

Original Article

Role of Paraoxonase-1 Enzyme in Prediction of Severity and Outcome of Acute Organophosphorus Poisoning: A Prospective Study



Nour A.A. Eltramsy¹, Rabab Shaban El-Shafey², Abeer A.I. Sharaf El-Din³, Prashant Shankarrao Adole⁴, Haidy M. Fakher⁵

¹ *Demonstrator of Forensic Medicine and Clinical Toxicology, Faculty of Medicine, Benha University.*

² *Associate professor of Forensic Medicine and Clinical Toxicology, Faculty of Medicine, Benha University*

³ *Professor of Forensic Medicine and Toxicology, Faculty of Medicine, Benha University.*

⁴ *Associate professor of biochemistry, Jawaharlal Institute of Postgraduate Medical Education & Research, Pondicherry, India.*

⁵ *Lecturer of Forensic Medicine and Clinical Toxicology, Faculty of Medicine, Benha University.*

ABSTRACT

*Corresponding author:

Nour Abo-Bakr
Ali Eltramsy

Email:
nour.abubakr@fmed.bu.edu.eg

Mobile:
01063215693

Background: Human serum paraoxonase-1 (PON-1) hydrolyzes organophosphate compounds (OPC) and so significantly alters an individual's susceptibility to the toxicity of these chemicals. **Aim:** The study was designed to assess the serum PON-1 activity in patients with OPC poisoning and to correlate its level with the severity and outcome of acutely organophosphate poisoned patients. **Patients and methods:** This was a prospective clinical study that was performed at Benha Poison Treatment and Toxicological Research Unit (BPTTRU), Benha University Hospitals, Egypt, for one year, from 1 August 2020 till 31 July 2021. Patients were divided into case and control groups. Socio-demographic information of patients, clinical findings, treatments given, length of hospital stay and outcome were collected into datasheets. Patients were classified according to degree of toxicity according to Peradeniya Organophosphorus Poisoning (POP) scale. Blood samples were collected from patients to assess pseudocholinesterase and PON-1 activities. **Results:** Reduction of serum pseudocholinesterase and paraoxonase-1 (PON-1) activities in poisoned patients and patients can be graded according to (POP) scale into: mild, moderate and severe cases. **In conclusion:** This study concluded that serum paraoxonase-1 (PON-1) activity was significantly lower in patients with severe organophosphorus compounds (OPC) poisoning as compared to patients with moderate poisoning. Lower PON-1 activity was significantly associated with lower serum cholinesterase and poorer outcomes. PON-1 activity may be considered as an indicator of prognosis in OPC poisoning.

Keywords: Pseudocholinesterase; Organophosphorus compounds; POP Scoring; Paraoxonase-1
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I. Introduction

Pesticides refer to a wide range of chemicals that are employed to increase agricultural output. Several pesticides have been shown to have severe negative impacts on human health, including acute toxicity (accidental poisoning deaths, particularly in impoverished nations) and chronic toxicity (even at low concentrations) (Trellu et al., 2021). In the central nervous systems of mammals and insects, organophosphate compounds (OPC) inhibit acetylcholinesterase irreversibly by inhibiting acetylcholine breakdown during nerve impulse transmission. Continuous neuronal excitation causes a variety of hazardous symptoms in mammals and insects, **including slowed heart rate, pinpoint eye pupils, and seizures and respiratory failure (RF)** which is the leading cause of OPC poisoning morbidity and fatality (Zhai et al., 2021).

The diagnosis is based on the individual's medical history, physical examinations, and toxidromes of acute poisoning. Predicting the severity, prognosis, and complications related to poisoning requires a variety of clinical observations, electrocardiography, and blood or urine sample results. Electrolytes, the complete blood count, and arterial blood gas are virtually always tested (Kim et al., 2022).

Acetylcholine is found to be considerably in almost whole of the autonomic preganglionic fibers which consists of the efferent postganglionic fibers along with the peripheral parts of the ANS (Autonomic nervous system). In addition it also comprises of the cholinergic fibers which are the sympathetic post ganglionic nerve fibres (Kaur et al., 2019).

The paraoxonases family consists of three enzymes: Paraoxonase-1 (PON-1), paraoxonase-2 (PON-2) and paraoxonase-3 (PON-3), all having antioxidant and hydrolase

activities. Despite the fact that PON enzymes are found throughout the human body, they are mostly generated in the liver. They are found in a variety of tissues and are mostly linked to cell membranes and certain lipoproteins, while a free enzyme has been discovered in the blood (Reichert et al., 2021).

Analyzing PON-1 activity in those who have ingested OPC would be helpful in: (I) evaluating the severity of poisoning, (II) estimating the capability of the patient to detoxify OPC, and (III) recognizing PON-1's prognostic significance due to interindividual differences in PON-1 activity (Samy et al., 2019).

Aim of work:

The aim of this work is to evaluate serum paraoxonase-1 (PON-1) activity in patients with organophosphorus poisoning and to correlate serum PON-1 with the severity and outcome of acutely organophosphate poisoned patients admitted to the Benha Poison Treatment & Toxicological Research Unit (BPTTRU).

II. Patients and methods:

2.1 Type of study:

This is a prospective clinical study that was performed at Benha Poison treatment and toxicological research unit (BPTTRU), Benha University Hospitals, Egypt, for one year, from 1 August 2020 till 31 July 2021 after obtaining the approval from the Ethical Committee of the Faculty of Medicine, Benha University. Written informed consent (in Arabic language) was taken prior to participation from study subjects or their guardians. The study protocol was approved by the Local Ethical Committee of Benha University at 4th of March 2020, approval number was 305.

2.2 Patients grouping:

Group I (control group): which included 20 healthy volunteers who were selected based on their clinical examination, recent clinical history, and age and sex matching to the case group. All included participants were divided into 5 groups according to age per year :

- 18-29 years
- 30-39 years
- 40-49 years
- 50-59 years
- ≥ 60 years

Group II (case group): which has 70 participants, including both genders, 52 of them were symptomatic and diagnosed as acute organophosphates compounds (OPC) toxicity. There were 18 participating asymptomatic patients of both sexes who had positive history of acute organophosphates compounds toxicity excluded from the study.

Inclusion criteria :

According to Patil (2014)'s recommendations, the following criteria are used to make the diagnosis of OPC poisoning:

- Previous OPC exposure.
- The cholinergic toxidrome-specific features of OPC toxicity
- After using atropine, muscarinic symptoms and signs improved.
- low pseudo-cholinesterase activity in serum.

Exclusion criteria :

- Patients under the age of 18.
- Cases with no symptoms.
- Patients who have a history of severe renal, cardiac, pulmonary, or nephritic syndrome.
- Patients with any of the following conditions which reduce pseudo-cholinesterase activity:
 - ✓ Patients who have a history of parenchymal liver disease, acute infection, metastatic cancer, malnutrition, iron deficiency anemia, or dermatomyositis.
 - ✓ Patients who are pregnant or who are using narcotics or poisonous substances (such as cocaine, carbon disulfide, benzalkonium salts, organic mercury compounds, ciguatoxins, and solanines) (oral contraceptive pills and metoclopramide).

2.3. Study design:

All included individuals in the study (case and control groups) were subjected to:

2.3.1. Socio-demographic data: Personal data collection: age, sex, residence, occupation and marital status.

2.3.2. Exposure history: manner of poisoning, route of exposure, place of exposure

2.3.3. Physical examination for clinical study:

1) Vital signs

a. Pulse:

Bradycardia is described as a sustained heart rate less than 60 BPM (Umeh et al., 2022) while heart rate of more than 100 beats per minute is considered tachycardia (Linton et al., 2022).

b. Temperature :

Hyperthermia is an increase in internal body temperature by 0.5 °C (Dervisevic et al., 2022). Hypothermia is defined as a core body temperature of <36 °C (Cumin et al., 2022).

c. Respiratory rate:

Normal range of respiratory rate in adults is 12-20 breaths per minute. Bradypnea is respiratory rate below 12 breaths per minute. Adults with a respiratory rate of more than 20 breaths per minute are considered to have tachypnea (Longhitano et al., 2022 and Luca et al., 2022).

d. Blood pressure:

Hypotension is defined as mean arterial pressure less than 65 mmHg (Murabito et al, 2022), while when mean arterial pressure $\geq 140/90$ mmHg is known as hypertension (Hamrahian et al., 2022).

2) Cholinergic toxidrome:

a. Central manifestations: Level of consciousness was evaluated by GCS, confusion, convulsion and coma. A GCS score of less than 8 is a well-known indicator for intubation (Alsulimani et al., 2022).

b. Muscarinic signs and symptoms (excess salivation, lacrimation, bradycardia, bronchospasm, diarrhea and urinary incontinence).

c. Nicotinic manifestations (fasciculations and muscle paralysis).

2.3.4. Clinical severity scoring:

According to the Peradeniya Organophosphorus Poisoning (POP) Scale, severity was determined, which included pupil size, respiratory rate, pulse rate, fasciculations, level of consciousness and whether there were any convulsions or not. Accordingly, subjects were divided into mild (POP scale 0-3), moderate (POP scale 4-7) and severe poisoning (POP scale 8-11) groups according to Amir et al. (2020). Peradeniya Organophosphorus Poisoning (POP) Scale was calculated to each patient admitted.

2.3.5. Treatment, hospital admission & Outcome:

Delay time and total duration of hospital stay. All the patients were observed for short - term outcomes; that they were either discharged or died and the total duration of hospital stay (Mohamed et al., 2019).

