

## **A Study of Socio-demographic Profile and Role of Serum Amylase, Lipase and Creatine Phosphokinase Level in Prognosis of Organophosphorus Poisoning**

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### **Abstract**

**Introduction:** Organophosphates are the most common suicidal poisons in developing countries and mortality continuous to be high due to these. A causal relationship between organophosphate exposure and development of acinar cell injury had been demonstrated in experimental animal model. The need for newer biomarkers in relation to organophosphorus poisoning started a very long time ago. Present study was conducted to assess parameters like serum amylase, serum lipase and creatine phosphokinase to predict the severity and prognosis in organophosphorus poisoning cases.

**Materials and methods:** A hospital based observational study was carried out at Department of Medicine of a tertiary care centre at Western Rajasthan (India) from April 2017 to March 2018. Permission from institutional ethics committee was taken and 100 organophosphorus poisoning cases were recruited for

the study. After obtaining socio-demographic informations, detailed history was taken and medical examination was done. Biochemical tests like serum amylase, serum lipase and creatinine phosphokinase were done. The data were statistically analysed using student 't' test. Pearson's correlation coefficient (r) was calculated for amount of organophosphorus substance consumed with serum enzyme levels. P-value < 0.05 was considered as statistically significant.

**Results:** Out of 100 cases 55 were males and 45 were females. Maximum cases (66%) were in the age group of 14-25 years. 85% cases were survived and 15% were expired. Mean serum amylase, serum lipase and creatinine phosphokinase levels in survived cases were 89.40±62.36 IU/L, 84.44±71.44 IU/L and 628.21±524.90 IU/L respectively, while in expired cases these enzyme levels were 308.73±84.31 IU, 245.53±34.21 IU/L and 1995.73±636.46 IU/L respectively (p-value<0.01). 27% cases needed

ventilator support. Mean serum amylase, serum lipase and creatinine phosphokinase levels were significantly high ( $p$ -value $<0.01$ ) in intubated cases as compared to non-intubated cases  $243.18 \pm 109.01$  v/s  $77.6 \pm 51.38$ ,  $203.22 \pm 81.20$  v/s  $78.26 \pm 62.42$  and  $1737.62 \pm 642.67$  v/s  $498.87 \pm 402.68$  IU/L respectively.

**Conclusion:** Mean duration of hospital stay in survived cases was 6.4 days. Higher enzyme levels were associated with increased mortality, longer duration of stay in hospital and need for intubation of cases.

**Keywords:** Organophosphorus, Poisoning, Serum amylase, Serum lipase, Serum creatinine kinase.

### Introduction

The organophosphorus compounds mainly used in agriculture as pesticides. Some preparations are used as veterinary and human medicine. In commerce, organophosphorus compounds have been used as lubricants, plasticizers and flame retardants. The development and use of some of these compounds as very potent agents of warfare is of clinical significance. The importance of pesticides in India can be understood from the fact that currently, India is the largest producer of pesticides in Asia and ranks 12<sup>th</sup> in the world for the use of pesticides. A vast majority of the population in India is engaged in agriculture and is therefore exposed to the pesticides used in agriculture.<sup>1</sup>

Organophosphate based pesticides are widely used and have emerged as the major contributors to ill health associated with pesticides worldwide. Poisons are subtle and silent weapons that can easily use without violence and often without arousing suspicion. Most of these poisons are usually ingested with a suicidal intent. WHO in year 2012 reported that more than 90% of fatal poisoning cases are seen in middle and low income countries.<sup>2</sup>

National poison information centre India, reported that

suicidal poisoning with house hold agents such as organophosphorus, carbamates, pyrethrinoidsetc; being cheap, highly toxic, capable of being taken along with food or drink and easy availability, is the most common modality of poisoning. In India, the exact incidence cannot be defined due to gross under reporting of cases of poisoning and also due to lack of research in this area.<sup>3</sup>

Previously, various studies were conducted regarding mortality, morbidity and clinical manifestations of organophosphorus toxicity. Multisystem manifestations of organophosphorus toxicity were highlighted in these studies including cardiovascular, neurological and respiratory manifestations.<sup>4</sup> Apart from few case reports, very few studies were conducted till date to evaluate the effect of organophosphorus compounds on hepatobiliary system and pancreas.<sup>5</sup>

