Research Article

Eurasian Journal of Toxicology

Serum Creatine Phosphokinase as a Biomarker in Organophosphorus Poisoning

Rajib Kumar DEY[1,2], Gunjan KHADKA[1]

[1]Consultant in Internal Medicine, Indira Gandhi Memorial Hospital, Male, Maldives
[2]Consultant in Internal Medicine, Treetop Hospital, Hulhumale, Maldives

Abstract

Background: Organophosphorous poisoning is a common problem in Nepal. Biochemical markers play an important role in the diagnosis and assessment of severity of Organophosphorous poisoning. Presently cholinesterase level which is an expensive biomarker is being used. However, new and cheaper biochemical markers are being studied. The objective of this study was to compare two laboratory biomarkers, creatine phospsokinase and Acetylcholine Esterase and its prognostic significance in Organophosphorous poisoning.

Methodology: A cross-sectional hospital-based study was conducted involving 40 patients with organophosphorus poisoning. Informed consent was obtained from caregivers, and patients of either sex who presented within 12 hours of ingestion/exposure were included. Cases of mixed poisoning, chronic alcoholism, liver/kidney disease, myositis, or use of medications (statins, fibrates, or steroids) were excluded from the study.

Clinical severity was categorized using the Peradeniya Organophosphorus Poisoning Scale. Venous blood samples were collected to measure serum creatine phospsokinase and Acetylcholine Esterase levels. Patients were treated with intravenous pralidoxime and atropine as per hospital protocol, avoiding intramuscular injections. After one week of admission, repeat serum creatine phospsokinase levels were re-measured.

The Pearson correlation coefficient was used to assess the relationship between Peradeniya Organophosphorus Poisoning score and creatine phospsokinase levels at admission, and the paired t-test was used to compare initial and final creatine phospsokinase and Acetylcholine Esterase levels, with a significance level of 0.05.

Results: Majority of patients enrolled in this study had mild Organophosphorous poisoning 32(80%) as per POP score whereas 6(15%) had moderate Organophosphorous poisoning and 2(5%) had severe poisoning. In patients with mild Organophosphorous poisoning the mean initial creatine phospsokinase level was 333.91±182.52 (IU/L). Patients with moderate Organophosphorous poisoning had a mean initial creatine phospsokinase level of 355.40±115.17(IU/L) where as in severe Organophosphorous poisoning the mean initial creatine phosphokinase level was 462.5±279.3(IU/L). The calculated Pearson correlation coefficient of Peradeniya Organophosphorus Poisoning with initial serum creatine phospsokinase level was 0.544 implying distinct positive correlation. The creatine phospsokinase levels in recovering patients showed a tendency to decrease, which was statistically significant in mild and moderate cases but not in severe cases.

Conclusions: Serum creatine phospsokinase level can be used as an alternative marker in the diagnosis and assessment of severity and prognostication in Organophosphorous poisoning especially in mild to moderated cases as shown in our study. Besides, the fall in the serum creatine phospsokinase level may also be used as marker of recovery.

Keywords: Organophosphorus Poisoning, Creatine phosphokinase, Acetyl Cholinesterase, Peradeniya Organophosphorus Poisoning Scale

Introduction

Acute poisoning by Organophosphorus pesticides (OP) is common in most parts of the developing world, particularly in Asia including Nepal where agriculture is the most common occupation in the country. The toxicity of OP compounds and the lack of appropriate medical facilities accounts for a high fatality rate. Easy accessibility of these pesticides has an important role in the choice of OP as a self-poison, and the incidence is particularly high among young people who are engaged in agriculture[1].

According to World Health Organization (WHO) one million serious unintentional poisonings occur annually, and an additional two million people seek hospital care for pesticide related suicide attempts[2]. Ravi et al reported in 2007 that the incidence of OP poisoning was around 126,000 over the period of 12 months in India[3]. In the year 1999-2000, 31% of all suicidal deaths in the country were due to poisoning[4]. Multicenter studies including five major hospitals across India in 1999- 2000 reported OP compounds were the commonest cause of poisoning, which comprised 52% of total cases[5].

