e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2025; 17(12); 471-475

Original Research Article

Efficacy of Micronutrients and Cumulative Impact of Steroid Utilization in Moderate to Severe Cases of COVID Pneumonia, Harping to Latent Avascular Necrosis of Head of the Femur: A Retrospective Analysis

Y. Devadas[1], Y. Hadassah Vathsalya[2], P. Umanadh[3]

[1]Associate Professor, Department of Orthopaedics, Viswabharathi Medical College, Penchikalapadu. Kurnool, Andhra Pradesh, India

[2] Assistant Professor, Department of Biochemistry, Santhiram Medical College, Nandyala, Andhra Pradesh, India

[3]Professor and Head, Department of Orthopaedics, Viswabharathi Medical College, Penchikalapadu. Kurnool, Andhra Pradesh, India

Received: 01-09-2025 / Revised: 15-10-2025 / Accepted: 21-11-2025

Corresponding author: Dr. Y. Hadassah Vathsalya

Conflict of interest: Nil

Abstract

The COVID-19 pandemic that hit globally has left devastating effects economically, bodily and psychosociological. The results of post viral complications and its remedy protocols have been substantially studied, published in various journals but sequalae of long duration steroidal treatment effects & coping efforts, has been restrained mainly in the third world countries like India. The micronutrients in bodily frame play a pivotal function in fighting the contamination by distinctive mechanisms. Of them zinc, ascorbic acid and vitamin D have crucial function in controlling the entry of virus into host cells and modifying the anti-inflammatory markers in reaction to body immunology. As the covid infection results in multiorgan involvement with raised CRP, (C reactive protein) and D dimer in reaction to infection, therefore the steroids dexamethasone, methylprednisolone, performed a crucial function in preventing the dangerous outcomes of anti-inflammatory cascade, but the excessive doses that has necessitated to manipulate the storm of inflammation, resulted in shorterm and long-term effects in patients like Avascular necrosis of femoral head, mainly in post-menopausal females, elderly males or even younger people, who have been admitted and discharged from Govt Hospital and Medical college, Kurnool, Andhra Pradesh.

Keywords: COVID-19, CRP, (C-Reactive Protein), D-dimer, Zinc, Ascorbic Acid And Vitamin D.

Introduction

The coronavirus disease 2019 (COVID-19) pandemic has led to unprecedented morbidity and mortality worldwide, with severe pneumonia representing a major clinical challenge. In the management of moderate to severe cases, two important therapeutic domains have been explored: micronutrient supplementation and corticosteroid therapy.[1]

Micronutrients such as zinc, ascorbic acid, and vitamin D are known to play a pivotal role in immune modulation and antiviral defense, particularly in respiratory viral infections. Early reports suggested their potential to attenuate the hyper-inflammatory response associated with COVID-19, thus generating considerable global interest.[2]

Several studies have documented widespread micronutrient deficiencies during the pandemic, particularly in Asian populations, highlighting the relevance of zinc and vitamin C depletion in infected patients compared to healthy controls. Interventional trials, however, have provided mixed evidence, with some demonstrating improvements in inflammatory markers and oxygen requirements, while others reported no significant reduction in symptom duration or disease severity. Despite theoretical benefits, the inconsistency of clinical outcomes has limited their stand-alone therapeutic value. [3]

In contrast, corticosteroids such as methylprednisolone and dexamethasone have shown consistent benefit in radiologically confirmed severe cases (CORADS 4–6), offering rapid symptomatic relief, improved oxygenation, and facilitated ventilatory weaning.

Nevertheless, these gains come at the cost of well-documented adverse effects, including steroid-induced hyperglycemia, impaired bone mineralization, and long-term complications such as avascular necrosis (AVN) of the femoral head. The cumulative impact of prolonged steroid use in COVID-19 survivors is now a pressing concern in post-pandemic clinical practice. [4]

This retrospective analysis aims to critically evaluate the efficacy of micronutrient supplementation and the cumulative burden of steroid utilization in moderate to severe COVID-19 pneumonia. Particular emphasis is placed on the emerging sequelae of avascular necrosis of the femoral head, underscoring the need for a balanced therapeutic strategy that maximizes survival while minimizing delayed musculoskeletal morbidity.

Methods and Materials

This will be a retrospective study conducted in a tertiary care hospital of the Govt of Andhra Pradesh in the department of Orthopedics. Ethical clearance for the study was obtained from the Institutional ethical committee prior to the commencement of the study.

Study Design: Retrospective study.

Study Period: April 2021- August 2021.

Sample Size: 650 Cases.

Inclusion Criteria:

1. All patients of age between 15-75 yrs admitted in COVID designated blocks for moderate (requiring CPAP/BIPAP), and severe cases (Requiring ventilatory support), whose SPO2 on admission is less than 80%, after RT-PCR positivity.

