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Original Article

CLINICAL SPECTRUM, ECG FINDINGS, AND OUTCOMES OF AMINOPHYLLINE TOXICITY IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Background: Aminophylline is a bronchodilator with a narrow therapeutic range and a risk of toxicity, which may cause gastrointestinal, neurological, and cardiovascular complications.

Objective To determine the clinical spectrum, ECG findings, and outcomes of aminophylline toxicity in patients admitted to a tertiary care hospital in Peshawar.

Methodology: A retrospective observational study was conducted from May 2024 to November 2024 among patients with documented aminophylline exposure and features of toxicity. Data regarding demographics, clinical manifestations, aminophylline use, ECG findings, comorbidities, management, and outcomes were collected from medical records. Descriptive statistics, Chi-square tests, and analysis of potential confounding variables were performed. A p-value <0.05 was considered statistically significant.

Results: A total of 246 patients were included, with 126(51.2%) males and 120(48.8%) females. The mean age was 53.41±15.21 years. COPD exacerbation was present in 159(64.6%) patients and asthma exacerbation in 87(35.4%) patients. Mild, moderate, and severe toxicity occurred in 144(58.5%), 77(31.3%), and 25(10.2%) patients, respectively. Sinus tachycardia was the most frequent ECG abnormality, observed in 132(53.7%) patients, while normal sinus rhythm was recorded in 114(46.3%) patients. ICU admission occurred in 32(13.0%) patients and mortality in 1(0.4%) patient. Toxicity severity was significantly associated with ICU admission (χ^2=186.130, p<0.001), and sinus tachycardia was also associated with ICU admission (χ^2=12.570, p<0.001). COPD (p=0.471), chronic kidney disease (p=1.000), drug interaction risk (p=0.154), and polypharmacy (p=0.657) were not significant confounders.

Conclusion: Aminophylline toxicity presents with diverse clinical features, and ECG abnormalities, particularly sinus tachycardia, may indicate the need for closer monitoring. Early recognition of toxicity severity and appropriate management may improve outcomes in patients receiving aminophylline.

Keywords: Aminophylline; Drug Toxicity; Electrocardiography; Bronchodilator Agents; Adverse Drug Reaction

INTRODUCTION

Aminophylline is a methylxanthine drug that contains theophylline and acts as a bronchodilator. It has been used for many years to treat asthma, chronic obstructive pulmonary disease and other breathing problems [1]. The drug has a narrow therapeutic window, with a target blood level of 10 to 20 mg/L, and levels above 20 mg/L can cause adverse effects [2]. Toxicity from aminophylline can affect the stomach, the heart, the nervous system and the metabolism [3].

Theophylline works by blocking adenosine receptors and by raising the level of certain cell messengers, which helps the airways to open, but the same actions also cause harm such as tachycardia, cardiac arrhythmias and seizures [4]. Because of this danger, the drug is no longer a preferred treatment in many countries, yet it remains widely used in low- and middle-income countries, where most people with asthma live [5]. In these settings inhaled medicines are often too expensive or simply unavailable, so many patients rely on oral salbutamol, theophylline or prednisolone instead [6]. Some experts even recommend oral theophylline as a preventer for asthma when resources are scarce [7].

Aminophylline is also given as a second-line drug in hospital for severe asthma attacks when the first treatments fail [8]. Asthma affects more than 250 million people worldwide and is responsible for over 1,000 deaths each day [9]. Even so, guidance from the United Kingdom states that intravenous aminophylline is unlikely to give extra bronchodilation in adults with acute asthma compared with inhaled bronchodilators and steroids [10]. In practice, however, aminophylline injections are still given in many emergency departments.

The safety of aminophylline remains a real concern. A meta-analysis compared aminophylline with doxofylline in bronchial asthma and found that aminophylline was linked with significantly more adverse events [11]. Other medicines can add to the risk. Ciprofloxacin, for example, reduced theophylline clearance by 19 to 32 per cent, and patients taking both drugs had nearly twice the risk of hospital admission for theophylline toxicity [12]. Herbal products that affect the liver enzyme CYP1A2 can also raise or lower theophylline levels in the blood [13].

