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Original Research Manuscript

Correlation Of Serum Amylase with Outcome in Acute Organophosphorous Poisoning

Running Title Serum Amylase Levels in Acute Organophosphorous Poisoning

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Abstract

Context: Organophosphorus (OP) poisoning is a common mode of suicidal poisoning. These compounds are widely available in developing country like India, resulting in high morbidity and mortality. The use of serum amylase in determining the severity of OP poisoning has showed promise.

Aims: This study was undertaken to estimate serum amylase levels in acute OP poisoning and to correlate it with the outcome.

Settings and Design:
Setting – tertiary care treating hospital
Design -cross-sectional observational study

Methods and Material:A hospital-based cross-sectional study was conducted on 80 patients who were clinically diagnosed with acute OP poisoning. Serum amylase was measured on days 1 and 2 of admission and correlated with clinical features and the end result.

Statistical analysis used was SPSS 23.0 version software, and the data was analyzed. To compare the variables across the groups, the H test and Chi-square test were used.

Results: The majority of the cases in the study (41%) were between the ages of 21 and 30. Males made up 65 % of the group, while females 28 %. Serum amylase levels were significantly elevated in patients with clinical features of OP poisoning. The median serum amylase level was 80 IU/l (IQR 50–224.5). Serum amylase levels were normal in 62.5 % (n-50), but elevated in

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37.5 % (n-30). A bad outcome was linked to a persistently elevated serum amylase level on day 2.

Conclusions: Serum amylase levels is also considered as a prognostic marker of OP poisoning since it enables the first recognition of severity and to spot those in danger of developing the complications of OP poisoning.

Keywords: Organophosphorus poisoning, serum amylase.

Introduction

Organophosphates (OP) became the foremost widely used agricultural insecticide worldwide. Suicidal attempts with these easily accessible agents are a significant problem in developing countries. [1] These agents are also used in chemical warfare as nerve agents. [2]

Acute organophosphorus poisoning occurs after or oral exposure to either low volatility pesticides (e.g., chlorpyrifos, dimethoate) or high volatility nerve agents (e.g., sarin, tabun). [3,4] Inhibition of acetylcholinesterase at synapses results in accumulation of acetylcholine and overactivation of acetylcholine receptors at the neuromuscular junction and in the autonomic and central nervous systems.Early clinical features (the acute cholinergic crisis) reflect involvement of the parasympathetic system and include bronchorrhoea, bronchospasm [5,6], miosis, salivation, defecation, urination, and hypotension. Features indicating involvement of the neuromuscular junction (muscle weakness and fasciculations) and central nervous system (seizures, coma, and respiratory failure) are common at this stage. Respiratory failure may also occur many hours later, either separated in time from the cholinergic crisis (intermediate syndrome) or merged into the acute cholinergic crisis. [4, 11]

The pathophysiology of this late respiratory failure seems to involve downregulation of nicotinic acetylcholine receptors. [3, 4] Intermediate syndrome is particularly important since people who are apparently well can progress rapidly to respiratory arrest. Late motor or motor/sensory peripheral neuropathy can develop after recovery from acute poisoning with some organophosphorus pesticides.Acute poisoning may result in long-term neurological and psychiatric effects, but the evidence is still unclear.Its widespread use and easy availability has increased the likelihood of poisoning with these compounds in developing countries like India. [7].

OP compound poisoning is associated with various biochemical abnormalities, among which hyperamylasemia is well documented and may be due to excessive cholinergic stimulation of the pancreas. Acute pancreatitis is frequent in OP poisoning, and increased serum amylase is less specific and sensitive. Several studies [8,9] reported elevated serum amylase levels in patients with organophosphorous compound poisoning (OP) and found hyperamylasaemia to be closely related to clinical severity and the presence of shock.[10]

However, the toxic effects of OPs are associated with significant morbidity and mortality and are a major global clinical problem. Mortality ranges from 4-30% in Indian studies. Occupational, suicidal (or) homicidal exposure to OPs produces a characteristic but treatable syndrome in humans. Thus, early recognition and timely intervention of toxicity from these compounds are of great importance to emergency physicians and patients [10].

