ORIGINAL RESEARCH PAPER

Internal Medicine

# STUDY OF SERUM AMYLASE LEVELS IN ORGANOPHOSPHATE POISONING

**KEY WORDS:**
Organophosphate, Intoxication, Amylase, Prognosis

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**ABSTRACT**

Organophosphate (OP) insecticides are the most probable common cause of acute poisonings in developing countries. OP intoxication often presents as medical emergencies, and its related morbidity and mortality have not decreased despite major advances in critical care. This study aims to determine the impact of serum amylase level for estimation of prognosis in patients with acute OP poisoning. **Method:** This prospective observational hospital-based study was performed on 100 patients with acute OP poisoning. Demographics data, clinical profile, serum amylase levels, complications, hospital stay and outcome were determined. Data were analyzed in the form of a frequency distributions using SPSS 26.0 version software. **Result:** Most patients were young adults with mean age of 29yrs ± 11yrs with slightly male predominance. Mean serum amylase level was significantly higher among patients with morbidity and mortality. **Conclusion:** Among patients with OP poisoning, higher serum amylase than normal was associated with severe clinical course and increased risk for mortality. Determination of serum amylase can be an effective marker of the prognosis and clinical course among OP poisoning patients.

## INTRODUCTION:

Poison is a substance (solid, liquid, gaseous) which if introduced in the living body or brought into contact with any part thereof will produce ill-health or death by its constitutional or local effects or both. Thus, almost anything is poison.

"THE DOSE MAKES THE POISON" ……Paracelsus once said.[1] Insecticides have significant economic, environmental and public health impacts. Their usage helps to improve human nutrition through longer storage life, greater availability, and lower costs of foods. They also assist in the control of food-borne and vector borne diseases.[2] Organophosphate insecticides are one of the most predominant insecticides used today all over the world. The insecticides which have been developed to protect crops are now themselves causing significant morbidity and mortality by means of environmental pollution and acute poisoning.

The widespread and negligent use, not so stringent legislation and personal problems have made the pesticides, the most commonly encountered substance in human poisoning. The organophosphates are considered as the king of pesticides, because of their magnitude of use in agriculture. Acute poisoning by organophosphate pesticides has reached epidemic proportions in most parts of the world, particularly in developing agrarian countries, where the toxicity of available poisons and the paucity of appropriate medical facilities trigger a high fatality rate[3]. The ease of access and socio-cultural factors plays important role in choice of organophosphate as a self-poison and the incidence is higher in a young economically active group with a common fatality ratio of 20%[4].

According to WHO, worldwide estimates of pesticide poisoning is 3 million each year, with 2 million hospitalized due to suicidal attempts resulting in 2,20,000 deaths, the majority of which are actually intentional[5]. Poisoning due to occupational exposure, account for about one-fifth of the incidents, with a fatality rate of less than 1%. More than 90% of the non-occupational incidents are suicidal, with a fatality rate of more than 10% and the majority of the subjects are young males. Accidental exposures account for 8-10% of the incidents and homicidal uses (less than 1%) are other forms of poisoning. The reported overall mortality following organophosphate insecticide poisoning varies from 4% to 30% in different countries and institutions. In India, organophosphate compounds cause more self-poisoning deaths in southern and central India. In northern part of India, aluminum phosphide causes most deaths with a fatality rate of 90%. Other pesticides used for self-poisoning includes organochlorines, carbamates and pyrethroids. Organophosphate compounds are particularly used as pesticides and their exposure is highly prevalent in developing countries[4]. Toxic effects of organophosphates are associated with significant morbidity and mortality and are a major global clinical burden. Occupational, suicidal or homicidal exposure to organophosphate compounds produces a characteristic syndrome which is treatable in humans. Early recognition and timely intervention of toxicity from these compounds are of great importance to emergency physicians and patients[6]. Mortality ranges from 4-30% in Indian studies. Neurologic, cardiac, and respiratory complications are the main causes of morbidity and mortality in organophosphate poisoning patients. The involvement of other systems can also occur but it is very uncommon[7].

Chemically, organophosphate compounds are alkyl phosphates and aryl phosphates. Alkyl phosphates compounds which are commonly used include hexaethyl tetraphosphate (HETP), tetraethyl pyrophosphate (TEPP), octamethyl pyrophosphoramide (OMPA) and Malathion whereas Parathion and Diazinon are commonly used aryl phophates compounds. Poisoning from these compounds can occur from inhalation, ingestion and absorption through unbroken skin. The organophosphate compounds act by inhibiting the function of enzyme acetylcholine esterase (AChE) primarily found at postsynaptic neuromuscular junctions causing overstimulation of acetylcholine receptors. Signs and symptoms of poisoning are mainly due to muscarinic, nicotinic and central nervous system receptor over stimulation[8].