2.3.6. Laboratory data:

The individuals' venous blood was taken five milliliters under strict aseptic conditions of both control and case groups (before antidotal therapy). Then the blood was left to be coagulated for 10-20 minutes at room temperature, then centrifugation was done for 20 min at the speed of 2000-3000 r.p.m by Laboratory centrifuge 800D (Changsha Weierkang Xiangying Centrifuge, China). Serum samples were obtained, then half of the separated serum was used for pseudocholinesterase enzyme assay and the other one was kept at -20° C to be used for paraoxonase-1 (PON-1) analysis later.

Pseudo-cholinesterase enzyme: It was measured by clichem 2 apparatus using cholinesterase DGKC kits that was purchased from Spectrum Diagnostics, Al-Obour city, industrial zone. Block 20008, piece 19 A., PO Box 30 Obour, Egypt .

Serum PON-1: The enzyme-linked immunosorbent assay was used to measure it (ELISA) using human paraoxonase (PON)

ELISA kits. Shanghai Sunred Biological Tec., HNOLOGY CO., China, Shanghai, Baoshan District, Hutai Road, LTD No. 6497.

2.4. Statistical Analysis

A report form was used to capture the clinical data. Using the computer program SPSS (Statistical package for social science) version 26, these data were tabulated and examined to produce according to Khamankar et al. (2021):

Descriptive statistics were calculated for the data in the form of :

1. Mean and standard deviation for quantitative data.
2. Frequency and distribution for qualitative data.

One of the following tests was used to determine the significance of difference in the statistical comparison between the studied groups:

- a) Student's t-test for comparing mean of two groups of quantitative data .
 - b) The ANOVA test, which compares the means of more than two groups of quantitative data, is done using the F value.
 - c) Inter-group comparison of categorical data was done by using chi square test (X²-value) and fisher exact test (FET).
 - d) Mann–Whitney U test, ANOVA, or Kruskal-Wallis test, where appropriate used to compare group means of the continuous variables.
 - e) Dunn test was used to perform comparisons between independent groups and to tell which groups are statistically different.
 - f) Tukey test was used to perform comparisons as a post hoc analysis after an ANOVA has shown significant difference.
 - g) Depending on the pattern of the variable's distribution, correlations were evaluated using either the Pearson correlation test or the Spearman's rank test.
 - h) A receiver-operating characteristic (ROC) curve analysis was done to find out what PON-1's cut-off value should be for case prediction.
- P value <0.05 was considered statistically significant(*) while >0.05 statistically insignificant.
 - P value <0.01 was considered highly significant (**) in all analyses.

III. RESULTS

The present study was performed at Benha Poison Treatment and Toxicological Research Unit (BPTTRU), Benha University hospitals during the period from 1 august till 31 July 2020. A total 72 participants were enrolled into this prospective study (52 who fulfilled the inclusion criteria served as patient group and 20 healthy volunteers served as control group). Their personal history (sociodemographic

data), exposure history, clinical data, and clinical severity scoring based on POP scale were performed. Laboratory parameters, total dose of atropine needed, delay time, total duration of hospital stay as well as outcome for all patients were recorded.

The total number of acute pesticides poisoning was 441 patients out of 2549 cases (17.3%) during the period of the study.

Sociodemographic data and exposure history

Table 1 showed socio-demographic characteristics of case and control groups. The mean age (\pm SD) of the patients (n=52) was 33.67 (\pm 5.24) years. The mean (\pm SD) age of control group (N=20) was 32.91 (\pm 2.43) years. There was non-significant statistical difference between control group and case group according to age, sex, residence, and marital status. While statistical analysis showed

significant difference between control group and case group according to occupation.

Most patients (20 patients, 38.5%) were falling in the age group 18-29 years, followed by patients aged 30-39 years (18; 34.6%), 40-49 years (7; 13.5%), then those aged between 50-59 years (4; 7.7%) while the least percentage occurred in cases aged > 60 (3; 5.8%) years old. As regarding the sex, the male patients showed a high incidence in number and percentage (29; 55.8%) as compared to female patients (23; 44.2%) with a sex ratio of 1.26:1.

The majority of presented cases were married (28; 53.8%) compared to single patients (24; 46.2 %), and (55.8 %) of the patients (29) lived in rural areas, as compared with 23 patients (44.2%) who were referred from urban areas. Another finding was that most of the presented patients worked as farmers (16; 30.8%), followed by unemployed and housewife who compromised about 26.9%

Table 1: Comparison between studied groups according to socio-demographic characteristics.

Variables	Case group (52)		Control group (20)		Test	P value
	N	%	N	%		
Age (years)						
18-29	20	38.5	8	35.0	FET= 1.82	0.81
30-39	18	34.6	8	25.0		
40-49	7	13.5	2	20.0		
50-59	4	7.7	1	10.0		
\geq 60y	3	5.8	1	10.0		
Sex						
Male	29	55.8	12	70.0	X ² = 1.22	0.27
Female	23	44.2	8	30.0		
Residence						
Urban	23	44.2	11	55.0	FET= 1.22	0.29
Rural	29	55.8	9	45.0		
Marital status						
Married	28	53.8	17	50.0	X ² = 0.09	0.77
Single	24	46.2	3	50.0		
Occupation						
Unemployed	14	26.9	3	15.0	X ² = 15.1	0.004*
Farmer	16	30.8	8	40.0		
Student	1	1.9	2	10.0		
Employer	7	13.5	5	25.0		
Housewife	14	26.9	2	10.0		

X²: chi square test FET: fisher exact test N: number y: years * significant

As regard exposure history, the majority of toxic exposures occurred indoor (46; 88.5%) rather than outdoor (6; 11.5%), it also showed that the highest manner of exposure was suicidal (29; 55.8%) then accidental manner (23; 44.2%) without any homicidal cases (0;

0%), and the most important route of exposure to OPC cases was oral ingestion (44; 84.6 %), followed by inhalation (7; 13.5%), and lastly the dermal exposure (1; 1.9%) as shown in (Figure 1).

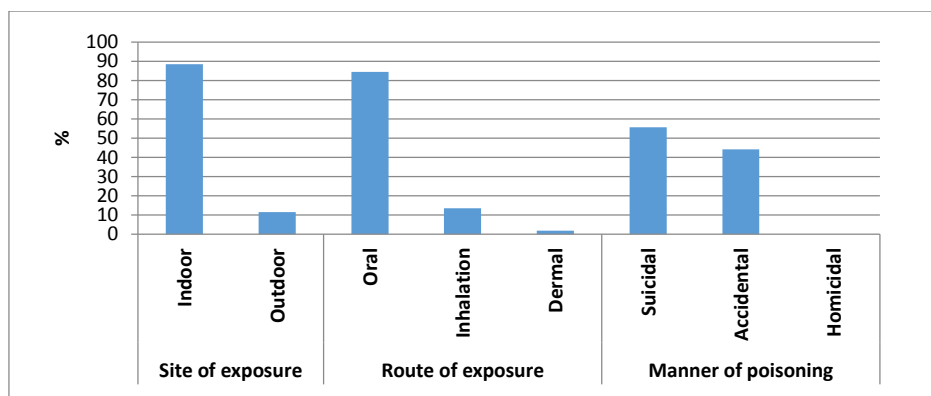


Figure 1: Distribution of exposure history among case group.

Physical examination for clinical data

Regarding vital signs, case group showed that 39 cases (75%) had normal pulse rates, bradycardia was the commonest pulse abnormalities presented in 9 cases (17.3%) followed by tachycardia in four cases (7.7%). There were thirty cases (57.7%) had normal blood pressure. Hypotension displayed more prevalent abnormality in 18 cases (34.6%)

followed by hypertension in four cases (7.7%). Forty-nine cases (94.2%) acquired proper respiratory rates. Bradypnea occurred in two cases (3.8%), while tachypnea was found in one case (1.9%). There were 50 cases (96.2%) possessed normal temperature and two cases only (3.8%) showed hypothermia as shown in (Table 3).

Table 2: Number and percentage of the studied patients as regard vital signs.

Vital signs	Case group (52)	
	N	%
Heart rate (beat/min)		
Normal	39	75.0
Bradycardia	9	17.3
Tachycardia	4	7.7
Blood pressure (mmHg)		
Normal	30	57.7
Hypotension	18	34.6
Hypertension	4	7.7
Respiratory rate (beat/min)		
Normal	49	94.2
Bradypnea	2	3.8
Tachypnea	1	1.9
Temperature (°C)		
Normal	50	96.2
Hypothermia	2	3.8

N: number

The clinical presentation of the patients is shown in (Table 3), Almost all patients had muscarinic symptoms and signs (52; 100%). The most frequent clinical signs were bronchorrhea (45, 86%), pinpoint pupil (41, 78.8%), emesis (32, 61.5 %), sweating (30, 57.7) and increased urinary frequency (25.48%), followed by bradycardia (9, 17.3 %), lacrimation (two patients, 3.8%) and diarrhea (one patient, 1.9%). Whereas nicotinic

manifestations were present in 20 cases (38.5%), manifested by fasciculation and weakness (20, 38.5% for each), hypertension and tachycardia (four patients, 7.7%) and mydriasis in two patients (3.8%). As regard central nervous system (CNS) manifestations, ten cases had altered mental status ranging from confusion to coma. No reported cases had convulsions.

Table 3: Number and percentage of the studied patients as regard cholinergic toxidrome.

Cholinergic toxidrome	Case group (52)	
	N	%
Muscarinic manifestations		
Bronchorrhea	45	86.5
Pinpoint pupil	41	78.8
Emesis	32	61.5
Sweating	30	57.7
Urination	25	48
Bradycardia	2	17.3
Lacrimation	9	3.8
Diarrhea	1	1.9
Nicotinic manifestations		
Fasciculations	20	38.5
Weakness	20	38.5
Hypertension	4	7.7
Tachycardia	4	7.7
Mydriasis	2	3.8
CNS manifestations		
Coma	5	9.6
Disturbed conscious level	3	5.8
Confusion	2	3.8
Convulsion	0	0.0

N: number CNS: Central Nervous System

On arrival to the hospital, the level of consciousness was evaluated by Glasgow Coma Scale (GCS), the results denoted that about (43; 82.7%) of cases were fully awake (GCS=15),

(four patients; 7.7%) were drowsy (GCS=9-14), and (five patients; 9.6%) presented with coma (GCS<8) as shown in (Figure 2).

