International Journal of Medical and Pharmaceutical Research

Online ISSN-2958-3683 | Print ISSN-2958-3675
Frequency: Bi-Monthly
Website: https://ijmpr.in/

Original Article

Low Serum Calcium as an Early Predictor of Adverse Outcomes in Critical Illness: A Prospective Analysis

Mukesh K Sarna[1], Akash Aggarwal[2], Animesh Gaur[3], Manish Pahadia[4], Ankit Beniwal[5], Saurabh Singh[6], Shubham Sharma[7], Nikhil Mehta[8], Sudha Sarna[9]

[1]Professor & Unit Head, Department of General Medicine, Mahatma Gandhi Medical College & Hospital, Jaipur
[2]Junior Resident, Department of General Medicine,
[3]Associate Professor, Department of General Medicine,
[4]Professor, Department of General Medicine,
[5]Junior Resident, Department of General Medicine,
[6]Junior Resident, Department of General Medicine
[7]Junior Resident, Department of General Medicine,
[8]Junior Resident, Department of General Medicine
[9]Professor and Head, Department of Palliative Medicine

Corresponding Author:

Mukesh K Sarna
Mahatma Gandhi Medical College & Hospital, Jaipur.
Email: mukeshsarna@gmail.com

Received: 16-03-2026
Accepted: 05-04-2026
Published: 21-04-2026

ABSTRACT

Electrolyte disturbances, particularly hypocalcemia, are frequently observed in critically ill patients and may significantly influence disease severity and outcomes. Calcium plays a crucial role in cardiovascular stability, neuromuscular function, and intracellular signaling (1). This study aimed to evaluate the association between serum calcium levels and disease severity as well as prognosis in critically ill patients admitted to the ICU. This observational study was conducted in the ICU of a tertiary care hospital over 18 months (April 2024–September 2025), including 205 critically ill patients aged 18–65 years. Serum calcium levels were measured within 24 hours of ICU admission, and disease severity was assessed using the APACHE II score. Statistical analysis included correlation, chi-square test, and comparison of means. Hypocalcemia was present in 53.1% of patients. A significant negative correlation was observed between serum calcium levels and APACHE II score ($r = –0.396$, $p = 0.001$). Hypocalcemia was more prevalent in severe disease (65.8%) compared to mild cases (40.9%) ($p = 0.01$), and lower calcium levels were significantly associated with mortality ($p < 0.001$). The study concludes that hypocalcemia is highly prevalent in critically ill patients and is significantly associated with increased disease severity and mortality, suggesting that serum calcium may serve as a useful prognostic biomarker in ICU settings.

Keywords*: Hypocalcemia, critically ill patients, Serum calcium, APACHE II score, ICU mortality.*

INTRODUCTION

Critical illness represents a complex and dynamic state of physiological dysregulation involving multiple organ systems and requiring intensive monitoring and organ support in the ICU. Electrolyte imbalances are common in such patients and play a crucial role in determining clinical outcomes. Calcium, a vital extracellular cation, is essential for myocardial contractility, vascular tone, coagulation, neuromuscular transmission, and intracellular signaling pathways (1,2). Even minor disturbances in calcium homeostasis can lead to significant physiological impairment, particularly in critically ill patients with limited compensatory reserve.

Hypocalcemia is one of the most common electrolyte abnormalities in ICU settings, with prevalence reported between 40% and 80% . It is multifactorial in origin, resulting from systemic inflammation, sepsis, renal dysfunction, vitamin D deficiency, impaired parathyroid hormone activity, and altered protein binding due to hypoalbuminemia (3–6). Inflammatory cytokines interfere with calcium regulation by suppressing parathyroid hormone function and impairing vitamin D metabolism, leading to decreased calcium availability . Additional contributing factors include gastrointestinal

dysfunction, poor nutritional intake, fluid shifts, and iatrogenic causes such as citrate-containing transfusions and medications.

