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Correlation of Serum Amylase with Serum Cholinesterase in Assessing the Severity of Acute Organophosphorus Poisoning

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Abstract:-
Background: The aim of the study was to estimate serum amylase and serum cholinesterase levels in patients of acute OP poisoning and to correlate serum amylase levels with serum cholinesterase and outcome in term of mortality in same patients.
Material and Methods: A prospective observational study was conducted in 106 clinically proven cases of OP poisoning attending the Emergency Department of Sir Takhtsinhji General Hospital, Bhavnagar. Serum amylase and Cholinesterase were measured on fully auto analyzer I-Lab at the time of admission. Patients were followed up for final outcome.
Results: Serum cholinesterase levels were decreased in all the three groups. Serum amylase was significantly elevated in group III when compared to group I and II. Correlation between serum cholinesterase levels and serum amylase showed significant negative correlation. Mean value of serum cholinesterase and serum amylase at the time of admission in survivor were 1265±866.5 and 146±68.24 respectively while in non-survivor 756.4±741 and 417±138.6 respectively.
Conclusion: Acute OP poisoning is associated with increased serum amylase levels and decreased serum ChE levels. Serum cholinesterase inhibition & lt;10% and hyper-amylasemia & gt;300 U/L has been associated with high degree of mortality. Serum amylase estimation can be used as
a prognostic indicator along with the serum cholinesterase activity in assessing severity of OP poisoning. Further studies with estimation of isoenzymes of amylase and correlation with clinical severity in larger population is necessary to know the type of hyperamylasemia and its clinical significance in acute OP poisoning

Keywords:- *Amylase, Cholinesterase, Organophosphorus poisoning.*

I. INTRODUCTION

Pesticides are chemicals that have been employed to eradicate or injure undesired environmental living forms. Pesticides come in a wide range of chemical forms, from straightforward heavy metal salts to intricate, high-molecular-weight organic molecules. The most often used pesticides are insecticides. The most widely used insecticides in terms of chemical makeup are the organophosphates, which also include halogenated hydrocarbons and carbamates. Out of all organophosphate pesticides, organophosphates account for around one-third of all pesticide poisonings.[1]Suicidal, unintentional, and intentional poisoning are the main causes. Suicidal poisoning is more frequent in underdeveloped nations because organophosphates are inexpensive and accessible on the market.[2]

These agent's main effect is to inhibit acetylcholinesterase, a neurotransmitter found in both the central and peripheral nervous systems. Acetylcholinesterase inhibition results in synaptic acetylcholine accumulation and overstimulation of muscarinic and nicotinic receptors, which triggers symptoms in the muscarinic, nicotinic, and central nervous systems like blurred vision, confusion, bradycardia, hypotension, and salivation.[3] The most frequent cause of death is respiratory failure, which is brought on by nicotinic receptor-mediated muscle paralysis along with bronchoconstriction, bronchorrhea, and CNS depression.[5]

It is well known that more poison is consumed in suicide poisoning cases, endangering the tissues and organs. In order to confirm poisoning and organ damage, laboratory testing becomes just as important as clinical evaluation. The gold standard for diagnosing organophosphorus poisoning is to check the blood serum cholinesterase level because it drops in OPC toxicity.[6]

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Because of physiological differences that exist within and between persons, the influence of illness status, genetic variances, and pharmaceutical interactions, the decline in the cholinesterase activity in patients with the same signs and symptoms varies greatly. Hyperamylasemia is a common metabolic abnormality among others in severe organophosphate poisoning. Numerous investigations between serum amylase and organophosphorus toxicity have been conducted. It has not been determined whether serum amylase levels and cholinesterase levels can be utilized to monitor OP toxicity.[5]

In this study, we aim to determine the clinical value of serum amylase levels in OP poisoning cases at the time of admission in diagnosing the severity of poisoning as plasma cholinesterase is now the most frequently utilized biochemical marker in assessing the severity of poisoning.

II. MATERIALS &METHODS

- *Ethical Consideration*

The protocol for this study was approved by the Ethics Committee of the Government Medical College Bhavnagar (IRB (HEC) no. 589//2016).

