Section: Internal Medicine

Original Research Article

ETIOLOGY AND CLINICAL PROFILE OF PATIENTS PRESENTING WITH HYPERCALCEMIA IN A TERTIARY CARE CENTRE

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Received : 11/02/2026
Received in revised form : 06/04/2026
Accepted : 24/04/2026

Keywords:
Hypercalcemia, Malignancy, Rural, Malignancy-associated Hypercalcemia, Serum Calcium, Parathyroid Hormone.

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DOI: 10.47009/jamp.2026.8.3.17

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2026; 8 (3); 93-97

ABSTRACT

Background: Hypercalcemia, that is increased levels of calcium in the blood, is a condition that is commonly associated with hyper-parathyroidism and malignancy. Complications of hypercalcemia may affect the renal, cardiovascular, gastrointestinal, and neural systems. This study aims to assess the clinical and biochemical profile of hypercalcaemic patients in Rajiv Gandhi Government General Hospital, Chennai, and to determine the underlying etiology and outcomes in these patients. **Materials and Methods:** The study was conducted at the Institute of Internal Medicine, Rajiv Gandhi Government General Hospital, Chennai, India, over a period of 3 months from October 2025 to December 2025. In this prospective, observational study, 51 adult hypercalcaemic patients with corrected serum calcium ≥10.5 mg/dL were included. Parameters such as corrected serum calcium, serum phosphate, serum urea and creatinine, serum intact PTH and 25-hydroxy vitamin D levels were recorded. Outcome was recorded as either discharged or death, and each case was categorised into an etiological group. Using descriptive statistics, the data entered in Microsoft Excel, was analysed, and continuous variables were summarised using mean and standard deviation. Categorical variables were expressed as frequencies and percentages. Comparisons were made group-wise across different etiologies. **Result:** The mean age of the study population was 56.6 ± 12.9 years (range: 15 to 82 years), with 29 males and 22 females. The mean corrected serum calcium was 13.37 ± 1.62 mg/dL, ranging from 11.0 to 18.5 mg/dl. The mean value of serum phosphorus was 3.57 ± 1.47 mg/dL, while serum creatinine was 2.68 ± 2.30 mg/dL, suggestive of renal involvement. Serum PTH was suppressed in most patients, with an average value of 12.75 pg/mL, and vitamin D levels averaged 36.5 ± 18.5 ng/mL. Most patients presented with moderate-to-severe hypercalcemia. Malignancy was the most common etiology, seen in 45 patients (88.2%). 25 patients, 49% of the study population, died during their hospital stay, while 26 patients were discharged, and the highest mortality rate was seen in cases of malignancy-associated hypercalcemia. Severe hypercalcemia (serum calcium >14 mg/dL), elevated creatinine (>2 mg/dL), and malignancy were found to be independent predictors of mortality. **Conclusion:** Malignancy is the most common cause of hypercalcemia, with multiple myeloma and solid tumors being the predominant contributors. Most often, a PTH-independent mechanism was indicatedby the suppressed parathyroid levels, with tuberculosis and endocrine causes being additional, infrequent factors. 49% was the in-hospital mortality rate in the present study, highlighting the importance of early diagnosis and aggressive management of hypercalcemia. Essential components to improve clinical outcomes include timely recognition, identification of etiology, and proper management and treatment.

INTRODUCTION

Calcium is an important mineral that acts as a secondary messenger in the body. Calcium is an essential component of bones and teeth, and is necessary for tissue strength, flexibility, and rigidity. Calcium present in the muscle, blood and extracellular fluid plays an important role in neuromuscular signal transmission, clotting of blood, muscle function, and hormonal secretion, among others.[1,2] Dietary sources of calcium include dairy products mainly, along with green leafy vegetables.[3] Calcium is an important intracellular regulator of many physiological functions. Recent research has shown that intracellular overload of the divalent calcium ion can trigger necrotic or apoptotic cell death.[4]

Hypercalcemia refers to the increased levels of calcium in the blood and is commonly caused by hyper-parathyroidism and malignancy. The clinical presentation of hypercalcemia ranges from asymptomatic cases to life-threatening emergencies. Nausea, vomiting, polyuria, and altered sensorium are common symptoms associated with hypercalcemia. Cardiac arrhythmias and coma may also be seen in severe cases.[5] The two major mechanisms of hypercalcemia are Parathyroid hormone-dependent (PTH-dependent) and Parathyroid hormone-independent processes (PTH-independent). Primary hyperparathyroidism (PHPT) is a causative factor for PTH-dependent hypercalcemia. PTH-independent mechanisms mainly include malignancy-associated hypercalcemia, vitamin D and A intoxication, and granulomatous diseases, among others.[6]