Clinically, hypocalcemia may lead to myocardial depression, hypotension, arrhythmias, prolonged QT interval, and neuromuscular irritability, all of which contribute to worsening prognosis (4,5). Several studies have demonstrated a strong association between calcium levels and disease severity indices such as APACHE II and SOFA scores (7,8). Furthermore, hypocalcemia has been identified as an independent predictor of mortality in critically ill patients (9–11). Despite this, data from Indian ICU settings remain limited. Therefore, this study was undertaken to evaluate the association between serum calcium levels, disease severity, and clinical outcomes in critically ill patients.

MATERIALS AND METHODS

This hospital-based observational study was conducted in the ICU of Mahatma Gandhi Medical College & Hospital, Jaipur, over 18 months (April 2024–September 2025). A total of 205 critically ill patients aged 18–65 years were included after obtaining informed consent. Patients with known disorders affecting calcium metabolism, including pancreatitis, vitamin D disorders, and those on dialysis, were excluded. Serum calcium levels were measured within 24 hours of ICU admission, and disease severity was assessed using the APACHE II scoring system. Patients were followed until discharge, death, or leaving against medical advice. Statistical analysis was performed using SPSS version 23, applying chi-square test, Pearson correlation, and t-test, with $p < 0.05$ considered statistically significant.

RESULTS AND OBSERVATIONS

Table 1: Demographic, Clinical, and Serum Calcium Profile of Critically Ill Patients (n = 205)

Variable	Category	n (%)	Mean ± SD (Range)
Age (years)	≤50 years	66 (32.1)	48.2 ± 11.20 (21–67)
	>50 years	139 (67.9)	
Gender	Male	113 (55.2)	
	Female	92 (44.8)	
Locality	Urban	134 (65.4)	
	Rural	71 (34.6)	
APACHE II Score	Overall	205 (100)	16.07 ± 4.79 (4–20)
Disease Severity	Mild (0–9)	33 (16.1)	
	Moderate (10–19)	115 (56.1)	
	Severe (20–29)	57 (27.8)	
Serum Calcium	Hypocalcemia	109 (53.1)	8.62 ± 0.45 (7.40–10.00)
	Normocalcemia	96 (46.9)	
Cause of ICU Admission	Sepsis	56 (27.3)	
	Acute Kidney Injury	54 (26.3)	
	Chronic Liver Disease	41 (20.0)	
	Acute Exacerbation of COPD	38 (18.5)	
	Meningitis	16 (7.8)	
Oxygen Requirement (days)	1–3 days	75 (36.6)	4.39 ± 1.96 (1–10)
	4–6 days	110 (53.7)	
	≥7 days	20 (9.7)	
CPAP Requirement (days)	0 days	18 (8.8)	2.37 ± 1.28 (0–6)
	1–2 days	99 (48.3)	
	3–4 days	75 (36.6)	
	≥5 days	13 (6.3)	
Mechanical Ventilation	Not required	166 (81.0)	
	Required	39 (19.0)	5.7 ± 2.1 days

Table1: Description: The study population predominantly consisted of patients aged above 50 years with a slight male predominance and majority urban residence. Most patients had moderate disease severity (56.1%) with a mean APACHE II score of 16.07 ± 4.79. Hypocalcemia was observed in 53.1% of patients. Sepsis and acute kidney injury were the most common causes of ICU admission. The majority required short-term oxygen and CPAP support, while only a minority required mechanical ventilation.

Table 2: Association of Serum Calcium with Disease Severity, Clinical Parameters, and Outcomes (n = 205)

Variable	Category	n (%)	Mean ± SD (Range)
Correlation with APACHE II Score	All patients	205 (100)	r = –0.396, p = 0.001
Correlation with ICU Stay	All patients	205 (100)	r = –0.093, p = 0.186