The clinical picture of aminophylline toxicity is wide. A hospital study from Iran found that vomiting, nausea, sinus tachycardia, hyperglycaemia and respiratory alkalosis were the most common symptoms, with hyperglycaemia seen in 47.1 per cent of patients [14]. In another study from Egypt, 366 patients with acute methylxanthine intoxication were reviewed, and life-threatening events occurred in 16.1 per cent of them, with T-wave inversion the most frequent serious arrhythmia [15]. A report from French intensive care units described metabolic acidosis in 80 per cent of patients and low potassium levels in 60 per cent, with a median theophylline level of 40 mg/L, and warned that poisoning can be fatal above 100 mg/L [16].

Cardiac problems deserve special attention in this condition. A case report described symptomatic supraventricular tachycardia that did not respond to adenosine in a patient on chronic theophylline treatment [17]. Another report linked aminophylline with rapid atrial fibrillation in a patient who came to the emergency department with palpitations [18]. Heart biomarkers may also help predict the outcome, since a study from Egypt concluded that troponin I could predict the severity of theophylline toxicity, as well as the need for intensive care admission and haemodialysis [19].

Severe toxicity requires urgent and careful management. Treatment focuses on stabilising the heart and lungs, correcting metabolic problems, controlling seizures and removing the drug from the body [20]. Multi-dose activated charcoal is recommended in severe poisoning, together with fluids and supportive care [20]. In life-threatening cases, kidney replacement therapy is used. In one reported case, an 85-year-old woman with status epilepticus and a theophylline level of 119.8 mg/L recovered after continuous haemodiafiltration [21].

Acute poisoning is common in Pakistan. A study at a hospital in Abbottabad found that medicinal poisoning was the most frequent type of poisoning among patients coming to the emergency department [22]. Another study in Bahawalpur recorded 2261 poisoning cases in a single year, with 72% being male and most patients between 21 and 40 years old [23].

Despite this heavy burden, drug safety systems remain weak, although research in Lahore and Karachi found that health workers have good general knowledge of adverse drug reaction reporting, reporting rates remain very low and the systems are underdeveloped [24], [25].

Aminophylline and theophylline are widely prescribed in Pakistan, but recent local studies on their toxicity remain scarce. Most of the available evidence comes from other countries and may not reflect local prescribing habits, where blood level monitoring is rarely available. Understanding this problem in a local tertiary care setting can help doctors recognise toxicity earlier and treat it more effectively. The objective of this study was to determine the clinical spectrum, electrocardiographic findings and outcomes of aminophylline toxicity in patients presenting to a tertiary care hospital in Peshawar.

METHODS

Study design

A retrospective observational study was conducted to evaluate the clinical spectrum, electrocardiographic findings, and outcomes of aminophylline toxicity among patients admitted to a tertiary care hospital in Peshawar. The study was based on the review of existing medical records of patients who had received aminophylline and developed features suggestive of toxicity. No intervention was performed, and patients were not exposed to any additional risk during the study period.

Study setting and duration

The study was conducted in the Department of Medicine of a tertiary care hospital located in Peshawar, Khyber Pakhtunkhwa, Pakistan. The hospital served as a referral centre for patients from Peshawar and surrounding districts and provided emergency and inpatient care for respiratory and medical conditions. Data were collected from patient records between May 2024 and November 2024. The study included records of patients who fulfilled the predefined eligibility criteria during this period.

Study population

The study population consisted of adult patients who had received aminophylline therapy during hospital admission and developed clinical features or laboratory findings consistent with aminophylline toxicity. Patient records were reviewed from hospital admission files, emergency department records, medication charts, ECG reports, laboratory investigations, and discharge summaries.

