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STUDY ON THE ASSOCIATION OF SERUM CALCIUM LEVELS IN PATIENTS WITH COPD AND BRONCHIAL ASTHMA IN A TERTIARY CARE HOSPITAL IN NORTHERN INDIA

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ABSTRACT

Introduction: Hypocalcemia is a recognized, but underreported, contributor to bronchospasm.In patients with COPD and asthma, it may mimic or exacerbate acute respiratory symptoms, especially during steroid therapy.

Aim: To evaluate serum calcium levels during exacerbation and stability in COPD and asthma patients and assess their association with pulmonary function and clinical outcomes.

Materials and Methods: A prospective cohort study was conducted on 378 patients admitted with acute exacerbations of COPD or asthma. Serum calcium levels were measured at admission and during clinical stability.Spirometry, ABG, comorbidity profiles, and medical history were recorded.Statistical analyses included t-tests, correlation, logistic regression, and survival analysis.

Results: Hypocalcemia (<8.5 mg/dL) was observed in 32.1% of patients during exacerbations.The mean calcium level increased significantly during the stability phase ($p < 0.0001$).Hypocalcemia was associated with lower FEV1%, higher $PaCO_2$, and greater prevalence in patients on steroids or with kidney disease. Regression analysis confirmed that steroid use and renal comorbidity were independent predictors.

Conclusion: Routine monitoring and correction of calcium may improve outcomes and reduce misdiagnosis of exacerbations.

KEYWORDS: Association, Serum Calcium, Levels, COPD, Bronchial Asthma

INTRODUCTION

Bronchospasm due to hypocalcemia is well-documented in pediatric emergencies but underreported in adults. In COPD and asthma, where steroids and beta-agonists are mainstays of therapy, calcium depletion may worsen symptoms or mimic exacerbations. This study investigates the role of serum calcium in respiratory function and clinical outcomes.

Introduction

Bronchial asthma is a common chronic respiratory disorder characterized by variable respiratory symptoms, variable expiratory airflow limitation, airway inflammation, and airway hyperresponsiveness. Patients commonly present with recurrent episodes of wheezing, dyspnea, chest tightness and cough, with the intensity and frequency of symptoms varying over time. Asthma is a heterogeneous disease, and its clinical expression is influenced by genetic, environmental, inflammatory and metabolic factors. Current understanding recognizes that asthma involves complex interactions between airway epithelial cells, inflammatory cells, cytokines, airway smooth muscle and structural changes within the bronchial wall. The Global Initiative for Asthma (GINA) describes asthma as a heterogeneous disease usually characterized by chronic airway inflammation and variable expiratory airflow, with objective assessment of lung function playing an important role in diagnosis and monitoring.[1]

Acute exacerbations of asthma are clinically important events characterized by a progressive increase in symptoms and deterioration in expiratory airflow. They may require intensified bronchodilator therapy, systemic corticosteroids, emergency care or hospitalization. Although airway inflammation and bronchial smooth-muscle constriction are central to asthma exacerbations, several systemic and metabolic abnormalities can influence respiratory symptoms and lung function. Identifying potentially reversible metabolic abnormalities may therefore be clinically relevant, particularly in hospitalized patients with severe respiratory symptoms. Recent literature emphasizes the importance of recognizing patients at increased risk of exacerbation and using objective clinical and biological markers to improve assessment of disease severity and treatment response.[2]

Pulmonary function testing, particularly forced expiratory volume in one second (FEV1), forced vital capacity (FVC), peak expiratory flow rate (PEFR) and other expiratory flow indices, provides objective information regarding airflow limitation. FEV1 is widely used to assess the degree of airflow obstruction and response to treatment. Biomarkers and lung-function measurements may complement clinical assessment because symptoms alone do not always accurately reflect the underlying inflammatory or physiological state. Recent reviews have highlighted the growing importance of biomarkers in asthma for diagnosis, phenotyping, prediction of exacerbations, assessment of disease progression and evaluation of treatment response.[3]

Among the various metabolic factors potentially relevant to bronchial smooth-muscle function, calcium has attracted attention because of its fundamental role in muscle contraction and cellular signaling. Calcium ions participate in excitation–contraction coupling within smooth-muscle cells, and alterations in extracellular calcium concentrations may influence neuromuscular excitability and bronchial tone. Although hypocalcemia is not considered a routine cause of asthma, marked reductions in serum calcium have been reported in association with bronchospasm. Recent case-based literature has emphasized that hypocalcemia-induced bronchospasm is uncommon but may present with wheezing, dyspnea and respiratory distress and can therefore clinically resemble an obstructive airway exacerbation.[4]
The relationship between serum calcium and respiratory symptoms is potentially important because bronchospasm can arise through mechanisms other than classical allergic or inflammatory airway disease. Severe hypocalcemia may increase neuromuscular excitability and produce a range of clinical manifestations. In susceptible patients, this may contribute to bronchial smooth-muscle constriction and respiratory symptoms. A recent report describing hypocalcemia-associated bronchospasm demonstrated improvement after correction of the underlying calcium abnormality, emphasizing the importance of considering metabolic abnormalities when bronchospasm is persistent or disproportionate to the expected clinical course.[4]

The calcium–respiratory relationship may also be influenced by vitamin D status. Vitamin D is closely linked to calcium homeostasis and has been investigated extensively in relation to asthma because of its potential immunomodulatory and airway effects. Recent systematic reviews have suggested that vitamin D may influence airway inflammation, airway smooth-muscle behavior and airway remodeling, although clinical trials have produced inconsistent results regarding its ability to improve asthma control or prevent exacerbations.[5,6] A 2023 systematic review reported potential effects of vitamin D on airway smooth-muscle contraction, inflammatory pathways, collagen synthesis and bronchial remodeling, although the evidence remains insufficient to establish a definitive therapeutic role.[6]
Similarly, the clinical relationship between vitamin D status and asthma exacerbations remains controversial. An updated Cochrane review published in 2023 found that vitamin D or its metabolites did not significantly reduce the proportion of patients experiencing severe asthma exacerbations requiring systemic corticosteroids.[5] Other meta-analyses have reported possible reductions in exacerbation frequency in selected populations, particularly children, demonstrating that the interaction between vitamin D, calcium metabolism and asthma may be complex and influenced by age, baseline nutritional status, disease severity and treatment characteristics.[7] Thus, although vitamin D and calcium metabolism are biologically interconnected, serum calcium itself requires independent evaluation in patients with acute respiratory disease.

Electrolyte abnormalities may be particularly relevant during acute respiratory exacerbations because critically ill or hospitalized patients may have disturbances related to poor nutritional intake, systemic inflammation, renal dysfunction, medications and alterations in fluid and acid–base balance. The present study therefore considers serum calcium together with other biochemical variables, including magnesium, sodium and potassium, as well as arterial blood-gas parameters. The original study protocol specifically includes corrected serum calcium at admission and during clinical stability, along with spirometric indices and ABG parameters.

Medication exposure represents another potentially important factor. Systemic corticosteroids are a cornerstone of treatment for moderate-to-severe asthma exacerbations and are frequently administered to patients with acute respiratory deterioration. Prolonged or repeated corticosteroid exposure can influence bone and mineral metabolism, although the immediate relationship between corticosteroid administration and serum calcium during acute asthma remains incompletely defined. Other therapies commonly used during exacerbations, including bronchodilators and antibiotics, may also occur alongside changes in electrolyte and metabolic status. Consequently, evaluation of calcium levels should ideally account for medication exposure and important comorbidities.

Comorbid conditions may further modify calcium homeostasis and respiratory outcomes. Renal dysfunction, for example, can disturb calcium and phosphate metabolism and may contribute to persistent abnormalities in serum calcium. Similarly, nutritional deficiencies and other systemic disorders may influence mineral metabolism. In the present study, comorbidities and medication history are therefore included among the clinical variables assessed. The study also evaluates the relationship between calcium concentration and objective respiratory parameters, including FEV1%, FVC%, PEFR and FEF25–75%.

The clinical importance of this relationship lies in the possibility that hypocalcemia may either contribute to bronchospasm or act as a marker of systemic illness during acute respiratory deterioration. If lower calcium levels are consistently associated with poorer pulmonary function, calcium measurement could provide an additional, inexpensive biochemical

parameter for identifying patients who require closer monitoring. Conversely, if calcium levels normalize as respiratory status improves, this may suggest that calcium abnormalities are at least partly associated with the acute phase of illness. The present study is designed to evaluate these relationships by comparing serum calcium during exacerbation with levels obtained during clinical stability.

The study was therefore undertaken to assess serum calcium levels among patients with bronchial asthma and COPD during acute exacerbation and clinical stability and to determine their relationship with pulmonary function and clinical characteristics. The principal objectives include comparison of calcium concentrations between exacerbation and stable phases, assessment of correlations between calcium and spirometric parameters, identification of clinical predictors of hypocalcemia, and evaluation of its potential relationship with hospital outcomes. By examining calcium status alongside respiratory physiology, treatment exposure and comorbid conditions, this study seeks to clarify whether serum calcium has a clinically meaningful association with respiratory impairment and whether recognition of hypocalcemia may contribute to a more comprehensive assessment of patients presenting with acute bronchial asthma.

Aims and Objectives
Primary Objective:
- To assess serum calcium levels during acute exacerbations in COPD and asthma patients.

Secondary Objectives:
- To compare calcium levels during exacerbation and stability.
- To correlate calcium levels with spirometry parameters.
- To identify predictors of hypocalcemia.
- To evaluate its impact on hospital stay and outcomes.

MATERIALS AND METHODS
StudyDesign: Prospective cohort study
Setting: Dr. RMLIMS, Lucknow (General Medicine ward, ICU, Emergency)

Sample Size: 378 patients

Inclusion Criteria:
- Age >18 years
- Spirometry-confirmed COPD or asthma (GOLD 1–4)
- History of ≥1 exacerbation
- BMI 19–25
- Smoking history

Exclusion Criteria:
- Intubated or NIV-dependent patients
- Inability to perform spirometry
- Serious comorbidities (e.g., CVA, IHD, alcoholism)
- Use of calcium-altering drugs (PPIs, thiazides, digoxin)

Data Collection:
- Serum calcium (corrected for albumin) at admission and stability
- Spirometry (FEV1%, FVC%, PEFR, FEF25-75%)
- ABG, comorbidities, medication history
- Outcome: discharge or death

