

How to Cite:

Thirunavukkarasu, S., Radhakrishnan, S., & Shankar, R. (2022). Serum amylase a prognostic indicator in acute organophosphorous compound poisoning. *International Journal of Health Sciences*, 6(S8), 5028–5035.
<https://doi.org/10.53730/ijhs.v6nS8.13357>

Serum amylase a prognostic indicator in acute organophosphorous compound poisoning

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Abstract---Background: OPC is being considered as the most important agent of self-poisoning among the younger generation people because of its easy availability. Recent studies have reported an early increase in serum amylase levels among patients with OP compound poisoning and found hyperamylasemia to be closely associated with the clinical signs and symptoms and more so with respiratory failure. Aim: To study the serum amylase levels among patients with OPC poisoning and correlate its levels with the clinical features on the day of presentation. Methodology: A prospective longitudinal study was conducted for a period of two years in a Government medical college hospital at TamilNadu. A total of 278 patients reported to our hospital with history of OPC poisoning during the said period among which 157 patients satisfying our inclusion and exclusion criteria are selected as our study subjects. Severity of OPC intoxication was measured using POP (Peradeniya OP poisoning) scale and it was graded as mild, moderate and severe. Serum amylase level was measured for all the patients on the day of admission. Results: The mean serum amylase level was found to be in normal levels for patients with mild grade (94U/L) of OPC poisoning, whereas the mean levels of serum amylase was increased to 162 U/L and 304 U/L for patients with moderate and severe grades of OPC poisoning and the difference was found to be statistically significant ($p<.0001$). Serum

amylase levels were significantly elevated among patients who have developed respiratory failure and the levels were also high among the patients who have died due to OPC poisoning. Conclusion: Serum amylase levels can be considered as a marker for assessing the prognosis and severity of OPC poisoning.

Keywords---organophosphorous compound poisoning, serum amylase, peradeniya scoring scale, correlation.

Introduction

Poisoning by Organophosphorous Pesticide Compounds (OPC) has reached epidemic proportions in most parts of the world, particularly in developing agrarian countries like India. Toxicity of these types of available poisons and paucity of appropriate medical facilities ensure a high case fatality rate.¹ OPC is being considered as the most important agent of self-poisoning among the younger generation people because of its easy availability. According to the reports of WHO, annually 3 millions cases of OPC poisoning are reported every year in which 2 million cases are getting hospitalized and among them 2,20,000 are dying on an average. The numbers might be still bigger as underreporting is a major factor in poisoning cases.²

In India the commonest OPC agents available in market are malathion, chlorpyrifos and parathion which when classified based on their toxicity they are low toxic, intermediate toxic and high toxic respectively.^{3,4} The mortality rate due to OPC ranges between 10 and 30% in our country mainly due to respiratory failure because of bronchospasm and bronchorrhoea. OPC act by inhibiting acetylcholine esterase enzyme at nerve endings and neuromuscular junction, causing overstimulation of acetylcholine receptors, thereby triggering the activity of parasympathetic nervous system at muscarinic, nicotinic and central nervous system receptors. Severity of signs and symptoms directly correlates with decrease in the pseudocholinesterase levels.^{5,6} Still today plasma cholinesterase level has been considered as a gold-standard investigatory tool to assess the severity of OPC poisoning and to determine the clinical course. However, because of few limitations such as wide inter-individual variability, lack of availability at all places particularly in rural areas and its high cost had led to the search of a cheap and readily available biomarkers.⁷

Of late recent studies have reported an early increase in serum amylase levels among patients with OP compound poisoning and found hyperamylasemia to be closely associated with the clinical signs and symptoms and particularly in patients with very high values of serum amylase, the presence of shock and respiratory failure was found to be inevitable.⁸ Theories have suggested that parasympathetic over stimulation of pancreas is the reason for increased serum amylase in OPC poisoning.^{9,10} Studies done earlier had shown a mixed response in the prognostic significance of serum amylase in OPC poisoning. However, this association still has not been widely used as a prognostic indicator in OPC poisoning as there is no local data available regarding the frequency of high amylase levels and the severity of OP poisoning and so the present study was

aimed to study the serum amylase levels among patients with OPC poisoning and correlate its levels with the clinical features on the day of presentation.

