

OUTCOME PREDICTION IN INDIVIDUALS WITH ORGANOPHOSPHORUS AND CARBAMATE POISONING: A PROSPECTIVE COHORT STUDY.

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ABSTRACT

Objective

The study evaluated the predictive utility of Erythrocyte Acetylcholinesterase (E-AChE) and Butyrylcholinesterase (BChE) levels in individuals presenting with OP and carbamate poisoning.

Methods

Of the 60 patients, 42 had Organophosphorus (OP) poisoning, and 18 had Carbamate poisoning in the ER. Vital signs, symptoms, and POP Severity Scale scores were recorded. E-AChE levels were measured using the Rapid ChE Check Mobile, and BChE levels were assessed through standard lab techniques. SPSS was used for statistical analysis, examining correlations between E-AChE levels and outcomes like ICU stay, mechanical ventilation, and mortality.

Results

The study involved 60 patients (mean age 32.5 years, \pm 10.7), 66.7% male and 33.3% female. Of these, 60% consumed OP chemicals and 40% carbamate. Severe poisoning was associated with significantly lower E-AChE levels (mean = 2.1 U/g Hb) compared to moderate (3.5 U/g Hb) and mild cases (5.1 U/g Hb) ($p < 0.001$), showing a strong negative correlation with POP Severity scores ($\rho = -0.76$, $p < 0.001$). Butyrylcholinesterase (BChE) levels also showed a significant decrease in severe poisoning cases, aligning with clinical outcomes, although the correlation was less robust than with E-AChE. Delays in care led to severe consequences in 80% of low-income patients. Lower E-AChE levels correlated with prolonged ICU stays ($r = -0.68$, $p < 0.001$), increased ventilation needs ($r = -0.62$, $p < 0.01$), and higher mortality ($r = -0.74$, $p < 0.001$). Rural patients faced worse outcomes due to inadequate healthcare access.

Conclusion

Although BChE levels were also measured, their correlation with outcomes was less pronounced but still valuable. Incorporating early measurements of both E-AChE and BChE could enhance clinical decision-making in OP and carbamate poisoning cases.

Recommendations

Incorporating rapid diagnostic tools for cholinesterase measurement in emergency settings could improve clinical decision-making and patient outcomes.

Keywords: Organophosphorus Poisoning, Carbamate Poisoning, Erythrocyte Acetylcholinesterase, Butyrylcholinesterase, Prognosis, Emergency Management.

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INTRODUCTION

Organophosphorus (OP) and carbamate poisoning are significant global health concerns, particularly in agricultural regions where these compounds are widely used as pesticides. Acute poisoning by these chemicals remains a common cause of morbidity and mortality, especially in low- and middle-income countries, where pesticide regulation and control measures are often inadequate [1]. OP and carbamates inhibit acetylcholinesterase, leading to an accumulation of acetylcholine at synaptic junctions, causing a cholinergic

crisis characterized by a range of symptoms from miosis, salivation, and bradycardia to severe respiratory failure and death. This cholinergic toxidrome often requires rapid and intensive medical intervention, including the administration of atropine and mechanical ventilation, to counteract the severe effects of poisoning [2].

The management of OP and carbamate poisoning poses significant challenges due to the variability in clinical presentation and the need for rapid diagnosis and treatment. Recent studies emphasize the importance of early and accurate prognostication to guide the clinical

management of these patients. The Peradeniya Organophosphorus Poisoning (POP) Severity Scale has been widely used as a tool to assess the severity of poisoning at presentation, but its predictive accuracy can be variable depending on patient characteristics and the extent of exposure [3]. Biomarkers, such as erythrocyte acetylcholinesterase (E-AChE) and plasma butyrylcholinesterase (BChE) levels, have emerged as potential prognostic indicators, offering objective measures to assess the severity of poisoning and guide therapeutic decisions [4].

Despite advances in the management of OP and carbamate poisoning, there is still a lack of consensus regarding the most reliable prognostic markers that can be used in routine clinical settings. E-AChE levels, in particular, have shown a strong correlation with clinical outcomes in several studies, suggesting that they could be a valuable tool for risk stratification [5]. However, the availability and use of rapid testing methods, such as the Rapid ChE Check Mobile, are still limited in many healthcare settings, particularly in resource-constrained environments [6]. Moreover, the relationship between cholinesterase levels, clinical presentation, and patient outcomes remains under-explored in many contexts.

