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Predictors of Severity and Survival in Acute Cases of Organophosphorous Poisoning at Zagazig University Hospitals: Prospective Cohort Study

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Abstract

Organophosphorous Insecticides (OPIs) have been profusely used and toxicity by them are common. Scoring systems are used as predictors of survival in severely ill patients. OPIs toxicity is associated with multiple biochemical abnormalities like changes in serum lactate. The aim of this study was evaluation the role of Acute physiology and chronic health evaluation II (APACHE II), Sequential Organ Failure Assessment (SOFA) scores, acetyl cholinesterase (AChE), and lactate enzymes in assessing severity, outcome and complications in acutely OPIs poisoned patients. This prospective cohort study was carried out on 36 OPIs poisoned patients admitted to Zagazig University Hospitals in seven months' period from the beginnings of May 2019 till the end of November 2019. The Peradeniya Organophosphorus Poisoning (POP), APACHE II and SOFA scores were calculated on the first day of admission. Serum lactate, and AChE enzymes were measured on admission and after 24 h. The cases were aged from 3 to 66 years old. As result of the study: APACHE II and SOFA scores were predictors of severity. The decrease in AChE level was correlated with the severity and complications but it was not predictor of them. Lactate was predictor of outcome and complications. Thus, APACHE II and SOFA scores can have used as predictors of severity. Also, lactate can be used as a predictor of outcome and complications.

Keywords: Acetyl Cholinesterase, Acute Physiology and Chronic Health Evaluation II (APACHE II), Lactate, Organophosphorous Insecticides, Sequential Organ Failure Assessment (SOFA) Score

1. Introduction

Organophosphorous Insecticides (OPIs) are used through the world and its related compounds can also be used as chemical weapons[1]. Poisoning with OPIs is responsible for large numbers of morbidities and mortalities all over the world especially in developing countries including Egypt. This high morbidity and mortality may be due to their easy availability and lack of awareness about their dangers[2,3]. Even with proper treatment, the death rate could reach 40% of all cases[4].

Organophosphorous insecticides work by inhibition of acetyl cholinesterase enzyme (AChE) leading to massive accumulation of acetylcholine (Ach) within the synaptic cleft. This leads to overstimulation of cholinergic receptors (nicotinic and muscarinic receptors) in both central and peripheral nervous system inducing the characteristic manifestations of organophosphorous poisoning[5].

The cause of death in OPIs poisoning is mainly due to respiratory failure, but also, it may be due to other complications as arrhythmia, pulmonary edema, pneumonia, pancreatitis, and renal failure[6].

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Prognostic factors are measurable substances associated with the outcome in people with a given disease or health condition including simple measures such as body mass index and complex measures such as biomarkers. They can contribute to diagnose and may even predict treatment response. In acute OP poisoning, many factors can be applied to detect poisoning severity and fatality[7].

Prediction of morbidity at presentation might help in decision making in places of limited resources like rural settings in the developing countries[8].

Scoring systems have been continuously developed to predict outcome in patients with severe illness and to assist clinical decision-making particularly for intensive care unit patients. Acute physiology and chronic health evaluation II (APACHE II) system serves as a useful index for evaluating the severity of poisoning due to multiple organ system involvement. Moreover, the Sequential Organ Failure Assessment (SOFA) score has been shown to have a good correlation between predicted and observed patient outcome[9,10].

Lactate levels are often used as alternative indicator for illness severity and response to the therapy. Many medications and toxins are associated with elevated lactate levels[12]. Patients with elevated lactate levels may be at higher risk for significant morbidity and mortality[13].

The aim of this work was to evaluate the role of APACHE II, SOFA scores, AChE, and serum lactate in assessing severity, outcome and complications in acutely OPIs poisoned patients admitted to the Poison Control Center (PCC) or intensive care units at Zagazig University Hospitals.

2. Patients and Methods

This prospective cohort study was carried out at the period between the beginnings of May 2019 till the end of November 2019. Approval for performing the study was obtained from Forensic Medicine and Clinical Toxicology Department and Ethical committee of scientific research (Institutional Research Board "IRB"), Faculty of Medicine, Zagazig University (ZU-IRB # 5528, August 2019). Informed consent was obtained from all patients or their legal guardian before recruitment for the study.

The selected patients of both sexes with acute OPIs exposure diagnosed through four criteria:

1. History of exposure to OPIs.
2. Characteristic toxic syndrome of OPIs toxicity.
3. Improvement of muscarinic symptoms and signs after atropine administration.
4. Low serum AChE activity.

Patients with any disease which can reduce AChE activity, patients with comorbidities as severe heart disease, heart failure, kidney disease, diabetes or cancer and patients who had received an intravenous injection of Ringer solution or sodium lactate Ringer solution prior to or within 6 h after admission to the hospital were excluded7. As result to these exclusion criteria, this study included only 36 subjects. Informed consent from the patients about the study was obtained.

Personal history including name, age, sex and occupation, poisoning history including history of OPIs exposure, route of exposure, type of substance and treatment before arrival were obtained. In addition, we scored the cases on admission using Peradeniya Organophosphorous Poisoning (POP) scale, APACHE II and SOFA scores.

POP scale has described sex clinical parameters that can grade severity without laboratory tests which are pupil size, respiratory rate, heart rate, fasciculation, conscious level and seizures. APACHE II score relays on 12 standard tests and gives a score from 0 to 71 and higher scores suggest a more serious illness and a greater risk of death. SOFA score based on the rate of organ dysfunction in six organs (respiratory, cardiovascular central nervous system, renal, coagulation, and liver) and scored on a scale of 0-4 to give the final score [6–24 (maximum)].

On admission and after 24 h, arterial blood samples were taken to measure arterial blood gas according to the method described by Dominiczak and Szczepanska-Konkel[14], another blood samples were taken to measure complete blood picture, liver function tests, renal function tests at Zagazig university hospitals laboratories, Egypt. Serum lactate, and AChE were measured in Ultra laboratories, Zagazig branch, Egypt.