During the study period, 106 clinically confirmed cases of OP poisoning presented to the emergency department of Sir Takhtsinhji General Hospital, Bhavnagar, were included. The presumptive diagnosis of OP poisoning was made based on the patient's medical history, circumstantial consumption evidence, typical clinical signs, and routine laboratory tests. After receiving approval from the Govt. Medical College, Bhavnagar's Institutional Review Board and Ethics Committee, the work was completed between June 2016 and June 2017 at the Clinical Biochemistry Laboratory of Sir Takhtsinhji General Hospital. 106 clinically confirmed patients with acute OP poisoning were chosen after applying inclusion and exclusion criteria, and their serum amylase and serum ChE levels were assessed. First degree relatives of the patient provided written informed consent before an examination could begin.We continued with the trial without including any patients who met the exclusion criteria or who refused to participate.

Blood samples were collectedin plain vaccutainer in patients of acute OP poisoning at the time of admission for estimation of serum cholinesterase and serum amylase on fully auto analyzer I-Lab 650 at Clinical Biochemistry Section, Laboratory Services Sir Takhtsinhji General Hospital, Bhavnagar.

All the patients were divided in following groups with reference to Biological reference interval (BRI): 4000-10,000 IU/L

Group I: 20-50% of serum ChE activity (1400-3500 IU/L)
Group II: 10-20% of serum ChE activity (700-1400 IU/L)
Group III: <10% of serum ChE activity (<700 IU/L)

- *Statistical Analysis*

Data have been analyzed by Kolmogorov-Smirnov test for the normality assumption of all measurements. They were not meeting the assumption, so non-parametric statistical methods were used to evaluate data. The groups were compared by using Kruskal-Wallis analysis of variances; numerical data was expressed as mean ± Standard Deviation (SD) and median (min, max).Comparison of serum amylase and serum ChE in patients of acute OP poisoning with outcome were carried out by applying unpaired t-test and their correlation were studied by applying Pearson Correlation test.

$p < 0.05$ was considered as statistically significant. All these statistical calculations were done using Graph pad 3 demo version.

*$p < 0.05$ – significant
**$p < 0.001$ – highly significant
#$p \geq 0.05$ – not significant

III. RESULT

Table 1, depicts the distribution of cases among the groups. Out of 106 patients, 29 patients (27.35%) placed in group I, followed by 37 patients (34.90%) in group II and 40 patients (37.73%) in group III. Maximum numbers of cases belongs to group III who had serum ChE level <10% of normal activity (<700 IU/L).

It is evident from table 2, that 9 patients lost their lives who had serum ChE level <10% of normal activity (<700 IU/L); followed by 4 patients in group II who had serum ChE level 10-20% of normal activity (700-1400 IU/L) and only 1 patient in group I who had serum ChE level 20-50% of normal activity (1400-3500 IU/L).

Table 3, shows that out of 106 patients, 10 patients (83.33%) lost their lives who had serum amylase >300 U/L, followed by 3 patients (16.67%) who had serum amylase between 200-300 U/L, followed by only 1 patient (2.56%) who had serum amylase between 100-200 U/L and no deaths occurred whose serum amylase levels within normal range . Maximum deaths occurred in patients (83.33%, 10/14) who had serum amylase > 300 U/L.

As seen in table 4, out of 106 patients, 14 (13.20%) died and 92 (86.79%) survive. Mean ± SD ofserum amylase was 417 ± 138.6 in non-survivor patients versus 146 ± 68.24 in patients who survive which is statistically more significant ($p<0.0001$) than serum ChE level which was 1265 ± 866.5 in survivor versus 756.4 ± 741 in non-survivor ($p<0.05$). Serum amylase and serum ChE levels in OP poisoning patients was statistically highly significant with 'p' value of <0.0001. Pearson's correlation test shows significant negative correlation (-0.4799) in OP poisoning patients.