Sample size calculation

The sample size was calculated using the WHO recommended formula for prevalence studies, the standard normal value at a 95% confidence interval (1.96), p represented the expected prevalence of aminophylline toxicity, and d represented the margin of error. A previous clinical study reported cardiac adverse effects among patients receiving intravenous aminophylline, with arrhythmias observed in approximately 20% of treated patients. This prevalence value was considered for sample estimation. Using an estimated prevalence of 20%,[26] a 5% margin of error, and a 95% confidence level, the minimum calculated sample size was approximately 246 patients.

Sampling technique

A non-probability consecutive sampling technique was used. All available patient records from May 2024 to November 2024 that fulfilled the inclusion criteria were reviewed and included in the study. Every eligible case during the study period was considered to reduce selection bias.

Inclusion criteria

Patients were included if they were adults aged 18 years or above, had received aminophylline therapy during hospital admission, and had documented clinical features, ECG abnormalities, or laboratory findings suggestive of aminophylline toxicity. Patients were included regardless of the route of administration if adequate information regarding drug exposure and clinical outcomes was available in the medical record.

Exclusion criteria

Patients were excluded if their medical records were incomplete, if aminophylline exposure could not be confirmed, if ECG reports were unavailable, or if the observed symptoms were clearly explained by another medical condition without evidence of possible aminophylline involvement. Patients with incomplete outcome documentation were also excluded from final analysis.

Randomization and blinding

Randomization was not performed because the study was retrospective in design. No treatment allocation was involved. Data extraction was performed from existing records, and patient identifiers were removed before analysis to maintain confidentiality. Blinding was not applicable for this study.

Data collection procedure

Data were collected using a structured data collection form developed according to the study objectives. The required information was obtained from hospital records, including demographic characteristics, clinical history, indication for aminophylline use, dose and duration of therapy, presenting symptoms, physical examination findings, ECG changes, laboratory investigations, management strategies, and clinical outcomes.

The collected clinical information included symptoms such as nausea, vomiting, abdominal discomfort, tremors, agitation, seizures, palpitations, hypotension, and altered mental status. ECG findings were reviewed for abnormalities including sinus tachycardia, atrial arrhythmias, ventricular ectopic beats, conduction abnormalities, and other rhythm disturbances. Patient outcomes were assessed according to recovery, complications, intensive care admission, and mortality.

Assessment criteria and operational definitions

Aminophylline toxicity was defined as the development of clinical symptoms or cardiovascular abnormalities occurring after aminophylline administration and considered related to excessive drug effect. Toxicity was assessed through documented clinical findings, ECG changes, and available serum theophylline or aminophylline concentration levels when performed.

Clinical severity was assessed according to the presence of mild, moderate, or severe manifestations. Mild toxicity included gastrointestinal symptoms and mild neurological complaints. Moderate toxicity included significant tachycardia, persistent vomiting, agitation, or marked electrolyte abnormalities. Severe toxicity included seizures, serious arrhythmias, haemodynamic instability, intensive care admission, or death.

ECG abnormalities were defined as any newly documented rhythm or conduction abnormality occurring after aminophylline exposure. Treatment outcomes were classified as improved clinical condition, development of complications, prolonged hospital stay, or death.

Medication assessment

Information regarding aminophylline administration was recorded, including dose, route of administration, duration of therapy, and concurrent medications. Other drugs that could potentially influence aminophylline metabolism or increase toxicity risk were also documented when available. Supportive treatments provided during management of toxicity, including antiarrhythmic therapy, electrolyte correction, oxygen therapy, or intensive monitoring, were recorded from patient files.

Data management and handling of missing data

All collected data were checked for completeness before statistical analysis. Missing information identified in patient records was documented, and cases with critical missing variables were excluded when accurate assessment was not possible. For variables with limited missing information, available case analysis was performed, and missing values were not replaced or estimated. The number of missing observations for important variables was

recorded and reported during data analysis to maintain transparency.

Statistical analysis

The collected data were analysed using SPSS version 23. Continuous variables were presented as mean and standard deviation or median with interquartile range depending on data distribution. Categorical variables were presented as frequencies and percentages.