A national study done in Bangladesh showed that self-poisoning caused 14 percent of all cause mortality among women of age group 10-50 years (3971 out of 28,998), with pesticides being the commonest[6]. The problem is particularly severe in Sri Lanka where pesticide poisoning was the commonest cause of hospital death in six rural districts during 1995[7]. The OP compounds had the largest

Corresponding Author: Rajib Kumar DEY **e-mail:** dr_rajibdey@yahoo.co.uk
Received: 24.03.2025 • **Revision**: 27.03.2025 • **Accepted:** 28.03.2025
Cite this article as: Dey RK, Khadka G. Serum Creatine Phosphokinase as a Biomarker in Organophosphorus Poisoning Tox. 2025;1(1): 5-10

burden of poisoning related morbidity and mortality in Nepal as shown in several hospital-based studies[5].

Organophosphate compounds inhibit the acetylcholinesterase enzyme (AchE) at muscarinic and nicotinic receptors. As a result, the patient develops symptoms like miosis, bradycardia, vomiting, profuse sweating, tachypnea, hypersalivation, lacrimation, altered sensorium, fasciculation, bronchospasm, blurred vision, photophobia, urination and defecation. If not treated promptly, patient can develop complications like respiratory paralysis, acute renal failure, seizures, arrhythmias, aspiration, coma and even death.[8]

Early recognition and timely intervention are of great importance to critical care providers and patients. OP toxicity is a clinical diagnosis which is confirmed by the measurement of cholinesterase activity. These investigations are not readily available everywhere. Although Red Blood Cell (RBC) and plasma (pseudo) cholinesterase (PChE) levels can both be used, RBC cholinesterase correlates better with CNS acetylcholinesterase activity and is, therefore, a more useful marker of OP poisoning. Erythrocyte cholinesterase is the more accurate of the two tests, however, plasma cholinesterase is easier to assay and is more widely available. Since RBC cholinesterase levels are not done in Nepal, plasma cholinesterase is the only option, which is not done in most laboratories and is an expensive investigation.[8]

There are novel alternatives to inexpensive and easily measurable biochemical markers of interest in OP poisoning, such as creatine phosphokinase (CPK), lactate dehydrogenase (LDH), serum immunoglobulins (IgG, IgA), and circulating complement components C3 and C4.

According to studies, OP poisoning is associated with elevated serum CPK levels, which could be used as a biomarker[8,9]. Hence this study was undertaken to see association and the prognostic significance of creatine phosphokinase in OP poisoning.

Methodology

Forty patients with OP poisoning were enrolled in this cross-sectional hospital-based study, conducted at Bir Hospital and SBH Army Hospital, Kathmandu, Nepal, over a period of 9 months after approval from Institutional Review Board. The patients were enrolled from the emergency department along with detailed history from the patient and/or caregiver. Confirmation of OP poisoning was done by label of packet/container of the poison consumed and serum Acetyl Choline Esterase (AChE) level at the time of admission. Informed consent was taken from the caregivers and patients were of either gender with history of ingestion or exposure to OP poison presenting to emergency department within 12 hours were included. However, patients who had mixed poisoning; chronic alcoholic intake, had history of chronic liver disease, chronic kidney disease or myositis; and patients taking any of medications including statins, fibrates, or steroids were excluded from the study Clinical severity was categorized according to Peradeniya Organophosphorus Poisoning (POP) scale as shown in Table 1.

Table 1: Peradeniya Organophosphorus poisoning (POP) Scale

Parameter	Criteria	Score
Pupil Size	≥ 2mm	0
	<2mm	1
	Pinpoint	2
Respiratory rate	<20/min	0
	≥ 20 min	1
	≥ 20 min with central cyanosis	2
Heart rate	>60/min	0
	41-60/min	1
	≤40/min	2
Fasciculation	None	0
	Present, generalized, continuous	1
	Both generalized/continuous	2
Level of consciousness	Conscious and rational	0
	Impaired response to verbal command	1
	No response to verbal command	2
Seizures	Absent	0
	Present	1

0-3: Mild poisoning, 4-7: moderate poisoning, 8-11: severe poisoning.

Venous blood sample was collected from a peripheral vein and sent for serum CPK and Acetyl Choline Esterase levels.

Patients were treated with intravenous PAM and atropine as per hospital protocol. Intramuscular injection was avoided in all the patients during the course of treatment.

At the end of one week from admission, the levels of serum CPK and serum AChE were measured.

