An analytical study to evaluate the levels of serum creatine kinase and serum magnesium in patients admitted with diagnosis of organophosphorus consumption.

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KEYWORDS

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ABSTRACT

Introduction: Organophosphorus poisoning (OPP) is a serious health issue caused by the inhibition of acetylcholinesterase, leading to cholinergic toxicity. This study aimed to evaluate serum creatine kinase (CK) and magnesium levels as diagnostic and prognostic markers in OPP patients.
Methodology: A prospective observational study was conducted at Krishna Hospital from February 2022 to January 2024, including 75 patients diagnosed with acute OPP.
Observations: The mean age of patients was 36.44 years, with 66.67% males. Chlorpyriphos was the most common poison (81.33%). The mortality rate was 22.67%, with a significant association between CK and magnesium levels and patient outcomes. Mean CK levels were significantly higher in non-survivors (1388.71 IU/L) compared to survivors (712.10 IU/L) ($p < 0.001$), while mean magnesium levels were significantly lower in non-survivors (1.50 mg/dl) compared to survivors (1.82 mg/dl) ($p < 0.001$).
Conclusion: Serum CK and magnesium levels can serve as reliable prognostic markers for OPP severity and outcomes.

Introduction:

Organophosphorus compounds are protease and serine esterase inhibitors, widely used as insecticides in agriculture. Organophosphate (OP) pesticide are a class of substances frequently encountered in agro-industrial settings despite their deleterious effect on human health.[1,2]
Organophosphate poisoning (OPP) is a poisoning due to OPs, which are compounds containing carbon and phosphorous acid derivatives. OPs are potent inhibitors of acetylcholinesterase (ACE) that can cause severe cholinergic toxicity after dermal contact, inhalation, and ingestion.[3] Chlorpyrifos, parathion, diazinon, dichlorvos, tetrachlorvinphos, fenitrothion, and azinphos-methy are among the frequently used OPs.[4] It is one of the leading causes of emergency hospitalization.[5]
Organophosphorus (OP) pesticides predominantly in Asian countries pose a significant risk of causing either acute or chronic health problems in these nations and are thought to affect 3 million or more individuals annually, resulting in roughly 300,000 fatalities worldwide.1,2 India being an agriculture-based country, OP pesticide remains the main agent for crop protection and pest control and thus increased risk of OP poisoning both intentional and inhalational is prevalent among Indian farmers.
Organophosphorus compound act by inhibiting the acetylcholinesterase enzyme (AchE) at muscarinic and nicotinic receptors, producing a group of symptoms like papillary constriction,

low heart heart, increased gastrointestinal motility, vomiting, profuse sweating, respiratory distress, salivation, lacrimation, altered sensorium, fasciculation, bronchospasm, blurred vision, photophobia, urination and defecation. The major complications associated with organosphosphorus compound poisoning include acidosis, respiratory paralysis, acute renal failure, seizures, arrythmias, aspiration, coma and even death. Furthermore, these insecticides increase reactive oxygen species level which results in oxidative stress that contributes to cell membrane lipid peroxidation, DNA damage and cell death.5,6

Laboratory evidence of OP poisoning is usually confirmed by measuring the decreases in the blood and erythrocyte cholinesterase activities. However, because of wide inter-individual variability and also the cost factor the serum EChE or BChE levels are not routinely performed.7 There are emerging options for newer economically viable and easily quantifiable biochemical markers in relation to OP poisoning like creatine phosphokinase (CPK), lactate dehydrogenase (LDH) and serum immunoglobulins (IgG, IgA).8

There will be the elevation of serum CPK in OP poisoning due to myonecrosis caused by persistent depolarization at the neuromuscular junction and oxidative cellular damage to muscle membrane.[10,11] Hypomagnesemia in acute organophosphorus poisoning cases might be due to GI losses, vomiting, diarrhoea, prolonged gastric aspiration, etc., magnesium is one of the omitted electrolyte in any illness. Since, many manifestations of hypomagnesemia overlap with features of organophosphorus poisoning, it may be the contributory factor in severity and outcome.