Lactate was calculated by enzymatic colorimetric method using Spectrum lactate liquizyme (LOX /PAP), serum AChE was determined by colorimetric test using the method of Ellman *et al.*[15].

3. Statistical Designs

Data were analyzed by Statistical Package of Social Science (SPSS), software version 20 **(SPSS, Chicago, IL, USA, 2009)**. The comparison was done using ANOVA (analysis

of variance) test, followed by Least Significance Difference test "LSD" for multiple comparisons between groups, student "t" test, paired t- test, chi-square test, correlation co-efficient rank test, multiple linear regression analysis and Receiver operating characteristic curve (ROC) using the Area under the Curve (AUC), cut off points, sensitivity, specificity, positive predictive value and negative predictive value.

For all above-mentioned statistical tests done, the threshold of significance was fixed at 5% level (P-value). P value of > 0.05 indicates non-significant results. P value of < 0.05 indicates significant results. The smaller the P value obtained, the more significant results are.

4. Results

Thirty-six organophosphorous insecticide poisoned patients were enrolled in this study. The age was range from 3-66 years with the mean 32.7±17.96. There was a significant difference in age and sexes among the studied patients (p< 0.05) (Figures 1, 2).

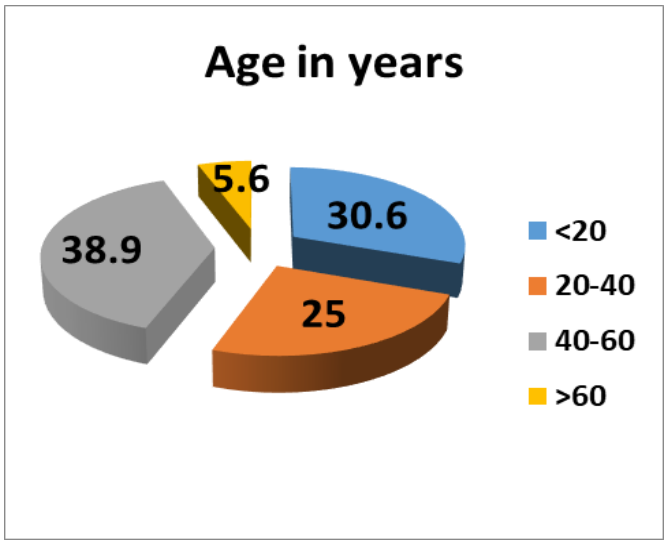


Figure 1. Frequency and percentage of age among studied patients (n=36).

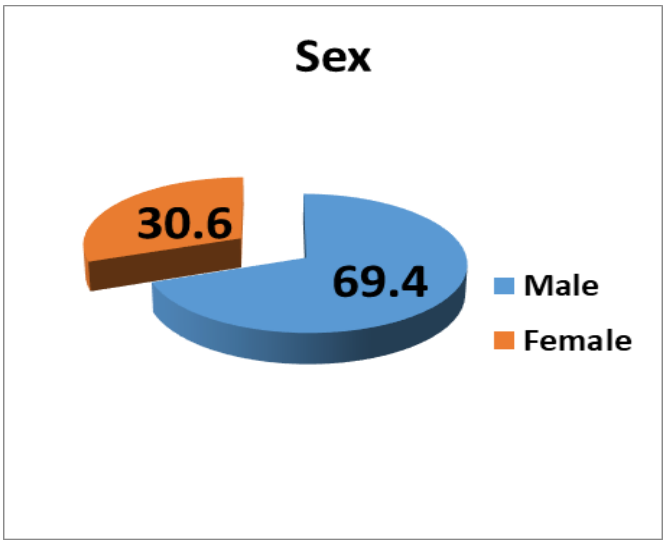


Figure 2. Frequency and percentage of sex among studied patients (n=36).

There were statistically non-significant differences in the frequency and percentage of toxic substances (p>0.05), but there was statistically significant difference in the route of exposure among studied patients (p<0.05) (Figures 3, 4).

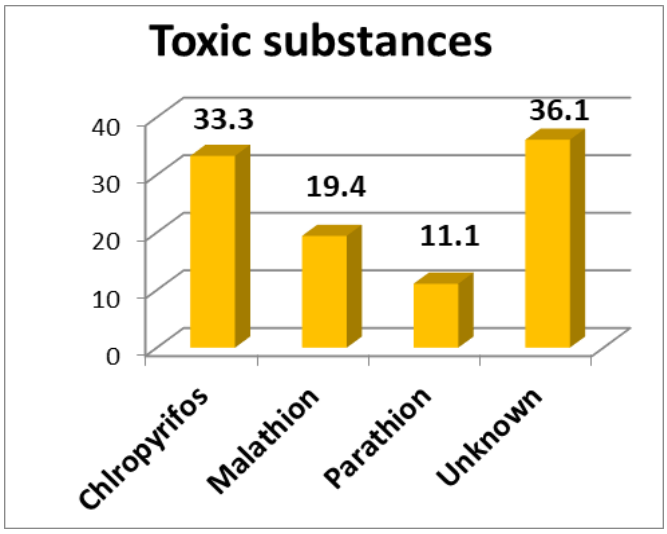


Figure 3. Frequency and percentage of toxic substances among studied patients (n=36).

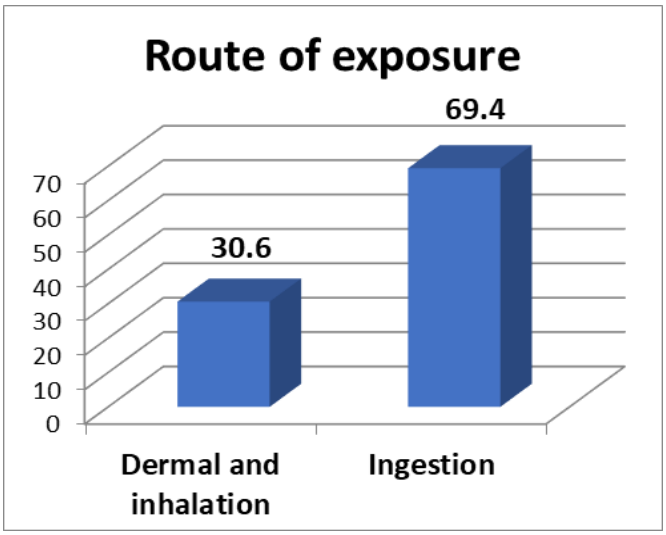


Figure 4. Frequency and percentage of route of exposure among studied patients (n=36).

