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To Study the Utility of Plasma Cholinesterase and RBC Cholinesterase in Organophosphorus Compound Poisoning in a Tertiary Care Centre

[1]Dr Abdul Haris KK , [2]Dr Thiruvanath Varriam Kunjulakshmy ,[3]Dr D B Bhusare, [4]Dr Sagar Sinha

[1]Junior resident, [2]Senior resident, [3]Head of department,[4]Professor
Department of Emergency Medicine
MGM hospital, kamothe,Navi Mumbai

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I. INTRODUCTION

Intentional self-harm and suicidality are serious public health concerns, particularly in middle- and low-income countries.[1] Suicide statistics from less developed nations provide the impression that self-harm and suicide are hastily chosen actions. Instead of considering a poison's lethality, consider its availability.[2] Among the most popular suicide techniques used worldwide are pesticide ingestion, hanging, and using a weapon. [3] Significant psychopathology is frequently absent in suicide victims, too.

Pesticides are the most frequent cause of poisoning, and according to estimatesfrom the World Health Organization (WHO), there are more than 220,000 fatalities globally from pesticide poisonings each year.[3] The third of pesticide poisoningincidents in the third world occur in India, with farm labourers suffering the harshest effects. Suicidal poisoning was most frequently used (53%), then accidental (47%). Themajority of the exposure (88%) occurred orally. The combined effects of the dermal (5%), inhalation, and ocular exposure were 7%.
Household agents (44.1%), pharmaceuticals (18.8%), agricultural pesticides (12.8%), industrial chemicals (8.9%),animal bites and stings (4.7%), plants (1.7%), unidentified (2.9%), and other groups (5.6%) were the causes of poisoning with the highest incidence.[4] According to earlierresearch, poisoning was among the top four leading causes of death in rural India, wheremortality rates range from 15 to 30 percent, before the COVID-19 pandemic.[5] Due to the accessibility of poisons, the rising use of chemicals for residential and industrial purposes, and the low cost of dangerous chemicals, poisoning instances are relatively common in India. Suicidal poisoning was most frequently used (53%), then accidental(47%). The majority of the exposure (88%) occurred orally. The combined effects of the dermal (5%), inhalation, and ocular exposure were 7%. Household agents (44.1%),pharmaceuticals (18.8%), agricultural pesticides (12.8%), industrial chemicals (8.9%),animal bites and stings (4.7%), plants (1.7%), unidentified (2.9%), and other groups (5.6%) were the causes of poisoning with the highest incidence.[4] According to earlierresearch, poisoning was among the top four leading causes of death in rural India, wheremortality rates range from 15 to 30 percent, before the COVID-19 pandemic.[5] Due tothe accessibility of poisons, the rising use of chemicals for residential and industrial purposes, and the low cost of dangerous chemicals, poisoning instances are relatively common in India. Organophosphorus compounds (OPC) are frequently used as insecticides in residences as well as in horticulture and agriculture to reduce the spread of diseases including dengue fever and malaria. Organophosphates (OPs) are poisonous substancesmade by the esterification process as well as various other methods. They are the primary ingredients in pesticides, insecticides, and herbicides. They are also frequently employed in the manufacture of polymers and solvents. While the great majority of recorded pesticide poisonings and the socioenvironmental effects of their use are unknown, poisonings like organophosphate poisoning among farmers have been well-documented.[6] Additionally, occupational exposure was a major factor in a large number of OP poisoning cases that required

hospital admission, particularly in agricultural nations.[7] Common uses of OP for residential and agricultural pest management, particularly in farming settings, include improper handling, unintentionalingestion, and suicide attempts. The issues were especially common in India's rural communities.

OPC substances are either derivatives of phosphoric or phosphonic acids that permanently inhibit serum cholinesterase, leading to a syndrome complex of excessivecholinergic activity including muscarinic, nicotinic, and central nervous system receptors.

In addition to having a direct toxic effect on the cardiac muscle and the vascular system, myocardial injury is caused by sympathetic system stimulation, parasympathetic overactivity, hypoxia, metabolic acidosis, dyselectrolytemia, and other factors. Respiratory failure is the main reason for mortality. Although there is therapy for OP poisoning, it has not advanced significantly in more than 50 years. Atropine, a muscarinic antagonist, and supportive care have continued to be the cornerstones of treatment, with reactivators playing a contentious role.

Increased musculature activity, such as respiratory difficulty, bronchorrhea, bradycardia, etc., frequently indicates organophosphate intoxication. Following organophosphate poisoning, monitoring a patient's cholinesterase status permits the confirmation of significant anticholinesterase chemical exposure. Future use of these tests may make it easier to decide when to cease administering oxime and to gradually wean a patient off of a ventilator when butyrylcholinesterase activity is rising. Studies are being conducted to verify the clinical utility of this strategy.

AIMS AND OBJECTIVES AIM:

Aim of the present study is to find out the utility of plasma and RBC cholinesterase level in management and prognosis of OP poisoning.

PRIMARY OBJECTIVES.

We conducted the study with the objectives to find out:

1) To assess the severity of Organophosphorus compound poisoning by correlating the levels of plasma and RBC cholinesterase at zero and 72 hours.
2) To correlate the level of plasma and RBC cholinesterase in assessing total ICU days.

SECONDARY OBJECTIVE:

1) To evaluate the relevance of RBC cholinesterase and plasma cholinesterase as a mortality predictor.

EXPECTED OUTCOME OF THE STUDY

1. To confirm the exposure to organophosphorus compound poisoning using plasma cholinesterase assay.
2. To determine severity of organophosphorus compound poisoning using RBC cholinesterase assay.

II. MATERIALS AND METHODS

Ethics and consent: "Institute Ethics Committee Clearance was obtained before start of study". Written and informed consent shall was taken from all patients or reliatives. All patients were informed regarding the purpose, procedures, risks .

Type of study: Prospective and Observational study

Data collection: Primary data collection

Type of sampling: Random sampling

Sampling method: Non-probability (convenient) sampling method

Sample size: 50

Period of study: Study was conducted from MARCH 2021 to DECEMBER 2022

INCLUSION CRITERIA

1. Adults patients (≥ 18 years of age) presenting to the emergency department of MGM medical college and hospital, Navi Mumbai.
2. Patients with clinical features of organophosphate poisoning .
3. Patients willing to give consent.

EXCLUSION CRITERIA

1. Patients who were previously treated with atropine in an outside treatment facility before admission.
2. Patients with history of mixed poisoning. 3.Pregnant women

4.Patients less than 18 years of age.

III. METHODOLOGY

Clearance from the Institutional Ethical Committee was sought before the start this study. Informed consent was obtained from all patients or relatives. All patients were informed regarding the procedures, purpose of the study. A detailed history, thorough clinical examination and significant biochemical investigations were carried out. The detailed clinical examination was done during the initial resuscitation and through the course of their treatment.

Peradeniya organophosphate poisoning scale was used to assess the clinical severity as mild, moderate, and severe in all the patients. In the present study 5ml of plain blood was collected on admission before administration of atropine and pralidoxime for estimation of plasma cholinesterase I (0 Hours) and RBC cholinesterase I(0 Hours) and 5ml of plain blood was collected at 72 hours of hospital stay for estimation of plasma cholinesterase II (72 Hours) and RBC cholinesterase II (72 Hours). All samples collected were kept at 20 degree Celsius for at least 3 days. The determination of RBC cholinesterase was done by measuring the rate of hydrolysis of acetylcholine by a red cell at pH 7.2 at 412 nm by the reaction of thiocholine with DTNB to give the yellow 5-thio-2-nitrobenzoate anion. The normal range of RBC cholinesterase is 8-13kU/l.

All the patients who were part of the present study were managed starting with decontamination. Intravenous atropine was administered, 2mg every 5 minutes until atropinization. Cardiorespiratory parameters like reduced secretions and absence of bronchospasm were used to guide the atropinization. All patients received 2g of pralidoxime chloride over 15 minutes after admission to the emergency department. Patients were observed thoroughly during the course of hospital stay.

STATISTICAL ANALYSIS

The data was collected and compiled in MS Excel. Descriptive statistics has been used to present the data. To analyse the data SPSS (Version 26.0) was used. Significance level was fixed as 5% ($\alpha = 0.05$. Qualitative variables are expressed as frequency and percentages and Quantitative variables are expressed as Mean and Standard Deviation. To compare the proportion between groups chi-square test was applied. To compare mean values between groups student t-test and ANOVA test was used. Pearsons correlation was used to compare correlation between values.

