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Original Research Paper

An array of Metabolic Disturbances Associated with Status Asthmaticus

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ABSTRACT:

Background: Status asthmaticus is a severe and potentially life-threatening asthma exacerbation refractory to standard treatments, associated with significant morbidity and mortality. It is significantly associated with electrolyte imbalances resulting in metabolic disturbances that considerably adds to the deterioration of clinical condition. **Objective:** The aim of our study is to illuminate the incidence of electrolyte imbalance and metabolic disturbances, including both metabolic acidosis and alkalosis, in patients with status asthmaticus. **Material & Methods:** An observational, hospital-based, retrospective chart review was conducted on patients with status asthmaticus admitted over the period of past two years, January 2021 to December 2022. The sample comprised of 72 known asthmatic patients of age 12-65 years. The data was based on serum electrolyte levels (sodium, potassium, magnesium, calcium, and phosphate) and results of arterial blood gases at the time of presentation in ER. Statistical analysis was performed by using SPSS v.20. **Results**: All the status asthmaticus patients were having acute electrolyte and metabolic disturbances. Metabolic acidosis (n=13, 18%) was more prevalent than metabolic alkalosis. However, respiratory acidosis with metabolic alkalosis was found more common, associated with the severity and poor outcome (n=26, 36%). Among all, 13%, 15%, 35%, and 38% had 1, 2, 3 and >3 electrolyte disturbances, respectively. **Conclusion**: Electrolytes and metabolic profile derangements are common amongst the status asthmaticus patients. While managing the life-threatening status asthmaticus, it is also essential to monitor serum electrolytes and acid-base levels to improve prognosis.

Keywords: status asthmaticus, electrolyte imbalance, metabolic disorder, pathophysiology, complications

INTRODUCTION:

Status asthmaticus is an extreme and potentially life-threatening form of asthma that is unresponsive to standard treatment modalities. It is characterized by persistent bronchospasm that can trigger severe and protracted attacks, potentially leading to respiratory failure. [1] The underlying pathophysiology of status asthmaticus is multi-factorial and complex, involving an interplay of inflammation, bronchial hyper-reactivity, and various biochemical alterations. [2] Asthma is a chronic respiratory disease affecting 339 million people worldwide, making it one of the most common noncommunicable diseases. The estimated prevalence of asthma ranges from 1% to 18% in different countries. [3] Asthma prevalence is increasing with urbanization and exposure to environmental exposure. Recent studies show the burden of the disease is almost equally distributed in countries of various socioeconomic status. [4] The epidemiology of status asthmaticus is hard to estimate due to its varying definition and the ubiquitous nature of asthma itself. However, severe asthma, which status asthmaticus is a subset of, affects about 5-10% of the total asthmatic population globally. Some studies suggest that in United States, about 2% of all the medical emergencies represents status asthmaticus with the mortality rate of 2% [5] Despite advancements in medical care, there is significant mortality associated with asthma accounting for approximately 1000 deaths per day, globally. [6]

Asthma, at its core, is an inflammatory disease of the airways. The pathophysiology of status asthmaticus, while complex and multifaceted, is an exaggeration of the typical pathophysiology seen in chronic asthma. It involves a combination of bronchoconstriction, inflammation, and mucous plugging leading to severely impaired airflow. Mucous plugging is a result of hypertrophy and hyperplasia of the mucus-secreting goblet cells in the airway epithelium and the overproduction of mucus. These plugs can cause near-complete occlusion of the airways, contributing to the severity of status asthmaticus. [6,7]

Inflammation is typically mediated by an influx of inflammatory cells into the bronchial wall, including eosinophils, mast cells, lymphocytes, and neutrophils. These cells release an array of inflammatory mediators, cytokines, and chemokines, causing increased vascular permeability, edema, and further recruitment of inflammatory cells. [6-8] The bronchoconstriction seen in status asthmaticus is due to the hyperresponsiveness of bronchial smooth muscle to various stimuli, such as allergens, cold air, exercise, or irritants. This hyperresponsiveness leads to severe and often refractory bronchoconstriction during an episode of status asthmaticus. [8,9]

Risk factors for status asthmaticus include uncontrolled asthma, nonadherence to maintenance therapy, abrupt discontinuation of corticosteroids, allergen exposure, viral respiratory infections, exercise without prior use of a bronchodilator, and stress or emotional upheaval. Certain comorbid conditions like obesity, chronic sinusitis, or gastroesophageal reflux disease can also exacerbate asthma and increase the risk of status asthmaticus. [10]