Any exposure to organophosphate compounds can cause

inhibition of enzyme acetylcholinesterase, thereby showing signs & symptoms of toxicity such as hyper salivation, nausea, diaphoresis, blurring of vision, headache, diarrhea and bronchorrhea. Following ingestion of organophosphate compounds, the symptoms developed by a patient can vary, with SLUDGE (salivation, lacrimation, urination, defecation, gastric cramps, emesis) symptoms occurring within minutes to hours (acute manifestations)[9]. Some patients may develop delayed (24 hours to 2 weeks) or late (>2 weeks) complications from organophosphate poisoning[10]. The complications include seizures, acidosis, acute renal failure, respiratory paralysis, arrhythmia, aspiration etc. and death may be due to one or combination of above complications[11]. Acetylcholinesterase (AChE) is a cholinergic enzyme primarily found at postsynaptic neuromuscular junctions, especially in muscles and nerves and is primarily responsible for degradation of neurotransmitter acetylcholine leading to the termination of nerve impulses. Organophosphate compounds irreversibly block the active site of serine residue of AChE by undergoing nucleophilic attack to produce serine-phosphoester adduct. This irreversible inactivation leads to an excess accumulation of acetylcholines in the peripheral and central nervous system causing cholinergic manifestations[12]. Amylase is an enzyme related to gastrointestinal system of human body and helps in digestion of starch by cleaving it into smaller carbohydrate groups and finally into monosaccharides, by hydrolysis of internal alpha 1,4 gycoside bonds, which results in the production of maltose and oligosaccharides[13].

Elevated serum amylase levels a.k.a. Hyperamylasemia secondary to pancreatic injury because of parasympathetic overstimulation and hypersecretion has been noted in human beings. Studies have shown that serum amylase levels above normal range on the day of admission was related to the development of respiratory failure[14]. Organophosphate compound poisoning is associated with numerous biochemical abnormalities, among which hyperamylasemia is well documented and may be due to excessive cholinergic stimulation of pancreas. Acute pancreatitis is frequent in organophosphate poisoning and increased serum amylase is less specific and sensitive. Several studies reported elevated serum amylase levels in patients with organophosphate compound poisoning and found hyperamylasemia to be closely related to clinical severity and the presence of shock[15]. It is known that in cases of poisoning due to suicidal intention, amount of poison ingested is more which can damage the tissues and organs. Hence along with the clinical assessment, laboratory evaluation also becomes very important to confirm the poisoning and extent of organ damage[16]. In India, organophosphate compounds are principally used as pesticides and their exposure is highly prevalent as these compounds are easily available. Neurologic, cardiac and respiratory complications are the main causes of morbidity and mortality due to suicidal, occupational or homicidal exposure to organophosphate compounds. Few studies have been conducted in this part of country where use of serum amylase as a predictor of severity and outcome in organophosphate poisoning has been studied. In this study we intend to know the clinical significance of serum amylase levels in organophosphate poisoning patients at the time of admission in assessing the severity and outcome of patients.

**STUDY**

A prospective observational hospital-based study was performed on 100 patients admitted in Medicine Department of Jhalawar Medical College, Jhalawar with history of exposure and clinical manifestations of organophosphate poisoning w.e.f. March 2021 to November 2021. Permission was obtained from the ethics committee of the institution.

**1. SOURCE OF DATA:**

Patients admitted under Department of General Medicine, Jhalawar Medical College, Jhalawar, Rajasthan during the study period fulfilling the inclusion and exclusion criteria were included in this study. The patients were followed up till their recovery, discharge or death.

**2. METHOD OF COLLECTION OF DATA:**

Socio demographic, history, clinical and laboratory data was elicited in the patients as per preformed proforma and final analysis was made at the end of the study to achieve the fore mentioned goals.

**3. INCLUSION CRITERIA:**

1) Patient aged above 18 years, regardless of sex of the patients.
2) Patient with history of exposure to organophosphate poisoning with clinical features of organophosphate poisoning

**4. EXCLUSION CRITERIA:**

1) Patients aged below 18 years regardless of sex were excluded.
2) Patient with indication of exposure to an entirely different poison other than organophosphate poison.
3) Patient who consumed poison along with alcohol.
4) Patients who are chronic alcoholics.
5) Patients with history suggestive of gall stone disease.
6) Patients with history of intake of drugs e.g., Azathioprine, 6-Mercaptopurine, Thiazides, Furosemide, Pentamidine, Steroids, Valproate and Sulphonamides.
7) History of abdominal trauma.
8) Gone through ERCP in previous 24 hours.
9) Pregnancy.
10) Patient with history of renal or hepatic disease.
11) Patient with history of lipid disorders.
12) History of parotid gland disease.
13) Pre-existing pancreatic disease.