IV. RESULTS

A prospective and observational study was done in 50 patients to confirm the exposure of the patient to organophosphorus compound poisoning using plasma cholinesterase level and to determine severity of organophosphorus compound poisoning using RBC cholinesterase levels.

Table 1: Distribution of patients based on age

AGE GROUP	FREQUENCY	PERCENT
19-20	5	10.0
21-30	17	34.0
31-40	9	18.0
41-50	12	24.0
51-60	5	10.0
61-70	2	4.0
Total	50	100.0
MEAN+SD	37.00+13.245	

In the present study, 17(34%) of patients were in the age group of 21-30 years. Mean age of patients were 37±13.2 years.

Figure 1: Distribution of patients based on age

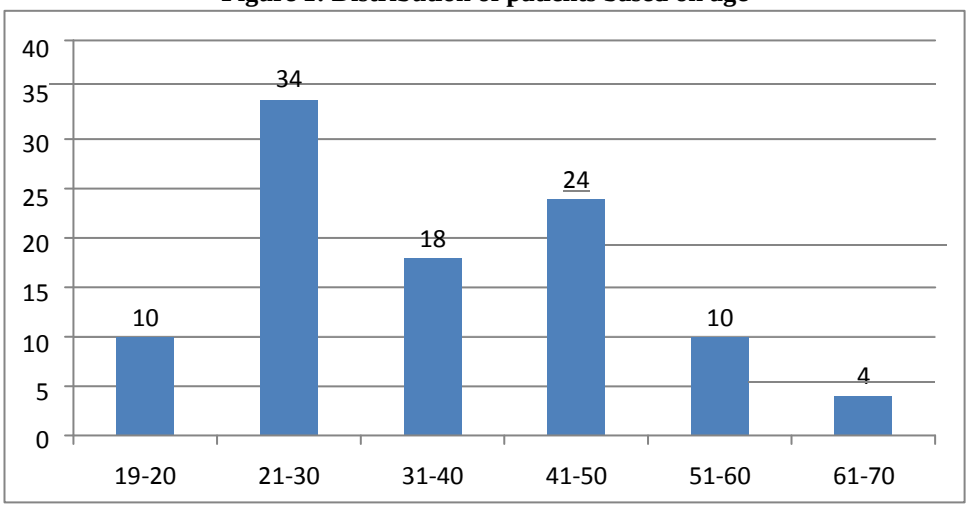


Table 2: Distribution of patients based on Gender

GENDER	FREQUENCY	PERCENT
MALE	31	62.0
FEMALE	19	38.0

In the present study, 31(62%) of cases were males.

Figure 2: Distribution of patients based on Gender

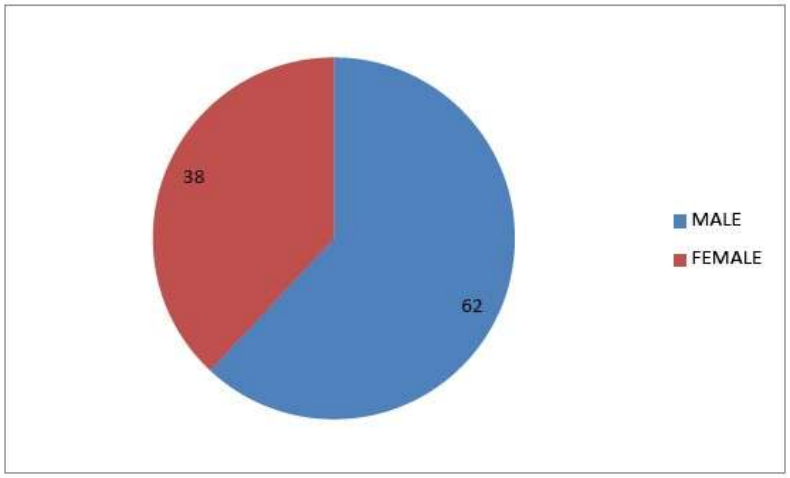


Table 3: Distribution of patients based on type of ingestion

TYPE OF INGESTION	FREQUENCY	PERCENT
INTENTIONAL	49	98.0
ACCIDENTAL	1	2.0

In this study conducted with 50 cases of OP poisoning 49(98%) patients ingested OP intentionally in an attempt commit suicide or cause self-harm.

Figure 3: Distribution of cases based on type of ingestion.

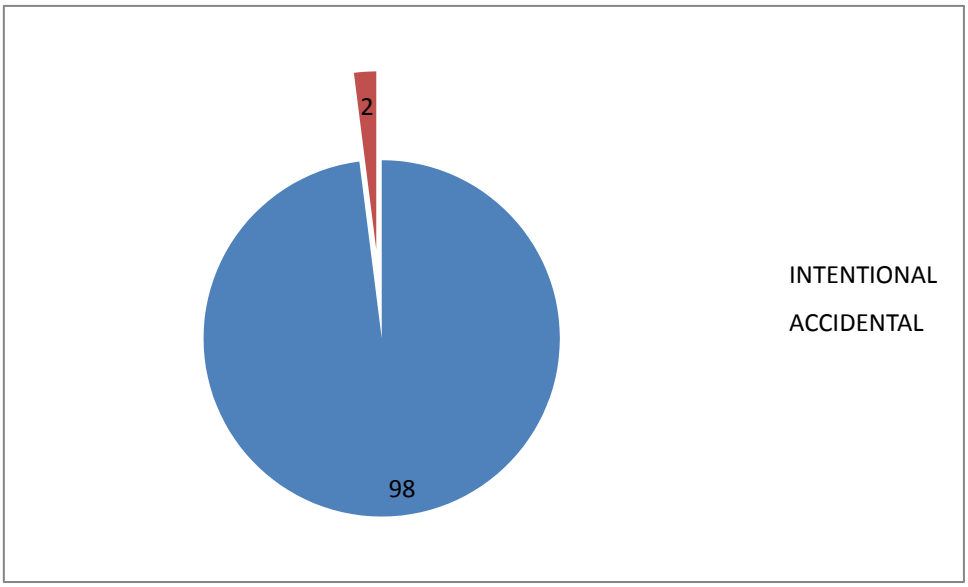


Table 4: Distribution of cases based on Residence

RESIDENCE	FREQUENCY	PERCENT
RURAL	35	70.0
URBAN	15	30.0

In the present study, most of the cases were i.e. 35(75%) were from rural area.

Figure 4: Distribution of cases based on Residence

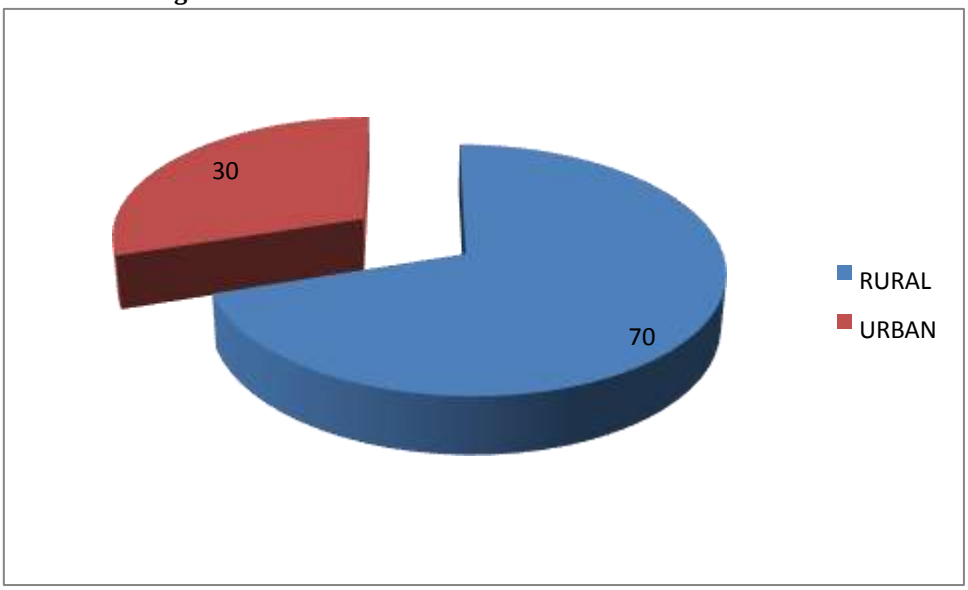


Table 5: Distribution of cases based on agent

AGENT	FREQUENCY	PERCENT
Dimethoate	15	30.0

Chlorpyrifos	14	28.0
Dichlorfos	9	18.0
Methyl parathion	5	10.0
Phorate	2	4.0
Parathion	1	2.0
Peridone	1	2.0
Monochrotophos	1	2.0
Profufor	1	2.0
Trichlorphos	1	2.0