Status asthmaticus can be associated with various electrolyte and metabolic disturbances, most commonly hypokalemia and hypomagnesemia. Hypokalemia is typically caused by the use of β2-agonists, a mainstay of treatment in status asthmaticus. β2-agonists stimulate the Na+/K+-ATPase pump leading to an intracellular shift of potassium, resulting in hypokalemia. [11] Hypomagnesemia is another potential disturbance, possibly linked to the severity of asthma. Magnesium acts as a natural calcium antagonist, and hence a deficiency could contribute to bronchial smooth muscle contraction and hyperresponsiveness. [9-11]

Metabolic disturbances commonly seen include lactic acidosis and respiratory alkalosis. The former can occur due to the administration of β2-agonists, which leads to increased anaerobic glycolysis. The latter is often a compensatory mechanism for metabolic acidosis but can also occur independently due to hyperventilation. [12]

The primary goals in managing status asthmaticus are to correct hypoxemia, rapidly reverse airflow obstruction, and reduce the risk of relapse. Medications used in status asthmaticus include short-acting β2-agonists (SABAs) such as albuterol, anticholinergics like ipratropium bromide, systemic corticosteroids, and in some cases, magnesium sulfate. The initial treatment typically involves the administration of high-flow oxygen to correct hypoxemia, along with a combination of rapid-acting inhaled β2-agonists and ipratropium bromide to reverse airflow obstruction. [11,12] Systemic corticosteroids are started as soon as possible to decrease airway inflammation and are typically continued for at least five days. Intravenous magnesium sulfate can be used as an adjunct therapy to induce bronchodilation in patients not responding to initial treatments. [13] In cases where these treatments are ineffective, the patient may require mechanical ventilation. [14]

SABAs can cause tachycardia, hypokalemia, hyperglycemia, and in rare cases, lactic acidosis. Ipratropium bromide is generally well-tolerated but can cause dry mouth, cough, and in rare cases, urinary retention. [15] Corticosteroids can cause hyperglycemia, hypertension, fluid retention, mood alterations, and, with prolonged use, osteoporosis, and adrenal suppression. Magnesium sulfate, generally safe, can cause hypotension and muscle weakness at high doses. [16]

In summary, status asthmaticus is a severe, potentially life-threatening form of asthma that requires immediate medical attention. Understanding its pathophysiology, associated electrolyte, and metabolic disturbances, and the side effects of its treatment can significantly improve patient outcomes and help in developing new, more effective therapies. However, despite a growing body of research dedicated to understanding these intricate pathways, there remains a paucity of literature exploring the potential link between serum electrolyte imbalances, metabolic disturbances, and status asthmaticus. This study is an endeavor to bridge this knowledge gap and offer new insights into patient management and therapeutic approaches.

MATERIAL AND METHODS:

This retrospective, observational study was conducted over a two-year period in a tertiary care hospital. Serum electrolyte concentrations and metabolic parameters were evaluated at the time of admission. The features collected on detailed history and clinical examinations during the hospital admission helped in the diagnosis of status asthmaticus, including the previous history of asthma, acute onset of respiratory distress, poor response to initial bronchodilators, necessitating the use of either high dose of bronchodilators or assistance of mechanical ventilation. Regular arterial blood gas (ABG) analyses were performed to evaluate for any potential metabolic acid-base disturbances. Data regarding patient demographics, clinical features, vital monitoring, asthma control test (ACT) scores, and medication use were also collected.

Data was entered into a statistical software database and analyzed using descriptive and inferential statistics. Continuous variables were described as mean ± standard deviation, and categorical variables were expressed as frequencies and percentages. A p-value of less than 0.05 was considered statistically significant.

This study strictly adhered to the guidelines for human research, and ethical clearance was obtained from the Institutional Ethics Committee. Informed consent was acquired from all patients or their legal representatives. All data were handled confidentially and anonymously to maintain patient privacy.

Inclusion Criteria:

- Previously diagnosed cases of asthma were presented in medical emergency department with status asthmaticus within the duration of this study.
- Patients with complete medical record and written informed consent to use the information in conducting research, taken at the time of admission.
- Patient who stayed admitted in the hospital until fully recovered and discharged.
- Patients with no recent history of toxin ingestion/poisoning, diarrhea, starvation, or alcohol consumption may affect the metabolic profile.

