# Do Lab Parameter Could be used as Indicators of Severity in Case of Acute Cholinestrase Inhibitor Insecticides?

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## Abstract

**Background:** Cholinestrase inhibitor insecticides considered one of the most common causes of morbidity and mortality due to poisoning especially in developing countries like Egypt. This work aims to study the possible role of Creatine Phosphokinase (CPK), Amylase, Lactate Dehydrogenase (LDH), C-Reactive Protein (CRP) and blood sugar status in predicting the severity of acute cholinesterase inhibitor insecticides poisoning at the time of admission.

**Subjects and Methods:** This work was done at Poison Control Center of Ain Shams University Hospitals – Egypt, and was carried on 150 patients admitted with acute (CEI) insecticides poisoning. Clinical evaluation of the patients and poisoning severity was graded according to Peradynia organophosphorus poisoning (POP) scale, then venous blood sample was collected from patients and examined for CPK, Amylase, LDH, CRP and random blood sugar (RBS).

There is significant increase of CPK, LDH, CRP RBS and amylase enzyme specially with increase the severity in those patients admitted to ICU rather than inpatient, and in mechanically ventilated patients rather than non mechanically ventilated and in died patients rather than survivors.

**Conclusion:** CPK, Amylase, LDH, CRP and random blood sugar could be used to predict severity of cholinesterase inhibitor insecticides poisoning. They can also predict ICU admission, mechanical ventilation need and mortality. Amylase is a better predictor of respiratory failure and need of mechanical ventilation.

***Keywords:****Amylase, , C-Reactive Protein , Lactate Dehydrogenase, Peradynia organophosphorus poisoning scale.*

## Introduction

Cholinestrase enzyme inhibitor (CEI) insecticides, are most commonly used to get rid of agricultural, household and structural pests[1]**.** The easy reach to these insecticides with lack of knowledge about its serious hazards resulting in increased its accidental and suicidal poisoning[2]**.**

According to the World Health Organization (WHO), one million accidental and two million suicidal toxicity with insecticides take place worldwide yearly with approximately 200,000 die, most of them developing countries[3].

Organophosphates (OPs) irreversibly bind to cholinestrase enzyme by forming covalent bond between it and active site of enzyme leading to accumulation of acetylcholine at synaptic gap and myoneuronal junctions resulting into cholinergic crisis[4] . Carbamates also bind

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to cholinesterase enzyme ; however, the formed bond is weaker than that formed by OPs, hydrolyze more rapidly and enzyme returns functioning again within 2 days[5] .

Cholinergic symptoms are in the form of muscarinic, nicotinic and central. Muscarinic symptoms include excessive salivation, lacrimation, urination, diarrhea, gastrointes-tinal colics, vomiting, blurring of vision, miosis, slow pulse, and wheezing. Nicotinic symptoms include fasciculation, paresis or paralysis, increased blood pressure and rapid pulse. Central symptoms include anxiety, confusion, convulsions, psychosis and ataxia[6].

Peradeniya Organophosphorus Poisoning (POP) scale is a simple scoring system was used by by N Senanayake, HJ de Silva and L Keralliceede in 1993. The score is done at initial entrance to the Emergency Room on admission before doing any medical intervention[7].

## Subjects and Methods:

This work presents a cross sectional prospective study carried out at Poison Control Center (PCC) of Ain Shams University hospitals, cairo, Egypt, during the period from March 2017 to January 2018 ,it was done on 150 patients admitted with acute cholinesterase inhibitor (CEI) insecticides poisoning. The study was approved by Institutional ethical committee and an informed written consent was obtained from each patient or from his/her guardian.

**Inclusion criteria:**

The selected patients were adults of both sexes with acute (CEI) insecticides poisoning presented to PCC within 12 hours of exposure to insecticide and without receiving any previous treatment. Diagnosis of cases was based on history of exposure to an insecticide, clinical manifestations according to POP score and low serum pseudocholinesterase activity.

**Exclusion criteria:**

Patients who consumed other poisons along with (CEI) insecticides, Patients with renal, hepatic, cardiac diseases or chronic lung diseases, Patients known to be diabetics or addicts, Patients with septic manifestations, pancreatitis, epilepsy, autoimmune diseases or known cases of malignancy, Patients who presented to PCC with delay time more than 12 Hours, Patients who received any previous treatment before reaching PCC and Patients less than 18 years old.

