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Original Research Article

Acute pancreatitis, a significant mortality predictor in acute organophosphate poisoning: an observational study in a tertiary care centre in north India

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ABSTRACT

Background: Organophosphate compounds are one of the most common agents used as poison and acts by accumulation of acetylcholine hormone at neuronal synapses resulting in the symptoms like excessive salivation, vomiting, urination, and increased serum amylase and lipase levels. APACHE 2 score along with ultrasound modality can be used to assess the acute pancreatitis. The primary aim of the study is to find correlation of serum amylase and lipase levels with duration of ICU stay and with radio-logical variables like bulky pancreas.
Methods: This observational study conducted at GSVM medical college, Kanpur from December 2020 to October 2022 included 58 out of total 94 admitted patients with acute organophosphate intoxicationn on the basis of inclusion and exclusion criteria. Patients were divided in 3 groups as mild, moderate and severe using q SOFA score at the time of admission.
Results: Acute organophosphate poisoning was more prevalent among 20-40 years of age group. Mean serum amylase level values in q SOFA category 0, 1, 2, 3 were 65.2, 82.0, 118.4, 329.9 IU/l respectively and that of mean serum lipase levels on day 1 of admission values were 42.0, 44.3, 38.6 and 115.5 IU/l respectively. Serum amylase levels were positively correlated with duration of ICU stay and were better predictor for acute pancreatitis.
Conclusions: In this study we concluded that serum amylase is a better predictor of duration of ICU stay and acute pancreatitis in patients admitted with acute organophosphate poisoning.

Key words: Organophosphates, qSOFA, Serum amylase, APACHE2 score, Acute pancreatitis

INTRODUCTION

Self-inflicted violence accounts for almost half of the total violent deaths that occur every year worldwide. About 63% of global deaths due to suicide occur in the Asia Pacific region. According to National crime records bureau India, every 5 minutes a person commits suicide and 7 attempt to kill themselves, accounting for 1,00,000 deaths per year. Suicide rates are highest in the state of Uttar Pradesh. Majority of the victims belonged to the age group 14-34 years and organophosphate compounds (OPC) are the most common agent used for suicide purpose.[1] As time advances, pesticides are now a days widely used for modern cultivation methods and therefor, they are readily available as over the counter drugs even in village shops and act as common agents for suicidal purposes. Most of these deaths occur in rural areas, where easy access to highly toxic pesticides turns many impulsive acts of self-poisoning into suicide.[2] In India OPC intake is the commonest method of suicide (40.5%)

after hanging (49%). Hospital-based data suggest that barbiturates and copper sulfate were the commonly used agents for suicide in the years, 1972-1977; however, later they were replaced by OP compounds and aluminium phosphide. Organophosphate insecticides are responsible for as much as 75% of all poisonings in our country today.[3] The gastrointestinal symptoms following Organophosphate compound poisoning are excessive salivation, nausea, vomiting, abdominal pain and diarrhea. Both in experimental studies and in humans exposed to these compounds pancreatic damage had been reported. Pancreatic injury in humans may be painless and marked by elevated serum amylase, elevated serum lipase, hyperglycemia and glycosuria.[4] Occasionally, symptomatic acute pancreatitis can occur. The incidence of the latter varies from 7–22% depending on type of study, compound characteristics and level of work up and investigations done.[5]

The OP compounds act by inhibiting acetylcholine esterase enzyme at nerve endings and neuromuscular junction, causing overstimulation of acetylcholine receptors. Signs and symptoms of poisoning are mainly due to muscarinic, nicotinic and central nervous system (CNS) receptor overstimulation.[6] The muscarinic receptor stimulation in pancreas yields increase in serum amylase and lipase levels. In acute OP poisoning, the severity of poisoning correlates with increase in serum amylase levels.[7]

Various scoring systems such as acute physiology and chronic health evaluation score (APACHE 2) are available, but laboratory evaluation plays an important and vital role for confirmation of poisoning, diagnosing the first acute organ damage and assessing the severity of poisoning.[8] In laboratory evaluation of OP poisoning, assessment of plasma cholinesterase is most specific lab test for OP poisoning, but serum amylase levels comes out to be the most sensitive lab test for OP poisoning. Increase levels of amylase and lipase are well documented in various studies and may be due to excessive cholinergic stimulation of pancreas.[9] The present study was conducted to find the incidence of increased levels of serum amylase and serum lipase in OPC poisoning and to identify the relation with prognosis and clinical outcome, out of which one outcome was acute pancreatitis.