Correlation with Oxygen Requirement	All patients	205 (100)	r = –0.194, p = 0.005
Correlation with CPAP Duration	All patients	205 (100)	r = –0.095, p = 0.174
Correlation with Ventilation Duration	All patients	205 (100)	r = –0.044, p = 0.531
Disease Severity	Mild	18 (40.9%)	
	Moderate	39 (47.5%)	
	Severe	52 (65.8%)	p = 0.01
Cause of Admission	COPD	21 (55.2%)	
	Acute Kidney Injury	24 (44.4%)	
	Chronic Liver Disease	19 (46.3%)	
	Meningitis	13 (81.2%)	
	Sepsis	32 (57.1%)	p = 0.669
Outcome	Death	61 (29.8)	8.13 ± 0.46
	Discharge	83 (40.5)	8.75 ± 0.47
	LAMA	61 (29.8)	8.23 ± 0.25
Hypocalcemia in Death Cases	Present	42 (68.8)	
	Absent	19 (31.2)	
Severity among Death Cases	Mild	1 (1.6)	
	Moderate	5 (8.2)	
	Severe	55 (90.2)	
Cause of Death	Acute Kidney Injury	18 (29.5)	
	Meningitis	13 (21.3)	
	Sepsis	13 (21.3)	
	Chronic Liver Disease	12 (19.7)	
	COPD	4 (6.6)	

Table2: Description: Serum calcium levels demonstrated a significant inverse correlation with disease severity (APACHE II score). Hypocalcemia increased with worsening disease severity and was significantly associated with mortality. Lower calcium levels were observed among patients who died compared to those discharged. Hypocalcemia was highly prevalent among death cases (68.8%), particularly in patients with severe illness. These findings establish serum calcium as an important prognostic marker in critically ill patients.

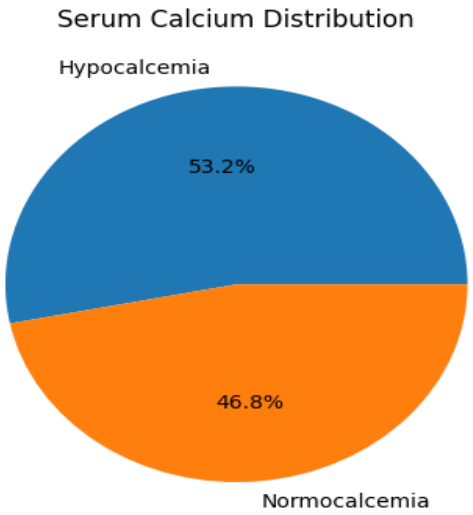

Figure 1:

Figure 1: This figure shows the distribution of serum calcium levels among critically ill patients. Hypocalcemia was observed in 53.2% of patients, while 46.8% had normal calcium levels, indicating a high prevalence of calcium imbalance in the ICU population.

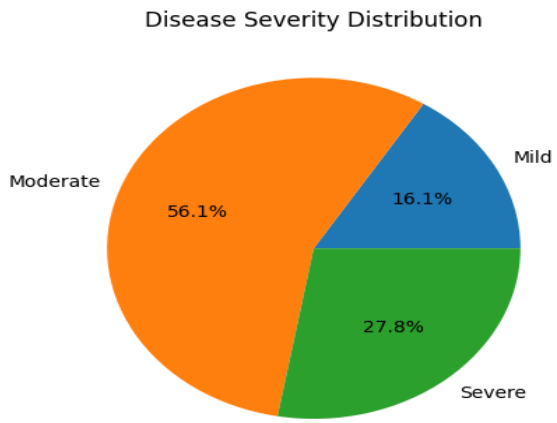

Figure 2

Figure 2: This figure represents disease severity based on APACHE II score. The majority of patients had moderate disease (56.1%), followed by severe (27.8%) and mild (16.1%) categories, reflecting the critically ill nature of the study population.

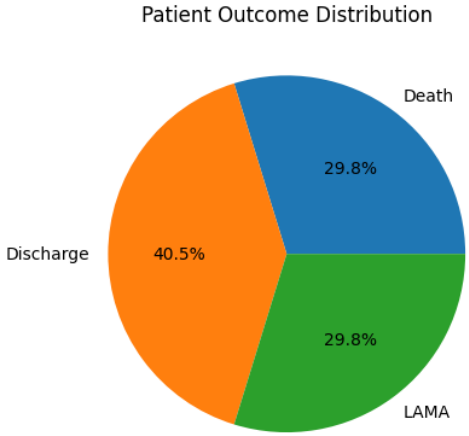

Figure 3

Figure 3: This figure depicts patient outcomes, with discharge being the most common (40.5%), while death and LAMA each accounted for 29.8% of cases. This highlights the significant mortality burden among critically ill patients.

