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ORIGINAL ARTICLE

Evaluation of The Role of Cortisol, Glycemic state and Poison Severity Score in Prognosis of Acute Organophosphate Poisoning

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ABSTRACT

Background: Organophosphate Poisoning **(**OP) is a worldwide health problem, early evaluation of cases using scores, metabolic and hormonal changes is mandatory for predicting prognosis and outcome. Little reports were found on this subject before at Zagazig university hospital. So, we aimed to assess the prognosis of cases with acute organophosphorus compounds poisoning in order to improve the course of management.

Methods: This was a prospective cohort study included 52 cases of acute organophosphorus poisoning presented to the poison control center (PCC) and intensive care units (ICU) of Zagazig University Hospitals. Cortisol, glycemic state and poison severity score (PSS) were measured in all cases.

Results: Serum cortisol on admission, 6 and 12 hours was highly significantly related to poisoning severity and intensive care unit (ICU) admission. Specifically, its measurement at 6 hours was the best in prediction of severity and the need for ICU with 87.8% Specificity. Random blood sugar (RBS) on admission and discharge was highly significantly related to poisoning severity and ICU admission. Specifically, its measurement on admission was the best in prediction of severity and the need for ICU with 92.7% Specificity. According to PSS, 15.4 % of cases were grade 3 (severe grade) that were highly significantly related to the need for ICU admission with 100% specificity.

Conclusions: PSS, RBS (on admission) and Cortisol (6 hrs after admission) respectively are good predictors for poisoning severity and need for ICU admission in acute organophosphate poisoning.

Keywords: Cortisol ;Glycemic State ;Poison Severity Score ;Acute Organophosphate Poisoning.

INTRODUCTION

Although organophosphorus compounds (OPs) are widely used pesticides, poisoning from them poses a threat to global health, particularly in impoverished nations [1].

The enzymatic inert state of cholinesterase is achieved via covalent phosphate binding, which is the mechanism by which OPs cause toxicity. After then, there is an initial overstimulation of the cholinergic synapses, neuromuscular junctions, and central nervous system. Paralysis of the central and peripheral nervous systems ensues. Cholinergic excess will then cause symptoms in the central nervous system, muscarinic, and nicotinic pathways [2].

OPs raise morbidity and death rates, particularly in underdeveloped nations. Self-poisoning deaths in impoverished nations range from 10% to 20%, with the primary causes being respiratory insufficiency brought on by respiratory center depression, muscular weakness, and/or direct lung consequences from bronchospasm and bronchorrhea [3].

When someone has acute organophosphorus compound (OP) poisoning, there are numerous ways to determine the severity and mortality of the poisoning [4].

Severe OP poisoning patients frequently have unstable conditions and a significant death rate. It is critical to quickly determine the severity and prognosis of patients and to start appropriate treatment as soon as possible [5].

Cortisol level fluctuations, disrupted glucose homeostasis, and other metabolic abnormalities are linked to OP poisoning and are important factors in determining the prognosis [6, 7]. Serum cortisol variations during critical illness have been explained by a number of processes; they include decreased cortisol metabolism or increased synthesis as a result of activating the hypothalamic-pituitary-adrenal (HPA) axis [8].

A common consequence of serious disease is hyperglycemia. It was thought to be a component of the survival-enhancing adaptive stress response. Nonetheless, there has been mounting evidence over the last 20 years linking hyperglycemia to higher rates of morbidity and death. It is critical to demonstrate that hyperglycemia is merely a symptom of disease severity and does not, by itself, result in a bad clinical outcome [9].

In order to help with clinical decision-making, particularly for patients in critical care units, scoring systems have been created continually to predict outcomes in patients with severe illness. One tool used to estimate poisoning severity and quality assessment, identify actual dangers, and compare data is the Poisoning Severity Score (PSS) [10].

METHODS

This was a prospective cohort study on 52 cases of acute organophosphorus poisoning presented to the Poison Control Center (PCC) and Intensive Care Units (ICU) of Zagazig University Hospitals over the period from the beginning of September 2023 to the end of March 2024. Informed consent from the patients' relatives or the patient himself if he was adult and conscious was taken. The study was performed after approval from the ethical committee of scientific research (Institutional Research Board "IRB" number ZU-IRB #10463/1-3-2023).

The chosen patients were above 18 years [11] both sexes with acute organophosphorus chemical poisoning who were admitted to the PCC or ICU. The following factors are used to diagnose OP poisoning: a history of exposure to OPs, a distinctive toxidrome of OP toxicity, and low levels of pseudo-cholinesterase activity in the blood.

Exclusion criteria included pregnancy, chronic alcoholism, liver/kidney illness, cancer, and medications like aspirin, metoclopramide, and monoamine oxidase inhibitors [12]. Patients with comorbidities like diabetes, heart failure, severe heart disease, kidney disease, pancreatic disease, cancer, or any other comorbidity that could affect the patients' cortisol level or glycemic status were also excluded. Patients with a history of co-ingestion, patients who received treatment prior to presentation, patients on steroid therapy, patients on medication, and patients with a history of ingestion of medications that could affect the cortisol level were also excluded.

These cases were excluded by history, clinical symptoms and tests, such as complete blood counts , electrolytes, liver function tests , and renal function tests.

The following steps were performed on all enrolled patients: full history taking with special emphasis on history of exposure to OP and asking about the active ingredient, route of exposure and symptoms following ingestion before presentation to the emergency department, clinical assessment of conscious level using The Glasgow Coma Scale (GCS) [13], vital indicators, such as blood pressure, heart rate, breathing rate, and temperature, as well as the patient's overall state, such as the pupil of the eye (normal, constricted, dilated or pin point), the mouth odor and fasciculation of the tongue or lip, skin condition (sweeting or not), chest condition if either clear or contain secretions and neurological condition of seizures and fasciculations.

Laboratory investigations were done for all patients; serum cortisol level, serum random glucose level and serum pseudo-cholinesterase activity.