The pathology behind the development of acute pancreatitis in cases after organophosphorus ingestion is not very clear. Pancreatic ductal hypertension and stimulation of exocrine, pancreatic secretion secondary to cholinergic stimulation are considered to be responsible for the development of pancreatitis. Furthermore, organophosphates such as echothiophate, which inhibit the two cholinesterase isoenzymes (butyryl cholinesterase and acetyl cholinesterase) in the human pancreas, increase pancreatic sensitivity to acetylcholine. Liver involvement observed in these cases was mostly secondary to pancreatic involvement.<sup>6</sup>

Previous studies had shown that serum cholinesterase can be a useful tool in the diagnosis of organophosphorus poisoning but it's prognostic role is very minimal. The present study was planned to know the prognostic role of pancreatic enzymes like serum amylase, serum lipase and creatinine phosphokinase in

organophosphorus poisoning cases.

### Material and Methods

It was a hospital based descriptive study, carried out in Department of Medicine, Dr. S.N. Medical College, Jodhpur (Rajasthan) from April 2017 to March 2018. Approval from institutional ethics committee was obtained before the start of study. Total 100 organophosphorus poisoning cases were recruited in the study after taking informed written consent. Cases confirmed by history, circumstantial evidence of ingestion, admitted within 12 hours of ingestion with characteristic clinical findings and basic and relevant laboratory investigations were included in the study while patients with feature of exposure to another compound not relating to organophosphorus poison, mixed poisoning, chronic alcoholic, history suggestive of liver disease, myopathy, malignancy, autoimmune disease, renal disease and cardiac disease were excluded from the study.

Eligible cases or their close relatives were interviewed and in-depth history was taken. Socio-demographic information like age, sex, locality, religion, marital status, occupation, type of family and socio-economic status were noted in a pre-designed performa. General and systemic examination was done and blood samples were obtained for biochemical examination. Serum amylase, serum lipase and creatinine phosphokinase (CPK) titre were noted. The collected data were entered in Microsoft Excel 2016 Spreadsheets and statistically analysed using unpaired 't' test. Pearson's correlation coefficient (r) was calculated for amount of organophosphorus substance consumed with serum enzyme levels. P-value < 0.05 was considered as statistically significant.

### Results

Out of 100 organophosphorus poisoning cases included in the present study, 55 were males and 45 females. Highest number of cases (66%) were belonged to age group 14-25 years with equal distribution, followed by 26-35 years (22%). 71% cases were literate while 29% cases were illiterate. Farmers were most commonly involved in organophosphorus poisoning (29%) followed by housewives and students (26% each). Others were labourers (10%), drivers (2%) and self-business (7%). 60% cases were married and 40% were unmarried. About 86% cases belonged to joint families while only 14% were from nuclear families. Majority of cases (90%) were from rural areas while only 10% cases were from urban localities (Table-1).

Figure-1 shows the type of organophosphorus compound used by study population. Most common type was chlorpyrifos (28%) followed by malathion (23%), monocrotophos (19%), endosulphan (9%), tik-20 (8%), parathion (7%) and metacid (6%). 81% patients consumed poison with suicidal intention while 10% patients had accidental exposure and 9% had occupational exposure (Figure-2).

Out of 100 subjects, 85 survived and 15 expired. Mean serum amylase, lipase and CPK levels in survived subjects were  $89.40 \pm 62.36$  IU/L,  $84.44 \pm 71.44$  IU/L and  $628.21 \pm 524.90$  IU/L while in expired patients these were  $308.73 \pm 84.31$  IU/L,  $245.53 \pm 34.21$  U/L and  $1995.73 \pm 636.46$  IU/L. The difference was statistically significant in each enzyme (p-value < 0.01). Out of 100 patients, 27 required mechanical ventilation and among them 12 (44.44%) were survived and 15 (55.56%) were expired. The mean serum amylase, lipase and CPK levels in intubated patients were  $243.18 \pm 109.01$  IU/L,  $203.22 \pm 81.20$  IU/L and  $1737.62 \pm 642.67$  IU/L while in non-intubated patients these levels were  $77.6 \pm 51.38$

IU/L, 78.26±62.42 IU/L and 498.87±402.68 IU/L. The difference was statistically significant in each enzyme (p-value<0.01). Out of 100 patients, 34 were admitted in intensive care unit. The mean serum amylase, lipase and CPK levels in patients admitted in ICU were 222.09±114.52 IU/L, 195.30±89.51 IU/L and 1554.36±680.54 IU/L while in patients admitted in ward, these levels were 73.16±44.28 IU/L, 70.97±49.48 IU/L and 478.20±430.51 IU/L. The difference was

statistically significant in each enzyme (p-value<0.01) (Table-2).