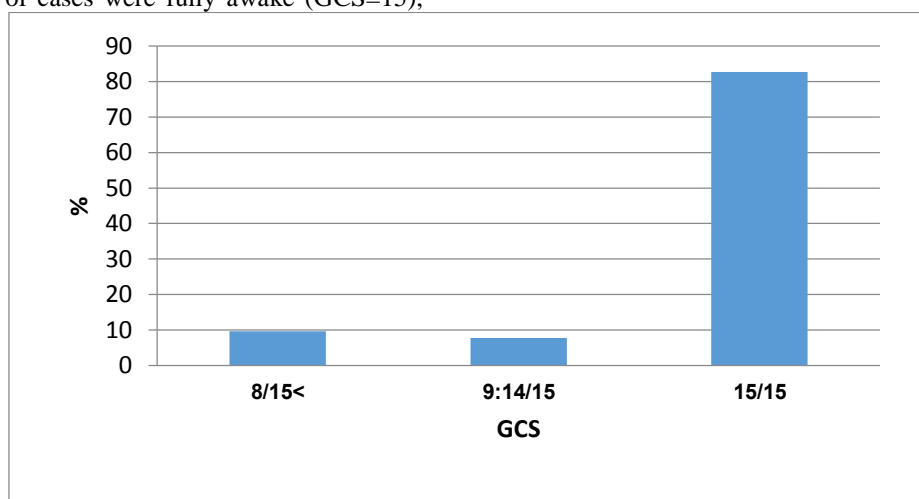


Figure 2: Distribution of case group according to Glasgow Coma Scale (GCS).

Clinical severity scoring based on POP scale

Regarding Peradeniya Organophosphorus Poisoning scale (POP), The cases were classified in severity of poisoning according to POP scale into mild (41 cases, 78.8%),

moderate (six cases, 11.5%) and severe (five cases, 9.7%) as shown in (Figure 3).

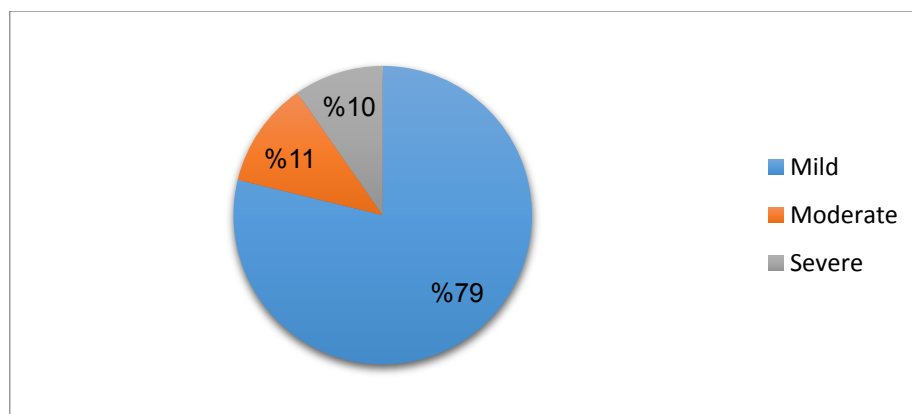


Figure 3: Severity of cases according to Peradeniya Organophosphorus Poisoning (POP) scale.

Treatment, hospital admission and outcome

The current study revealed that about 80.8% (42 patients) of the total studied cases were admitted to the hospital within one hour of exposure, followed by 1-2 hours delay (10; 19.2%) and no cases were delayed > 6 hours. About 92.3% (48 patients) were admitted for 6-48 hours, while 7.7% (4 patients) were admitted for > 48 hours. The mean value (\pm SD) of elapsed time between acute poisoning and

hospital arrival was 2.09 (\pm 1.4) hours. At the same time, the mean (\pm SD) duration of hospitalization was 34.75 (\pm 21.38) hours. The mean (\pm SD) of total atropine dose needed was 7.67 (\pm 6.26) as shown in (Table 4).

The outcome of the patients was as the following: 49 patients were discharged after complete recovery representing about (94.2%) and only three patients were died representing about (5.77%).

Table 4: Number and percentage of the studied patients as regard delay time, duration of hospitalization and outcome of patients.

Variables	Case group (52)	
	N	%
Delay time (hours)		
1-2 h	42	80.8
2-6 h	10	19.2
\geq 6 h	0	0.0
Duration of hospitalization (hours)		
< 6 h	0	0.0
6 -48 h	48	92.3
\geq 48 h	4	7.7
Complete recovery	49	94.2
Death	3	5.77

N: number h: hour

Demography and poisoning severity score (POP)

There was a non-significant difference between different age group and between both sexes among the three grades of poisoning. There was a significant relation according to

residence, but a non-significant relation according to marital status and occupation as illustrated in (Figure 4).

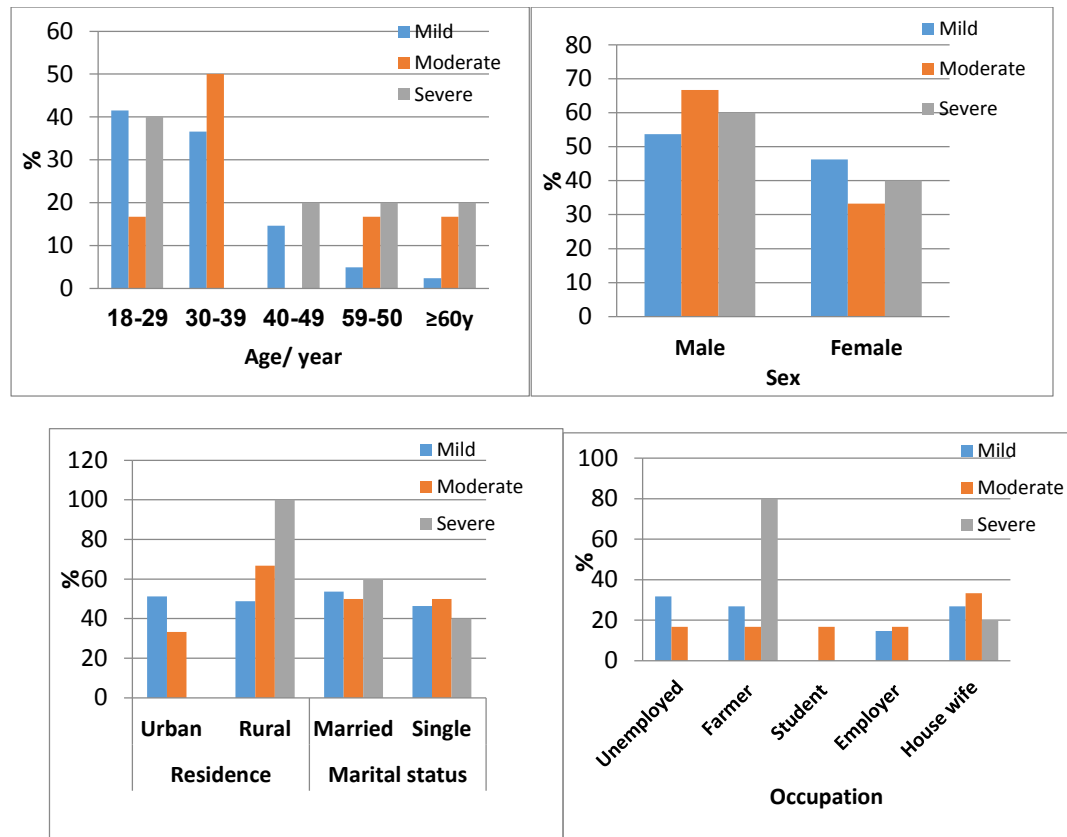


Figure 4: Distribution pattern of socio-demographic data among the three grades of poisoning according to Peradeniya Organophosphorus Poisoning scale (POP).

There was a significant relation among case group according to manner of poisoning, being more severe with suicidal cases, but non-

significant relation according to site and route of exposure as illustrated in (Figure 5).

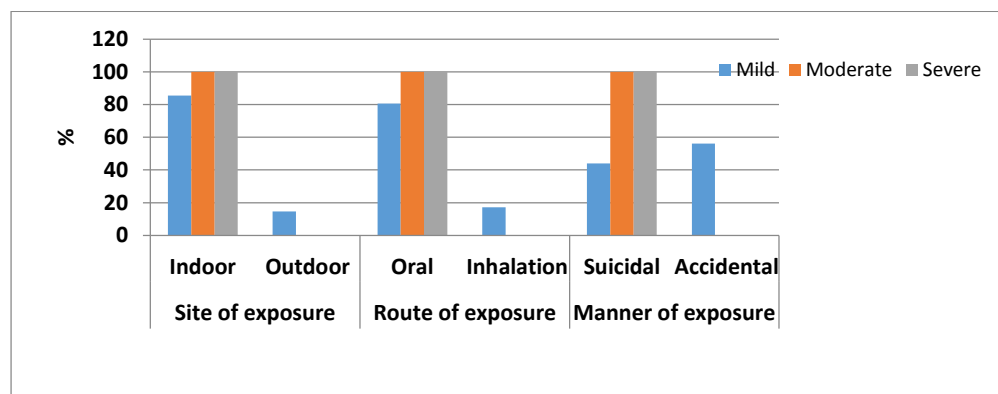


Figure 5: Distribution pattern of site, route, manner of exposure among the three grades of poisoning according to Peradeniya Organophosphorus Poisoning scale (POP).