This study aims to evaluate the predictive utility of E-AChE and BChE levels in patients presenting with OP and carbamate poisoning.

METHODOLOGY

Study Design

A prospective cohort design.

Study Setting

The study took place at the Rajendra Institute of Medical Sciences (RIMS) in Ranchi, India, over 11 months from September 2023 to August 2024.

Participants

The study included 60 adult patients. Participants were adults aged 18 years or older who presented to the Emergency Room (ER) with symptoms of cholinergic toxidrome or confirmed ingestion of organophosphorus (OP) or carbamate within 24 hours, as evidenced by the presence of a chemical bottle or its photograph from the scene.

Inclusion Criteria

Adults aged 18 years and above presenting to the ER with clinical signs of cholinergic toxidrome or evidence of OP or carbamate poisoning within 24 hours of ingestion were included.

Exclusion Criteria

Patients excluded from the study were those who were brought in dead due to OP or carbamate poisoning, cases of unknown poisoning without typical cholinergic signs, and pregnant women.

Sample Size

Given the lack of larger studies correlating erythrocyte acetylcholinesterase (E-AChE) levels with the severity of poisoning or atropine requirements, the study included all eligible cases of OP or carbamate poisoning during the study period.

Bias

To reduce bias, the E-AChE results were kept confidential from ER physicians, ensuring that patient management was not influenced by these data.

Variables

The study documented demographic information, baseline characteristics, details of the ingested substance, medical history, clinical signs, and symptoms, time between ingestion and ER presentation, E-AChE levels (units per gram hemoglobin), plasma butyrylcholinesterase (BChE) levels (units per liter), and laboratory findings. Additional variables included atropine toxicity, the occurrence of intermediate syndrome, duration of hospitalization, mechanical ventilation needs, use of inotropes, HDU or ICU stay duration, concurrent illnesses, and patient outcomes.

Data Collection and Procedure

E-AChE levels were assessed using the Rapid ChE Check Mobile, while plasma BChE levels were assessed using conventional laboratory methods. Blood samples were collected in EDTA tubes (2 mL), and E-AChE estimation was conducted using a modified Ellman method, providing results within 5 minutes. To avoid influencing clinical decisions, E-AChE results were not shared with ER physicians. Management in the ER adhered to established clinical guidelines, with atropine administered based on the physician's assessment. Atropine toxicity and the need for physical or chemical restraints were monitored using the Confusion Assessment Method (CAM).

Statistical Analysis

Data were entered into Excel and analyzed with SPSS 22.0. Descriptive statistics summarised demographic and clinical data. Spearman's correlation analyzed associations between ranked variables, and ANOVA compared group means. Statistical significance required a p-value below 0.05.

Ethical considerations

The study protocol was approved by the Ethics Committee and written informed consent was received from all the participants.

RESULTS

The average age was 32.5 years (± 10.7), with a male-to-female ratio of 2:1. The mean systolic blood pressure was 98.6 mmHg (± 15.2), and the average diastolic blood

pressure was 64.3 mmHg (\pm 10.5). The average heart rate was 82.4 beats per minute (\pm 14.8), while the average respiratory rate was 20.3 breaths per minute (\pm 5.2). Pupillary constriction (miosis) was observed in 78.3% of

the cases, and 55% of patients exhibited excessive salivation. The POP Severity Scale revealed that 40% of individuals had mild poisoning, 35% had moderate poisoning, and 25% had severe poisoning.

Table 1: POP Severity Scale and Vital Signs/Symptoms at Emergency Room Presentation

Parameter	Value
Mean Age (years)	32.5 \pm 10.7
Gender	
- Male	66.7%
- Female	33.3%
Mean Systolic Blood Pressure (mmHg)	98.6 \pm 15.2
Mean Diastolic Blood Pressure (mmHg)	64.3 \pm 10.5
Mean Heart Rate (beats per minute)	82.4 \pm 14.8
Mean Respiratory Rate (breaths per min)	20.3 \pm 5.2
Pupillary Constriction (Miosis)	78.3%
Excessive Salivation	55.0%
POP Severity Scale	
- Mild	40%
- Moderate	35%
- Severe	25%

The toxicants ingested were identified in all cases, with the majority (70%) ingesting organophosphorus compounds, while the remaining 30% had ingested carbamate compounds. Toxidromes were assessed, with 83.3% of the patients exhibiting cholinergic toxidrome and the remainder displaying a mixed toxidrome. Among those with cholinergic toxidrome, 45% presented with bradycardia, and 60% had bronchorrhea.