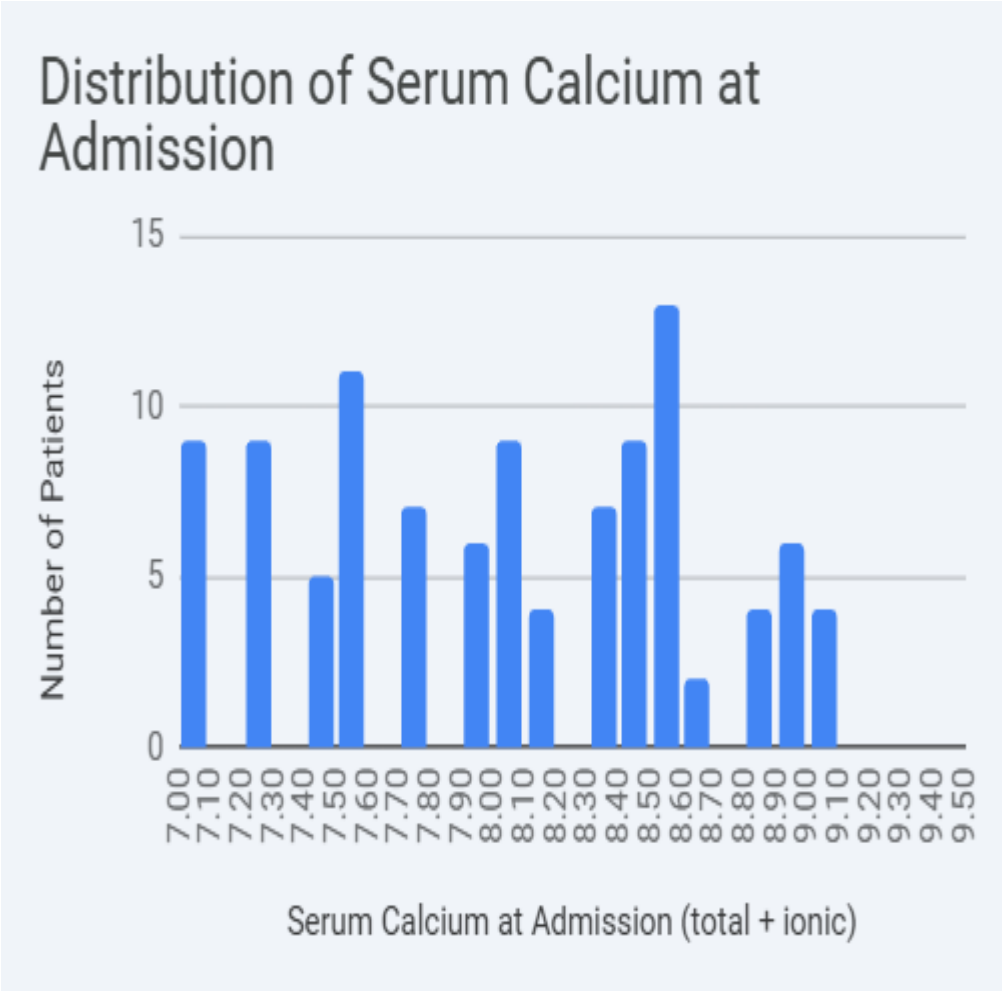
Statistical Analysis:
- Descriptive statistics
- Paired t-test
- Pearson correlation
- Logistic regression
- Kaplan-Meier survival curves
- Cox proportional hazards model
- Software: R v4.23

RESULTS
Key Variables Analyzed

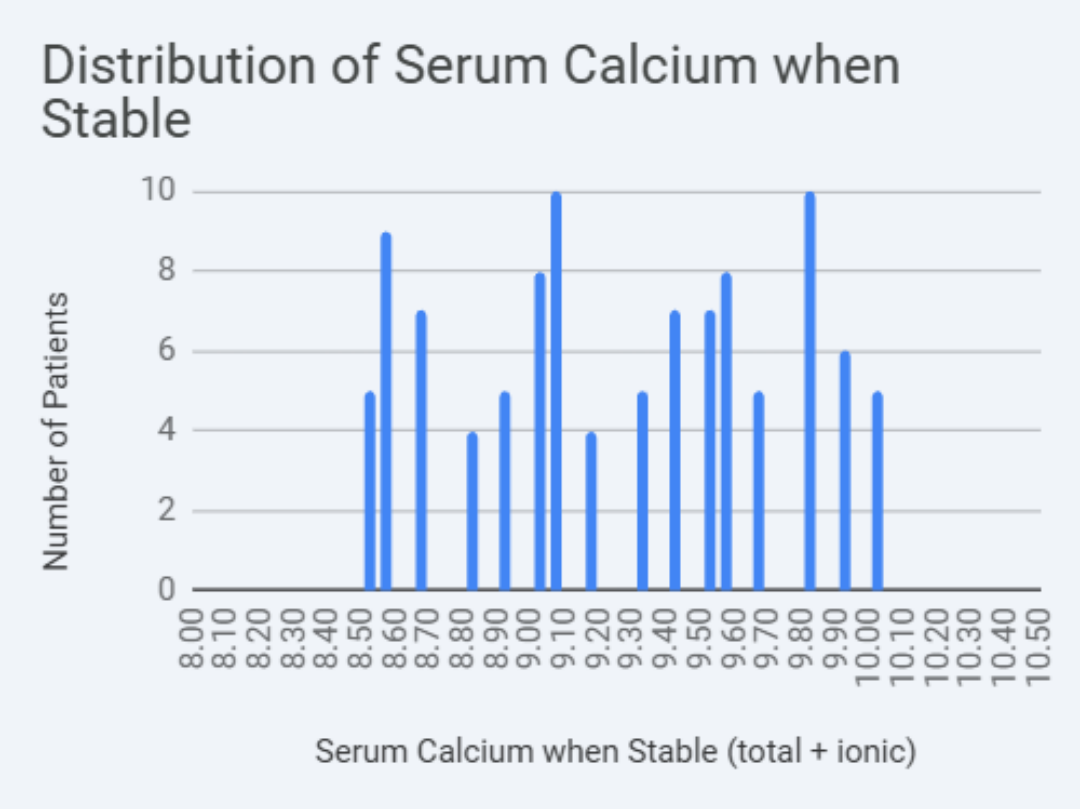
Category	Variables
Demographics	Age, Sex, BMI, Smoking history

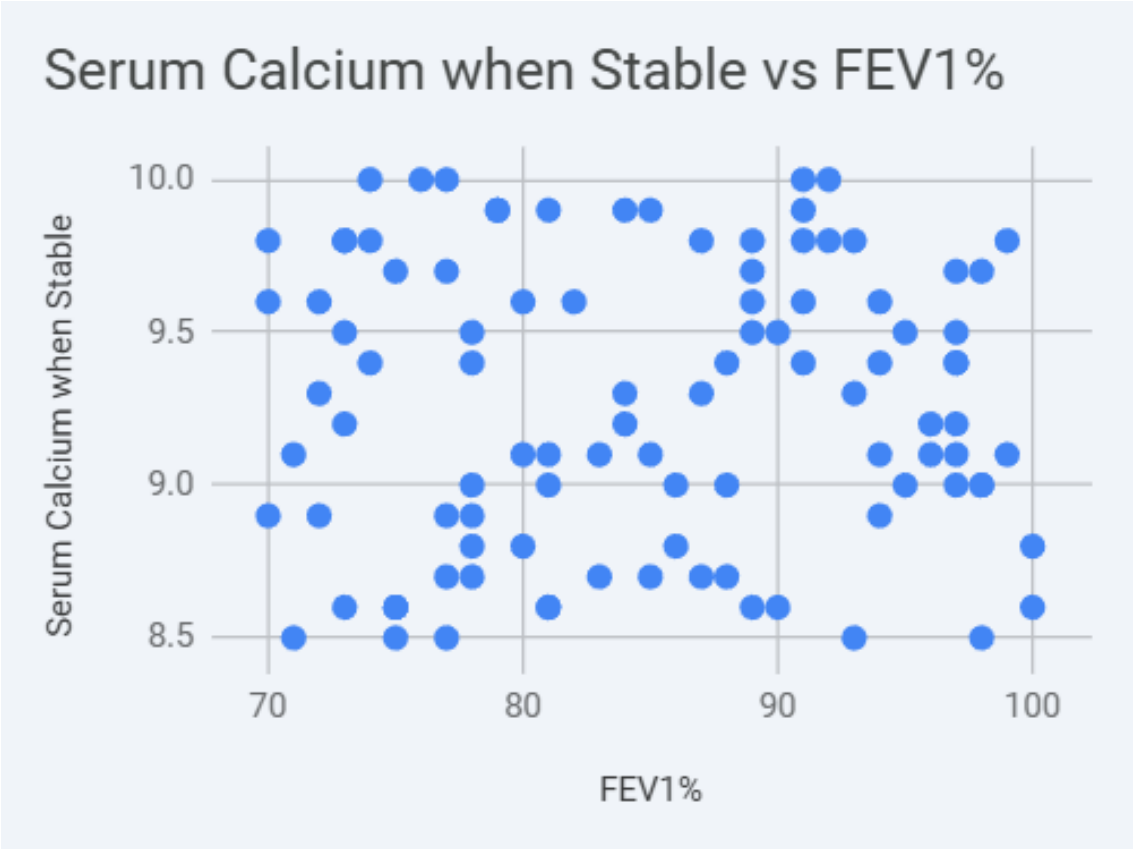
Clinical	Diagnosis (COPD/Asthma), Duration of symptoms, Comorbidities
Respiratory	FVC%, FEV1%, PEFR%, FEF25-75%, SPO2, PaO2, PaCO2, pH
Biochemical	Serum calcium (exacerbation & stable), Magnesium, Sodium, Potassium
Treatment	Steroid use, Medication type
Imaging	Chest X-ray findings

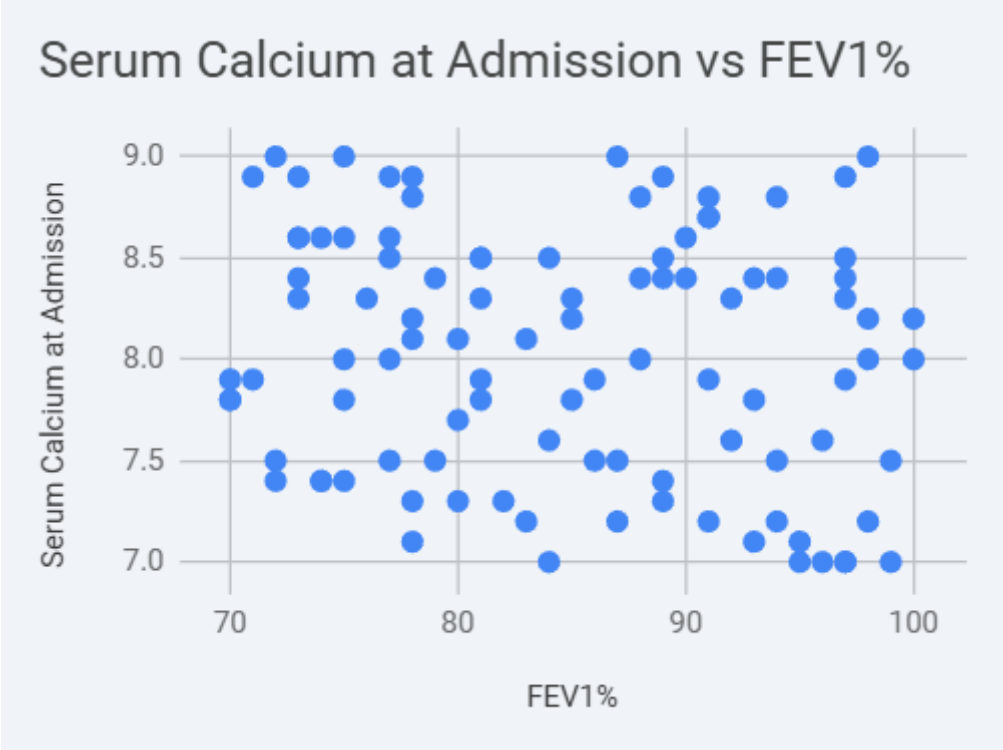
Serum Calcium Analysis
1. Distribution of Serum Calcium
During exacerbation:
Mean: ~8.7 mg/dL
Range: 7.1–10.0 mg/dL
Hypocalcemia