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Rationale of this study was to findout whether the only increased serum amylase, or persistently raised serum amylase, had any bearing on the outcome.

Aim and objective was:

1. To measure the serum amylase level in cases of acute OP poisoning at the time of admission and then after 24 hours, and 2. to correlate with the outcome.

Subjects and Methods:

Study design:

Type of study: cross-sectional

Study setting: tertiary care hospital

Place of study: M.K.C.G Medical College, Brahmapur, Odisha, India.

Study period - November 20th, 2018 to November 20th, 2020

Sample size- 80 (80 or more measurements/surveys are needed to have a confidence level of 95% that the real value is within ± 5 % of the measured/surveyed value)

After the calculation of the sample size, 80 cases of acute OP poisoning admitted to the hospital were included after considering the following inclusion and exclusion criteria and IEC – 776/IEC M.K.C.G Medical College, Brahmapur, Odisha, India.

Inclusion criteria

Patients with a history of OP poisoning with clinical features and physical evidence of poisoning were the study subjects.

Exclusion criteria

Patients with an evidence of exposure to an entirely different poison other than OP poison or mixture of OP and non OP poison or consumed poison along with alcohol or chronic alcoholics or history of pancreatitis or history suggestive of cholelithiasisorhistory of intake of drugs – e.g., Azathioprine, Mercaptopurine, Thiazides, Furosemide, Pentamidine were excluded from the study.

Sample collection

Approximately 3 ml of venous blood was collected from each of the selected patients on two occasions, the first within 24 hours of poison consumption (Sample I) and the second after 24 hours of the first sample (Sample II).The samples were centrifuged at 3000rpm for 15 minutes. The supernatant serum was separated and frozen. Serum amylase was estimated with the help of a kit manufactured by Diasys Diagnostic System Gmbh ALTE Strasse g 65558 Holzheim, Germany by using the CNP-G3 method Autoanalyzer AUTOPAK with the department of Biochemistry.

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Serum amylase levels between 30 and 110 U/l were considered normal.

Informed written consent was obtained from each of the patients and/or attendants before taking any interviews, after describing the study's purpose and methods, the confidentiality of the interviews, risks, and benefits of participating in the study. All information was collected confidentially with complete respect to the patient without any force or pressure.

Statistical analysis

Data will be collected in a Case Investigating Proforma that has been pre-designed. The cases will then be submitted to the appropriate investigations, with the results being documented in a methodical manner. The statistical analysis was carried out using the statistical packages for social sciences (SPSS) software for Windows, version 23.0. Measurable variables with normal distributions were provided as mean standard deviation (SD), while those with non-normal distributions were presented as median and interquartile range (IQR). To compare the variables across the groups, the H test and Chi-square test were used. Signs and symptoms of poisoning were correlated with outcome.

Elimination of bias: The most common type of Bias which might be encountered during the study was Selection Bias, which was ruled out by including all the patients satisfying the Inclusion and Exclusion criteria into the study. Information bias was ruled out by accurately measuring and cross-checking all the key study variables at least 3 times before classifying them in the study.

Results:

Majority of the patients (41%) were between the age groups of 21–30 yrs, followed by those aged 40 and older**.** 52 (65%) were males and 28 (35%) were females**.** The male to female ratio was nearly two-thirds (1.9:1) (**Table 1).**The reasons for poisoning were mainly familial stress, with 54 (63%) of the other 14 (18%) reasons being love failure and work-related stress. Chlorpyripous+cypermethrine, diamethate, and monocrotophos are the poisoning agents. The median serum amylase is 80 (IQR 50–224) **(Table 2**).