Vital signs and poisoning severity score

Chi-square statistical analysis between different proportions of the overall clinical parameters showed significant differences

among the three grades of poisoning as shown in (Table 5).

Table 5: Distribution pattern of vital signs among the three grades of poisoning according to Peradeniya Organophosphorus Poisoning scale (POP).

Vital signs	POP score			Statistical test (X ²)	P value
	Mild	Moderate	Severe		
Heart rate (beat/min)					
Normal	87.8%	33.3%	20%	20.25	<0.001**
Bradycardia	4.9%	66.7%	60%		
Tachycardia	7.3%	0%	20%		
Blood pressure (mmHg)					
Normal				26.1	<0.001**
Hypotension	73.2%	0%	0%		
Hypertension	19.5%	100%	80%		
	7.3%	0%	20%		
Respiratory rate (breath/min)					
Normal	97.6%	100%	60%	10.63	0.031*
Bradypnea	0%	0%	40%		
Tachypnea	2.4%	0%	0%		
Temperature (°C)					
Normal	100%	100%	60%	10.22	0.006**
Hypothermia	0%	0%	40%		

* significant ** highly significant

The main bulk of patients with mild manifestation (40, 97.6%) experienced normal GCS (> 15/15), followed in order of frequency by those with severe (5, 10%) with GCS (> 8/15) and moderate (3, 50%) with GCS

(9:14/15). There was a highly significant difference among the three grades of poisoning groups according to GCS as illustrated in (Figure 6).

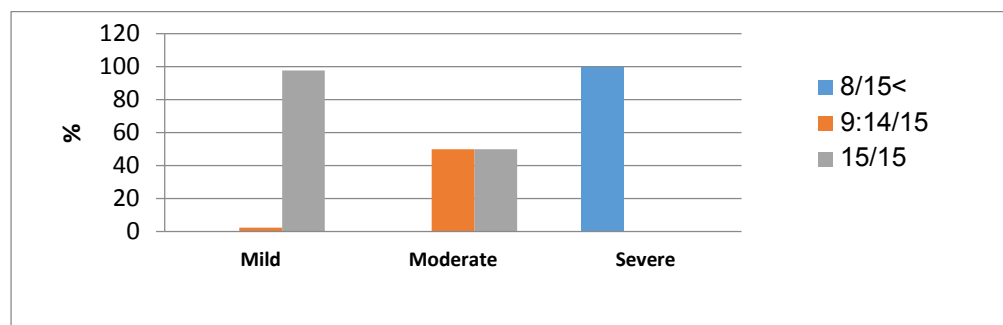


Figure 6: Distribution pattern of Glasgow coma scale (GCS) among the three grades of poisoning according to Peradeniya Organophosphorus Poisoning scale (POP).

- Treatment & outcome and poisoning severity score

Thirty-four patients (82%) with mild manifestations recorded delay of admission about 1-2 hours, followed by five patients (83.3%) with moderate manifestations and severe manifestations were present in three patients (60%). While seven patients (17.1%) with mild manifestations recorded delay of admission about 2-6 hours, followed by two patients (40%) with severe manifestations and moderate manifestations were present in only one patient (16.7%).

Forty patients (97.6%) with mild manifestations recorded hospital stay of 6-48 hours, followed by six patients (100%) with moderate manifestations and severe manifestations were present in two patients (40%). While three patients (60%) with severe manifestations recorded hospital stay of more than 48 hours, followed by one patient (2.4%) with mild manifestations and no one with moderate manifestations recorded hospital stay more than 48 hours.

There was a significant relation among case group according to duration of hospitalization

of patients, being more severe with cases who had duration of hospitalization more than 48 hours, but non-significant difference according to delay. All patients with mild and moderate grade of POP severity scale survived. Three

(40%) from five patients with severe grade of POP scale had expired. There was a significant (P value < 0.001) difference between three groups as shown in (Figure 7).

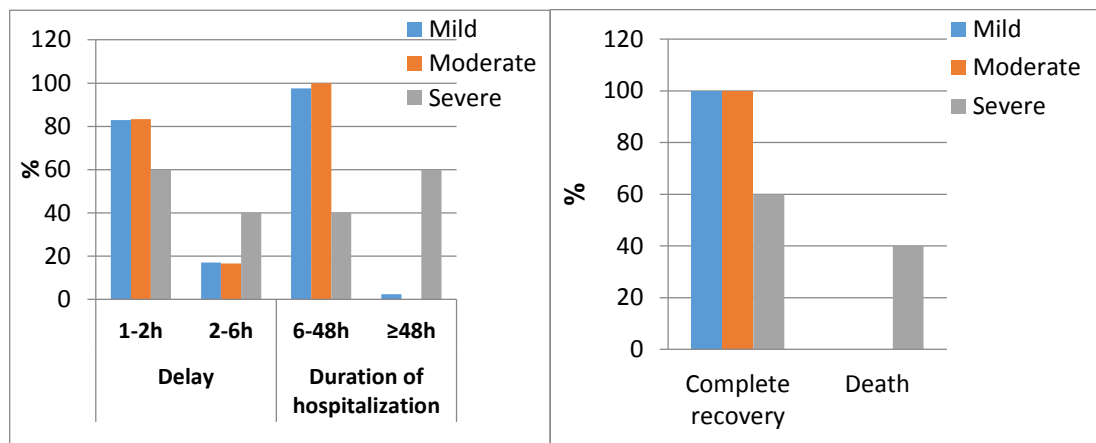


Figure 7: Relation between Peradeniya Organophosphorus Poisoning scale (POP) and treatment & outcome among case group.

Laboratory data:

Student t-test analysis showed a significant decrease as regard pseudocholinesterase and paraoxonase-1 levels in patients as compared to controls (Table 6). At the same time, the mean

(± SD) levels of PChE in patients was 2611.78 (± 1162.42), significantly lower than that of controls 8274.75 (± 2168.44). Mean levels of paraoxonase in patients and controls were 33.79 ± 9.07 and 137.73 ± 32.34 respectively.

Table 6: Statistical analysis of the difference of pseudocholinesterase (PChE) and paraoxonase-1 (PON-1) levels in patient and control groups using student t-test.

		PChE (U/L)	PON-1 (U/L)
Case group (52)	Mean	2611.78	33.79
	±SD	1162.42	9.07
Control group (20)	Mean	8274.75	137.73
	±SD	2168.44	32.34
t test		14.23	21.31
P value		<0.001**	<0.001**

t: student t test; SD: standard deviation; PON: paraoxonases; PChE: Pseudocholinesterase; * significant; ** highly significant

- Sociodemographic data and Paraoxonase-1 level (PON-1):

As regard relation between sociodemographic data and PON-1 level among the case group, there was non-significant

difference between the groups based on age, sex, residence, marital status, and occupation as shown in (Figure 8)

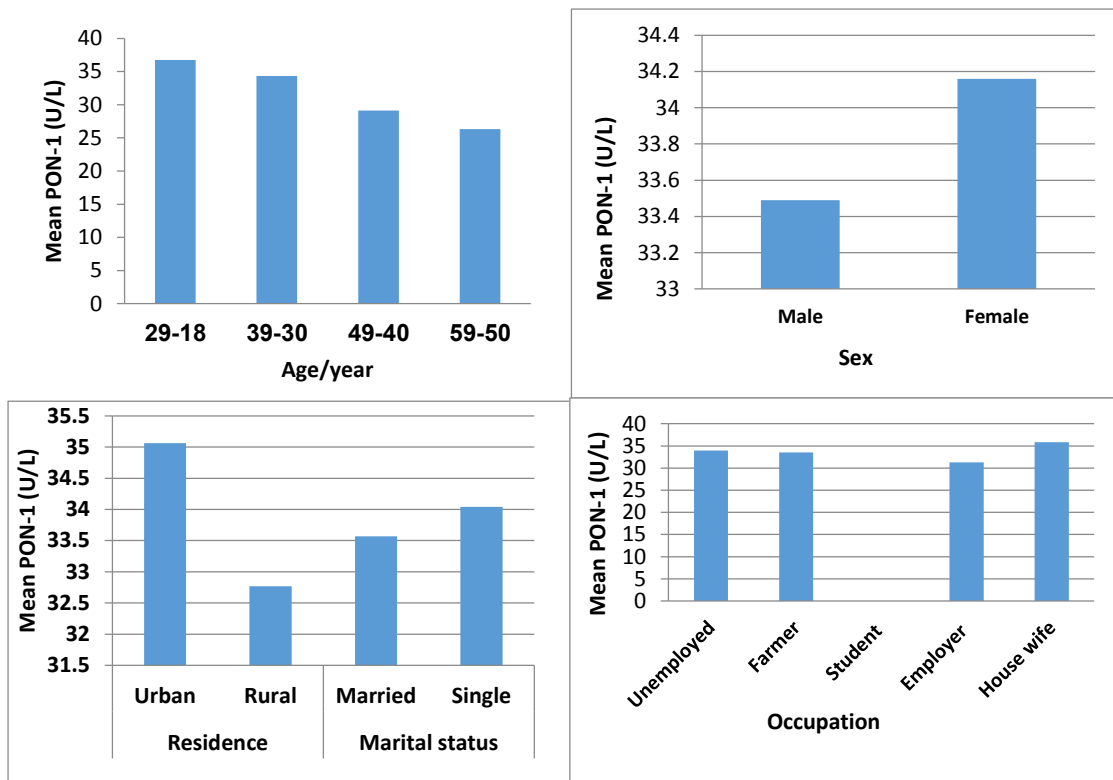


Figure 8: Relation between paraoxonase-1 (PON-1) level and occupation among case group.

