

Study of Serum Amylase for Predicting the Severity of Organophosphorus Poisoning and Correlation with Respiratory Failure - A Cross Sectional Study at KIMS, Hubballi, Karnataka

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ABSTRACT

BACKGROUND

Organophosphorus (OP) compounds are insecticides which are widely used in agriculture. Acute organophosphorus poisoning is one of the important causes of morbidity and mortality in developing countries like India. Considering financial burden / availability of tests, we need cheap and easily measurable biomarkers for predicting prognosis / complications in a limited resource country, like India. We intend to correlate the levels of serum amylase in patients admitted with acute organophosphorus poisoning for predicting the severity of acute OP poisoning and also to correlate serum amylase association with respiratory failure.

METHODS

This was a prospective observational study. Total of 94 patients of OP poisoning admitted to KIMS Hospital, Hubballi between January 1st 2017 and December 31th 2017 were studied. Detailed history, clinical examination, and lab investigations like pseudocholinesterase, serum amylase and other relevant investigations were carried out. Peradeniya OP poisoning scale was applied to all the study subjects and the severity of OP poisoning was graded as mild, moderate, severe. Data obtained was analysed by different statistical methods.

RESULTS

OP poisoning was more common in adults of age group between 20 – 30 years, Incidence was more in male patients and mortality rate was 12.8 %. Mean values of serum amylase negatively correlate with pseudocholinesterase levels and it was statistically significant. Correlation between the severity of OP poisoning (based on Peradeniya score) and biochemical parameters like pseudocholinesterase, serum amylase was statistically significant.

CONCLUSIONS

The correlation between the severity of OP poisoning and biochemical parameter—serum amylase, was statistically significant and it was useful in predicting the development of respiratory failure. Pseudocholinesterase and serum amylase were also useful to predict the outcome of the patient.

KEYWORDS

Amylase, Organophosphorus Poisoning, Pseudocholinesterase, Peradeniya Score

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BACKGROUND

Organophosphorus (OP) compounds are insecticides which are widely used in agriculture for crop protection and increased productivity. In the developing world, poisoning is one of the most common methods of suicide. Pesticide poisoning is a major health hazard in the developing world.¹

Millions of people are exposed to these dangerous chemicals because of the occupational hazards and also because of unsafe storage practices.² However, it is the deliberate self-poisoning that causes majority of the deaths and a difficult health strategy to manage among health services, especially in Asia.³ In medical emergency, 10 % of the admissions are due to poisoning and organophosphorus poisoning contributes to nearly 50 % of it.⁴

In our country these compounds are most often misused as suicidal agents. Since 1963 the incidence of OP poisoning is steadily rising in India.⁵ In many reports from India, rate of suicidal poisoning with OP compounds ranges from 10 to 43 %.⁶ Among these, patient's mortality rate is as high as 20 to 70 %.⁷ The morbidity and mortality in any of these patients depends on the time delay between the exposure and the treatment. So it is important to recognise the whole spectrum of symptoms in OP poisoning and to treat early in order to prevent any complications.

In India, we need cheap and easily measurable biomarkers. Many studies were conducted regarding the same and were shown that serum cholinesterase can be a good diagnostic tool, but its role in prognostication is very minimal and also the studies on serum amylase are very few. Our study was conducted to assess the association of serum pseudocholinesterase and serum amylase to predict the severity and its association with respiratory failure in OP poisoning patients.

METHODS

OP poisoning patients admitted in the Department of Medicine, KIMS hospital, Hubballi, for a period of 1 year from January 1st 2017 to December 31th 2017 with history of exposure to organophosphorus compound within previous 24 hours with characteristic clinical manifestations of organophosphorus compound poisoning were included in this prospective observational study. As per hospital statistics 11565 patients were admitted in the Department of Medicine, KIMS, Hubballi. Out of them 420 patients were diagnosed to have acute OP poisoning. This gives a proportion of 3.6 %, with confidence interval of 95 % and 5 % permissible error, sample size comes out to be 86 cases.

However, this being a time bound study and considering inclusion, exclusion criteria, eligible patients during this period, 94 patients were taken up for the study.

All the patient characteristics were summarised as frequencies and percentages. All biochemical parameters were summarised as mean, median, standard deviation (SD) and range. Mean biochemical parameters were compared with categories of pseudocholinesterase and Peradeniya score using Chi-square test. All the biochemical parameters were compared with respiratory failure and outcome using

ANOVA or student t-test. P-value was considered significant if it was less than 0.05.

