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Essential micronutrients in the clinical progression of SARS-CoV-2 in hospitalized patients

Micronutrientes esenciales en la evolución clínica del SARS-CoV-2 en pacientes hospitalizados

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Abstract

The present study aims to evaluate the relationship between the intake of essential micronutrients -selenium, zinc and vitamin C- and the clinical course of acute respiratory infection (ARI) caused by SARS-CoV-2 in hospitalized patients of the HNCASE (Hospital Nacional Carlos Alberto Seguín Escobedo), Arequipa, Peru. The research starts from the hypothesis that previous nutritional deficiencies could have negatively influenced the immune response, increasing the severity of the clinical picture. Through a descriptive-correlational approach, the patients' dietary habits before infection were analyzed, as well as clinical indicators such as lung damage and the need for supplemental oxygen. The results obtained allow us to establish that an insufficient intake of these micronutrients is associated with a greater severity of the disease. Consequently, the need to consider nutritional status as a modifiable risk factor in the management of patients with COVID-19 is highlighted, promoting preventive strategies based on nutrition. The study provides relevant evidence for the formulation of nutritional guidelines applied to respiratory viral diseases.

Keywords: Micronutrients, acute respiratory infection, SARS-CoV-2

Resumen

El presente estudio tiene como objetivo evaluar la relación entre la ingesta de micronutrientes esenciales —selenio, zinc y vitamina C— y la evolución clínica de la infección respiratoria aguda (IRA) provocada por el SARS-CoV-2 en pacientes hospitalizados del HNCASE (Hospital Nacional Carlos Alberto Seguín Escobedo), Arequipa, Perú. La investigación parte de la hipótesis de que deficiencias nutricionales previas podrían haber influido negativamente en la respuesta inmune, incrementando la gravedad del cuadro clínico. A través de un enfoque descriptivo-correlacional, se analizaron los hábitos alimentarios de los pacientes antes del contagio, así como indicadores clínicos como el daño pulmonar y la necesidad de oxígeno suplementario. Los resultados obtenidos permiten establecer que una ingesta insuficiente de estos micronutrientes se asocia con una mayor severidad de la enfermedad. En consecuencia, se resalta la necesidad de considerar el estado nutricional como un factor de riesgo modificable en el manejo de pacientes con COVID-19, promoviendo estrategias preventivas desde la alimentación. El estudio aporta evidencia relevante para la formulación de guías nutricionales aplicadas a enfermedades virales respiratorias.

Palabras clave: Micronutrientes, infección respiratoria aguda, SARS-CoV-2

Introduction

The pandemic caused by SARS-CoV-2 has had a profound impact on health, economics, and society on a global scale, affecting the world's population unevenly. Although public health measures have been implemented to contain the spread of the virus, such as social distancing, personal hygiene, and isolation, the burden of the disease has fallen more heavily on immunocompromised individuals or those in vulnerable situations. In this context, the clinical evolution of patients infected with COVID-19 has been the subject of numerous investigations, identifying factors that may predispose individuals to a more severe progression, including the presence of comorbidities, advanced age, and increasingly, nutritional status.

Deficiencies in certain micronutrients such as selenium, zinc, and vitamin C have been identified as critical factors that could negatively influence immune responses to viral infections (Carr & Maggini, 2017). These

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compounds, found in specific foods within the typical diet, actively participate in the modulation of inflammation, antioxidant function, and activation of the immune system.

Vitamin C, for example, has been shown to not only act as an antioxidant by neutralizing free radicals but also to enhance the production of anti-inflammatory cytokines such as IL-10, reduce pro-inflammatory cytokines like TNF-α, and even accumulate in high concentrations in leukocytes, thereby strengthening the immune response (Shakoor et al., 2020). Similarly, zinc has been identified as an essential mineral in regulating both innate and acquired immune responses, influencing epithelial barrier function, cytokine modulation, and viral replication (Khatiwada & Subedi, 2021; Zabetakis et al., 2020). Zinc deficiency has also been associated with increased pulmonary inflammation, making supplementation a preventive resource against the progression of severe respiratory complications (Wolfgruber, 2023).