In the present study, common agent consumed by cases was dimethoate i.e. 15(30%)

Figure 5: Distribution of cases based on agent

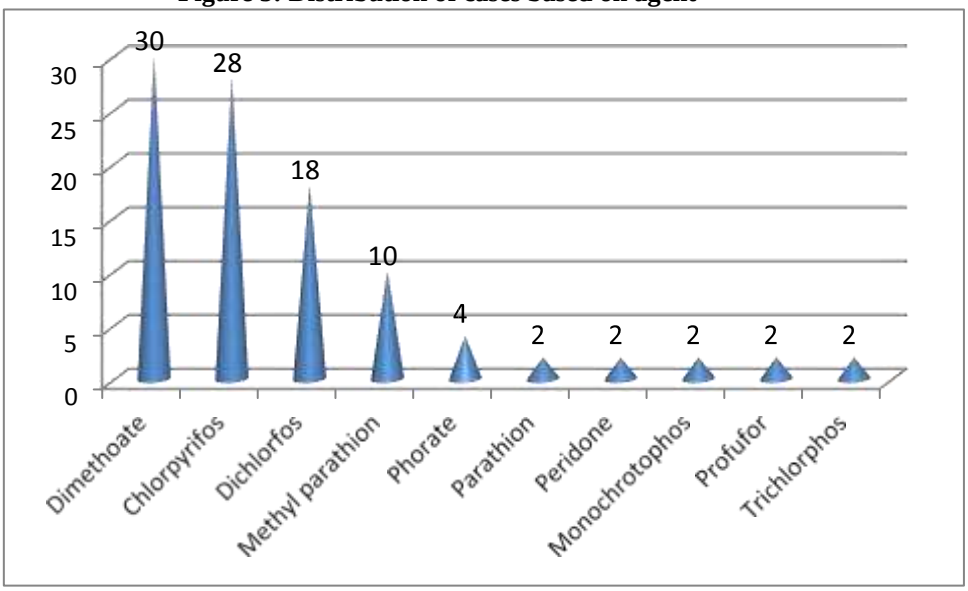


Table 6: Distribution of cases based on symptoms

SYMPTOMS	FREQUENCY	PERCENT
Nausea/Vomiting	45	90.0
Stool/Urinary Incontinence	22	44.0
Miosis	31	62.0
Altered sensorium	18	36.0
Secretions	46	92.0

In the present study, majority 45(90%) cases reported nausea and vomiting as common symptom.

Figure 6: Distribution of cases based on symptoms

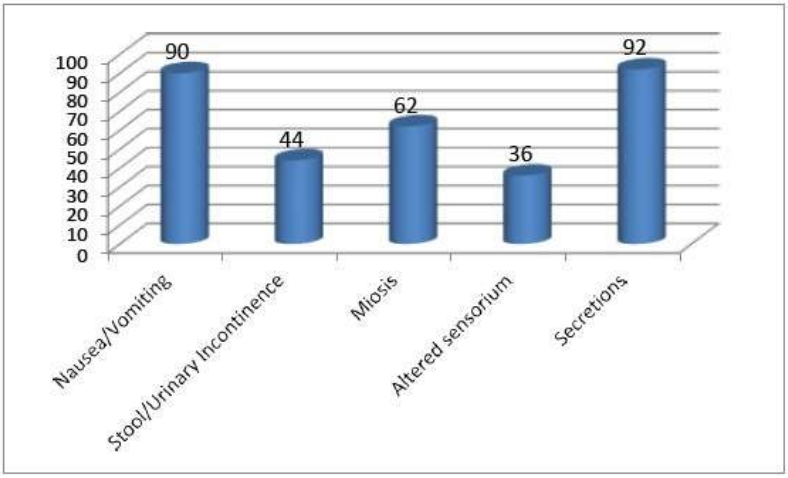


Table 7: Distribution of cases based on basic parameters

BASIC PARAMETERS		FREQUENCY	PERCENT
Heart rate	**B**	7	14.0
	N	22	44.0
	T	21	42.0
Blood Pressure	**LOW**	1	2.0
	N	40	80.0
	HIGH	9	18.0

In the present study, most of the i.e. 44% cases had normal heart rate and 42% of cases had tachycardia.

Figure 7: Distribution of cases based on heart rate

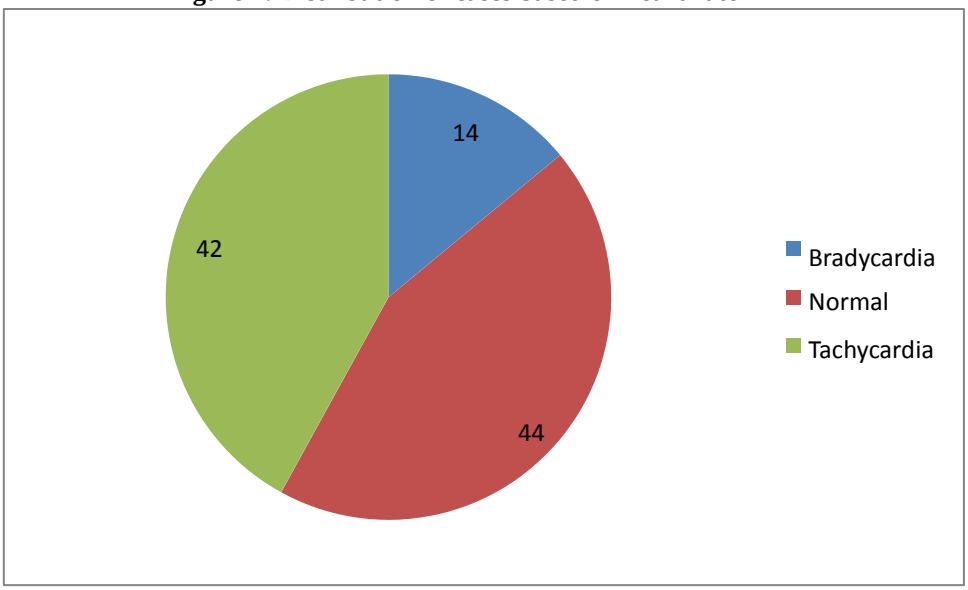


Table 8: Distribution of cases based on basic findings

FINDINGS	FREQUENCY	PERCENT
Fasciculations	15	30.0
Convulsions	3	6.0
Respiratory failure	18	36.0
Impaired level of consciousness	11	22.0

In the present study, most common finding was respiratory failure seen among 36% of study cases.

Figure 8: Distribution of cases based on findings

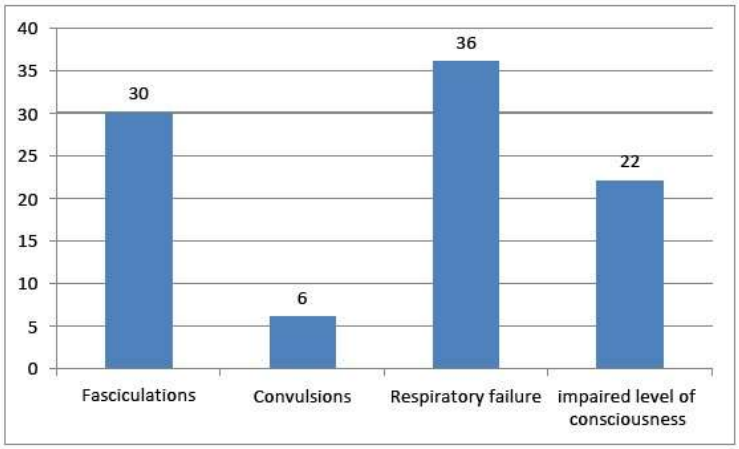


Table 9: Distribution of cases based on outcome

OUTCOME	FREQUENCY	PERCENT
ALIVE	44	88.0
DEAD	6	12.0

In the present study of 50 cases of organophosphorus poisoning, 44 patients survived and 6(12%) patients succumbed to it. Mortality of 12% was observed.