Clinical evaluation of patients was done on arrival to ER according to POP score (Table 1).

POP score ***(Senanayake et al., 1993)***

(0-3) mild poisoning, (4-7) moderate poisoning, (8-11) severe poisoning.

**Sampling:**

Venous blood sample (5 ml) was collected before admission and after stabilization of the patient under complete sterile conditions. The samples were centrifuged, the serum was stored at refrigerator in (-80 degrees) until they were examined.

**Laboratory parameters:**

Pseudocholinesterase (PCHE) level was measured to confirm the diagnosis using kinetic colorimetric method (reference range between 4900–11900 U/L), Serum Creatine Phosphokinase (CPK) was measured by kinetic method (reference range between 36–174 U/L for men and 26–140 U/L for women), Serum Amylase was measured by kinetic method (reference range Up to 100 U/L),

Serum Lactate Dehydrogenase (LDH) was measured by kinetic ultraviolet method (reference range between 240–280 U/L), C-Reactive Protein (CRP) was measured by turbidimetric immunoassay method (reference range < 6 mg/L) and blood glucose was measured by enzymatic colorimetric method (reference range 70–105 mg/dl).

## Statistical Analysis

The collected data were statistically analyzed using SPSS software statistical computer package version 18 (SPSS Inc, USA). For quantitative data, the mean and standard deviation (SD) were calculated. One-way ANOVA was used in comparing between three groups while Independent t-test was used to compare between two groups. Qualitative data were presented as number and percentages, chi square ($\chi 2$) was used as a test of significance. ROC curve was used to determine the cut-off point in which highest sensitivity and specificity of several parameters as a predictor for severity.

For interpretation of results of tests of signifi-cance, significance was adopted at $P \leq 0.05$.

## Results

Out of 150 patients included in this study, 41.3% were mild, 31.3% were moderate and 27.3% were severe according to POP scale.

The study showed that the mean age of patients was 29.9 ± 12.3 years and there was significant positive correlation between age of patients and severity of poisoning (Figure 1).

59.3 % of patients were females and 40.7 % were males, 56.6 % of patients were from urban areas and 43.3 % were from rural areas.

Organophosphorus compounds (OPCs) were responsible for poisoning in 54.7% of all patients and carbamates were responsible for poisoning in 45.3% of all patients and (OPCs) were associated with more sever poisoning than carbamates.

Suicidal exposure was responsible for 79.3% of all studied patients and accidental exposure was responsible for only 20.7 %.

60.7% of all patients were admitted in the inpatient department and 39.3% of the all patients were admitted in the ICU and there was significant positive correlation between severity and ICU admission (Figure 1).

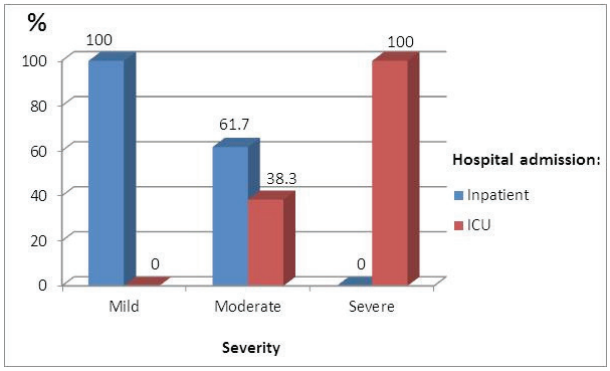


**Figure (1): Place of admission and severity**

As regard need for mechanical ventilation in ICU admitted patients, none of moderate patients admitted in ICU needed mechanical ventilation and 85.4% of sever patients admitted in ICU needed mechanical ventilation. There was significant positive correlation between severity and need for mechanical ventilation in ICU admitted patients (Figure 2).