Exclusion Criteria:

- Patients with other significant co-morbidities affecting electrolyte balance, including kidney disease, diabetes mellitus, liver disease, heart failure, or those receiving dialysis, were excluded.
- Pregnant patients and those who refused to give informed consent were also excluded from the study.

RESULTS:

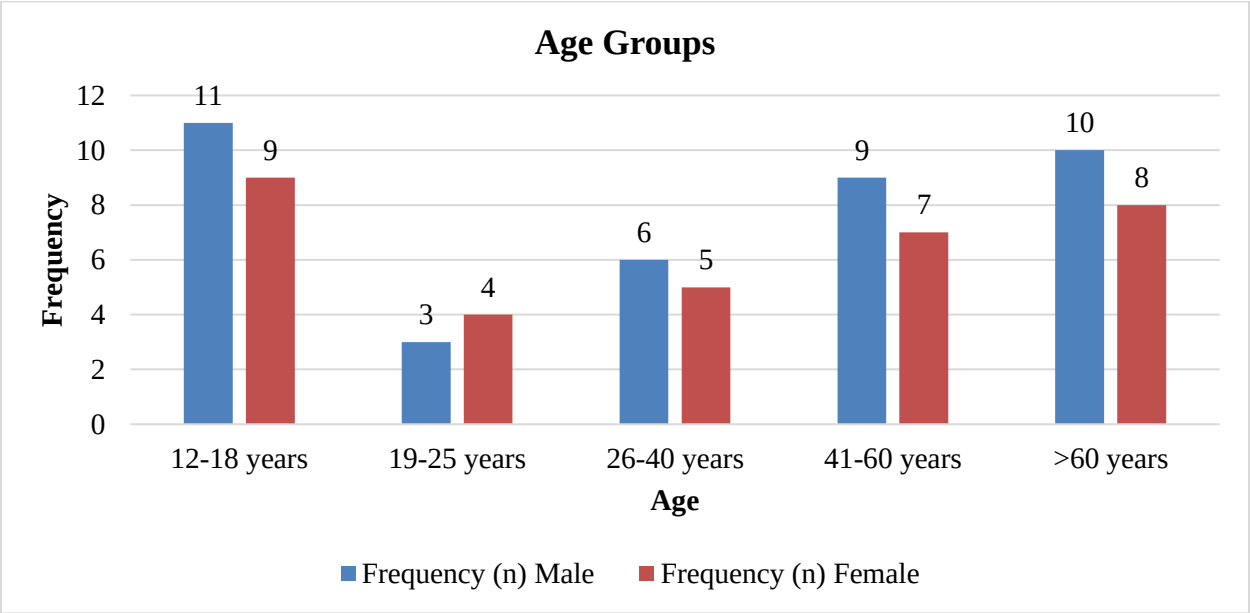
According to the collected data, 72 patients were presented with status asthmaticus in medical emergency of a tertiary care hospital, over the period of 2 years. All the patients were known asthmatics.

During data collection, there was an unremarkable gender discrepancy. However, cases were common at the extremes of the age spectrum, 12-18 years (n=20, 27.7%) and >60 years (n=18, 25%). Asthma and then status asthmaticus was more common in chronic passive (n=59, 81.9%) and active smokers (n=28, 38.9%). The prevalence of such patients was more common in urban areas (n=52, 73%). (Table 1)