As regard relation between exposure history and PON-1 level among the case group, there was a significant relation regarding manner of

poisoning, being more reduced with suicidal cases, but a non-significant according to site and route of exposure as shown in Figure (9)

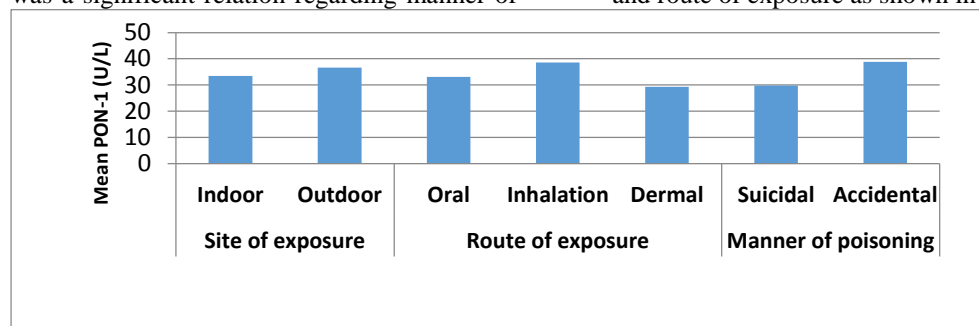


Figure 9: Relation between paraoxonase-1 (PON-1) level and exposure history among case group.

As regard relation between vital signs and mean PON-1 among the case group, there was a significant relation according to temperature, being more reduced with hypothermic patients,

but non-significant according to heart rate, respiratory rate and blood pressure as shown in (Figure 10).

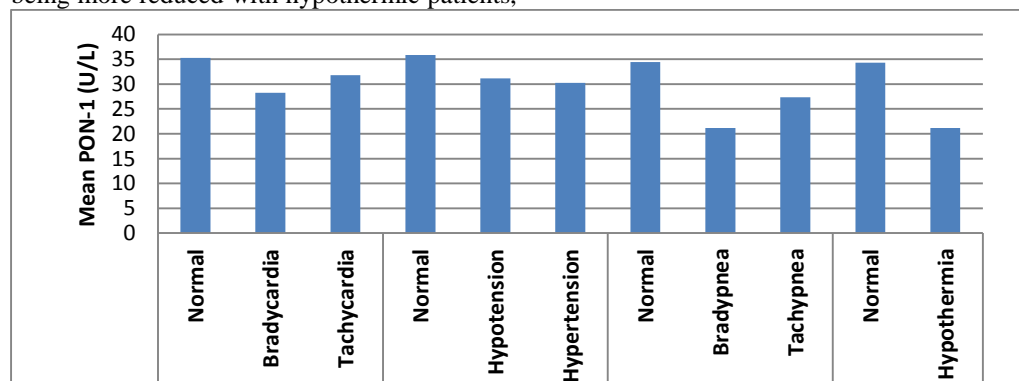


Figure (10): Relation between paraoxonase-1 (PON-1) level and vital signs among case group.

Regarding relation between GCS and serum PON-1 level among the case group, there was a highly significant relation between them, being

more reduced with cases who had GCS < 8 (Figure 11).

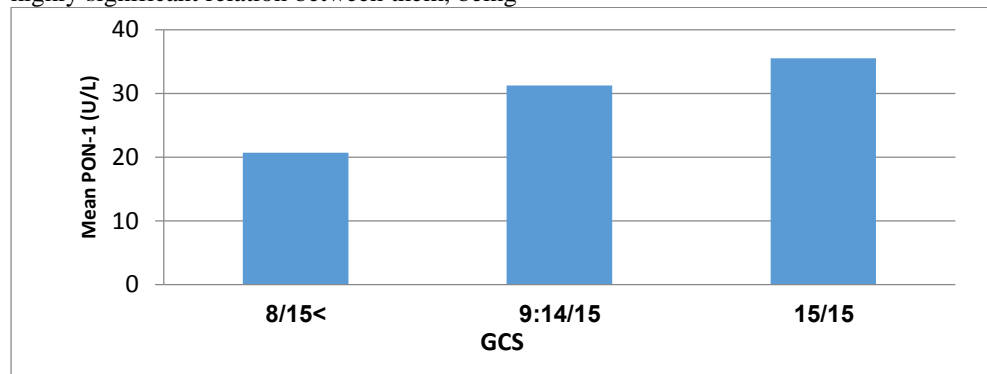


Figure 11: Relation between paraoxonase-1 (PON-1) level and Glasgow coma scale (GCS) among case group.

Correlation between paraoxonase-1 (PON-1) level and treatment

As regard relation between treatment and mean value of PON-1 among the case group, there was a significant relation regarding duration of hospitalization of patients and time

elapsed between exposure and admission, being more reduced with patients who presented two to six hours after exposure and duration of hospitalization more than 48 hours, as shown in (Figure 12).

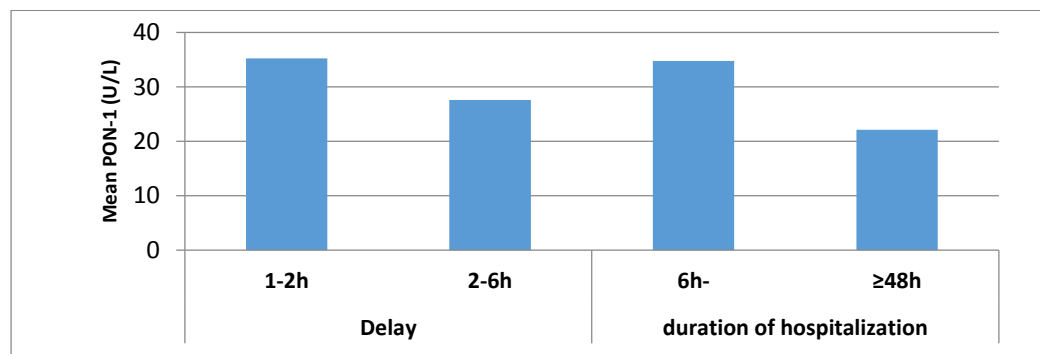


Figure 12: Relation between paraoxonase-1 (PON-1) level and treatment among case group

Correlation between paraoxonase-1 (PON-1) level with severity and outcome.

Table 7 demonstrates the association between POP scoring and PON-1 enzyme level. Regarding the initial levels of PON-1 enzyme. Regarding the initial levels of PON-1 enzyme, there was a statistically significant difference

between the three groups ($P < 0.001$), being more reduced with severe cases. As well, statistically significant differences were found between mild and moderate groups ($P = 0.036$), moderate and severe groups and between mild and severe groups ($P = 0.001$, each).

Table 7: Correlation between paraoxonase-1 (PON-1) level and severity based on Peradeniya Poisoning Organophosphorus scale (POP) scale among studied case group.

Case group (52)		POP scale		
		Mild	Moderate	Severe
PON-1 level (U/L)	N	41	6	5
	Mean	45.66	38.9	19.81
	±SD	6.32	6.08	1.02
Statistical test		F= 41.99		
P value		<0.001** P1: 0.036* P2: <0.001** P3: <0.001**		

SD: standard deviation F: ANOVA test N: number PON: paraoxonases * significant ** highly significant P1: difference between mild and moderate group, P2: difference between mild and severe group, P3: difference between moderate and severe group.

Among the 52 studied patients, three patients (5.77%) had all fatalities. (Figure 13) clarifies that mean PON-1 was significantly ($P < 0.001$) decreased among patients with an unfavorable outcome (death) as compared with

those with a favorable outcome (complete recovery) denoting that the serum level of PON-1 at admission had significant association with the patient’s outcome as the level of it was low in died patients compared to survived patients.

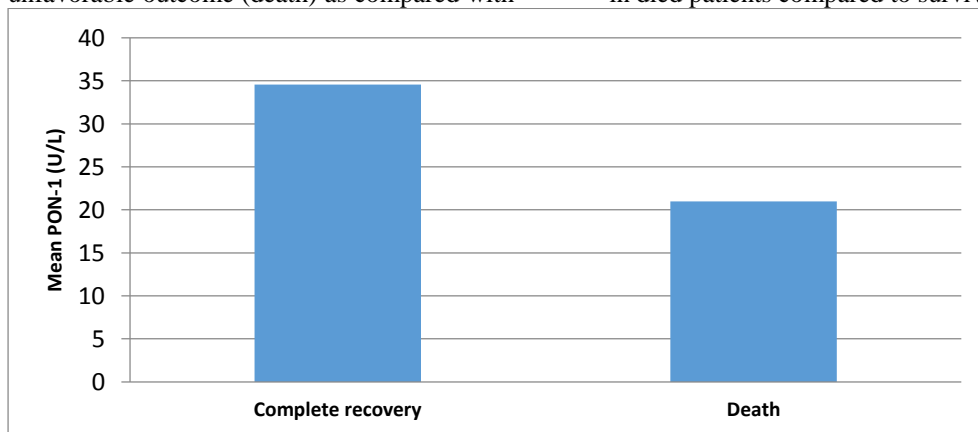


Figure 13: Relation between paraoxonase-1 (PON-1) level and outcome among case group.

There was a significant negative correlation between the severity of poisoning categorized by the POP scale and the serum PON-1 at the time of admission of the patients ($r = 0.408$, $P < 0.001$), duration of hospital stay ($r = -0.653$, $P < 0.001$), and total amount of atropine needed (r

$= -0.589$, $P < 0.001$). At the same time, there was a significant positive correlation between PON-1 and GCS ($r = 0.254$, $P = 0.032$) and Pseudo-choline esterase ($r = 0.873$, $P < 0.001$) as showed in (Table 8).

Table 8: Correlation between PON-1 and different variables in the study participants.