Serum cortisol level assessment:

Serum samples were collected from patients under a septic condition at admission then after 6 and 12 hrs from admission and stored at -80 till time of assay.

The assay was based on the electrochemiluminescence immunoassay “ECLIA” method [14, 15].

Serum random glucose level assessment:

Serum samples were collected from patients at admission and discharge under a septic condition.

The assay was based on Enzymatic reference method of hexokinase [16, 17], and was done using Cobas 8000 (c702) analyzer available in Zagazig university hospitals.

Serum pseudo-cholinesterase activity assessment:

The assay was based on Kinetic method Deutsche Gesellschaft für Klinische Chemie method (DGKC

method), using Cholinesterase DGKC kits and was done using sat 450 chemistry analyz88er [18].

Poison Severity Score calculation:

PSS calculated for each patient admitted. PSS is divided into categories that cover a wide range of clinical features [19], and it is meant to be used adaptably to incorporate the most important laboratory and clinical aspects of the poisoning along with the available data. PSS generates a qualitative evaluation of the morbidity brought on by different kinds of poisoning [20].

In our study, PSS shown in **Table 1** was calculated by evaluation of some selected criteria chosen from the cardiovascular, neurological, and respiratory systems [21].

Treatment of the cases

All cases were treated corresponding to management protocol of poison control center at Zagazig University Hospitals. Treatment includes the following:

1-Stablization (ABC)

First of all, maintain the airway opened and suction of secretion then maintain breathing. Mechanical ventilation is the most useful advance in management of severe and fatal cases. Also, Succinylcholine must be avoided.

Insert two IV lines (one for fluid and drugs, and the other for atropine).

Criteria for intensive care unit admission [22, 23]:

The patients admitted to ICU had any of the following:

Endangered airway, cardiac arrest, respiratory arrest, sudden decrease in conscious level according to GCS (more than 2 points), seizures which were recurrent or constant, respiratory acidosis with elevating arterial carbon dioxide tension, respiratory rate > 40 or < 8 breaths/min, oxygen saturation below 90%, pulse rate < 40 or >140 beats/minute or systolic blood pressure < 90 mmHg.

2-Decontamination [24].

-Eye: irrigation with tab water or saline for 20 minutes.

-Skin: remove all clothes, body and hair wash with water and soap must be done, washing should be repeated every 2-6 hours.

-Gastric lavage: patient kept in left lateral position as that delays spontaneous absorption. Tab water used in lavage is 5-10ml/kg as a full amount. Although it is believed to be beneficial for up to four hours after administration, lavage works best within thirty minutes of ingestion. - Activated charcoal: 1 g/kg of activated charcoal, (One dose) is enough.

3- Antidotes

- **Atropine** [25].

  Use atropine in case of OPs poisoning with bronchorrhea or bradycardia

  -Loading dose: 1–2 mg initial dose **.**

  Every five minutes, increase the dosage by doubling, and if there is no improvement, increase it again. Oxygen inhalation and removing nasopharyngeal secretions were done during atropine use. Also, taking care of heart rate during loading is very important. Full Atropinisation means clear lungs, dry skin, and tachycardia.

  -Maintenance dose:

  Every hour, try administering 10–20% of the total atropine dose needed to load the patient; an infusion rate of 3–5 mg/hour is required. To begin, use 10% of the entire dosage, if criteria of atropinization decreased try to increase to 12% and so on. Every fifteen minutes, evaluate the patient to make sure the atropine infusion rate is appropriate.

- ***Oximes*** [26].

  Oximes are given in case of CNS manifestations or generalized fasciculation.

  Toxogonin (obidoxime) 250 mg /ampoule: parallel with atropine.

  -Loading dose: 4-8 mg/kg in 100 cm saline over 20 min.

  -Maintenance dose: 4 mg/kg in 100 cm saline over 20 min every 8 hrs.

  For best results, it should be given as soon as possible after exposure.

- ***Benzodiazepines (diazepam, midazolam):*** [27].

  Used in case of agitation, seizures, elevated heart rate to maintain the patient's sedation and tolerance to the endotracheal tube or while loading atropine.

- ***Sodium bicarbonate*** [25].

  recommended for the management of related metabolic acidosis.

4 -General observation:

Because they are unstable, patients need to be observed frequently in order to quickly identify changes in their overall health and atropine needs.

5 -Discharge:

All symptomatic patients are to be hospitalized for at least 24 hours after completing their management due to the risks of respiratory impairment or recurrent symptoms. Asymptomatic patients can be discharged after 12 hours of organophosphate exposure.

Statistical designs

Version 28 of the SPSS (Statistical Package for the Social Sciences) program was used to analyze the data. Chi-square for trend test (§), The Mann

Whitney (Z) test and Receiver operating characteristic (ROC) curve were the tests that were used.

RESULTS

This was a prospective cohort study of acute organophosphorus poisoning cases that were brought to Zagazig University Hospitals poison control center and intensive care units. and fulfilled the inclusion criteria. 52 patients, ages ranging from 19 to 53 years, with a median age of 23 years, were included in this study. Males were more than females representing 53.8% of patients. About 67% of patients came from rural residence. About 67.3% of patients had no job and 71.2% of patients were accidentally poisoned and 78.8% of patients exposed to organophosphates via ingestion. Patients were presented with time range from 1 to 24 hours with median 4 hours**.** Regarding the clinical picture, vomiting was the most, representing 80.8% of cases followed by Abdominal pain, Miosis, Drowsy/DCL, Sweating, General fasciculation and Chest secretion representing 53.8%, 30.8%, 28.8%, 19.2%, 19.2% and 13.5% of cases respectively**.** Median serum cortisol in admission was 23.55 (µg/dl) which decreased to 12.2 (µg/dl) at 6 hours then increased to 17.8 (µg/dl) after 12 hours. Median random blood sugar (RBS) on admission was 120.5 mg/dl while mean RBS on discharge was 109.67 mg/dl. Pseudo-choline level ranged from 240 to 5466.7. Regarding our patient's prognosis**,** (21.2%) of them needed ICU admission and one patient died (1.9%) by the end of the study **(Table 2).**