**5. METHODOLOGY:**

After obtaining approval and clearance from the institutional review board, only those patients meeting the inclusion and exclusion criteria were enrolled for the study.

Informed consent was obtained from each participant.

Data regarding name, age, gender, religion, occupation, address was noted.

After enrollment, detailed history & clinical examinations findings were noted.

Organophosphate poison particulars like name of poison (chemical/trade name), nature of poison (liquid/powder), mode and intension of consumption (alone, with water, accidental, suicidal etc.), signs and symptoms after consumption (shortness of breath, cough, chest pain, syncope, vomiting etc.), past history of similar attempts, psychiatric illness, co morbid illness, personal history.

All patients were subjected to laboratory investigations including-

- Complete Blood Count
- Blood urea & Serum creatinine
- Blood sugar level
- Serum electrolytes (sodium, potassium)
- Serum bilirubin
- Urine routine examination
- Chest x-ray, USG abdomen and ECG.
- Serum amylase estimation on admission and after 24 hours

**6. DIAGNOSTIC CRITERIA**

Normal Range of Serum Amylase = 25-115 U/L
Serum Amylase levels >115 U/L is considered as Hyperamylasemia.

## 7. STUDY DESIGN
Hospital based prospective observational study in patients admitted under Department of General Medicine in Jhalawar Medical College and Hospital, Jhalawar.

## 8. STUDY PERIOD
The study was carried out from March 1, 2021 to November 30, 2021

## 9. SAMPLE SIZE
n = t2 x p x (1-p)/e2
Where t = 95% confidence interval (t=1.96)

p = Proportion of Organophosphate poisoning patients among total IPD of Medicine Department SRG Hospital, Jhalawar in month of September 2020 (p = 81/1354 = 0.05982 ~ 0.06)
e = allowed error 5% (e = 0.05)
Putting these values
n = (1.96)2 x 0.06 x (1-0.06) / (0.05)2
n = 86.63 ~ 87

Effect of error N = n + 5% = 87 + 5% of 87 = 87 + 4.35 = 91.35 ~ 92

Now we increased the sample up to a minimum of 100 cases. So, minimum 100 cases of patients above 18 years with organophosphate compound poisoning were included in the study.

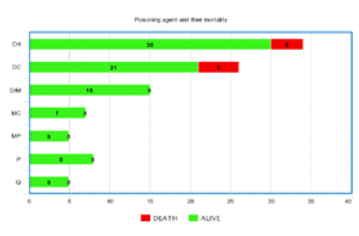
## 10. SAMPLING TECHNIQUE
Systematic random allocation method.

## 11. STATISTICAL ANALYSIS:
The Data collected was entered on Excel Spreadsheet after coding. It was processed and analyzed using SPSS 26.0 version statistical software. Mean, standard deviation and proportions were calculated. Appropriate test of significance was used based on type of data. A p value of <0.05 was considered significant.

## RESULT
Out of 100 patients, 52 were male and 48 were females, Mean age was 29.04yrs ±11.03yrs and most common age group involved was 21-30yrs (45%).

Most of the patients belong to rural areas (76%) in comparison to urban areas (24%). Most common occupation was farming. In the identified cases Chlorpyrifos and Dichlorvos were among most commonly used substance. Other substance were Dimethoate, Monochrotophos, Methylparathion, Parathion and Quinophos (Fig.01).

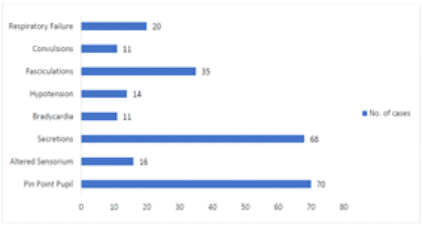
**Figure 1 : Poisoning Agent and their mortality**




CH- Chlorpyrifos DC- Dichlorvos DIM- Dimethoate MC- Monochrotophos
MP- Methylparathion P- Parathion Q- Quinophos

Most frequent clinical features were Miotic pupils (70%), excessive secretions (68%), Muscle Fasciculations (35%), Respiratory failure (20%), Altered sensorium (16%), Hypotension (14%) (Fig. 02). Clinically significant bradycardia was seen in 11% cases. The mean hospital stay was 4days±1days and 30% of patients admitted in ICU. Serum amylase levels at the time of admission (170.46±136.80 U/l) were significantly higher in comparison to at 24hrs of admission (135.87±110.91 IU/L).