Figure 9: Distribution of cases based on outcome

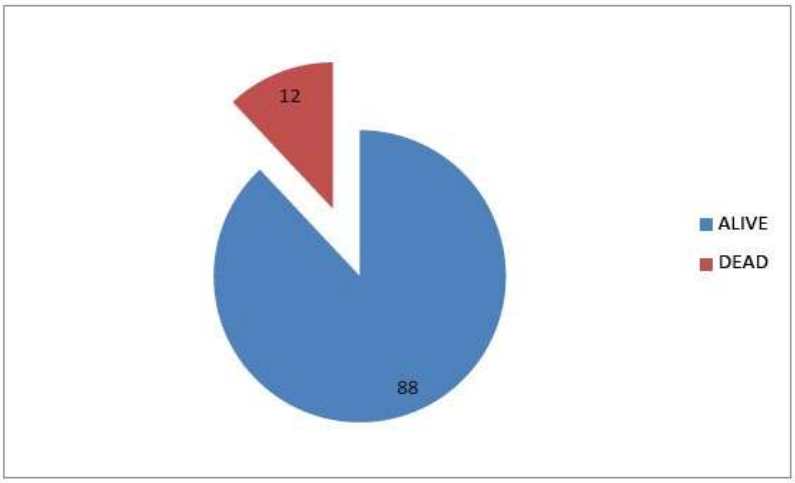


Table 10: Distribution of cases based on POP Score Severity

POP Score Severity	FREQUENCY	PERCENT
MILD	31	62.0
MODERATE	16	32.0
SEVERE	3	6.0

In the present study, POP score was mild for 62% of cases.

Figure 10: Distribution of cases based on POP Score Severity

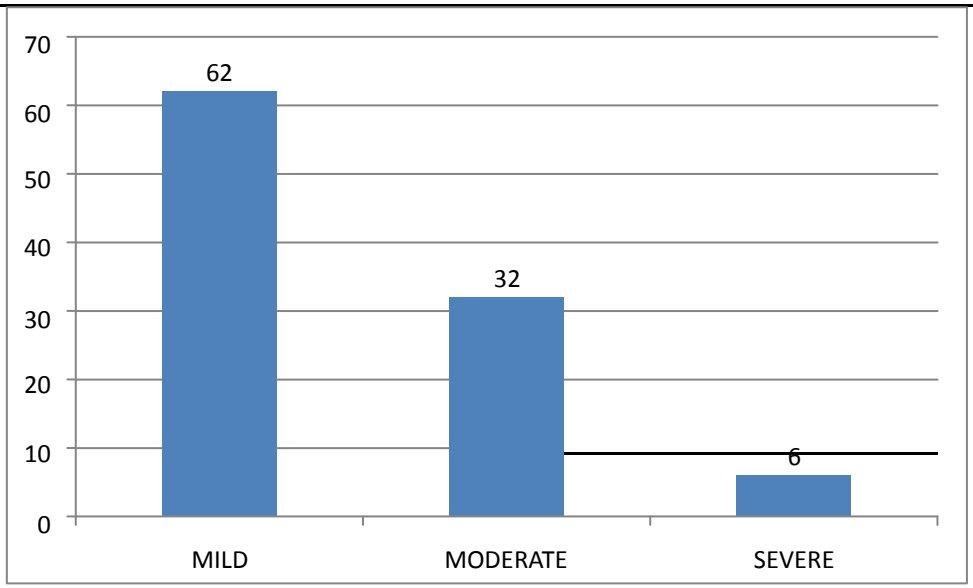


Table 11: Distribution of cases based on complications

Complications	FREQUENCY	PERCENT
Acute Cholinergic crisis	18	36.0
Aspiration Pneumonia	13	26.0
Sepsis	8	16.0
Intermediate syndrome	6	12.0

In the present study, majority i.e. 18(36%) of cases had acute Cholinergic crisis as complication of organophosphorus poisoning

Figure 11: Distribution of cases based on complications

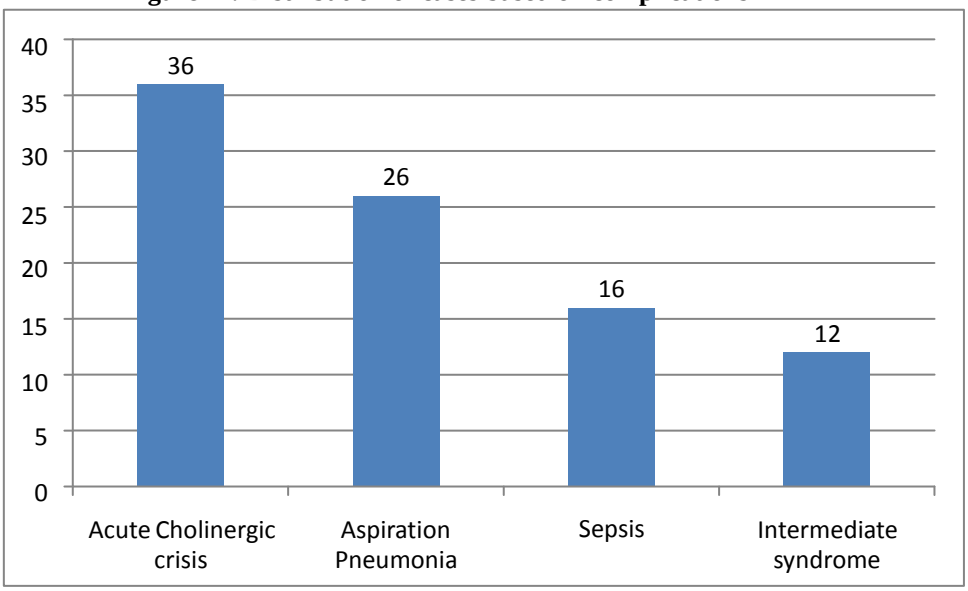


Table 12: Distribution of cases based on Cholinesterase level

	Minimum	Maximum	Mean	Std. Deviation
Plasma Cholinesterase I	200	8800	2961.98	2084.652
Plasma Cholinesterase II	200	7850	2861.86	1832.757
RBC cholinesterase I	0.66	7.55	3.4812	1.50175
RBC cholinesterase II	0.72	10.30	3.5994	1.64144

In the present study, plasma cholinesterase I(on admission) values were 2961±2084.652, plasma cholinesterase II(72 hours) was 2861.86±1832.757, RBC cholinesterase I values were 3.4812±1.5 & RBC cholinesterase II was 3.599±1.641.