According to POP score, there was statistically significant difference between degrees of severity of poisoning. Regarding outcome, there was statistically significant difference between discharged and died cases. In the aspect of complications, there was statistically significant difference between complicated and non-complicated patient (Table 1). As regard to scoring systems, there were significant differences in SOFA scores and APACHE II scores regarding the severity of the poisoning using POP score (Table 2). By Least Significant Difference test (LSD), as regard to both scores, the results of comparison revealed significant increase in moderate and severe cases of toxicity when compared to mild cases. Also, there was significant increase in the mean value of SOFA and APACHE II scores in severe cases when compared to moderate ones.

Table 1. Statistical analysis of patients according to severity using pop score, outcomes, and complications (n=36)

		N	Percent	X2 test	P. value
Severity according to pop score	**Mild**	9	25.0	12.465	0.002*
	Moderate	22	61.1		
	Severe	5	13.9		
Outcomes	**Discharged**	31	86.1	18.778	<0.001**
	Died	5	13.9		
Complications	**Not Complicated**	29	80.6	13.44	<0.001**
	Complicated	7	19.4		
Types of Complications	**Cardiac (Arrest & shock)**	2	5.6	0.245	0.88 (ns)
	Chest complications	3	8.3		
	Others as Coma	1	2.8		
	Seizures	1	2.8		

n: number (ns): statistically non-significant (p>0.05) *: statistically significant(p<0.05). **: statistically highly significant (p<0.01) X2 test: Chi square test

Table 2. Statistical comparison among mild, moderate and severe groups as regard groups as regard mean values of SOFA score, APACHE II score, AChE, and lactate on admission and post 24 hours using ANOVA, LSD and paired t-test (n=36).

Parameters	Periods in hours	Mild(n=9)	Moderate(n=22)	Severe(n=5)	F	p. value
		Mean ±SD				
SOFA score		2.89±0.33	5.14±1.28 a	9.2±1.3 a b	49.96	<0.001**
APACHE II		6±1.12	9.18±3.4 a	21.8±5.54 a b	37.48	<0.001**
AChE (U/L)	0 hrs.	1650±267	1207.2±342.7 a	755.2±484 ab	11.24	<0.001**
	24 hrs.	2684.9±48	2036.5±493.6 a	1579.4±790 a	7.814	0.002**
	t-test	4.875	11.85	3		
	P	0.001**	<0.001**	0.04*		
Lactate (mmol/L)	0 hrs.	1.22±0.29	2.03±0.37 a	3.76±0.83 a b	54.12	<0.001**
	24 hrs.	0.69±0.17	0.88±0.18 a	2.42±0.35 a b	130.7	<0.001**
	t-test	4.239	14.017	2.89		
	P	0.003*	<0.001**	0.045*		

n: number SD: standard deviation (ns): statistically non -significant (p>0.05) *: statistically significant (p<0.05)
**: statistically highly significant (p<0.01) SOFA: Sequential assessment of organ dysfunction.
APACHE II: acute physiology and chronic health evaluation hrs.: hours. AChE: acetyl cholinesterase enzyme
U/L: Units per liter mmol/L: mille moles per liter
By LSD test - a: statistically significant when compared to mild cases
-b: statistically significant when compared to moderate cases

According to biochemical tests, there were significant differences in the mean values of AChE, and lactate on admission and after 24 hours regarding severity of the poisoning using POP score (Table 2).

By LSD test, our results showed statistically significant low AChE level on admission in both moderate and severe cases when compared to mild cases. In addition, there was significant decrease in AChE level in severe cases in comparison with that in moderate cases (Table 2).

By LSD test, our results showed statistically significant increase in serum lactate on admission in both severe cases and moderate cases when compared to those in mild. In addition, severe cases showed significant increase in serum lactate when compared to that in moderate cases (Table 2).

As regard outcome (discharged or died), there were statistically significant increases in the mean values of SOFA score and APACHE II score in died cases in comparison to those discharged cases. Also, there were significant decreases in the mean values of lactate on admission and after 24 hours in died patients compared to discharged ones with non-significant difference in the mean values of AChE on admission and after 24 hours (Table 3).

Table 3. Statistical comparison between discharged and died groups as regard mean values of SOFA score, APACHE II score, AChE, and lactate on admission and post 24 hours using student t-test and paired t-test (n=36).

Parameters	Periods in hours	Discharged (n=31)	Died (n=5)	t-test	P1
SOFA score		4.65±1.79	8.2±2.17	3.995	<0.001**
APACHEII		8.55±3.44	20±8.8	2.873	0.043*
AChE (U/L)	0 hrs.	1307.13±405.6	932.8±532.6	1.838	0.08(ns)
	24 hrs.	2168.38±659	1928.6±405.7	0.784	0.44(ns)
	Paired-t	10.063	6.933		
	P2	<0.001**	0.002*		
Lactate (mmol/L)	0 hrs.	1.8±0.53	3.72±0.87	6.9	<0.001**
	24 hrs.	0.88±0.42	2.06±0.58	5.537	<0.001**
	Paired-t	11.250	4.263		
	P2	<0.001**	0.013*		

SD: standard deviation (ns): statistically non-significant (p>0.05) hrs. hours *: statistically significant (p<0.05) **: statistically highly significant (p<0.001) (P1: P of t- test, P2: P of Paired t- test) SOFA: Sequential assessment of organ dysfunction APACHE II: acute physiology and chronic health evaluation

Regarding complications, there were statistically significant increases in the mean values of SOFA score and APACHE II score in complicated group in comparison to those of non-complicated group (Table 4). In addition, there were significant decreases in the mean values of AChE and significant increase in the mean values lactate on admission and after 24 hours in complicated group compared to non-complicated group (Table 4).