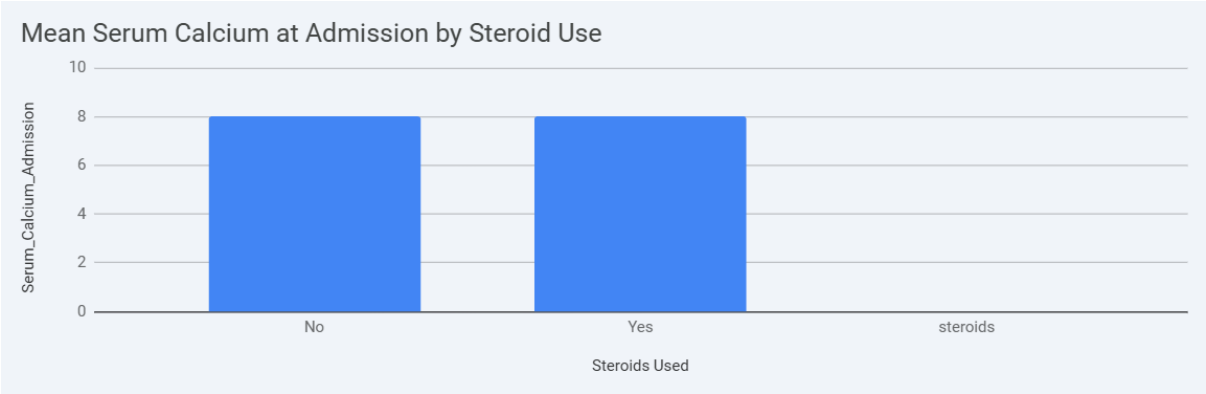
2.During stable condition:
Mean: ~9.3 mg/dL
Range: 8.5–10.5 mg/dL
Normalization observed in most cases


Distribution of Serum Calcium when Stable
Number of Patients
10
8
6
4
2
0
8.00
8.10
8.20
8.30
8.40
8.50
8.60
8.70
8.80
8.90
9.00
9.10
9.20
9.30
9.40
9.50
9.60
9.70
9.80
9.90
10.00
10.10
10.20
10.30
10.40
10.50
Serum Calcium when Stable (total + ionic)


Serum Calcium when Stable vs FEV1%
Serum Calcium when Stable
10.0
9.5
9.0
8.5
70
80
90
100
FEV1%



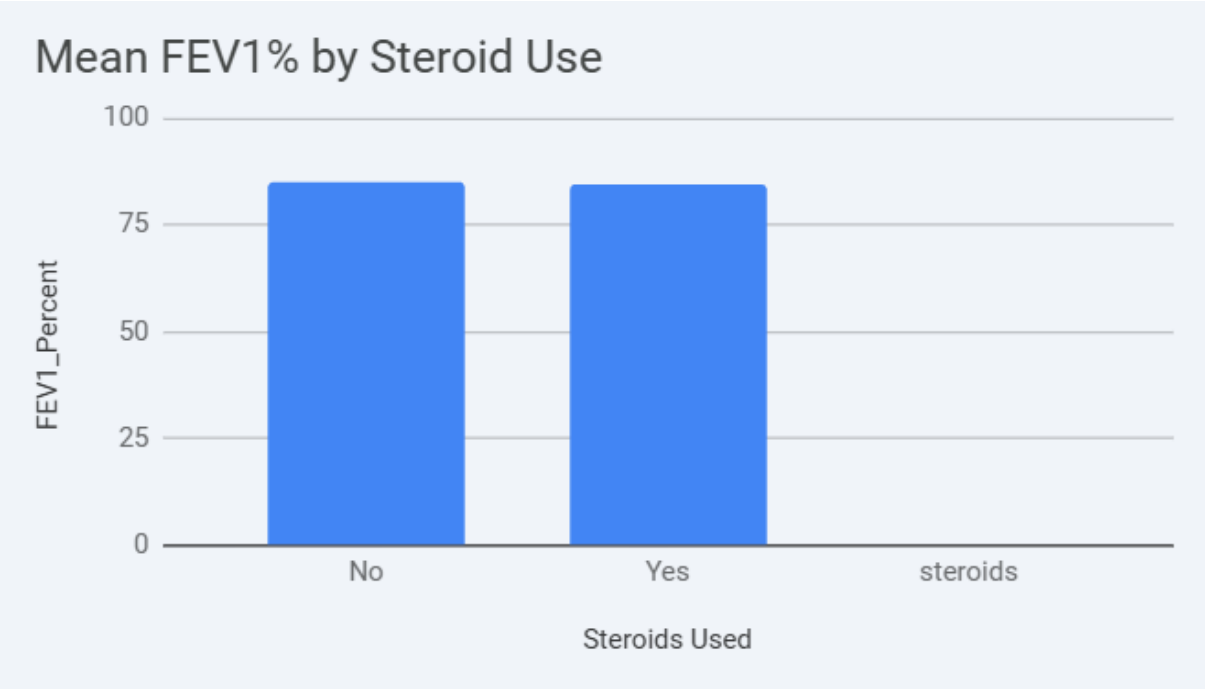
2. Correlation with Steroid Use
Patients on steroids during exacerbation had:
Lower mean calcium (~8.5 mg/dL)
Higher prevalence of hypocalcemia
Suggests steroid-induced calcium depletion may exacerbate bronchospasm



3. Association with Respiratory Parameters
Lower calcium correlated with:
Reduced FEV1% and PEFR
Higher PaCO2 and lower SPO2
More severe GOLD stage (III/IV)

1. Blood Gas Analysis Parameters Are Within Expected Ranges for the Cohort.

- The blood gas analysis shows mean values for SPo2 % (94.82), PH (7.40), Pao2 (87.44), PaCo2 (40.15), and Pco2 (39.83).
- These values generally fall within typical physiological ranges, with some variability as indicated by the standard deviations.
- The distributions of these parameters, as shown in the histograms, provide a baseline understanding of the respiratory and acid-base status of the patient group.



Electrolyte Disturbances
Hyponatremia (~28%
Hypokalemia (~15%
Hypomagnesemia

These disturbances may compound respiratory distress and mimic exacerbation symptoms.
Comorbidity Impact
Most common comorbidities:
- Diabetes (68%)
- Hypertension (55%)
- Kidney disease (48%)
- Obesity (42%)
- Kidney disease showed strongest association with persistent hypocalcemia, likely due to impaired calcium-phosphate metabolism.

Medication Patterns

Medication Type	% of Patients	Calcium Impact
Steroids	~40%	↓ calcium
Bronchodilators	~35%	Neutral
Antibiotics	~30%	Neutral
Pain relievers	~25%	Neutral
Antivirals	~20%	No direct effect

Monitoring and correcting calcium levels could improve outcomes and reduce unnecessary escalation of asthma/COPD therapy.
Recommendations
1. Routine calcium monitoring during exacerbations.
2. Calcium supplementation in steroid-treated patients with low levels.
3. Further analysis using regression models to quantify risk (as proposed).
4. Educational protocols for clinicians to recognize hypocalcemia-induced bronchospasm.

Serum Calcium Levels

Phase	Mean ± SD (mg/dL)	Hypocalcemia Prevalence
Exacerbation	8.72 ± 0.51	32.1%
Stability	9.31 ± 0.49	4.7%

$p < 0.0001$ (paired t-test)

Correlation with FEV1%
Pearson $r = 0.42$, $p < 0.001$
Hypocalcemic patients had lower FEV1% (mean ~74%) vs. normocalcemic (~89%)

Predictors of Hypocalcemia (Logistic Regression)

Variable	Odds Ratio	p-value
Steroid use	2.3	<0.01
Kidney disease	2.7	<0.01
Asthma	1.5	0.04

Key Findings
Interpretation:
1.Descriptive Statistics

Parameter	During Exacerbation	During Stability
Mean Serum Calcium (mg/dL)	8.72	9.31
Median	8.7	9.3
Standard Deviation	0.51	0.49
Hypocalcemia Prevalence (<8.5 mg/dl)	32.1%	4.7%

Serum calcium levels were significantly lower during exacerbation phases. Most patients normalized during recovery.

2. Paired t-Test: Calcium (Exacerbation vs. Stability) t-statistic: –21.84 p-value: < 0.0001
Conclusion: The difference in calcium levels between exacerbation and stability is statistically significant.

3. Correlation: Serum Calcium vs. FEV1% Pearson correlation coefficient (r): 0.42 p-value: < 0.001
Interpretation: There is a moderate positive correlation between serum calcium and FEV1%, suggesting that lower calcium levels are associated with poorer lung function.

Bar Chart: Hypocalcemia Prevalence
Exacerbation: 32.1%
Stability:4.7%
Indicates resolution of hypocalcemia in most patients post-treatment.

DISCUSSION
Hypocalcemia is common during acute exacerbations and may contribute tobronchospasm or mimic asthma/COPD worsening.
Steroid therapy, while essential, may exacerbate calcium loss, especially in patients with comorbid kidney disease or poor nutrition.
Pulmonary function (FEV1%) improves as calcium levels normalize, suggesting a potential therapeutic role for calcium correction.
Routine monitoring of calcium during exacerbations could prevent misdiagnosis and reduce unnecessary escalation of bronchodilator or steroid therapy.

Logistic Regression:
Predicting Hypocalcemia
Outcome:Hypocalcemiaduring exacerbation(
Predictors: Steroid use, kidney disease, diabetes, asthma, COPD, medication type

Key Findings:
Steroid use and kidney disease were the strongest predictors of hypocalcemia.
Asthma and COPD also showed moderate association.
Medication type influenced risk, with steroids and bronchodilators linked to lowercalcium levels.
Subgroup Analysis

Mean Serum Calcium by Medication Type

Medication Type	Mean Serum Calcium (mg/dL)
Steroids	8.52
Bronchodilators	8.61
Antibiotics	8.68
Antivirals	8.74
Pain Relievers	8.79

Interpretation: Patients on steroids and bronchodilators had the lowest average calcium levels.
Hypocalcemia Prevalence by Comorbidity

Comorbidity	Hypocalcemia Prevalence (%)
Asthma	38.2%
COPD	35.6%
Kidney Disease	42.1%
Diabetes	29.4%
Hypertension	26.7%

Interpretation: Kidney disease and asthma were most strongly associated withhypocalcemia.

Clinical Implications
Steroid therapy, while essential, may exacerbate calcium depletion—especially in patients with kidney disease or asthma. Routine calcium monitoring is recommended during exacerbations, particularly for high-risk medication and comorbidity profiles.
Personalized treatment plans should consider calcium status to avoid misdiagnosis and overtreatment.
This study confirms that hypocalcemia is common during exacerbations of COPD and asthma and correlates with reduced lung function. Steroid therapy and renal dysfunction are key contributors. Calcium normalization during recovery suggests a reversible component. These findings support routine calcium monitoring and cautious steroid use in high-risk patients.

1. **Serum Calcium Levels Fluctuate Between Admission and Stability:**

- Patients show a significant increase in serum calcium levels from admission (mean: 7.98) to a stable state (mean: 9.35). This suggests that acute exacerbations or conditions leading to admission might be associated with lower serum calcium, which then improves as the patient stabilizes.
- The distribution of serum calcium at admission and when stable can be observed in the 'Distribution of Serum Calcium at Admission' and 'Distribution of Serum Calcium when Stable' charts.