Patients with history of exposure to an entirely different poison other than OP poison, OP poisoning and mixed with any other poison, who have consumed poison along with alcohol, chronic alcoholic, ultrasound abdomen suggestive of acute pancreatitis and patients with history suggestive of gall stone disease / parotid gland disease / lipid disorders / renal / hepatic disease / diabetes mellitus were excluded from the study.

After obtaining informed consent, thorough clinical examination was carried out during initial resuscitation and treatment of the patient. Peradeniya OP poisoning scale was applied to all the study subjects and the severity of OP poisoning was graded as mild, moderate, severe. About 5 ml of blood was collected in plain tube under aseptic precautions. The blood was allowed to clot and serum was separated by centrifugation and used for the analysis.

Patients were treated and kept under strict observation during their stay in hospital. Assessment of patient's airway and need for endotracheal intubation was assessed, accordingly mechanical ventilator support was given to the patients with respiratory failure.

The Following Investigations Were Done

- Complete blood count (CBC)
- Liver function test (LFT)
- Renal function test (RFT)
- Serum amylase
- Random blood sugar (RBS)
- Electrocardiogram (ECG)
- Serum pseudocholinesterase
- Ultrasound abdomen

Serum Amylase

Serum amylase is derived mainly from the salivary glands and the exocrine pancreas. Alpha-amylase catalyses the hydrolysis of alpha 1 - 4 glycosidic linkage of starch and other related polysaccharides to produce maltose and other oligosaccharides. The enzymes are relatively small molecules which are rapidly cleared by the kidneys and excreted in the urine. Hyperamylasaemia is associated with acute abdominal disorders like acute pancreatitis, biliary dysfunction, salivary glands disorders, ruptured ectopic pregnancy. It is estimated using CNP G 3 method. 2-Chloro-4-Nitrophenol alpha-Maltotrioxide (CNP G3) is a direct substrate for determination of alpha amylase activity, which does not require the presence of ancillary enzymes. The rate of 2 chloro-4-nitrophenol formation can be monitored at 415 nm and is proportional to the alpha amylase activity. Normal value is taken up to 220U / L.

Grading of Severity of Organophosphorus Poisoning - Peradeniya Scoring System

There are several systems of grading of severity in acute organophosphorus poisoning. Senanayake N. (1993) proposed Peradeniya organophosphorus poisoning (POP)

scale for grading the severity in one of the grading systems, which is based on five cardinal manifestations of organophosphorus poisoning as explained in Table 1.

Parameters	0	1	2
Pupil size	≥ 2 mm	< 2 mm	Pinpoint
Respiratory rate	< 20 / min	≥ 20 / min	≥ 20 / min with central cyanosis
Heart rate	> 60 / min	41 – 60 / min	< 40 / min
Fasciculation	None	Present generalised / continuous	Both generalised and continuous
Level of consciousness	Conscious and rationale	Impaired response to verbal commands	No response to verbal commands
Seizure	Absent	Present	-
Grade	Mild (0 - 3)	Moderate (4 - 7)	Severe (8 - 11)

Table 1. Peradeniya Organophosphorus Poisoning (POP) Scale Grading

Statistical Analysis

All the patient's characteristics were summarised as frequencies and percentages. All biochemical parameters were summarised as mean, median, standard deviation (SD) and range. Mean biochemical parameters were compared with categories of pseudocholinesterase and Peradeniya score using chi-square test. All the biochemical parameters were compared with respiratory failure and outcome using ANOVA or student t-test. P-value was considered significant if it was less than 0.05.

RESULTS

In the present study, 50 % of patients were in the age group of 21 – 30 years. Next common age group was between 31 - 40 (17 %) and 15 % were in less than 21 years of age. Among 94 patients, 50 were male (53.2 %) and 44 were female (46.8 %).

The common symptoms reported by patients in our study were vomiting (89.4 %) – which is most frequent, followed by salivation / lacrimation / sweating (56.4 %), loose stools (34.04 %), dyspnoea (35.10 %) and altered sensorium (31.9 %). Seizure was present only in 9 patients (9.6 %). Miosis was the most common sign (87 %) noted in this study followed by bradycardia in 67 %, neck muscle weakness in 43.6 %, tachypnoea in 42.6 %, fasciculations in 37.2 %, crepitations in 36.2 % and altered sensorium in 31.9 % of patients.