Regarding the relation between severity using POP score and SOFA, and APACHE II scores, a positive significant correlation between SOFA score, APACHE II, and severity. While AChE showed a negative significant correlation with severity. However, there were no significant correlations between lactate, and severity (Table 5).

Regarding outcome, there was a positive significant correlation between POP, SOFA, APACHE II scores, lactate, and outcome (p<0.001). While AChE showed non-significant correlation with outcome (p>0.05) (Table 6).

In the present study, POP, SOFA, APACHE II scores, and lactate were positively significant correlated with complications. While AChE showed a negative significant correlation with complications (Table 7).

By using multiple regression analysis for factors predicting severity, SOFA and APACHE II were statistically significant as predictors of severity of poisoning in OPIs (p<0.001), but AChE, and lactate, were statistically non-significant as predictors of the severity (p>0.05) (Table 8).

Table 4. Statistical comparison among complicated and non-complicated groups as regard mean values of SOFA score, APACHE II score, AChE, and lactate, on admission and post 24 hours using ANOVA and student t-test (n=36)

Parameters	Periods in hours	Not Complicated (n=29)	Complicated (n=7)	t- test	P1
SOFA score		4.38±1.47	8.29±1.98	5.893	**<0.001****
APACHEII		8.24±3.3	18±8.04	3.147	**0.018***
AChE (U/L)	0 hrs.	1307.21±368.31	832.29±469.2	3.212	0.003*
	24 hrs.	2266.07±548.5	1592.43±702	2.765	0.009*
	Paired-t	10.966	3.893		
	P2	<0.001**	0.008*		
Lactate (mmol/L)	0 hrs.	1.7±0.45	3.5±0.8	5.242	0.001**
	24 hrs.	0.81±0.2	2 ±0.78	4.01	0.007*
	Paired-t	11.395	4.430		
	P2	<0.001**	0.004*		
	Paired-t	2.835	1.322		
	P2	0.008*	0.234(ns)		

n: number (ns): statistically non-significant (p>0.05) *: statistically significant(p<0.05). **: statistically highly significant (P<0.01). AChE: acetyl cholinesterase enzyme. P1: P of t- test, P2: P of Paired t- test SOFA: Sequential assessment of organ dysfunction. APACHE II: acute physiology and chronic health evaluation

Table 5. Correlation coefficient test of severity using POP score and SOFA Score, APACHE II, AChE, and lactate

Parameters	Severity (POP score)	
	R	p. value
SOFA Score	0.903	<0.001**
APACHE II	0.815	<0.001**
AChE (U/L)	-0.754	<0.001**
Lactate (mmol/L)	0.213	0.211(ns)

(ns): statistically non-significant (p>0.05) **: statistically highly significant (p<0.001). r: correlation coefficient AChE: acetyl cholinesterase enzyme U/L: Units per liter mmol/L: mille moles per liter

Table 6. Correlation coefficient statistical test of outcomes and POP score, SOFA Score, APACHE II, AChE, and lactate

Parameters	Outcomes	
	R	p. value
POP score	0.545	0.001**
SOFA Score	0.565	<0.001**
APACHE II	0.677	<0.001**
AChE (U/L)	-0.219	0.200(ns)
Lactate (mmol/L)	0.637	<0.001**

(ns): statistically non-significant (p>0.05) **: statistically highly significant (p<0.001). r: correlation coefficient AChE: acetyl cholinesterase enzyme U/L: Units per liter mmol/L: mille moles per liter

Table 7. Correlation coefficient statistical test of complications and POP score, SOFA score, APACHE II, AChE, and lactate

Parameters	Complications	
	R	p. value
POP score	0.711	0.001**
SOFA score	0.711	<0.001**
APACHE II	0.661	<0.001**
AChE (U/L)	-0.489	0.002**
Lactate (mmol/L)	0.589	<0.001**

(ns): statistically non-significant (p>0.05) **: statistically highly significant (p<0.001). r: correlation coefficient AChE: acetyl cholinesterase enzyme. U/L: Units per liter mmol/L: mille moles per liter

Table 8. Multiple regression analysis for factors predicting severity

Model	Unstandardized Coefficients		Standardized Coefficients	t_ test	p. value
	B	Std. Error	Beta		
(Constant)	1.932	1.357		1.424	0.165
SOFA	0.483	0.115	0.554	4.211	<0.001**
APACHE II	0.133	0.036	0.411	3.709	0.001**
AChE	-0.001	0.000	-0.183	-1.815	0.080(ns)
Lactate	-0.017	0.060	-0.019	-0.280	0.781(ns)

(ns): statistically non-significant (p>0.05). **: statistically highly significant (p<0.001). AChE: acetyl cholinesterase enzyme. SOFA: Sequential assessment of organ dysfunction. APACHE II: acute physiology and chronic health evaluation

Receiver operating characteristic (ROC) curve analysis to assess the predictors of severity of OPIs poisoning (Table 9, Figure 5).

By using multiple regression analysis for factors predicting outcome, serum lactate level was statistically significant as predictors of the outcome (p<0.001), but POP score, SOFA score, APACHE II score, and AChE were statistically non-significant predictors of the outcome (p>0.05) (Table 10).

Receiver operating characteristic (ROC) curve analysis to assess the predictors of the outcome of OPIs poisoned patients (Table 11, Figure 6).

By using multiple regression analysis for factors predicting complications, serum lactate level was statistically significant as predictor of complications (p<0.001), but POP score, SOFA score, APACHE II score, and AChE were statistically non-significant predictors of complications (p>0.05) (Table 12).
Receiver operating characteristic (ROC) curve analysis to assess the predictors of complication in OPIs poisoned patients (Table 13, Figure 7).