Methodology

A prospective longitudinal study was conducted for a period of two years in a Government medical college hospital at TamilNadu. The study was started after obtaining permission from Institutional Ethics Committee. All patients presenting to our hospital with history of organophosphorous compound poisoning are taken as our study subjects. Since we are assessing the serum amylase we want to avoid the factors which are going to influence the serum amylase levels such as chronic alcoholics, who had consumed poison along with alcohol, history of gallstone disease, history of lipid disorder, history of intake of drugs that are likely to produce pancreatitis like azathioprine, mercaptopurine etc. Apart from these patients with chronic lung or cardiac illness, women with history of OCP intake, pregnant or lactating females and people with neuromuscular disorders such as myasthenia are excluded from the study. A total of 278 patients reported to our hospital with history of OPC poisoning during the said period among which 157 patients satisfying our inclusion and exclusion criteria are selected as our study subjects. All patients initially received at casualty where it was registered in the MLC (Medico Legal Case) register and the patient was shifted to the medicine ward. Severity of OPC intoxication was measured using POP (Peradeniya OP poisoning) scale which takes into account the five common clinical manifestations of OP poisoning such as miosis, fasciculations, respiration, heart rate and level of consciousness. Each of these factors are assessed on a 3-point scale varying between 0 and 2 and based on that score the poisoning was graded as mild (score 0-3), moderate (score 4-7) or severe (score 8-10). 2 ml of venous blood sample was collected from all the patients and it was allowed to coagulate at room temperature for 10-15 minutes, later the serum was separated by centrifugation for 15 minutes at 2500 rpm. Serum amylase level was measured by Vitros-350 auto-analyzer by using enzymatic and colorimetric assay and the serum amylase level of <110 U/L was considered as normal. All data were entered and analysed using SPSS version 23. Mean and standard deviation was derived for all parametric variables and percentage was calculated for the frequency variables. Chi-square test, Kruskal Wallis test and Spearman's correlation test were used to derive the statistical inference, considering $p < .05$ as statistically significant.

Results

The demographic characteristics of the study subjects show that majority of the patients who had consumed OPC poisoning are in the age group between 20 and 40 years (50%) and nearly 70% of them were males. Majority of our patients (34%) were agricultural workers followed by house wife and 18% of the patients were unemployed. In our study majority of the patients belong to lower socio-economic status (47%), followed by middle and upper. The POP scoring scale which takes into account the pupil size, heart rate, respiration, muscle fasciculation and level of consciousness and for each variable the scoring was between 0 and 2 with a total score of minimum 0 and maximum 10. Based on this scoring system patients were categorised as mild, moderate and severe, with majority of the patients were belonging to mild category (46.4%) and 14% of the

patients were under severe category. In the present study 71% of the patients had raised serum amylase levels (>110 U/L) and the mortality rate in our study was 15.2% (table 1). In our study all patients had the history of suicide attempt and the most common reason for suicide quoted by them were heavy debts and family disputes. The most common OPC compound used as poisoning agent among our patients was Monochrotophos followed by methyl parathion. The mean serum amylase level was found to be in normal levels for patients with mild grade (94U/L) of OPC poisoning, whereas the mean levels of serum amylase was increased to 162 U/L and 304 U/L for patients with moderate and severe grades of OPC poisoning and the difference was found to be statistically significant ($p<.0001$) (table 2). A scatter plot was made between serum amylase levels and grading of OPC poisoning and it shows a strong positive linear correlation between these two parameters which is to be statistically significant ($r = 0.920$, $P <.001$) (fig 1). Apart from this association between OPC grading and serum amylase levels, we also found a strong significant association between serum amylase levels and the time interval between the intake of poison and the patient reporting to the hospital, as the time interval increases there was an increase in the serum amylase levels. Similarly serum amylase levels were significantly elevated among patients who have developed respiratory failure and the levels were also high among the patients who have died due to OPC poisoning ($p<.0001$) (table 3).