METHODS

The study was conducted at Post graduate department of Medicine, GSVM medical college, Kanpur among the patients suffering from acute Organophosphate poisoning and admitted in emergency/ICU/medicine ward within 24 hours of intoxication event. This was an observational study conducted from December 2020 to October 2022 with sample size of 94 patients out of which only 58 patients fulfill the inclusion and exclusion criteria. Patients of age >18 years of age (male and female) with acute (within 24 hours) organophosphate poisoning were included in this study.

Patients excluded from this study were those with history of acute pancreatitis in last 3 months, previous history of organophosphate poisoning, patients with chronic diseases like diabetes mellitus, chronic alcoholic liver disease and chronic kidney disease. Patients with history of abdominal trauma, with parotid disorder and pregnant lady were also excluded from this study. Patients who are taking drugs like thiazides, furosemide, ecothiophate, steroids, oral contraceptives, valproate and various antipsychotic drugs were excluded from the study.

Procedure

Patient with history of acute OP poisoning (intake within last 24 hours) was admitted & selected for study as per inclusion and exclusion criteria. Using the qSOFA score, selected patients were divided into 3 groups (mild/moderate/severe). In all 3 groups (mild/moderate/severe), s. amylase and lipase levels were measured. In all 3 groups (mild/moderate /severe), Outcome variables like duration of ICU stay, need of intubation and radiological outcome variables like pancreatic size and echogenicity on ultrasound whole abdomen and relevant data is collected for statistical analysis.

Statistical analysis

Statistical analysis was done using the Jamovi project 2022(version 2.3), data was collected and frequency tables were created and appropriate tests were applied and P value <0.05 was considered significant.

RESULTS

Acute organophosphate poisoning was more prevalent among 20-40 years of age group with prevalence in females (62.1%) and males (37.9%) (Figure 1).

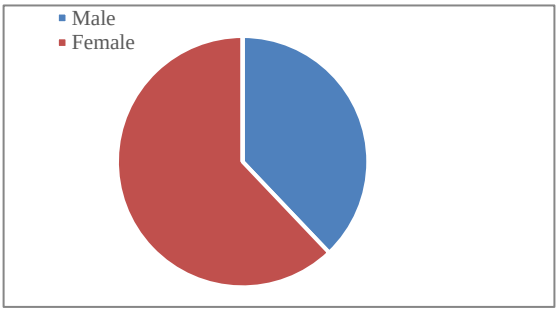

Figure 1: Gender wise distribution of cases (n=58).

The serum amylase and lipase levels were distributed among all the cases in this study with non-normal distribution in positively skewed manner with few outliers (Table 1). Mean serum amylase level values in various q SOFA categories (0, 1, 2 and 3) were 65.2, 82.0, 118.4 and 329.9 IU/l respectively with p value < 0.001 (Table 2) and that of mean serum lipase level values were 42.0, 44.3,

38.6 and 115.5 IU/l respectively with p value 0.059 (Table 3).

Table 1: Representative of total number of cases with mean, median serum amylase and lipase levels along with their standard deviation values.

Descriptive	Serum amylase	Serum lipase
N	58	58
Mean	198	75.7
Median	106	50
SD	260	98.7
Minimum value	45	27
Maximum value	1280	720

Table 2: Frequency table of serum amylase level in relation to q SOFA category (welch test).

q SOFA	N	Mean s. amylase	SD	SE
0	6	65.2	10.6	4.31
1	17	82.0	21.0	5.10
2	8	118.4	52.3	18.50
3	26	329.9	341.4	66.96

Table 3: Frequecny table of serum lipase levels in relation to q SOFA (welch test).

q SOFA	N	Mean s. lipase	SD	SE
0	6	42.0	5.4	2.21
1	17	44.3	10.92	2.65
2	8	38.6	10.23	3.62
3	26	115.5	136.72	26.81

Results of serum amylase levels were analyzed using one way ANOVA test or Welch test and it was found that higher serum amylase values were seen with higher values of q SOFA score which was statistically significant with p value < 0.001 (Figure 2).