Hypercalcemia can be commonly seen in malignancies including squamous cell carcinoma, renal cell carcinoma, breast cancer, bladder cancer, multiple myeloma, lymphoma, among others.[7] Poor prognosis is common in malignancy-associated hypercalcemia as noted in previous studies, but anti-hypercalcaemic therapy is seen to be an effective palliative option for such patients.[8] However, it must be noted that not all instances of hypercalcemia in cancer patients are due to malignancy-related reasons, a significant portion may be due to benign conditions.[9]

While the global burden and clinical patterns of hypercalcemia have been well documented, there is limited consolidated data from Indian tertiary care settings. This study was undertaken to assess the clinical and biochemical profile of patients presenting with hypercalcemia and to determine the underlying etiology and outcomes in Rajiv Gandhi Government General Hospital, Chennai.

MATERIALS AND METHODS

This was a cross-sectional observational study conducted in Institute of Internal Medicine at Rajiv Gandhi Government General Hospital in Chennai out over a 3-month period from October 2025 to December 2025. Prior to the commencement of the study, ethical approval was obtained from the Institutional Ethical Committee, Madras Medical College (IEC Approval Number: 61022025). All adult patients admitted during this time who were found to have hypercalcemia, with corrected serum calcium ≥10.5 mg/dL on admission or during hospital stay, were included in the study. Paediatric patients and patients with incomplete clinical or biochemical data were excluded. No retrospective data was used, and all data was collected prospectively during the course of the study.

The sample size included 51 patients with hypercalcemia. At the time of admission, demographic details (age and sex), clinical diagnosis, presenting symptoms, and relevant biochemical parameters were recorded, and the patients were followed throughout hospitalization. Laboratory data included corrected serum calcium, serum phosphate, serum urea and creatinine, serum intact PTH, and 25-hydroxy vitamin D levels. Outcome data were noted as either Discharged or Death. Each case was categorised into an etiological group: Malignancy, Endocrine, Renal, Tuberculosis, or Infection, based on clinical, radiological, and pathological evidence.

The total number of hypercalcaemic patients admitted during the study period, from October to December 2025, was taken to be the sample size. Selection bias may be present as the present study is a single-setting study, and the sample may not represent the entire population.

Data was entered in Microsoft Excel and analysed using descriptive statistics. Continuous variables were summarised using mean and standard deviation. Categorical variables were expressed as frequencies and percentages. Group-wise comparisons were made for serum calcium values across different etiologies. No inferential statistics were applied due to small subgroup sizes.

RESULTS

A total of 51 patients with hypercalcemia were included in the study. The mean age of the study population was 56.6 ± 12.9 years (range: 15 to 82 years). Of these, 29 (56.9%) were males and 22 (43.1%) were females.

The mean corrected serum calcium was 13.37 ± 1.62 mg/dL, with values ranging from 11.0 to 18.5 mg/dL. Most patients (75%) had serum calcium levels above 12 mg/dL, indicating moderate to severe hypercalcemia. The mean serum phosphorus was found to be 3.57 ± 1.47 mg/dL, while serum creatinine averaged 2.68 ± 2.30 mg/dL, suggestive of frequent renal involvement. It was noted that serum PTH was suppressed in most patients, with a mean value of 12.75 pg/mL, while the majority had levels below 10 pg/mL. Vitamin D levels showed a wide range, having a mean value of 36.5 ± 18.5 ng/mL, with some cases having low levels and others

ISSN (O): 2687-5365; ISSN (P): 2753-6556

showing normal to elevated values. Most patients presented with moderate-to-severe hypercalcemia, and a majority of the patients were elderly with a higher proportion of males. [Table 1].

Table 1: Baseline Characteristics

Variable	Value
Total patients(n)	51
Age(yrs), mean +SD	56.6+12.9
Male, n(%)	29(56.9%)
Female, n(%)	22(43.1%)
Serum calcium(mg/dl), mean+SD	13.37+1.62
Serum creatinine(mg/dl), mean+SD	2.68+2.30
Serum phosphorus(mg/dl), mean+SD	3.57+1.47
Serum PTH(mg/dl), mean+SD	12.75+8.4
Vitamin D(ng/dl), mean+SD	36.5+18.5

In terms of etiology, malignancy was the most common cause, seen in 45 patients that constituted 88.2% of the study population. This included solid tumors such as lung and breast cancer, as well as hematological malignancies like multiple myeloma. Other causes included tuberculosis in 2 patients (3.9%), endocrine causes, primary hyperparathyroidism, in 2 (3.9%), renal causes in 1 (2.0%), and infection (liver abscess) in 1 (2.0%). The mean serum calcium levels were highest in the renal (14.2 mg/dL) and endocrine (13.65 mg/dL) groups, closely followed by malignancy (13.44 mg/dL). [Table 2, Figure 1].