**Figure 2: Clinical features**




Symptomatic patients had higher level of serum amylase at admission. Table shows number of patients with elevated amylase levels among different clinical feature groups. In our study mortality rate was 9%. Out of these Chlorpyrifos was most common compound responsible for mortality (56%) (Fig. 01). Patients with respiratory failure and convulsions had higher mortality. Mean serum amylase level at presentation of non-survivors was 488.33±89.58IU/L which is significantly higher in comparison to survivals (139.02±93.64IU/L, p value <0.001).

## CONCLUSIONS:
By analyzing our study data, we found that poisoning was predominant in the age group of 21-31 years (45%) followed by age group of less than 20 years (22%). These findings are consistent with the findings of Guven et al., & Saadeh et al.[17,18], where mean ages were 24.1 and 23.95 respectively. The main reason for poisoning in this group was familial problems followed by financial problems & other reasons like breakup, work related stress etc.

Male preponderance was observed in our study. 52% males as compared to 48% of females were present in our study. Similar observations were made by Dalal et al. & Agarwal et al.[19], where 63% and 72% male subjects were involved in poisoning respectively.

In our study, we observed that the number of cases from rural population (76%) were higher as compared to urban population (24%) which shows that organophosphate poisoning is more prevalent in the rural population. These findings are consistent with the findings of Thunga et al. & Dalal et al.[19], who reported 66.6% and 70.5% involvement of rural population respectively. Reasons for higher rural population being involved in organophosphate poisoning is easy availability of pesticides as majority of rural population is involved in agriculture practices.

In our study population the most marked muscarinic sign was Miosis (70%) followed closely by excessive secretions (68%) and the most marked nicotinic effect was muscle weakness and fasciculations (35%) followed by Respiratory failure (20%) due to muscle end plate blockade. Depressed mental status was found in 16% patients. Similar findings were present in the study by Sungur et al. & Vishwanathan et al.[20] The clinical findings and their association with severity of poisoning were present in our study as well as study by Mood et al. The results of prospective observational study done at Department of Chest Medicine, King Edward Memorial Hospital, Mumbai showed that clinical features like miosis, unconsciousness & fasciculations were strong predictors of severity of poisoning and the need for ventilator support for these patients.

Biochemical parameters in our study were similar to study conducted by Mood et al. and showed no statistical significance. Various parameters like blood sugar, serum urea, creatinine, total WBC count have not shown much variation from the normal levels in our study.

Of all the complications seen in OPC, most troublesome complication was Respiratory depression which was observed in 20% cases in our study. Similar observation was reported by Eddleston et al.[3] (2006) where 24% of patients

required ventilation. Various reasons could lead to respiratory depression in OPC like aspiration of gastric contents, excessive secretions, pneumonitis, and septicemia complicating acute respiratory distress syndrome. Early recognition, prompt endotracheal intubation and mechanical ventilator support could be lifesaving in severe OPC poisoning cases. In our study, we observed that the mean amylase level was significantly elevated at the time of admission (170.46) and gradual remission was observed with treatment. Hyperamylasemia was noted in 53% of our patients. Severe manifestations of OPC poisoning like respiratory failure, fasciculation, convulsions, bradycardia, hypotension, altered sensorium, pinpoint pupil and secretions had a significant correlation with hyperamylasemia. A significant correlation was also observed between elevated serum amylase levels with severity & outcome in OPC poisoning. Similar findings were reported by Lee et al.,[21] (1998) were 36% of patients were found to have hyperamylasemia. A significant correlation was also reported between elevated amylase levels and clinical severity and development of shock.

Badiger S et al.22(2016) concluded that serum amylase levels more than 200 U/L has been associated with increased chances for respiratory failure and poor prognosis. Sumiya et al. also observed in his study that 50% of patients who developed respiratory failure had an increase in serum amylase levels above the normal range.

Out of 100 patients, 9 deaths were reported in our study population. Overall mortality was 9% in our study and all those who died had increased serum amylase levels.

Overall mortality reported in different countries and institution including India varies from 4% to 30% in organophosphate poisoning cases. Causes of morbidity and mortality in OPC poisoning cases are due to complications involving the nervous, cardiac and respiratory system Adhil SM et al.[7]

From our study data we analyzed that age, sex, place of residence (rural/urban), poison particulars and laboratory parameters do not have a significant relation with serum amylase levels but there is a significant relation between serum amylase levels and severity of symptoms like pinpoint pupil, fasciculations, secretions, hypotension, bradycardia, convulsion, altered mental status, respiratory failure and outcome in organophosphate poisoning patients. In other studies, this correlation was confirmed and recommended check of plasma amylase in all of the OP poisoning for prediction of severity of clinical sign, respiratory failure, shock, and coma.11-14. So we recommend that hyperamylasemia can be used as a marker of severity and outcome of OP poisoning.

