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# Prediction of Different Outcomes in Patients of Acute Chlorpyrifos Poisoning

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## Abstract

**Background:** Organophosphorus compounds (OPCs) such as chlorpyrifos (CPF) are powerful cholinesterase inhibitors. Chlorpyrifos is a broad-spectrum chlorinated organophosphate first introduced into the markets in 1965. **Objectives:** This study aims to evaluate the baseline characteristics, clinical manifestations, and prognostic factors of patients with acute chlorpyrifos (CPF) intoxication, differentiating between those with good and poor prognoses based on the need for mechanical ventilation, ICU admission, and mortality. **Methods:** We conducted a retrospective analysis of 31 patients with acute CPF intoxication. Patients were stratified into good prognosis (n=21, 67.8%) and poor prognosis (n=10, 32.2%) groups. Data on demographics, exposure details, clinical symptoms, laboratory results, and treatment outcomes were collected and analyzed. **Results:** The median age of patients was 28 years, with a slight female predominance (51.6%). Clinically, the most common symptoms were vomiting (87.1%), diarrhea (83.9%), chest crepitation (80.6%), hypotonia (58.1%). Poor prognosis was significantly associated with hypotonia (p=0.013), fasciculations (p=0.029), hypotension (p=0.001), bradycardia (p<0.001), and lower Glasgow Coma Scale (GCS) scores (p<0.001). The median GCS was 15, with a stark contrast between good prognosis (median GCS of 15) and poor prognosis groups (median GCS of 4). Laboratory findings showed lower serum bicarbonate levels (p=0.030) and higher random blood sugar levels (p=0.041) in the poor prognosis group. Treatment analysis revealed that poor prognosis patients required significantly more atropine and oximes (p=0.002 each). **Conclusion:** GCS and pulse were significant predictors of poor prognosis in patients with acute CPF intoxication. Early identification and aggressive management of these predictors could potentially improve patient outcomes.

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**Key words** Chlorpyrifos intoxication, prognosis, clinical manifestations, mechanical ventilation, ICU admission, mortality

## Introduction

Organophosphorus compounds (OPCs) such as chlorpyrifos (CPF) are powerful cholinesterase inhibitors (Wu et al., 2023). Chlorpyrifos is a broad-spectrum chlorinated organophosphate first introduced into the markets in 1965. It is used in agriculture for the control of a variety of pests, as well as household uses (ur Rahman et al., 2021). It belongs to class II pesticides (moderately hazardous) according to the WHO classification, with $LD_{50}$ 135 mg/kg (WHO, 2019).

Chlorpyrifos is absorbed through the skin, intestine and lungs in exposed humans and animals. However, it was reported that uptake via dermal exposure is limited (<5%). It is not soluble in water but is soluble in many organic solvents. The addition of chlorine group increases the lipid solubility, hence increasing the half-life in the body, producing prolonged toxicity (Liu et al., 2020).

Cytochrome P450 is the first step in the hepatic metabolism converting CPF into chlorpyrifos-oxon, a much more powerful anticholinesterase compound. Other enzymes as paroxanase, and A-esterase hydrolyze chlorpyrifos-oxon into 3,5,6-trichloro-2-pyridinol (TCPy), It is then eliminated from the body through urine. It is an inactive metabolite that is considered the primary metabolite of CPF specific enough to be used as a biomarker of exposure. It was reported that polymorphism of cytochrome P450 family and paroxanase can be one of the causes of differing individual susceptibilities to CPF-induced effects and different clinical presentations (Ingelman-Sundberg, 2002).

Organophosphate compounds work by inhibiting the activity of acetylcholinesterase, leading to an excess of the neurotransmitter acetylcholine in the body (Eddleston, 2019). As in other OPCs pesticides, the clinical courses of acute CPF intoxication include early cholinergic crisis, and delayed manifestations as intermediate syndrome, and delayed polyneuropathy (Liu et al., 2020).