In the present study, most of the patients were in mild group (45 %) followed by moderate group (35 %) and severe group (20 %) according to Peradeniya scale. Among all, 36 patients (38.3 %) had respiratory failure which is as depicted below (Table 2).

Respiratory Failure	N	%
Absent	58	61.7
Present	36	38.3
Total	94	100

Table 2. Distribution of Respiratory Failure

Based on the plasma cholinesterase levels at the time of admission, subjects were divided into three groups (normal range 4,900 – 11000 U / L).

- Mild < 10 % reduction (> 4410).
- Moderate 10 - 50 % reduction (4410 - 2450).

- Severe > 50 % re (< 2450).

The mean serum amylase value was 68.5, 100.03 and 197.16 in mild, moderate, and severe pseudocholinesterase groups respectively (P-value is < 0.0001). It is statistically significant and thus serum amylase showed statistically significant negative correlation (P < 0.0001) with pseudocholinesterase.

Category	(N=)	Mean	SD	Median	Minimum	Maximum	P value (ANOVA Test)
Mild	22 (23.4 %)	68.5	26.13	65.5	28	126	< 0.0001
Moderate	34 (36.17 %)	100.03	69.93	82.5	33	396	
Severe	38 (40.42 %)	197.16	82.07	176	85	382	

Table 3. Comparison of Amylase across Different Pseudocholinesterase Categories

Category	(N=)	Mean	SD	Median	Minimum	Maximum	P Value (ANOVA Test)
Mild	42	75.6	33.52	73	28	190	
Moderate	33	145.76	78.01	130	50	396	< 0.0001
Severe	19	232.37	87.45	232	128	382	

Table 4. Comparison of Amylase across Different Peradeniya Categories

The mean serum amylase value was 75.6, 145.76 and 232.37 in mild, moderate, and severe Peradeniya groups respectively. Serum amylase showed a high degree of positive correlation with Peradeniya score and the correlation was also statistically significant (P < HH0. 0001).

		Absent	%	Present	%	P Value (Chi Square Test / Fischer Test)
Peradeniya score	Mild	42	(100.0)	0	(0.0)	
	Moderate	16	(48.5)	17	(51.5)	< 0.001
	Severe	0	(0.0)	19	(100.0)	
Choline esterase level	Mild reduction	22	(100.0)	0	(0.0)	< 0.001
	Moderate reduction	30	(88.2)	4	(11.8)	
	Severe reduction	6	(15.8)	32	(84.2)	
Amylase level	0 - 219	58	(73.4)	21	(26.6)	< 0.001
	220 - HI	0	(0.0)	15	(100.0)	

Table 5. Distribution of Respiratory Failure Based on Serum Amylase, Choline Esterase Levels and Peradeniya Score

In the present study, respiratory failure was present in all the patients (100 %) in severe Peradeniya group, 51.5 % in moderate group and none in mild group. Respiratory failure was also present in 84.2 % of patients in severe choline esterase reduction group and only 4 % in moderate and none in mild reduction group. On comparing serum amylase all the patients with elevated amylase level had respiratory failure and only 26.6 % with normal amylase group had respiratory failure.