Figure 12: Distribution of cases based on Plasma Cholinesterase level

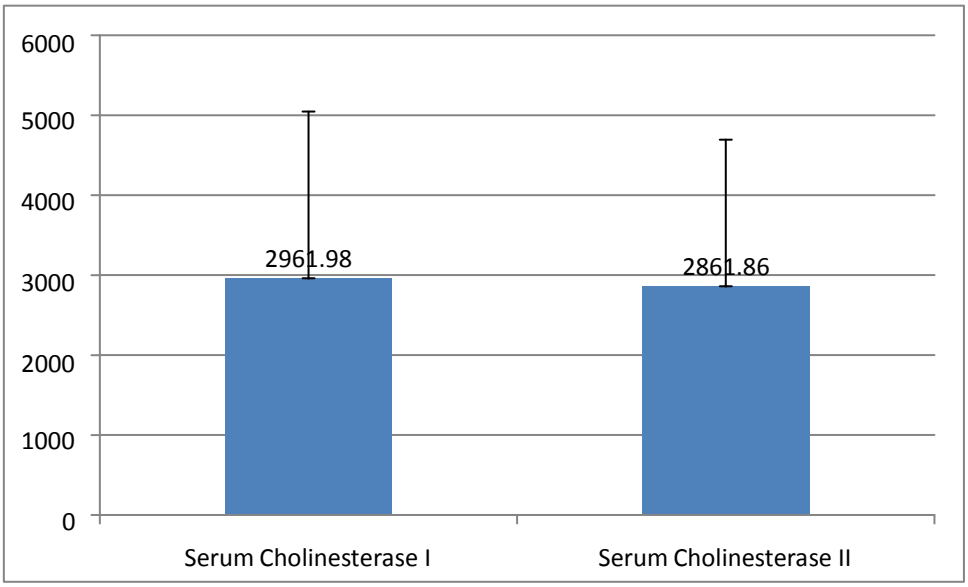


Figure 13: Distribution of cases based on RBC Cholinesterase level

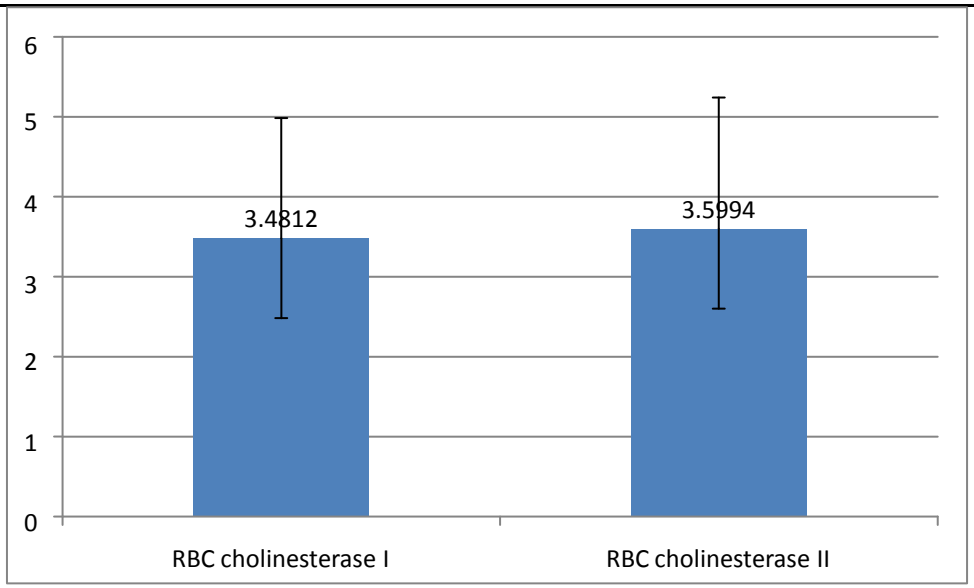


Table 13: Distribution of cases based on Cholinesterase level & POP Score

POP Score Severity		Plasma Cholinesterase I	Plasma Cholinesterase II	RBC cholinesterase I	RBC cholinesterase II
MILD	Mean	3261.16	3126.55	3.7016	3.9252
	N	31	31	31	31
	S. D	2137.596	1747.571	1.33129	1.59474
MODERAT E	Mean	2408.31	2371.50	3.1250	3.0956
	N	16	16	16	16
	S. D	1886.339	1876.683	1.72768	1.64040
SEVERE	Mean	2823.33	2742.00	3.1033	2.9200
	N	3	3	3	3
	S. D	2715.885	2653.249	2.07365	1.82033
P VALUE		0.419	0.414	0.424	0.200

The mean value of Plasma cholinesterase on admission in POP mild case was higher in mild cases as compared to POP moderate and severe cases. However the mean value of

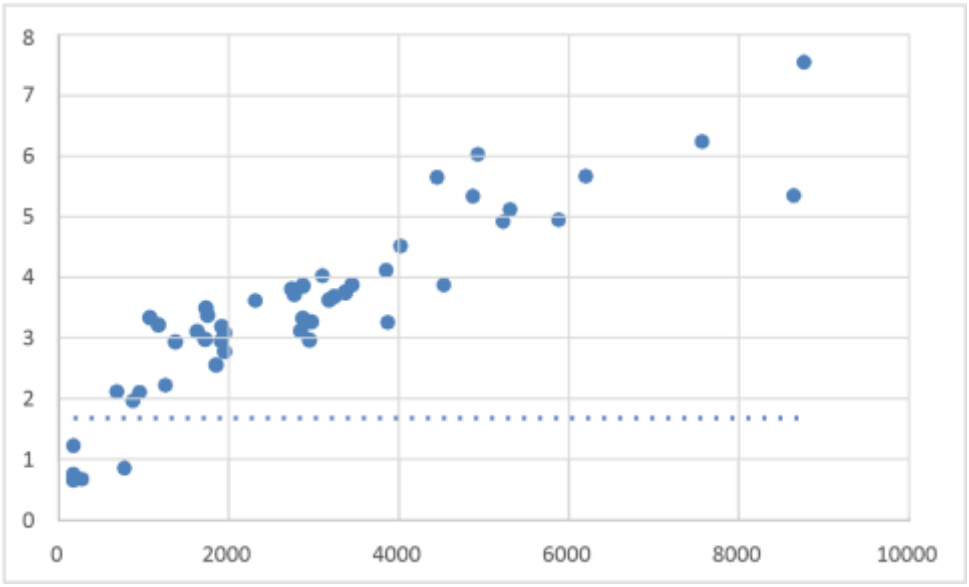
Plasma cholinesterase after 72 hours of admission (following standard treatment with atropine and oximes)did not always show an increase in the mean value hence making Plasma cholinesterase suitable for detecting or diagnosing exposure to organophosphorus. The mean value of RBC cholinesterase on admission was lower in POP severe and moderate cases as compared to POP mild cases and the mean value of RBC cholinesterase after 72 hours showed a decline making it suitable for assessing severity.

Table 14: correlation based on plasma & RBC Cholinesterase

		RBC cholinesterase I	RBC cholinesterase II
Plasma Cholinesterase I	Pearson Correlation	0.908	0.880
	Sig. (2-tailed)	**0.000**	**0.000**
Plasma Cholinesterase II	Pearson Correlation	0.882	0.821
	Sig. (2-tailed)	**0.000**	**0.000**

Strong positive correlation was seen between plasma cholinesterase at the time of admission and 72 hrs with RBC cholinesterase and this association was found to be statistically significant.

AT ADMISSION



AT 72 HOURS

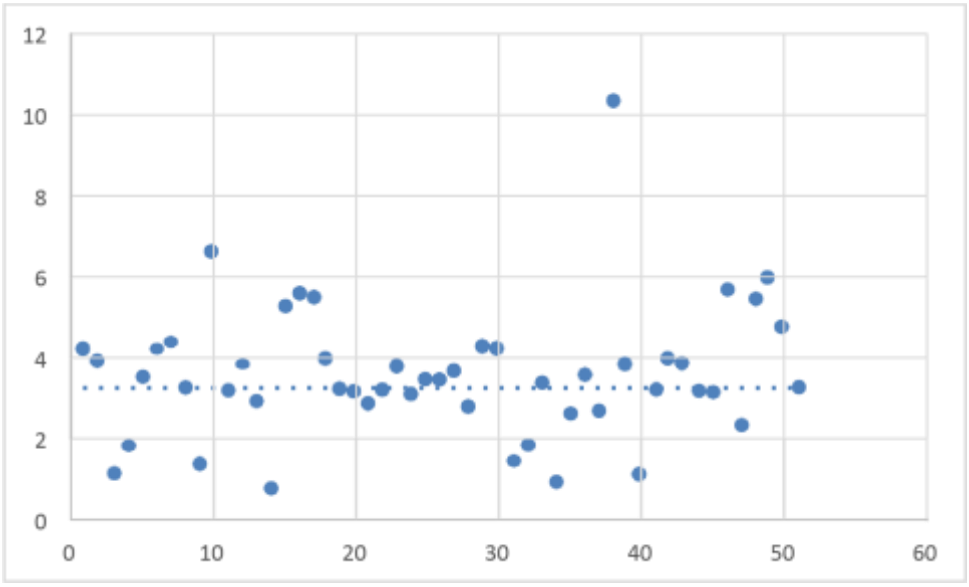


Table 15: correlation based on plasma cholinesterase, RBC Cholinesterase & outcome

Outcome		Plasma Cholinesterase I	Plasma Cholinesterase II	RBC cholinestera se I	RBC cholinestera se II	ICU days
ALIVE (44)	Mean	3071.73	2950.93	3.6000	3.7639	9.64
	S. D	2089.908	1811.231	1.46629	1.59574	4.188
DEAD (6)	Mean	2157.17	2208.67	2.6100	2.3933	19.17
	S. D	2035.432	2030.660	1.60512	1.58805	6.306
P VALUE		0.318	0.357	0.131	0.054	**0.000**

The mean values of plasma cholinesterase were higher among patients who survived as compared to the patients who succumbed to organophosphate poisoning. Mean RBC cholinesterase at admission among patients who survived was 3.60Ku/L and theaverage number of ICU stay was 9.64 days.