Among the total cases, secretions (56%), pin-point pupils (41%), fasciculation (41%), respiratory failure (29%), depressed mental status (24.4%), and hypotension (17%) were the most common clinical features. This study shows that patients with pin-point pupils, depressed mental status, and increased secretions, fasciculations, bradycardia, convulsions, and respiratory failure had a persistent increase in serum amylase. The mean serum amylase level in patients with clinical features was significantly higher (**Table 3).**

On Day 1, out of 80, 50 (62.5%) cases had normal serum amylase, i.e., mean ± SD (68±25 U/L), and 30 cases had an increase in serum amylase, i.e., mean ± SD (264±172 U/L) on day 1 or at the time of admission **(Table 4).**

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On Day 2, 58 cases (71%) had normal serum amylase levels. 22 (76%) of the 30 cases , who had increased serum amylase on day1 remained persistently increased levels also in day2.In7 (24%) cases, the amylase level decreased to normal. (**Table 5) (Figure 1)**

During this study period, the total number of deaths were 9 (11.25%) . Out of 22 cases with persistent hyperamylasemia on day 2, death occurred in 6 cases. Whereas only 3 cases out of 58 who had either normal or non persistenthyperamylasaemia did not survive in this study. On correlating serum amylase with survival, it was observed that the number of deaths among the cases with persistent hyperamylaesemiawith those with either normal or non-persistent serum amylaseamia was significantly high, p value 0.043 (p value<0.5). (**Table 5)**

Discussion:

In the current study, the majority of the patients (41%) were between to the age group 21–30 yrs, followed by those aged 40 and older. This research is comparable to that of DeveeAnjana et al. [11, 15]. Females and males comprised 52% and 48% of the cases in this study, respectively. This shows that there was no significant difference between the sexes in the case of OP compound poisoning. Kora S et al. [16] found slightly different percentages: 56.08% and 43.98% for females and males, respectively.

The primary cause of poisoning was familial stress, with love failure and work-related stress accounting for 54 (63%) and 14 (18%), respectively. According to Subash Chandra Joshi et al. (2011), the most common reason for poisoning in bothmales (50.80%) and females (43.01%) was suicidal ideation. [17]

The most prevalent clinical characteristic at presentation was secretions (56 percent), followed by pin-point pupils (51 percent), fasciculation (41 percent), and respiratory failure (29 percent). Less frequent symptoms were hypertension (17%) and convulsions (2.6%). However, the majority of patients' presenting symptoms overlapped.

Hyperamylasemia was found to be linked to three of the most severe symptoms of OPC poisoning: secretions, fasciculation, and bradycardia. In this study, there was a significant correlation between betweenelevated serum amylase and symptoms.

In the study, the amylase levels were significantly elevated at the time of admission [264±72] and have shown a gradual remission with proper treatment. 30 (37.5%) of our patients were found to have persistent hyperamylasemia.

According to **Singh et al.** [18], mild elevations of serum amylase are common in OP poisoning, but acute pancreatitis is uncommon. Serum amylase was elevated > 200 (○1.U) in 37 (46.95%) patients. Only one had acute pancreatitis. Similarly, no patient developed symptomatic acute pancreatitis in this study.

Ahmed Arshia et al. [19] found hyperamylasemia in 28 (31%) of patients amongst 90. And pancreatitis was seen in 2 (2.2%) patients. Hyperamylasemia is more frequently seen in organophosphorus poisoning than in acute pancreatitis as a complication.

The overall mean value of serum amylase was significantly higher in non-survivors than in survivors, i.e., 296 ± 108 U/L.

The current study has several limitations, including the lack of a control arm, the inability to determine the chemical makeup of diverse OP compounds due to the lack of facility, and the inability to generalise hyperamylasemia to all types of OP compounds.

Conclusion

Based on the findings of this study, it can be concluded that increased serum amylase levels and persistent hyperamylasemia can be used as a prognostic marker for organophosphorous poisoning, as it allows for early detection of severity and helps to identify those who are at risk of developing organophosphorous poisoning complications. In the current investigation, there was no significant association between patient age and gender and amylase levels, however there was a significant correlation between persistently higher amylase levels with the outcome.

However, a larger study would shed more light on the finer link between blood amylase levels and clinical severity and outcome in various types of OP poisoning.