By using Mann Whitney test, there was statistically highly significant relationship (P <0.001) between ICU admission and cortisol on admission, at 6 hours and 12 hours (significantly higher among patients needed ICU admission) **(Table 3).**

Receiver operating characteristic curve analysis to assess the performance of cortisol level on admission, at 6 and 12 hours in prediction of need of ICU admission of OPs poisoning showed that the best cutoff of serum cortisol on admission in prediction of need of ICU admission was ≥30.32 (µg/dl) with area under curve 0.895 with sensitivity 90.9% and specificity 80.5% (p<0.001)**.** The best cutoff of serum cortisol at 6 hours in prediction of need of ICU admission was ≥27.35 (µg/dl) with area under curve 0.979 with sensitivity 90.9% and specificity 87.8% (p<0.001)**.** The best cutoff of serum cortisol at 12 hours in prediction of need of ICU admission was ≥21.25 (µg/dl) with area under curve 0.878 with sensitivity 90.9% and specificity 82.9% (p<0.001)**.** The area under curve for cortisol at 6 hours was the highest and was the best in prediction of need of ICU admission **(Table 4&Figure 1).**

By using Mann Whitney test, there was statistically highly significant relationship (P <0.001) between ICU admission and all of RBS on admission, and on discharge (significantly higher among patients who needed ICU admission) **(Table 3).**

Receiver operating characteristic curve analysis to assess the performance of RBS on admission, and on discharge in prediction of need for ICU admission of OPs poisoning showed that the best cutoff of RBS on admission in prediction of need for ICU admission was ≥180 mg/dl with area under curve 0.978 with sensitivity 90.9% and specificity 92.7% (p<0.001). The best cutoff of RBS on discharge in prediction of need for ICU admission was ≥120 with area under curve 0.853 with sensitivity 90.9% and specificity 73.2% (p<0.001). The area under curve for RBS on admission was the highest and was the best in prediction of ICU admission **(Table 4&Figure 1S).**

Patients were categorized using PSS into 63.5% had mild form (grade1), 21.2% had moderate form(grade2) and 15.4% had severe form(grade3). The main bulk of patients experienced mild toxic manifestations. Concerning components of PSS grading, 13.5% of our cases had been intubated (grade 3), 5.8% had seizures (grade 3), 1.9% had low conscious level (3-8) grade 3 and 3.8% had low blood pressure (≤80 mmHg) (grade 3) **(Table 5).**

By using Chi square test, there was a statistically highly significant relationship (p<0.001) between ICU admission and PSS grades. All patients with severe grade were admitted to ICU. Having Severe grade can predict need for ICU admission with 72.7% sensitivity and 100% specificity **(Table 6).**

Only one patient died by the end of the study. This patient was male, aged 48 years old, from rural area and received organophosphate (chlorpyrifos) via ingestion, accidentally, came to emergency room (ER) after 5hours from ingestion. At time of examination, he was disturbed, Glasgow coma scale 9/15, pin point pupil, chest secretions, fasciculation, heart rate 145, blood pressure 90/65, arterial blood gas showed respiratory acidosis and pseudocholine esterase was 1260. Patient intubated at ER and admitted to ICU completing the treatment protocol. The patient severity grade according to PSS was grade 3 (severe grade). RBS on admission was 267 mg/dl which decreased to 160 mg/dl in the last measurement before death. Serum cortisol on admission was 50 then decreased to 41.3 at 6 hours

then became 36.8 at 12 hours. The patient died after 2 days.

Table (1): Criteria used to calculate poison severity score (PSS) **[21].**

	Grade 1 (mild)	Grade 2 (moderate)	Grade 3 (severe)
Respiratory Intubated	No	-	Yes
Neurological GCS	14-15	9-13	3-8
Seizures	No	-	Yes
Bradycardia (pulse)	>50	41-50	≤40
Tachycardia (pulse)	≤140	141-180	>180
Hypotension (systolic BP)	>100	81-100	≤80

GCS Glasgow coma scale BP blood pressure

Table (2): Distribution of the studied patients according to demographic data, clinical picture, laboratory data and prognosis

	N=52	%
Age (year)		
Median (IQR)	23(19 – 41.5)	
Mean ± SD	29.29 ± 11.72	
Range	19 – 53	
Gender		
Female	24	46.2%
Male	28	53.8%
Residence		
Rural	35	67.3%
Urban	17	32.7%
Working		
No	35	67.3%
Yes	17	32.7%
Method		
Accidental	37	71.2%
Suicidal	15	28.8%
Route		
Ingestion	41	78.8%
Inhalation	5	9.6%
Skin and inhalation	6	11.5%
Organophosphate		
Azamethiphos	2	3.8%
Chlorpyrofos	7	13.5%
Diazinon	3	5.8%
Malathion	11	21.2%
Unknown	29	55.8%
Presented within		
Median (IQR)	4(3 – 5)	
Range	1 – 24	
Clinical picture		
Vomiting	42	80.8%
Abdominal pain	28	53.8%
Miosis	16	30.8%
Drowsy/DCL	15	28.8%
Sweating	10	19.2%

	N=52	%
General fasciculation	10	19.2%
Chest secretion	7	13.5%
Cortisol on admission (µg/dl)	23.55(18.05 – 34.7)	8.6 – 50
Cortisol at 6 hours (µg/dl)	12.2(10 – 28.93)	3.11 – 41.3
Cortisol at 12 hours (µg/dl)	17.8(15.93 – 25.9)	6.3 – 157
RBS on admission (mg/dl)	120.5(93.5 – 158.75)	53 – 292
RBS on discharge (mg/dl)	109.67 ± 27.56	66 – 180
Pseudo choline level (from upper)	**Median (IQR)** 3645(1796.75 – 4045)	**Range** 240 – 5466.7
ICU		
No	41	78.8%
Yes	11	21.2%
Outcome		
survivors	51	98.1%
Non-survivors	1	1.9%