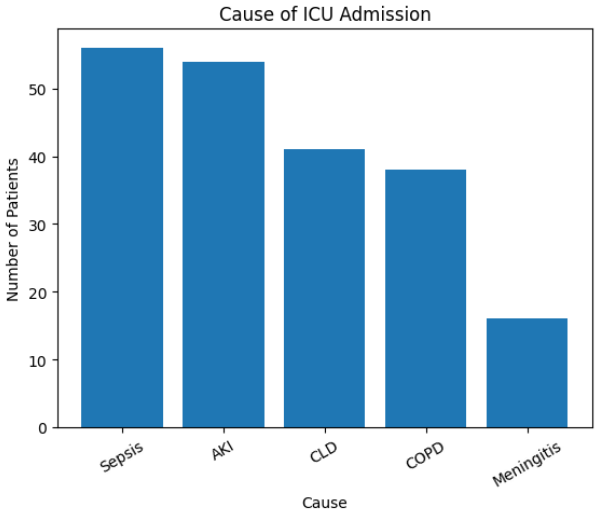

Figure 4

Figure 4: This bar graph represents the distribution of underlying causes of ICU admission among study participants. Sepsis (56 cases) was the most common cause, followed closely by acute kidney injury (54 cases). Chronic liver disease

(41 cases) and COPD (38 cases) were also significant contributors, while meningitis (16 cases) was the least common. This distribution highlights the predominance of infectious and organ failure-related conditions in critically ill patients.

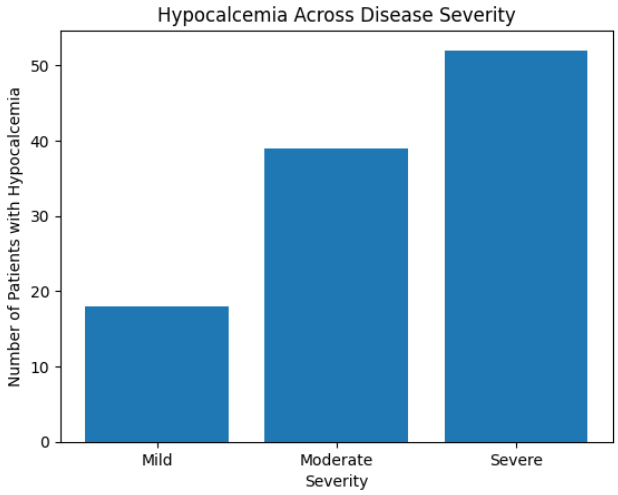

Figure 5

Figure 5: This graph demonstrates the relationship between hypocalcemia and disease severity. The number of patients with hypocalcemia increased progressively from mild (18 patients) to moderate (39 patients) and severe (52 patients) disease categories. This trend supports the significant association between hypocalcemia and increasing disease severity, reinforcing its role as a prognostic marker in critically ill patients.

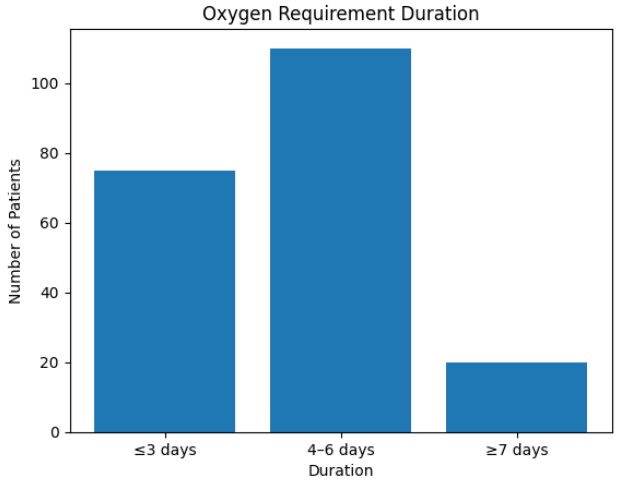

Figure 6

Figure 6: This bar graph illustrates the duration of oxygen therapy among ICU patients. The majority of patients (110 cases) required oxygen support for 4–6 days, followed by 75 patients requiring ≤3 days and only 20 patients requiring prolonged oxygen therapy (≥7 days). This indicates that most critically ill patients required moderate-duration respiratory support.