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Table 1 Demographic profile in OP poisoning

VARIABLE	SUBGROUPS	CASE (%)
	0-20	10(13)
	21-30	33(41)
	31-40	17(21)
	41 AND ABOVE	20(25)
	MALE	52(65)
	FEMALE	28(35)

Table 2 Reason and agent of poisoning in relation to OP poisoning

	FAMILIAL	54(63)
	FINANCIAL	10(13)
	JOB STRESS	4(6)
REASON OF	OTHERS	14(18)
	CHLORPYRIPHOUS AND CYPERMETHRINE	37(46)
	DIMETHOATE	24(30)
	MONOCOROTOPHOS	11(13)
	TRIAZOPHOS AND DELTAMETHRIN	6(8)
AGENT OF POISONING	PARATHION	2(3)

Table 3 Clinical Features and the Value of Serum Amylase in Op Poisoning

CLINICAL FEATURE	CASE 80(%)	SERUM AMYLASE D1 MEAN± SD (**U/L)**	SERUM AMYLASE D2 MEAN± SD (**U/L)**
PIN PONT PUPIL	41(51)	182 ±108	136 ±83
DERPRESSED MENTAL STATUS	19(23)	204 ±131	158± 97
SECRETION	45(56)	172 ± 106	158± 97
FASCICULATION	33(41)	205±107	158±85
HEART RATE	20(25)	239 ± 106	187± 82
CONVULSION	5(6)	318± 93	240±54
RESPIRATORY FAILURE	23(29)	229±106	177± 86

BLOOD PRESSURE	14(17)	168 ± 93	136 ± 102

TABLE 4 Serum Amylase on Day 1

SERUM AMYLASE	CASES	SERUM MAYLASE MEAN SD D1(U/L)
NORMAL	50(62.5)	68 ± 25
INCREASED	30(37.5)	264 ±172

Table 5 Number of Cases with Abnormal Serum Amylase on Day 1 and Day 2 with Outcome

SERUM AMYLASE	NO OF CASE %		OUTCOME DEATH 9 (%)	
	DAY 1	DAY 2		
INCREASED	30(37.5%)	22 (27.5 %)	6(67)	
NORMAL	50(62.5 %)	58 (72.5%)	3(23)	P<0.047

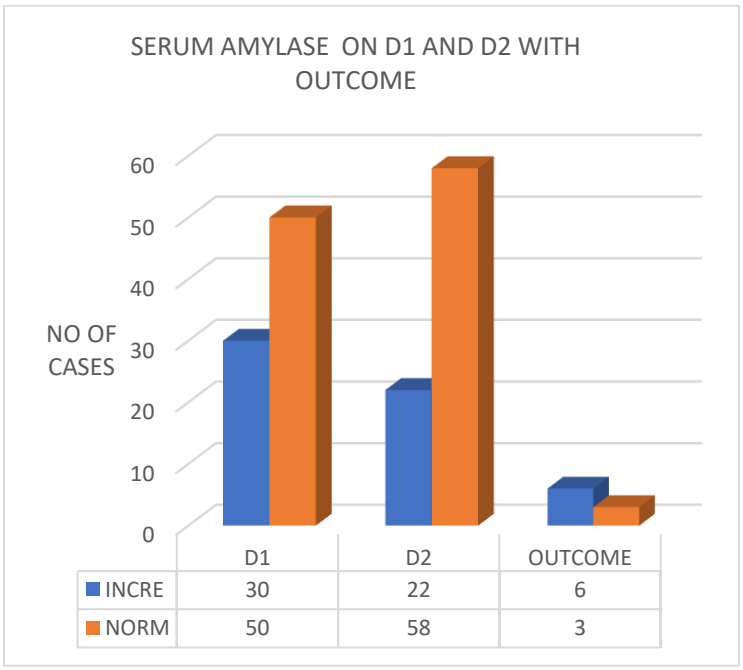

Figure 1 Numbers of Cases with Abnormal Serum Amylase on Day 1 and Day 2 with Outcome