As of today only very few studies has shown that CPK level estimations are useful in diagnosis of organophosphorus poisoning in acute phase.9,10 Considering the potential correlation between serum creatine phosphokinase (CPK) or serum magnesium levels and OPC poisoning is crucial as early detection of poisoning severity can greatly reduce the burden on patients and mortality rates.

Hence, this study was planned for assessing serum creatine kinase and serum magnesium levels as diagnostic and prognostic marker in a patient with acute organophosphorus poisoning.

Methodology:

This was a prospective observational study conducted at Krishna Hospital and Research Center, Krishna Vishwa Vidhyapeeth, Karad, from February 2022 to January 2024. The study focused on patients admitted to the ICU with a diagnosis of organophosphorus (OP) poisoning. A total of 75 patients, irrespective of the route of exposure, age, or sex, were selected for the study after obtaining informed consent.

The inclusion criteria consisted of acute OP poisoning cases of both genders who provided written informed consent. Exclusion criteria included patients with other pesticide poisoning (such as organocarbamates) as determined by history and clinical features, those with mixed poisoning, individuals who had consumed compounds with alcohol, and those with pre-existing medical conditions such as chronic liver disease, myopathy, malignancy, renal failure, autoimmune diseases, seizure disorder, or coronary artery disease. Additionally, patients on chronic drug usage (statins, steroids, diuretics), as well as pregnant patients, were excluded.

Eligible patients were clinically assessed upon admission using the Peradeniya Organophosphorus Poisoning (POP) scale and categorized based on the severity of poisoning. Routine blood investigations were performed, including blood sugar, blood urea, serum creatinine, liver function tests, serum acetylcholinesterase, electrocardiogram (ECG), and arterial blood gases (ABG). Additionally, serum creatine kinase and magnesium levels were estimated at the time of admission.

According to the study, **Ajitha Kesi Chellappan et al** [78], using prevalence of OP Poisoning cases of 8% in all ICU admissions, with z of 1.96 and precision of 0.10 , minimum sample size calculated is 71. Rounding it off to 75, we considered 75 cases in our study, using the formula

$n = 4pq/d^2$. The study was approved by Institutional Ethics Committee (IEC) after discussion of the study protocol with committee.
Data was collected using a semi-structured pre-tested questionnaire, data Collected was entered in Microsoft Excel. Data is represented in frequencies and percentages, charts and graphs. Mean and standard deviation of quantitative variables is shown. Appropriate statistical tests are applied using SPSS software trial version 21 for analysis. Chi square test is used for association and student's t-test is used for comparison wherever applicable. Other statistical tests are used as per study requirements. The P value < 0.05 is taken as statistical significance.
Observations and results:
Out of the 75 cases, the mean age 36.44 SD (± 7.85) years, age range is 22 – 56 years. 18 patients (24.00%) were within the age group of 21 to 30 years, 37 patients (49.33%) were between 31 and 40 years old, 17 patients (22.67%) were aged 41 to 50 years, and 3 patients (4.00%) fell within the 51 to 60 years age range. We had 50 male (66.67%) and 25 (33.33%) were female participants. The distribution of occupation for the study population shows that 40 patients (53.33%) were engaged in agriculture, while 35 patients (46.67%) were involved in other occupations.
Table 1: Distribution of study population according to the type of poison consumption

Poison	Number (n=75)	Percent
Diazinon	1	1.33
Malathion	2	2.67
Dimethoate	3	4.00
Temephos	3	4.00
Prophenofos	5	6.67
Chlorpyriphos	61	81.33
Total	75	100.00

The distribution based on the type of poison ingested is as follows: Diazinon was involved in 1 case (1.33%), Malathion in 2 cases (2.67%), Dimethoate in 3 cases (4.00%), Temephos in 3 cases (4.00%), and Prophenofos in 5 cases (6.67%). The majority of cases involved Chlorpyriphos, accounting for 61 cases (81.33%). This distribution indicates that Chlorpyriphos was the most commonly encountered poison in the study. (Table 1)
The distribution of study population based on POP scores, categorizing them into mild, moderate, and severe categories. Among the total 75 cases analyzed, the majority fall under the moderate category, comprising 46.67% of the cases. Mild cases account for 28.00%, while severe cases make up 25.33% of the total. (Fig 1)

