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# "Study of Serum Amylase and Serum Cholinesterase Levels in Cases of Organophosphosphorous Poisoning and It's Correlation With Severity of Disease"

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**ABSTRACT**

**BACKGROUND**

Organophosphorus (OP) compounds are the most common suicidal poison in developing countries and mortality continues to be high.

**MATERIALS AND METHODS**

The study was conducted in the Department of Medicine, Netaji Subhash Chandra Bose Medical College and Hospital city of Jabalpur in the state of Madhya Pradesh, India. 80 patients presented with consumption of Organophosphate compound were included in the study. Serum cholinesterase and serum amylase levels were estimated on admission.

**RESULTS**

Patients were grouped into 3 categories based on reduction in serum cholinesterase activity. Clinical severity was classified on the basis of POP scale(Peradeniya Organophosphate Poisoning).Proportion of patients with serum cholinesterase(U/L):- <2500 U/L{Group III} was significantly higher in POP score 8-11{severe} and 4-7{moderate} as compared to 0-3 {Mild}. (<2500 U/L{Group III}:- 100%, 87.50% vs 46.15% respectively). (p value=0.003).Proportion of patients with serum amylase(U/L):- >160 U/L{Elevated} was significantly higher in POP score 4-7{moderate} and 8-11{severe} as compared to 0-3 {Mild}. (>160 U/L{Elevated}:- 83.33%, 75% vs 51.92% respectively). (p value=0.019).Mean ± SD of serum cholinesterase(IU/mL) in patients who did not require ventilatory support was 2525 ± 1403.91 which was significantly higher as compared to patients who required ventilatory support (931.81 ± 852.52).(p value <.0001)The mean ± SD of serum amylase (IU/mL) in patients who did not require ventilatory support was 169.76 ± 45.76 and patients who required ventilatory support was 178.76 ± 28.45 with no significant association between them. (p value=0.3)

**CONCLUSION:**

The present study concluded that serum cholinesterase levels decrease whereas serum amylase levels are elevated in patients with organophosphorus poisoning. There is a significant correlation between the severity of poisoning and the degree of derangement of serum cholinesterase and serum amylase level at the initial presentation. The higher the POP score, the higher the degree of derangement. A significant negative correlation was seen between serum cholinesterase(U/L) with serum amylase(U/L). There is a significant correlation between serum cholinesterase levels with mortality and requirement of ventilatory support. However, there was no significant association between serum amylase levels with mortality and requirement of ventilatory support. Therefore, serum cholinesterase can be used as a marker to assess the prognosis of the disease in organophosphate poisoning whereas role of serum amylase as a prognostic marker needs further studies and evaluation.

## I. INTRODUCTION

Organophosphates (OP) are chemical substances produced by the process of esterification between phosphoric acid and alcohol. Organophosphates can undergo hydrolysis with the liberation of alcohol from the ester bond. These chemicals are the main components of herbicides, pesticides, and insecticides. OPs are also the main components of nerve gas. Acute or chronic exposure to OPs can produce varying toxicity levels in humans, animals, plants, and insects. From the clinical perspective, OPs are of interest because of the toxicity produced from exposure. Nerve gas and organophosphate pesticides (OPP) are particularly important from a clinical standpoint because of the cholinergic symptoms produced from exposure.[1,2]

Manifestation of OP poisoning is categorized as the muscarinic, nicotinic, and central nervous system. Overstimulation of muscarinic receptor present with parasympathetic excitement, including miosis, bradycardia, and bronchorrhea. The nicotinic reaction consists of muscle fasciculation, cramping, and weakness, while loss of consciousness, respiratory depression, and seizures are due to central nervous system effects. Diagnosis mainly is based on clinical signs.[3]

Laboratory evaluation plays an important and vital role for confirmation of poisoning, diagnosing the first acute organ damage and assessing the severity of poisoning. In laboratory evaluation of OP poisoning, assessment of plasma cholinesterase is most specific lab test for OP poisoning.[4]

Elevated serum amylase (hyperamylasaemia) secondary to pancreatic injury because of parasympathetic overstimulation and hypersecretion has been noted in human beings and both of this are found closely related in different studies.[5] A clinical scale to assess severity or organophosphorus (OP) intoxication is used commonly which is also known as POP(Peradeniya Organophosphate Poisoning) scale. Five common clinical manifestations of OP poisoning have been used as parameters, each to be assessed on a 3 point scale varying from 0-2. Poisoning is then graded as mild (score 0-3), moderate (score 4-7) or severe (score 8-11) .[6]

## II. MATERIALS AND METHODS

The study was conducted in the Department of Medicine, Netaji Subhash Chandra Bose Medical College and Hospital city of Jabalpur in the state of Madhya Pradesh, India. 80 patients presented with consumption of Organophosphate compound were included in the study. Serum cholinesterase and serum amylase levels were estimated on admission.

