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Original Article

Internal Medicine Section

Correlation of Serum Amylase, Lipase and Creatine Kinase with Severity of Organophosphate Poisoning- A Cohort Study

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ABSTRACT

Introduction: Organophosphate Compounds (OP) are widely used pesticides in agriculture. It is easily available and OP poisoning is most common cause of poisoning and hospital admissions. Severe poisoning is associated with high mortality. Severity of poisoning can be assessed by Peradeniya Organophosphorus Poisoning (POP) scale, Acute Physiology and chronic Health Evaluation (APACHE) II, Glasgow Coma Scale (GCS) or serum Cholinesterase Level (ChE). Serum amylase, lipase, and creatine kinase are important biomarkers raised in OP poisoning.

Aim: To correlate serum amylase, lipase, and creatine kinase with severity of OP poisoning.

Materials and Methods: This was a hospital based observational cohort study conducted on 130 patients of organophosphate poisoning admitted in General Medicine wards of SCB Medical College, Cuttack, Odisha from June 2019 to December 2020. Serum Acetylcholine Esterase (AChE), amylase, lipase and creatinine kinase were estimated at admission, day 2, and at discharge. Other routine investigations were done. Acetylcholine Esterase (AChE) was used to confirm the diagnosis. The severity of poisoning was assessed using POP scale and graded as mild, moderate and severe. The severity of poisoning and the level of enzymes were correlated. The parameters were tabulated and mean values and Standard Deviation (SD) were analysed using Statistical Package For The Social Sciences (SPSS) software version 22.0.

Results: Out of 130 patients 91 were males and 39 were females, mostly from rural areas, both farming and non-farming community. Age ranged from 14 years to 79 years, with majority in 19 to 39 years. AChE decreased in all cases depending on severity confirming OP poisoning. Severity as assessed by POP score were mild (52 patients), moderate (46 patients) and severe (32 patients). At admission, the Amylase (U/L), Lipase (U/L), and Creatine kinase (U/L) level (mean±SD) in mild poisoning were 83.7±41.9 U, 70.9±18.6, 72.5±34.9, in moderate poisoning 153.6±109.7, 91.9±47.4, 92.6±81.5, and in severe poisoning 243.9±113.8, 195.3±147.7, 298.8±207.4, respectively. Measurements on second day also remained elevated. Among the severe cases 24 patients developed Intermediate Syndrome (IMS), and 26 patients died. There was positive correlation between increase of enzyme levels and the severity of OP poisoning as per POP score.

Conclusion: Serum amylase, lipase, and creatine kinase level correlated well with the severity of organophosphorus poisoning and scan be used additionally as an indicator to assess the severity. Serum amylase is a better indicator of severity than lipase and Creatine Kinase (CPK).

Keywords: Insecticide, Intermediate syndrome, Serum cholinesterase, Severity scale

INTRODUCTION

The Organophosphate Compounds (OPs) are widely used pesticides in agriculture since the World War II. Insecticides are the most common cause of poisoning and hospital admissions in developing countries especially South East Asia with around 2,00,000 deaths each year [1]. It has been estimated that approximately one-third of world's suicide is by consuming pesticides accounting for an estimated death of 2,60,000 deaths per year [2]. The official data of National Crime Records Bureau, India 2014 estimated 10.9% of Indian suicides resulted from insecticides [3]. In another survey in India, suicide by poisoning accounted for 25.8% during 2019 [4]. Patel V et al., survey estimated that in 2010, 38.8% of total suicidal deaths in India are due to pesticides [5]. Organophosphates are the third most common cause of pesticide poisoning in India [6]. Psychosocial factor is a major underlying cause of suicidal poisoning [7]. In the developing countries mortality is as high as 70%, probably due to lack of facilities like transport and medical services, delayed treatment, misdiagnosis or increased patient-doctor ratio or lack of antidotes [8].