## REFERENCES:


1. Patricia Frank, M. Alice Ottoboni. The DOSE MAKES the POISON: A plain-language guide to Toxicology,Third edition 2011.
2. Weiss B, Amler S, Amler RW, Pesticides. Pediatrics 2004; 113:1030-1036.
3. Eddleston M, Sinicize L, Eyer P. Oximes in acute organophosphate pesticide poisoning: A systematic review of clinical trials. QJ Med J 2002: 275-83.
4. Elango P, Indumathi G. A study of serum amylase levels in acute organophosphate poisoning at Government Dharmapuri Medical College Hospital, Dharmapuri. IAIM 2017; 4(9): 6-11.
5. Cherian MA, Roshini C, Visalakshi J. Biochemical and clinical profile after organophosphate poisoning- a placebo-controlled trial using pralidoxime. JAPI 2005; 53: 427-30
6. Srinivas Rao Ch, Venkateswaralu V, Surender T. Pesticide poisoning in south India: Opportunities for prevention and improved medical management. Trop Med Inter Health 2005; 10(6): 581-88
7. Adhil SM, Sudharsan S. Estimation of serum amylase and lipase levels in correlation with clinical outcome of organophosphate poisoning. Int J Mod Res Revs 2015; 3(10): 849-51.
8. Pore NE, Pujari KN, Jadkar SP. Organophosphate poisoning. J Pharma Biosci 2011; 2: 604-12.
9. Peter J, Sudarsan T, Moran J. Clinical features of organophosphate poisoning: A review of different classification system and approaches. Indian J Crit Care Med 2014; 18(11): 805.
10. Dhunputh P, Mohammed AP, Bhatt A, Saraswat PP, Umakanth S. Pancreatic pseudocyst, a delayed complication of organophosphate poisoning. MJMS 2018; 3 (1): 40-44.
11. Panda S, Nanda R, Mangaraj M, Mishra PK, Venkata Rao E. Laboratory abnormalities in patients with organophosphate poisoning. Indian Medical Gazette 2014: 6-12.
12. Manu MS, Prashant V, Akila P, Suma MN, Basavanagowdappa H. A retrospective analysis of serial measurement of serum cholinesterase in acute poisoning with organophosphate compounds. Toxicol Inter 2012; 19 (3): 255-59.
13. Satyanarayana U, Chakrapani U. Digestion and absorption. In: Biochemistry 3rd edition, Books and allied (P) Ltd. Kolkata, 2009: 165-81.
14. Patil SL, Vasepalli P. Prognostic value of clinical and lab parameters in assessing the severity of organophosphate compound poisoning. Indian J Basic Appl Med Res 2014; 4 (1): 77-91.
15. Harputluoglu MM, Damirel U, Alan H, Ates F, Aladag M, Karincaoglu M, et al. Pancreatic pseudocyst development due to organophosphate poisoning. Turk J Gastroenterol 2007: 18(2): 122-25.
16. Sitaram CSKSKD, Sumathi ME. Clinical Significance of serum amylase in acute organophosphate poisoning. IOSR-JBB 2016; 2(5): 54-57.
17. Mcihammet Guven, Ayban DOGUKAN, Hulyan TASKAPAN, Lcukocytosis as a parameter in Management of Organophosphate Intoxication. Turk J Med Sci 2000; 30: 499-500
18. A.M. Saadeh, N.A. Farsakh, M.K. Al. Ali. Cardiac manifestations of acute carbonate and organophosphate poisoning. Heart 1997; 77: 461-464.
19. Dalal et al., "poisoning trends: A postmortem study". Journal of Indian Academy of Forensic Medicine 1998; 20(2): 27-31.
20. Murat Sungur, Muhammed Guiven. Intensive care management of organophosphate insecticide poisoning. Crit Care 2001; 5 (4)211-215.
21. Lee WC, Yang CC, Deng, JF, Wu ML, Ger J, Lin HC, et al. The clinical significance of hyperamylasemia in organophosphate poisoning. J Toxicol Clin Toxicol 1998; 36 (7): 673-81.
22. Badiger S, Vishok M. Study of serum amylase and serum cholinesterase in organophosphate poisoning. JKIMSU 2016; 5(2): 49-56.