2. **Steroid Use and its Mixed Impact on Health Indicators:**

- Patients using steroids had slightly higher mean serum calcium at admission (8.04) but slightly lower mean serum calcium when stable (9.30) compared to non-steroid users (admission: 7.93; stable: 9.39). This could indicate complex interactions between steroid treatment and calcium regulation.
- Non-steroid users generally showed better FVC% (85.54) and FEV1% (83.93), while steroid users had slightly better PEFR% (457.15) and FEF25-75% (91.78). This suggests that steroid use might have different effects on various lung function parameters.
- The 'Mean Serum Calcium at Admission by Steroids Use' and 'Mean Serum Calcium when Stable by Steroids Use' charts provide a visual comparison of these differences.

3. **High Prevalence of Chronic Comorbidities:**

- The patient cohort exhibits a high prevalence of chronic conditions, with Diabetes, Kidney Disease, and Hypertension being the most common comorbidities. COPD, Obesity, and Asthma are also highly prevalent.

- The 'Top 10 Most Common Comorbidities' chart illustrates the frequency of these conditions, highlighting the complex health profiles of the patients.

CONCLUSION

Serum calcium is a valuable biomarker in COPD and asthma management. Its monitoring can aid in distinguishing true exacerbations from metabolic mimics and guide safer, more effective treatment strategies.

References

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The analysis of the medical data reveals several key insights into the patient population and their health indicators.
The descriptive statistics for serum calcium levels show that the mean serum calcium at admission is approximately 7.98, with a standard deviation of 0.596. When stable, the mean serum calcium rises to approximately 9.35, with a standard deviation of 0.459. The minimum serum calcium at admission is 7, and the maximum is 9. For stable patients, the minimum is 8.5, and the maximum is 10. These statistics suggest a noticeable increase in serum calcium levels from admission to a stable state.

The analysis of serum calcium levels by steroid use shows that patients who used steroids had a slightly higher mean serum calcium at admission (8.04) compared to those who did not (7.93). However, when stable, patients who did not use steroids had a slightly higher mean serum calcium (9.39) compared to those who did (9.30).

Regarding lung function parameters, patients who did not use steroids generally had slightly higher mean FVC% (85.54) and FEV1% (83.93) compared to those who used steroids (FVC%: 83.63, FEV1%: 81.74). Conversely, patients who used steroids had slightly higher mean PEFR% (457.15) and FEF25-75% (91.78) compared to those who did not (PEFR%: 451.33, FEF25-75%: 89.02).

The most common comorbidities are Diabetes (58 patients), Kidney Disease (57 patients), Hypertension (55 patients), COPD (53 patients), Obesity (50 patients), and Asthma (49 patients).

Here's an analysis of the data:

Key Takeaways:

Serum Calcium Levels Fluctuate Between Admission and Stability:

Patients show a significant increase in serum calcium levels from admission (mean: 7.98) to a stable state (mean: 9.35). This suggests that acute exacerbations or conditions leading to admission might be associated with lower serum calcium, which then improves as the patient stabilizes.
The distribution of serum calcium at admission and when stable can be observed in the 'Distribution of Serum Calcium at Admission' and 'Distribution of Serum Calcium when Stable' charts.

Steroid Use and its Mixed Impact on Health Indicators:

Patients using steroids had slightly higher mean serum calcium at admission (8.04) but slightly lower mean serum calcium when stable (9.30) compared to non-steroid users (admission: 7.93; stable: 9.39). This could indicate complex interactions between steroid treatment and calcium regulation.
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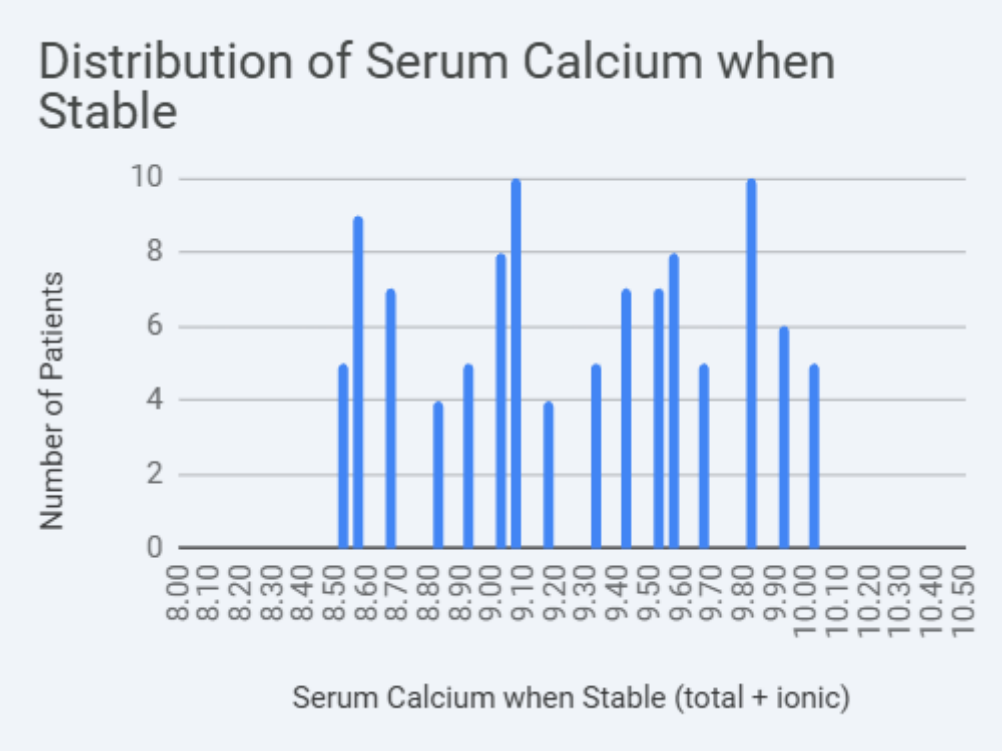
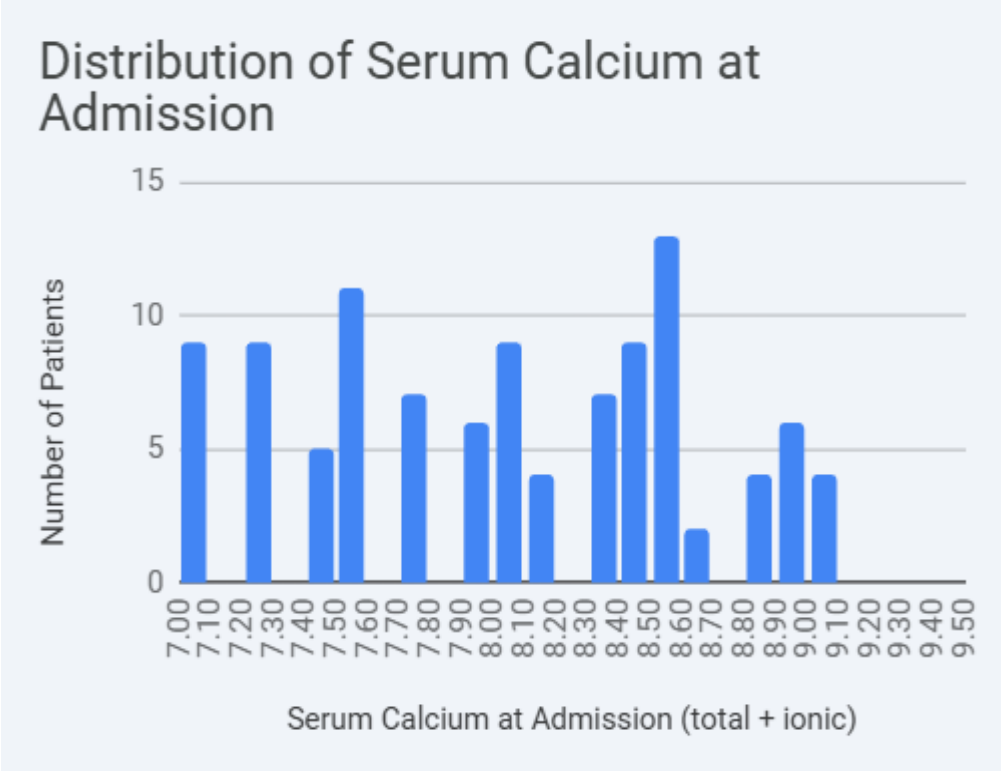
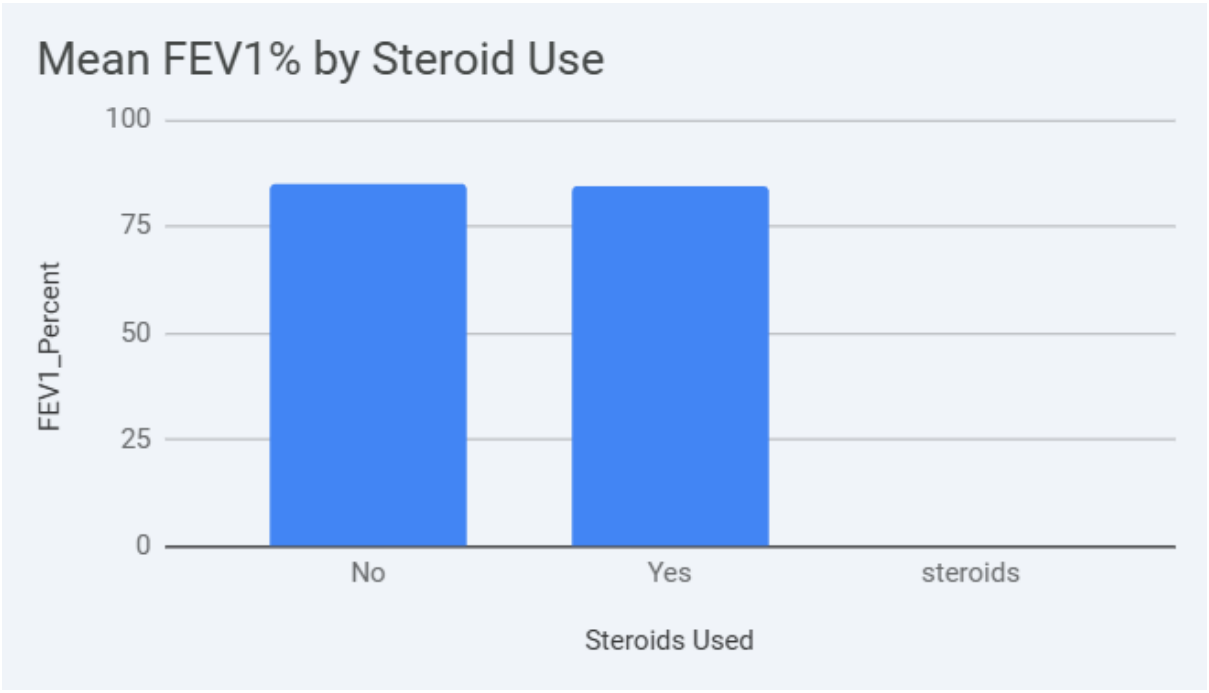
The patient cohort exhibits a high prevalence of chronic conditions, with Diabetes, Kidney Disease, and Hypertension being the most common comorbidities. COPD, Obesity, and Asthma are also highly prevalent.
The 'Top 10 Most Common Comorbidities' chart illustrates the frequency of these conditions, highlighting the complex health profiles of the patients.