Table 9. Sensitivity, specificity, and accuracy rate of predictors of severity

Parameters	Cut off point	AUC	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy rate (%)
SOFA	>7.5	1.0	100.0	100.0	100.0	100.0	100.0
APACHE II	>14	0.987	100.0	93.5	71.4	100.0	94.4

AUC: Area under Curve (Receiver Operating Curve) PPV: Positive Predictive Value NPV: Negative Predictive Value %: percent SOFA: Sequential assessment of organ dysfunction APACHE II: acute physiology and chronic health evaluation

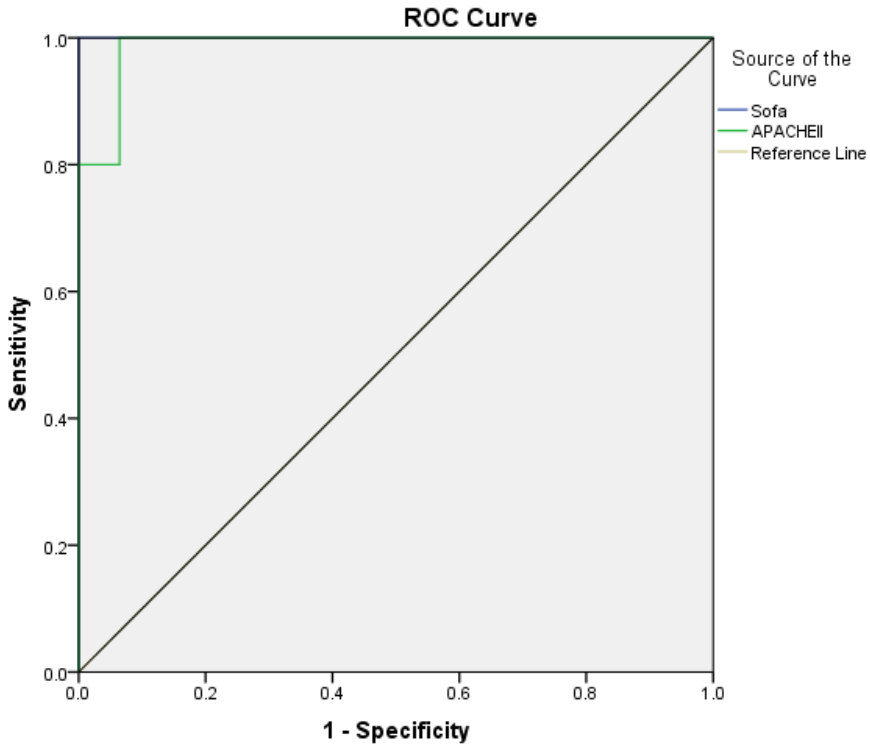


Figure 5. AUC curve analysis to assess the predictors of severity in OPIs poisoned cases.

Table 10. Multiple regression analysis for factors predicting outcome

Model	Unstandardized Coefficients		Standardized Coefficients	t- test	p. value
	B	Std. Error	Beta		
(Constant)	-0.631	0.300		-2.102	**0.045**
POP score	0.045	0.040	0.248	1.121	**0.272(ns)**
SOFA	-0.019	0.031	-0.121	-0.615	**0.544(ns)**
APACHE II	0.015	0.009	0.255	1.608	**0.120(ns)**
AChE	0.000	0.000	0.228	1.825	**0.079(ns)**
Lactate	0.077	0.013	0.466	6.025	**<0.001****

(ns): statistically non-significant (p>0.05). **: statistically highly significant (p<0.001). AChE: acetyl cholinesterase enzyme. SOFA: Sequential assessment of organ dysfunction. APACHE II: acute physiology and chronic health evaluation.

Table 11. Sensitivity, specificity, and accuracy rate of predictors of outcome

Parameters	Cut off point	AUC	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy rate (%)
Lactate	>2.18	0.987	100	96.8	83.3	100	97.2

AUC: Area under Curve (Receiver Operating Curve). PPV: Positive Predictive Value. NPV: Negative Predictive Value %: percent SOFA: Sequential assessment of organ dysfunction. APACHE II: acute physiology and chronic health evaluation

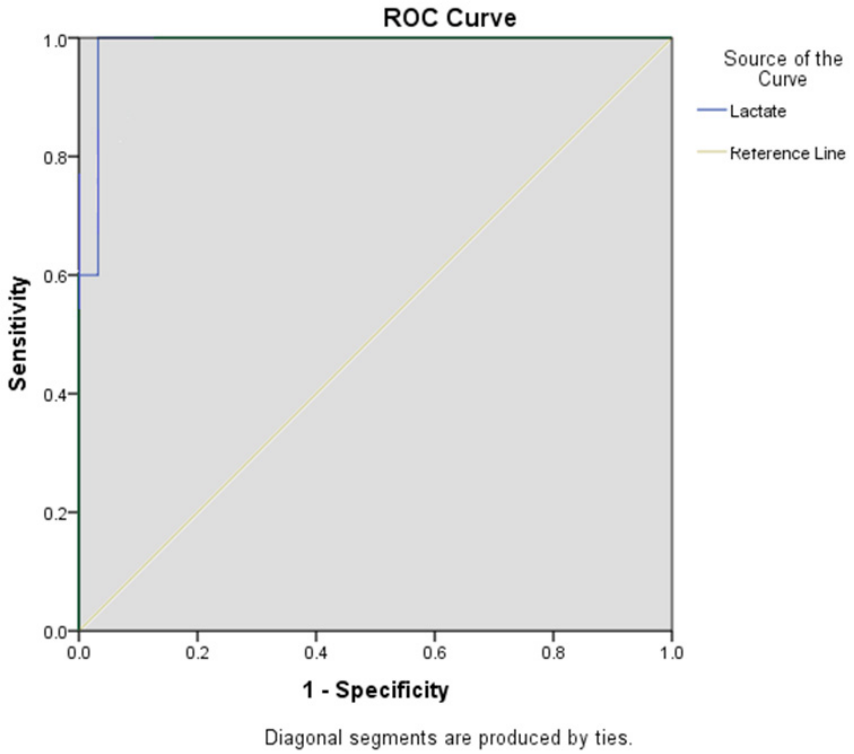


Figure 6. ROC curve analysis to assess the predictors of outcome of OPIs poisoned cases.