The normality of continuous variables was assessed using the Shapiro-Wilk test. The Chi-square test or Fisher's exact test was applied to evaluate associations between categorical variables, including ECG findings and clinical outcomes. Independent sample t-test or Mann-Whitney U test was applied for comparison of continuous variables where appropriate. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The final analysis included 246 patients who fulfilled the eligibility criteria during the study period from May 2024 to November 2024. All patients were included according to the predefined retrospective study methodology. The demographic characteristics showed that 126(51.2%) patients were male and 120(48.8%) were female. The mean age of the study population was 53.41±15.21 years. The demographic distribution is presented in Table 1.

Table 1. Demographic and baseline characteristics of study participants

Variable	Frequency (%)
Male	126(51.2%)
Female	120(48.8%)
COPD exacerbation	159(64.6%)
Asthma exacerbation	87(35.4%)

Most patients were admitted with COPD exacerbation 159(64.6%), while 87(35.4%) patients were admitted with acute asthma exacerbation. Intravenous aminophylline was used in 190(77.2%) patients, whereas oral therapy was documented in 56(22.8%) patients. The mean aminophylline dose was 602.35±118.42 mg/day and the mean duration of therapy was 4.12±2.06 days.

The clinical spectrum of toxicity showed that mild toxicity was observed in 144(58.5%) patients, moderate toxicity in 77(31.3%) patients, and severe toxicity in 25(10.2%) patients. The distribution of toxicity severity is shown in Figure 1. Gastrointestinal symptoms were common, while seizures and altered mental status were mainly observed among patients with severe toxicity.

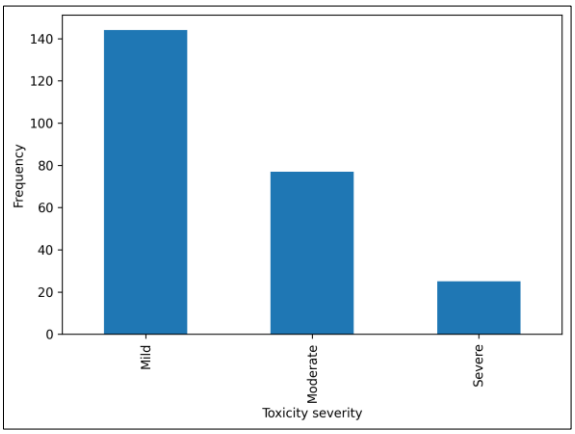

Figure 1. Distribution of aminophylline toxicity severity

Electrocardiographic assessment demonstrated that sinus tachycardia was the most frequent ECG abnormality, occurring in 132(53.7%) patients. Normal sinus rhythm was observed in 114(46.3%) patients. Ventricular tachycardia was uncommon and was recorded in 3(1.2%) patients. The ECG distribution is presented in Figure 2.

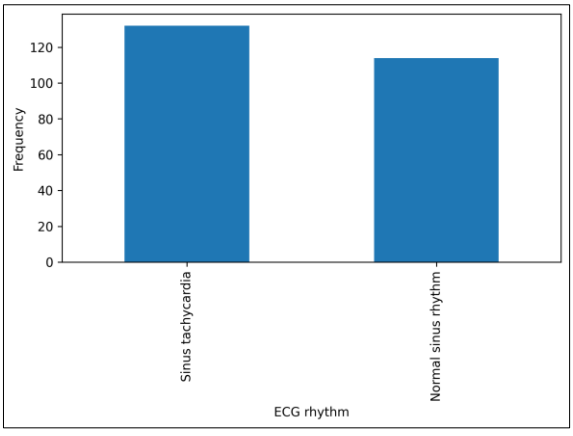

Figure 2. Distribution of ECG rhythm findings

The association between toxicity severity and clinical outcomes was statistically significant. Patients with severe toxicity had higher ICU admission rates compared with patients with mild and moderate toxicity (χ^2=186.130, p<0.001). This finding indicated that increasing toxicity severity was associated with greater need for intensive monitoring and supportive care.

Sinus tachycardia was significantly associated with ICU admission (χ^2=12.570, p<0.001). This suggested that early ECG abnormalities may help identify patients requiring closer observation. The association between major clinical variables, ECG findings, and outcomes is presented in Table 2.