Participants' follow-ups varied based on clinical severity. While most were followed until hospital discharge, the average length of stay in the ICU for those admitted was 6.8 days (\pm 3.2 days). Some patients required prolonged hospitalization, while five patients (8.3%) died during the study.

Table 2: Patients' Ingested Toxicants and Toxidrome When They Visit the Emergency Department

Ingested Toxicant	Patients (N = 60)	Cholinergic Toxidrome	Mixed Toxidrome
Organophosphorus Compounds	42 (70%)	35 (83.3%)	7 (16.7%)
Carbamate Compounds	18 (30%)	15 (83.3%)	3 (16.7%)
Bradycardia (within Cholinergic)	-	27 (45%)	-
Bronchorrhea (within Cholinergic)	-	36 (60%)	-

All patients received immediate medical attention upon ER presentation, with atropine being the primary treatment administered. The mean dose of atropine required for initial stabilization was 32.5 mg (\pm 18.7 mg). Mechanical ventilation was necessary for 28.3% of the patients, and 35% required ICU admission. The mean ICU stay was 6.8 days (\pm 3.2 days). Complications included atropine toxicity in 18.3% of cases, intermediate

syndrome in 10%, and acute renal failure in 6.7%. The overall hospital mortality rate was 8.3%.

The primary outcome measures were ICU stay duration, mechanical ventilation requirements, and mortality. Throughout the study, 28.3% of patients required mechanical ventilation, 35% were admitted to the ICU, and 8.3% died. Lower E-AChE and BChE levels were associated with worse outcomes, including prolonged ICU stays and increased mortality.

Table 3: Managing Individuals in the Emergency Department and Hospital Results

Management/Outcome Parameter	Value
Mean Atropine Dose for Stabilization (mg)	32.5 (± 18.7)
Mechanical Ventilation Required	17 (28.3%)
ICU Admission	21 (35.0%)
Mean ICU Stay (days)	6.8 (± 3.2)
Atropine Toxicity	11 (18.3%)
Intermediate Syndrome	6 (10.0%)
Acute Renal Failure	4 (6.7%)
Hospital Mortality	5 (8.3%)

The RBC cholinesterase (E-AChE) levels were measured upon presentation, and their correlation with patient prognosis was assessed. Patients with severe poisoning had significantly lower E-AChE levels (mean = 2.1 U/g Hb, ± 0.5) compared to those with moderate (mean = 3.5 U/g Hb, ± 0.6) and mild poisoning (mean = 5.1 U/g Hb, ± 0.7) ($p < 0.001$). A strong negative correlation was found

between E-AChE levels and the POP Severity Scale score (Spearman's rho = -0.76, $p < 0.001$). Additionally, lower E-AChE levels were significantly related to longer ICU stays ($r = -0.68$, $p < 0.001$), higher mechanical ventilation requirements ($r = -0.62$, $p < 0.01$), and increased mortality ($r = -0.74$, $p < 0.001$).

Table 4: Relationship Between Prognosis and RBC Cholinesterase (E-AChE) Levels

Prognosis Parameter	Mean E-AChE (U/g Hb)	Correlation (Spearman's rho)	p-value
Mild Poisoning	5.1 (± 0.7)	-0.76	<0.001
Moderate Poisoning	3.5 (± 0.6)		
Severe Poisoning	2.1 (± 0.5)		
ICU Stay	6.8 (± 3.2)	-0.68	<0.001
Mechanical Ventilation Requirement	-	-0.62	<0.01
Hospital Mortality	-	-0.74	<0.001

While the study primarily emphasized the prognostic utility of E-AChE, BChE levels were also measured to assess their correlation with patient outcomes. A significant relationship was found between BChE levels and the severity of poisoning. Patients with lower BChE levels (mean BChE < 2000 U/L) experienced more severe clinical outcomes, including:

- Prolonged ICU stay: A significant correlation was observed between lower BChE levels and longer ICU stays ($r = -0.45$, $p < 0.01$).
- Mechanical ventilation: The need for mechanical ventilation increased with decreasing BChE levels ($r = -0.52$, $p < 0.01$).
- Mortality: Mortality rates were higher in patients with significantly reduced BChE levels (mean BChE in deceased patients = 1500 U/L, compared to survivors = 3200 U/L, $p < 0.001$).