IQR interquartile range SD standard deviation N number % percent

Table (3): Relation between each of serial cortisol levels (on admission,6hrs, 12hrs) , random blood sugar levels (RBS) (on admission, on discharge) and intensive care unit (ICU) admission using Mann Whitney test (Z):

	No ICU admission Median (IQR)	ICU admission Median (IQR)	Z	p
Cortisol				
On admission	19.1(17.4 – 28.1)	40.8(35.4 – 45.9)	-3.99	<0.001**
6 hour	12(9.9 – 15.13)	35.5(34.1 – 38.7)	-4.843	<0.001**
12 hour	16.9(15.75 – 18.95)	29.5(25.3 – 36.8)	-3.822	<0.001**
RBS				
On admission	115(89.5 – 135.5)	225(210 – 270)	-4.83	<0.001**
On discharge	94(83.5 – 123.5)	135(123 – 145)	-3.565	<0.001**

Z Mann Whitney test **p≤0.001 is statistically highly significant IQR interquartile range

Table (4): Performance of cortisol level on admission, at 6 and 12 hours and random blood sugar (RBS) (on admission and on discharge) in prediction of need of intensive care unit (ICU) admission

Time	Cutoff	AUC	95% CI		Sensitivity	Specificity	p
Cortisol							
On admission	≥30.32	0.895	0.746	1	90.9%	80.5%	<0.001**
At 6 hours	≥27.35	0.979	0.946	1	90.9%	87.8%	<0.001**
At 12 hours	≥21.25	0.878	0.717	1	90.9%	82.9%	<0.001**
RBS							
On admission	≥180	0.978	0.945	1	90.9%	92.7%	<0.001**
On discharge	≥120	0.853	0.749	0.956	90.9%	73.2%	<0.001**

AUC area under curve CI Confidence Interval **p≤0.001 is statistically highly significant % percent

Table (5): Distribution of the studied patients according to poison severity score (PSS) grades

	Grade 1(mild) n(%)	Grade 2 (moderate)n(%)	Grade 3 (sever)n(%)
Respiratory (intubated)	45 (86.5%)	-	7 (13.5%)
GCS	42 (80.8%)	9 (17.3%)	1 (1.9%)
Seizures	49 (94.2%)	-	3 (5.8%)
Bradycardia	52 (100)%	0 (0%)	0 (0%)
Tachycardia	48 (92.3%)	4 (7.7%)	0 (0%)
Blood pressure	39 (75%)	11 (21.2%)	2 (3.8%)
Total	33 (63.5%)	11 (21.2)	8 (15.4)

n number % percent

Table (6): Relation between poison severity score (PSS) and intensive care unit (ICU) admission by Chi square test (§)

	No ICU admission N(%)	ICU admission N(%)	§	p
PSS **Mild (Grade 1)** **Moderate (Grade 2)** **Severe (Grade 3)**	 32 (78%) 9 (22%) 0 (0%)	 1 (9.1%) 2 (18.2%) 8 (72.7%)	 30.64	 <0.001**
Predictive performance of severe	Sensitivity =72.7%	Specificity=100%		

**p≤0.001 is statistically highly significant N: number of cases % percentage §Chi square for trend test

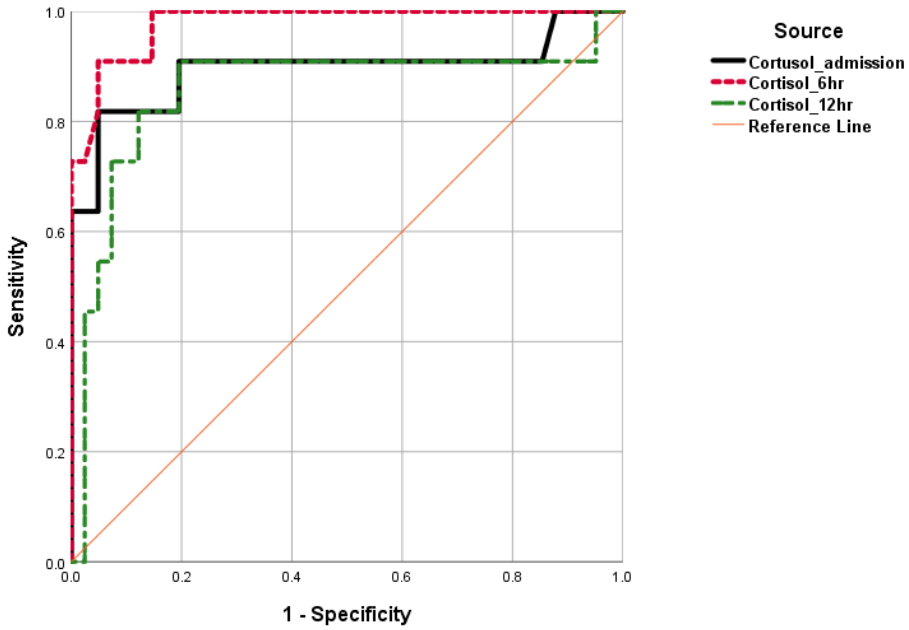

Figure 1. Receiver operating characteristic (ROC) curve showing performance of cortisol level on admission, at 6 and 12 hours in prediction of need of intensive care unit (ICU) admission

DISCUSSION

Organophosphorus chemical toxicity is a serious health issue. According to the WHO, there are three million cases of severe pesticide poisoning annually. The global average for pesticide-related suicides is around one-third of all suicides; the

number of deaths globally attributed to pesticide poisoning is estimated to be between 234,000 and 326,000 every year [28]. 40% of instances may still result in mortality even with appropriate care [29].