Exclusion Criteria:

1. Paediatric age group (age < 15 years).
2. Pregnant women.
3. On admission ventilatory support.
4. Previous comorbidities (HTN, TYPE IIDM, COPD, Bronchial Asthma, On steroid dependency for any reason).

Methods

1. Patients' Blood samples have been processed on day of admission for Zinc, vitamin C, Vitamin D, CRP, D Dimer values.

2. Patients who have progressed from mild to moderate and patient who tolerated severe disease and who have been administered long course of steroids during hospital stay, have been followed during treatment and 02 months post discharge, and 06 months and 1 year in medical OPD data base registry.

Statistical Analysis: All collected data were compiled and analyzed using SPSS software (Version 24.0,) Descriptive statistics were expressed as mean ± standard deviation for continuous variables, and categorical variables were presented as frequencies and percentages.

Associations between micronutrient levels, steroid exposure, and outcomes were assessed using appropriate inferential tests, with $p < 0.05$ considered statistically significant.

Results

In this retrospective study of 650 COVID-19 patients, 312 developed moderate disease requiring CPAP and 300 severe disease requiring ventilatory support, while 38 with mild illness improved on micronutrients alone. Among severe cases, 247 survived and 53 succumbed. A total of 559 patients (86%) received intravenous methylprednisolone for 12–21 days. Steroid-related complications included impaired glucose in 264 (47.2%), spontaneous pneumothorax in 74 (13.2%), hydropneumothorax in 148 (26.5%), bilateral pedal edema with right heart strain in 73 (13.0%), wedge compression fractures in 33 (5.9%), and acute gastritis in 163 (29.1%). Most glucose abnormalities resolved, except in four patients requiring oral hypoglycemics. Pneumothorax cases were managed with ICDs; three patients developed DVT. On long-term follow-up, 23 patients (4.1%) developed avascular necrosis (AVN) of the femoral head, predominantly among those with pneumothorax, hydropneumothorax, and pedal edema.

These findings highlight the dual challenge of managing COVID-19 severity with steroids while mitigating their musculoskeletal and systemic sequelae.

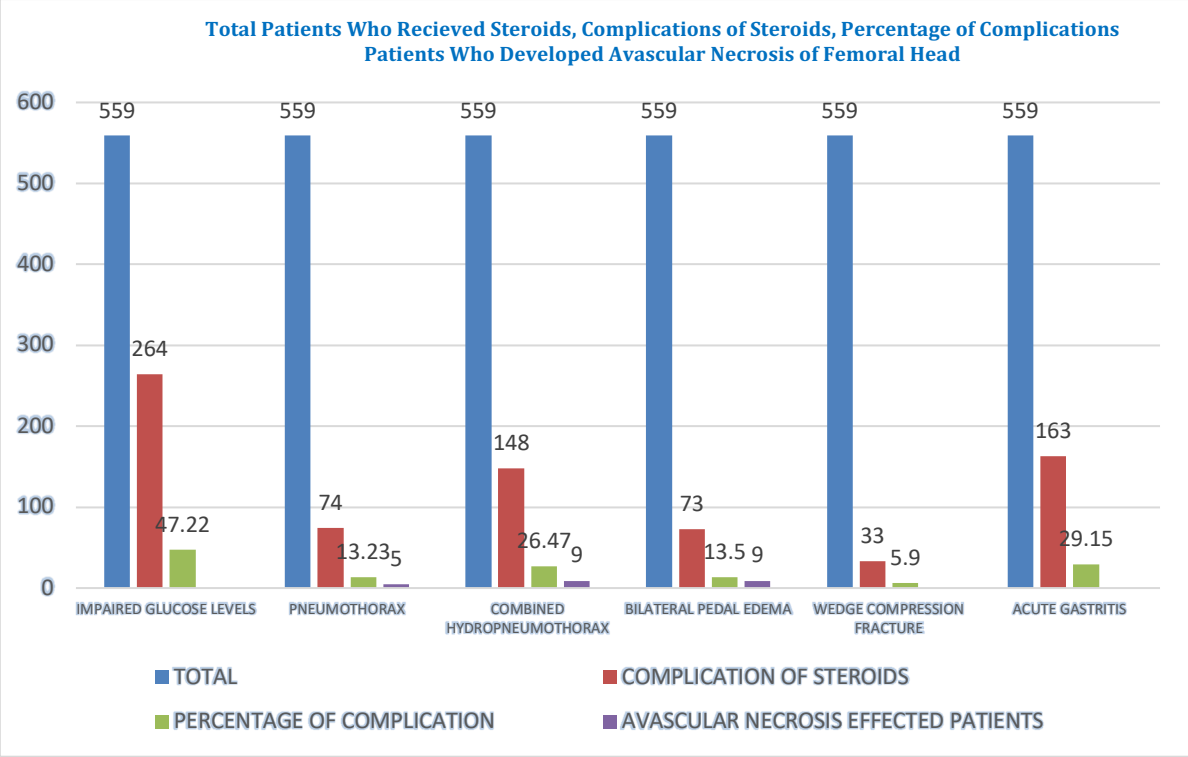

Figure 1: Total Patients Who Received Steroids, Complications of Steroids, Percentage of Complications Patients Who Developed Avascular Necrosis of Femoral Head