DISCUSSION

The study evaluated 60 adult patients with organophosphorus and carbamate poisoning, presenting with various degrees of severity as assessed by the POP Severity Scale. The mean age was 32.5 years, with a predominance of male patients (66.7%). Key symptoms at presentation included pupillary constriction (78.3%) and excessive salivation (55.0%). Vital signs such as blood pressure, heart rate, and respiratory rate were recorded, showing variations consistent with the severity of poisoning. The POP Severity Scale categorized 40% of

patients as having mild poisoning, 35% as moderate, and 25% as severe. These findings suggest that a significant proportion of patients presented with life-threatening symptoms, emphasizing the need for prompt medical intervention.

The toxicants ingested were predominantly organophosphorus compounds (70%), with carbamates accounting for the remaining 30%. Most patients (83.3%) exhibited cholinergic toxidrome, characterized by symptoms such as bradycardia and bronchorrhea, highlighting the classic presentation of poisoning with these substances. A smaller proportion of patients presented with a mixed toxidrome, indicating the potential for varied clinical manifestations depending on the toxicant involved. The identification of specific toxidromes underscores the importance of targeted clinical assessment to guide appropriate treatment.

Management in the emergency room primarily involved atropine administration, with an average dose of 32.5 mg required for initial stabilization. Mechanical ventilation was necessary for 28.3% of patients, and 35% required admission to the ICU, with an average stay of 6.8 days. Complications observed included atropine toxicity (18.3%), intermediate syndrome (10%), and acute renal failure (6.7%). The overall hospital mortality rate was 8.3%, indicating the serious nature of these poisonings and the potential for fatal outcomes despite aggressive management. These findings highlight the critical role of

early intervention and intensive care in improving patient outcomes.

A key finding of the study was the strong negative correlation between RBC cholinesterase (E-AChE) levels and the severity of poisoning, length of ICU stay, need for mechanical ventilation, and mortality. Patients with severe poisoning had significantly lower E-AChE levels compared to those with moderate or mild poisoning. The correlation analysis showed that lower E-AChE levels were strongly associated with poorer outcomes, including longer ICU stays and higher mortality rates (Spearman's $\rho = -0.76$, $p < 0.001$). This data suggests that E-AChE levels can serve as a valuable prognostic marker in the management of organophosphorus and carbamate poisoning, aiding in the stratification of patients according to their risk of adverse outcomes.

The study confirms that E-AChE levels are a robust marker for predicting the severity of OP and carbamate poisoning. Patients with lower E-AChE levels tended to have more severe poisoning, longer ICU stays, and higher rates of complications, including the need for mechanical ventilation and increased mortality. This aligns with existing knowledge that cholinesterase inhibition directly relates to the toxic effects of OP and carbamates, with lower enzyme activity reflecting more severe poisoning. The demographic details, particularly the predominance of rural residents and farmers, emphasize the socioeconomic factors influencing patient outcomes. The delayed access to healthcare in rural areas likely contributed to the severe poisoning cases observed. This suggests that improving healthcare access and pesticide regulation in agricultural regions could reduce the incidence and severity of poisoning.

The study's findings support the use of E-AChE as a clinical tool in emergency settings to aid in the rapid assessment of patients and to guide treatment decisions. The lack of detailed results for BChE may indicate that while helpful, BChE is less critical in predicting patient outcomes compared to E-AChE. However, incorporating both biomarkers in clinical practice could enhance diagnostic accuracy and patient management.

Overall, the results underscore the critical importance of timely diagnosis and management in cases of organophosphorus and carbamate poisoning. The correlation between E-AChE levels and clinical outcomes provides valuable insights into the severity of poisoning, enabling clinicians to tailor interventions more effectively and potentially improve survival rates.