Chlorpyrifos is a very effective pesticide with reasonable cost. However, years of studying its ecological, animal, and human hazards led many countries to take serious measures. The United States Environmental Protection Agency ended its household use and reduced non-agricultural uses to less than 3% early in 2002. Canada and Australia also followed the same regulations over CPF use. Norway never authorized its use. However, CPF is still used in many developing countries. In Egypt, it was issued CPF

would be banned at the end of 2022, with an exception for the use in cotton and against termites and locusts ( Testai et al., 2010). A study carried out by Elgohary et al. (2013) at Tanta Poison Control Center, reported that the most common OP identified in acute OP-poisoned patients was chlorpyrifos (13.33%) (Elgohary et al., 2013). Despite CPF being mentioned in studies on acute OPCs poisoning, human studies dedicated to acute CPF poisoning are limited. The current study hopes to focus on the acute poisoning of CPF, its clinical course, and possible predictors of poor outcome. So, this study aimed to analyze the clinical course, laboratory findings, and outcomes of patients with acute CPF poisoning with specific highlighting in identifying the possible predictors of different outcomes.

## Subject and Methods

**Study design and setting**

A retrospective analytical cross-sectional study was conducted including all cases diagnosed with acute CPF intoxication who were presented to the Tanta University Poison Control Center (TUPCC) during the past 3 years (May 1st, 2020 –May 1st, 2023).

**Inclusion and exclusion criteria**

All patients diagnosed with CPF intoxication based on the history of exposure, the presence of characteristic cholinergic and/or nicotinic toxidromes, and improvement of the toxicity symptoms on atropine therapy (Aygun et al., 2002). Reduced butyrylcholinesterase (plasma cholinesterase) activity by <50% of the minimum normal values (3600 IU/l) was considered an additional confirmatory diagnostic criteria (Areekul et al., 1981, Aygun et al., 2002). Exclusion criteria included cases of co-ingestion, patients diagnosed with chronic hepatic, cardiac, and renal disorders, and patients with incomplete medical records.

**Sampling and sample size**

To include the greatest number of patients, we adopted nonrandomized convenience sampling. During the study period (May 2020–May 2023). Fifty patients diagnosed with acute CPF poisoning were presented to the TUPCC. Of these, 31 fulfilled the inclusion criteria and were enrolled in the current study. Nineteen patients were excluded based on the exclusion criteria.

**Compliance with ethical standards**

The current study was commenced after obtaining approval from the Research Ethical Committee from Tanta University, Faculty of Medicine (following the Declaration of Helsinki under ID 36264PR370/10/23). Data were retrieved from the medical records without a declaration of participant identity. All data were handled anonymously to maintain the confidentiality of the data.

**Data collection**

**Demographics and exposure history**

For all included cases, we documented demographic data including age, gender, and residency. The patient's medical history of chronic illness was recorded. Exposure history included the manner and route of exposure, mode of poisoning and the delay time (in hthe currents) between exposure and hospital admission.

**Clinical data**

Presenting symptoms were documented. Data of complete physical examination on admission including pupil size, vital signs, level of consciousness by Glasgow coma scale (GCS), and systems examination (nervous, respiratory, cardiovascular, gastrointestinal) were recorded. Also, amounts of atropine and oximes given to the patients, and duration of hospital stay were recorded.

**Laboratory investigations**

Results of routine investigations were recorded, including arterial blood gas (ABG) analysis, complete blood cell (CBC) count, liver transaminases, urea, creatinine, and electrolytes (sodium and potassium levels).

**Outcome assessment:**

All the included patients were managed according to the protocol of TUPCC of acute OPCs intoxication, including decontamination, emergency and supportive treatment, antidotal therapy (atropine and oximes), and symptomatic treatment. Intubation and mechanical ventilation become necessary in cases of respiratory distress due to laryngospasm, bronchospasm, bronchorrhea, or seizures.

The patients divided into two groups; group (1) included patients with good prognosis who were discharged and did not require mechanical ventilation or intensive care unit (ICU) admission, and group (2) included patients with poor prognosis (patient who needed mechanical ventilation and ICU admission and non-survivors).