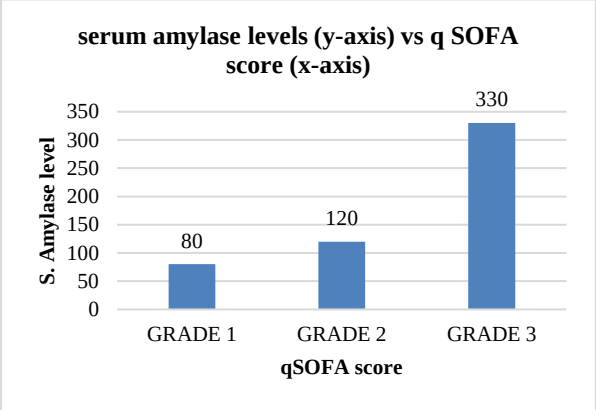

Figure 2: Component bar chart representative of serum amylase level distribution as per q-SOFA category using one way ANOVA test or Welch test.

Results of serum lipase levels using Welch test were not significant with p values 0.059. Following ROC curve is representative of accuracy of serum amylase levels in prediction of acute pancreatitis in patients with acute OP poisoning with sensitivity 97.9% and specificity 44.4% with Area under the curve (AUC) 0.965, which was statistically significant with p value 0.003 (Figure 3). In our study, 6.9% patients developed acute pancreatitis and showed edematous pancreas on ultrasound whole abdomen. Out of these acute pancreatitis patients, 50% died and 50% survived. Overall mortality was 17.2% in our study while 82.7% of recruited patients survived. Among the individual clinical severity group, mortality in mild group (q-SOFA=0 or 1) was 5.8%, in moderate group (q-SOFA=2) was 19.8% and in severe group (q-SOFA=3) was 30.8% (Figure 4). Estimates in (Table 4) represents log of odds of acute pancreatitis (bulky pancreas/normal pancreas).

Table 4: Binomial logistic regression analysis was also used to find out correlation between serum amylase levels and ultrasonographic variable (bulky or echogenic pancreas/normal pancreas).

Predictor	Estimate	SE	Z	P value
S. amylase	-0.00572	0.00192	-2.97	0.003
S. lipase	0.016	0.01111	0.71	0.12

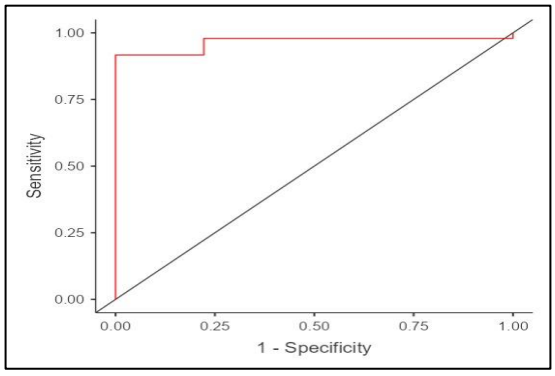

Figure 3: ROC curve representing predictablity of acute pancreatitis using serum amylase levels in patients with acute organophosphate poisoning.

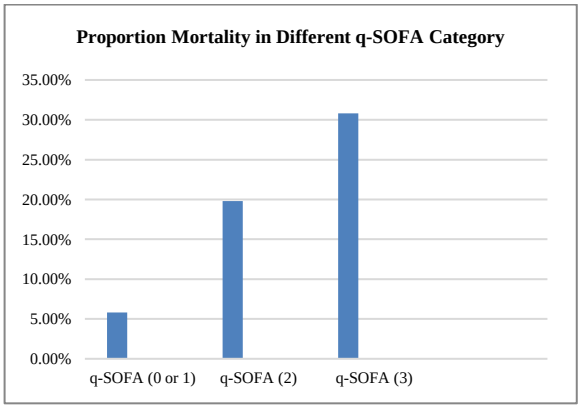

Figure 4: The number of deaths among individual clinical severity group using q-SOFA score.

DISCUSSION

Studies have been conducted in past to assess prognostic role of serum amylase and lipase levels in acute organophosphate poisoning and their relation with prognostic clinical scores like q SOFA score and APACHE 2 score.[10] In our study, statistically significant increase in serum amylase and lipase level values were seen in patients with higher q SOFA score values using one way ANOVA test analysis. A positive correlation was also seen between serum amylase values and outcome variable(duration of ICU stay) with p value 0.041, however , correlation between serum lipase values & duration of ICU stay was not significant (p value 0.591), as per linear regression analysis. Binomial regression analysis shows that serum amylase was better predictor than serum lipase, of acute pancreatitis with AUC, sensitivity and specificity are 0.965, 97.9% and 44.4% respectively.