The presence of muscarinic and nicotinic symptoms indicates the clinical diagnosis of OPs poisoning. The cholinesterase enzyme level dropping is proof positive. A 25% drop in butyrylcholinesterase levels indicates a significant hazardous exposure. Any delay in diagnosing poisoning could result in inadequate care and raise the death rates associated with these cases [30].

Respiratory failure is the primary cause of death in individuals poisoned with OPs. Arrhythmia, pulmonary edema, pneumonia, pancreatitis, and renal failure are possible further consequences [31].

In settings with limited resources, such as rural areas in developing nations like Egypt, the prediction of morbidity at presentation may aid in decision-making **[32].**

This study aimed to determine the significance of serum cortisol levels and glycemic states in predicting the severity of acute organophosphorus compound poisoning. Additionally, patients were evaluated using the PSS to determine the prognosis of cases of OP poisoning that were admitted to the intensive care unit and poison control center of Zagazig University Hospitals.

This prospective cohort research had 52 patients that met inclusion and exclusion criteria. Personal history, poisoning history and past history were taken. Also, clinical assessment and investigations were done.

In the current study, the affected age group had a median age of 23 years and ranged from 19 to 53 years. This result was consistent with those noted by **Prasad** [33] who reported that 50 OP poisoned patients were with median age of 27.1 years. Also, **Gifford et al.** [34] discovered that the median age of the 70 patients with pure acute OPs poisoning admitted to the Bangladesh center was 22 years old. Males represented 53.8% of poisoned cases which outnumbered females 46.2% which is consistent with similar studies done in Tabriz and Iran **Shahsavarinia et al.** [35] who found that in their study done on 82 patients, 45 (54.9%) were males and 37 (45.1%) were females and other countries like Western India **Muley et al.** [32] who found that in their study done on 76 cases, males patients were 46 (60.52%) of cases and females patients were 30 (39.57%). Also, males represent (60.53 %) of **Amin et al.** [36] study.

Nevertheless, other research revealed that the most of poisoning victims were female. **Sah and Mandal** [37] whom study was on 50 patients with OPs poisoning. Among the total cases 22(44%) were male and 28(56%) were female. Also, **Tallat et al.** [38] study which was done on 30 patients with acute OPs poisoning, 53.3% of the cases were females and 46.7% were males**.** Furthermore, **Gunduz et al.** [39] reported in their study, that included 296 patients, 219 (74%) of them were females. We could explain that male predominance by rural area of our study and the males more exposed to occupational exposure than females.

Our results showed that 67.3% of patients came from rural area of residence and 32.7% of cases were from urban area. This is similar to **El-Gendy et al.** [40] who found in their study that done in the PCC at Tanta University Hospitals and included 40 patients that 60% of their patients from rural areas. Also, **Elgohary et al.** [41] reported similar findings in their work in the Delta region explaining that high exposure to OP is due to its low price.

Occupation-wise, most of the patients in our study (67.3%) were non workers while the remaining (32.7%) of cases had a work. **Hassan and Madboly** [42] research conducted at Benha University Hospitals' Benha Poisoning Control Unit (BPCU), included 60 patients with OPs poisoning, 36.7% were students, 23.3% housewives, 21.7% farmers, 8.3% 0ther jobs and 10% non workers.

Regarding **Mohamed et al.** [43] study that was done in Cairo on 200 cases, 43 % were unemployed, 23 % were students, 12 % were housewives, 11 % were civil employers, 7 % were manual workers and 4 % were farmers. These differences from our study may be due to different area of the study.

Regarding mode of exposure, 71.2% of patients in our study were accidentally poisoned while 28.8% were suicidal cases. This coincides with **Elgazzar et al.** [44] who revealed that 65.5% of the patients they looked at had unintentionally been exposed to OPs. Furthermore, in **Ghonem et al.** [26] study that was done on 30 cases at PCC of Tanta University Emergency Hospital, 56.7% of the cases were accidentally exposure. This can be interpretated by the mistaken intake of OPs due to their wide availability in agricultural areas of these governments.

However, there are other studies which found that suicidal exposure to OPs represents the majority of their cases. **Tallat et al.** [38] recorded 76.7% suicidal cases of the total studied cases and the whole 29 cases included in **Masoud et al.** [6] were

attempts at suicide. Poverty, money issues, unstable economies, unemployment, marital disputes, and the disintegration of the family support structure could all contribute to this [45].

Poisoning from OPs can occur from a variety of sources, including ingestion, inhalation, and skin absorption. Oral consumption was the most common method of poisoning in this research (78.8%) followed by inhalation (9.6%) while cases of mixed inhalation and dermal absorption represented 11.5%, which is consistent with other studies such as **Banday et al.** [46] who found that the main route of poisoning was oral ingestion (98.5%) and only 1.5% of their patients had dermal/inhaled exposure. **Patil et al.** [47] reported in their study done on 100 cases of OPs poisoning, that 90 % of cases were poisoned through oral ingestion and 10 % of cases were poisoned through inhalation.

Regarding toxic substances, malathion (21.2%), chlropyrifos (13.5%), diazinon (5.8%), azamethiphos (3.8%) were the primary hazardous chemical kinds that caused poisoning in the cases included in this study. On the other hand, in 55.8% of cases, the harmful OP was unknown. These substances have also been more widely used and frequent in other studies, including **Elshamy et al.** [48] They discovered in their research conducted in Egypt that the most widely used pesticides were dimethoate (8.4%), parathion (20.8%), and malathion (20.8%). Additionally, 50% of pesticides comprise more than one chemical. Moreover, similar to our findings, **Tallat et al.** [38] reported that malathion (40%) was the most predominant OP between cases followed by diazinon and chlorpyrifos (30% for each type).

Patients in our study were presented with time range from 1 to 24 hours with median time of 4 hours and interquartile range (IQR) (3-5) hours. This is similar to delay time in mild cases of **Beltagy et al.** [24] study. **Gifford et al.** [34] reported also the same median for delay time in all cases admitted to Bangladesh center.