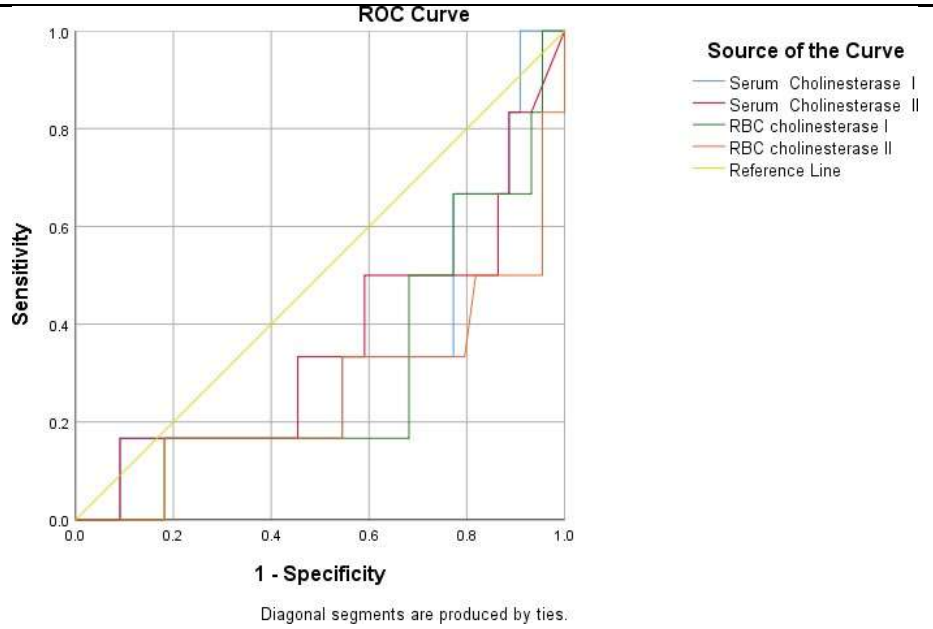
Table 16: correlation based on plasma, RBC Cholinesterase & ICU stay

		ICU STAYS
Plasma Cholinesterase I	Pearson Correlation	-0.080
	Sig. (2-tailed)	0.580
Plasma Cholinesterase II	Pearson Correlation	-0.117
	Sig. (2-tailed)	0.417
RBC cholinesterase I	Pearson Correlation	-0.130
	Sig. (2-tailed)	0.367
RBC cholinesterase II	Pearson Correlation	-0.133
	Sig. (2-tailed)	0.356

A lower level of RBC cholinesterase and plasma cholinesterase at admission and at 72 hours corresponded to longer ICU stay this translated to a negligible negative correlation however this correlation was not found to be statistically significant.

TABLE 17: ROC ANALYSIS IN PREDICTION OF MORTALITY

Area Under the Curve					
			Asymptotic	95% Confidence Interval	
Test Result Variable(s)	Area	Std. Error	Sig	Lower Bound	Upper Bound
Plasma Cholinesterase I	0.337	0.124	0.199	0.095	0.580
Plasma Cholinesterase II	0.358	0.131	0.263	0.101	0.615
RBC cholinesterase I	0.299	0.114	0.114	0.076	0.522
RBC cholinesterase II	0.259	0.124	0.058	0.016	0.503



Test Result Variable(s)	CUTOFF	Sensitivity	Specificity
Plasma Cholinesterase I	505.00	0.833	0.909
Plasma Cholinesterase II	300.00	0.833	0.932
RBC cholinesterase I	0.7200	0.833	0.955
RBC cholinesterase II	0.9950	0.833	0.977

V. DISCUSSION

- **Age:**

In the present study, 17(34%) of cases were in the age group of 21-30 years. Mean age of cases were 37±13.2 years. Similarly in a study done by Chaudhary SC et al[28] mean age of patient was 24.99 ± 8.7 years. In a study done by Kothiwale V et al [29] patient age ranged from 18 to 87 years. Maximum number of cases were in the age group of below 30 years, i.e., 47 patients (55.29%). Many factors increase the risk of developing or triggering depression in younger age group including: Having issues that negatively impact self-esteem, such as obesity, peer problems, long-term bullying or academic problems.

- **Gender:**

In the present study, 31(62%) of cases were males. Similar findings seen in a study done by Kothiwale V et al [29] there was male preponderance with a ratio of male to female – 2.4:1. This observation is similar to the study by Kang et al.[30] and Patil et al.[31] In contrast, Rehiman et al.[32] and Sen et al.[33] observed more number of females in their study. Easy accessibility of OP compounds to males is the reason for this.

- **Residence area:**

In the present study, most of the cases were i.e. 35(75%) were from rural area. Similarly in a study done by Chaudhary SC et al[28] majority of patients were from rural areas (71.43%) and were agricultural workers by occupation Cases of OP poisoning were predominantly young males (below 40 years of age) and belonged to rural areas. This could be due to the facts that males have easy accessibility to OP compounds because they work in agriculture fields.

- **Reason for ingestion**

In the present study, majority of the patients i.e. 49(98%) gave reason for ingestion as deliberate or intentional. Likewise in a study done by Chaudhary SC et al[28] 49 patients (70%) of Organophosphorus poisoning were with suicidal intent, while 21 (30%) cases were accidentally poisoned. In all accidental cases, route of poisoning was

inhalational, whereas in all the attempt to suicide and suicide cases, route of exposure was ingestion. Due to the taste and smell of organophosphorus compounds it is very rarely that these compounds are ingested accidentally. Patients who initially gave history of having accidentally ingested organophosphate was later revealed to have taken it deliberately with intention to cause self-harm or suicide.

- **Agent:**

In this study, majority of the cases consumed dimethoate i.e. 15(30%). In a study done by Kothiwale V et al [29] the commonly consumed compounds were malathion in 21 patients (24.71%), chlorpyrifos in 14 patients (16.47%), and parathion in 14 patients (16.47%). In studies by Nouira *et al*.[34] and Rehiman *et al*.,[35] the most commonly consumed compounds were parathion and dichlorvos. In contrast, a study by Kumar *et al*.,[36] found that the most commonly consumed compounds were monocrotophos and chlorpyrifos.

- **Symptoms:**

In the present study, majority 45(90%) cases reported nausea and vomiting as common symptom. In a study done by Kothiwale V et al [29] majority 74 patients (87.06%) had vomiting, 60 patients (70.59%) had sweating, 57 patients (67.06%) had breathlessness; other symptoms were diarrhoea in 53 patients (62.35%), muscle twitching in 46 patients (54.12%), and only two patients presented with seizures.

Similarly, studies by Nouira et al.[34] and Venkateshwarlu et al.[37] observedcombination of symptoms of nausea, vomiting, fasciculations, diarrhoea, etc.

- **Basic parameters & outcome:**

In the present study, most of the i.e. 44% cases had normal heart rate and 42% of cases had tachycardia & mortality was observed among 12% of cases. Similar findings seen in a study done by Kothiwale V et al [29] the outcome of patients was evaluated and we found that 13 patients (15.29%) had expired and 72 patients (84.71%) had survived. A study by Kang et al.[30] found almost similar outcomes of patients. In contrast, Siva et al.[38] had observed a significantly higher percentage of deaths in their study. When death occurs, the most common reason is respiratory failure stemming from bronchoconstriction, bronchorrhea, central respiratory depression or weakness/paralysis of the respiratory muscles.

- **Complications:**

In the present study, 18(36%) of patients presented with acute Cholinergic crisis. Likewise in a study done by Kothiwale V et al [29] various complications of Organophosphorus compound poisoning: acute renal failure in six patients (23.08%), intermediate syndrome in five patients (19.23%), respiratory failure in five patients (19.23%), and cardiac arrhythmia in four patients (15.38%) (2 ventricular tachycardia and 2 QTc prolongation). This is in contrast to a study by Venkateshwarlu et al.[10] who observed that pulmonary edema was the most common complication seen in their patients. In a study done by Sen et al.[32] respiratory acidosis was found to be the most common complication followed by intermediate syndrome.

- **Peradeniya organophosphate poisoning scale :**

In this study, POP scalewas mild for 62% of cases. Similar findings seen in a study done by Kothiwale V et al [29] POP score revealed severe intoxication in nine patients (10.59%), moderate intoxication in 50 patients (58.82%), and mild intoxication in 26 patients (30.59%). This is in contrast with study by Rehiman et al.[33] who noticed 70% of their cases had mild intoxication, 26% cases had moderate intoxication, and only 4% cases had severe intoxication. Five common clinical manifestations of OP poisoning have been selected as parameters, each to be assessed on a 3 point scale varying from 0-2. Poisoning can then be graded as mild (score 0-3), moderate (score 4- 7) or severe (score 8-11) when the patient first presents.

- **Cholinesterase level & outcome:**

In the present study, plasma cholinesterase I values were 2961±2084.652, plasma cholinesterase II was 2861.86±1832.757, RBC cholinesterase I values were 3.4812±1.5 & RBC cholinesterase II was 3.599±1.641. The mean values of cholinesterase levels were higher among survived patients than who succumb to it. In the 6 subjects who succumbed, the mean plasma cholinesterase I levels was 2157.17±2035.342 and the mean plasma cholinesterase II levels were 2208.67±2030.66, the mean RBC cholinesterase I was 2.61±1.605 and mean RBC cholinesterase II value was 2.393±1.588. In these 6 patients the mean RBC cholinesterase level showed a decreasing trend which may indicate the increasing severity of the poisoning and hence the prolonged mean ICU stay of 19.17±6.306 days. Similar finding were seen in a study conducted by Patel P et al(40) that showed that

majority of patients[6] who had a severe POP score have 10-20% RBC cholinesterase level. Similar findings seen in a study done by Kothiwale V et al [29] that 1st-day Plasma cholinesterase was directly correlating with hospital stay which is depicted above ($P < 0.001$; statistically significant) Similar observations were made by Khazi et al.[39] and Rehiman et al.[35] where in a significant correlation was established between deranged plasma cholinesterase level and morbidity of the patients in terms of prolonged durationof hospital stay.