INCLUSION CRITERIA:All cases of OP poisoning confirmed by history, circumstantial evidence of poisoning, specific clinical examination, and basic laboratory reports were included in the study.

EXCLUSION CRITERIA:Patients with history of intake of OP compound mixed with any other poison or alcohol, chronic alcoholism, disorders of salivary gland were excluded from the study.

SAMPLING METHOD:
Considering the best availability of the patients by reviewing the previous records of the health facility, to achieve the maximum sample size we randomly screened all patients and selected those who fulfilled the inclusion and exclusion criteria and were ready to give the written informed consent.

TOOLS USED :
1. Detailed History of symptoms onset and risk factors.
2. Clinical examination
3. Hematological investigations were done at N.S.C.B Medical College, Jabalpur.
4. Serum Cholinesterase: Estimation of serum cholinesterase activity by kinetic method based on hydrolysis of butyrylthiocholine by choline esterase.
5. Serum Amylase: Estimation of serum amylase by chromogenic method using dyed amylopectin.

## III. STATISTICAL ANALYSIS

The presentation of the Categorical variables was done in the form of number and percentage (%). On the other hand,the quantitative data were presented as the means ± SD and as median with 25th and 75th percentiles (interquartile range). The following statistical tests were applied for the results:
1. The association of the variables which were quantitative in nature were analyzed using Independent t test (for two groups) and ANOVA test (for more than two groups).
2. The association of the variables which were qualitative in nature were analyzed using Chi-Square test. If any cell had an expected value of less than 5 then Fisher's exact test was used.
3. Pearson correlation coefficient was used for correlation of Serum cholinesterase (U/L) and Serum amylase (U/L) with duration of stay(days) and POP score.
4. Receiver operating characteristic curve was used to find cut off point, sensitivity, specificity, positive predictive value and negative predictive value of Serum cholinesterase (U/L) and Serum amylase (U/L) for predicting mortality.
The data entry was done in the Microsoft EXCEL spreadsheet and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, ver 25.0.
For statistical significance, p value of less than 0.05 was considered statistically significant.

## IV. RESULTS

35 patients belonged to the age group 20-30 years followed by 31-40 years [15] and <20 years [14].Mean value of age(years) of study subjects

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was 30.91 ± 13.1. 40(50.00%) patients were females and males each.

**Table 1:-Distribution of age(years) of study subjects.**

| Age(years) | Frequency | Percentage |
|---|---|---|
| <20 | 14 | 17.50% |
| 20-30 | 35 | 43.75% |
| 31-40 | 15 | 18.75% |
| 41-50 | 8 | 10.00% |
| >50 | 8 | 10.00% |
| Mean ± SD | 30.91 ± 13.1 | |
| Median(25th-75th percentile) | 26(20.75-38.5) | |
| Range | 15-65 | |

In majority [56(70.00%)] of patients, area of residence was rural. Area of residence was urban of only 24 out of 80 patients (30.00%).

In majority [49(61.25%)] of patients, serum cholinesterase(U/L) was <2500 U/L{Group III} followed by 2500 to 4500 U/L {Group II} [23(28.75%)]. Serum cholinesterase(U/L) was >4500 U/L {Group I} in only 8 out of 80 patients (10.00%). Mean value of serum cholinesterase(U/L) of study subjects was 2106.79 ± 1458.99.

In majority [50(62.50%)] of patients, serum amylase(U/L) was >160 U/L{Elevated}. Serum amylase(U/L) was <=160 U/L {Normal} in only 30 out of 80 patients (37.50%). Mean value of serum amylase(U/L) of study subjects was 172.12 ± 41.93

Clinical severity was based on POP scoring- 8-11{severe}, 4-7{moderate} and to 0-3 {Mild}.