Selenium, for its part, has been extensively studied for its antioxidant capacity, its role in the expression of key selenoproteins, and its influence on both cellular and humoral immunity. Recent research has documented that low selenium levels are associated with greater severity and mortality in COVID-19 patients (Roldán & Capuchino, 2023; Zhou & Yuan, 2023). Selenium not only protects against oxidative stress but also helps limit viral replication, enhances T cell function, and modulates systemic inflammation (Hardy et al., 2019; Manzanares et al., 2019). Furthermore, areas with selenium-poor soils tend to report higher incidences and adverse progressions of viral diseases due to weakened immune defenses and the promotion of more aggressive viral mutations (Kieliszek & Lipinski, 2020; Taylor et al., 2022). Thus, scientific evidence reinforces the importance of ensuring adequate intake of these micronutrients in both preventive contexts and clinical treatments.

Various studies have underscored the relevance of selenium, zinc, and vitamin C in strengthening the immune system against SARS-CoV-2. Shakoor et al. (2020) highlight that COVID-19 patients exhibit elevated levels of pro-inflammatory cytokines such as IL-6, IL-2, and IL-7, which trigger severe systemic inflammation. In this context, adequate levels of micronutrients like selenium and vitamin C contribute to a more effective immune response by reducing oxidative damage and modulating inflammatory responses. Manzanares et al. (2019) and Hardy et al. (2019) indicate that selenium deficiency is linked to greater clinical severity and impaired immune responses, recommending its supplementation in critically ill patients to improve clinical outcomes. Additionally, Kieliszek and Lipinski (2020) note that sodium selenite could inhibit viral infectivity by altering protein structures essential for the virus's entry into cells. This therapeutic potential is reinforced by findings from Khatiwada and Subedi (2021), who associate selenium deficiency with higher mortality in hospitalized patients.

On the other hand, Zabetakis et al. (2020) argue that healthy nutrition plays a key role in mitigating severe inflammatory processes, emphasizing the importance of consuming foods rich in antioxidants and micronutrients. In line with this, Zhou et al. (2023) demonstrate a significant decrease in metalloid levels such as selenium and zinc in COVID-19 patients, affecting immune homeostasis. Similarly, Taylor et al. (2022) suggest that optimal selenium levels enhance both T and B lymphocyte responses, improving viral clearance. In a recent meta-analysis, Roldán and Capuchino (2023) conclude that infected patients exhibit lower serum selenium levels than healthy individuals, although without substantial differences according to clinical severity. Finally, Wolfgruber (2023) reports significant antiviral effects of zinc oxide nanoparticles against SARS-CoV-2, particularly against variants such as Delta and Omicron. Collectively, these findings support the role of certain micronutrients as adjuncts in the immune response to emerging viral infections.

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Table 1

Food Sources of Selenium, Zinc, and Vitamin C (per 100 g of product)

Food	Selenium (µg)	Zinc (mg)	Vitamin C (mg)
Beef	36.04	4.32	-
Lamb	38.5	-	-
Poultry (hen)	30.3	-	-
Poultry (chicken)	25.2	1.21	-
Fresh cow's milk	15.47	0.4	-
Chicken egg	10	4.62	-
Fresh fish (jurel, etc.)	46.8	-	-
Seafood (shrimp, mussels)	56.5	1.60	-
Lamb liver	24	4.66	-
Common wheat bread	20.5	-	-
White bread or butter	10.23	-	-
Oats	7.98	-	-
Brown rice	7.64	-	-
Refined rice	3.25	-	-
Nuts	29.76	-	-
Peanuts	3	-	-
Garlic	14.2	-	-
Tuna	108.3	-	-
Turkey meat	-	2.20	-
Pork meat	-	1.74	-
Chicken/Hen liver	-	6.59	-
Yogurt	-	0.59	-
Fresh cheese (Andean)	-	4.43	-
Paria cheese	-	3.39	-
Lentils/beans	-	4.78	-
Quinoa flour	-	5.19	-
Wheat flour	-	2.98	-
Orange	-	-	92.30
Lemon	-	-	44.20
Mandarin	-	-	48.70
Strawberry	-	-	42
Kiwi	-	-	86.76
Northern papaya	-	-	47.70
Red tuna	-	-	33.66
Lime	-	-	36
Guava	-	-	60
Broccoli	-	-	114
Tomato	-	-	18.40
Cabbage	-	-	31.40
Cucumber	-	-	12.60
Potatoes	-	-	14
Cassava	-	-	36

Considering the above, this study aims to evaluate the correlation between the intake of sources of selenium, zinc, and vitamin C, and the progression of acute respiratory infections caused by SARS-CoV-2 in hospitalized patients at HNCASE. This is crucial for establishing preventive strategies and strengthening nutritional care as a key component in the comprehensive management of COVID-19.