DISCUSSION

The present study demonstrates a high prevalence of hypocalcemia among critically ill patients, consistent with previous reports in ICU populations (3,6,12). This high prevalence reflects the complex pathophysiology of calcium imbalance in critical illness, involving inflammatory cytokine activity, endocrine dysfunction, renal impairment, and altered protein binding .

A significant inverse correlation between serum calcium levels and disease severity was observed, supporting the concept that hypocalcemia is a marker of physiological derangement. Similar findings have been reported in earlier studies correlating calcium levels with APACHE II and SOFA scores (7,8). The underlying mechanisms include cytokine-mediated suppression of parathyroid hormone, impaired vitamin D metabolism, and reduced calcium mobilization (3–5). The strong association between hypocalcemia and mortality further highlights its prognostic significance. Patients with lower calcium levels had significantly higher mortality, consistent with previous studies identifying hypocalcemia as an independent predictor of adverse outcomes (9–11). Hypocalcemia contributes to mortality through impaired myocardial contractility, reduced vascular tone, and increased risk of arrhythmias.

The observed association between calcium levels and oxygen requirement suggests its role in respiratory muscle function and overall physiological stability. However, no significant correlation was found with ICU stay duration, indicating that calcium reflects acute severity rather than recovery trajectory.

It is important to note that total serum calcium may not accurately reflect biologically active calcium in critically ill patients due to hypoalbuminemia. Ionized calcium is a more reliable indicator and should be preferred when available (13). Furthermore, some evidence suggests that hypocalcemia may represent an adaptive response rather than a direct therapeutic target, and routine correction should be guided by clinical context rather than laboratory values alone .

Overall, hypocalcemia serves as both a marker of disease severity and a predictor of adverse outcomes, reinforcing its importance in critical care practice.

CONCLUSION

Hypocalcemia is a common and clinically significant abnormality in critically ill patients. It shows a strong inverse relationship with disease severity and is significantly associated with increased mortality. Serum calcium measurement is simple, cost-effective, and widely available, making it a valuable prognostic biomarker in ICU settings. Early identification and appropriate interpretation of calcium abnormalities may aid in risk stratification and improve clinical outcomes in critically ill patients.

REFERENCES

1. Cooper MS, Gittoes NJ. Diagnosis and management of hypocalcaemia. *BMJ*. 2008;336:1298–1302.
2. Dickerson RN. Electrolyte disturbances in critical illness. *JPEN*. 2009;33:255–259.
3. Zaloga GP, Chernow B. Hypocalcemia during sepsis. *Ann Intern Med*. 1987;107:36–41.
4. Steele T, Kolamunnage-Dona R, Downey C, et al. Hypocalcemia in critical illness. *Crit Care*. 2013;17:R106.
5. Zivin JR, Gooley T, Zager RA, et al. Hypocalcemia in critically ill patients. *Am J Kidney Dis*. 2001;37:689–698.
6. Chernow B, Zaloga GP, McFadden ER Jr, et al. Hypocalcemia in ICU patients. *Crit Care Med*. 1982;10:848–851.
7. Zhang Z, Xu X, Ni H, Deng H. Ionized calcium and ICU outcomes. *PLoS One*. 2014;9:e95204.
8. Carlstedt F, Lind L, Rastad J, et al. Calcium and severity of illness. *Eur J Clin Invest*. 1998;28:898–903.
9. Akirov A, Gorshtein A, Shraga-Slutzky I, et al. Calcium and prognosis. *Endocrine*. 2017;55:842–848.
10. Cai B, et al. Ionized calcium and ICU mortality. *Crit Care*. 2018.
11. Meng K, et al. Serum calcium and mortality in ICU patients. *Front Med*. 2021.
12. Burchard KW, Gann DS. Electrolyte balance in ICU. *Surg Clin North Am*. 1983;63:413–430.
13. Slomp J, van der Voort PHJ, Gerritsen RT, et al. Albumin-adjusted calcium limitations. *Crit Care Med*. 2003;31:1389–1393.