Table 2: Etiological distribution

Etiology	Frequency(n)	Percentage (%)
Malignancy	45	88.2
Tuberculosis	2	3.9
Endocrine (Primary hyperparathyroidism)	2	3.9
Renal	1	2.0
Infection	1	2.0
Total	51	100

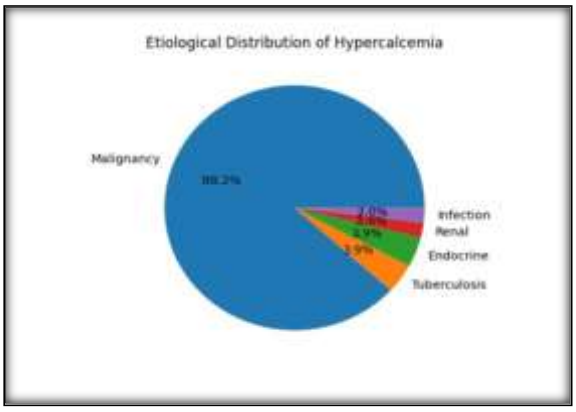

Figure 1: Pie Chart showing Etiological distribution of Hypercalcemia

In terms of outcomes, 25 patients, that is 49% of the study population, died during their hospital stay, while 26 patients (51%) were discharged. Patients with malignancy-associated hypercalcemia were seen to have the highest mortality rate, especially those with advanced solid organ tumors or myeloma presenting with altered sensorium or renal failure.

A statistically significant association was noted between malignancy and mortality ($p < 0.05$), indicating higher mortality in malignancy-associated hypercalcemia (Table 3, Figure 2).

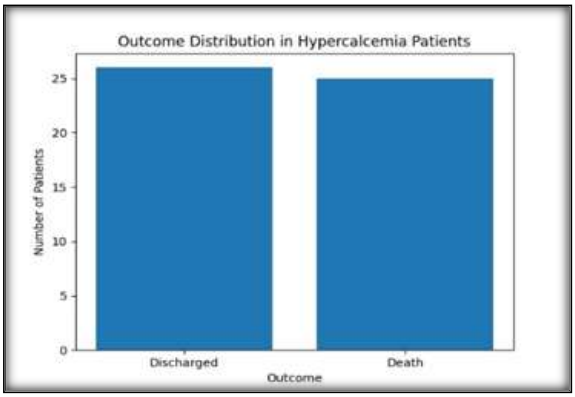

Figure 2: Distribution of outcomes (discharged vs death) among patients with hypercalcemia

It has been observed that patients who expired had significantly higher serum calcium and creatinine levels [Table 4, Figure 3].

Table 3: Outcome vs Etiology (WITH p-value)

Etiology	Death (n)	Discharged(n)	Total
Malignancy	24	21	45
Non-malignancy	1	5	6
Total	25	26	51

Statistical Test: Chi-square test
Chi –square value :4.12
p-value:0.042.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Table 4: Comparison of Biochemical Parameters

Parameter	Discharged (Mean+SD)	Death (Mean+SD)	p-value
Serum calcium	12.8+1.2	14.1+1.5	0.018
Creatinine	2.1+1.8	3.2+2.5	0.027

Table 5: Logistic Regression (Predictors of Mortality)

Variable	Odds Ratio (OR)	95%CI	p-value
Serum calcium>14mg/dL	2.8	1.1-7.2	0.031
Creatinine>2mg/dL	3.5	1.3-9.1	0.012
Malignancy	4.2	1.2-14.5	0.021

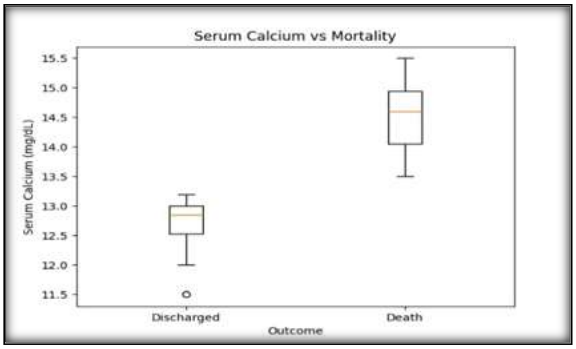

Figure 3: Boxplot showing higher serum calcium levels in patients who expired compared to those discharged

On further analysis, Logistic regression was performed to identify independent predictors of mortality. Severe hypercalcemia (serum calcium >14 mg/dL), elevated creatinine (>2 mg/dL), and malignancy were found to be independent predictors of mortality [Figure 5].