The correlation of serum enzymes level (amylase, lipase and CPK) with amount of organophosphorus compound consumed in both survived and expired patients was seen. Linear correlation was found significant in survived patients while it was non-significant in expired patients (Tables-3-5 & Figure-3-5).

Table 1: Socio-demographic profile of study subjects (N=100)

Socio-demographic factor	Male (n)	Female (n)	Total (n)
Age:			
14-25	33	33	66
26-35	14	8	22
36-45	6	3	9
46-55	2	1	3
Education status:			
Illiterate	18	11	29
Literate	37	34	71
Occupation:			
Farmer	28	1	29
House wife	0	26	26
Driver	2	0	2
Student	8	18	26
Labour	10	0	10
Self-business	7	0	7
Marital status:			
Married	34	26	60
Unmarried	21	19	40
Family type:			
Joint	47	39	86
Nuclear	8	6	14
Locality:			
Rural	53	37	90
Urban	2	8	10

Table 2: Association of mean serum enzyme levels with patient's outcome, need for mechanical ventilation and need for ICU admission

Event of interest	Serum Amylase (Mean±SD)	Serum Lipase (Mean±SD)	CPK (Mean±SD)
Outcome of patient:			
Survive	89.40±62.36	84.44±71.44	628.21±524.90
Expired	308.73±84.31	245.53±34.21	1995.73±636.46
P-value*	<0.0001	<0.0001	<0.0001
Need of mechanical ventilation:			
Yes	243.18±109.01	203.22±81.20	1737.62±642.67
No	77.6±51.38	78.26±62.42	498.87±402.68
P-value*	<0.0001	<0.0001	<0.0001
Mode of admission:			
ICU	222.09±114.52	195.30±89.51	1554.36±680.54
Ward	73.16±44.28	70.97±49.48	478.20±430.51
P-value*	<0.0001	<0.0001	<0.0001

\*Unpaired 't' test

Table-3: Correlation of serum amylase level with amount of organophosphorus substance consumed in patient outcome

Outcome	Amount consumed (ml)	Serum amylase (IU/L)	Pearson's correlation coefficient (r)	P-value
Survived	55.17±27.72	89.40±62.36	0.255	0.018
Expired	149.33±39.86	308.73±84.31	0.151	0.59

Table-4: Correlation of serum lipase level with amount of organophosphorus substance consumed in patient outcome

Outcome	Amount consumed (ml)	Serum lipase (IU/L)	Pearson's correlation coefficient (r)	P-value
Survive	55.17±27.72	84.44±71.44	0.225	0.037
Expired	149.33±39.86	245.53±34.21	-0.157	0.575

Table-5: Correlation of serum creatine kinase level with amount of organophosphorus substance consumed in total patient

Outcome	Amount consumed (ml)	Creatinine phosphokinase (IU/L)	Pearson's correlation coefficient (r)	P-value
Survive	55.17±27.72	628.21±524.90	0.204	0.06
Expired	149.33±39.86	1995.73±636.46	-0.487	0.067

Figure 3: Correlation of serum amylase level with amount of OP substance consumed in patient outcome

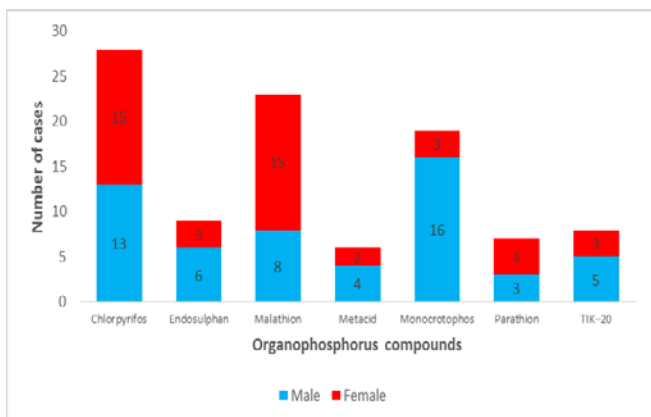


Figure 1: Type of organophosphorus compound consumed

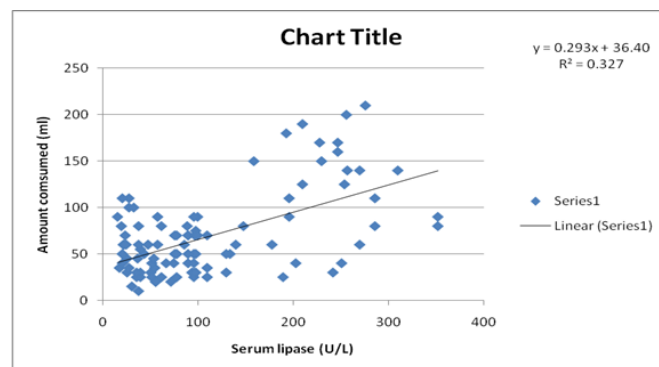


Figure 4: Correlation of serum lipase level with amount of OP substance consumed in patient outcome