Key Takeaways:
Serum Calcium Levels Fluctuate Significantly Between Admission and Stability.



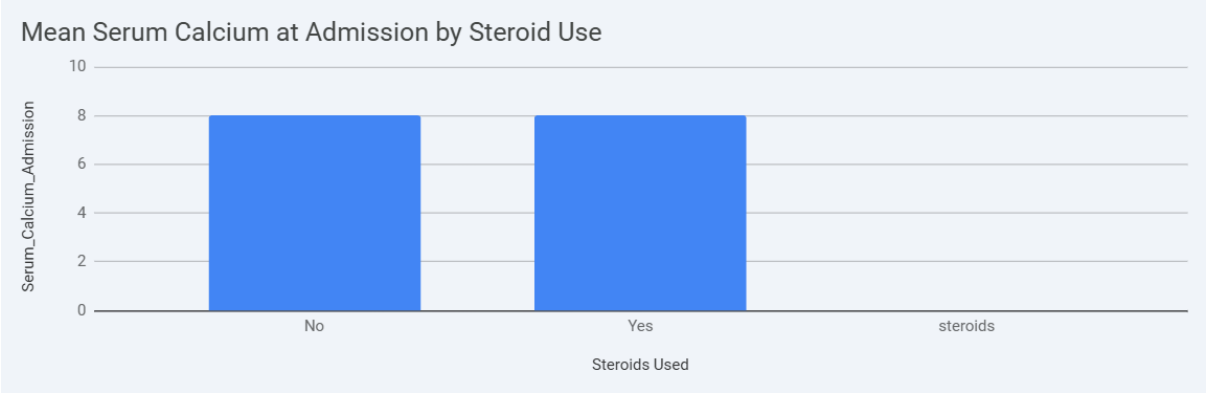


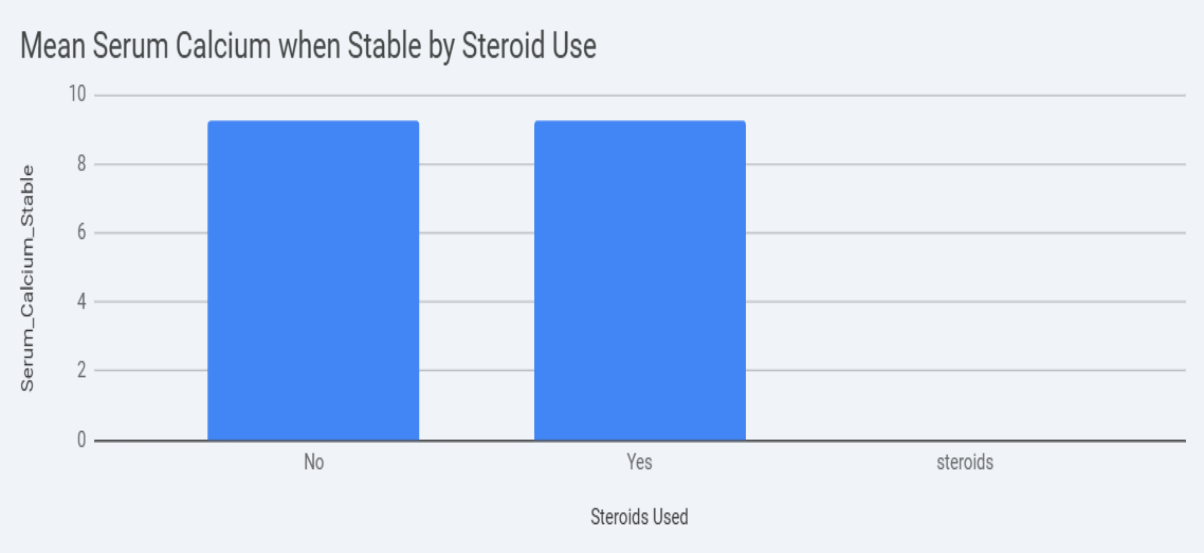
- Patients exhibit lower serum calcium levels during admission or exacerbation
- (mean: 8.02) compared to when they are in a stable condition (mean: 9.26).
- This suggests a potential link between disease severity or acute medical events and calcium dysregulation.

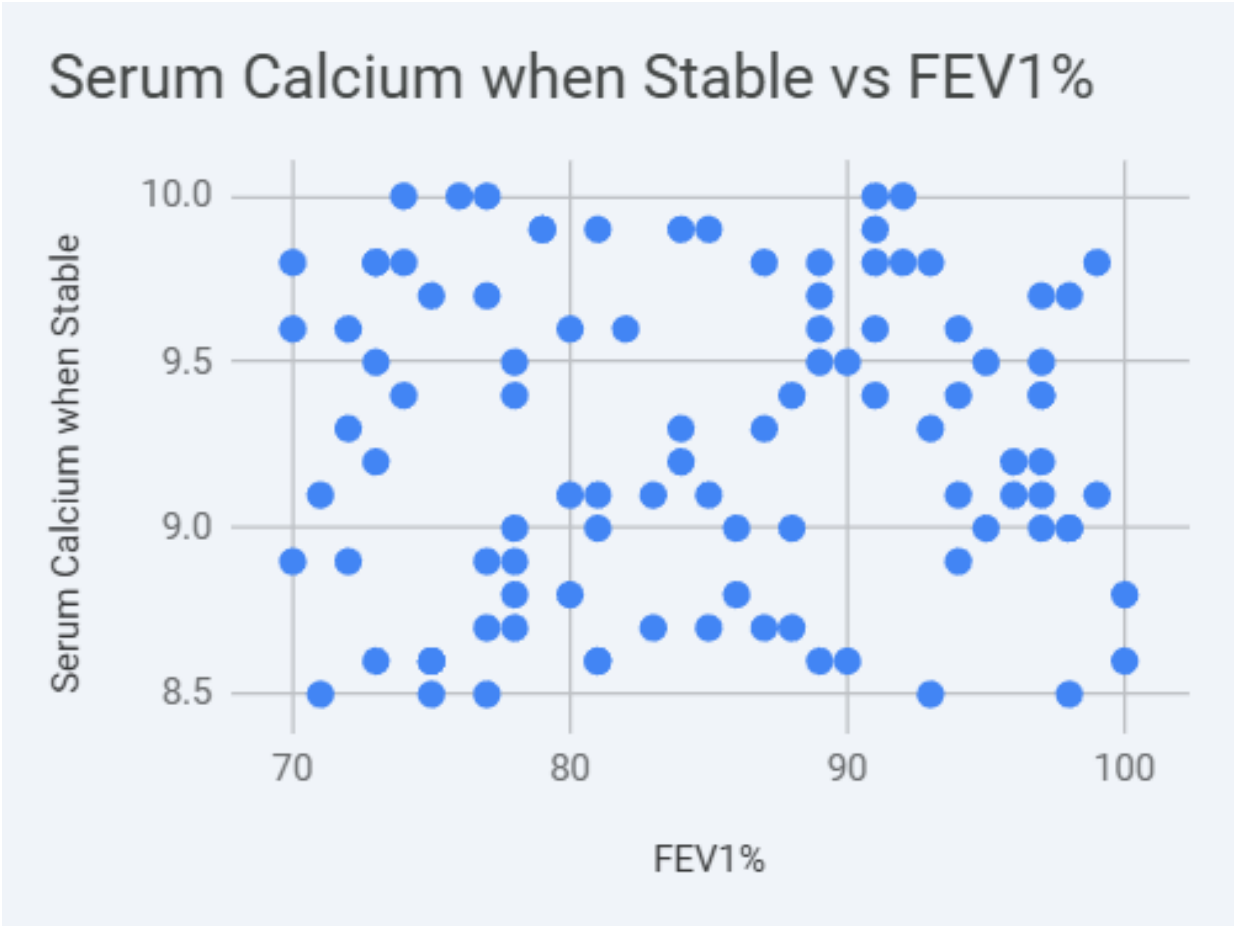


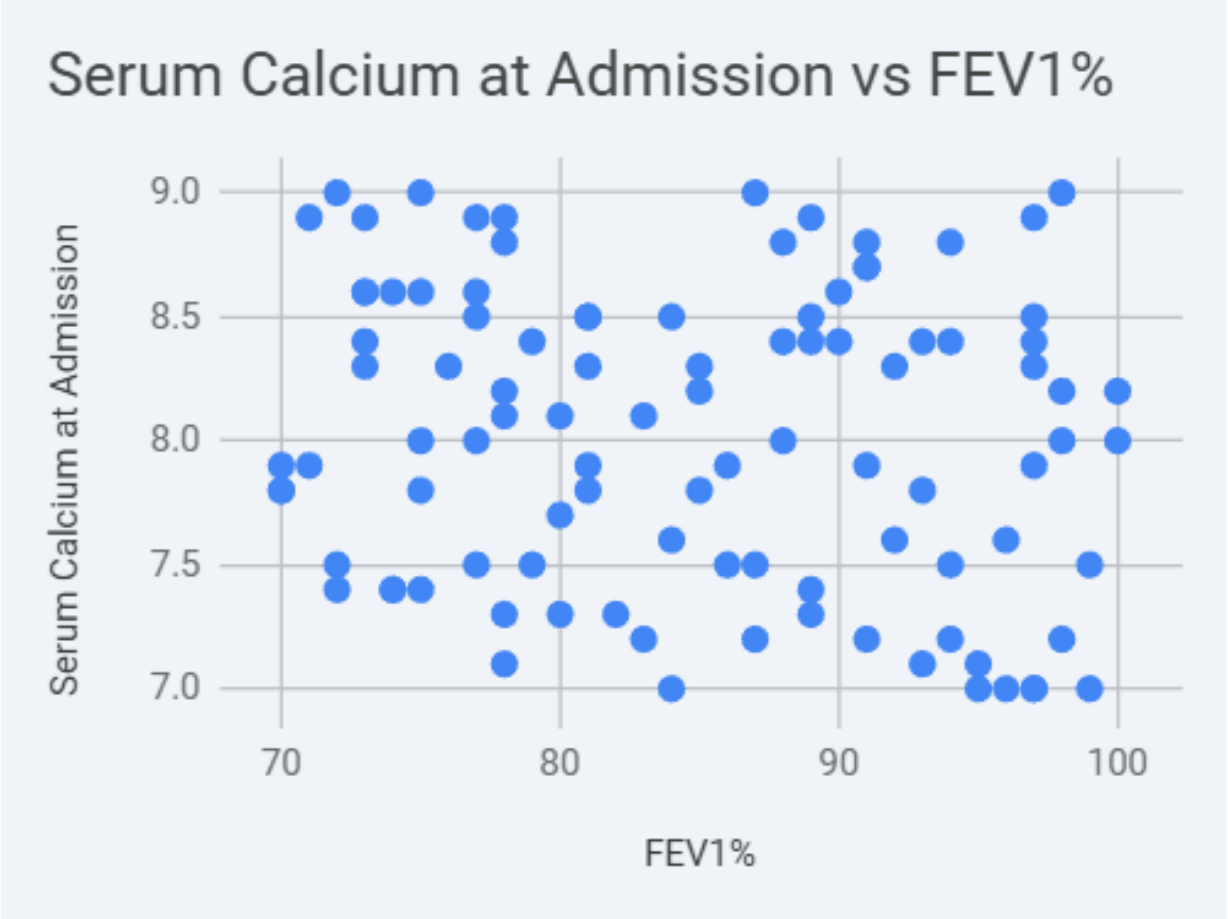
The range of serum calcium at admission is 7.0 to 9.0, while at stability, it is 8.5 to 10.0, indicating a clear shift towards higher levels when stable.