Data was entered in Statistical Package of Social Science (SPSS) version 16 (SPSS Inc., Chicago IL, USA), and Microsoft Excel spreadsheet. Data analysis was done using SPSS (16 version) program and was depicted as tables and charts. Correlation of severity (POP score) with CPK level at admission was tested using Pearson correlation coefficient. The paired t test was used to analyze the difference between initial and final CPK and AChE levels with level of significance of 0.05.

Results

During the period of data collection of nine months (May 2013 to January 2014) there were a total of 40 patients enrolled into this study.

As shown in Figure 1, out of the 40 patients enrolled into the study 15(37%) were males and 25(63%) were females. The male: female ratio was 1: 1.7.

As illustrated in Figure 2, the majority of OP poisoning patients were in the age group ≥ 35 years which was 15 patients (37.5%). The next highest number of patients were in the age group 15-19 years where there were 12 (30%) patients. There were 7(17.5%) patients in the age group of 20– 24yrs. There were a similar number of patients in the age group 25- 29 years and 30-34 years 3 (7.5%).

The pie chart in Figure 3 shows that majority of patients enrolled in this study had mild OP poisoning patients. As per POP score, 32(80%) patients had mild OP poisoning, 6(15%) patients had moderate OP poisoning and 2 (5%) patients had severe poisoning.

The Table 2 shows that in patients with mild OP poisoning the mean initial AchE level was 2079.8±1361.17(IU/L). Patients with moderate OP poisoning had a mean initial AchE level of 525.83±133.45(IU/L) where as in severe OP poisoning the mean initial AchEe level was 147.0±93.33(IU/L). The mean initial AChE level was 1151.8±1131.4(IU/L) when all the patients were combined. This table shows that the POP score increases as the AChE levels decreases, which is illustrated in scatter diagram in Figure 4. The Pearson correlation coefficient was computed to be -0.576 indicating distinct negative correlation with p-value of <0.001.

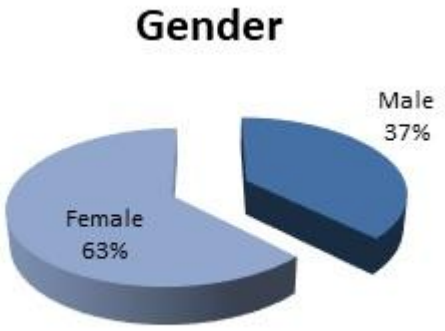

Figure 1: Sex distribution among OP poisoning patients

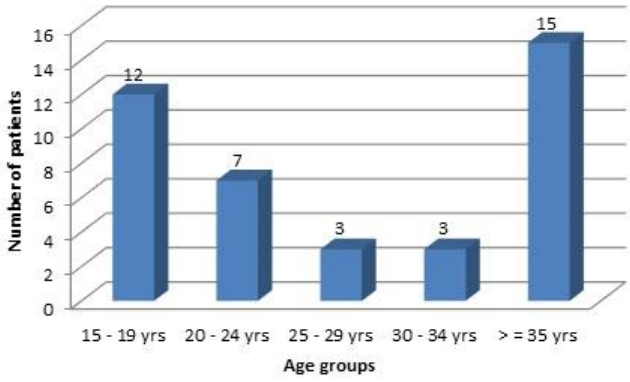

Figure 2: Age distribution among patients.

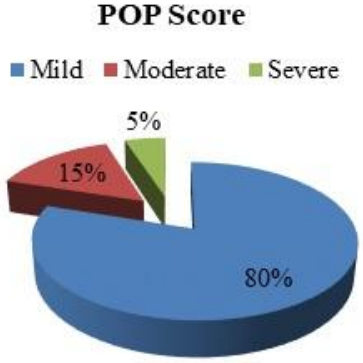

Figure 3: Severity of OP poisoning according to POP score

Table 2: Distribution of initial Ach E levels in relation POP score

POP score	Number of patients	Mean Initial AchE levels (IU/L)	± SD
Mild	32	2079.8	1361.17
Moderate	6	525.83	133.45
Severe	2	147.0	93.33
Total	40	1151.8	1131.47

In patients with mild OP poisoning, the mean initial CPK level was 333.91±182.52 (IU/L). Patients with moderate OP poisoning had a mean initial CPK level of 355.40±115.17(IU/L) where as in severe OP poisoning the mean initial CPK level was 561.25±60.85(IU/L). Table 3 shows that as the POP score increases the mean initial CPK level increases. Using scatter diagram as shown in Figure 5, Pearson correlation coefficient was calculated to be 0.544 implying distinct positive correlation.