Variables	PON-1	
	r	P value
POP scale	-0.408	<0.001**
Duration of hospital stay	-0.653	<0.001**
Total dose of atropine	-0.589	<0.001**
GCS	0.254	0.032*
Pseudo choline esterase	0.873	<0.001**

r: correlation coefficient; GCS: Glasgow coma scale; POP: Peradeniya Organophosphorus Poisoning scale ; PON: paraoxonases; * significant; ** highly significant

Receiver-operating characteristic (ROC) curve showed that the area under the curve was 0.973 which shows that serum PON-1 is the excellent predictor of mortality with P value <

0.001. Serum PON-1 level ≤ 21.58 was predictive of mortality, with 100% sensitivity and 95.92% specificity as shown in (Table 9) and (Figure 14).

Table 9: Sensitivity and specificity of paraoxonase-1 (PON-1) as an early predictor of mortality.

PON-1 level (U/L)	
AUC	0.973
95% CI	0.929 – 1.000
Cut-off point	≤ 21.58
Sensitivity	100
Specificity	95.92
PPV	60
NPV	100
Accuracy	96.16
P value	<0.001**

AUC: area under curve CI: confidence interval PPV: positive predictive value NPV: negative predictive value PON: paraoxonases ** highly significant

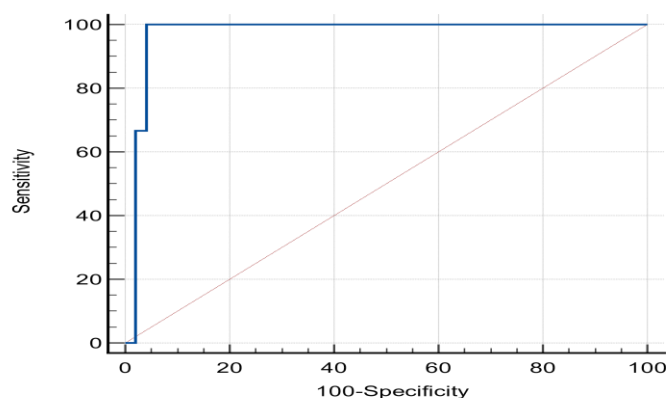


Figure 14: Sensitivity and specificity of paraoxonase-1 (PON-1) as an early predictor of mortality.

IV. Discussion

Since they are used to kill insects that destroy crops in the field, organophosphorus pesticides fall under the category of insecticides. They function by blocking the enzyme acetylcholinesterase (AChE), which is crucial for the production of nerve impulses. Inhibition of AChE causes acetylcholine to accrete, which results in persistent depolarization, convulsions, respiratory arrest, and eventually death (Kaushal, 2021).

The present study was performed at Benha Poison treatment and toxicological research unit (BPTTRU), Benha University hospitals during the period from 1 August till 31 July 2020. A total 72 participants were enrolled into this prospective study (52 who fulfilled the inclusion criteria served as patient group and 20 healthy volunteers served as control group).

Their personal history (sociodemographic data), exposure history, clinical data, and clinical severity scoring based on POP score were performed. Laboratory parameters, total dose of atropine needed, delay time, total

duration of hospital stay as well as outcome for all patients were recorded.

The current study revealed that the mean age was 33.67 ± 5.24 for case group and 32.91 ± 2.43 for control group. Patients between the ages of 18 and 29 made up the majority, followed by those between the ages of 30 and 39 while the least percentage occurred in cases aged > 60 years old.

This was in agreement with Amir et al. (2020) and Ananthi et al. (2018). Also, Dutta et al. (2015) found that the mean age of organophosphorus compounds (OPC) patients was 30.1 ± 10.3 years

These age groups (18-29 years) are the most dynamic in regards to their physical, mental, and social lives, making them more vulnerable to stress throughout their lives (Kumar et al., 2020). On the other hand, another study by Chuang et al. (2019) found that the mean age of cases was 53.3 (16.1) years and the mean age of controls was 53.2 (16.3) years, with 43.3% of the subjects being in the 20–49 age range. As regarding the sex, the male

patients showed a high incidence in number and percentage (29; 55.8%) as compared to female patients (23; 44.2%) with a sex ratio of 1.26:1. These findings harmonized with those achieved by Ananthi et al. (2018). El-moneim et al. (2019) stated that 80% of patients were males due to easy availability of OPC in agriculture fields and stressors in males than females. According to Shivaramu et al. (2015), the shift in lifestyle, psychological issues, and financial issues that have primarily afflicted men over the past few decades are to blame for this gender disparity in OPC poisoning cases. On the other hand, Ahmed et al. (2016) and Acikalin et al. (2017) found higher incidence in female patients. The same outcomes were found by Tallat et al. (2020), who suggested that this observation may be explained by the emotional susceptibility of females to life's difficulties as well as the accessibility of insecticides at home.

In the present study, the results revealed that the majority of presented cases were lived in rural areas and worked as farmers, followed by unemployed and housewife.

These findings were in the accordance with other studies (Eddleston et al., 2004, Prasad et al., 2013, Elagamy et al., 2019 and Shusil et al., 2020). According to Denbath et al. (2018), the majority of OPC patients (80%) are from rural areas, with agricultural workers topping the list of patients (51.91%), followed by housewives (28.68%), because use of the OPC compound as an insecticides, pesticides and fungicides was more in rural areas than urban.

The extensive use of organophosphate compounds in agriculture and their common presence and easy availability lead to high prevalence in rural dwellers homes (Elagamy et al., 2019).

The current findings announced that most patients were married. This was similar to the results observed by Sunny et al. (2019) and Bajracharya et al. (2018) who explained these results by the fact that they bear the bulk of the family's obligations, may be constantly stressed out, and are more likely to be exposed to OPC.

The current results showed that the most important route of exposure to OPC cases was oral ingestion, which was followed by inhalation and cutaneous exposure. These findings were in agreement with the studies of Al Jumaan et al. (2015), Dundar et al. (2015) and Lin et al. (2016) as they explained this by easy ingestion of poisons by mouth especially with liquid consistency of insecticides.

Lack of knowledge in dealing with these products may play a significant role in exposure to these compounds through dermal and inhalation routes (Bilal et al., 2014 and Coskun et al., 2015).

The present study's findings revealed that most of the cases were consumed poison with a suicidal intention via oral route.

These findings agreed with those achieved by Coskun et al. (2015) and Lin et al. (2016) who found most of the enrolled OPC patients were suicidal.

The higher percentage of suicidal ingestion of organophosphorus compounds (OPC) could be attributed to the low-price, easy availability, stressful lifestyle and jobs, loneliness, emotional liability in addition to, the lack of adequate regulations controlling their sale. They usually ingested a large amount, which can lead to rapid onset of the clinical features and complicating the management (Darwish et al., 2017 and Kumar et al., 2018).

Concerning the vital signs, the present study's findings demonstrated that thirty-nine cases had normal pulse rates, bradycardia was the commonest pulse abnormalities, followed by tachycardia. There were thirty cases had normal blood pressure. Hypotension displayed more prevalent abnormality, followed by hypertension. Forty-nine cases acquired proper respiratory rates. Bradypnea occurred in two cases, while tachypnea was found in one case. There were 50 cases possessed normal temperature and only two cases showed hypothermia. As regard relation between POP scale and vital signs among the three grades of poisoning, there were significant differences among the three grades of poisoning according to heart rate, blood pressure, respiratory rate, and temperature of patients, being more increased in severity with bradycardia, hypotension, bradypnea and hypothermia.

Zayed et al. (2015) showed that bradycardia and hypotension were the main profound cardiovascular disorders in the symptomatic group. The results of Pannu et al. (2021) showed that the most prevalent respiratory symptom, shortness of breath, was present in 75.7% of cases. The study of El-moneim et al. (2019) showed that 60% of patients in the present study presented with hypotension, 82% had tachycardia and 50% of patients presented with tachypnea. Most of patients (80%) had normal body temperature, but only 20% had hyperthermia.

Shusil et al. (2020) discovered that 134 OPC patients (83.75%) had tachypnoea, 115 had altered consciousness, 86 had miosis, 70 had fasciculation, and 36.25 had tachycardia.

Vijayakumar et al. (2011) and Gunduz et al. (2015) showed that tachycardia is most likely present in OPC patients due to excessive cholinergic nicotinic effects on the CNS, then it may be followed by bradycardia due to parasympathetic stimulation which was more

common in patients who presented to the hospital later.

Organophosphorus poisoning can cause cardiac toxicity by a number of pathways, such as increased sympathetic and parasympathetic activity, acidosis, electrolyte abnormalities, hypoxia, and direct toxicity on the myocardium (Cherian et al., 2005).

The combination of central and peripheral effects, paralysis of the respiratory muscles, and depression of the respiratory center can result in respiratory failure, which can appear as respiratory dysfunction (Jokanovic et al., 2011 and Zayed et al., 2015).

Almost all patients had muscarinic symptoms and signs. The most frequent clinical signs were bronchorrhea, pinpoint pupil, emesis, sweating and increased urinary frequency, followed by bradycardia, lacrimation, and diarrhea. Whereas nicotinic manifestations were present in 20 cases, manifested by fasciculation and weakness, hypertension and tachycardia and mydriasis. As regard central nervous system (CNS) manifestations, ten cases had altered mental status ranging from confusion to coma. No reported cases had convulsions.

Symptoms presented were in coincidence with Shusil et al. (2020), Kamath et al. (2021) and Zayed et al. (2015) as they noted that vomiting the most prevalent symptom. This could be explained by the fact that during cholinergic syndrome, the muscarinic affection usually precedes nicotinic (Seabury et al., 2013).

According to Glasgow coma scale (GCS), the current results displayed that most patients were fully awake (GCS=15) followed by drowsy (GCS=9-14) and finally stuporous or comatosed (GCS< eight) patients. There was a significant relation of POP scale levels among the three grades of poisoning according to GCS, being more severe with cases who had GCS less than eight.