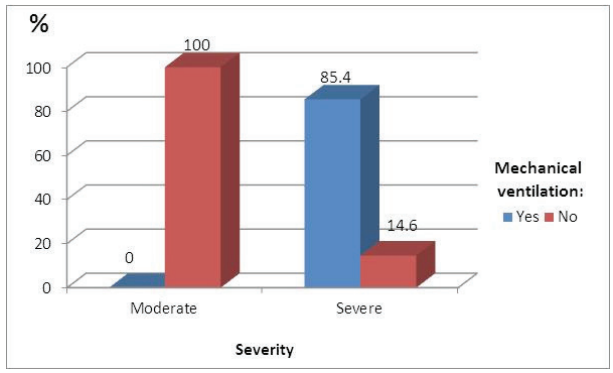


**Figure (2): Mechanical ventilation need and severity**

87.3% of all patients were discharged and 12.7% of all patients were died and there was significant positive correlation between severity and death outcome of the patients (Figure 3).

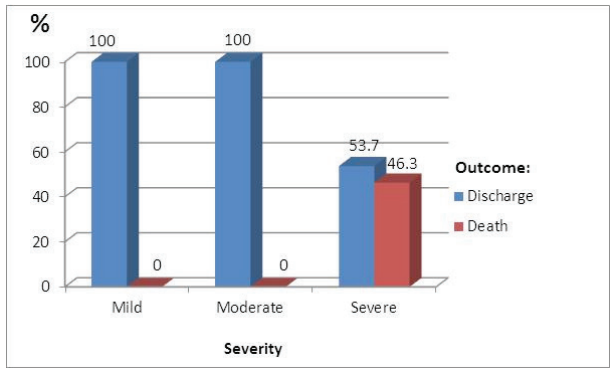


**Figure (3): Outcome and severity**

There was significant negative correlation positive pseudocholinestrase (PHCE) level and severity , also there was significant positive correlation between CPK, Amylase, LDH, CRP, RBS levels and severity according to POP score (Table 1).

**Table (1): Differences in laboratory parameters levels according to severity**

| Parameters | Severity | | | P |
|---|---|---|---|---|
| | Mild (N=62) | Moderate (N=47) | Severe (N=41) | |
| | Mean ± SD | | | |
| PChE | 1730.95 ± 765.33 | 1313.36 ± 419.76 | 939.46 ± 264.10 | <0.0001#* |
| CPK | 218.56 ± 15.29 | 329.19 ± 43.20 | 676.51 ± 77.42 | <0.0001#* |
| Amylase | 69.69 ± 13.71 | 127.72 ± 17.48 | 264.32 ± 41.95 | <0.0001#* |
| LDH | 521.60 ± 19.70 | 687.77 ± 54.16 | 884.66 ± 65.65 | <0.0001#* |
| CRP | 6.27 ± 2.37 | 17.34 ± 3.89 | 39.10 ± 11.40 | <0.0001#* |
| RBS | 104.40 ± 7.06 | 129.81 ± 8.84 | 176.90 ± 22.54 | <0.0001#* |

# Independent t-test *Significant

There was significant negative correlation between pseudocholinestrase level and incidence of ICU admission while there was significant positive correlation between

CPK, Amylase, LDH, CRP, RBS levels and incidence of ICU admission (Table 2).

**Table (2): Differences in laboratory parameters levels according to place of admission**

| Parameters | Place of Admission | | P |
|---|---|---|---|
| | Inpatient (N=91) | ICU (N=59) | |
| | Mean ± SD | | |
| **PChE** | 1576.23 ± 716.03 | 1086.92 ± 364.65 | **<0.0001#*** |
| **CPK** | 247.66 ± 49.56 | 580.05 ± 161.12 | **<0.0001#*** |
| **Amylase** | 84.88 ± 25.76 | 227.75 ± 65.99 | **<0.0001#*** |
| **LDH** | 570.64 ± 76.37 | 830.63 ± 106.26 | **<0.0001#*** |
| **CRP** | 9.65 ± 5.67 | 32.69 ± 13.81 | **<0.0001#*** |
| **RBS** | 111.24 ± 12.31 | 164.47 ± 26.91 | **<0.0001#*** |

# Independent t-test *Significant

There was significant negative correlation between pseudocholinestrase level and the need for mechanical ventilation while there was significant positive correlation between CPK, Amylase, LDH, CRP, RBS and the need for mechanical ventilation (Table 3).