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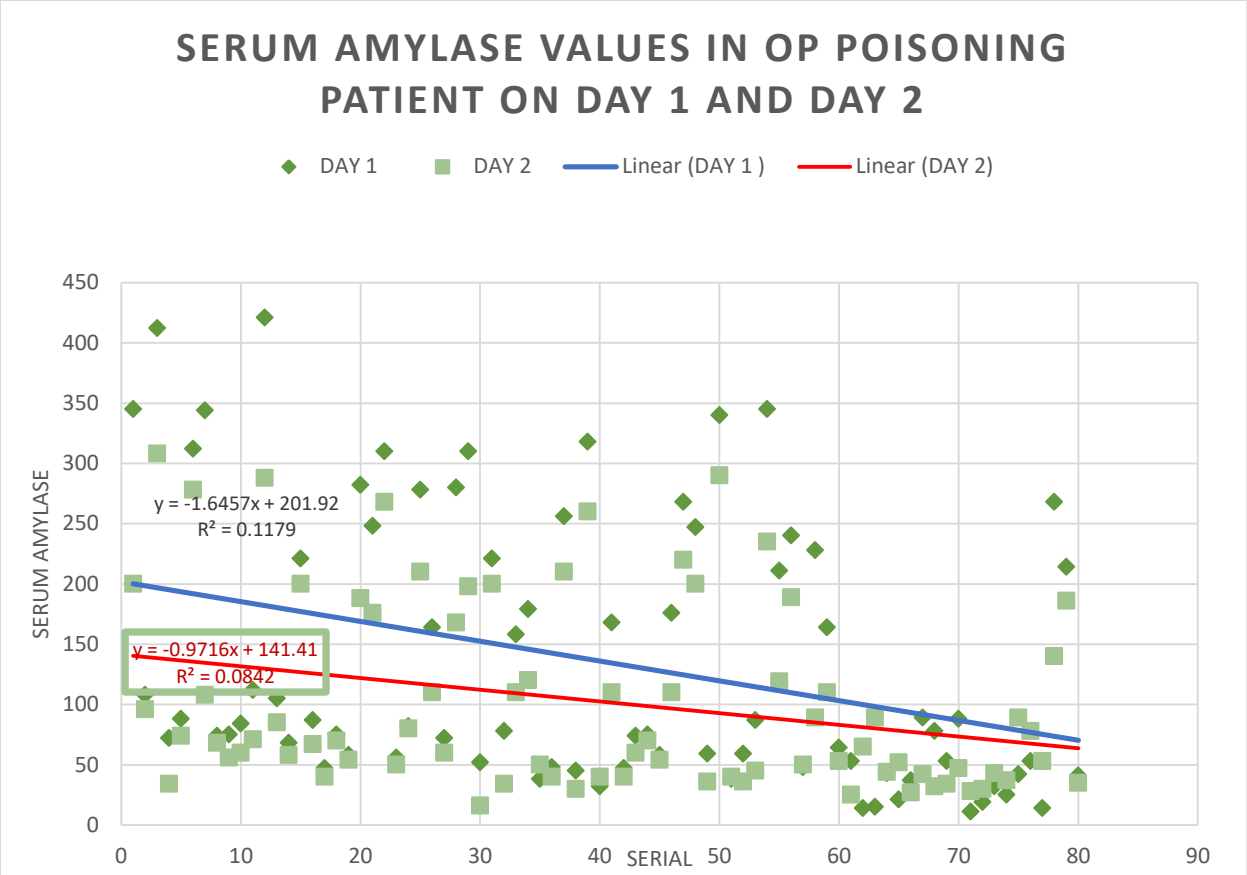

Figure 2 Serum amylase values in OP poisoning patient on Day 1 and Day 2

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Ethical policy and Institutional Review board statement

INSTITUTIONAL ETHICS COMMITTEE

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CERTIFICATE

(For Post Graduate Students)

The Institutional Ethics Committee has approved the Thesis protocol titled **A STUDY ON SERUM AMYLASE LEVEL IN PATIENTS OF ACUTE ORGANOPHOSPHOROUS POISONING IN SOUTHERN ODISHA** of **Dr. Deepak Kumar Naik** under the guidance of **Dr. S. S. Acharya** of **General Medicine** Department for M.D./M.S. **(General Medicine)** to be conducted for two years at M.K.C.G. Medical College, Brahmapur- 4, Orissa.

Member Secretary
Prof. C. S. Maharana
Prof. & HOD of Pharmacology
M.K.C.G. Medical College,
Brahmapur-4.

* *The original certificate is to be preserved by the candidate.*