Methodology

The present research adopted a correlational quantitative approach, aimed at determining the relationship between dietary habits—specifically the consumption of micronutrients such as selenium, zinc, and vitamin C—and the clinical respiratory status in patients hospitalized due to SARS-CoV-2 infection. The study was conducted during the COVID-19 health emergency at the Carlos Alberto Seguín Escobedo National Hospital (HNCASE),

EsSalud-Arequipa, and was executed under a field design of a documentary-relational type, in two phases spanning from July 2021 to August 2023, following formal approval from the relevant institutional ethics committee.

To address the variable "dietary habits," a communication technique was utilized through a structured interview, applying a validated food anamnesis format based on a consumption recall. This instrument, developed and approved by the Nutrition Department of EsSalud (Resolution of the Central Management of Health Benefits No. ia_GCPS-ESSALUD-2017), enabled the identification of both the frequency and quantity of foods consumed by the patients, with an emphasis on estimating daily intake of selenium, zinc, and vitamin C. The procedure was based on the nutritional protocol of EsSalud designed for immunocompromised patients due to chronic illnesses such as cancer or severe infections.

Regarding the variable “clinical status of acute respiratory infection (ARI),” an observational-documentary technique was employed using a data collection format derived directly from the patients' medical records. This instrument allowed for the recording of parameters such as the percentage of lung damage diagnosed, the severity level of the respiratory infection, and the need for oxygen therapy, expressed as the fraction of inspired oxygen (FiO_2) administered via a simple nasal cannula.

The study took place in the hospitalization area of HNCASE, located in the city of Arequipa. The nature of the research was situational, coinciding with the critical context of the COVID-19 pandemic. Following the presentation and approval of the protocol by the Training, Research, and Teaching Office of the Arequipa Health Network of EsSalud, data collection was carried out during the specified period.

The target population consisted of 60 adult patients of both sexes, hospitalized for COVID-19 with a confirmed diagnosis of acute respiratory infection and atypical pneumonia, who were also receiving oxygen therapy via nasal cannula. The sample was non-probabilistic and convenience-based, comprising 15 patients who voluntarily agreed to participate, signing the informed consent and meeting the inclusion criteria.

Among the criteria considered were: confirmed diagnosis of ARI due to SARS-CoV-2, mild to moderate clinical status, treatment with oxygen via simple nasal cannula, and preserved communicative ability to conduct the interview. Conversely, patients in critical condition, in intensive care, using high-flow masks that impeded communication, or who declined to participate were excluded.

Data collection was carried out using the food anamnesis instrument for dietary habits and an observational format for extracting clinical data from medical histories. Prior to this, each patient received a detailed explanation of the study and signed the respective informed consent.

The anamnesis instrument used for dietary data collection has been previously validated by experts from EsSalud, in accordance with Resolution of the Central Management of Health Benefits No. ia_GCPS-ESSALUD-2017, which approves the “Nutritional Intervention Guide for Patients with Cancer and Severe Infections,” adapted to the context of the present study.

The obtained information was systematized into matrices created in Microsoft Excel and subsequently processed using SPSS statistical software. To establish associations between quantitative variables, Pearson’s correlation coefficient was employed, a statistical test that evaluates the degree of linear relationship between two continuous variables. This can range from +1 to -1, indicating positive or negative relationships of varying magnitudes, while a value of 0 suggests no association. The interpretation of these values allowed for the establishment of the strength and direction of correlations between micronutrient intake and respiratory indicators.