**Table (3): Differences in laboratory parameters levels according to mechanical ventilation need in ICU admitted patients**

| Parameters | Mechanical Ventilation | | P |
|---|---|---|---|
| | Yes (N=35) | No (N=24) | |
| | Mean ± SD | | |
| PChE | 911.09 ± 273.97 | 1343.33 ± 329.70 | <0.0001#* |
| CPK | 698.40 ± 59.91 | 407.46 ± 88.09 | <0.0001#* |
| Amylase | 276.49 ± 32.02 | 156.67 ± 24.12 | <0.0001#* |
| LDH | 903.23 ± 51.19 | 724.75 ± 69.88 | <0.0001#* |
| CRP | 41.46 ± 10.45 | 19.92 ± 5.65 | <0.0001#* |
| RBS | 181.57 ± 20.62 | 139.54 ± 10.21 | <0.0001#* |

# Independent t-test *Significant

There was significant negative correlation between pseudocholinestrase level and death outcome of patients while there was significant positive correlation between CPK, Amylase, LDH, CRP, RBS and death outcome of patients .

By ROC curve analysis to predict ICU admission and need for mechanical ventilation; CPK, Amylase, LDH, C-RP and RBS had higher sensitivity and specificity than pseudocholinestrase and Amylase had the highest sensitivity and specificity among these parameters in predicting ICU admission and MV need .

## Discussion

The mean age of patients included in our study was 29.9 ± 12.3 years, this was in accordance with ***Kaumar and Sahna, (2017)*** [8]. ***and Banday et al., (2015)*** [9]. as they noticed that the highest incidence of poisoning was seen in patients in the middle age group which may be due to the increased stress conditions because of unemployment, poverty and depression that can happen during this age of life. Significant positive correlation was noticed between severity of poisoning and age, as noticed by ***Akdur et al., (2010)*** [10].

Female patients represented 59.3% of patients while male patients represented 40.7% with a female to male ratio of 1.46:1. This was also seen in the study of ***Hassan and Madboly, (2013)*** [11]. *and* ***Gündüz et al., (2015)*** [12]. where females were more affected than males. On the contrary, ***Sumathi et al., (2014)*** [13]. studies showed that males were more affected than females. This may be due to the emotional liability of females to stresses and easy availability of insecticides at home as household

products.

56.7% of patients were from urban areas compared to those from rural areas who were 43.3%. The same result was also reported by ***Dubey et al., (2016)*** [14] ***and Ismael et al., (2013)*** [15]**.** This may be explained by that the study was done in Cairo which is a wide urban community and most of rural patients included in the study came from only the near rural areas.

54.7% of patients were intoxicated by (OPCs) while 45.3% were intoxicated by carbamates, In their study, ***Sun et al., (2015)*** [16]**.** reported that 79% of patients were due to (OPCs) toxicity while 21% were due to carbamates poisoning.

79.3% of patients were suicidal while, the remaining 20.7% were accidental, these results agreed with ***Ismael et al., (2013)*** [15]**.** **,** ***Banday et al., (2015)*** [9]**.** .

60.7% of patients were admitted in the inpatient department and 39.3% were admitted in the ICU of which 59.3% needed mechanical ventilation (MV) and all of them were from the severe group of patients. The remaining 40.7% of ICU admitted patients did not need MV. Significant positive correlation was noticed between severity of poisoning and each of ICU admission and the need for MV, these results are in accordance with the results reported by ***Girish et al. (2016)*** [17]**.** *and* ***Kaumar and Sahna, (2017)*** [8]**.** **.**

Death represented 12.7% of patients while the remaining 87.3% were discharged. This in accordance with the results reported by ***Sun et al., (2015)*** [16]**.** where death was 12% of cases and cure was observed in 88% of cases, significant positive link was observed between severity of poisoning according to POP score and death with increased severity was associated with increased death rate and this in accordance with the results reported by ***Girish et al. (2016)*** [17]**.** and ***Vernekar and Shivaraj, (2017).*** [18]**.**

Significant negative relation was found between level of Pseudocholinestrase (PChE) and severity of poisoning, ICU admission, the need for Mechanical Ventilation and mortality. ***Muley et al., (2014)*** [19]**.** *and* ***Kaumar and Sahna, (2017)*** [8]**.** agreed with the present study regarding the associated relation between the severity and PChE level.