Table 2. Association of toxicity severity and ECG findings with ICU admission

Variable	χ^2 value	p value
Toxicity severity	186.130	<0.001
Sinus tachycardia	12.570	<0.001

Potential confounding variables were assessed. COPD, chronic kidney disease, polypharmacy, and drug interaction risk did not show statistically significant associations with ICU admission in this dataset. These findings suggested that toxicity severity and ECG changes were stronger indicators of poor clinical course than baseline comorbid conditions. The confounding analysis is shown in Table 3.

Table 3. Confounding variable analysis for ICU admission

Confounder	**χ^2 value**	**p value**
COPD	0.520	0.471
Chronic kidney disease	0.000	1.000
Drug interaction risk	2.030	0.154
Polypharmacy	0.200	0.657

Overall, 214(87.0%) patients recovered without ICU admission, 32(13.0%) patients required ICU care, and 1(0.4%) patient died. The outcome analysis is summarised in Table 4.

Table 4. Clinical outcomes of patients with aminophylline toxicity

Outcome	Frequency (%)
Recovered	245(99.6%)
ICU admission	32(13.0%)
Mechanical ventilation	8(3.3%)
Mortality	1(0.4%)

DISCUSSION

The present study evaluated the clinical manifestations, ECG findings, and outcomes of aminophylline toxicity among 246 patients admitted to a tertiary care hospital in Peshawar between May 2024 and November 2024. Toxicity produced gastrointestinal, cardiovascular, and neurological effects of varying severity. Sinus tachycardia was the most common ECG abnormality, and greater toxicity severity was significantly associated with ICU admission, highlighting the importance of early recognition and continuous monitoring.

This study provides real-world evidence from Pakistan, where aminophylline remains widely used because of its affordability and availability. Despite its narrow therapeutic range, it may cause multisystem toxicity through excessive catecholamine activity and cardiac stimulation. The observed gastrointestinal, cardiovascular, and neurological manifestations were consistent with the recognised toxic effects of methylxanthines.

The clinical severity pattern in this study showed that mild toxicity was the most frequent presentation, occurring in 144(58.5%) patients, followed by moderate toxicity in 77(31.3%) and severe toxicity in 25(10.2%) patients. Similar findings were reported in previous clinical studies where most patients with theophylline toxicity developed mild to moderate symptoms, while a smaller proportion progressed to severe complications requiring intensive management.[27] Sessler et al. evaluated consecutive cases of theophylline toxicity and reported that severe toxicity was associated with higher drug exposure and increased risk of complications, particularly cardiac and

neurological events .[27] The current findings support the observation that although severe toxicity is less common, it represents an important clinical concern due to its potential for rapid deterioration.

The presence of severe toxicity and its association with ICU admission in the present study indicates that toxicity severity can be an important marker of clinical instability. Patients with severe manifestations require closer monitoring because complications may develop quickly. Previous research has shown that chronic theophylline toxicity may be difficult to predict only from symptoms and requires careful assessment of cardiovascular and neurological status.[28] Therefore, early identification of worsening symptoms may improve clinical decision-making and reduce adverse outcomes.

Cardiovascular effects were an important focus of this study because aminophylline toxicity has a well-established relationship with cardiac rhythm abnormalities. Sinus tachycardia was the most common ECG abnormality, observed in 132(53.7%) patients, while normal sinus rhythm was present in 114(46.3%) patients. Previous studies from the United States reported that sinus tachycardia and supraventricular ectopic activity were among the most frequently observed cardiac changes during theophylline toxicity.[4] A study conducted continuous ECG monitoring in patients with theophylline toxicity and found that rhythm disturbances occurred frequently, although life-threatening ventricular arrhythmias were less common .[17] The findings of the current study are consistent with these observations.