Results and discussion

Table 2

Frequency of sex distribution of patients hospitalized with SARS-CoV-2 at HNCASE

SEX	No.	%
Male	11	73,3
Female	4	26,7
Total	15	100

The sex distribution of patients hospitalized with SARS-CoV-2 at the Carlos Alberto Seguín Escobedo National Hospital (HNCASE) reveals a marked prevalence of the male gender, representing 73.3% of the total cases compared to 26.7% corresponding to the female sex. This difference suggests a greater clinical vulnerability of males to complications requiring hospitalization, a trend reported in various studies on the impact of COVID-19, possibly linked to biological, immunological, and behavioral factors differing between the sexes. The total number of patients considered in this sample was fifteen, which, although limited, allows for the observation of a pattern consistent with international scientific literature.

Table 3
Age of patients hospitalized with SARS-CoV-2 at HNCASE

Statistics	Age
Mean	43,40
Std. Deviation	12,04
Minimum	25
Maximum	65
N	15

Data regarding the age of patients hospitalized with SARS-CoV-2 at HNCASE show a mean age of 43.40 years, with an age range between 25 and 65 years, and a standard deviation of 12.04. This age profile indicates that the majority of affected individuals fall within the middle-aged adult group, a segment that, while not representing the most vulnerable in terms of lethality, does show significant risks of hospitalization, especially when comorbid factors or immune deficiencies are present. The dispersion of the data suggests a moderately broad distribution within the adult group, reinforcing the need for prevention and monitoring strategies in this population segment.

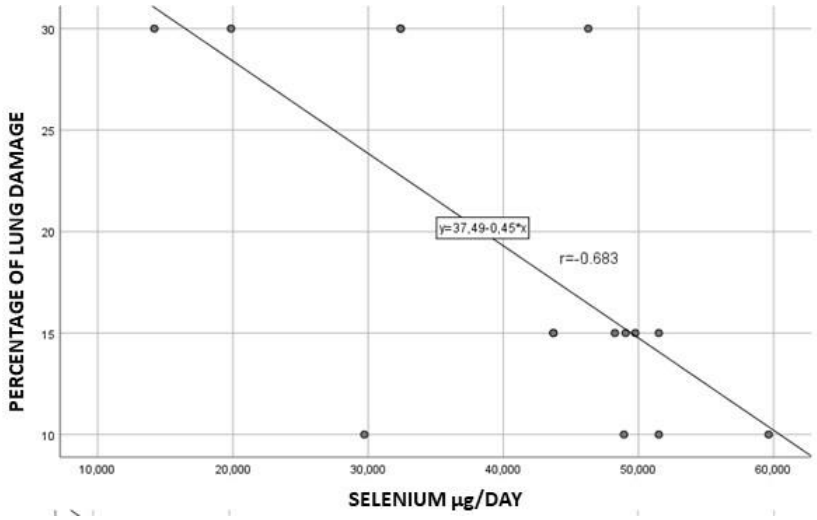
Table 4
Clinical and nutritional indicators in patients hospitalized with SARS-CoV-2 at HNCASE

Indicator	Mean	Standard Deviation	Minimum	Maximum
Selenium Intake (µg/day)	41,39	12,83	14,19	59,62
Zinc Intake (mg/day)	3,79	1,76	0,69	5,96
Vitamin C Intake (mg/day)	44,41	13,29	25,00	60,30
Percentage of Lung Damage (%)	18,67	8,55	10,00	30,00
Fraction of Inspired Oxygen (FiO_2%)	18,33	8,16	10,00	30,00

The integrated assessment of clinical and nutritional indicators in patients hospitalized with SARS-CoV-2 at HNCASE reveals a concerning pattern of nutritional deficiency that may be linked to the deterioration of observed respiratory parameters. The average selenium intake was 41.39 µg/day, with considerable dispersion (SD = 12.83), while zinc intake reached only 3.79 mg/day, significantly below the recommended values for adequate immune function. Similarly, the average consumption of vitamin C was 44.41 mg/day, indicating insufficient intake compared to the established daily requirements for adults. These reduced levels coincide with an average lung damage percentage of 18.67% and a fraction of inspired oxygen (FiO_2) of 18.33%, suggesting a possible relationship between micronutrient deficiency and the clinical severity of respiratory conditions.