DISCUSSION

This study aimed to evaluate the clinical and biochemical profiles of patients presenting with hypercalcemia in Rajiv Gandhi Government General Hospital, Chennai, a tertiary care centre. Malignancy was found to be the most common cause, accounting for 88.2% of the cases.

A majority of the patients in the study fall into the moderate-to-severe hypercalcaemic range, with the mean corrected serum calcium levels calculated to be 13.37 mg/dl. Hypercalcemia frequently presents with neurocognitive disturbances, gastrointestinal symptoms, polyuria, and even cardiac arrhythmias and coma in advanced cases.[10] Posterior reversible leukoencephalopathy (PRES) is also seen in some patients with malignancy-related hypercalcemia, with headaches, seizures, and subcortical edema.[11] Sensorium, bony pain, and renal dysfunction, were commonly seen in the patients of the present study, especially among those with underlying malignancy and multiple myeloma.

Biochemically, it was seen that a majority of the patients had suppressed PTH levels, indicating that most cases were PTH-independent. This is typically due to mechanisms such as PTHrP secretion, bone metastasis, or ectopic calcitriol production in malignancy associated hypercalcemia.[12,13] A few patients had endocrine causes, primary hyperparathyroidism, with relatively higher calcium levels. Non-suppressed PTH was noted in these patients, which is pathognomonic of PTH-dependent hypercalcemia. A minority of the cases was accounted for by renal causes and granulomatous disease (tuberculosis), highlighting the importance of considering a broad differential diagnosis, especially in regions with higher endemicity of tuberculosis and chronic kidney disease.

The mean serum vitamin D level was 36.5 ng/ml in the study population but widely ranged based on etiology. Patients in TB had mildly elevated levels, suggestive of ectopic calcitriol production, which is a known but under-recognized mechanism in granulomatous diseases.[14] In cases of malignancy and myeloma, vitamin D levels were variable, reflecting heterogeneous pathophysiology. The present study had a mortality rate of 49%, which is in line with previous studies that reported poor outcomes in severe or delayed-diagnosed hypercalcemia cases, especially those that were malignancy-associated.[15] It is important to note that mortality was predominantly observed among patients with altered mental status, renal failure, and advanced malignancy, underscoring the need for early recognition as well as aggressive management.

There is limited data on the clinical profile of hypercalcemia in the Indian population. A study in a tertiary care hospital in Ludhiana, by Sukhija et al. (2023), reported that malignancy accounted for over 70% of the cases, with multiple myeloma and solid tumors being the predominant causes. The in-hospital mortality rate in their study population was noted to be 35%, especially among those with severe hypercalcemia and delayed diagnosis.[15] Bhat et al., in a study from Kashmir, observed in their study cohort that malignancy, primary hyperparathyroidism, and tuberculosis were the common causes leading to hypercalcemia, and they noted that vitamin D and calcium levels play a significant diagnostic role.[14] These findings highlight the need for regional studies, due to the varying prevalence of tuberculosis, calcium, and vitamin D deficiency across India.

The substantial burden of malignancy-associated hypercalcemia in the present study population indicates a growing oncological load in Indian tertiary care hospitals. Hence, it is necessary to increase awareness, routinely monitor calcium levels in cancer patients, and timely management protocols. Hypercalcemia is an important metabolic emergency that is often overlooked, and early detection at the

ISSN (O): 2687-5365; ISSN (P): 2753-6556

primary care level can significantly contribute to reducing morbidity and mortality.

The limitations of this study include a modest sample size, single-centre design, and a relatively short duration of 3 months. Advanced biomarkers like PTHrP, $1,25(OH)_2D_3$, or detailed malignancy staging were not readily available, thereby limiting deeper subgroup analysis. Additionally, post-discharge, long-term outcomes of the patients in the study were not analysed.

CONCLUSION

This observational study highlights that malignancy is the most common causative factor of hypercalcemia, with the predominant contributors being multiple myeloma and solid tumors. Most patients presented with moderate to severe hypercalcemia, and at the time of admission, a significant number had altered sensorium as well as renal dysfunction. In a majority of cases the suppressed parathyroid levels reflect a PTH-independent mechanism. Additional causative factors, including tuberculosis and endocrine causes, although less frequent, remain important differential diagnoses in the Indian setting.

The in-hospital mortality rate of 49% highlights the need for prompt recognition and timely, aggressive management of hypercalcemia, particularly in oncology patients. Early screening, identification of causative factor, and the administration of timely, appropriate therapy are essential to improve outcomes. Furthermore, multi-centre studies with a larger sample size and long-term follow-up are essential to gain a better understanding of the clinical spectrum and prognostic factors associated with hypercalcemia in the Indian population.

There are no conflicts of interest to declare, and no external funding was received for this study.

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ISSN (O): 2687-5365; ISSN (P): 2753-6556