In agreement with **Abd Alkareem and Khater [49],** vomiting (80.8%) and abdominal pain (53.8%) were the most common clinical manifestations in our study. Also, **Hassan and Madboly** [42] reported that vomiting and abdominal pain together (93.3%) were the most common manifestations. On the other hand, conjunctival congestion and miosis respectively took the upper hand according to **Prasad** [33]. The type of OP used, the amount absorbed, and the exposure method may all have an impact on the differences in clinical symptoms observed between studies.

A key challenge for clinical toxicologists treating acutely poisoned individuals is determining prognosis. Prognostic indicators enable the proper allocation of scarce ICU beds [50]. Prognostic value of cortisol has previously been evaluated in critically ill patients. Some studies suggest the mechanism is related to lipid depletion, bleeding and adrenal cortex necrosis in patients in serious condition. Stress, hypotension, and shock in people with critical illnesses are additional possible pathways that impact cortisol levels. Changes in glucocorticoid secretion, responsiveness, protein binding, and activity could be the basis for this [51].

In our study we found that there is a statistically significant positive relation between disease severity and serum cortisol level. This finding is similar to that mentioned by **Satar et al.** [52], They found that stressful situations raised cortisol levels, and that these increases were correlated with the severity of the illness. They also discovered that loss of AChE activity is akin to a generalized stress reaction, in which the plasma cortisol concentration should increase. These findings suggest that this condition may be caused by a lack of circadian rhythm and increased production.

Also, our finding was similar to **Güven et al.** [53] who pointed out in their research that several animal experiments had been conducted, which had revealed elevated cortisol levels in cases of acute anticholinesterase poisoning and demonstrated a correlation between the degree of elevation and the severity of the sickness.

In our investigation, we relied on the necessity for ICU hospitalization to determine the prognosis. A statistically significant correlation was seen between cortisol levels on admission, at 6 and 12 hours and ICU admission. This matched what was discovered by **Masoud et al.**[6] who attributed that cortisol at these three measurements could predict need for ICU admission with a good advantage for 2nd and 3rd measurements. While in our study the best performance was at 6 hours.

Masoud et al.[6] acknowledged that cortisol levels at admission can predict death and discovered a significant difference between survivors and non survivors on admission alone.

The hypothalamic-pituitary-adrenal axis is activated in response to stressful situations or life-threatening illnesses, which raises cortisol levels [54]. Nevertheless, some patients experience severe illness-related corticosteroid insufficiency, a disease

in which their body fails to produce enough cortisol in reaction to stressful situations critical illness-related corticosteroid insufficiency (CIRCI) [55].

Furthermore, anticholinesterase insecticides can influence transcription factors, hormone synthesis, and hormone receptors to impact the endocrine system [56].

Shadnia et al. [51] found that cortisol was the best predictor of outcome for usage in their toxicology intensive care unit (ICU) out of all the characteristics they examined. Furthermore, **Dutta et al.** [57] had discovered that their OP-poisoning patients had elevated baseline cortisol levels.

In our investigation, the random blood sugar levels at admission and discharge showed a statistically significant positive link with the severity of the condition and ICU admission (with the correlation being much larger among patients who required ICU admission). The best performance in predicting the requirement for an ICU admission was on the admission measurement.

Similar to our result**, Makloph et al.** [58] found that there was a strong positive association between RBS at the time of admission and severity based on the Peradeniya Organophosphorus Poisoning scale, supporting the idea that RBS might be utilized to predict the severity of cholinesterase inhibitor pesticide poisoning. **Sagah and Elhawary,** [2] **and Panda et al.,** [11] found that there was a rise in the RBS with increase in severity, that makes blood glucose status at time of admission may help in identifying the severity of poisoning.

Also, Bhat et al. [7] found that extremes of glycemic status at presentation were significantly associated with the clinical severity and hyperglycemia had a significantly positive correlation with it. In addition, they observed that patients with extremes of glycemia had moderate to severe disease in the majority. These findings agree with the observations documented in the earlier studies [59].

Moon et al. [60] **and Khalaf et al.** [61] showed in their research that there was a highly significant rise in blood glucose levels in severely OP-intoxicated patients as compared to the control. Additionally, a noteworthy association was documented between the extent of BChE inhibition and the elevation of serum glucose levels.

Regarding the glycemic state at discharge, our result was similar to **Panda et al.**[11] **and Koirala et al.** [62] who additionally disclosed the RBS's decline to normal levels on the day of discharge. elucidating how stress caused glucocorticoid, ACTH, and catecholamine excess symptoms, which had a cholinergically mediated effect during the incident and were also explained by the blood sugar returning to normal at discharge.

Gunduz et al.[39] found that glucose was one of the independent predictors of mortality examined in their study on patients with OP poisoning explaining that the hyperglycaemia in OP poisoning is generally associated with the catecholamine discharge from the adrenal medulla. **Mir et al.** [63] found that glycemic changes (hyperglycemia and glycosuria) were observed more in patients of grade II and III OP poisoning and these changes were associated with increased morbidity and mortality.

Makloph et al.[58] found a significant positive correlation between RBS and death outcome of OP-patients. **Rao and Raju,** [64] discovered that high blood glucose levels at the time of admission were a good indicator of the severity, and that levels of RBS greater than 200 mg/dl were a reliable indicator of death and the requirement for ventilatory support. **Sagah and Elhawary,** [2] discovered a substantial correlation between RBS and death.

Also, **Godinjak et al.**[9] noted that patients with stress-hyperglycemia had a greater death rate in their study of critically ill patients.

A number of researchers declared that when anticholinesterase poisoning occurs, hyperglycemia is a frequent consequence and a clinically relevant result [65].

Rahimi and Abdollahi [66] claimed that a number of causes, including pancreatitis, oxidative stress, nitrosative stress, physiological stress, suppression of the cholinesterase enzyme, and disruption in the liver's tryptophan metabolism, could be to blame for the spike in serum glucose levels.