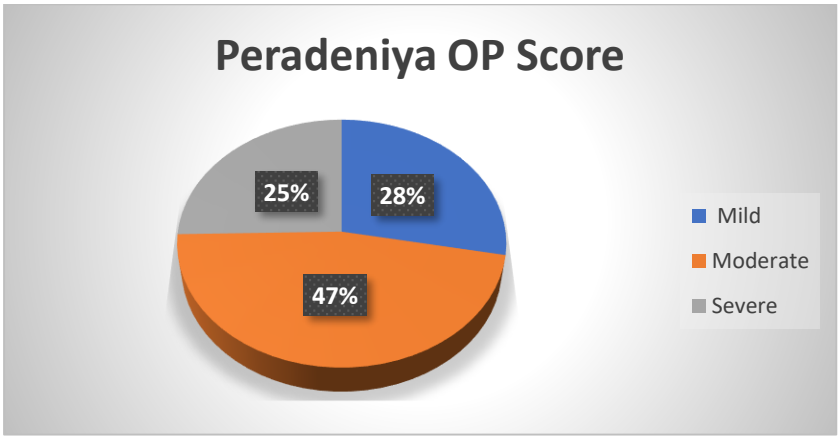

Fig 1: Distribution of the study population according to Peradeniya OP score

Out of a total of 75 cases, 58 patients survived, constituting 77.33% of the cohort. Tragically, 17 patients did not survive, representing 22.67% of the total study population.

Table 2: Relation between the quantity of the poison exposed and deaths in the study population

Quantity Exposed	Non survivors	Survivors	Total
<50 ml	4	36	40
50 - 100 ml	8	15	23
>100 ml	5	7	12
Total	17	58	75

Chi square= 8.06, df = 2, p = 0.018, Significant

The relationship between the quantity of poison exposed and outcomes (survivors and non survivors) among the study population. The table categorizes cases based on the amount of poison exposure: less than 50 ml, 50-100 ml, and more than 100 ml. Out of the total 75 cases, 40 cases had exposures of less than 50 ml, resulting in 4 deaths (10%) and 36 survivors (90%). For exposures between 50-100 ml (23 cases), 8 resulted in deaths (34.78%) and 15 in survivors (65.22%). For exposures exceeding 100 ml (12 cases), 5 resulted in deaths (41.67%) and 7 in survivors (58.33%). Overall, the table indicates a statistically significant association between the quantity of poison exposure and deaths ($\chi 2 = 8.06$, $p = 0.018$), highlighting the impact of poison quantity on patient outcomes. (Table 2)

Table 3: Relation between the Hospital stay and ICU stay and Peradeniya OP Scores and deaths in the study population

	Non survivors	Survived	Total	P Value
Hospital Stay ≤ 7 days	0	22	22	Chi square = 14.61, df= 2, p = 0.001
Hospital Stay 8 - 14 days	11	32	43	
Hospital Stay 15 - 21 days	6	4	10	
ICU Stay < 5 days	0	29	29	Chi square = 33.78, df=2, p < 0.001
ICU Stay 6 - 10 days	7	27	34	
ICU Stay 11 - 20 days	10	2	12	
POP Score Mild	0	21	21	Chi square= 12.77, df= 2, p = 0.002
POP Score Moderate	8	27	35	
POP Score Severe	9	10	19	

p < 0.05, Significant

The relationship between Peradeniya OP poisoning scale (POP) scores and outcomes (non survivors and survivors) among the study population. The table categorizes cases into mild, moderate, and severe based on their POP scores. Among the total 75 cases, all 21 cases

categorized as mild resulted in survival (100%). For moderate cases (35 cases), 8 cases resulted in deaths (22.86%) and 27 in survivors (77.14%). In severe cases (19 cases), 9 cases resulted in deaths (47.37%) and 10 in survivors (52.63%). Statistical analysis ($\chi 2 = 12.77$, $p = 0.002$) indicates a significant association between POP scores and deaths. (Table 3)