In a research by Chandrasekhar et al. (2019) on 100 OPC patients, they reported that GCS scores were < ten in 25 patients and GCS scores were \geq ten in 75 patients. Also, Jha. (2018) reported that 30.5% of OPC had GCS < eight, 5.1% had GCS 8-12 and 64.4% had GCS >13.

Also, Kozaci et al. (2012) had stated that altered mental status is represented 76% of intoxicated patients. Direct cerebral toxicity of OPC and hypoperfusion or hypoxemia due to respiratory failure usually causes low GCS scores which is seen frequently in severe OPC poisoning cases (Acikalin et al., 2017).

Regarding Peradeniya Organophosphorus Poisoning score (POP) is an important tool for the diagnosis of the severity of OP poisoning. In

this study, the cases were classified as mild poisoning (41 cases), moderate (six cases) and severe (five cases) according to POP scale. At the same time, there was a significant relation among the three grades of poisoning according to residence and manner of poisoning, being more severe in rural areas and suicidal cases, but non-significant relation according to age, sex, residence, marital status, occupation, site, and route of exposure.

Kumar et al. (2020) stated that out of 80 patients, 29 were classified as mild poisoning, 31 as moderate poisoning, and 20 as severe as per POP scale. Chaudhary et al. (2019) reported that out of 100 OPC patients, 57 (57%) were classified as mild, 38 (38%) moderate and five (5%) as severe poisoning. On the other hand, Eisa et al. (2021) stated that 61.1% of studied patients had moderate toxicity, 25% had mild toxicity, while 13.9% had severe toxicity according to POP score. Also, Elagamy et al. (2019) concluded that most patients presented with mild status but persons who tend to harm themselves usually ingest large amounts of rapidly acting highly toxic compounds and so more poisoning severity.

Samy et al. (2018) reported that there were no statistical significance differences with respect to age and gender distribution between severe and moderate poisoning. On the contrary, Eisa et al. (2021) reported that there was statistically significant relation between age of the studied patients and route of exposure with severity according to POP scale.

The current findings revealed that about most of the total studied cases were admitted to the hospital within one hour of exposure, followed by 1-2 hours delay and no cases were delayed more than six hours. Most of patients were admitted for 6-48 hours. The mean value (\pm SD) of elapsed time between acute poisoning and hospital arrival was 2.09 (\pm 1.4) hours. At the same time, the mean (\pm SD) duration of hospitalization was 34.75 (\pm 21.38) hours.

Shama et al. (2022) stated that the median of delay time between exposure and hospital admission in their study, at Tanta University Poison Control Center, was 4 h.

Abd alkareem et al. (2019) stated that the hospital stay duration in their study ranged from one to 21 days with mean 3.7 days, with positive significant correlation between POP score and hospital stay duration. Thus, by applying Pearson correlation, the hospital stay duration was longer in severe group more than in moderate and mild groups. This could be explained by that most of severe patients might be vulnerable to variant complications that require prolonged ICU stay.

Vandana et al. (2021) conducted a study on 225 patients and stated that majority of patients (63.59%) were admitted to the hospital after a delay of more than two hours following the exposure to the poison and most of the deaths (73.68 %) occurred when the time lapse was more than two hours. On the other hand, 83 (36.40%) patients reported more than two hours of exposure and five deaths (26.31 %) occurred in cases with the time lapse of less than two hours. Time lapse had a significant role in mortality in case of acute poisoning.

According to atropine dosage, the mean (\pm SD) needed was 7.67 (\pm 6.26) which remains the main antidote in OPC poisoning. Hiremath et al. (2016) found that the mean dose of atropine given to their studied patients was about 24 mg. These findings were in coincidence with Pannu et al. (2021).

The relation between POP scale and treatment, there was a significant relation among the three grades of poisoning according to duration of hospitalization of patients, being more severe with cases who had duration of hospitalization less than 48 hours, but non-significant difference according to delay.

This was in agreement with Samy et al. (2018), Eisa et al. (2021) and Senarathne et al. (2022) who reported that the POP scale's severity and days of admission had a statistically significant relationship.

Twayana et al. (2019) noticed that the correlations of POP scale with lag time and atropinization dose, showed no statistical significance.

The current data showed that all patients with mild and moderate grade of POP severity scale survived. Three (40%) from five patients with severe grade of POP scale had expired. There was a significant difference between three groups denoting that there was a high significant relation between POP scale among the three grades of poisoning according to outcome of patients, being more increased with those who had death outcome.

Banday et al. (2015) concluded that mortality is usually higher in cases that consume large amount of OPC substances. So, severity is increased with suicidal cases rather than accidental ones. Gunduz et al. (2015) reported that mortality was the outcome in 41(13.9%) cases.

The mortality rate in the Amin et al. (2018) study was 11.53%. Also, Moussa et al. (2018) study reported mortality rate by 10 %. Furthermore, Abdel Baseer et al. (2021) reported that mortality rate was 5.5%. Sungur et al. (2001) reported a study with a greater fatality rate (27.6%).

The high survival rate can be explained by early referrals, adequate first aid, early

administration of antidotes and oxygen when indicated (Amir et al. 2020).

Chaudhary et al. (2019) had demonstrated that the POP scale is a reliable predictor of the severity of OPC poisoning and that it can access the intensity, morbidity, and mortality of individuals who have been exposed to OPC. Also, Samy et al. (2018) revealed the mortality rate was considerably greater in patients with severe poisoning compared to those with moderate poisoning.

Kamath et al. (2021) stated that in cases of mild to severe poisoning, the fatality rate was 5.4% and 52.8%, respectively.

Hassan et al. (2019) noticed a strong link exists between death and poisoning severity as measured by the POP score as increased severity was associated with increased mortality.

Death from OPC poisoning is not solely predicted by one predictor; rather, all the predictors overlap. Greater lag time, more severe poisoning, and longer mechanical breathing all work together to cause death (Ahmed et al., 2014).

According to biochemical investigations, the findings of this study demonstrated a statistically significant decrease in pseudo-cholinesterase (PChE) among organophosphate intoxicated cases compared to control group.

These findings were in line with El-gohary et al. (2013), Acikalin et al. (2017) and El-moneim et al. (2019) who found a substantial drop in PChE in patients who were intoxicated compared to a healthy control group. This finding can be explained on the basis that in acute OP exposure, there is marked phosphorylation of cholinesterase under the influence of the high dose of OP exposure in a very short time (Balali-Mood and Balali-Mood, 2008).

Additionally, when compared to the control group, the patients in the current study who were acutely organophosphorus intoxicated had a significantly lower level of serum PON-1 at admission.

This finding was in line with the study of Elgohary et al. (2013), Zhang et al. (2014) and Zayed et al. (2015) who found a linear relationship between low serum PON-1 activity and pesticide exposures.

The reduction of PON-1 activity induced by OPC may be due to direct inhibition without affecting enzyme synthesis or clearance (El-moneim et al., 2019).

The mean PON-1 level of the case group showed a significant relation regarding manner of poisoning, being more reduced with suicidal cases, but insignificant when taken into account variables including age, sex, place of residence, marital status, job, and exposure route.

Our findings are consistent with previous study of Sato et al. (2016). On the contrary, Zhang et al. (2014) stated that PON-1 activity in both populations for men was higher than that for women.

As regard relation between treatment and mean value of PON-1 among the case group, there was a significant relation regarding duration of hospitalization of patients and time elapsed between exposure and admission, being more reduced with patients who presented two to six hours after exposure and duration of hospitalization more than 48 hours.

Samy et al. (2018) found that serum PON-1 concentration was negatively associated with length of hospital stay. Although the amount and toxicity of the pesticide as well as the route of exposure determine how severe the poisoning will be, the genotype of the patient may also play a role.

In the present study, the POP scale was calculated for all patients at initial presentation. Regarding the blood level of PON-1, there was a statistically significant difference between the three levels of poisoning severity, being more reduced with severe cases. The association between POP scoring and the initial levels of PON-1 show significant differences between mild and moderate POP scale, mild and severe POP scale, and moderate and severe POP scale groups, suggesting that initial PON-1 levels are specific indicators of the clinical severity.

This was consistent with El-moneim et al. (2019) who stated that there was significant association between development of symptoms and level of paraoxonases, as its activity in mild cases was significantly higher than moderate and severe cases, indicating a protective effect of PON-1 against insecticides toxicity. Also, Sözmen et al. (2002) have demonstrated that those with mild clinical manifestations of OP poisoning had higher PON-1 activity.

Meanwhile, Richard et al. (2013) observed that the severity grade didn't significantly affect the PON-1 enzymes activities.

Concerning outcome, among the 52 studied patients, three patients (5.77%) had all fatalities. Mean PON-1 was significantly ($P < 0.001$) decreased among patients with an unfavorable outcome (death) as compared with those with a favorable outcome (complete recovery) denoting that the serum level of PON-1 at admission had significant association with the patient's outcome as the level of it was low in died patients compared to survived patients. The data obtained from ROC curve analysis suggest that the predictive cut - off value of the serum PON-1 was ≤ 21.58 (U/I), with sensitivity 100% and specificity 95.92%, which shows that serum PON-1 is the excellent predictor of mortality with P value < 0.001 . In

addition, the blood PON-1 level at the time of the patients' admission was found to significantly negatively correlate ($r = -0.408$, $P 0.001$) with the severity of poisoning as measured by the POP scale. This indicates a lower PON-1 level and a more severe POP scale.

Moreover, The POP scale's classification of the severity of poisoning was significantly inversely correlated with both the total amount of atropine required ($r = -0.589$, $P 0.001$) and the length of hospital stay ($r = -0.653$, $P < 0.001$), which is a morbidity indicator. At the same time, there was a significant positive correlation between PON-1 and GCS ($r = 0.254$, $P = 0.032$) and Pseudo- choline esterase ($r = 0.873$, $P < 0.001$).