Moreover, a variety of theories have been proposed to explain hyperglycemia as the culmination of many pathways. excessive production of catecholamines from the adrenal medulla due to overstimulation of nicotine receptors on sympathetic ganglia. Furthermore, the anterior pituitary may release more adrenocorticotropic hormone in response to intense cholinergic stimulation.[11]. In addition, According to **Xiao et al.** [67], Pancreatitis and increased glycogenolysis may be also responsible for this rise.

PSS is broken down into three grades, with its constituent parts chosen based on **Shrestha et al.** [21].

Our present results showed predominance of patients with mild grade of PSS (63.5%). This goes

parallel with **Tawfik and ElHelaly** [68] and **Khodeary and Elkholy** [65] who stated that mild grade patients made up the bulk of their patient base. Conversely, **Azab** [69] has revealed that the majority of individuals in his study had severe OP-toxicity and higher PSS grades.

The dosage, the mode of exposure, the kind and pharmacokinetic characteristics of the chemical, and the victim's prior health state all influence how severe an OP poisoning is. [70].

There was a statistically highly significant relationship ($p<0.001$) between ICU admission and PSS grades. All patients with severe grade were admitted to ICU. Having Severe grade can predict need for ICU admission with 72.7% sensitivity and 100% specificity.

That matched with **Khodeary and Elkholy** [65] and **Yuan et al.** [20] who demonstrated that PSS is a useful tool for assessing the severity and prognosis of patients hospitalized with OP poisoning.

Also, **Hodeib and Ghonem** [23] found that the median value of PSS in ICU admitted patients was significantly higher than ICU-not admitted patients ($p<0.001$) with 86.67% sensitivity and 100% specificity noting that PSS predicted ICU admission with excellent performance.

Shama et al. [71] found that PSS predict ICU admission with fair performance in organophosphorus poisoned cases. **El Sarnagawy et al.** [72] found a statistical difference between ICU admission and PSS grades.

The mortality following OP poisoning ranges from 4 to 30% [73, 74] but mortality rate in our study was one case (1.9%) which was comparable to **Beltagy et al.** [24] where no mortalities were reported in their study. Low mortality rate may be due to limited number of the study cases.

Hulse et al. [75] made clear that the majority of deaths following OP poisoning are brought on by hypoxia, which is brought on by a confluence of central apnea and acute cholinergic effects. Subsequent deaths have happened as a result of problems with reduced consciousness, neuromuscular junction dysfunction, or cardiovascular shock.

CONCLUSIONS

In conclusion, the availability of OPs makes OP poisoning a serious health concern, particularly in undeveloped nations like Egypt where it is more common. We concluded from our findings that serum cortisol on admission, 6 and 12 hours was highly significantly related to poisoning severity and ICU admission. Specifically, its measurement at 6 hours was the best in prediction of severity and the need for ICU. RBS on admission and discharge was highly significantly related to poisoning severity and ICU admission. Specifically, its measurement on admission was the best in prediction of severity and the need for ICU. PSS was highly significantly related to ICU admission. PSS, RBS (on admission) and Cortisol (6 hrs) respectively are good predictors for poisoning severity and need for ICU admission in acute organophosphate poisoning.

RECOMMENDATIONS

- Evaluation of patients according to PSS at the time of admission.
- Using serum cortisol level in every case of acute OPs poisoning especially at 6 hours as predictor for prognosis.
- Using serum random blood glucose level as predictor for prognosis in every case of acute OPs poisoning.
- Using serum random blood glucose level as predictor at time of admission as it is easy, simple, cheap bed side test and available in any hospital.
- Performing more clinical studies on a larger scale of population to confirm our results.
- Upcoming studies should include more moderate and severe cases.
- Further studies needed also to evaluate other parameters which can assess the prognosis and severity of organophosphorus poisoning

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Competing interests

The authors declare that they have no competing interest.

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Table (1): Criteria used to calculate poison severity score (PSS) **[21].**

	Grade 1 (mild)	**Grade 2 (moderate)**	**Grade 3 (severe)**
Respiratory Intubated	No	-	Yes
Neurological GCS	14-15	9-13	3-8
Seizures	No	-	Yes
Bradycardia (pulse)	>50	41-50	≤40
Tachycardia (pulse)	≤140	141-180	>180
Hypotension (systolic BP)	>100	81-100	≤80

GCS Glasgow coma scale BP blood pressure

Table (2): Distribution of the studied patients according to demographic data, clinical picture, laboratory data and prognosis

	N=52	**%**
Age (year) **Median (IQR)** **Mean ± SD** **Range**	 23(19 – 41.5) 29.29 ± 11.72 19 – 53	
Gender **Female** **Male**	 24 28	 46.2% 53.8%
Residence **Rural** **Urban**	 35 17	 67.3% 32.7%
Working **No** **Yes**	 35 17	 67.3% 32.7%
Method **Accidental** **Suicidal**	 37 15	 71.2% 28.8%
Route **Ingestion** **Inhalation** **Skin and inhalation**	 41 5 6	 78.8% 9.6% 11.5%
Organophosphate **Azamethiphos** **Chlorpyrofos**	 2 7	 3.8% 13.5%

	N=52	%
Diazinon	3	5.8%
Malathion	11	21.2%
Unknown	29	55.8%
Presented within		
Median (IQR)	4(3 – 5)	
Range	1 – 24	
Clinical picture		
Vomiting	42	80.8%
Abdominal pain	28	53.8%
Miosis	16	30.8%
Drowsy/DCL	15	28.8%
Sweating	10	19.2%
General fasciculation	10	19.2%
Chest secretion	7	13.5%
Cortisol on admission (µg/dl)	23.55(18.05 – 34.7)	8.6 – 50
Cortisol at 6 hours (µg/dl)	12.2(10 – 28.93)	3.11 – 41.3
Cortisol at 12 hours (µg/dl)	17.8(15.93 – 25.9)	6.3 – 157
RBS on admission (mg/dl)	120.5(93.5 – 158.75)	53 – 292
RBS on discharge (mg/dl)	109.67 ± 27.56	66 – 180
Pseudo choline level (from upper)	**Median (IQR)** 3645(1796.75 – 4045)	**Range** 240 – 5466.7
ICU		
No	41	78.8%
Yes	11	21.2%
Outcome		
survivors	51	98.1%
Non-survivors	1	1.9%