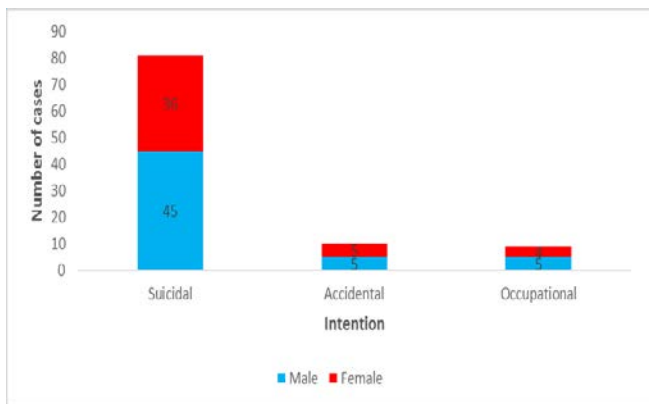


Figure 2: Intention of organophosphorus consumption

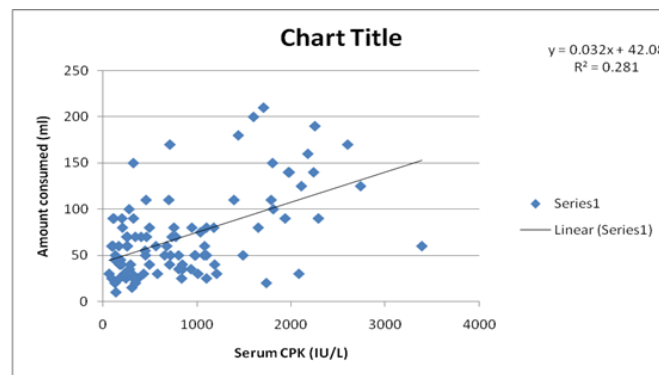
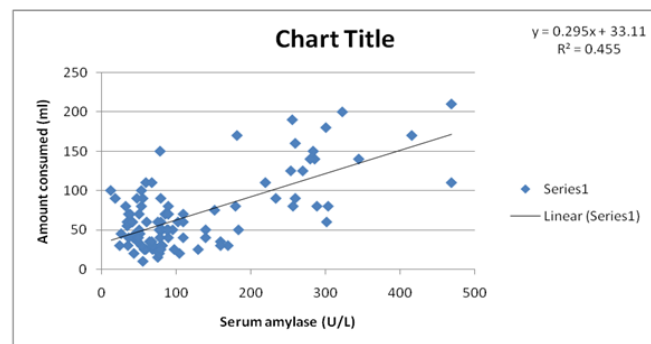


Figure 5: Correlation of serum creatine kinase level with amount of OP substance consumed in patient outcome



### Discussion

The present study was a hospital based, observational, cross-sectional study carried out in western Rajasthan. The socio-demographic profile and role of serum levels of amylase, lipase and creatine phosphokinase (CPK) as prognostic marker in organophosphorus poisoning

cases were assessed. The serum enzyme levels were determined at the time of admission.

The median age of the study subjects was found to be 25 years and 88% of them were from age group of 14-35 years. Earlier, Gupta et al<sup>7</sup> found major age group was 21-30 years (47.5%) and Sarkar et al<sup>8</sup> found major age group was 16-30 years (65.6%). The younger age group was commonly involved in organophosphorus poisoning. It may be due to lack of stress bearing capacity and unemployment among youths. In present study, out of 100 study population, 71 were literates and 29 were illiterate. Contrary results were observed by Bag et al<sup>9</sup> where they found 62% case were illiterates.