Table 12. Multiple regression analysis for factors predicting complications

Model	Unstandardized Coefficients		Standardized Coefficients	t- test	p. value
	B	Std. Error	Beta		
(Constant)	-0.894	0.488		-1.832	0.078
POP score	0.076	0.066	0.363	1.156	0.258(ns)
SOFA	0.006	0.051	0.031	0.110	0.913(ns)
APACHE II	-0.005	0.015	0.001	0.006	0.995(ns)
AChE	-0.005	0.000	0.031	0.177	0.861(ns)
Lactate	0.068	0.021	0.358	3.256	**0.003****

(ns): statistically non-significant (p>0.05). **: statistically highly significant (p<0.001). AChE: acetyl cholinesterase enzyme. SOFA: Sequential assessment of organ dysfunction. APACHE II: acute physiology and chronic health evaluation

Table 13. Sensitivity, specificity, and accuracy rate of predictors of complications

Parameters	Cut off point	AUC	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy rate (%)
Lactate	>1.6	0.99	100.0	86.2	63.6	100.0	88.9

AUC: Area under Curve (Receiver Operating Curve) PPV: Positive Predictive Value. NPV: Negative Predictive Value %: percent. SOFA: Sequential assessment of organ dysfunction. APACHE II: Acute physiology and chronic health evaluation.

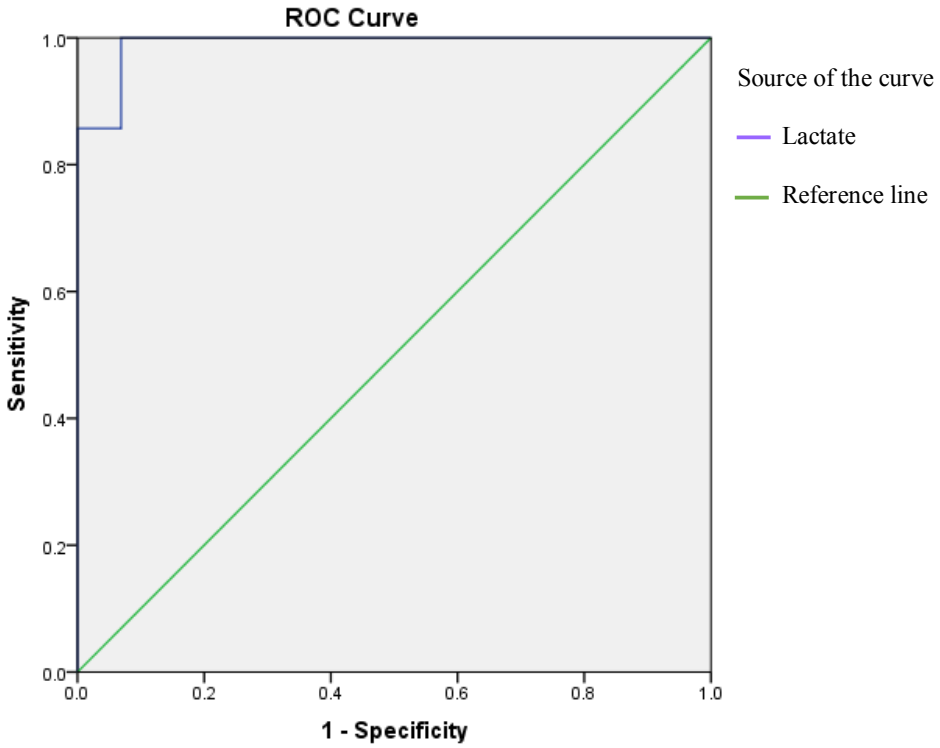


Figure 7. ROC curve analysis to assess the predictors of complications in OPIs poisoned case.

5. Discussion

Toxicity with OPIs is a major health problem. World Health Organization reported that three million cases of serious pesticide poisoning occur each year. The average percentage of pesticide suicides in the world is about one-third of the world's suicides, with estimated annual worldwide deaths from pesticide poisoning ranging between 234,000 and 326,000[16].

The main cause of death in OPIs poisoned patients is respiratory failure, but also other complications as arrhythmia, pulmonary edema, pneumonia, pancreatitis, and renal failure may occur[6].

Diagnosis of OPIs poisoning is mainly clinical that needs an experienced clinician and high index suspicion. It is confirmed by decrease in the level of cholinesterase enzyme (acetyl cholinesterase or pseudo-cholintesterase)[17]. Any delay in the diagnosis of poisoning may lead to insufficient treatment, and increase mortality rates of these cases[18].

The affected age group in the current study was ranged from 3 to 66 years with mean age 32.7±17.96. This finding was similar to those recognized by Sungur and Guven[19] and Ibrahim *et al.*[10] with mean age 30 ±15 years.

The majority of poisoned cases were men (69.4 %). These results are consistent with other studies like Ahmed *et al.*[20], Amin *et al.*[21] and Hodeib and Khalifa[22]. However, there are additional studies found that women represented the majority of poisoned patients as Sungur and Guven[19], Ibrahim *et al.*[10] and Gunduz *et al.*[23]

Regarding toxic substances, chlropyrifos (33.3 %), malathion (19.4 %), parathion (11.1 %) and unknown substances (36.1 %) were mainly the types of toxic substances by which the cases in the present study were poisoned. Such compounds have also been popular and more prevalent in other studies such as Elshamy *et al.*[24] who found that the most common used pesticides in their study that have done in Egypt were malathion (20.8%), parathion (20.8 %), dimethoate (8.4 %) and pesticides contain more than one substance (50.0 %). Also, Mahto *et al.*[25] study included diclorovos, chlropyrifos, and methyl parathion in the majority of the poisoned cases.