Discussion

Acute OPC poisoning is often considered as a medical emergency as it requires close monitoring and in most of the patients it would lead onto respiratory failure for which ventilator support is needed. Early intervention based on the severity of the disease, which depends on clinical signs and symptoms and the laboratory parameters is the key factor in reducing the morbidity and mortality of the disease as such. Various scales for assessing the clinical manifestations and different laboratory markers had been developed for grading the severity of the disease condition.¹¹

Peradeniya Organophosphorus Poisoning (POP) scale has been widely used by many researchers for grading the OPC poisoning patients as mild, moderate and severe based on certain clinical parameters. Recently few studies had shown the serum amylase level as an important laboratory marker for assessing the severity of OPC poisoning.¹²⁻¹⁵ In India as such very few studies have measured serum amylase levels in OPC poisoning patients and those studies reported an increase of serum amylase levels which was found to be directly proportionate to the clinical severity of the disease. With this background, the present study was aimed to evaluate the significance of raised amylase levels in organo phosphorus compound poisoning.

In the present study, the mean age of the patients was 24.3 ± 5.8 years. This result correlated with study done by Gunosindhu Paul et al in which the mean age was 23.68 ± 6.8 years and another study by Kozac et al reported the mean age of OPC poisoning patients as 23.6 ± 12.4 years.^{16,17} In this study, most participants (32.4%) belonged to the age group 21- 30 years, followed by 27.3% of patients in the age group of 14-20 years. Other researchers also reported a similar type of finding.¹⁸⁻

²⁰ Age group between 20 and 40 years is being considered as the most critical period, where the person is more likely to face various problems that might lead onto psychological stress making that person to take the extreme step of ending the life. The male: female ratio of the current study was 2.1: 1, and most of the previously done studies were also shown that the males have outnumbered females, female predominance was also reported in few studies.¹⁶⁻¹⁸

A study done by Badiger and Vishok found that farmers were the most common victims of OPC poisoning, followed by students and homemakers.¹³ Our observation was almost quite similar, farmers are being more prone to OPC poisoning because of its easy availability and accessibility of pesticides to them. Based on the POP scoring our study shows 46.4% had mild grade, 39.4% moderate grade and 14% had severe grade of OPC poisoning based on their clinical presentation and it was similar to the study done by Patil, Vasepalli and Gunosindhu Paul et al.^{5,16} The present study showed elevated amylase levels in 71.3% of the patients with a median of 142.5 U/L which could be because of acute OPC poisoning causing acute pancreatitis, whereas the prevalence of elevated serum amylase levels among OPC poisoning patients assessed in different studies was between 20 and 45% and the median level was ranging between 130 and 204 U/L. In the present study the mean serum amylase levels was 94U/L among patients with mild grade and it was 162 U/L and 304 U/L among moderate and severe grade of OPC poisoning. A study done by Dubey T et al in 2016 ranked mild, moderate and severe based on POP scale and their mean serum amylase concentration was 59.45 (± 18.78), 246.84 (± 172.798) and 864.00 (± 162.84) respectively and the analysis of variance (ANOVA) showed statistically highly significant relationship (p value < 0.0001) between POP level of severity and the serum amylase concentration.²¹ Our study was in par with the study done by Palash Kumar Biswas et al showed a strong positive spearman correlation between serum amylase levels and the POP score among these patients.²² Our study further highlighted the association between serum amylase levels and respiratory failure, higher the levels more the chances of respiratory failure and also a similar association between the outcome of the patients and the amylase levels. A study done by Subhash L. Patil et al and Palash Kumar Biswas et al showed that majority of the patients with high amylase levels needed ventilator support compared to patients with normal serum amylase levels which was found to be statistically significant.^{5,22} The above mentioned study along with the study done by Ganiger I et al reported a statistically significant difference between amylase level of alive and dead patient, which was in accordance with the present study.²³ The limitations of the present study were, sample size not being too large, follow-up serum amylase levels was not measured due to logistic constraints and there was no control group for comparing the results.