Organophosphates combine irreversibly with AChE which results in rapid accumulation of acetylcholine at the cholinergic sites in the nervous system with excessive cholinergic stimulation causing toxicity [9]. The severity depends on potency and dose of poison, and time lag between exposure and management [10]. Death results from respiratory failure due to respiratory center depression, respiratory muscle paralysis, bronchospasm, and bronchial secretions in cholinergic crisis (Type I paralysis), and from IMS; Type II paralysis, a complication of OP poisoning [11]. Diagnosis of OP poisoning is done clinically by history and the toxidrome, and confirmed by decreased serum ChE level. Severity of poisoning can be assessed by using serum ChE, POP scale, APACHE II score, and GCS score. Serum AChE is useful for confirmation of OP poisoning [9]. Proudfoot classification is used for severity assessment based on serum ChE level [12]. But serum ChE does not always correlate properly with severity and the scale is not reliable [13].

The POP scale devised by Senanayake N et al., is a 3-point scale (0-2) taking six clinical parameters to asses severity of OP poisoning. The severity graded as mild (score 0-3), moderate (score 4-7), severe (score 8-11) when the patient first presents to the emergency ward [14]. It is an easy bed side procedure taking only the clinical parameters, but need to be done before starting treatment.

Many studies using other factors are available but there is no consensus regarding those factors to determine severity and to predict morbidity and mortality. Lee WC et al., reported that amylase is frequently increased in severe OP poisoning but lipase assay is indicated for early diagnosis of pancreatitis [15]. Matsumiya N et al., reported that elevated amylase is related to respiratory failure in OP poisoning [16]. Sumathi ME et al., reported that serum amylase, lipase and Creatine Phospokinase (CPK) could be used as additional prognostic indicator with amylase being the better predictor in OP poisoning [17]. High serum CPK level reflects the severity of acute muscle necrosis and is a sensitive indicator of muscle injury [18]. CPK was found elevated in acute phase and significantly increased in IMS [19,20]. Mural R et al., reported that CPK can be used for diagnosis and assessment of severity in OP poisoning [21], but in their study only 34 out of 100 patients had raised CPK level, so cannot be a reliable indicator of severity if taken alone. Most of the studies are based on correlation of serum ChE with amylase and as there is lack of local data regarding the severity assessment by using POP scale and enzyme levels. This study was taken up to determine the serum level of amylase, lipase, and CPK and correlating them with the severity of OP poisoning assessed by POP scale.

MATERIALS AND METHODS

The hospital based observational cohort study was conducted on 130 OP poisoning cases admitted to Medicine Ward of SCB Medical College, Cuttack from June 2019 to December 2020. Prior ethical approval from the institution ethics committee and written informed consent from each patient were taken. The study was duly approved by Institutional Ethical Committee vide letter No. 330 dtd. 26.08.2020. Patients satisfying the inclusion and exclusion criteria were included in the study.

Inclusion criteria: Directly admitted OP poisoning cases were included in the study.

Exclusion criteria: Referred OP poisoning cases, mixed poisoning and any co-morbid conditions like chronic alcoholism, respiratory, hepatic and renal diseases, old pancreatitis, salivary gland disorders were excluded from the study.

Study Procedure

Each patient was subjected to detailed history, thorough clinical examination and investigations. Standard treatment was given as per the protocol. Serum ChE, amylase, lipase and creatine phosphokinase were estimated at admission and repeated on the second day and at discharge. OP poisoning was confirmed by Serum ChE level. Severity was assessed by Serum ChE level and POP scale. Patients were monitored during the treatment, and were followed-up by telephonic conversation weekly and OPD visit at the end of one month after discharge.

STATISTICAL ANALYSIS

The parameters were tabulated and mean values and Standard Deviation (SD) were analysed using Statistical Package For The Social Sciences (SPSS) software version 22.0. One-way ANOVA (Analysis of Variance) and Paired t-test were used for comparison of Mean and SD between the groups. Biochemical parameters were co-related with POP score using Pearson's coefficient. Chi-square test was the test of significance. For assessment of diagnostic accuracy of biochemical parameters, Area Under Curve (AUC) in Receptor Operating Curve (ROC) were calculated.