Organophosphate poisoning can be acquired by all routes such as inhalation, ingestion, and cutaneous absorption. The most popular route of poisoning in this study was oral ingestion in (69.4%) followed by inhalation absorption and dermal absorption (30.6%), which is consistent with other studies as Adinew *et al.*[26] and Hodeib and Khalifa[22].

Senanayeke *et al.*[27] and Chaudhary *et al.*[28] have shown that the POP score can effectively access the intensity, morbidity and mortality of OPIs poisoned patients. POP score is a useful predictor of severity of OPIs poisoning. So, in this study, we have used POP score as severity indicator.

In the present study, the overall mortality rate was 13. 9%. These results go parallel with Gunduz *et al.*[23] who reported mortality rate of 13.9 % in their study. Another study done at Zagazig University Hospitals where mortality rate reached 11.53 %.[21] Also, in Moussa *et al.*[29] study 10 % of patients died.

In the present study, the incidence rate of complications was 19. 4% and the most common complications were chest complications in 8.3% of all cases followed by cardiac complications in 5.6 % of all cases, while coma in 2.8 % and seizures in 2.8 % of cases.

The incidence rate of complications in the study of Bilal *et al.*30 agreed with these results, which reported that 10 % of patients complicated with respiratory failure, 10 % complicated with coma and 6 % complicated with circulatory failure. In addition, Gunduz *et al.*[23] study found that the cause of death was respiratory failure in 68 % of died cases followed by cardiac arrest in 20%, then renal failure 12%. Moreover, Chintale *et al.*[31] confirmed that respiratory failure was the most common complication.

Hulse *et al.*[32] explained that most fatalities after OPIs poisoning occur due to hypoxia caused by a combination of acute cholinergic effects with central apnea. Other deaths have occurred later due to cardiovascular shock, Neuromuscular Junction (NMJ) dysfunction, or complications of decreased level of consciousness.

As regard to scoring systems, we found that there was significant increase in the mean value of the SOFA score with increasing the severity. There was increase in the mean values of SOFA score of moderate and severe patients when compared to that of mild cases. Also, there was significant increase in mean values of SOFA score of severe patients compared to moderate cases.

In addition, there was an increase in mean values of SOFA score in died cases when compared to mean values of SOFA score in discharged ones. Moreover, there was highly a significant relation between mean values of SOFA score and incidence of complications as the average SOFA score of complicated cases was double the average score of non-complicated cases. Furthermore, SOFA had highly significant positive correlation with severity, outcome, and complications. These results were in agreement with Vosylius *et al.*[33], Kim *et al.*[3], Coskan *et al.*[34] and Moussa *et al.*[29].

In the current study, there were rises in the mean values of APACHE II score with increasing the severity of the poisoning. Moreover, there was an increase in the mean values of APACHE II score in died cases than in discharged ones. Also, our results showed that there was correlation between mean values of APACHE II scores and incidence of complications as the average APACHE II score of complicated cases was more than double the average score of non-complicated cases. In addition, APACHE II score had a positive highly significant correlation with severity, outcome, and complications. Sam *et al.*[35], Lee and Tai[18], Jabalameli *et al.*[36], Kang *et al.*[37] and Hrabetz *et al.*[38] agreed with these results.

Using multiple regression analysis with the indices used in the current study, it was found that SOFA and APACHE II are highly statistically significant predictors of the severity of OPIs poisoning. This findings were consistent with Moussa *et al.*[29], which indicated that the SOFA score and the APACHE II score were predictors of severity.

In the present study, Receiver Operating Characteristic (ROC) curve analysis to assess the predictors of severity of OPIs poisoning showed that the area under the curve for SOFA score was 1.0, APACHE II score was 0.987. Also, it was found that SOFA score at cut off value > 7.5 had corresponding sensitivity 100 % and specificity 100%. APACHE II score at cut off > 14 had sensitivity 100 % and specificity 93.5 %.

These results agreed with those of Moussa *et al.*[29] where the area under the curve for SOFA score was 0.896 and for APACHE II score was 0.716, the accuracy rate of SOFA score was 83.2% which was higher than that of APACHE II score 67.9%.

Sequential assessment of organ dysfunction (SOFA) score and APACHE II score could predict the prognosis of patients with OPIs, with recommending the SOFA score, which has the maximum accuracy and predictive capacity more than APACHE II score[39–41].

Regarding to biochemical parameters, our results found that, there was statistically significant differences in AChE values (on admission and after 24 h) and the severity of the toxicity graded using POP score. There was a significant decrease in AChE activity with increasing degree of severity on admission and after 24 h of admission. Moreover, we found that the decrease in AChE was more in severe cases than moderate and mild cases and more on admission than after 24 h.

Moreover, AChE levels showed no relation with the outcome of the cases on admission or after 24 h. Also, we found that AChE was significantly more decreased in complicated cases when compared to that in non-complicated ones. In addition, AChE showed a negative significant correlation with severity, negative significant correlation with complications, and no correlation with outcome.

These results are similar to Bardin *et al.*[42], Nigg and Knaak[43] and Bhattarai *et al.*[44] who illustrated that AChE level was decreased significantly in all grades of the severity of OPIs poisoning. Moreover, Sen *et al.*[45] and Hiremath *et al.*[46] stated that AChE is a reliable indicator of the severity of OPIs poisoning. As well as, Arafa *et al.*[47] results showed a significant decrease in AChE activity with increasing the degree of severity on admission, 6 and 24 h post admission. Also, they found a negative correlation between AChE level and severity of poisoning.