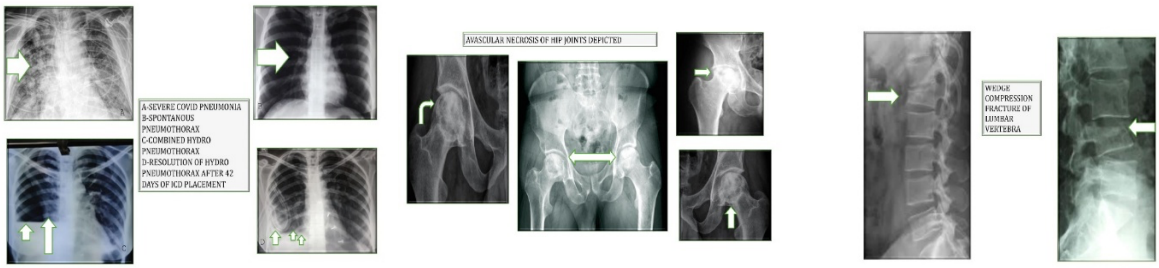

Figure 2: X rays showing Pneumonia and complications of steroids

Discussion

Zinc, vitamin C, and vitamin D have long been recognized as modulators of immunity and antiviral defense. A study from June 2020 demonstrated that zinc deficiency was more prevalent in affluent societies (17.5%) compared to Asian populations (8.9%). Similarly, an Indian prospective observational study in May 2021 reported significantly lower zinc levels in COVID-19 patients (74.5 µg/dL) versus healthy controls (105.8 µg/dL; $p<0.01$).[5] These findings corroborate the results of cohort, where reduced zinc was associated with greater severity of disease.

The mechanistic basis for zinc's protective role lies in its regulation of innate and adaptive immunity. Zinc deficiency impairs maturation of lymphoid tissue and NK cells, reduces interferon-mediated viral clearance, and disrupts apoptosis regulation by altering caspase activity and BCL-2/Bax ratios. Despite this, randomized clinical trials have shown mixed benefits. For instance, supplementation with zinc gluconate (50 mg) and high-dose vitamin C (8,000 mg/day) did not significantly shorten symptom duration compared to standard care. [6]

Vitamin C, a potent antioxidant, has been associated with protection against viral pneumonia and attenuation of inflammatory cascades. In Indian studies, administration of 1 g vitamin C thrice daily for 3 days reduced inflammatory markers such as ferritin and D-dimer, while lowering oxygen requirements. [7] Similarly, a trial at Zhongnan Hospital, Wuhan University, demonstrated that high-dose intravenous vitamin C (up to 24 g/day) improved chest radiograph findings and reduced systemic inflammation. However, these benefits remained supportive rather than definitive. [8]

Vitamin D has been linked to respiratory outcomes through epidemiological data. The NHANES 2001–2006 survey and Indonesian studies found

higher mortality in COVID-19 patients with deficiency (<20 ng/mL) or insufficiency (21–29 ng/mL). Vitamin D enhances epithelial barrier integrity and induces antimicrobial peptides such as cathelicidins and defensins, while also mitigating cytokine storm–driven alveolar injury. In cohort, vitamin D deficiency correlated with prolonged hypoxia and delayed recovery, highlighting its role in host protection. [9]

Despite these theoretical and supportive roles of micronutrients, the most consistent survival benefit in moderate-to-severe COVID-19 has been with systemic corticosteroids. A prospective meta-analysis of seven randomized controlled trials confirmed that corticosteroid therapy reduced 28-day mortality. The Surviving Sepsis Campaign COVID-19 guidelines accordingly recommend their use in ARDS and refractory shock. Mechanistically, methylprednisolone and dexamethasone suppress proinflammatory cytokines (IL-1, IL-6, TNF-α, IFN-γ) and upregulate anti-inflammatory mediators (IL-10, lipocortin). [10]

In present study, 559 patients (86%) received intravenous methylprednisolone for 12–21 days. Steroid therapy was associated with rapid clinical improvement, reduced ventilatory dependency, and symptomatic relief, consistent with global data. However, complications were frequent: impaired glucose in 47.2%, spontaneous pneumothorax in 13.2%, hydropneumothorax in 26.5%, pedal edema with right heart strain in 13.0%, wedge compression fractures in 5.9%, and acute gastritis in 29.1%. These highlight the double-edged nature of corticosteroid therapy.