Figure 1

Relationship between percentage of lung damage and dietary selenium deficiency in patients before hospitalization with SARS-CoV-2 at HNCASE

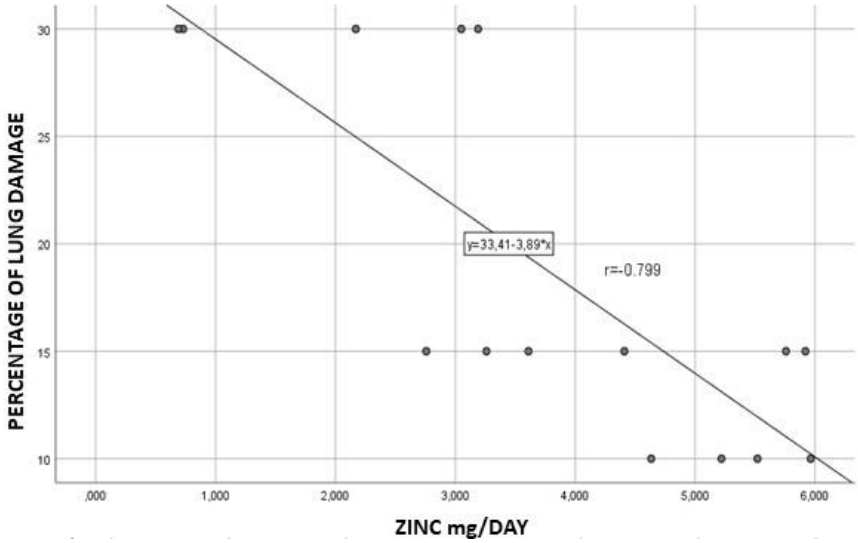


The figure demonstrates a significant inverse relationship between daily selenium intake and the percentage of lung damage in patients with SARS-CoV-2, represented by a negative slope in the linear regression (y = 37.49 - 0.45x) and a correlation coefficient of r = -0.683, suggesting a moderate to strong correlation.

This finding indicates that higher selenium consumption is associated with lower degrees of lung impairment, which may be attributed to the antioxidant and immunomodulatory properties of this micronutrient. Likewise, a selenium-deficient diet prior to infection and hospitalization increases the likelihood of greater lung damage.

Figure 2

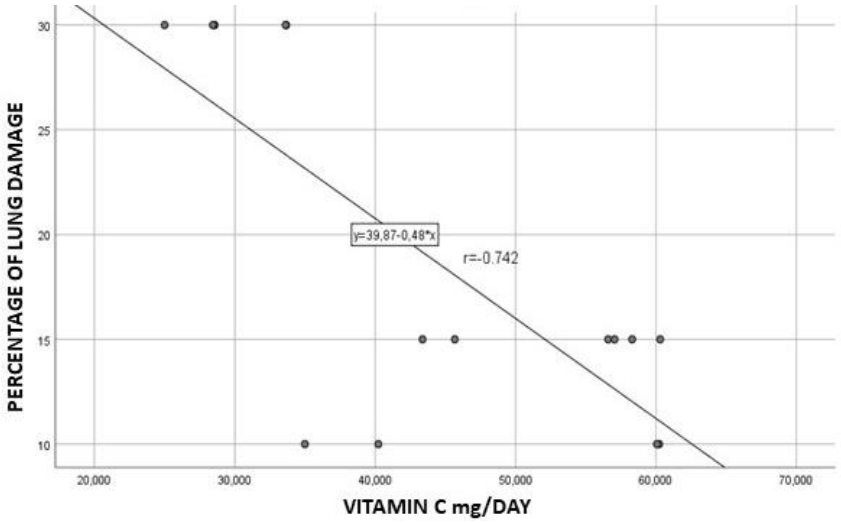
Relationship between percentage of lung damage and dietary zinc deficiency in patients before hospitalization with SARS-CoV-2 at HNCASE



The graph shows a significant negative correlation between zinc intake and the percentage of lung damage in patients infected with SARS-CoV-2. The slope of the linear regression (y = 33.41 - 3.89x) and the correlation coefficient r = -0.799 indicate a strong inverse relationship: as zinc consumption increases, the degree of lung damage decreases. This association can be explained by the protective immune role of zinc, an essential trace element in regulating the inflammatory response and maintaining pulmonary epithelial integrity. Therefore, a zinc-deficient diet prior to infection and hospitalization increases the probability of greater lung damage.