The results from the present study are similar to the results of Yardan *et al.*[48], Tang *et al.*[7] and Chaudhary *et al.*[28] as they found that no significant changes between the admission levels of AChE, 6-hour post-admission levels of AChE in survival and non-survival groups. So, the changes in blood AChE levels did not represent the extent of clinical intoxication in these cases and it should not be used as the principal reference for estimating OPIs outcome.

The results of the current study are in parallel with studies as Amin *et al.*[21], who found significant decrease in AChE in cases required mechanical ventilation than the cases did not require mechanical ventilation. Also, Chaudhary *et al.*[28] observed a significant correlation between the decrease of AChE level and complications.

Our results were different from El- Naggar *et al.*[17] that their results showed no significant association between the severity of the disease and the plasma AChE level.

Lactate is the end product of the anaerobic glycolysis and may be used as an indicator for illness severity and to measure the response to therapy.[12] Patients with elevated lactate levels may be at higher risk for significant morbidity and mortality and need a systematic approach for both diagnosis and treatment[13].

Generally, the mechanisms of hyperlactatemia include hypo perfusion that led to cellular hypoxia, increased lactate and pyruvate due to increased anaerobic glycolysis. Decreased lactate clearance, muscle hyperactivity due to seizures, impaired electron transfer and oxidative phosphorylation are also causes of hyperlactatemia[49–52].

Blood lactate measurement is commonly used in detection of patients with signs and symptoms of sepsis or shock[53]. The role of blood lactate levels had also been studied as a prognostic factor in drug and chemical poisoning[54].

The present study found an increase in lactate enzyme levels with increased severity on admission and 24 h post-admission, as well as there were differences between lactate enzyme on admission and after 24 h of mild, moderate, and severe cases. In addition, we found an increase in the mean values of lactate in dead patients when compared to discharged patients. Also, the results demonstrated an increase in the mean values of lactate in patients who had complications compared to patients without complications.

However, there was no significant correlation between lactate and severity. But there was highly significant positive correlation between serum lactate and both outcome and complications. By using multiple regression analysis, serum lactate level was statistically highly significant predictor of the outcome and complications.

Cases with arterial lactate rates greater than 5 mmol / L and pH lower than 7.35 are critically ill and have very poor prognosis. Multicenter studies showed a mortality rate of 75% in these cases.[55] Moreover, Gunnerson *et al.*[56] demonstrated that, the concentration of blood lactate has a prognostic value, and serum lactate levels greater than 2.5 mmol / L have been associated with an increase in the mortality rate.

Inoue *et al.*[57] and Moon *et al.*[58] suggested that the first lactate value is an accepted factor in determining the need for specialized medical treatment and that it may be useful in predicting prognosis. Also, Tang *et al.*,[7] found that lactate on admission, after 6 h and after 24 h are predictors of outcome. In addition, Lionte *et al.*[59] illustrated in their study presence of correlations between the increase in lactate level on admission, and both complications and mortality following exposure to systemic poisons. So, lactate can be

used to predict morbidity and mortality following exposure to systemic poisons.

Keep matching with Arafa *et al.*[47], who detected a strong positive correlation between lactate and severity of poisoning was found. Also, they reported that lactate level can be used as predictor of intensity in acute OPIs poisoning because they are cost effective and easily available in developing countries. The only weakness in using serum lactate as predictors is that other reasons of its elevation are largely dismissed.

Moussa *et al.*[29] suggested that complications following OPIs poisoning particularly respiratory complications leads to hypo perfusion and increase in anaerobic glycolysis causing increase in lactate level. Yuan *et al.*[41] also found that lactate was markedly higher in the non-survival than the survival groups in OPIs poisoned patients, and elevated lactate was shown to be correlated with mortality in critically ill patients. In addition, lactate significantly improves the predictive ability of the scoring systems when combined with these systems specially SOFA score.

In a study done on systemic poisoning included pesticides, Lionte *et al.*[59] found that the cut off for lactate on admission as predictor of mortality was 3.3 mmol/L. AUC was 0.92 with CI 95%, sensitivity 86% and specificity 88%.

Moreover, Yuan *et al.*[41] found that lactate at cut off value > 2.6 had corresponding sensitivity 67 % and specificity 93 % with PPV 79 % and NPV 88 %. Also, Masyuk *et al.*[60] concluded that changes in serum lactate over 24 h have been strongly associated with mortality (short and long term) in critically ill patients, making lactate measurement a quick and easy risk stratification parameter. Dong *et al.*[61] had developed a scoring system for severe OPIs poisoning including blood lactic acid. This predicted score was found to be useful and with good accuracy in such cases.

6. Conclusion

Poisoning with OPIs is a major health problem mainly in developing countries like Egypt. The mean value of the SOFA score and APACHE II score were significantly related to poisoning severity, outcome, and complications. SOFA but APACHE II scores were predictors of OPIs poisoning severity only.

SOFA score was more useful, and easier and simpler than the APACHE II and can help emergency physicians to quickly detect the severity of OPIs poisoned patients. The decrease in AChE activity was statistically related to the degree of poisoning severity and complications and more on admission than after 24 h. AChE level showed no relation with the outcome. It was not a good predictor of severity, outcome, and complications. Serum lactate level was statistically highly significant predictor of the outcome and complications.

6.1 Limitation of the Study

The limitations in our present study are the sample size is small, so the results cannot be generalized to all populations. we suggest a multi-center or a randomized trial to be conducted in the future to avoid these limitations and confirm our results. Also, we are unable to control for the dose of OPIs.

6.2 Recommendations

On the light of the results of the present study, we recommend further studies with large sample size for more accurate evaluation of the correlation with OPIs poisoning. Widespread public health education programs to increase awareness about OPIs poisoning hazards. Training the emergency physician how to diagnose OPIs poisoning and how to deal with that poisoning. Using SOFA score and APACHE II score as predictors of OPIs poisoning severity. Using serum lactate level as predictor of outcome and complication. Using serum acetyl cholinesterase level, lactate level, on admission and repeating them are not beneficial. Furthers studies to find more accepted predictor for OPIs poisoning.

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