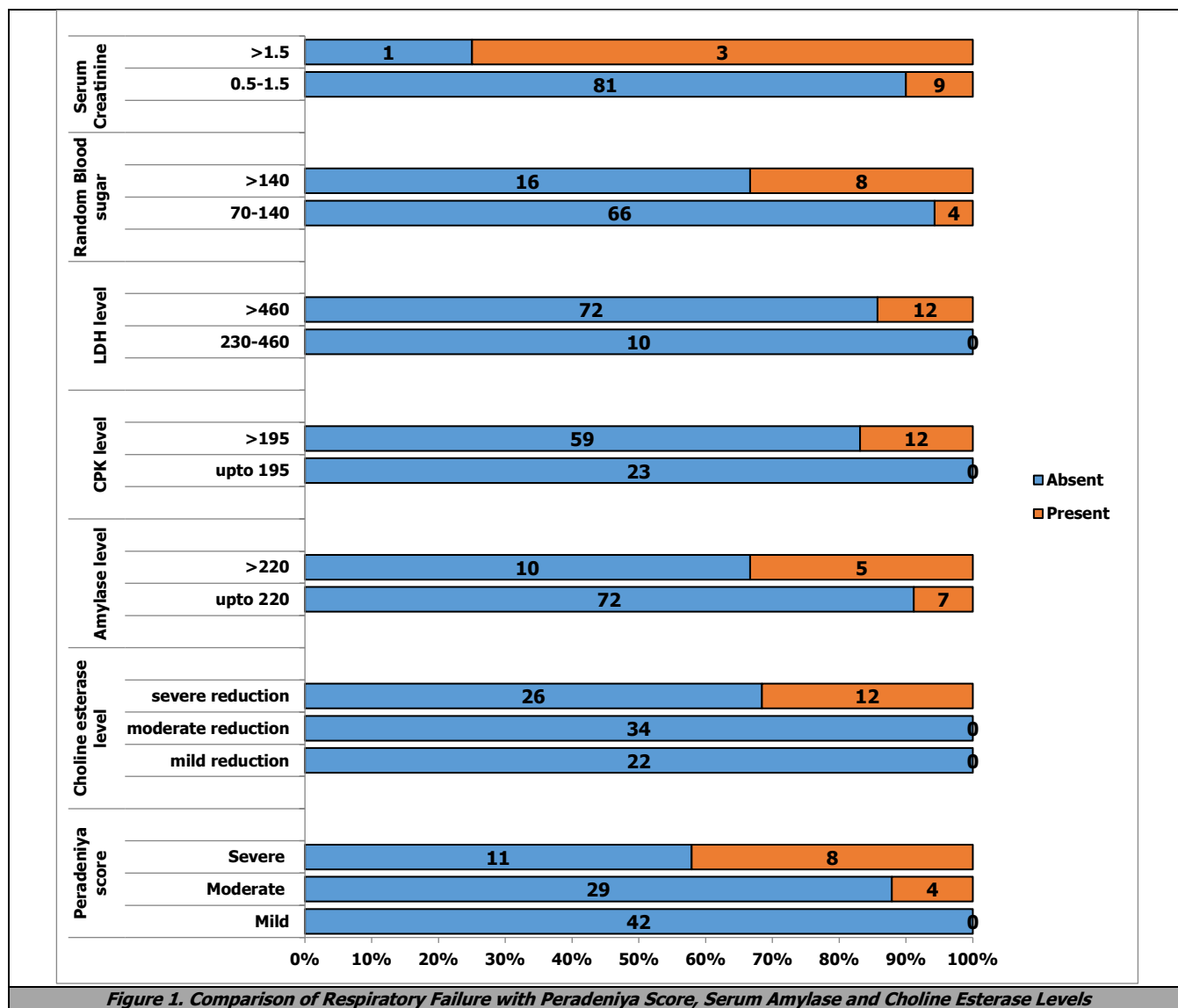


Figure 1. Comparison of Respiratory Failure with Peradeniya Score, Serum Amylase and Choline Esterase Levels

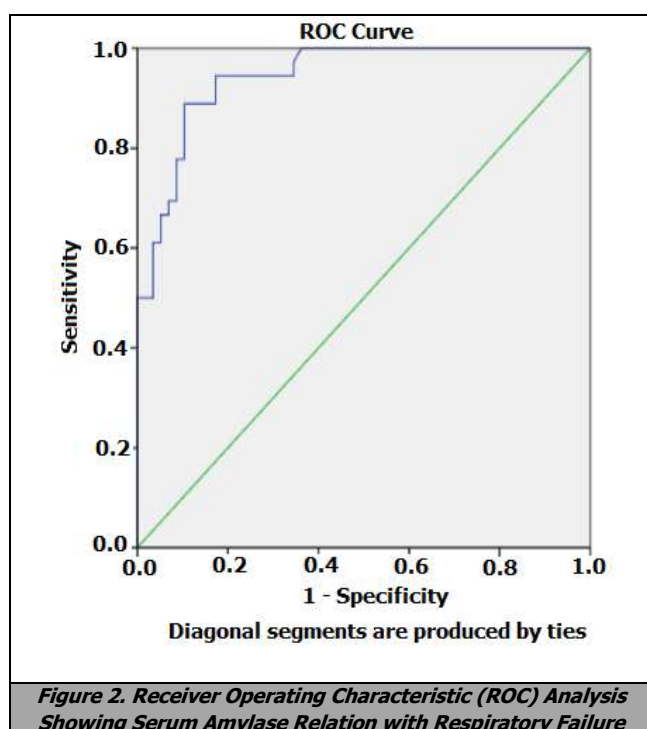


Figure 2. Receiver Operating Characteristic (ROC) Analysis Showing Serum Amylase Relation with Respiratory Failure

Serum amylase is the predictor of respiratory failure with the area under the curve of 0.948 (0.902 - 0.986) which shows that serum amylase is the excellent predictor of respiratory failure with P-value < 0.001.