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Table 1: Distribution of Cases

Groups	Total		Male		Female	
	N	Percent	N	Percent	N	Percent
Normal	00	0%	00	0%	00	0%
Group I	29	27.35%	21	30%	08	22.22%
Group II	37	34.90%	22	31.42%	15	41.67%
Group III	40	37.73%	13	18.57%	13	36.11%

Fig 1: Distribution of cases

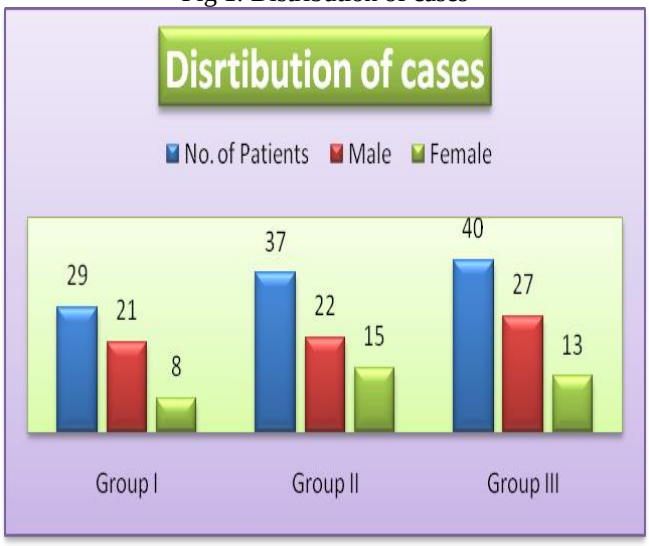

Table 2: Serum ChE and outcome

Groups	No. of Patients & Percentage	No. of death & Percentage	No. of discharge & Percentage
Group I	29 (27.35%)	01 (3.44%)	28 (96.55%)
Group II	37 (34.90%)	04 (10.81%)	33 (89.18%)
Group III	40 (37.73%)	09 (22.5%)	31 (77.5%)
Total	106 (100%)	14 (13.20%)	92 (86.79%)

Table3: Serum amylase and outcome

Serum Amylase level (BRI : 28-100 U/L)	No. of Patients & Percentage	No. of Death & Percentage	No. of Discharge & Percentage
0-100	37 (34.90%)	00 (0%)	37 (100%)
100-200	39 (36.79%)	01 (2.56%)	38 (97.43%)
200-300	18 (16.98%)	03 (16.67%)	15 (83.33%)
>300	12 (11.32%)	10 (83.33%)	02 (16.67%)
Total	106 (100%)	14 (13.20%)	92 (86.79%)

Table 4: Relationship of serum amylase and serum ChE levels with outcome

Outcome	Serum amylase (mean ± SD)	Serum ChE (mean ± SD)
Survivor (N=92)	146±68.24	1265±866.5
Non survivor(N=14)	417±138.6	756.4±741
P value	<0.0001**	<0.05*

Note: *p < 0.05 – significant, **p s< 0.001 – highly significant,#p≥0.05 – not significant

Table 5:Correlation of Serum ChE with serum Amylase

Parameter	'r' value	'p' value
Serum Amylase	-0.4799	<0.0001**

Note: *p < 0.05 – significant, **p < 0.001 – highly significant, #p≥0.05 – not significant

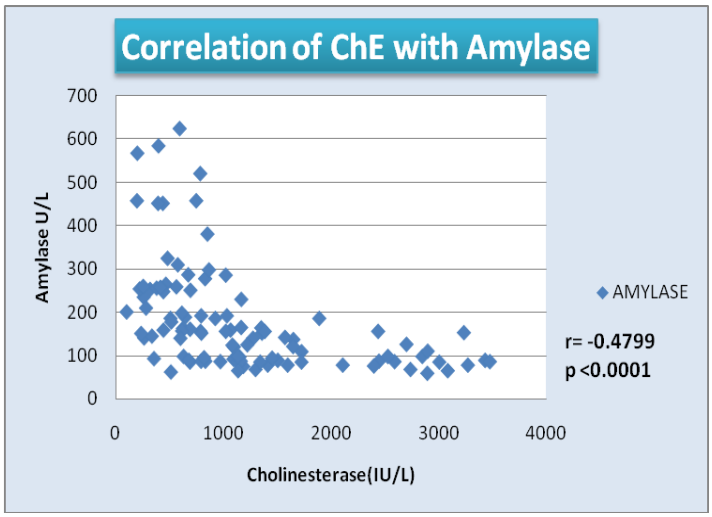

Fig 2: Correlation of Serum ChE with Serum Amylase

IV. DISCUSSION

A good and stealthy weapon that may be used frequently and without raising any suspicion is poison. Currently, a substantial number of novel compounds have emerged as new dangerous substances as a result of the rapid expansion in all spheres of life, including industries, medicine, and agriculture. The pesticides that were created to safeguard crops are now responsible for a considerable amount of sickness and mortality due to environmental damage and suicidal behaviour. The OP compounds are frequently employed as suicidal poison, which can result in major pesticide-related sickness and death in developing nations like India because of their simple availability, lower cost, and lethal impact in lesser doses.[7]