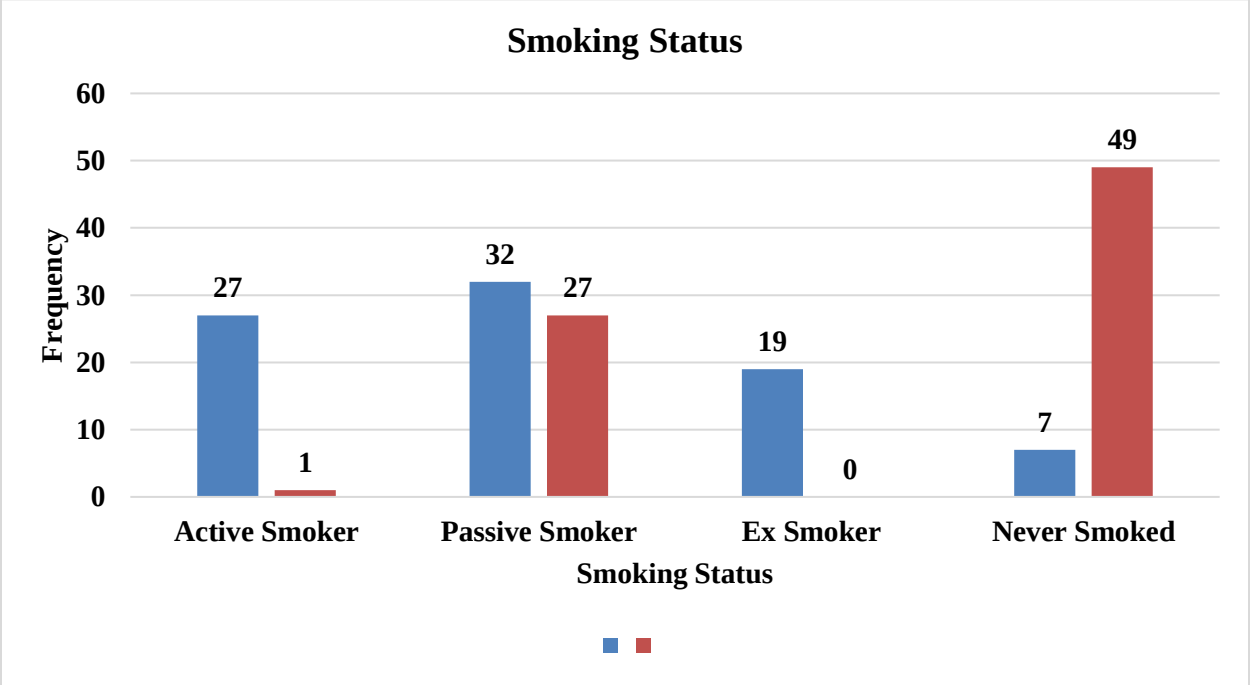
Age	Frequency (n)		Percentage (%)	
	Male	Female	Male	Female
12-18 years	11	9	15%	13%
19-25 years	3	4	4%	6%
26-40 years	6	5	8%	7%
41-60 years	9	7	13%	10%
>60 years	10	8	14%	11%
Total	39	33	54%	46%

Smoking Status				
Active Smoker	27	1	38%	1%
Passive Smoker	32	27	44%	38%
Ex Smoker	19	0	26%	0%
Never Smoked	7	49	10%	68%
Residence				
Rural	12	8	17%	11%
Urban	27	25	38%	35%

Table 1. Patient's demographic data including age, smoking status and residence.



Graph 1. Showing frequency of males and females segregated based on their ages.



Graph 2. Smoking status based on the personal history of asthmatic patients.

Patients were assessed based on their past medical history, clinical examination, and functional assessment. At presentation, the most common signs were dyspnoea/tachycardia (n=69, 96%), irritability/confusion/altered sensorium (n=66, 92%), use of accessory muscles (n=63, 88%), cyanosis (21%), and exhaustion/bradycardia (26%). On clinical examination, most of the patients had decreased air entry to bilateral lungs (69%) while some had silent chest and imminent respiratory failure (31%). The results of functional assessment are summarized in table 2. (p-value of less than 0.05 is considered significant). Table 2

Functional Assessment	Mean±SD	p-value
FVC%	53.8±11.2	0.005
FEV1%	33.2±7.3	0.001
PEFR%	25.5±8.5	0.05
FEF%	16.9±10.2	0.01
PEF	<48% of predicted value	0.02
PaO2	<55 mmHg	0.003
PaCO2	>41 mmHg	0.004
SaO2	<85%	0.002

Table 2. Functional assessment of patients of status asthmaticus.

All patients with status asthmaticus developed moderate to severe electrolyte imbalance and metabolic disturbances at early stages. Based on samples collected in emergency, hypokalemia, hypocalcemia, hypomagnesemia, hypophosphatemia, and hyponatremia were noticed with significant p-value. The results are summarized in table 3.