The relationship between hospital stays duration and outcomes (non survivors and survivors) among the study population. The table categorizes study population based on the length of hospital stay: (≤ 7 days, 8-14 days, and 15-21 days). Out of the total 75 cases, all 22 cases with a hospital stay of (≤ 7 days) resulted in survival (100%). For cases hospitalized for 8-14 days (43 cases), 11 resulted in deaths (25.58%) and 32 in survivors (74.42%). In the 15-21 days category (10 cases), 6 cases resulted in deaths (60%) and 4 in survivors (40%). Statistical analysis ($\chi 2 = 14.61$, $p = 0.001$) reveals a significant association between hospital stay duration and deaths. (Table 3)

The relationship between ICU (Intensive Care Unit) stays duration and outcomes (non survivors and survivors) among the study population. The table categorizes cases into three groups based on ICU stay duration: A (< 5 days), B (6-10 days), and C (11-20 days). Among the total 75 cases, all 29 cases with an ICU stay of < 5 days resulted in survival (100%). For cases staying in the ICU for 6-10 days (34 cases), 7 resulted in deaths (20.59%) and 27 in survivors (79.41%). In the 11–20-day category (12 cases), 10 cases resulted in deaths (83.33%) and 2 in survivors (16.67%). Statistical analysis ($\chi 2 = 33.78$, $p < 0.001$) indicates a highly significant association between ICU stay duration and deaths. (Table 3)

Table 4: Comparison of mean Serum CK Levels, mean serum magnesium levels with outcome

Outcome	Mean Serum CK Levels (IU/L)	Mean Magnesium levels (mg/dl)
Survivors (58)	712.10 ± 527.57	1.82 ± 0.25
Non survivors (17)	1388.71 ± 1029.81	1.50 ± 0.23
	t= 3.66, p < 0.001, Significant	t = 4.721, p < 0.001, Significant

The mean Serum Creatine Kinase (CK) levels between outcomes (survivors and non survivors) among the study population. The table indicates that among those who survived, the mean Serum CK level was 712.10 IU/L with a standard deviation (SD of 527.57 IU/L). In contrast, among those who died, the mean Serum CK level was higher at 1388.71 IU/L, with a (SD of 1029.81 IU/L). For the total cases studied, the mean Serum CK level was 865.47 IU/L, with a (SD of 609.98 IU/L). The statistical analysis ($P = 0.014$) indicates a significant difference in Serum CK levels between survivors and non-survivors, suggesting that higher CK levels may be associated with increased mortality in cases of poisoning. (Table 4)

The mean serum Magnesium levels between outcomes (survivors and non survivors) among the study population. Among patients who survived, the mean serum Magnesium level was 1.82 mg/dl (SD = 0.25 mg/dl), whereas among those who died, the mean level was lower at 1.50 mg/dl (SD = 0.23 mg/dl). Across all cases studied, the mean Serum Magnesium level was 1.75 mg/dl (SD = 0.28 mg/dl). The statistical analysis ($P < 0.001$) indicates a significant difference in Serum Magnesium levels between survivors and non-survivors, suggesting that

lower Magnesium levels may be associated with increased mortality in cases of poisoning. (Table 4)

Discussion:

The study to evaluate the levels of serum creatinine kinase and serum magnesium in patients with acute organophosphate poisoning, aiming to understand the extent of muscle injury and the physiological disturbances associated with this condition. We compared our study with other similar studies from India and overseas. Also, the present study was done on patients admitted in the hospital setting.

In this study, frequency distribution of study population shows a predominance of middle-aged individuals, with the highest percent of patients (49.33%) in the 31-40 years age group. This finding aligns with other studies indicating that organophosphorus (OP) poisoning is more common among the middle-aged population due to occupational exposure and socio-economic stressors (Singh et al.) [82] Another study by Bhatt et al. [83] found similar age distribution, with a significant number of patients in the (31-40 years) age group, underscoring the vulnerability of this age group to OP poisoning.