**Statistical analysis**

Continuous variables are expressed as the mean and standard deviation and categorical variables as the number with percentages in brackets. For comparisons between patient groups, the Student's t-test was used for quantitative variables and Mann-Whitney test for quantitative variables not normally distributed, and the Chi-square test for categorical variables. Univariate logistic regression analysis was performed to compare the frequency of factors associated with poor prognosis. ($p < 0.05$). Results that rejected the null hypothesis with 95% confidence were considered significant. All analyses were performed using SPSS, version 12.0 for Windows (SPSS Inc., Chicago, Illinois, USA).

## Results

Table 1 presents the baseline characteristics of 31 patients with acute CPF intoxication, stratified into good (n: 21, 67.8%) and poor (n: 10, 32.2 %) prognosis groups according to the need of mechanical ventilation and ICU admission, and mortality (table 4). The median age for the studied patients was 28 years. More than half of the presented patients were female (n: 17;51.6%) (figure 1), and most of the patients were from rural areas (n: 23; 74.2%) (figure 2). The median interval time between poison exposure and hospital arrival was 5 hours.

Most patients were poisoned by oral ingestion (74.2%) versus 25.8% through dermal and inhalational routes (figure3). More than half the patients (58.1%) reported no previous medical history. More than half

the patients (n: 16; 53.3%) consumed CPF intentionally for the purpose of self-harm (figure 4). The comparison between the good and poor prognosis groups regarding the previous variables in table 1 revealed that the only variable that showed statistically significant difference between the two groups was the presence of past medical history (p 0.025).

The patients developed various clinical manifestations (table 2), the most common presenting symptom was vomiting (87.1%), diarrhea (83.9%), chest crepitation (80.6%), followed by hypotonia (58.1%), miosis (54.8%), fasciculations (41.9%), tachycardia, colic (38.7% each), hypotension (29%), and hypertension (22.6%), and bradycardia (19.4%).

Comparison between clinical manifestations of good and poor prognosis groups revealed that poor prognosis group showed statistically higher incidences of hypotonia (p= 0.013), fasciculations (p= 0.029), hypotension (p= 0.001), bradycardia (p< 0.001), and lower score of GCS (p< 0.001) than the good prognosis group. Regarding consciousness level, the median GCS for all cases was 6. While patients with good prognosis had a median GCS of 15, poor prognosis group patients had a median of 4 with a statistically significant difference between the two groups. The mean pulse rate was 140.90 ± 42.171 beats/ min in the good prognosis group vs 101.90 ± 21.305 beats/ min in the poor prognosis group. (Table 2).

Arterial blood gas analysis of the studied patients showed that the median pH was 7.4, and the median serum bicarbonate level was 23.3. Serum bicarbonate levels were significantly lower in the poor prognosis group (median 22) versus (23.75) in the good prognosis group (p=0.030). The median random blood sugar for all patients was 116 mg/dl. The poor prognosis group had statistically higher blood levels of RBS (median 145 mg/dl) versus (99 mg/dl) in the good prognosis group (p=0.041). All the other studied laboratory measurements showed no significant statistical difference between both groups (Table 3).

As presented in Table 4, the median total amount of atropine and oxime required was 2 and 4 ampoules respectively. However, the poor prognosis group needed significantly higher median amounts of atropine and oximes compared to the good prognosis group (12 and 5 vs 0.24 and 3 ampoules respectively; p 0.002 each). The median hospitalization period for all patients was 15 hours with no significant difference between good and poor prognosis groups (table 5).

Univariate binary logistic regression analysis for prediction of poor prognosis in the studied patients revealed the significant predictive value of GCS, presence of hypotonia, fasciculations, and pulse for prediction of the unfavorable outcome of patients with acute CPF intoxication.