Conclusion

Elevated serum amylase levels are significantly less common in mild grade of OPC poisoning compared to moderate and severe grade of poisoning. A statistically significant strong positive correlation exists between serum amylase levels and the scoring of OPC poisoning. Serum amylase levels can be considered as a marker for assessing the prognosis and severity of OPC poisoning. Still multi-centric studies with a larger sample size along with a control arm should be

conducted to derive more evidence to firmly conclude that serum amylase level is the marker for assessing the severity of OPC poisoning.

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Table 1: Demographic and baseline characteristics of the study subjects

Variable		Frequency (n=157)	Percentage
Age	10 – 20 years	12	7.6%
	21 – 30 years	51	32.4%
	31 – 40 years	43	27.3%
	41 – 50 years	21	13.3%
	51 – 60 years	19	12.1%
	>60 years	11	7%
	Mean $\pm$ SD	24.3 $\pm$ 5.8	
Gender	Male	109	69.4%
	Female	48	30.5%
Occupation	Student	11	7%
	House wife	35	22.2%
	Farmer	52	33.1%
	Daily wager	31	19.7%
	Unemployed	28	17.8%
SES	Lower	74	47.1%
	Upper middle	38	24.2%
	Middle	31	19.7%
	Upper	14	8.9%

Severity of OPC poisoning based on POP score	Mild	73	46.4%
	Moderate	62	39.4%
	Severe	22	14%
Serum amylase levels	Normal	45	28.6%
	Raised	112	71.3%
Outcome of patient	Alive	133	84.7%
	Dead	24	15.2%

Table 2: Grading of OPC poisoning and their mean serum amylase levels

Grading of OPC based on POP scale score	Serum amylase			P value
	Mean	SD	95%CI	
Mild (0 – 3) (n=73)	94	21	77 – 118	<.0001
Moderate (4 – 7) (n=62)	162	28	130 – 191	
Severe (8 – 11) (n=22)	304	13	290 – 318	

P value derived using ANOVA

Fig 1: Scatter plot between serum amylase levels and POP scale score

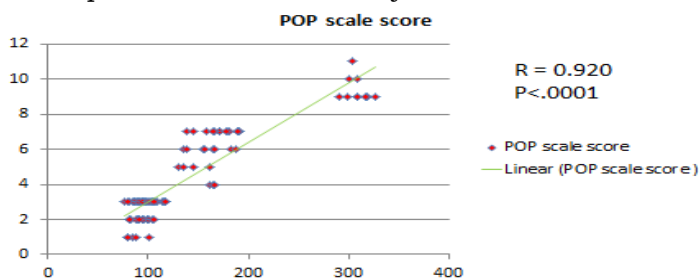


Table 3: Association between serum amylase and clinical features and outcome

Variables		Serum amylase		P value
		Normal (n=45)	Elevated (n=112)	
Time interval between the intake of poison and hospital reporting	<6 hrs (n=89)	42 (93.3%)	47 (41.9%)	<.0001 Chi-square= 34.5
	>6 hrs (n=68)	3 (6.6%)	65 (58%)	
Respiratory failure	Present (n=43)	5 (11.1%)	38 (33.9%)	P=0.0037 Chi-square=8.41
	Absent (n=114)	40 (88.8%)	74 (66%)	
Outcome	Alive (n=133)	44 (97.7%)	89 (79.4%)	P = 0.0039 Chi-square=8.31
	Dead (n=24)	1 (2.2%)	23 (20.5%)	