—	1.72 (0.92–3.22)	0.09

and adverse prognosis in SARS-CoV-2 infection. Iranian hospital-based research (Shakoor et al., 2021)[15] also revealed severely depleted retinol in severe versus non-severe COVID-19 cases, implying that deficiency may predispose individuals to uncontrolled inflammation and worse pulmonary injury. Vitamin C is a powerful water-soluble free radical that maintains neutrophil function, lowers reactive oxygen species, and modulates cytokine response. Our observation of mean vitamin C levels being reduced by half among critical patients relative to mild patients (20.3 μmol/L vs. 45.8 μmol/L) corroborates earlier research such as Chiscano-Camón et al. (2020)[16] documented undetectable or extremely low vitamin C levels among most ICU-admitted COVID-19 patients, while Tomasa-Irriguible (2021)[17] also reported extreme hypovitaminosis C among critically ill populations. These findings agree with previous findings in acute respiratory distress syndrome (ARDS), in which vitamin C deficiency is prevalent because of enhanced metabolic usage under oxidative stress and inflammation.

The incidence of vitamin A deficiency (<0.70 μmol/L) from 8.8% in mild disease rose to 50.0% in critical illness, and vitamin C deficiency (<11 μmol/L) from 2.9% in mild disease to 38.9% in critical illness (p for trend < 0.001 for both).This evidence implies that increasing COVID-19 severity has strong correlation with micronutrient deficiency, especially in critical illness. Vitamin A deficiency was fairly rare in mild illness but seen in one-third of severe and half critical illness. This concurs with the findings of Jovic et al. (2020)[13], who also noted substantially lower serum retinol in hospitalized COVID-19 patients, particularly those necessitating ICU placement. Likewise, Shakoor et al. (2021)[15] observed that deficiency in retinol correlated with longer hospital stay and unfavorable outcomes in Iranian patients. Aside from COVID-19, Stephensen (2001)[18] identified vitamin A deficiency as a predictor of compromised immune functions in respiratory infections, which may account for its role in exacerbating COVID-19. The stepwise worsening of vitamin C deficiency, up to almost 40% in critical patients, is consistent with the findings of ICU-based studies such as Chiscano-Camón et al. (2020)[16] found that a majority of ICU-admitted Spanish COVID-19 patients had undetectable or extremely low plasma vitamin C concentrations. Similarly, Tomasa-Irriguible (2021)[17] presented that hypovitaminosis C was nearly ubiquitous in critically ill patients and correlated with higher inflammatory markers. These findings reflect previous evidence in sepsis and ARDS, wherein Truwit JD et al. (2019)[19] stated significant depletion of vitamin C as a result of heightened metabolic utilization during systemic inflammation.