RESULTS

A total of 130 confirmed direct cases of OP poisoning were enrolled in the study. There were 91 males and 39 females. The age ranged from 14 to 79 years with median age 32 years [Table/Fig-1]. A total of 89 cases were from rural areas, mostly from farming background. A total of 119 cases were suicidal poisoning, 11 cases were stated accidental poisoning. The common compounds were Chlorpyriphos, Dimethoate and Monocroptophos. Common clinical features were vomiting, diarrhea, sweating, lacrimation, salivation, altered sensorium, pin-point pupils, bradycardia, and tachypnoea. Severity of poisoning as assessed by POP score and serum ChE level in mild, moderate and severe cases at admission was shown in [Table/Fig-2]. Patients were categorised as mild (52 cases, 33 males and 19 females), moderate (46 cases, 37 males and 9 females) and severe (32 cases, 20 males and 12 females). [Table/Fig-3] depicts mean level and SD of serum ChE, amylase, lipase and CPK on day 1, day 2 and day of discharge. Amylase was raised in 83 cases (26 mild, 29 moderate, 28 severe cases). Lipase was raised in 67 cases (19 mild, 31 moderate, 17 severe cases). CPK was raised in 48 cases (13 mild, 12 moderate, 23 severe cases). All the patients were given standard treatment as per the protocol. Out of the 32 severe cases, 24 cases developed IMS, 27 patients were put on ventilator, and 26 patients (17 males and 9 females) died, seven patients on first day, six patients on second day and subsequently 13 patients during treatment. [Table/Fig-4] shows enzyme values in IMS and death cases. Almost all cases who developed complications or died having high level of all the three biochemical parameters. After successful treatment 104 patients were discharged. All patients were normal on follow-up.

	Sex		
Age group (years)	Male, N (%)	Female, N (%)	Total, N (%)
14-19	15 (11.5)	7 (5.4)	22 (16.9)
20-29	23 (17.7)	11 (8.4)	34 (26.1)
30-39	22 (16.9)	13 (10)	35 (26.9)
40-49	17 (13.1)	4 (3.1)	21 (16.2)
50-59	7 (5.4)	2 (1.5)	9 (6.9)
60-69	4 (3.1)	1 (0.8)	5 (3.9)
70-79	3 (2.3)	1 (0.8)	4 (3.1)
Total	91 (70)	39 (30)	130 (100)
Median age=32 years.			

[Table/Fig-1]: Age and sex distribution.

Severity	No of patients (N=130) (%)	Serum ChE(U/L) (Mean±SD)	POP score (Range)
Mild	52 (40%)	5276±2237	0-3
Moderate	46 (35.4%)	3897±2146	4-7
Severe	32 (24.60%)	486±359	8-11
p-value		<0.01	<0.01
Confidence interval: 95%, One-way ANOVA			

[Table/Fig-2]: Severity assessed by POP score at admission.

[Table/Fig-5-10] depict the correlation and diagnostic accuracy values of the enzymes under study. Pearson's correlation coefficient (r) of - 0.874 between POP score and ACHE which signifies strong negative correlation and (r) of 0.618, 0.551 and 0.644 between POP score and amylase, lipase and CPK respectively signifies strong positive relationship between these parameters. The AUC in ROC for AChE is 0.987, amylase is 0.633, lipase is 0.595 and CPK is 0.579 [Table/Fig-6,11] which suggests that AChE, amylase, lipase and CPK were all good indicators of assessing severity of OP poisoning but AChE and Amylase were better predictors of severity than Lipase and CPK. The sensitivity and specificity values suggests AChE and amylase were more accurate in predicting severity of OP poisoning than Lipase and CPK.