Farmers were most commonly (29%) involved in organophosphorus poisoning followed by housewives (26%) and students (26%). In previous studies by Sarkar et al<sup>8</sup> and Kora et al<sup>10</sup> housewives were most commonly involved (37.4%, 37.76% respectively) followed by agricultural workers (23%, 18.24% respectively). In India, the farmers are economically very poor. Due to loss of crops by natural disasters and other economic loss, especially due to major illnesses, the farmers took the decision to commit suicide. Condition of women in rural area are also very bad due to unemployment, separated families and other social conditions. As organophosphorus compounds are commonly used as pesticides and insecticides in agriculture, so these substances are easily accessible and available to farmers and housewives in rural areas. In present study majority of the subjects (60%) were married. Almost similar results were observed by Sarkar et al<sup>8</sup> (70.7% married) and Kora et al<sup>10</sup> (60%). The level of stress and responsibility is higher among the married persons which may lead to more suicidal attempts. 86% cases belonged to joint family while

only 14% cases belonged to nuclear family which was contrary with the previous study by Gupta et al<sup>7</sup> where they found about two third of the cases were from nuclear families (74.5% vs 24.5%). Majority of the study subjects belonged to rural area (90%) in the present study. Findings of the authors like Sarkar et al<sup>8</sup> (89.6%), Bartra et al<sup>11</sup> (83%) and Dash et al<sup>12</sup> (58.2%) were consistent with the results of the present study. Agriculture is the main occupation in rural areas where organophosphorus compounds are abundantly used and easily available.

Suicide (81%) was the most common intention in organophosphorus poisoning cases followed by accidental (10%) and occupational (9%) ingestion. In study done by Sarker et al<sup>8</sup>; 77% of study population had suicidal intention to consume organophosphorus compound and in study done by Bartra et al<sup>11</sup>; this proportion was 64.3%. These findings were almost similar to present study. In the present study chlorpyrifos was found to be the most commonly consumed organophosphorus poison as it the widely used as pesticide in this area.

Acute organophosphorus poisoning often presents as a medical emergency requiring monitoring and management in intensive care unit. Management of poisoning depends on clinical severity and is assessed by clinical signs and symptoms as well as laboratory evaluation. In present study, mean CPK levels on day-1 was 628.21 IU/L in survived patients and 1995.75 IU/L in expired patients. The findings were consistent with previous study by Bhattacharyya et al<sup>13</sup> (mean CPK was elevated in survived and fatal cases, 456.06, 2139.8 IU/L respectively). The present study showed the high degree of correlation between initial serum CPK levels and outcome of patients, need for mechanical ventilation and need of ICU care. Initial high level of

CPK was associated with high mortality rate, increased need of ventilator support and increased need of ICU care. These correlations were found statistically significant (p-value<0.01). It is known that serum CPK levels increased in muscle injury and is used as an indicator in muscle injury. High serum CPK activity shows the magnitude of acute muscle necrosis. The presence of muscle fibre necrosis in organophosphorus poisoning has already been demonstrated in animal experiments by Calore et al<sup>14</sup>. It is also measured to determine the course of muscle injury.

Organophosphorus insecticides increase the intraductal pressure and exocrine pancreatic flow. The increase in pressure leads to extravasation of pancreatic fluid. This increased pancreatic exocrine flow could be due to direct cholinergic hyperstimulation of pancreatic acinar and ductal cells. In the present study mean plasma levels of amylase and lipase in survived patients were 89.40 IU/L and 84.44 IU/L respectively and in expired patients these were 308.73 IU/L and 245.53 IU/L. The high levels of serum amylase and lipase were associated with increase mortality. These correlations were found statistically significant (p-value<0.01).

The mean levels of amylase and lipase in patients who developed organophosphorus respiratory failure and need mechanical ventilation were 243.18IU/L and 203.22 IU/L while these values in patient who did not require mechanical ventilation were 77.6 IU/L and 78.26 IU/L. Again, the high levels of serum amylase and lipase were associated with increase need of mechanical ventilation. These correlations were found statistically significant (p-value<0.01). In a previous study by Lin et al<sup>15</sup>; plasma amylase level of the patient group with respiratory failure was significantly higher than those without respiratory failure (436.1±/-87.1 vs. 181.3±/-29.6, p-value<0.01). Of course, mean days of

hospitalization in the respiratory failure group were significantly longer than the other group (12.1±/-2.1 vs. 5.4±/-1.9, p<0.05).

### Conclusion

Estimation of serum amylase, lipase and CPK levels were high in organophosphorus poisoning patients who expired, needed prolonged stay and were intubated. So, these enzyme levels might be helpful in predicting as well as assessing the prognosis of patients of organophosphorus poisoning.

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