The Table 4 shows that in patients with mild OP poisoning there is a reduction from the mean initial CPK level (333.91±182.52 U/L) to the mean final CPK level (61.59±17.30 U/L) which was statistically significant (p<0.001). In patients with moderate OP poisoning there is a reduction from the mean initial CPK level (355.40±115.17 U/L) to the mean final CPK level (75.16±28.62 U/L) which was statistically significant (p=0.015). However, in the group of patients with severe poisoning the reduction from the mean initial CPK level (561.25±60.85 U/L) compared to

Table 3: Distribution of initial CPK levels in relation POP score

POP score	Number of patients	Mean Initial CPK levels (IU/L)	± SD
Mild	32	333.91	182.52
Moderate	6	355.40	115.17
Severe	2	561.25	60.85

Table 4: Comparison of the initial and final CPK levels

POP score	Initial CPK (U/L)		Final CPK (U/L)		p value
	Mean	±SD	Mean	±SD	
Mild (0-3)	333.91	182.52	61.59	17.30	<0.001
Moderate (4-7)	355.40	115.17	75.16	28.62	0.015
Severe (8-11)	561.25	60.85	112.80	28.28	0.27

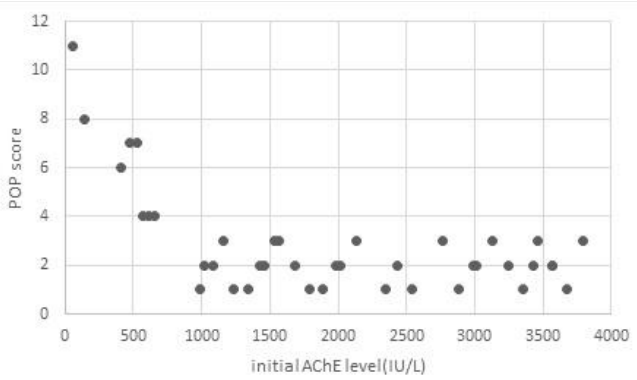

Figure 4: Severity of OP poisoning with initial AChE levels

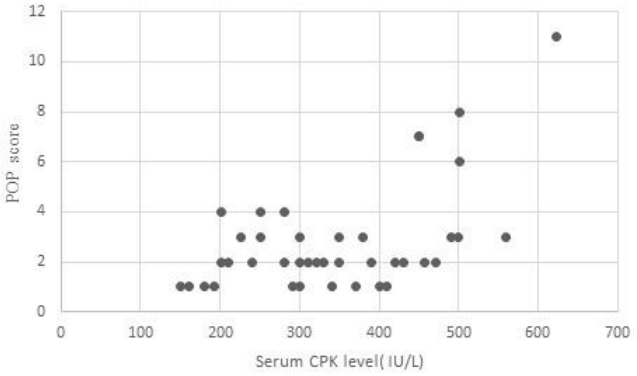

Figure 5: Scatter diagram showing correlation of severity of OP poisoning with CPK level

the mean final CPK (112.80±28.28 U/L) was statistically not significant (p=0.27).

Discussion

Organophosphate compounds are used for agriculture and industrial purposes and these compounds are easily available at a low cost. Poisoning with Organophosphates is a common cause of morbidity and mortality worldwide especially in South Asia. OP poisoning results in the inhibition of AChE at muscarinic and nicotinic receptors resulting in a range of symptoms. Complications of OP poisoning include acidosis, respiratory paralysis, renal failure, seizures, arrhythmias, aspiration, coma and even death. Early diagnosis is the key to cure. Till now estimation of serum cholinesterase and plasma cholinesterase levels have been used in the investigation and management of OP poisoning. However, these tests are costly and not done in most laboratories in the developing countries. Therefore, cheaper and easily available biochemical markers that can be used in OP poisoning are being studied. The aim of our study was to determine the association and prognostic significance of CPK in OP poisoning.