The present study showed thatboth vitamins A and C had significant positive correlations with oxygen saturation (SpO_2) and negative correlations with inflammatory and predictive markers like C-reactive protein (CRP), D-dimer, and hospital stay. The vitamin A and vitamin C positive correlations with oxygen saturation (r = +0.42 and r = +0.46, respectively) indicate that increased baseline levels of micronutrients are associated with improved pulmonary function. These results agree with Carr et al. (2020)[20,] who found that vitamin C supplementation enhanced oxygenation parameters in acute respiratory distress syndrome (ARDS) patients. Likewise, Semba (1999)[21] proved that vitamin A deficiency is implicated with heightened vulnerability to hypoxemia in lower respiratory tract infections, suggesting a potential protective effect on lung integrity. Both vitamins were negatively correlated with CRP, an important marker of systemic inflammation (vitamin A: r = -0.38; vitamin C: r = -0.41). This finding is consistent with the findings of Tomasa-Irriguible (2021)[17], who demonstrated that patients with hypovitaminosis C presented with elevated CRP values and poorer clinical outcomes. In the case of vitamin A, Jovic et al. (2020)[13] stated that decreased serum retinol was associated with increased inflammatory responses in COVID-19, which corroborated our results that compromised antioxidant defense might worsen inflammation. The inverse correlations of vitamin C (r = -0.33) and vitamin A (r = -0.29) with D-dimer indicate an association between antioxidant depletion and coagulopathy. Increased D-dimer has been a characteristic of serious COVID-19. Research by Chiscano-Camón et al. (2020)[16] noted that reduced levels of vitamin C were prevalent among thrombotic complication patients, indicating that oxidative stress and vitamin depletion can lead to endothelial dysfunction and hypercoagulability. Likewise, Trasino (2020)[14] speculated that vitamin A has a function in maintaining vascular integrity, and its deficiency can exacerbate microvascular injury during COVID-19. The negative correlations between vitamin A (r = -0.25) and vitamin C (r = -0.28) with hospitalization duration underscore their possible contribution to the speed of recovery. Holford et al. (2020)[22] stressed that optimal vitamin C shortens the duration of illness in respiratory infections, whereas Shakoor et al. (2021)[15] attributed vitamin A deficiency with extended lengths of stay in COVID-19 cases. These similarities support the clinical significance of ensuring adequate micronutrient status in acute illness. The multivariate logistic regression model demonstrates that decreased serum vitamin A and vitamin C were independently correlated with higher odds of having severe or critical COVID-19, even after controlling for age, diabetes, and hypertension. Every 0.1 µmol/L higher level of vitamin A was linked to a 25% decrease in risk (adjusted OR: 0.75, 95% CI: 0.62–0.90), and every 5 µmol/L increment in vitamin C was linked to an 18% lower risk (adjusted OR: 0.82, 95% CI: 0.71–0.94). These results suggest a possible protective effect of micronutrient adequacy against disease advancement. The reverse correlation between vitamin A levels and critical disease concurs with the findings of Jovic et al. (2020)[13], who found that patients with hyporetinolemia were at increased risk of ICU admission in COVID-19. Likewise, Trasino (2020)[14] theorized that retinoid signaling plays a key role in lung epithelial repair and immunomodulation, and deficiency could predispose to unchecked inflammation and tissue damage. Our results confirm this hypothesis by measuring the independent contribution of vitamin A to disease severity risk reduction. The independent action of vitamin C corroborates findings of Chiscano-Camón et al. (2020)[16], who observed that a majority of critically ill COVID-19 patients had undetectable plasma vitamin C, indicating speedy depletion under oxidative stress. Additionally, Carr & Rowe (2020)20 summarized evidence that vitamin C supplementation in sepsis and viral pneumonia enhances clinical outcome, such as decreased progression to multi-organ failure. As with previous research, age was identified as an independent risk factor, with each 10-year increase raising the risk of severe disease by 28%. This accords with Zhou et al. (2020)[8] and Williamson et al. (2020)[9], both of whom showed that older age was one of the strongest risk factors for COVID-19 death. Aging is linked to immunosenescence and loss of antioxidant defenses, which could provide an explanation for the synergistic risk in elderly patients with micronutrient deficiencies. Diabetes also independently predicted severe/critical disease (adjusted OR: 1.95, p=0.04). This was consistent with Zhu et al. (2020)[23], who observed greater ICU admission and mortality rates in patients with COVID-19 and diabetes. Poor glycemic control enhanced oxidative stress and inflammation, with possible worsening of vitamin deficiency effects in this population, Gupta et al. (2020)[24] added. While hypertension trended towards risk augmentation (OR: 1.72, p=0.09), it was not significant in our population. Previous research like Richardson et al. (2020)[12] documented hypertension as a significant comorbidity among hospitalized patients with COVID-19 but its independent impact has been different across populations, usually diluted once adjusted for age and obesity.

Conclusion

The current study proved that reduced baseline serum levels of vitamin A and vitamin C had a very strong association with greater severity of COVID-19. Severe and critical disease patients had significantly lower levels of both vitamins than patients with mild or moderate disease, and deficiency increased with the severity of the disease. Additionally, regression analysis also upheld that vitamin A and vitamin C individually lowered the risk of severe/critical disease even after controlling for age and comorbid conditions like diabetes and hypertension.

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