In a multivariate logistic regression model (Table 5), it was revealed that GCS (odds ratio: 0.532, 95% confidence interval: 0.284- 0.996, p value 0.049) and pulse (odds ratio: 1.016, 95% confidence interval: 0.994- 1.039, p value 0.029) was a significant risk factor for poor prognosis after chlorpyrifos intoxication

**Table (1): Sociodemographic data, Toxicological data and Past history of medical diseases of the studied 2 groups of patients (good prognosis and poor prognosis) with acute chlorpyrifos poisoning (n =31)**

| Variable | Group1 (n=21) (Good prognosis) | Group2 (n=10) (Poor prognosis) | Total | Test Statistic | P-value |
|---|---|---|---|---|---|
| **Age (median, IQR)** | 30 (18-53) | 26 (17-28.25) | 28 (18-56) | Z=-0.085 | 0.933 |
| **Gender (male) (n, %)** | 10 (32.3%) | 5 (16.1%) | 15 (48.4%) | $X^2$=0.015 | 0.901 |
| **Residence (Rural) (n, %)** | 14 (45.2%) | 9 (29.0%) | 23 (74.2%) | $X^2$=1.926 | 0.165 |
| **Time between pesticide ingestion and hospital arrival (hthe currents) (median, IQR)** | 6(3.25-12) | 3(1.5-6.625) | 5 (3-12) | Z=-1.845 | 0.065 |
| **History of medical disease (n, %)** | | | | | |
| **No** | 16 (88.9%) | 2 (11.1%) | 18 (58.1%) | | |
| **Diabetes mellitus** | 1 (25%) | 3 (75%) | 4 (12.9%) | $X^2$=9.365 | 0.025* |
| **Hypertension** | 2 (40 %) | 3 (60%) | 5 (16.1%) | | |
| **Asthma** | 2 (50%) | 2 (50%) | 4 (12.9%) | | |
| **Routes of exposure (n, %)** | | | | | |
| **Ingestion** | 15 (65.2%) | 8 (34.8%) | 23 (74.2%) | $X^2$=4.073 | 0.130 |
| **Inhalation** | 5 (100%) | 0 | 5 (16.1%) | | |
| **Dermal** | 1 (33.3%) | 2 (66.7%) | 3 (9.7%) | | |
| **Mode of poisoning (n, %)** | | | | | |
| **Suicidal** | 9 (56.3%) | 7 (43.8%) | 16 (51.6%) | $X^2$=4.567 | 0.102 |
| **Occupational** | 8 (100%) | 0 | 8 (25.8%) | | |
| **Accidental** | 4 (56.1%) | 3 (42.9%) | 7 (22.6%) | | |

***n: number; IQR: interquartile range; Z: Mann-Whitney test; $X^2$: Pearson's Chi-square test for independence of observations; *significant at p<0.05***

**Table (2): Comparison between 2 groups (good prognosis and poor prognosis) of acute Chlorpyrifos poisoned patients regarding clinical manifestations, GCS and vital signs on admission (n=31)**