In majority [52(65.00%)] of patients, POP score was 0-3 {Mild} followed by 4-7{moderate} [24(30.00%)]. POP score was 8-11{severe} in only 4 out of 80 patients (5.00%). Mean value of POP score of study subjects was 3.11 ± 2.42

Proportion of patients with serum cholinesterase(U/L):-<2500 U/L{Group III} was significantly higher in POP score 8-11{severe} and 4-7{moderate} as compared to 0-3 {Mild}. (<2500 U/L{Group III}:- 100%, 87.50% vs 46.15% respectively). (p value=0.003).Mean ± SD of serum cholinesterase(U/L) in POP score 0-3 {Mild} was 2731.13 ± 1363.52 which was significantly higher as compared to 4-7{moderate} (1017.25 ± 792.8) and 8-11{severe} (527.5 ± 224.8).(p value<.0001)

**Table 2:-Association of serum cholinesterase(U/L) with POP score.**

| Serum cholinesterase(U/L) | 0-3 {Mild}(n=52) | 4-7{Moderate}(n=24) | 8-11{Severe}(n=4) | Total | P value |
|---|---|---|---|---|---|
| >4500 U/L {Group I} | 8 (15.38%) | 0 (0%) | 0 (0%) | 8 (10%) | 0.003* |
| 2500 to 4500 U/L {Group II} | 20 (38.46%) | 3 (12.50%) | 0 (0%) | 23 (28.75%) | |
| <2500 U/L{Group III} | 24 (46.15%) | 21 (87.50%) | 4 (100%) | 49 (61.25%) | |
| Mean ± SD | 2731.13 ± 1363.52 | 1017.25 ± 792.8 | 527.5 ± 224.8 | 2106.79 ± 1458.99 | <.0001§ |
| Median(25th-75th percentile) | 2726 (1784.75-3440) | 727.5 (571.25-950.25) | 592 (480-639.5) | 1914 (812-3122) | |
| Range | 226-5622 | 212-3182 | 204-722 | 204-5622 | |

* **Fisher's exact test,** § **ANOVA**

Proportion of patients with serum amylase(U/L):->160 U/L{Elevated} was significantly higher in POP score 4-7{moderate} and 8-11{severe} as compared to 0-3 {Mild}. (>160 U/L{Elevated}:- 83.33%, 75% vs 51.92% respectively). (p value=0.019).Mean ± SD of serum amylase(U/L) in POP score 8-11{severe} was 202.75 ± 38.31 which was significantly higher as compared to 4-7{moderate} (188.62 ± 36.26) and 0-3 {Mild} (162.15 ± 41.72). (p value=0.011)

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**Table 3:-Association of serum amylase(U/L) with POP score.**

| Serum amylase(U/L) | 0-3 {Mild}(n=52) | 4-7{Moderate}(n=24) | 8-11{Severe}(n=4) | Total | P value |
|---|---|---|---|---|---|
| <=160 U/L {Normal} | 25 (48.08%) | 4 (16.67%) | 1 (25%) | 30 (37.50%) | 0.019* |
| >160 U/L{Elevated} | 27 (51.92%) | 20 (83.33%) | 3 (75%) | 50 (62.50%) | |
| Mean ± SD | 162.15 ± 41.72 | 188.62 ± 36.26 | 202.75 ± 38.31 | 172.12 ± 41.93 | 0.011§ |
| Median(25th-75th percentile) | 162 (132-188.25) | 190 (173.75-207) | 204 (187.25-219.5) | 176 (135.5-198) | |
| Range | 82-280 | 110-246 | 155-248 | 82-280 | |

* **Fisher's exact test,** § **ANOVA**

Mean ± SD of serum cholinesterase(IU/mL) in patients who did not require ventilatory support was 2525 ± 1403.91 which was significantly higher as compared to patients who required ventilatory support (931.81 ± 852.52).(p value <.0001)

Mean ± SD of serum amylase (IU/mL) in patients who did not require ventilatory support was 169.76 ± 45.76 and patients who required ventilatory support was 178.76 ± 28.45 with no significant association between them. (p value=0.3)

Mean ± SD of serum cholinesterase (IU/mL) in discharged patients was 2339.12 ± 1447.9 which was significantly higher as compared to died (1011.5 ± 942.08).(p value=0.0002)

Mean ± SD of serum amylase (IU/mL) in discharged patients was 170.42 ± 44.61 and in died was 180.14 ± 25.43 with no significant association between them. (p value=0.274)

Area under curve of Serum Cholinesterase(IU/mL) for predicting requirement of ventilatory support was significantly higher than serum amylase(IU/mL). (p value<.0001)