Time of assesent (Total cases)	Severity by POP score	Number of patients (N)(%)	S. ChE Level (U/L) (Mean±SD)	S. Amylase (U/L) (Mean±SD)	S. Lipase (U/L) (Mean±SD)	S. CPK (U/L) (Mean±SD)
Day 1 (130)	Mild	52 (40)	5276±2237	83.7±41.9	70.9±18.6	72.5±34.9
	Moderate	46 (35.4)	3897±2146	153.6 ±109.7	91.9±47.4	92.6±81.5
	Severe	32 (24.6)	486±359	243.9±113.8	195.3±147.7	298.8±207.4
Day 2 (123)	Mild	52 (42.3)	3987±1087	82.2±45.6	69.7±21,4	73.3±30.2
	Moderate	46 (37.3)	2849 ±1121	121.5±82.4	96.6±56.5	236.4±125.6
	Severe	25 (20.4)	421±324	283.8±186.9	199.5±105.7	656.6±427.9
Discharge (104)	Mild	52 (50)	5134±1213	62.7±19.2	65.3 ±28.8	71.7±28.6
	Moderate	46 (44.3)	4783±821	74.8±21.9	74.2±31.7	286.3± 231.7
	Severe	06 (5.7)	3898±1823	202.4±18.8	181.2 ±112.3	148.4±132.1
p-value			<0.01	<0.01	<0.01	<0.01
Confidence interval: 95%, One-way ANOVA						

[Table/Fig-3]: Clinical Severity with Mean serum ChE, Amylase, Lipase, and CPK levels.
CPK: Creatine kinase; ChE: Cholinesterase level; POP: Peradeniya organophosphorus poisoning

	No of cases	POP score	S. ChE (U/L) Mean±SD	S. Amylase (U/ml) Mean±SD	S. Lipase (U/L) Mean±SD	S. CPK (U/L) Mean±SD
IMS	24	Severe	489±362	245.8±108.7	199.2±142.5	299.9±208.1
Death	26	Severe	489±355	246.2±109.2	199.4±149.8	299.9±208.9
p-value			<0.01	<0.01	<0.01	<0.01
Confidence interval: 95%, Paired t-test						

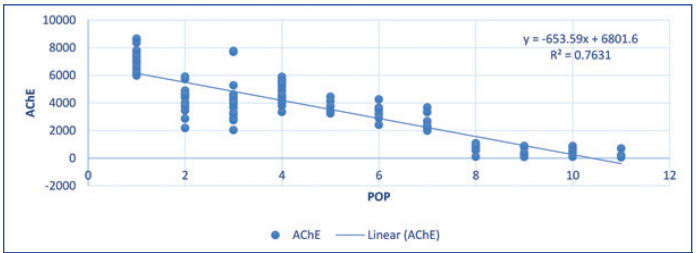
[Table/Fig-4]: IMS and death cases with severity and enzyme level at admission.
CPK: Creatine kinase; ChE: Cholinesterase level; POP: Peradeniya organophosphorus poisoning

Variables		POP	AChE	Amylase	Lipase	CPK
POP	Pearson correlation	1	-0.874**	0.618**	0.551**	0.644**
	Sig. (2-tailed)		0.001	0.001	0.001	0.001
	N	130	130	130	130	130
AChE	Pearson correlation	-0.874**	1	-0.506**	-0.516**	-0.587**
	Sig. (2-tailed)	0.001		0.001	0.001	0.001
	N	130	130	130	130	130
Amylase	Pearson correlation	0.618**	-0.506**	1	0.348**	0.450**
	Sig. (2-tailed)	0.001	0.001		0.001	0.001
	N	130	130	130	130	130
Lipase	Pearson correlation	0.551**	-0.516**	0.348**	1	0.798**
	Sig. (2-tailed)	0.001	0.001	0.001		0.001
	N	130	130	130	130	130
CPK	Pearson correlation	0.644**	-0.587**	0.450**	0.798**	1
	Sig. (2-tailed)	0.001	0.001	0.001	0.001	0.001
	N	130	130	130	130	130