The current results were consistent with results of Sozmen et al. (2002), Richard et al. (2013) and Ananthi et al. (2018) and study demonstrated the significant positive linear correlation between PON-1 and serum cholinesterase activity. Moreover, it was determined that individuals with more PON-1 activity may have a higher probability of successfully detoxifying the fatal effects of acute organophosphate poisoning (Richard et al., 2013).

V. Conclusions

Individuals with severe OPC poisoning have considerably lower serum paraoxonase-1 (PON-1) activity than patients with moderate intoxication. Reduced blood cholinesterase levels and worse outcomes were also substantially correlated with lower PON-1 activity. PON-1 activity may serve as a prognostic marker in OPC toxicity.

VI. Limitations:

The limited sample size of the present study might be one of its weaknesses as it is being a single-center study. Hence, we suggest future larger multicenter studies.

Another limitation was occurrence of the study during the first year of covid-19 epidemics which affected the rate of the flow and admission to hospital.

VII. Recommendations:

1. Complete documentation of sociodemographic data obtained from the patients with acute organophosphorus compounds (OPC) intoxications is better to be considered to allow monitoring the changes in the incidence, the pattern, the progress of the problem from year to year which allow the development of effective preventative plan to solve this problem.
2. Being the fact that delay in presentation affect both severity of poisoning and outcome so establishing a 'Poison Information Center (PIC) with a known telephone number, fax and web site to give

doctors round-the-clock assistance with knowledge and prompt guidance on how to treat different types of poisoning.

3. Reducing both accidental and suicidal exposure to these compounds could be achieved by :

- A. Short term plan including; the sale, distribution, and storage of these agrochemicals are governed by strict regulations; providing a safer formulations and withdrawal of highly toxic pesticides from market.
 - B. Long term plan including; promoting alternative non-chemical methods for pest control which is better to be extended and advanced to replace the use of highly toxic OPC pesticides.
 - C. Storing of such compounds in the original labeled containers that include hazards information and using instruction and also keeping household pesticides out of reach of children .
 - D. Community-level prevention efforts that can be accomplished by educational programs that conducted to the users and general public to create an awareness of the toxicity of these agents, how to avoid toxic exposure, symptoms of toxicity and first aid recommendations .
4. Because the length of the pre-hospitalization time might affect how severe the poisoning is when it manifests, physicians and nurses working in remote and rural areas need to be educated about the toxic effect of different OPC i.e., their clinical presentation, early diagnosis and proper management using supportive care and antidotes wherever available to avoid delay in management before referral to the specialized center to reduce the complications.
 5. Using of the clinical indices including Glasgow coma scale and Peradeniya organophosphorus poisoning scale “GCS and POP” which are two of the simple, rapid scoring systems that correlate to the severity and outcome of acute OPC poisoning are highly recommended in routine practice to provided beneficial information especially in emergency department and enables clinicians/nurses to determine the intensity of therapy and identify patients at high risk, allowing for more intensive monitoring.
 6. Pseudocholinesterase enzyme assay is better to be a part of routine investigations to confirm diagnosis.
 7. Paroxonase-1 enzyme assay is better to be a part of routine investigations to confirm diagnosis and to assess severity of poisoning.

VII. Conflict of interest

By signing this declaration, all authors of this study affirm that they have no conflicts of interest-financial or otherwise-with regard to this work to disclose.

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المخلص العربي

دور إنزيم الباراكسوناز-1 في التنبؤ بشدة ونتيجة التسمم الحاد
بالمركبات الفسفورية العضوية: دراسة مستقبلية

نور أبوبكر الترامسي¹ ورباب شعبان الشافعي² وعبيد عبد الوهاب شرف الدين³ وبراشنت شانكارو أدول⁴ وهايدي محمد عبد الرحمن فخر⁵

¹ معيد الطب الشرعي والسموم الإكلينيكية- كلية الطب- جامعة بنها
² أستاذ مساعد الطب الشرعي والسموم الإكلينيكية - كلية الطب- جامعة بنها
³ أستاذ الطب الشرعي والسموم - كلية الطب- جامعة بنها
⁴ أستاذ مساعد الكيمياء الحيوية- معهد جواهر لال للتعليم والبحث الطبي بعد التخرج، بونديشيرى، الهند
⁵ مدرس الطب الشرعي والسموم الإكلينيكية- كلية الطب- جامعة بنها

الخلفية: إنزيم الباراكسوناز-1 يحلل المركبات الفسفورية العضوية وبالتالي يغير بشكل كبير قابلية الفرد لسمية هذه المواد الكيميائية. تم تصميم الدراسة لتقييم نشاط إنزيم الباراكسوناز-1 في سلسلة من المرضى الذين يعانون من تسمم المركبات الفسفورية العضوية وربط مستواه مع شدة ونتائج المرضى المصابين بالتسمم الحاد بالفوسفات العضوي. **المرضى والطرق:** كانت هذه دراسة سريرية مستقبلية تم إجراؤها في وحدة علاج السموم وأبحاث التسمم في مستشفيات جامعة بنها بمصر، لمدة عام واحد، من 1 أغسطس 2020 حتى 31 يوليو 2021. تم تقسيم المرضى إلى مجموعة الحالات والمجموعة الضابطة. تم جمع البيانات الوبديولوجية للمرضى، والنتائج السريرية، وخطط العلاجات المقدمة، ومدة الإقامة في المستشفى والنتائج في أوراق البيانات. تم تصنيف المرضى حسب درجة السمية حسب مقياس تسمم الفسفور العضوي (بيرادينيا). تم جمع عينات الدم من المرضى لتقييم أنشطة إنزيم الكولينستيراز الباراكسوناز-1. **النتائج:** انخفاض أنشطة إنزيم الكولينستيراز الباراكسوناز-1 في المرضى المصابين بالتسمم ويمكن تصنيف المرضى وفقاً لمقياس تسمم الفسفور العضوي (بيرادينيا) إلى: حالات خفيفة ومتوسطة وشديدة. **الاستنتاج:** خلصت هذه الدراسة إلى أنه يمكن استخدام الباراكسوناز-1 للتشخيص والتنبؤ بنتائج المرضى المصابين بالتسمم الحاد بالمركبات الفسفورية العضوية.

التوصيات

من نتائج الدراسة الحالية، يمكن التوصية بما يلي:

1. يجب التأكد من التوثيق الكامل للبيانات الديموغرافية التي تم الحصول عليها من المرضى الذين يعانون من التسمم الحاد بمركبات الفسفور العضوي للسماح بمراقبة التغيرات في حدوث، ونمط، وتطور المشكلة من سنة إلى أخرى والتي تسمح بتطوير خطة وقائية فعالة لحل هذه المشكلة.
2. حقيقة أن التأخير في العرض يؤثر على كل من شدة التسمم والنتيجة، لذا فإن إنشاء "مركز معلومات السموم" كعنصر من وحدة علاج السموم وأبحاث التسمم برقم هاتف وفاكس وموقع ويب معروف لتقديمه على مدار الساعة وإيضاً خدمة تقديم المعلومات والنصائح السريعة للأطباء حول علاج أنواع التسمم المختلفة.
3. يمكن الحد من التعرض العرضي والانتحاري لهذه المركبات من خلال:
 - خطة قصيرة المدى بما في ذلك؛ تشريعات صارمة بشأن بيع وتوزيع وتخزين هذه الكيماويات الزراعية؛ وتوفير تركيبات أكثر أمناً وسحب مبيدات الآفات شديدة السمية من الأسواق.
 - خطة طويلة المدى بما في ذلك؛ الترويج لطرق بديلة غير كيميائية لمكافحة الآفات والتي ينبغي توسيعها وتطويرها لتحل محل استخدام مبيدات الآفات شديدة السمية من مركبات الفسفور العضوي.
 - تخزين هذه المركبات في العبوات الأصلية الموصوفة والتي تحتوي على معلومات عن المخاطر واستخدام التعليمات وكذلك إبقاء المبيدات المنزلية بعيدة عن متناول الأطفال.
 - كل التدابير الوقائية اللازمة على مستوى المجتمع والتي يمكن تحقيقها من خلال البرامج التعليمية التي يتم إجراؤها للمستخدمين والجمهور العام لخلق وعي بسمية هذه المركبات، وكيفية تجنب التعرض لها، وأعراض السمية شرح الإسعافات الأولية عند التعرض لها.
4. يوصى بشدة باستخدام المؤشرات الإكلينيكية بما في ذلك مقياس تسمم الفسفور العضوي (بيرادينيا) وهو نظام من أنظمة القياس البسيطة والسريعة التي ترتبط بأعراض ونتائج التسمم الحاد بالمركبات الفسفورية العضوية حيث أنه يمدنا بالمعلومات خاصة في قسم الطوارئ وتمكين الأطباء والمرضى من تحديد المرضى ذوي السمية الشديدة مما يسمح بمتابعتهم بدقة أكثر تركيزاً وذلك لتفادي المضاعفات التي تحدث بعد ذلك.
5. يمكن استخدام القياسات المبكرة لإنزيم الباراكسوناز-1 كأداة للتشخيص وتقييم الشدة وعلامة للتنبؤ بالنتائج.
6. يوصى بإجراء مزيد من الدراسات بما في ذلك القياسات التسلسلية لإنزيم الباراكسوناز-1 في حجم عينة كبير لتأكيد نتائج الدراسة الحالية. يجب أن يكون قياس إنزيم الباراكسوناز-1 جزءاً من الفحوصات الروتينية لتأكيد التشخيص ولتقييم شدة التسمم.