**Table 4 :- Receiver operating characteristic curve of Serum cholinesterase(IU/mL) and Serum amylase(IU/mL) for predicting requirement of ventilatory support.**

| Variables | Serum cholinesterase(IU/mL) | Serum amylase(IU/mL) |
|---|---|---|
| Area under the ROC curve (AUC) | 0.863 | 0.579 |
| Standard Error | 0.0517 | 0.0652 |
| 95% Confidence interval | 0.768 to 0.930 | 0.464 to 0.689 |
| P value | <0.0001 | 0.2227 |
| Cut off | ≤872 | >134 |
| Sensitivity(95% CI) | 76.19%(52.8 - 91.8%) | 95.24%(76.2 - 99.9%) |
| Specificity(95% CI) | 89.83%(79.2 - 96.2%) | 32.2%(20.6 - 45.6%) |
| PPV(95% CI) | 72.7%(49.8 - 89.3%) | 33.3%(21.7 - 46.7%) |
| NPV(95% CI) | 91.4%(81.0 - 97.1%) | 95%(75.1 - 99.9%) |
| Diagnostic accuracy | 86.25% | 48.75% |
| P value comparing AUC | <0.0001 | |

**DeLong et al test**

Area under curve of serum cholinesterase (IU/mL) for predicting mortality was significantly higher than serum amylase (IU/mL). (p value=0.002)

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**Table 5 :- Receiver operating characteristic curve of Serum cholinesterase(IU/mL) and Serum amylase(IU/mL) for predicting mortality.**

| Variables | Serum cholinesterase(IU/mL) | Serum amylase(IU/mL) |
|---|---|---|
| Area under the ROC curve (AUC) | 0.797 | 0.595 |
| Standard Error | 0.0721 | 0.0721 |
| 95% Confidence interval | 0.692 to 0.878 | 0.480 to 0.704 |
| P value | <0.0001 | 0.1867 |
| Cut off | ≤812 | >170 |
| Sensitivity(95% CI) | 71.43%(41.9 - 91.6%) | 78.57%(49.2 - 95.3%) |
| Specificity(95% CI) | 83.33%(72.1 - 91.4%) | 53.03%(40.3 - 65.4%) |
| PPV(95% CI) | 47.6%(25.7 - 70.2%) | 26.2%(13.9 - 42.0%) |
| NPV(95% CI) | 93.2%(83.5 - 98.1%) | 92.1%(78.6 - 98.3%) |
| Diagnostic accuracy | 81.25% | 57.50% |
| P value comparing AUC | 0.002 | |

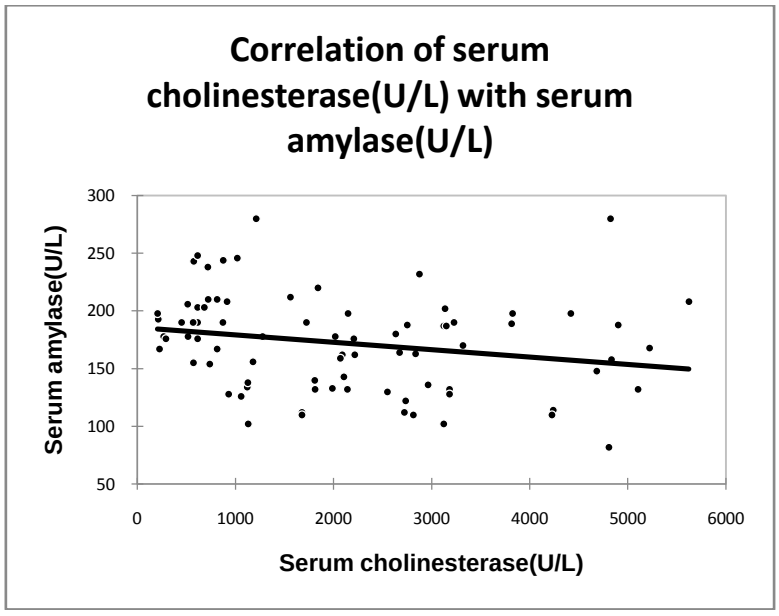
**DeLong et al test**

Significant negative correlation was seen between serum cholinesterase(U/L) with serum amylase(U/L) with correlation coefficient of -0.222.