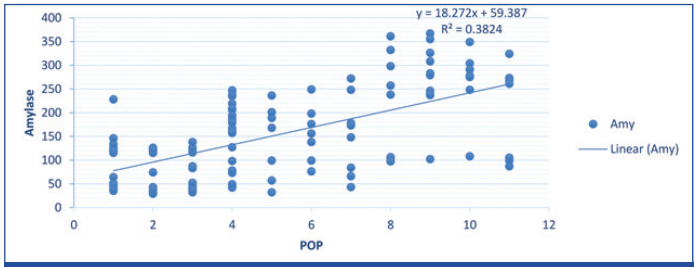
[Table/Fig-5]: Pearson Correlation between POP score and ACHE, Amylase, Lipase, CPK.
**Correlation is significant at the 0.01 level (2-tailed)

Test result variable	AUC	Cut-off value	Sensitivity	Specificity	p-value
AChE	0.987	6175	0.895	0.820	0.000
Amylase	0.633	153	0.679	0.822	0.035
Lipase	0.595	157	0.570	0.680	0.047
CPK	0.579	155	0.526	0.676	0.049

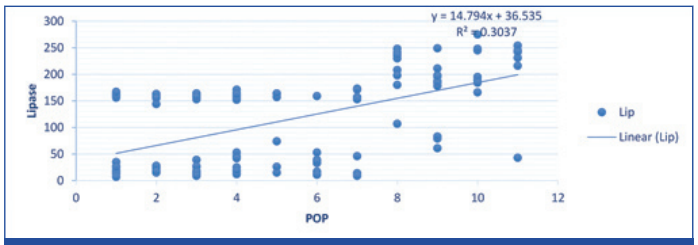
[Table/Fig-6]: AUC in ROC (p-values of AUC and Cut-off values with sensitivity and specificity).



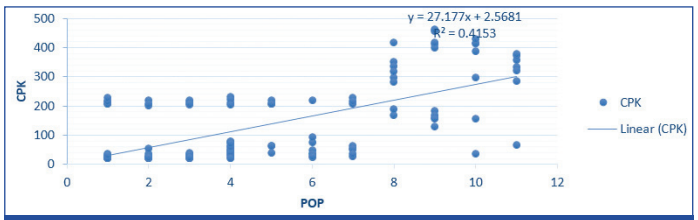
[Table/Fig-7]: Strong negative correlation between POP and AChE.



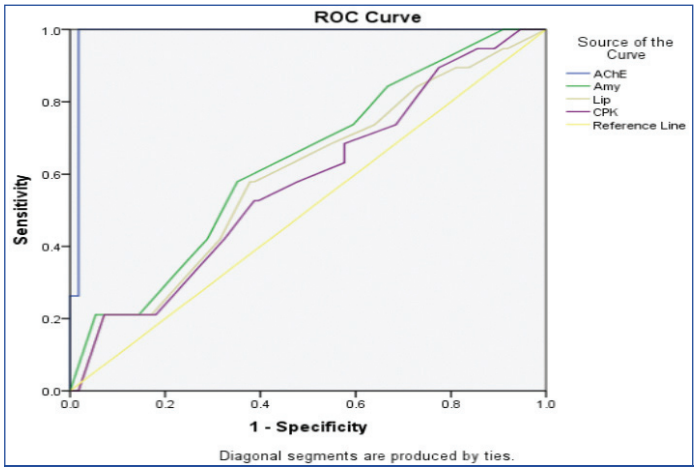
[Table/Fig-8]: Strong positive correlation between POP and amylase.



[Table/Fig-9]: Strong positive correlation between POP and lipase.



[Table/Fig-10]: Strong positive correlation between POP and CPK.



[Table/Fig-11]: ROC curve.