The significant association between sinus tachycardia and ICU admission (χ^2=12.570, p<0.001) suggests that ECG abnormalities may provide early warning signs of clinically significant toxicity. In clinical practice, ECG monitoring is a simple and accessible method that may help identify patients requiring closer observation. Previous studies have emphasised that cardiac monitoring is particularly important in patients with high theophylline exposure, older age, or underlying cardiovascular disease (4,5).

Although severe ventricular arrhythmias were uncommon in the present study, they remain a recognised complication of aminophylline toxicity. Previous reports have described atrial tachyarrhythmias, multifocal atrial tachycardia, premature ventricular contractions, and ventricular tachycardia during toxic exposure.[3,29] A study reported aminophylline-associated atrial fibrillation, highlighting that significant rhythm disturbances may occur even when toxicity initially appears mild.[30] The lower frequency of severe arrhythmias in the present study may be related to early recognition, supportive treatment, and differences in patient characteristics compared with older toxicity studies.

The current findings also need to be interpreted within the changing role of aminophylline therapy. In many European and North American guidelines, methylxanthines are used less frequently because inhaled bronchodilators and corticosteroids provide safer alternatives for many patients with obstructive airway disease.[31] However, in resource-limited healthcare settings, aminophylline remains commonly prescribed due to cost considerations and availability. Therefore, understanding its toxicity profile remains clinically relevant, particularly in countries such as Pakistan.

The outcome findings of the present study demonstrated that most patients recovered after discontinuation of aminophylline and supportive management. ICU admission was required in 32(13.0%) patients, while mortality occurred in 1(0.4%) patient. The relatively low mortality observed in this study may reflect early recognition of toxicity, availability of supportive care, and timely monitoring. Previous studies have shown that the outcome of theophylline toxicity depends on several factors, including the amount of drug exposure, duration of toxicity, patient age, and presence of underlying diseases.

Severe toxicity has been associated with seizures, haemodynamic instability, and life-threatening arrhythmias, particularly when diagnosis and treatment are delayed (3,8).

The significant association between toxicity severity and ICU admission in the present study (χ^2=186.130, p<0.001) indicates that increasing toxicity severity is an important predictor of clinical deterioration. This finding is clinically meaningful because it supports the use of severity assessment at the time of presentation. Patients with moderate or severe manifestations may benefit from early cardiac monitoring, repeated clinical assessment, and consideration for intensive care when required. Previous reports have similarly demonstrated that patients with severe theophylline toxicity require aggressive supportive management because complications may progress rapidly.[20]

Comorbid conditions and medication-related factors were also evaluated because they may influence aminophylline metabolism and toxicity risk. In the present study, COPD, chronic kidney disease, drug interaction risk, and polypharmacy were not significantly associated with ICU admission. However, these factors remain clinically relevant because previous studies have identified impaired drug clearance, interacting medications, and chronic illness as important contributors to methylxanthine toxicity.[3] The absence of statistical significance in the current analysis may be related to the sample characteristics, retrospective design, or limited availability of detailed medication and laboratory information.

The role of drug interactions is particularly important in clinical practice. Aminophylline metabolism can be affected by several commonly prescribed medications, including some antibiotics and drugs that alter hepatic enzyme activity. Previous pharmacological studies reported that antibiotics such as erythromycin and certain quinolones may increase serum theophylline concentrations and increase the risk of toxicity.[32] A Pakistani study evaluating potential drug-drug interactions in a tertiary care hospital reported clinically important interactions involving commonly prescribed medicines in hospital practice, highlighting the need for medication review before and during treatment.[33] Therefore, clinicians should consider concurrent medications when prescribing aminophylline, even if initial symptoms appear mild.

The present study provides important information from Pakistan, where evidence regarding aminophylline toxicity remains limited. Most available studies from the United States and Europe were conducted in poison control centres or intensive monitoring settings and focused mainly on theophylline overdose and cardiac complications.[34] In contrast, the current study reflects routine clinical practice in a tertiary care hospital in Peshawar, including patients treated for common respiratory conditions. This setting provides valuable information regarding how aminophylline toxicity presents in everyday hospital care rather than only in severe poisoning cases.