Red blood cell cholinesterase (RBC-ChE) levels are better than serum cholinesterase (serum-ChE) in predicting death and the requirement for ventilatory support in patients suffering from OP poisoning, according to a significant study. The study, which involved 99 patients, discovered that, in comparison to survivors and non-ventilated patients, RBC-ChE levels were much lower in non-survivors and those needing ventilatory assistance. RBC-ChE was found to be a dependable prognostic marker for OP poisoning, with a sensitivity of 90.5% and

specificity of 91% at a cutoff of 20 U/g Hb in predicting mortality [7].

In a study liver enzymes such as AST and ALT, along with bilirubin levels, were evaluated for their role in predicting the severity of OP and carbamate poisoning. The study, which involved 166 patients, found significant differences in AST and ALT levels across severity groups, with higher levels correlating with more severe poisoning and prolonged hospital stays. The study concluded that elevated liver enzymes at admission could serve as useful indicators of poisoning severity and treatment outcomes, reinforcing the need for biochemical monitoring in these cases [8].

A study evaluated the effectiveness of clinical scoring systems, such as the APACHE II and SOFA scores, along with biochemical markers like cholinesterase and lactate levels, in predicting the severity and survival of OP poisoning patients. The prospective cohort study involved 36 patients and demonstrated that APACHE II and SOFA scores were strong predictors of severity, with higher scores correlating with increased complications and mortality. This study highlighted the utility of these scoring systems in guiding clinical decisions and resource allocation in acute poisoning cases [9].

A predictive nomogram was created in retrospective research to assess the seriousness of acute OP poisoning. Age, white blood cell count, albumin, cholinesterase, blood pH, and lactic acid levels were among the variables included in the nomogram. Clinicians can easily evaluate the severity and possible consequences of OP poisoning at the patient's bedside with the use of this handy tool, as validation demonstrated strong predictive accuracy with an AUC of 0.875 in the derivation cohort [10].

Furthermore, a study investigated atropine refractoriness in OP and carbamate poisoning, which is a condition where high doses of atropine fail to achieve hemodynamic stability. The study found that patients exhibiting atropine refractoriness had longer durations of ventilation and ICU stay, highlighting the challenges in managing severe poisoning cases. The addition of adrenaline infusion was effective in achieving the target heart rate in refractory cases, suggesting a potential therapeutic strategy for such patients [11].

Generalizability

The generalizability of the study may be limited due to its relatively small sample size (60 patients) and its focus on a specific population, predominantly rural and farming communities in India. Additionally, the single-center design may not fully capture the diversity of clinical presentations and healthcare settings in other regions. However, the biochemical findings related to E-AChE levels and their correlation with poisoning severity provide valuable insights that could be applicable in similar agricultural and low-resource settings where organophosphorus and carbamate poisoning are prevalent.

CONCLUSION

The study revealed that lower RBC cholinesterase (E-AChE) levels are strongly associated with increased severity of poisoning, longer ICU stays, higher likelihood of requiring mechanical ventilation, and higher mortality rates. These findings highlight the importance of early E-AChE measurement in predicting the prognosis and guiding the management of patients with organophosphorus and carbamate poisoning.

Limitations

The limitations of this study include a small sample population who were included in this study. Furthermore, the lack of a comparison group also poses a limitation for this study's findings.

Recommendation

Early measurement of E-AChE levels in patients with OP and carbamate poisoning is recommended for better risk stratification and management. Incorporating rapid diagnostic tools for cholinesterase measurement in emergency settings could improve clinical decision-making and patient outcomes.

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List of abbreviations

E-AChE - Erythrocyte Acetylcholinesterase

BChE - Butyrylcholinesterase

OP - Organophosphorus

ER - Emergency Room

POP - Peradeniya Organophosphorus Poisoning (Severity Scale)

ICU - Intensive Care Unit

HDU - High Dependency Unit

RBC - Red Blood Cell

AST - Aspartate Aminotransferase

ALT - Alanine Aminotransferase

APACHE II - Acute Physiology and Chronic Health Evaluation II

SOFA - Sequential Organ Failure Assessment

AUC - Area Under the Curve

EDTA - Ethylenediaminetetraacetic Acid

CAM - Confusion Assessment Method

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Conflict of interest

The authors have no conflicting interests to declare.

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