Figure 3

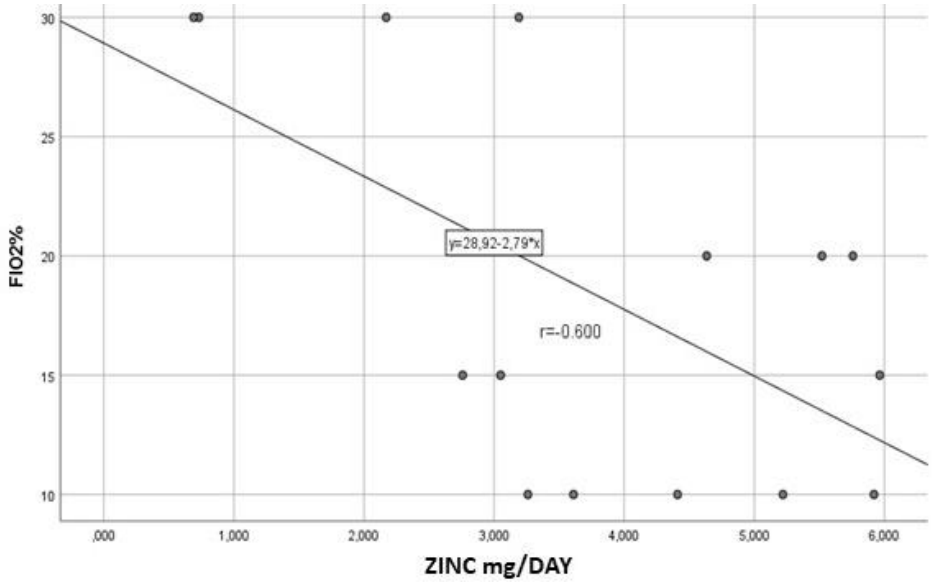
Relationship between percentage of lung damage and dietary vitamin C deficiency in patients before hospitalization with SARS-CoV-2 at HNCASE



The graphical analysis reveals a statistically significant inverse relationship between daily vitamin C intake and the percentage of lung damage in patients with SARS-CoV-2, represented by the regression equation y = 39.87 - 0.48x and a correlation coefficient of r = -0.742, indicating a strong association. Higher vitamin C consumption is associated with a lower proportion of lung impairment, reinforcing the antioxidant and anti-inflammatory roles of this vitamin in protecting respiratory tissue against damage induced by severe infectious processes such as COVID-19. Thus, a vitamin C-deficient diet prior to infection and hospitalization increases the likelihood of greater lung damage.

Figure 4

Relationship between fraction of inspired oxygen and dietary selenium deficiency in patients before hospitalization with SARS-CoV-2 at HNCASE