Hematological and biochemical alterations can result from OP compound's' effects on organs and systems such the immune system, pancreas, liver, lungs, and others, as well as the urinary system.[5] The classic laboratory test for OP poisoning is the inhibition of the serum cholinesterase which is apparent within few minutes or hours of absorption of OP compounds. Hyperamylasemia is a common metabolic abnormality among others in severe organophosphate poisoning.[4]

Finding of the present study showed, majority of patients were in age group 21-30 years (36.79%). Similar results have been obtained in studies conducted by Adhil et al.[8] and Gupta et al.[9] in which 36% and 33.6% of patients respectively were in the age group 21-30 years.This study revealed male predominance (66.03%), while females accounting for 33.97% of cases and the male to female ratio were 1.9:1.Male preponderance was also reported in studies conducted by Patil et al. [10] (1.14:1) and Badiger et al. [11] (1.3:1).Amanvermez and coworkers, in their study reported female preponderance and Gender preponderance in OP poisoning depends mainly on the geographical area, their occupation and socioeconomic status.[12] OP compounds are ChE inhibitors so the manifestation of OP poisoning is characterized by low serum ChE levels.

Mortality was higher (22.5%, 09/40)in group III in whom serum ChE level was <700 IU/L when compared to group II (10.81%, 04/37) and group I (3.45%, 1/29) in whom serum ChE levels were 700-1400 IU/L and 1400-3500 IU/L respectively.

In our study hyperamylasemia was reported in 65.09% of patients (69/106) and majority of the cases who had hyperamylasemia belonged to group III (87.5%) and group II (64.86%) as compared to group I (34.48%) (Table 7). Death occurred in 20.28% of patients who had serum amylase more than normal (>100U/L) (table 12) and mortality was higher in patients in whom serum amylase was more than 3 folds (>300 U/L) as in our study it was 83.33% (10/12) (Table 13). When the mean values of serum amylase and ChE were compared between the patients who survived and those who didn't survive, the value of serum amylase was statistically more significant ($p<0.0001$) as compared to serum ChE ($p<0.05$)

A negative correlation was observed between Serum Amylase and Serum ChE in patients of acute OP poisoning with a Pearson correlation coefficient of -0.4799 (Figure 26), which is statistically highly significant ($p<0.0001$). In this study total mortality was 13.20% (14/106) and all the patient have less than 50% of normal serum ChE activity (<3500 IU/L) whereas, in all the patient who lost their life, serum amylase level was more than normal (>100 U/L) and 71.42% of patients (10/14) have serum amylase level more than 3 fold (>300 U/L).

A recently published study byChoperla et al. [15] has shown that, 33.33% of total patients had hyperamylasemia. In his study, group of patients having serum ChE activity <10% of normal activity (group III), hyperamylasemia was seen in 50% and mortality was 10.5% in patients of acute OP poisoning.

V. CONCLUSION

In the current study, elevated serum amylase levels and lower serum ChE levels are related to the severity of acute organophosphorus poisoning. Death was observed in 13.20% of patients, and in those patients, serum amylase was elevated to a larger level (>300 U/L). Therefore, it may be concluded that estimate of serum amylase, coupled with serum ChE activity, can be employed as a predictive marker in determining the severity of OP poisoning. To determine the type of hyperamylasemia and its clinical importance in acute OP poisoning, additional research estimating amylase isoenzymes and correlating clinical severity in a broader population is required.

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Institutional Review Board Statement: The protocol for this study was approved by the Ethics Committee of the Government Medical College Bhavnagar (IRB (HEC) no. 589//2016.).

Informed Consent Statement: Informed written consent was obtained from all subjects involved in the study.

Conflicts of Interest: The authors declare no conflict of interest.

APPENDIX A

The following abbreviations are used in this manuscript:

OP	Organophosphate
ChE	Cholinesterase
CNS	Central Nervous system

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