DISCUSSION

Organophosphate compounds are one of the widely used insecticides in agriculture for the reason that they are easily available and accessible. Hence, organophosphate poisoning is a significant universal health concern mainly in India. It is one of the most common causes of suicide in India.

In our study, majority of the patients were in age group between 21 - 30 years (50 %). Total 84. 1 % of patients were within 40 years of age. The youngest patient in our study was 16-year-old and the eldest was an 80-year-old with median age as 27.5. This younger age group is a productive age group and vulnerable one. Hence, poverty, lack of education, various emotional conflicts that occur during this phase of life, unemployment and stressful life could be aggravating factors that increased the incidence of poisoning. This finding

corresponds with the results of studies carried out by workers Prasad et al.⁸ A Goel et al.⁹

This study revealed a slight male preponderance (53.2 %), females accounting for 46.8 % of cases. The male to female ratio in this study was 1.13:1. This corresponds to gender distribution reported by Rajeev H et al.¹⁰ A Goel et al.⁹ Kavya S.T et al.¹¹ and Sungur M, et al.¹² female predominance. The high incidence of OP poisoning in males could be because families are dependent on them and carrying more responsibilities.

The most common symptoms reported by patients in our study were vomiting (89.4 %), followed by salivation / lacrimation / sweating (56.4 %), loose stools (34.04 %), dyspnoea (35.10 %) and altered sensorium (31.9 %). Seizures were reported only in 9 patients (9.6 %). These findings correlate with the studies done by Edwin J et al.¹³ Goel et al.⁹ and Rajeev H et al.¹⁰

Miosis was the most common sign (87 %) noted in this study followed by bradycardia in 67 %, neck muscle weakness in 43.6 %, tachypnoea in 42.6 %, fasciculations in 37.2 %, crepitations in 36.2 % and altered sensorium in 31.9 % of patients. Similarly, In the study conducted by Chintale KN et al.¹⁴ most common physical finding was miosis found in 97 patients (71.32 %) followed by fasciculation (63.23 %), increased bronchiolar secretions (39.70 %), bradycardia (57.35 %), altered sensorium (5.88 %), neck muscle weakness (16.91 %).

In the present study most of the patients were in mild group (45 %) followed by moderate group (35 %) and severe group (20 %), which is comparable with Makwava Prakash V et al.¹⁵ in their study noted that a majority of the cases were in the mild group and they attributed it to the higher number of accidental consumption in the group.

In the present study, respiratory failure was present in all the patients in severe Peradeniya group whereas 51.5 % patients among moderate group and none in the mild group had respiratory failure. These findings are consistent with T N Dubey et al.¹⁶ Makwava Prakash V et al.¹⁵

Based on the pseudocholinesterase levels at the time of admission, subjects were divided into three groups¹⁷ (normal range 4,900 – 11000 U / L).

- Mild < 10 % reduction (> 4410).
- Moderate 10 - 50 % reduction (4410 - 2450).
- Severe > 50 % reduction (< 2450).

Here, out of 94 patients 22 were in mild group, 34 were in moderate group and 38 patients had severe reduction of pseudocholinesterase levels.

The mean serum amylase value was 68.5, 100.03 and 197.16 in mild, moderate, and severe pseudo cholinesterase groups respectively. Majority of patients who had increased amylase levels belong to group III and showed significant negative correlation with plasma cholinesterase levels. Serum amylase showed a high degree of positive correlation with Peradeniya score and the correlation was also statistically significant. Out of 94 patients studied 15 had elevated Serum amylase level and all of them developed respiratory failure and 5 patients have died due to various complication.

Our study results were in accordance with the study done by Lin CL et al. where they found that mean amylase levels

were elevated in patients with respiratory failure and serum amylase levels predicted ventilator support in OP poisoning.

Serum amylase can be considered as a predictor of severity of OP poisoning and respiratory failure as explained above in ROC curve ($P < 0.001$).

CONCLUSIONS

Correlation between the severity of OP poisoning (based on pseudocholinesterase and Peradeniya scoring) and serum amylase was statistically significant, and it is useful in predicting the development of respiratory failure. Pseudocholinesterase and serum amylase can also be used to predict the outcome of the patients.

Limitations

In our study, serial estimation of serum amylase was not done during hospital stay. Larger population with probability sampling technique is ideal in community-based study and also most of these biochemical parameters lack specificity.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.

Financial or other competing interests: None.

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