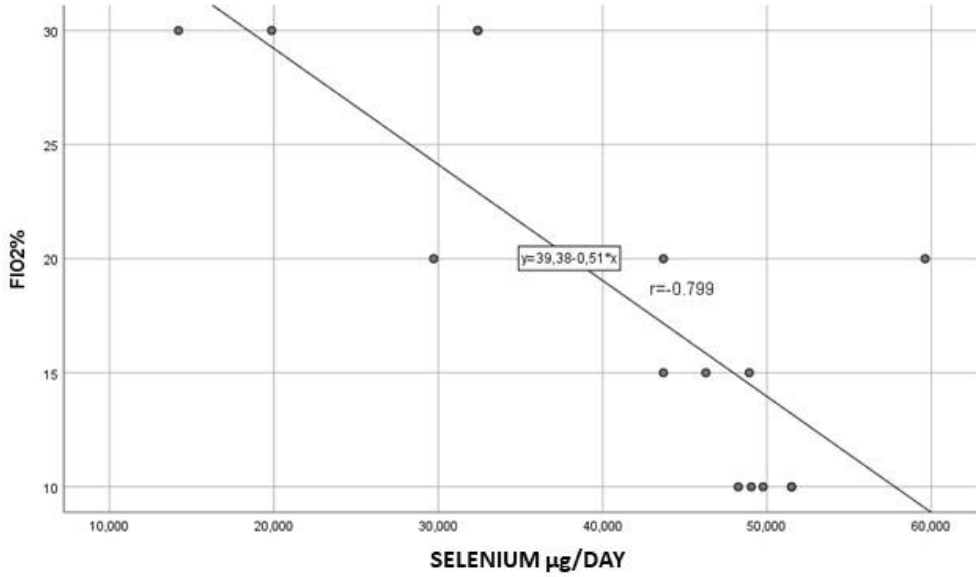


The figure shows a robust inverse correlation between daily selenium intake and the fraction of inspired oxygen (FiO_2%) in patients hospitalized with SARS-CoV-2, expressed through the regression equation y = 39.38 - 0.51x and a correlation coefficient r = -0.799, indicating a strong association. This finding suggests that higher selenium consumption is associated with a reduced need for supplemental oxygen therapy, potentially due to selenium's ability to modulate the inflammatory response and mitigate oxidative stress in lung tissue.

Consequently, selenium-deficient diets in patients prior to infection and hospitalization increase the likelihood of requiring greater supplemental oxygen via nasal cannula.

Figure 5

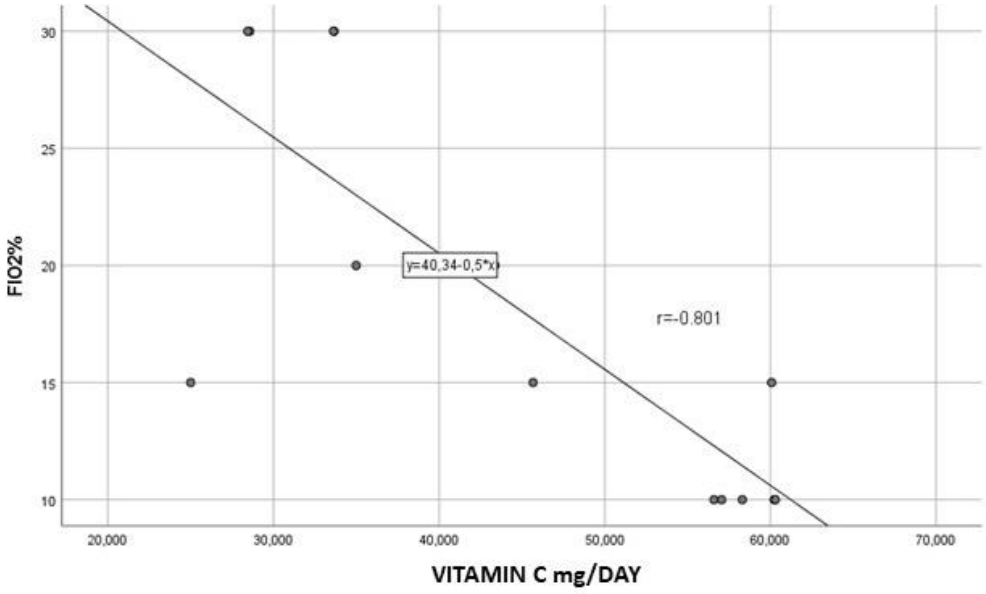
Relationship between fraction of inspired oxygen and dietary zinc deficiency in patients before hospitalization with SARS-CoV-2 at HNCASE



The graph demonstrates a moderate negative correlation between daily zinc intake and the fraction of inspired oxygen (FiO_2%) in hospitalized COVID-19 patients, represented by the regression equation y = 28.92 - 2.79x and a correlation coefficient r = -0.600. This relationship indicates that patients with higher zinc intake required a smaller proportion of supplemental oxygen, which may be associated with zinc's immunomodulatory role in reducing pulmonary epithelial damage and improving respiratory function. Therefore, a zinc-deficient diet in patients prior to hospitalization increases the likelihood of requiring greater oxygen assistance through oxygen therapy.

Figure 6

Relationship between fraction of inspired oxygen and dietary vitamin C deficiency in patients before hospitalization with SARS-CoV-2 at HNCASE



The figure shows a strong inverse correlation between vitamin C intake and the fraction of inspired oxygen (FiO_2%) in patients hospitalized with SARS-CoV-2, represented by the equation y = 40.34 - 0.5x and a correlation coefficient of r = -0.801. This association indicates that higher vitamin C consumption correlates with lower oxygen therapy needs, highlighting the crucial role of this micronutrient as an antioxidant in pulmonary defense. Vitamin C contributes to the preservation of alveolar integrity and the modulation of inflammation, thereby reducing the severity of respiratory compromise. A vitamin C-deficient diet prior to infection and hospitalization increased the likelihood of greater inflammation and consequently a higher requirement for oxygen.