IQR interquartile range SD standard deviation N number % percent

Table (3): Relation between each of serial cortisol levels (on admission,6hrs, 12hrs) , random blood sugar levels (RBS) (on admission, on discharge) and intensive care unit (ICU) admission using Mann Whitney test (Z):

	No ICU admission Median (IQR)	ICU admission Median (IQR)	Z	p
Cortisol				
On admission	19.1(17.4 – 28.1)	40.8(35.4 – 45.9)	-3.99	<0.001**
6 hour	12(9.9 – 15.13)	35.5(34.1 – 38.7)	-4.843	<0.001**
12 hour	16.9(15.75 – 18.95)	29.5(25.3 – 36.8)	-3.822	<0.001**
RBS				
On admission	115(89.5 – 135.5)	225(210 – 270)	-4.83	<0.001**
On discharge	94(83.5 – 123.5)	135(123 – 145)	-3.565	<0.001**

Z Mann Whitney test **p≤0.001 is statistically highly significant IQR interquartile range

Table (4): Performance of cortisol level on admission, at 6 and 12 hours and random blood sugar (RBS) (on admission and on discharge) in prediction of need of intensive care unit (ICU) admission

Time	Cutoff	AUC	95% CI		Sensitivity	Specificity	p
Cortisol							
On admission	≥30.32	0.895	0.746	1	90.9%	80.5%	<0.001**
At 6 hours	≥27.35	0.979	0.946	1	90.9%	87.8%	<0.001**
At 12 hours	≥21.25	0.878	0.717	1	90.9%	82.9%	<0.001**
RBS							
On admission	≥180	0.978	0.945	1	90.9%	92.7%	<0.001**
On discharge	≥120	0.853	0.749	0.956	90.9%	73.2%	<0.001**

AUC area under curve CI Confidence Interval **p≤0.001 is statistically highly significant % percent

Table (5): Distribution of the studied patients according to poison severity score (PSS) grades

	Grade 1(mild) n(%)	Grade 2 (moderate)n(%)	Grade 3 (sever)n(%)
Respiratory (intubated)	**45 (86.5%)**	**-**	**7 (13.5%)**
GCS	**42 (80.8%)**	**9 (17.3%)**	**1 (1.9%)**
Seizures	**49 (94.2%)**	**-**	**3 (5.8%)**
Bradycardia	**52 (100)%**	**0 (0%)**	**0 (0%)**
Tachycardia	**48 (92.3%)**	**4 (7.7%)**	**0 (0%)**
Blood pressure	**39 (75%)**	**11 (21.2%)**	**2 (3.8%)**
Total	**33 (63.5%)**	**11 (21.2)**	**8 (15.4)**

n number % percent

Table (6): Relation between poison severity score (PSS) and intensive care unit (ICU) admission by Chi square test (§)

	No ICU admission N(%)	ICU admission N(%)	§	p
PSS **Mild (Grade 1)** **Moderate (Grade 2)** **Severe (Grade 3)**	 32 (78%) 9 (22%) 0 (0%)	 1 (9.1%) 2 (18.2%) 8 (72.7%)	 30.64	 <0.001**
Predictive performance of severe	Sensitivity =72.7%	Specificity=100%		

**p≤0.001 is statistically highly significant N: number of cases % percentage §Chi square for trend test

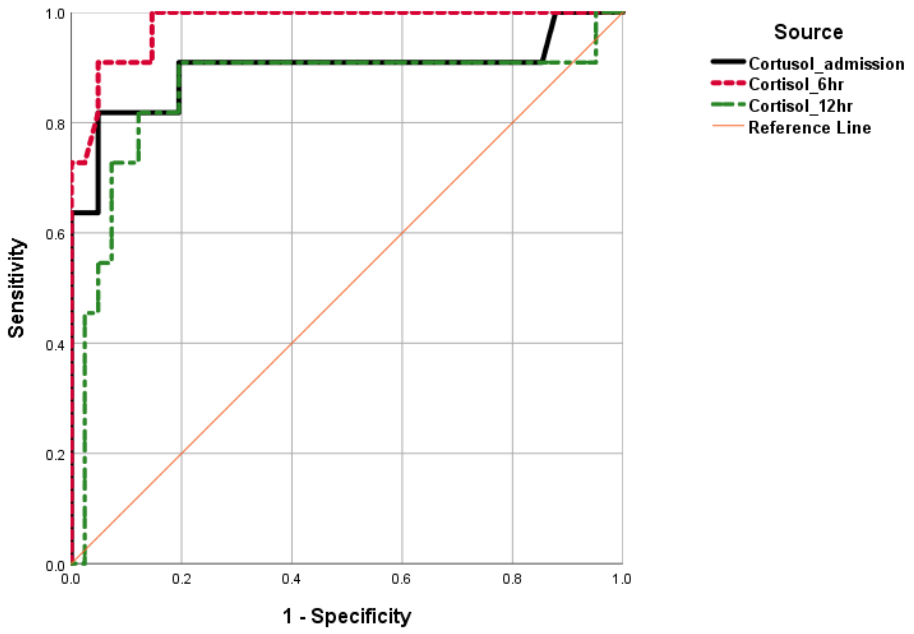

Figure 1. Receiver operating characteristic (ROC) curve showing performance of cortisol level on admission, at 6 and 12 hours in prediction of need of intensive care unit (ICU) admission.

Citation

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