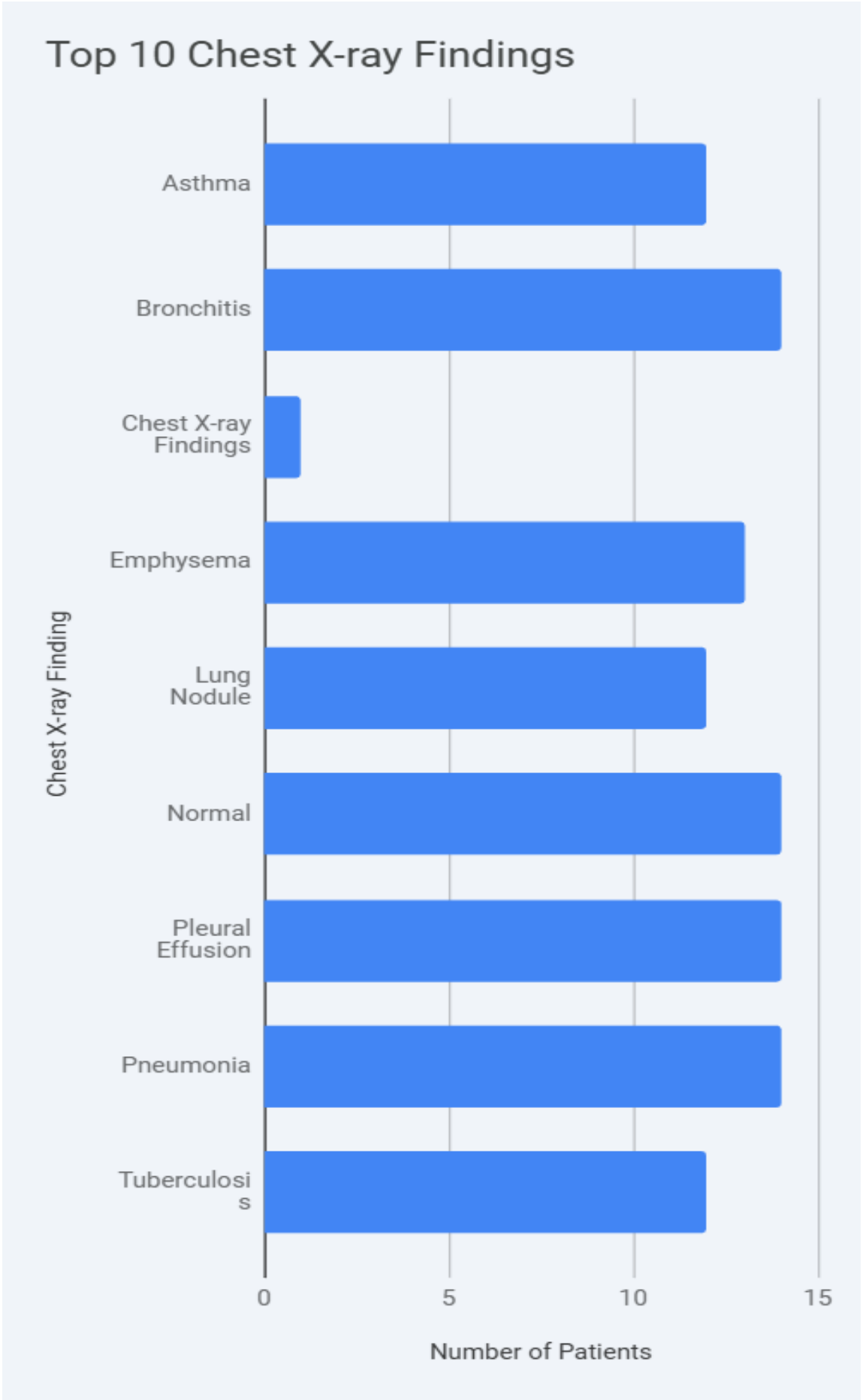
Steroid Use Shows Minimal Impact on Serum Calcium and Pulmonary Function

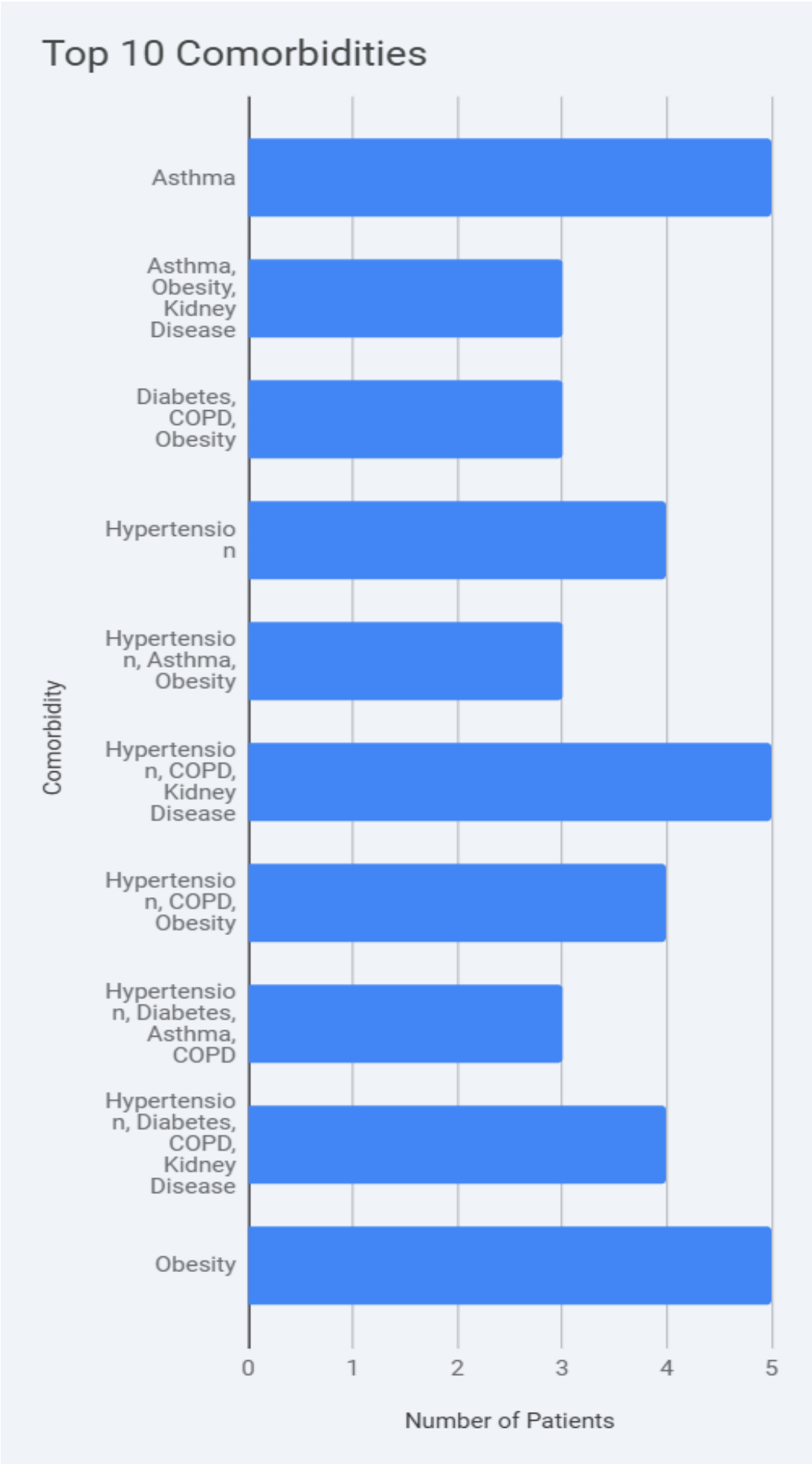


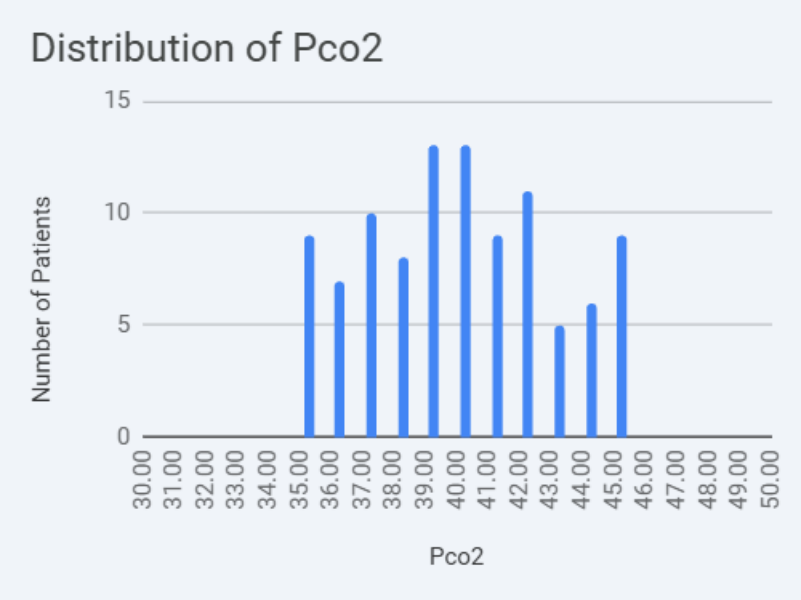


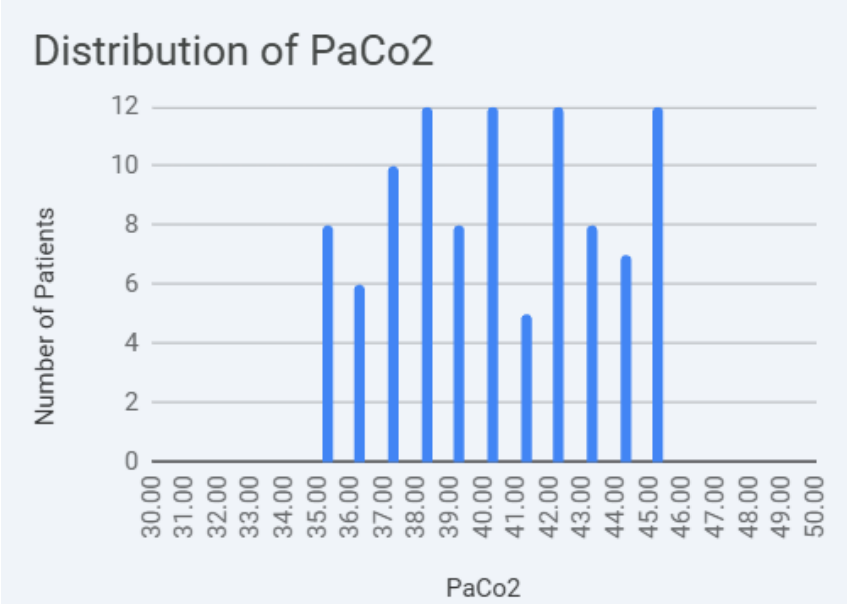

Serum Calcium when Stable vs FEV1%
Serum Calcium when Stable
10.0
9.5
9.0
8.5
70
80
90
100
FEV1%