A key long-term complication observed was avascular necrosis (AVN) of the femoral head, developing in 23 patients (4.1%) over one year. AVN risk is linked to daily and cumulative steroid dose, with parenteral regimens carrying greater risk. Early diagnosis is often missed due to lack of symptoms in initial stages, leading to late presentation requiring surgical management such as total hip replacement. The findings echo earlier reports linking prolonged steroid use to osteonecrosis, emphasizing the need for vigilance in post-COVID follow-up.

Thus, while micronutrient supplementation may provide an immunological advantage and supportive anti-inflammatory effect, their impact remains modest compared to corticosteroids in severe COVID-19. Yet, corticosteroids come at the expense of metabolic, pulmonary, gastrointestinal, and skeletal sequelae. Present study underscores the importance of balancing acute survival with long-term morbidity, highlighting the necessity of screening for steroid-induced AVN and metabolic complications during follow-up.

Conclusion

In this retrospective study of 650 COVID-19 patients, lower baseline levels of zinc, vitamin C, and vitamin D were associated with greater disease severity and delayed recovery. Patients with adequate micronutrient levels demonstrated better outcomes, supporting their potential role as prophylactic rather than purely therapeutic agents.

Corticosteroid therapy provided significant survival benefit in moderate-to-severe cases but was associated with multiple complications, including metabolic, pulmonary, gastrointestinal, and skeletal effects. Notably, 23 patients (4.1%) developed avascular necrosis on follow-up, underscoring the long-term risks of high-dose, and prolonged steroid use. The findings emphasize the dual need for micronutrient optimization and cautious, monitored steroid administration to balance survival with prevention of late morbidity.

Summary

Low levels of zinc, vitamin C, and vitamin D were linked to increased severity of COVID-19, while adequate levels aided early recovery.

Steroids improved survival in moderate-to-severe cases but caused significant complications, including hyperglycemia, pneumothorax, and gastritis.

On long-term follow-up, 23 patients (4.1%) developed avascular necrosis, highlighting the need for careful monitoring of steroid therapy.

References

1. Fowler AA, Truwit JD, Hite RD, Morris PE, DeWilde C, Priday A, et al. Effect of Vitamin C Infusion on Organ Failure and Biomarkers of Inflammation and Vascular Injury in Patients With Sepsis and Severe Acute Respiratory Failure: The CITRIS-ALI Randomized Clinical Trial. JAMA. 2019; 322(13): 1261–70.
2. Skalny AV, Rink L, Ajsuvakova OP, Aschner M, Gritsenko VA, Alekseenko SI, et al. Zinc and respiratory tract infections: Perspectives for COVID-19 (Review). Int J Mol Med. 2020; 46(1):17–26.
3. Thomas S, Patel D, Bittel B, Wolski K, Wang Q, Kumar A, et al. Effect of High-Dose Zinc and Ascorbic Acid Supplementation vs Usual Care on Symptom Length and Reduction Among Ambulatory Patients With SARS-CoV-2 Infection: The COVID A to Z Randomized Clinical Trial. JAMA Netw Open. 2021; 4(2):e210369.
4. Rastogi A, Bhansali A, Khare N, Suri V, Yaddanapudi N, Sachdeva N, et al. Short-term, high-dose oral vitamin D supplementation in symptomatic COVID-19 patients: A

randomized, double-blind, placebo-controlled trial. Postgrad Med J. 2020; postgradmedj-2020-139065.
5. Jothimani D, Kailasam E, Danielraj S, Nallathambi B, Ramachandran H, Sekar P, et al. COVID-19: Poor outcomes in patients with zinc deficiency. Int J Infect Dis. 2020;100: 343–9.
6. Hemilä H, Chalker E. Vitamin C as a Possible Therapy for COVID-19. Nutrients. 2020; 12(11):3266.
7. Kumari P, Mishra R, Chandra S, Singh P, Yadav S, Shekhar S, et al. Potential role of vitamin C in COVID-19: An observational study from northern India. Int J Infect Dis. 2021; 103:234–6.
8. Zhang J, Rao X, Li Y, Zhu Y, Liu F, Guo G, et al. High-dose vitamin C infusion for the treatment of critically ill COVID-19. Ann Intensive Care. 2021;11(1):5.
9. Raharusun P, Priambada S, Budiarti C, Agung E, Budi C. Patterns of COVID-19 Mortality and Vitamin D: An Indonesian Study. Med Rxiv. 2020;doi:10.1101/2020.04.30.20085676.
10. The WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group. Association between Administration of Systemic Corticosteroids and Mortality among Critically Ill Patients with COVID-19: A Meta-analysis. JAMA. 2020;324(13):1330–41.