Overall mortality in our study was 17.2% while 82.7% of recruited patients were survived. Among the indivudual clinical severity group, mortality in mild group (q SOFA-0/1) was 5.8%, in moderate group (q SOFA-2) was 19.8% and in severe group (q SOFA-3) was 30.8%. 6.9 percent patients admitted with acute OP poisoning developed acute pancreatitis and showed edematous pancreas on ultrasound whole abdomen. Out of these acute pancreatitis patients, approximatly 50% died and 50% survived. The positive correlation of serum amylase levels with poor clinical profile in our study was in accordance with the previous study like, in which the amylase levels were significantly elevated at the time of admission (178.21 U/l) and had shown a gradual remission with proper treatment.[4] The mean amylase level in severely poisoned patients in their study was 294.8 U/l, while the mean amylase level in our study in severely poisoned patients was 329.4 IU/l. Serum amylase levels may be considered as a marker of Organophosphorous intoxication, since it enables the early recognition of severity and to identify those at risk of developing the complications of Organophosphorous poisoning. Acute pancreatitis as a complication of OP intoxication is not a rare condition and significant number of patients developed this complication. In order to improve the outcome of OP poisoning, early diagnosis of acute pancreatitis is important and serum levels of amylase and lipase should be routinely considered carefully. Hyperamylasemia and associated clinical severity found in our study was in accordance with the previous studies in which they carried out a retrospective study of medical records of 121 patients with the diagnosis of OP poisoning over three years in Veterans General Hospital, National Yang-Ming University in 1998.[10,11] Serum amylase, pancreatic amylase, salivary amylase, lipase and cholinesterase levels and the clinical manifestations were analyzed. It was observed that 44 patients (36%) had hyperamylasemia (Amylase >360 U/l). Lipase was measured in 28 patients with hyperamylasemia; nine of 28 had hyperlipasemia (Lipase > 380 U/l). In our study also, mean serum amylase levels in patients with qSOFA score=3 is 329.4 IU/l and mean serum amylase levels in patients of OP poisoning with ventilatory support was 354 IU/l. The finding of hyperamylasemia was closely related to clinical severity and presence of shock. Hence, it was concluded that hyperamylasemia is frequent in severe OP poisoning. However, hyperamylasemia is not synonymous with acute pancreatitis and pancreatic amylase is not reliable parameter in the diagnosis of organophosphate induced pancreatitis due to its low sensitivity, as it is also seen in our study that sensitivity of serum amylase levels in predicting clinical severity is around 65%. Our study was well correlated with the previous studies in which they studied that serum amylase, lipase and CPK were negatively correlated with plasma cholinesterase levels.[9] Serum amylase showed statistically significant negative correlation with plasma cholinesterase. Serum amylase showed the highest diagnostic accuracy for assessing severity of poisoning followed by CPK and Lipase. OP poisoning is associated with hyperamylasemia. Serum amylase, lipase and CPK can be used as an additional prognostic indicator with plasma cholinesterase levels. Serum amylase could be considered as a better predictor of severity followed by CPK and lipase. Our study was also well correlated with the previous study[11] in which, they concluded that serum amylase levels were raised in 45.45% of the patients and serum lipase were raised in 37.37%. Computed tomography of the abdomen showed acute pancreatitis in 6.06% of the patients while mortality was noted in 13.13%. Strong positive correlation was noted between serum amylase and APACHE II scores and incidence of acute pancreatitis. There are also various studies which are well correlated with our study in one or other prospectives. Our study has several limitations also. Sample size was relatively small because all the patients of acute organophosphate poisoning does not meet the inclusion and exclusion criteria. Secondly, quality (chemical and trade name of poison) and potency of poison can not be assessed because many patients does not keep the documentation of type and amount of poison. Thirdly, only ultrasound modality was used to assess pancreatic anatomy and not CT scan.

CONCLUSION

The study found that levels of serum amylase & lipase were increased in statistically significant number of cases of acute organophosphate poisoning. These levels can be used as prognostic marker in cases of acute organophosphate poisoning as well as levels of amylase & lipase were well correlated with the severity of acute organophosphate poisoning, which was assessed clinically, on admission using q SOFA score. A positive correlation between levels of serum amylase & lipase with ultrasonographic variable of pancreatic size was well established in this study so we can use serum amylase & lipase levels had important role in diagnosis of acute organophosphate poisoning. In summary, data from this study shows that there was significant positive correlation between serum amylase & lipase levels with prognosis & clinical outcome (duration of ICU stay, need of intubation

& mortality) and radiological outcomes along with complications like acute pancreatitis. We can say that serum amylase levels were well correlated with ultrasonographic pancreatic size, and can be used to measure prevalence of acute pancreatitis, an important complication of acute organophosphate poisoning which also affects mortality of these patients.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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