Recent studies have shown that the immune response to SARS-CoV-2 can be significantly influenced by an individual's nutritional status, particularly by the adequate presence of micronutrients such as zinc, selenium, and vitamin C. Calder (2020), Maggini et al. (2018), and Shakoor et al. (2020) agree that these compounds play a protective role by modulating inflammation and enhancing both innate and adaptive immune responses. Vitamin C, in particular, has been highlighted by Carr and Maggini (2017) as a key antioxidant that reduces oxidative stress and improves the function of immune-competent cells, which is especially relevant in acute respiratory infections such as COVID-19.

Regarding zinc, multiple authors have evidenced its capacity to inhibit viral replication, stabilize cell membranes, and contribute to antibody production. Wollfgruber (2023) experimentally demonstrated the antiviral action of zinc oxide nanoparticles against SARS-CoV-2, while Díaz (2021) and Shakoor et al. (2020) indicated that patients with adequate levels of this trace element had a lower incidence of prolonged hospitalization and severe lung damage. Additionally, findings by Ping-Chiu and Chiu (2018) emphasize the regulatory role of zinc on endogenous antiviral proteins, reinforcing its use as an immune supplement in the early stages of the disease.

Selenium, for its part, has been extensively studied by authors such as Manzanares et al. (2020), Roldán and Capuchino (2023), Margaret et al. (2022), and Zhou and Yuan (2023), who demonstrated that its deficiency can worsen the clinical course of SARS-CoV-2 due to the loss of efficacy of selenium-dependent antioxidant enzymes. Hu and Zhao (2021) highlight that a diet rich in natural sources of selenium, such as whole grains and lean meats, can act as a preventive factor against viral respiratory diseases, reducing systemic inflammatory impact. This finding is consistent with observations by Kieliszek and Lipinski (2020), who associated low selenium levels with a higher probability of admission to intensive care units in COVID-19 patients.

From the perspective of the clinical evolution of lung damage in COVID-19 patients, research by Bösmüller et al. (2020), Ackermann et al. (2020), and Wu et al. (2020) describes pathological processes characterized by alveolar inflammation, thrombosis, and pulmonary fibrosis, which could be mitigated through nutritional support that enhances antioxidant activity and tissue oxygenation. Chan et al. (2020) and Sun et al. (2020) explored animal and structural models, respectively, demonstrating how the interaction between the virus and the respiratory system can be modulated by pre-existing systemic conditions, such as the deficiency of essential nutrients. The relationship among oxygen therapy, lung damage, and micronutritional supplementation thus represents a line of investigation with significant clinical potential.

Authors such as Combarnous et al. (2020), Junaid and Ejaz (2020), Maggini et al. (2018), Surai and Michele (2020), and Calder (2020) agree that micronutrients should not be considered isolated interventions but rather part of a comprehensive "pharmaconutrition" approach. These nutrients act synergistically, optimizing metabolic and cellular functions during acute inflammatory states. In this context, the present research reaffirms the necessity of integrating nutritional protocols into the hospital care of COVID-19 patients, particularly those in moderate phases receiving oxygen therapy.

Conclusions

The findings of this study affirm that adequate and sustained intake of micronutrients such as selenium, zinc, and vitamin C plays a crucial role in the clinical progression of patients hospitalized with acute respiratory infections caused by SARS-CoV-2. The analyzed evidence reinforces the hypothesis that a deficient nutritional state in these elements can exacerbate the inflammatory response and compromise the immune system, negatively affecting the recovery of those affected. Therefore, it is essential to incorporate specific nutritional guidelines as part of prevention and treatment protocols, not only in hospital settings but also from a public health perspective aimed at strengthening population immunity against future pandemics. This integrative approach, linking nutrition and immunity, represents a key opportunity to reduce morbidity and mortality associated with emerging viral respiratory diseases.

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