- **Cholinesterase level & ICU stay:**

There was a negligible negative correlation between plasma cholinesterase and RBC Cholinesterase at admission and at 72 hrs with ICU stay duration and this association was not found to be statistically significant. Similar findings seen in a study done by Kothiwale V et al [29] that a correlation of plasma cholinesterase estimation on serial days which showed a significant correlation of Plasma cholinesterase with hospital stay. Mean ICU stay was 9.40 ± 3.84 days in patients with an increasing trend of Plasma cholinesterase levels whereas in patients with a decreasing trend, the mean ICU stay was 11.50 ± 3.51 days. Acetylcholine is made more readily available overall by cholinesterase inhibitors. As a result, in the case of low levels, signs of overstimulation of the parasympathetic nervous system would be evident, such as enhanced hypermotility, hypersecretion, bradycardia, miosis, diarrhoea, and hypotension.

RBC cholinesterase level & ICU stay:

In the present study, RBC cholinesterase I values were 3.4812±1.5 & RBC cholinesterase II was 3.599±1.641. The normal range of RBC cholinesterase is 8 to 13Ku/l. A lower level of RBC cholinesterase and plasma cholinesterase at admission and at 72 hours corresponded to longer ICU stay this translated to a negligible negative correlation however this correlation was not found to be statistically significant. In a study done by Patel P et al.[40] 37 % of cases had subclinical poisoning and 6% of cases had severe poisoning according to RBC cholinesterase level. Patients who required ventilator support had moderate to severe organophosphorus poisoning and in majority of patients who had low grade of organophosphorus poisoning did not need ventilator support. Of the more than forty organophosphate insecticides now in use can cause acute or chronic organophosphate poisoning. Organophosphates block the breakdown of acetylcholine by inhibiting cholinesterase enzymes, such as plasma and red blood cell (RBC) cholinesterase.

RBC Cholinesterase Within the First 24 h After organophosphate poisoning.

Predicting the length of mechanical ventilation helps doctors prepare for tracheostomy in patients who require prolonged mechanical breathing and avoid needless delays in extubation. This study observed that decreased RBC cholinesterase levels within the first 24 hours after presentation were correlated with prolonged ICU stays following organophosphate intoxication. This was due to the noticeably different time courses of cholinesterase inhibition according to chemical properties of specific organophosphate. This finding is comparable to the results from a previous study by Thiermann et al[41] who suggested that RBC cholinesterase activity appears to be a suitable surrogate parameter of synaptic Ia activity during the first day of dimethyl or diethyl organophosphate intoxication. RBC cholinesterase activity at 24 h had a significant correlation with 96-h mortality in shrimp exposed to dimethyl organophosphate (malathion, azinphosmethyl) or diethyl organophosphate (chlorpyrifos).[42] In the present study, decreased RBC cholinesterase activity was associated with the prolonged length of ICU stay following organophosphate poisoning, but this association was not found to be statistically significant. Sample size inadequacy may be the cause for this lack of association.

VI. SUMMARY

This prospective study was conducted among 50 cases of organophosphate poisoning with age group above 18 years that presented to the Emergency room of a tertiary care hospital in Maharashtra, India to assess the severity of Organophosphorus compound poisoning by correlating the levels of plasma cholinesterase and RBC cholinesterase at zero(I) and 72 hours(II). To correlate the level of plasma and RBC cholinesterase in assessing total ICU days and To evaluate the relevance of RBC cholinesterase and plasma cholinesterase as a mortality predictor.

Study revealed the following:

1. Majority of study subjects were in the age group of 21-30 years.
2. Common organophosphorus agent consumed was dimethoate i.e. 15(30%).
3. The mean value of Plasma cholinesterase on admission in POP mild case was higher as compared to POP moderate and severe cases. The mean value of RBC cholinesterase on admission was lower in POP severe and moderate cases as compared to POP mild cases and the mean value of RBC cholinesterase after 72 hours showed a decline making it suitable for assessing severity.

4. Strong positive correlation was seen between plasma cholinesterase at the time of admission and 72 hrs. with RBC cholinesterase and this association was found to be statistically significant.
5. The mean values of plasma cholinesterase were higher among patients who survived as compared to the patients who succumbed to organophosphate poisoning. Mean RBC cholinesterase at admission among patients who survived was 3.60Ku/L and the average number of ICU stay was 9.64 days.
6. There was a negligible negative correlation between plasma cholinesterase and RBC Cholinesterase at admission and at 72 hrs with ICU stay duration and this association was not found to be statistically significant.

VII. CONCLUSION

A prospective and observational study was done with 50 patients of organophosphorus poisoning. Majority of cases were in the age group of 21-30 years. Mean age of patients were 37±13.2 years. Common among males in rural area.Common agent consumed was dimethoate and majority of patients consumed organophosphorus compound intentionally. Most common finding was respiratory failure among them. Strong positive correlation was seen between plasma cholinesterase at the time of admission and 72 hrs. RBC cholinesterase levels within the first 24 h after organophosphorus compound poisoning may be useful in predictingthe duration of ICU stay.

REFERENCES:

[1]. Ghosh AK, Brindisi M. Organic carbamates in drug design and medicinal chemistry. J Med Che. 2015 Apr 9 [cited 2022 Dec 13];58(7):2895–940. Available from:https://pubs.acs.org/doi/10.1021/jm501371s

[2]. Fukuto TR. Mechanism of action of organophosphorus and carbamate insecticides. Environmental Health Perspective. 1990 Jul [cited 2022 Dec 13];87:245–54. Available from: https://ehp.niehs.nih.gov/ doi/10.1289/ ehp.9087245

[3]. Amir A, Raza A, Qureshi T, Mahesar GB, Jafferi S, Haleem F, et al.

[4]. Organophosphate poisoning: demographics, severity scores and outcomes from national poisoning control centre, karachi. Cureus. 2020 May 31 [cited 2022 Dec 13]; Available from: https://www.cureus.com/articles/31727- organophosphate-poisoningdemographics-severity-scores-and-outcomes- from-national-poisoning-control-centre-karachi

[5]. Roberts DM, Aaron CK. Management of acute organophosphorus pesticide poisoning. BMJ [Internet]. 2007 Mar 24 [cited 2022 Dec 13];334(7594):629– 34. Available from: https://www.bmj.com/lookup/doi/10.1136/bmj. 39134.566979.BE

[6]. Loscalzo J, Fauci AS, Kasper DL, Hauser SL, Longo DL, Jameson JL, editors.

[7]. Harrison's principles of internal medicine. 21st edition. New York: McGraw Hill; 2022. 1023-56 p.

[8]. Peter JV, Sudarsan T, Moran J. Clinical features of organophosphate poisoning: A review of different classification systems and approaches. Indian Journal of Critical Care Medicine [Internet]. 2014 Nov [cited 2022 Dec 13];18(11):735–45. Available from: https://www.ijccm.org/doi/10.4103/0972-5229.144017

[9]. Tripathi KD. Essentials of medical pharmacology. Eighth edition. New Delhi: Jaypee Brothers Medical Publishers; 2019. 1064 p.

[10]. Wyatt JP, Clancy M, Robertson C, editors. Oxford handbook of emergency medicine. 4th ed. Oxford ; New York: Oxford University Press; 2012. 749 p.

[11]. Setlur R, Sharma RM. Severe metabolic acidosis secondary to organophosphate poisoning. Anesthesia & Analgesia [Internet]. 2005 Dec [cited 2022 Dec 13];101(6):1894. Available from: https://journals.lww.com/anesthesia-analgesia/fulltext/2005/12000/severe_metabolic_acidosis_secondary_to.87.asp x

[12]. Pajoumand A, Shadnia S, Rezaie A, Abdi M, Abdollahi M. Benefits of magnesium sulfate in the management of acute human poisoning by organophosphorus insecticides. Hum Exp Toxicol [Internet]. 2004 Dec [cited 2022 Dec 13];23(12):565–9. Available from:http://journals.sagepub.com/doi/10.1191/0960327104ht489oa

[13]. Balali-Mood M, Saber H. Recent advances in the treatment of organophosphorous poisonings. Iran J Med Sci. 2012 Jun;37(2):74–91.