In our study majority of the enrolled patients were women (63%) vs men (37%). The male to female ratio was 1:1.7. This was similar to the gender distribution in the study by Hassan et al where they had majority of female patients.[10] However, in the study by Bhattacharya et al men comprised the majority (male: female=2:1).[8] In our study, age of the patients ranged from 15-56yrs. It was observed that most of the OP poisoning cases were in the higher age groups and in very young patients. In the study by Hassan et al, the age of patients enrolled ranged from 13-68 years and Bhattacharya et al enrolled patients from 16-44 years.[10]

Majority of patients enrolled in this study had mild OP poisoning 32 patients (80%) as per POP score. Out of 40 patients, 6 (15%) patients had moderate OP poisoning and 2 (5%) patients had severe poisoning. Bhattacharya et al who studied serum CPK as a probable marker of severity in OP poisoning had 32(50.8%) patients in the group of moderate OP poisoning, 27% in the mild group and 22.2% in the severe group.[8] Sen R et al who studied the prognostic biomarkers in Organophosphorus poisoning reported that as per the POP Score, 29 patients (23 females and 6 male) had mild poisoning, 45 had moderate poisoning (22 females and 23 males) and 26 (12 females and 14 males) had severe poisoning.[11]

In our study patients with mild OP poisoning had a mean initial AchE level of 2079.8±1361.17 (IU/L). Patients with moderate OP poisoning had a mean initial AchE level of 525.83±133.45 (IU/L) where as in severe OP poisoning the mean initial AchE level was 147.0±93.3(IU/L). The relationship between severity and AchE level was found to be statistically significant (p<0.001) with r value of -0.576 indicating distinct negative correlation. Determination of AChE and PChE level in blood has remained important for the initial screening of acute OP exposure which helps health-care professionals in early diagnosis and immediate treatment plan. Several studies have shown the relationship between cholinesterase levels and severity of OP poisoning and it has been used as a prognostic marker.[9,11,12]

In our study the patients with mild OP poisoning, the mean initial CPK level was 333.91±182.52 (IU/L). Patients with moderate OP poisoning had a mean initial CPK level of 355.40±115.17(IU/L) where as in severe OP poisoning, the mean initial CPK level was 561.25±60.85(IU/L). Our results showed that as the POP score increases, the CPK level increases as seen in the scatter diagram. Also, the Pearson correlation coefficient(r) was calculated to be 0.544 implying distinct positive correlation with p-value of <0.001. These findings were comparable to the findings of the study by Hassan NM et al. They reported that as the initial CPK level increased, the POP score also increased. (Mild – 89.1±27, Moderate- 273±96.7, Severe-688.8±86.7 U/L) which was statistically significant p<0.001).[10] The study by Sen R et al also reported that the correlation between severity of poisoning and serum CPK (Mild-449.65±325.4, Moderate-768.2±485.4, Severe-1324.74±141.6) showed a high degree of positive correlation (r = 0.625) and the correlation was also statistically significant (p =0.001).[11]

The study by Bhattacharya et al also showed a similar result. They also reported a positive correlation between OP poisoning severity and CPK levels. (Mild – 273.53±108.71, Moderate-456.06±77.20, Severe-1032.57±205.57 U/L) which was statistically significant (p<0.001). It was found that the mortality was more in patients with high initial CPK levels. Patients with severe poisoning have been shown to exhibit elevated levels of CPK. The presence of rhabdomyolysis in 'intermediate syndrome' is associated with increased CPK levels. The findings revealed that serum CPK levels are elevated in patients with severe organophosphate poisoning, even when intermediate syndrome is not present, likely due to muscle fiber necrosis observed in muscle biopsies.[8]

Our study showed, patients with mild OP poisoning had a reduction from the mean initial CPK level (333.91±182.52 U/L) to the mean final CPK level (61.59±17.30U/L) which was statistically significant (p<0.001). In patients with moderate OP poisoning, there was a reduction from the mean initial CPK level (355.40±115.17 U/L) to the mean final CPK level (75.16±28.62 U/L) which was also statistically significant (p<0.015). However, in the group of patients with severe poisoning the reduction from the mean initial CPK level (561.25±60.85 U/L) compared to the mean final CPK (112.80±28.28 U/L) was statistically not significant (p=0.27). Only two patients presented with severe OP poisoning. The decrease in CPK levels may have been statistically insignificant, attributable to the limited sample size within that group. Cases of severe OP poisoning necessitated a longer recovery period, resulting in a less consistent decline in CPK levels.