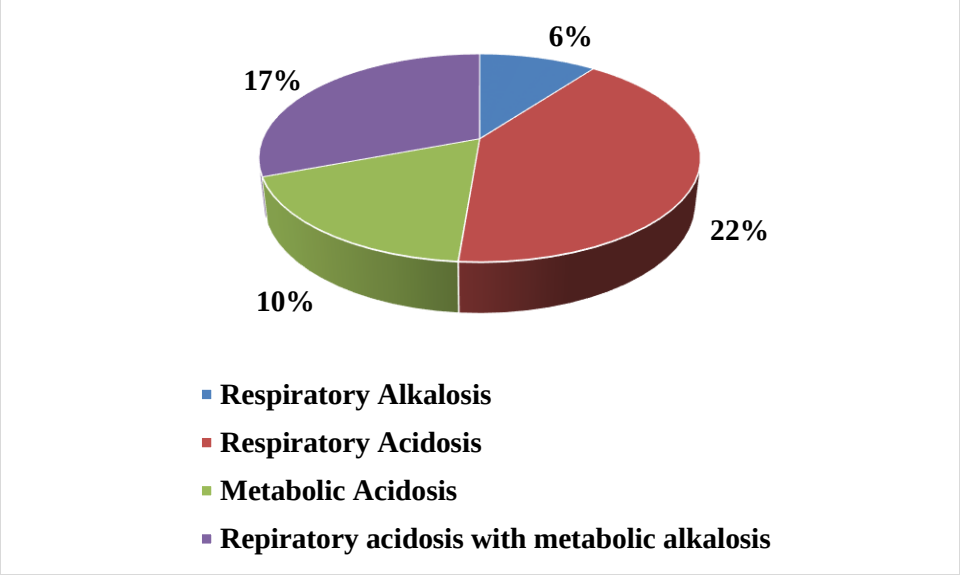
Serum Electrolytes	Mean±SD	p-value
Magnesium	1.11±0.74	0.02
Sodium	138.84±2.46	0.7
Potassium	3.21±0.56	0.001
Phosphate	0.72±1.3	0.02
Calcium	1.02±0.2	0.004

Table 3. Summary of Electrolyte Imbalances in selected patients

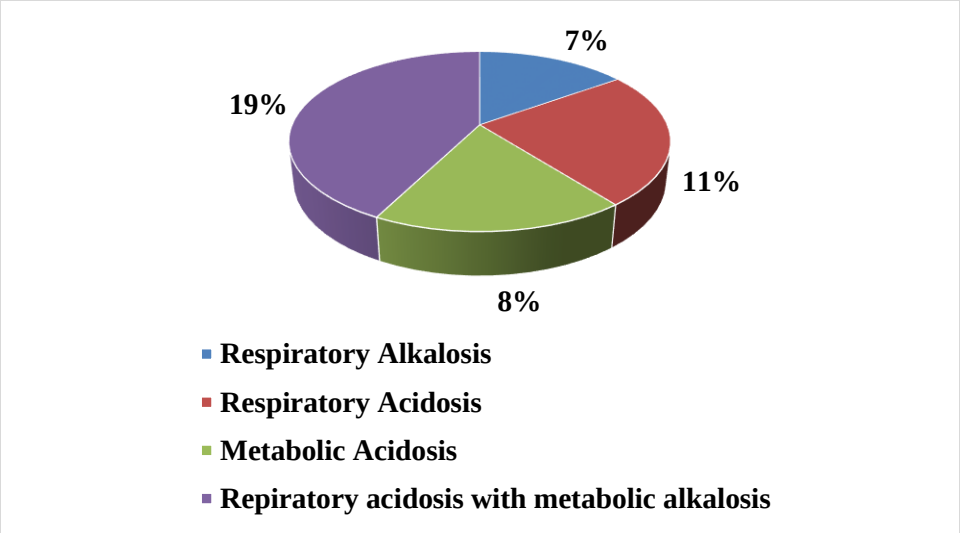
Among metabolic disturbances, respiratory acidosis with metabolic alkalosis was the most common one associated with difficult management and poor prognosis. (Table 4)

Metabolic Disturbances	Frequency (n)		Percentage (%)	
	Male	Female	Male	Female
Respiratory Alkalosis	4	5	6%	7%
Respiratory Acidosis	16	8	22%	11%
Metabolic Acidosis	7	6	10%	8%
Respiratory acidosis with metabolic alkalosis	12	14	17%	19%

Table 4. Spectrum of metabolic disturbances in status asthmaticus patients



Graph 3. Metabolic disturbances in males



Graph 4. Metabolic disturbances in females

The severity of the electrolyte disturbance was measured by the number of electrolytes that need to be corrected additional to the standard treatment. Most of the patients developed more than 3 electrolyte disturbances that needed prompt attention in order to improve patient's prognosis (n=27, 38%). Hypokalemia was found to be the most common electrolyte imbalance with significant p-value (mean±SD= 3.21±0.56, p-value 0.001). The rest of the findings are encapsulated in Table 5.