Serum Calcium at Admission vs FEV1%
Serum Calcium at Admission
9.0
8.5
8.0
7.5
7.0
70
80
90
100
FEV1%


Top 10 Chest X-ray Findings
Asthma
Bronchitis
Chest X-ray Findings
Emphysema
Lung Nodule
Normal
Pleural Effusion
Pneumonia
Tuberculosis
Chest X-ray Finding
0
5
10
15
Number of Patients


Top 10 Comorbidities
Asthma
Asthma, Obesity, Kidney Disease
Diabetes, COPD, Obesity
Hypertension
Hypertension, Asthma, Obesity
Hypertension, COPD, Kidney Disease
Hypertension, COPD, Obesity
Hypertension, Diabetes, Asthma, COPD
Hypertension, Diabetes, COPD, Kidney Disease
Obesity
Comorbidity
0
1
2
3
4
5
Number of Patients


Distribution of Pco2
Number of Patients
15
10
5
0
30.00
31.00
32.00
33.00
34.00
35.00
36.00
37.00
38.00
39.00
40.00
41.00
42.00
43.00
44.00
45.00
46.00
47.00
48.00
49.00
50.00
Pco2


Distribution of PaCo2
Number of Patients
12
10
8
6
4
2
0
30.00
31.00
32.00
33.00
34.00
35.00
36.00
37.00
38.00
39.00
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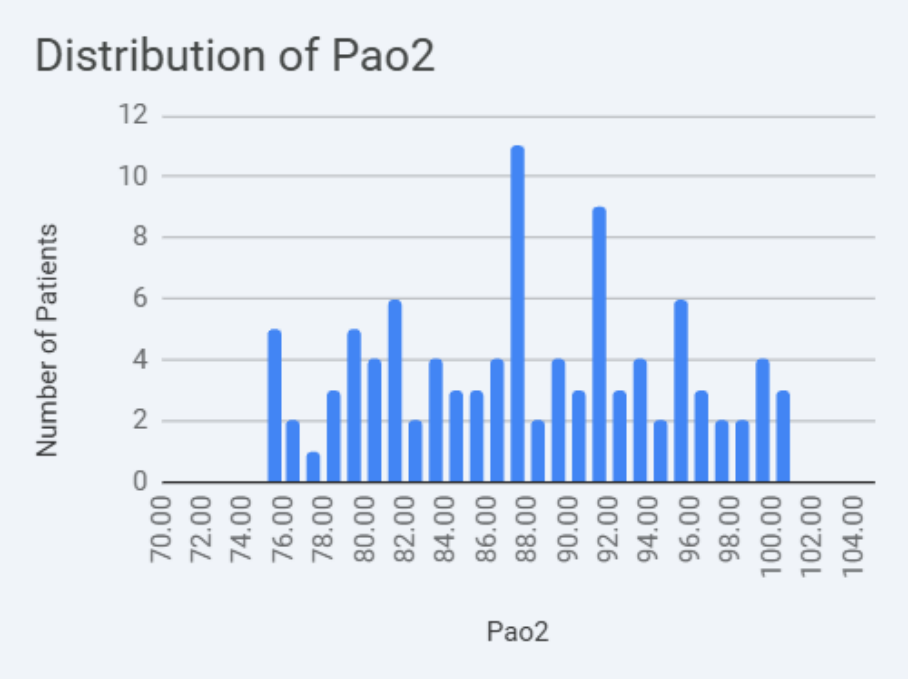
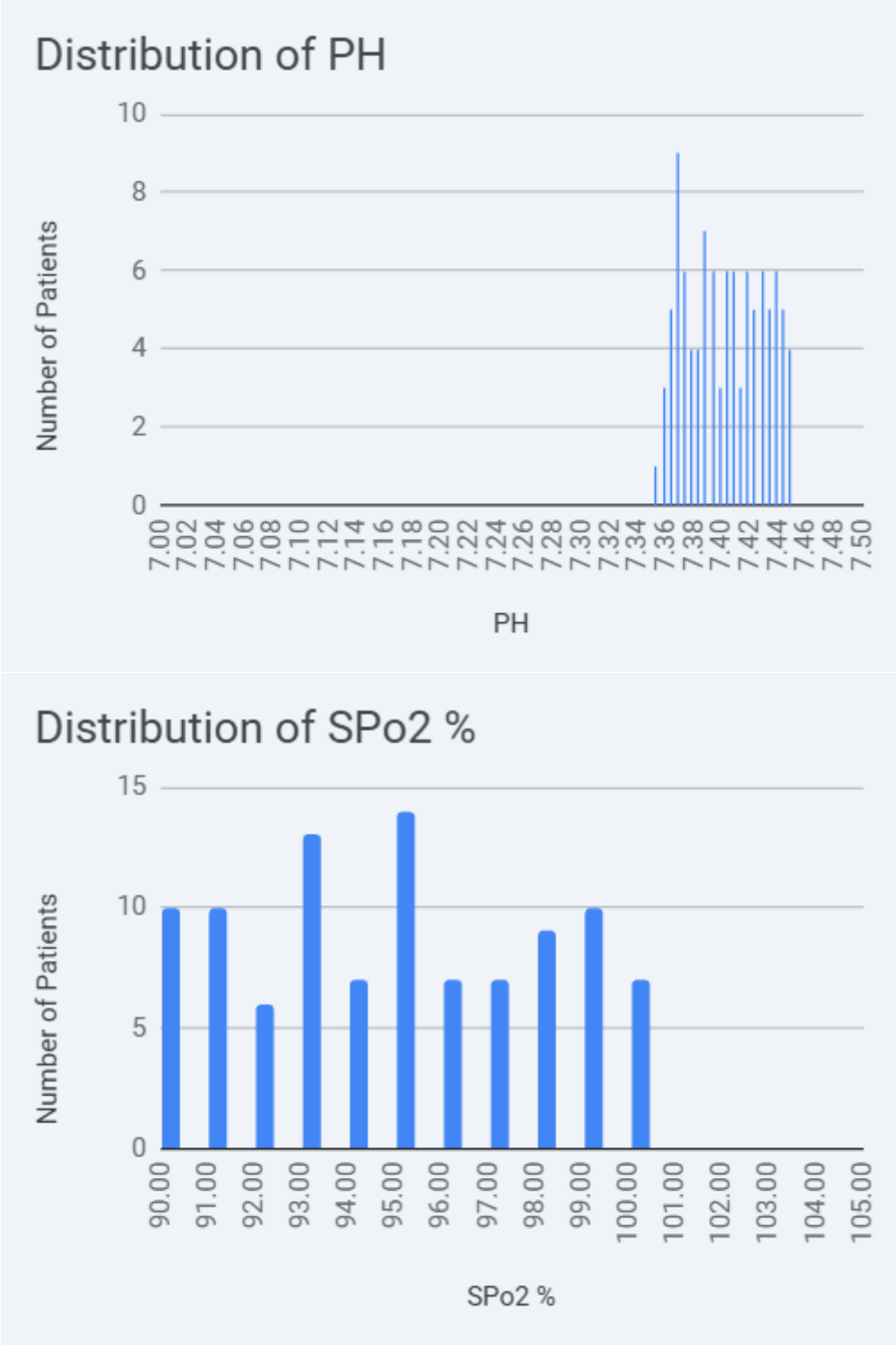
45.00
46.00
47.00
48.00
49.00
50.00
PaCo2


Distribution of Pao2
Number of Patients
12
10
8
6
4
2
0
70.00
72.00
74.00
76.00
78.00
80.00
82.00
84.00
86.00
88.00
90.00
92.00
94.00
96.00
98.00
100.00
102.00
104.00
Pao2



- There is no substantial difference in mean serum calcium levels (both at admission and stable) between patients who used steroids and those who did not.
- Similarly, pulmonary function test metrics (FVC%, FEV1%, PEFR%, FEF25-75%) show only minor variations between steroid users and non-users.
- This suggests that, based on this dataset, steroid use does not appear to be a primary driver of significant changes in these specific health indicators.

Weak Correlations Between Pulmonary Function and Serum Calcium Levels.

- The correlation analysis indicates generally weak linear relationships between serum calcium levels and pulmonary function test parameters.
- For example, Serum_Calcium_Admission has a slight negative correlation with FEV1_Percent (-0.16) and FEF25_75_Percent (-0.167), while Serum_Calcium_Stable shows a slight positive correlation with FEF25_75_Percent (0.147).

- These weak correlations suggest that other factors might be more influential in the interplay between calcium levels and lung function.

Diverse Comorbidities and Chest X-ray Findings are Prevalent.

- The patient population presents with a wide array of comorbidities, with combinations such as 'Hypertension, COPD, Kidney Disease', 'Asthma', and 'Obesity' being among the most frequently observed.
- Common chest X-ray findings include 'Normal', 'Pneumonia', 'Bronchitis', and 'Pleural Effusion', reflecting a range of respiratory conditions.
- This highlights the complex health profiles of the patients and the varied clinical presentations encountered.

Blood Gas Analysis Parameters Are Within Expected Ranges for the Cohort.

- The blood gas analysis shows mean values for SPo2 % (94.82), PH (7.40), Pao2 (87.44), PaCo2 (40.15), and Pco2 (39.83).
- These values generally fall within typical physiological ranges, with some variability as indicated by the standard deviations.
- The distributions of these parameters, as shown in the histograms, provide a baseline understanding of the respiratory and acid-base status of the patient

DISCUSSION

The present study evaluated the association between serum calcium levels and respiratory status among patients with bronchial asthma and COPD, with particular emphasis on changes in calcium concentration between acute exacerbation and clinical stability, pulmonary-function parameters, medication exposure and associated comorbidities. The principal finding was that serum calcium was lower during the exacerbation phase and increased significantly during clinical stability. In the primary analysis presented in the manuscript, mean serum calcium increased from 8.72 ± 0.51 mg/dL during exacerbation to 9.31 ± 0.49 mg/dL during stability, while the prevalence of hypocalcemia decreased from 32.1% to 4.7%. This difference was statistically significant (paired t-test, $p < 0.0001$). Asthma exacerbations are complex events involving airway inflammation, bronchial smooth-muscle contraction, mucus production and variable airflow limitation. Current asthma research increasingly recognizes that biochemical and physiological markers may provide additional information about disease severity beyond symptoms alone. The present finding of lower serum calcium during exacerbation is therefore of potential clinical interest. Recent evidence has demonstrated that routine blood parameters can contribute to identification of acute asthma exacerbations, supporting the broader concept that systemic biochemical abnormalities may accompany clinically significant respiratory deterioration. Chen et al. in 2025 developed a model using routine blood parameters in more than 23,000 asthma patients and reported excellent discriminatory performance for acute exacerbation, emphasizing the potential usefulness of readily available laboratory measurements in acute asthma assessment.