Previous Pakistani studies have mainly evaluated aminophylline use, prescribing patterns, or adverse drug interactions rather than comprehensive toxicity outcomes. A recent study from Khyber Pakhtunkhwa evaluated arrhythmias among patients receiving intravenous aminophylline for respiratory conditions and reported the occurrence of clinically relevant cardiac rhythm abnormalities requiring monitoring.[35] The current study extends local evidence by assessing the relationship between toxicity severity, ECG abnormalities, and patient outcomes. This contribution is important because local prescribing practices and patient characteristics may differ from those reported in Western healthcare systems.

The originality of this study lies in its integrated evaluation of three important clinical components: the clinical spectrum of toxicity, ECG findings, and outcomes among patients

receiving aminophylline in a Pakistani tertiary care hospital. While previous international studies have established the toxic potential of methylxanthines, limited research has examined these factors together in the Pakistani population. The findings provide a local perspective and may support the development of practical monitoring approaches for hospitals where aminophylline continues to be used.

The findings have direct implications for clinical decision-making. Patients receiving aminophylline should be monitored for early symptoms such as nausea, vomiting, palpitations, tremor, and neurological changes. ECG assessment may provide additional information for identifying patients at risk of deterioration, particularly when tachycardia or rhythm abnormalities are present. Careful dose selection, review of concurrent medications, and follow-up after toxicity episodes may reduce preventable complications.

This study has several limitations. First, the retrospective design depended on the accuracy and completeness of available medical records. Some variables, including serum theophylline concentrations, were not available for all patients, limiting direct assessment of concentration-related toxicity. Second, the study was conducted at a single tertiary care hospital, which may limit generalisation of the findings to other regions. Third, although important confounding variables were assessed, residual confounding from disease severity, treatment variation, and unrecorded medication factors cannot be completely excluded.

Future research should include multicentre prospective studies involving hospitals across Pakistan to determine the broader burden of aminophylline toxicity. Routine measurement of serum theophylline levels, detailed pharmacological assessment, and longer follow-up would help identify independent predictors of severe toxicity and poor outcomes. Development of local clinical monitoring protocols may improve the safe use of aminophylline in respiratory patients.

In conclusion, this study demonstrates that aminophylline toxicity remains an important clinical issue in tertiary care practice. The toxicity spectrum ranges from mild gastrointestinal symptoms to severe cardiac and neurological complications. ECG abnormalities, particularly sinus tachycardia, and increasing toxicity severity are important indicators for closer monitoring. Early recognition, appropriate assessment, and careful management may improve outcomes among patients receiving aminophylline.

CONCLUSION

The present study concluded that aminophylline toxicity showed a wide clinical spectrum among patients admitted to a tertiary care hospital in Peshawar. Gastrointestinal, cardiovascular, and neurological manifestations were observed, with sinus tachycardia being the most frequent ECG abnormality. The severity of toxicity was significantly associated with the need for intensive monitoring, indicating that early recognition of clinical symptoms and ECG changes may help identify patients at higher risk of complications.

The study findings demonstrated that careful assessment of patients receiving aminophylline is important, particularly in those with respiratory diseases, multiple medications, and underlying medical conditions. Regular monitoring of cardiac rhythm, clinical symptoms, and possible drug interactions may improve patient safety and reduce the risk of severe outcomes. The study provides local evidence from a Pakistani tertiary care hospital and highlights the importance of developing safer monitoring practices for aminophylline use.

Future studies should include larger multicentre populations from different regions of Pakistan to provide a broader understanding of aminophylline toxicity patterns. Prospective studies with routine measurement of serum theophylline levels and long-term follow-up are

recommended to identify independent predictors of severe toxicity and improve clinical management protocols.

AUTHORS' CONTRIBUTION

AH, AN, and AI conceptualized and designed the study. Data extraction and analysis were performed by AH, AN, and AI. All authors made substantial contributions to the writing and interpretation of the manuscript. AH, AN, and AI supervised the overall process, critically reviewed the manuscript, and provided guidance where necessary. All authors approved the final version of the manuscript for publication.

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