The gender distribution in this study shows a higher prevalence of males (66.67%) compared to females (33.33%). This pattern is consistent with the findings of Gupta et al., [84] who reported a higher incidence of OP poisoning among males due to their greater involvement in agriculture and pesticide handling. Similarly, Kar et al. [85] observed a male predominance in their study, attributing it to the higher likelihood of males engaging in high-risk occupations.

The study indicates that 53.33% of patients were engaged in agriculture, reflecting the significant occupational risk associated with pesticide use. This is supported by Patel et al., [86] who found a higher incidence of OP poisoning among agricultural workers. Similarly, Kumar et al. [87] reported that agricultural labourers are at increased risk due to frequent and unprotected exposure to pesticides.

The majority of study population in our study involved Chlorpyriphos (81.33%), highlighting its prevalent use and potential for misuse. Reddy et al. [88] also identified Chlorpyriphos as a common OP compound implicated in poisoning cases in their study. Another study by Sharma et al. [89] corroborates these findings, reporting a high incidence of Chlorpyriphos poisoning in agricultural settings.

The study found that 46.67% of cases had moderate Peradeniya OP scores, with 25.33% categorized as severe. This distribution is similar to findings by Singh et al., [82] who reported that moderate to severe cases constituted a significant proportion of OP poisoning incidents. In contrast, Verma et al. [90] found a higher percent of severe cases, which they attributed to delayed hospital presentations.

In the study, 77.33% of patients survived, while 22.67% succumbed to poisoning. This survival rate aligns with the findings of Reddy et al. [88], who reported a survival rate of around 75% in their cohort. Another study by Kumar et al. [87] showed similar outcomes, emphasizing the critical role of timely medical intervention in improving survival rates.

The analysis indicates a significant association between the quantity of poison exposure and mortality ($p = 0.018$), with higher exposure correlating with increased deaths. This finding is consistent with Gupta et al., [84] who found that larger quantities of poison ingestion were associated with higher fatality rates. Similarly, a study by Patel et al. [86] reported a direct correlation between the amount of poison ingested and the severity of clinical outcomes.

A significant association was observed between higher POP scores and increased mortality ($p = 0.002$), underscoring the utility of POP scores in prognosticating outcomes. This is supported by Singh et al. [82], who demonstrated that higher POP scores were linked with poorer outcomes. Verma et al. also highlighted the predictive value of POP scores in determining the severity and prognosis of OP poisoning cases.

Our study indicates a significant association between longer hospital stays and increased mortality ($p = 0.001$). This finding is supported by Reddy et al. [88], who observed that prolonged hospitalization was associated with poorer outcomes. Similarly, Kumar et al [87]. reported higher mortality rates in patients with extended hospital stays.
We found a highly significant association between longer ICU stays and increased mortality ($p < 0.001$), highlighting the severity of cases requiring prolonged intensive care. This is in line with Gupta et al. [84], who reported that extended ICU stays were indicative of severe poisoning and worse prognosis. Patel et al. [86] also found similar correlations in their study.
The study shows that higher mean Serum CK levels are significantly associated with increased mortality ($p = 0.014$). This finding is consistent with Singh et al. [82], who reported elevated Serum CK levels as a marker of severe poisoning and poor outcomes. Verma et al. [90] also found higher CK levels in non-survivors, suggesting its potential role as a prognostic biomarker.
We observed a significant association between lower mean Serum Magnesium levels and increased mortality ($p < 0.001$). This is supported by Reddy et al. [88], who found that hypomagnesemia was linked with poorer clinical outcomes in OP poisoning cases. Similarly, Sharma et al.[89] reported that lower magnesium levels were associated with higher mortality rates.

Conclusion:

The present study highlighted the significant association between serum creatine kinase and serum magnesium level with complication of organophosphorus poisoning while Peradeniya Organophosphorus Poisoning scale is used to categorized severity of the cases which found to be excellent classification system for categorising the severity of cases with acute organophosphorus poisoning. While serum creatine kinase can be an efficient biomarker as predictor of severity of acute organophosphorus poisoning and be used additional to serum acetylcholinesterase levels considering the cost and nonavailability. Serum magnesium can be used as the predictor of severity of acute organophosphorus poisoning to reduce the morbidity and mortality.

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