Number of Electrolyte Disturbances	Frequency	Percentage
1	9	13%
2	11	15%
3	25	35%
>3	27	38%

Table 5. Summary of the Electrolyte Imbalances observed in study subjects (n=72)

DISCUSSION:

Status asthmaticus is an acute, severe asthma exacerbation that remains unresponsive to first-line treatment with bronchodilators. [1,2] It represents a true medical emergency that can potentially lead to hypoxemia, hypercarbia, and even death if not treated promptly. [3] Our study included a total of 72 patients, with a near-equal gender distribution. Most of the patients had poor control of their asthma symptoms. In this study, the prevalence of electrolyte disturbances and metabolic upsets were recorded that needed urgent medical attention to improve the clinical condition and overall prognosis. [4-6]

The results of this study showed that there was a significant prevalence of hypokalemia (>70%) and hypomagnesemia (65%) in patients with status asthmaticus. [7] Hypokalemia is almost always first to develop among all other electrolyte disturbances and has been previously described in severe asthma exacerbations, attributed to the intracellular shift of potassium ions due to β2-adrenergic stimulation from administered bronchodilators. Even in the stable patients of chronic asthma, hypokalemia is a common finding. [8] Hypomagnesemia, however, has not been well documented in the existing literature in this context. Yet, considering the crucial role of magnesium as a natural calcium antagonist, its deficiency might contribute to bronchial smooth muscle contraction and hyperresponsiveness. These electrolyte disturbances result in persistent symptoms, refractory to the anti-asthmatic medication, resulting in hospitalization, increased morbidity, and mortality. [9-11]

Previous studies showed that intravenous aminophylline causes additional hypomagnesemia by increasing its urinary secretion. [12] This in turn can irritate the pulmonary lining and aggravate the severity of the acute episode of asthma. In current studies where patients were treated with intravenous aminophylline without intravenous magnesium sulphate, magnesium level monitoring is of prime importance. [13] Hypophosphatemia is another electrolyte abnormality frequently associated with IV aminophylline, corticosteroids, and IV beta2 agonists. [14] These anti asthmatic drugs cause influx of phosphate from the extracellular to the intracellular spaces resulting in decreased serum phosphate levels that results in cardiac depression, respiratory muscle fatigue, and reduced ventilation, exacerbating the effects of acute asthmatic attack. According to our studies, high number (>20%) of the patients developed hypophosphatemia. [15-17] Hyperlactatemia was also commonly observed among patients, causing metabolic acidosis. [18] The elevation of lactate levels in severe asthma is often attributed to β2-adrenergic stimulation, leading to increased anaerobic glycolysis. This could potentially mislead clinicians to suspect a diagnosis of sepsis or tissue hypoperfusion, hence, the importance of recognizing this biochemical alteration in the context of status asthmaticus. [19-21] Moreover, we noted a common trend of metabolic acidosis paired with respiratory alkalosis in these patients. The primary mechanism is thought to be due to increased lactate levels (lactic acidosis) and hyperventilation-induced respiratory alkalosis partially compensating for this acid-base disturbance. However, in the case of respiratory failure, patient goes into bradypnea and hypoventilation results in uncompensated respiratory acidosis with potentially fatal consequences.

CONCLUSION:

The findings of this observational study provide critical insights into the complex interplay of electrolyte imbalances and metabolic disturbances in status asthmaticus. Our study provides a valuable contribution to the understanding of biochemical alterations that can occur in status asthmaticus. Recognizing serum electrolyte imbalances and metabolic disturbances in these patients can aid in comprehensive patient management and monitoring. The prevalent incidence of hypokalemia, hypomagnesemia, hyperlactatemia, and metabolic acidosis underscores the importance of vigilance and proactive management of these disturbances in this patient population.

Early identification and appropriate correction of these disturbances could potentially mitigate the severity of status asthmaticus and prevent further complications. Additionally, understanding these biochemical alterations can guide clinicians in formulating personalized treatment plans and predicting patient outcomes.

However, it is pertinent to note that this study's findings need to be interpreted within the constraints of its design. As a single-center study, the applicability of the results may be limited by regional variations. Moreover, the study design was observational, which may introduce confounding factors. Therefore, multicenter prospective studies are required to substantiate these findings further. Nonetheless, our study underscores the importance of comprehensive biochemical assessment in status asthmaticus, offering a foundation for future research in this critical area.

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