**Table 6 :-Correlation of serum cholinesterase(U/L) with serum amylase(U/L).**

| Variables | Serum amylase(U/L) Serum cholinesterase(U/L) |
|---|---|
| Correlation coefficient | -0.222 |
| P value | 0.048 |

**Pearson correlation coefficient**



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## V. DISCUSSION

The study was conducted in the Department of Medicine, Netaji Subhash Chandra Bose Medical College and Hospital city of Jabalpur in the state of Madhya Pradesh, India. 80 patients presented with consumption of Organophosphate compound were included in the study. Serum cholinesterase and serum amylase levels were estimated on admission. Correlation of these laboratory parameters with outcome may help in defining important parameters which can predict the course of disease in organophosphate poisoning.

Majority of patients belonged to age group 20-30 years followed by 31-40 years. These findings are consistent with those of Vilas Honnakatti et al[7] and Gagarin et al[8] where majority of age group belonged to 20-30yrs (51%), 20 to 40 years (64%) and 21 to 40 years (66%) respectively.

In our study, males (50%) and females (50%) were equally affected whereas study done by Palash Kumar Biswas et al[9] had males (48%) and females (52%). This shows that there was no significant difference between incidence in males and females in case of organophosphate poisoning.

In our study, maximum patients belonged to rural areas which is consistent with findings of Palash Kumar Biswas et al[9] which may be due to easy access of pesticides to people belonging to rural areas. However, we cannot compare suicidal ideation due to stress in rural and urban areas.

The POP score was calculated for all patients at initial presentation.65% patients had a mild degree of poisoning whereas 30 % patients had moderate degree and 5 % had severe degree of poisoning. This is consistent with findings of Palash Kumar Biswas et al[9] and Vilas Honakatti et al[7] where majority of the patients belonged to mild severity. Dubey T et al in his study in 2016 found that 68% were mild ,27% moderate and 5% were in severe POP scale. In study of Yuri Gagarin[8] et al mild degree were 17%, moderate degree were 58% and severe were 25%. This variation in findings may be due to variability in time of presentation and amount of poison consumed.

In our study mean serum cholinesterase level was 2106.79 ± 1458.99 IU/ml. Patients were grouped into 3 categories based on reduction in serum cholinesterase activity. Group 1(>4500 U/L) were 10%, group 2(2500 to 4500 U/L) were 28.75% and group 3(<2500 U/L) were 61.25%.

On comparison of serum cholinesterase levels with POP score, Mean ± SD of serum cholinesterase(U/L) in POP score 0-3 {Mild} was 2731.13 ± 1363.52 which was significantly higher as compared to 4-7{moderate} (1017.25 ± 792.8) and 8-11{severe} (527.5 ± 224.8). (p value<.0001) which means that there is a significant correlation between the severity of poisoning categorized by the POP scale and the serum cholinesterase levels at the time of initial presentation of the patients.

Our findings are consistent with study of Vilas Honnakatti et al[7], Giridhar Patil et al[10] and V Agrawal[11] et al, where they also found a significant correlation between severity of disease and serum cholinesterase levels.

In our study, mean value of serum amylase(U/L) of study subjects was 172.12 ± 41.93 whereas in study done by Patil A et al it was 376.03. Mean serum amylase in study done by Biswas et al was 62.2 U/L ± 18.7 in patients with normal serum amylase and 376.56 U/L ± 266.12 in patients with elevated serum amylase.

On comparison of serum amylase levels with POP score Mean ± SD of serum amylase(U/L) in POP score 8-11{severe} was 202.75 ± 38.31 which was significantly higher as compared to 4-7{moderate} (188.62 ± 36.26) and 0-3 {Mild} (162.15 ± 41.72). (p value=0.011). Dubey T et al[5] in his study found stastically significant relationship between POP level of severity and serum amylase levels. Zoebiri et al also had similar findings where higher serum amylase than normal was associated with severe clinical course. In the study done by Biswas et al[12] and Dungdung et al[13], there was significant association between severity (assessed by POP scale) and elevated level of serum amylase.

Negative correlation between serum cholinesterase and serum amylase levels was seen in our study which was consistent with findings of Dungung et al[13].

Serum cholinesterase levels are decreased in patients of organophosphate poisoning and it also correlates with severity of poisoning. Serum amylase levels are increased in patients of organophosphate poisoning and it also correlates with severity of poisoning. However, serum cholinesterase is a better predictor of prognosis than serum amylase.

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