The CPK levels in recovering patients showed a tendency to decrease. Therefore, serial measurement of serum CPK level might be helpful in predicting the prognosis of OP poisoning.

In the study by Hassan NM et al, their comparison between initial and final CPK levels showed that there was a reduction in the final CPK levels with treatment in the mild and moderate cases which was statistically significant (p<0.001), while the changes among the severe group was not significant. They assumed that this was probably due to the widespread complication that occurred in the severe group in their study. These results were similar to our study.[10]

A more extensive study that encompasses a greater number of patients across each category (mild, moderate, and severe OP poisoning) will be beneficial in confirming our findings with increased reliability.

Conclusion

Serum CPK levels serve as a significant marker for assessing the severity of organophosphorus (OP) poisoning. This test is more accessible and cost-effective than measuring serum AChE levels. Consequently, serum CPK levels can be an invaluable resource for managing OP poisoning in resource-constrained areas. Furthermore, conducting serial CPK tests throughout the treatment process can aid in tracking the patient's recovery. Nonetheless, a key limitation is its non-specificity, making it essential to rule out other potential causes of elevated CPK levels.

Data availability

The datasets used in the study will be available from the corresponding authors upon reasonable request.

List of abbreviations

Ethics declarations

Ethical approval was taken from Institutional Review Board of National Academy of Medical Sciences, Kathmandu, Nepal.

Funding

No funding was received for this research

Competing interests

The authors declare no competing interests.

Consent for publication: Written informed consent was taken from the patients for the enrollment in study and publication of the article

Acknowledgements: The authors would like to thank the patients for their participation.

References

1. Balali-Mood M, Balali-Mood K, Moodi M, Balali-Mood B. Health aspects of organophosphorous pesticides in asian countries. Iran J Public Health. 2012;41(10):1-14. Epub 2012 Oct 1. PMID: 23304659; PMCID: PMC3494223.
2. Jeyaratnam J. Acute pesticide poisoning: A major global health problem. World Health Stat Q.1990;43:139–44.
3. Ravi G, Rajendiran C, Thirumalaikolundusubramanian P, Babu N. Poison control, training and research center, Institute of Internal Medicine, Government General Hospital, Madras Medical College, Chennai, India. Presented at 6th Annual congress of Asia Pacific Association of Medical Toxicology. Bangkok, Thailand: 2007.
4. His Majesty's Government of Nepal. Central Bureau of Statistics, National Planning Commission. Statistical Year Book of Nepal. 2001.
5. Gupta SK, Joshi MP. Pesticide poisoning cases attending five major hospitals of Nepal. J Nep Med Assoc 2002;41:447-56.
6. Yusuf HR, Akhter HH, Rahman MH, Chowdhary MK, Rochat RW. Injury related deaths among women aged 10-50 years in Bangladesh.Lancet, 2000; 355:1220-1224.
7. Sri lankan Ministry of Health. Annual Health Bulletin, 1995. Ministry of Health, Colombo, Srilanka.
8. Bhattacharyya K, Phaujdar S, Sarkar. Serum creatine kinase: A probable marker of severity in organophosphorus poisoning. Toxicol Int 2011;18:117-23.

9. Agarwal SB, Bhatnagar VK, Agarwal A, Agarwal U, Venkaiah K, Nigam SK, et al. Impairment in clinical indices in acute organophosphate insecticide poisoning patients in India. Internet J Toxicol. 2007;4:1.
10. Nermeen A. M. Hassan, Abdelmonem G. Madboly et al. Correlation between Serum Creatine Phosphokinase and Severity of Acute Organophosphorus Poisoning. IOSR Journal of Environmental Science, Toxicology And Food Technology (IOSR-JESTFT): May - Jun 2013: 4(5); 18-29.
11. Sen R, Nayak J, Khadanga S. Study of serum cholinesterase, CPK and LDH as prognostic biomarkers in Organophosphorus Poisoning. Int J Med Res Rev 2014; 2:185-189.
12. Hernández A F. Influence of exposure to pesticides on serum components and enzyme activities of cytotoxicity among intensive agriculture farmers. Environmental Research. 2006;102: 70–76.