DISCUSSION

An observational study was done by taking 130 organophosphorus poisoning cases applying inclusion and exclusion criteria, and confirming the poisoning by decreased serum ChE. Severity was

assessed by POP score and serum amylase, lipase and CPK were measured in each case.

In the study, the male female ratio was 2.3:1 which was same as that observed by Dungdung A et al., [22]; whereas it was 2.77:1 and 1.85:1 as observed by Sumathi ME et al., and Paul G et al., respectively [17,23]. Similar ratios were also observed in other studies [24]. In this study, 43% patients belong to age group 14-29 years and 43.1% to age group 30-49 years with median age of 32 years. These findings were similar as observed by Paul G et al., [23]. In a study, by Salame RN and Wani AS, 46% age group belonged to age group of 21-30 years [24]. Mean age was 30.6 years in the study by Dungdung A et al., [22]. The adolescent age groups are particularly vulnerable for suicidal attempts, particularly students who usually consume poisons following academic failures or failed relationships as well as conflict with parents. The middle aged peoples usually consume poisons because of poverty and financial liabilities.

In the present study, severity as assessed by POP scoring at admission was mild in 40%, moderate in 35.4% and severe in 24.6% and the severity correlated well with the serum ACHE levels. The number of severe cases were more in this study in comparison to the studies by Dungdung A et al., and Paul G et al., [22,23].

Many biochemical alterations correlate with the severity of OP poisoning. Serum amylase was one of them may be due to excessive stimulation of pancreas by cholinergic stimulation leading to acute pancreatitis. In this study, Serum amylase levels on the first day of admission was raised in 63.8% patients which was in accordance with Sumathi ME et al., but it was more than that as observed by Paul G et al., may be due to more number of patients in the moderate and severe group [17,23]. Salame RN and Wani AS observed raised amylase levels in 78% patients [24]. The presence of complications as well as mortality and the need of ventilatory support are more in patients with hyperamylasemia which was in accordance with studies by Sumathi ME et al., and Lin CL et al., [17,25]. Serum lipase is raised in 51.5% of cases which was in accordance with Dungdung A et al., (56%) but among severe cases only 53% cases have raised lipase levels. So, lipase level does not corroborate well with severity unlike amylase which was raised in 87.5% cases of severe patients [22].

Another biochemical parameter CPK had a promising role as a prognostic indicator in OP poisoning. Serum CPK usually get elevated in OP poisoning due to rhabdomyolysis or IMS which is a common and critical complication of OP poisoning. In the present study serum CPK was raised in 36.92% of patients. It was raised in almost all cases who developed IMS or succumbed. Sumathi ME et al., observed raised CPK level in 77% cases which may be due more percentage of severe cases [17]. Hassan NAM and Madboly AG have also similar observations in their prospective study [19]. Mural R et al., have observed serum CPK level showed a sensitivity of 70%, specificity of 82% and a positive predictive value of 95% [21].

In the present study, there was strong positive correlation with POP score and serum levels of amylase, lipase, and CPK as well as strong negative correlation with AChE levels. These biochemical parameters showed a declining trend as the patient followed-up and at discharge [Table/Fig-3]. The enzyme levels were highest in patients those who developed IMS or required ventilatory support or died [Table/Fig-4] which was in accordance with other observers [16,22,25]. Diagnostic accuracy of the biochemical parameters showed that serum amylase had highest diagnostic accuracy apart from AChE in comparison to lipase and CPK.

Limitation(s)

The sample size was small, compound wise assessment of severity was not done and pancreatitis was not assessed in some of the severe patients. Further studies with larger sample size and multicenter studies will provide a more definite conclusion.

CONCLUSION(S)

Serum Amylase, Lipase, and CPK rise with severity of organophosphorus poisoning and can be used as additional prognostic indicators. Serum amylase is most accurate in predicting severity of organophosphorous poisoning along with AChE in comparison to serum lipase and CPK.

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