The present study showed that there was significant positive relation between CPK level and severity of poisoning, ICU admission, need for MV, and result, this was in agreement with those found by ***Hassan and Madboly, (2013)*** [11]**.** and ***Dubey, et al., (2016)*** [14]**.** whom found that CPK levels were significantly positively related with the severity according to POP scale, Mechanical Ventilation need and death. In contrast, ***Khan et al., (2016)*** [20]**.** found that there was insignificant link between CPK levels and patients' severity and mortality and ***Gündüz et al., (2015)*** [12]**.** found no significant difference in levels of CPK between patients who died and those who survived.

There was significant positive relation between Amylase level and severity, ICU admission, Mechanical Ventilation need, and result. In their studies ***Patil and Vasepalli (2014)*** [8-9]**.** *and* ***Dubey, et al., (2016)*** [14]**.** found that serum amylase levels related well with the severity of poisoning according to POP scale, and admission to ICU, the need for Mechanical Ventilation and end. It was found in Previous studies that acute pancreatitis may develop following organophosphorus intake, this may be due to excessive cholinergic stimulation and hypertension in ducts ***(Ikizceli et al., 2005)*** [22]**.**

There was significant positive relation between LDH levels and severity, ICU admission, Mechanical Ventilation need, and result. ***Coskun et al., (2015)*** [23]**.** ***and Gündüz et al., (2015)*** [12]**.** found that LDH levels linked well with the severity of poisoning and can be used as a predictor of severity and mortality. On the contrary to that , the study done by ***Sen et al., (2014)*** [24]**.** **,** showed no significant difference in serum LDH levels between the survivor and non-survivor patients.

There was significant positive relation between CRP level and severity, ICU admission, MV need, and result, this agreed with the results of ***Wu et al., (2016)*** [25]**.** where they also found significant link between CRP level and the patients' severity and prognosis. In contrast, the study done by ***Yeo et al., (2012)*** [26]**.** showed no significant link between CRP level on admission and death. CRP may increased in (CEI) insecticides poisoning due to induced tissue and body organ damage ***(Lee et al, 2013)*** [27]**.** **.**

There was also significant positive link between RBS level and severity, ICU admission, Mechanical Ventilation need, and result.

***Panda et al., (2015)*** [28]**.** found that there was a rise in the random blood glucose with increase in severity and blood glucose status at time of admission may help in identifying the severity of poisoning. ***Rao and Raju, (2016)*** [29]**.** found that elevated blood glucose at the time of admission linked well with severity of cases and levels of RBS more than 200 mg/dl were fair parameters to guess mortality and the need for ventilatory support. The persistent increase of hormones (catecholamine and cortisone) associated with insecticides poisoning, lead to increased blood sugar level due to decrease the person's sensitivity to insulin ***(Clark, 2002).*** [30]**.**

The present study showed that Amylase had the highest sensitivity and specificity in prediction of respiratory failure and Mechanical Ventilation need, which was in accordance to results detected by ***Kozaci et al., (2012)*** [31]**.** and ***sumathi et al., (2014)*** [13]**.** which reported that the elevation of amylase levels was high in respiratory failure and could be used as a predictor for the need to mechanical ventilation.

## Conclusion

Poisoning severity can be monitored by using POP score, it facilitate the grouping of severity state of patients and can predict the end of the case.

Severity of toxicity according to POP score was significantly positively linked with ICU admission, need for Mechanical Ventilation and death.

Significant positive link was noticed between CPK, Amylase, LDH, CRP and RBS and severity, ICU admission, the need for Mechanical Ventilation and death, so they can be used as predictive tools in cholinesterase inhibitor insecticides toxicity.

Amylase had the highest sensitivity and specificity between all parameters in the guessing of the ICU admission and need for Mechanical Ventilation so it can be used as predictor of respiratory failure and need for Mechanical Ventilation in acute cholinesterase inhibitor insecticides poisoning.

**Conflict of Interest:** The author declare that there is no prescence for conflict of interest

**Source of Fund:** None

**Ethical consideration:** This study was approved by the Fayoum Faculty of Medicine Research Ethical Committee. Study was conducted after explaining the study's aims. Verbal and written consents were obtained from all patients (or their relatives) included in the study and each person had the right to refuse to participate in the study.

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