[14]. Açıkalın A, Dişel NR, Matyar S, Sebe A, Kekeç Z, Gökel Y, et al. Prognostic factors determining morbidity and mortality in organophosphate poisoning. Pak J Med Sci [Internet]. 2017 Jun 2 [cited 2022 Dec 13];33(3). Available from: http://pjms.com.pk/index.php/pjms/article/view/12395

[15]. Eddleston M, Buckley NA, Eyer P, Dawson AH. Management of acute organophosphorus pesticide poisoning. The Lancet [Internet]. 2008 Feb [cited 2022 Dec 13];371(9612):597–607. Available from: https://linkinghub.elsevier.com/ retrieve/pii/S0140673607612021

[16]. Bhattacharyya K, Sarkar R, Phaujdar S, Mullick O. Serum creatine phosphokinase: A probable marker of severity in organophosphorus poisoning. Toxicol Int [Internet]. 2011 [cited 2022 Dec 13];18(2):117. Available from: http://www.toxicologyinternational.com/text.asp?2011/18/2/117/84263

[17]. Mohammad FK, Alias AS, Ahmed OAH. Electrometric measurement of plasma, erythrocyte, and whole blood cholinesterase activities in healthy human volunteers. J Med Toxicol [Internet]. 2007 Mar [cited 2022 Dec 13];3(1):25–30. Available from: http://link.springer.com/10.1007/BF03161035

[18]. Shetab-Boushehri SV. Ellman's method is still an appropriate method for measurement of cholinesterases activities. EXCLI Journal; 17:Doc798; ISSN 1611-2156 [Internet]. 2018 [cited 2022 Dec 13]; Available from: https://www.excli.de/vol17/Shetab-Boushehri_13082018_proof.pdf

[19]. Blain PG. Organophosphorus poisoning (Acute). BMJ Clinical Evidence [Internet]. 2011 [cited 2022 Dec 13];2011. Available from:https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3217786/

[20]. M Nurulain S, Szegi P, Tekes K, Nh Naqvi S. Antioxidants in organophosphorus compounds poisoning. Archives of Industrial Hygiene and Toxicology [Internet]. 2013 Mar 1 [cited 2022 Dec 13];64(1):169–77. Available from: https://content.sciendo.com/doi/10.2478/10004-1254-64-2013-2294

[21]. Clement J. Hormonal consequences of organophosphate poisoning.

[22]. Fundamental and Applied Toxicology [Internet]. 1985 Dec [cited 2022 Dec 13];5(6):S61–77. Available from: https://linkinghub.elsevier.com/ retrieve/pii/ 0272059085901150

[23]. Rajak P, Ganguly A, Sarkar S, Mandi M, Dutta M, Podder S, et al. Immunotoxic role of organophosphates: An unseen risk escalating SARS-CoV-2 pathogenicity. Food and Chemical Toxicology. 2021 Mar [cited 2022 Dec 13];149:1120-27. Available from: https://linkinghub.elsevier.com/ retrieve/pii/ S0278691521000417

[24]. Paul UK, Bhattacharyya AK. ECG manifestations in acute organophosphorus poisoning. J Indian Med Assoc. 2012 Feb;110(2):98, 107–8.

[25]. Aman S, Paul S, Chowdhury FR. Management of organophosphorus poisoning: standard treatment and beyond. Critical Care Clinics [Internet]. 2021 Jul 1 [cited 2022 Dec 13];37(3):673–86. Available from: https://www.criticalcare. theclinics.com/article/S07490704(21)00022-1/abstract

[26]. Oxime - an overview | sciencedirect topics [Internet]. [cited 2022 Dec 13]. Available from: https://www.sciencedirect.com/topics/chemistry/oxime

[27]. Wani T, Gurcoo S, Farooqui A, Nisa W, Sofi K, Syed S. Is the World Health Organization-recommended dose of pralidoxime effective in the treatment of organophosphorus poisoning? A randomized, double-blinded and placebo- controlled trial. Saudi J Anaesth [Internet]. 2015 [cited 2022 Dec 13];9(1):49. Available from: http://www.saudija.org/text.asp?2015/9/1/49/146306

[28]. Peshin SS, Gupta YK. Poisoning due to household products: A ten years retrospective analysis of telephone calls to the National Poisons Information Centre, All India Institute of Medical Sciences, New Delhi, India. J Forensic Leg Med. 2018 Aug;58:205–11.

[29]. Indu TH, Raja D, Ponnusankar S. Toxicoepidemiology of acute poisoning cases in a secondary care hospital in rural South India: A five-year analysis. J Postgrad Med. 2015 Jul 1;61(3):159.

[30]. Vale A, Lotti M. Organophosphorus and carbamate insecticide poisoning.

[31]. Handb Clin Neurol. 2015;131:149–68.

[32]. Chaudhary SC, Singh K, Sawlani KK, Jain N, Vaish AK, Atam V, et al.

[33]. Prognostic significance of estimation of pseudocholinesterase activity and role of pralidoxime therapy in organophosphorous poisoning. Toxicol Int. 2013 Sep;20(3):214–7.

[34]. Kothiwale V, Shirol V, Yerramalla V, Somannavar V. Association between serum cholinesterase levels and clinical outcome in patients of organophosphorus compound poisoning – One-year hospital-based longitudinal study. APIK J Int Med. 2019 [cited 2023 Jan 6];7(4):109.

[35]. Kang EJ, Seok SJ, Lee KH, Gil HW, Yang JO, Lee EY, et al. Factors for determining survival in acute organophosphate poisoning. Korean J Intern Med 2009;24:362-7

[36]. Patil G, Nimbal NV, Joshi AV, Dambal A, Madhavaranga MP, Halki S. Role of serum cholinesterase in acute organophosphorus poisoning: A hospital based cross sectional study. J Evol Med Dent Sci 2015;4:5102-8.

[37]. Sen R, Nayak J, Khadanga S. Study of serum cholinesterase, CPK and LDH as prognostic biomarkers in organophosphorus poisoning. Int J Med Res Rev. 2014;2:185-9.

[38]. Rehiman S, Lohani SP, Bhattarai MC. Correlation of serum cholinesterase level, clinical score at presentation and severity of organophosphorous poisoning. JNMA J Nepal Med Assoc.`1 2008;47:47-52.

[39]. Nouira S, Abroug F, Elatrous S, Boujdaria R, Bouchoucha S. Prognostic value of serum cholinesterase in organophosphate poisoning. Chest. 1994;106:1811- 4.

[40]. Rehiman S, Lohani SP, Bhattarai MC. Correlation of serum cholinesterase level, clinical score at presentation and severity of organophosphorous poisoning. JNMA J Nepal Med Assoc. 2008;47:47-52.

[41]. Kumar CU, Kishan PV, Chandrashekhar E, Usharani P. The utility of serial serum cholinesterase as a prognostic marker in organophosphorus compound poisoning. Int J Basic Clin Pharmacol 2014;3:529-33.

[42]. Venkateshwarlu N, Gandiah P, Prabhakar KK, Indira G, Sivarajappa P. Significance of serum cholinesterase levels in patients of organophosphorus poisoning. Int J Recent Trends Sci Technol 2013;9:270-4.

[43]. Siva PV, Padma VS, Sarma DV, Reddy SM. Activity of serum cholinesterase in organo – Phosphorus poisoning cases: A prospective study. J Pharm Biomed Sci 2012;20:1-3.

[44]. Khazi MA, Sainath C, Parvez A. A cross sectional study of estimation of plasma pseudo cholinesterase and its correlation to mortality among organophosphorus poisoning patients. Indian J Basic Appl Med Res 2014;3:285-91.

[45]. Patel P, Patel VP, Patel H, Rathod GB. Study of prognostic value of serum and RBC acetyle cholinesterase level in organophosphorus poisoning and its correlation with the outcome. IAIM, 2016; 3(3): 147-157

[46]. Thiermann H, Zilker T, Eyer F, Felgenhauer N, Eyer P, Worek F. Monitoring of neuromuscular transmission in organophosphate pesticide-poisoned patients. Toxicol Lett 2009;191(2-3):297–304.

[47]. Key PB, Fulton MH. Correlation between 96-h mortality and 24-h acetylcholinesterase inhibition in three grass shrimp larval life stages. Ecotoxicol Environ Saf 2006;63(3):389–392.

[48]. Eddleston M, Worek F, Eyer P, Thiermann H, Von Meyer L, Jeganathan K, et al. Poisoning with the S-alkyl organophosphorus insecticides profenofos and prothiofos. QJM 2009;102(11):785–792.

[49]. Peter JV, Jerobin J, Nair A, Bennett A, Samuel P, Chrispal A, et al. Clinical profile and outcome of patients hospitalized with dimethyl and diethyl organophosphate poisoning. Clin Toxicol 2010;48(9):916–923.