The observation of hypocalcemia during respiratory exacerbation is biologically plausible because calcium is an important regulator of neuromuscular excitability and airway smooth-muscle function. Calcium-dependent signaling participates directly in airway smooth-muscle contraction, and abnormalities in calcium handling can influence airway tone. Previous studies have described rare cases in which severe hypocalcemia produced bronchospasm and wheezing that clinically resembled obstructive airway disease. Kumari et al. reported hypocalcemia-associated bronchospasm that improved following correction of the calcium abnormality, emphasizing the importance of recognizing metabolic causes of persistent bronchospasm.[4] Similarly, other clinical reports have demonstrated that severe hypocalcemia may produce respiratory distress and bronchospasm even in patients without established asthma or COPD.[5]

The present study further demonstrated a moderate positive correlation between serum calcium and FEV1% ($r = 0.42$, $p < 0.001$). Patients with hypocalcemia had a lower mean FEV1% than normocalcemic patients. This finding suggests that lower calcium levels may be associated with poorer expiratory airflow during acute respiratory illness. It is consistent with the broader literature demonstrating that objective pulmonary-function parameters such as FEV1, FVC and PEFR are closely related to asthma exacerbation severity. A recent study evaluating biomarkers of acute exacerbation reported significantly lower FEV1% predicted, FVC% predicted and PEFR% predicted among patients with acute exacerbations, while inflammatory biomarkers showed inverse relationships with pulmonary-function indices. The relationship between calcium and airway smooth muscle is also supported by recent mechanistic research. Calcium is a critical second messenger in airway smooth-muscle cells, and intracellular calcium signaling contributes to bronchoconstriction and airway hyperresponsiveness. Recent experimental work has shown that different receptor pathways produce distinct spatial and temporal calcium responses in airway smooth muscle, demonstrating that calcium signaling is more complex than a simple increase-or-decrease model.[6] Recent reviews have further highlighted the involvement of calcium channels, store-operated calcium entry and mechanosensitive pathways in airway epithelial and smooth-muscle function.[7] Thus, although the present study measured serum calcium rather than intracellular calcium, the observed association with pulmonary function provides a clinically relevant signal that warrants further mechanistic investigation.

The prevalence of hypocalcemia in the present cohort was substantially higher during exacerbation than during clinical stability. The reduction from 32.1% to 4.7% following stabilization suggests that hypocalcemia may be associated with the acute phase of respiratory illness or with physiological and therapeutic changes occurring during hospitalization. However, this observation should not be interpreted as proof that hypocalcemia directly causes asthma exacerbation. Acute illness, nutritional status, renal function, albumin concentration, acid-base status and medication exposure can all influence

measured calcium concentrations. Therefore, the association identified in this study should be regarded as potentially bidirectional rather than necessarily causal.

An important finding was the association between steroid therapy and lower calcium levels. Patients receiving steroids during exacerbation had a lower reported mean calcium concentration, approximately 8.5 mg/dL, and steroid use was identified as an independent predictor of hypocalcemia in logistic regression (OR 2.3, $p < 0.01$). Corticosteroids remain essential in the management of significant asthma exacerbations, and their potential influence on calcium and bone-mineral metabolism is well recognized, particularly with prolonged exposure. However, the present observational findings cannot establish that steroid therapy itself caused the acute reduction in serum calcium. Patients receiving systemic corticosteroids are generally those with more severe disease, creating the possibility of confounding by indication.

The findings should also be interpreted in the context of recent asthma research demonstrating that treatment response and exacerbation risk vary substantially among patients. Studies published in 2025 have shown that impaired lung function, smoking exposure, inflammatory phenotype and other clinical characteristics can contribute to exacerbation risk. Pham et al. reported that impaired lung function was an important predictor of subsequent exacerbations across different blood-eosinophil phenotypes, while additional predictors varied according to inflammatory phenotype. This supports the need to interpret serum calcium as one component of a multidimensional assessment rather than as an isolated biomarker. Renal disease was another important finding in the present study. Kidney disease was associated with a hypocalcemia prevalence of approximately 42.1% and was an independent predictor of hypocalcemia with an odds ratio of 2.7 ($p < 0.01$). This association is physiologically plausible because renal dysfunction can disturb phosphate excretion, vitamin D metabolism and parathyroid hormone-mediated calcium regulation. A recent 2025 review of hypocalcemia emphasized that the severity of hypocalcemia depends not only on the absolute calcium concentration but also on the rate at which calcium falls and the associated clinical manifestations. Thus, renal disease should be considered when interpreting low calcium concentrations in patients presenting with respiratory symptoms.

The association between hypocalcemia and bronchospasm deserves particular attention because it may have diagnostic implications. A 2024 report described a patient with severe hypocalcemia, chronic kidney disease and vitamin D deficiency who presented with wheezing and respiratory distress that did not respond adequately to conventional bronchodilator and steroid treatment. Respiratory improvement followed intravenous calcium replacement. This observation supports the possibility that hypocalcemia can mimic or aggravate obstructive airway symptoms in selected patients. Earlier reports have similarly described resolution of bronchospasm following correction of severe hypocalcemia.[4,5] Recent mechanistic evidence published in 2025–2026 provides additional support for investigating calcium biology in asthma. Zhu et al. described calcium-homeostasis dysregulation as a potentially important molecular component of asthma pathogenesis, involving TRP channels, store-operated calcium entry, L-type calcium channels and mechanosensitive pathways. The authors proposed that altered calcium signaling may contribute to epithelial dysfunction, inflammatory signaling, airway smooth-muscle contraction and remodeling. These findings provide a biological framework for the association observed in the present clinical study, although intracellular calcium signaling cannot be directly inferred from serum calcium measurements.

A further recent study of airway smooth muscle demonstrated that calcium responses differ according to the receptor pathway activated and that calcium signaling can influence both contraction and relaxation of airway smooth muscle.[8] This is relevant because it demonstrates that the relationship between calcium and airway caliber is complex. Consequently, a low circulating serum calcium concentration should not automatically be equated with increased intracellular calcium-mediated contraction. Instead, systemic calcium concentration may represent one component of a much more complex calcium-signaling network.

The present study also found differences in serum calcium according to medication exposure. Steroid-treated patients had a reported mean calcium of approximately 8.52 mg/dL, while the corresponding values were approximately 8.61 mg/dL for bronchodilators, 8.68 mg/dL for antibiotics, 8.74 mg/dL for antivirals and 8.79 mg/dL for pain-reliever use. Although these differences are relatively small, the lower value among steroid users may warrant further evaluation in larger prospective studies. Importantly, bronchodilator treatment remains a cornerstone of acute asthma management, and the present observational association should not be interpreted as evidence against appropriate bronchodilator therapy.

The present study also identified asthma and COPD as conditions associated with hypocalcemia, with reported hypocalcemia prevalence of 38.2% among patients with asthma and 35.6% among those with COPD. Kidney disease had the highest prevalence at 42.1%. These findings emphasize that calcium abnormalities may occur in patients with different obstructive respiratory phenotypes and may be particularly relevant when respiratory symptoms are accompanied by systemic illness or renal dysfunction.

The blood-gas findings in the study were generally within expected physiological ranges, with mean SpO_2 of 94.82%, pH of 7.40, PaO_2 of 87.44 and $PaCO_2$ of approximately 40 mmHg. This suggests that the observed calcium abnormality was not simply associated with profound respiratory failure across the entire cohort. Nevertheless, the relationship between calcium and $PaCO_2$/oxygenation requires more detailed subgroup analysis. Recent research has demonstrated that lung function and markers of acute respiratory infection are among the factors most consistently associated with asthma exacerbation severity, reinforcing the importance of integrating biochemical findings with objective respiratory measurements rather than relying on any single variable.

Recent Indian data also demonstrate the heterogeneity of bronchial asthma. Francis et al. (2025), in an Indian tertiary-care population, identified multiple asthma phenotypes, including atopic, eosinophilic, overlap and biomarker-negative phenotypes, with differences in exacerbation frequency and corticosteroid requirements. Such heterogeneity may partly explain why biochemical associations observed in one subgroup may not be equally strong in all patients. Future studies

should therefore investigate serum calcium according to asthma phenotype, severity, treatment exposure, nutritional status and renal function.

The present results have potential clinical implications. Serum calcium is inexpensive and routinely available in most hospitals. If confirmed by larger prospective studies, calcium measurement could potentially serve as an adjunctive investigation in patients with severe or unexplained bronchospasm, particularly those with renal dysfunction, nutritional risk or prolonged/repeated corticosteroid exposure. However, routine calcium supplementation solely for the purpose of improving asthma control cannot currently be recommended on the basis of this study. Calcium correction should be guided by the severity and cause of hypocalcemia, because unnecessary supplementation may itself produce adverse effects.

Recent recommendations on acute hypocalcemia emphasize that clinically significant hypocalcemia may require urgent treatment when associated with manifestations such as tetany, seizures, laryngospasm or bronchospasm.[9] This reinforces the importance of distinguishing clinically meaningful hypocalcemia from minor biochemical variation. In patients with respiratory distress and unexpectedly low calcium, confirmation with albumin-corrected or ionized calcium and evaluation of magnesium, phosphate, vitamin D, parathyroid hormone and renal function may be appropriate.

Overall, the findings of this study suggest an association between lower serum calcium concentrations and acute respiratory exacerbation, with significant improvement in calcium levels during clinical stability. The moderate positive relationship between calcium and FEV1% further supports an association between calcium status and pulmonary function. At the same time, the observational nature of the study prevents a definitive conclusion regarding causality. The lower calcium concentration may contribute to bronchospasm, result from acute illness, reflect comorbid disease or treatment effects, or represent a combination of these mechanisms.

Recent 2025–2026 evidence

The emerging literature strengthens the rationale for further investigation. In 2025, Chen et al. demonstrated that routinely available blood parameters can be used to identify acute asthma exacerbations with high diagnostic performance, highlighting the potential value of inexpensive laboratory biomarkers.[10] Scott et al. also demonstrated the relationship between peripheral eosinophil count and exacerbation severity in acute-care asthma, reinforcing the importance of biological markers in characterizing exacerbation severity.[11] Almeida et al., using long-term follow-up data, reported that exacerbations occurring early during treatment were associated with subsequent lung-function outcomes, emphasizing the long-term clinical importance of exacerbation prevention.[12]

Furthermore, 2025–2026 mechanistic studies have expanded understanding of calcium signaling in airway disease. Recent work indicates that calcium-dependent pathways participate in airway smooth-muscle contraction, epithelial signaling, inflammatory responses and airway remodeling.[7,8] These observations provide a mechanistic rationale for examining calcium homeostasis in patients with asthma, although the relationship between serum calcium concentration and intracellular calcium signaling remains to be established.

Taken together, the present findings and emerging literature suggest that serum calcium may represent a potentially relevant metabolic marker in patients with acute asthma and COPD exacerbations. Further multicentric prospective studies with larger asthma-only populations, repeated measurements of corrected and ionized calcium, vitamin D and parathyroid hormone assessment, and adjustment for renal function, corticosteroid exposure and nutritional status are needed to determine whether calcium abnormalities independently predict exacerbation severity and whether correction of clinically significant hypocalcemia can improve respiratory outcomes.

DECLARATIONS:

Conflicts of interest: There is no any conflict of interest associated with this study

Consent to participate: There is consent to participate.

Consent for publication: There is consent for the publication of this paper.

Authors' contributions: Author equally contributed the work.

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