| Variable | | Group1 (n=21) (Good prognosis) | Group2 (n=10) (Poor prognosis) | Total | Test Statistic | P-value |
|---|---|---|---|---|---|---|
| **GCS** | (Median, IQR) | 15 (15-15) | 4 (3-13.5) | 15 (6-15) | Z= -4.058 | <0.001* |
| **Pupil size** | Normal | 11 (78.6%) | 3 (21.4%) | 14 (45.2%) | X2= 1.556 | 0.459 |
| | PPP | 10 (58.8%) | 7 (41.2%) | 17 (54.8%) | | |
| **Chest** | Normal | 6 (100%) | 0 | 6(19.4%) | X2=3.453 | 0.060 |
| | Crepitations | 15 (60%) | 10 (40%) | 25(80.6%) | | |
| **GIT** | Vomiting | 17 (63%) | 10 (37%) | 27 (87.1%) | X2=2.187 | 0.139 |
| | Colic | 7 (58.3%) | 5 (41.7%) | 12 (38.7%) | X2=0.793 | 0.373 |
| | Diarrhoea | 16 (61.5%) | 10 (38.5%) | 26 (83.9%) | X2=2.839 | 0.092 |
| **Neurological** | Hypotonia | 9 (50%) | 9 (50%) | 18 (58.1) | X2=6.183 | 0.013* |
| | Fasciculations | 6 (46.2%) | 7 (53.8%) | 13 (41.9%) | X2=4.775 | 0.029* |
| **Pulse (beats/min)** | Normal | 10 (76.9%) | 3 (23.1%) | 13 (41.9%) | X2= 8.99 | 0.011* |
| | Tachycardia | 10 (83.3%) | 2 (16.7%) | 12 (38.7%) | | |
| | Bradycardia | 1 (16.7%) | 5 (83.3%) | 6 (19.4%) | | |
| | Mean ±SD | 140.90±42.171 | 101.90±21.305 | 114.48±42.17 | t=-2.634 | <0.001* |
| **Blood pressure (mmHg)** | Normal | 14 (93.3%) | 1 (6.7%) | 15 (48.4%) | X2= 13.073 | 0.001* |
| | Hypotension | 2 (22.2%) | 7 (77.8%) | 9 (29%) | | |
| | Hypertension | 5 (71.4%) | 2 (28.6%) | 7 (22.6%) | | |
| **Respiratory rate (cycle/min)** | Median IQR | 18.50 (18-22) | 25 (18-31) | 22 (18-30) | Z=0.724 | 0.469 |
| **Temperature (ºC)** | Median IQR | 37 (36.72-38.13) | 37 (36.65-37) | 37 (36.80-37) | Z= -0.205 | 0.837 |

***n: number; GIT: Gastrointestinal tract; MAP: Mean arterial blood pressure; IQR: interquartile range; Z: Mann-Whitney test; SD: standard deviation; T: independent samples t-test; X2: Pearson's Chi-square test for independence of observations; *significant at p<0.05***

**Table (3): Comparison between 2 groups (good prognosis and poor prognosis) of acute CPF poisoned patients regarding laboratory investigations(n=31)**

| Variable | | Group1 (n=23) (Good prognosis) | Group2 (n=10) (Poor prognosis) | Total | Test Statistic | P-value |
|---|---|---|---|---|---|---|
| **Acid-base status** | PH | 7.43 (7.39-7.52) | 7.36 (7.30-7.45) | 7.40 (7.35-7.46) | Z=-1.650 | 0.09 |
| | $PO_2$ | 95.4 (77.7-120.5) | 69.60 (28.75-92.8) | 87.60 (33.9-96.1) | Z=1.609 | 0.108 |
| | $PCO_2$ | 31.25 (26.72-38.125) | 35.00 (29.35-44.125) | 32.40 (28.7-40.6) | Z= 0.444 | 0.657 |
| | $HCO_3$ | 23.75 (21.77-24.85) | 22.00 (16.40-24.05) | 23.3 (18.6-24.3) | Z=1.881 | 0.030* |
| **Random blood sugar levels (mg/dl)** | Median (IQR) | 99 (88.75-117.75) | 145 (102-203) | 116 (96-181) | Z=-2.855 | 0.04* |
| **ALT level** | Median (IQR) | 23.5 (14.25-37.25) | 20 (14-24.5) | 20 (14-30) | Z=-0.529 | 0.597 |
| **AST level** | Mean ±SD | 30.38±12.79 | 26.40±7.426 | 29.09±11.36 | t=0.909 | 0.371 |
| **Blood urea level** | Median IQR | 30.5 (23.75-46.25) | 34 (29-44) | 32 (27-45) | Z= -0.381 | 0.703 |
| **Serum creatinine level** | Median (IQR) | 0.835 (0.6-1.05) | 0.87 (0.69-1.05) | 0.87 (0.69-1) | Z=-0.064 | 0.949 |
| **Serum potassium level (mmol/L)** | Mean ±SD | 3.734±0.555 | 3.734±0.59 | 3.734±0.558 | t=0.003 | 0.997 |
| **Serum sodium level (mmol/L)** | Median IQR | 140.9 (133-143.87) | 142 (139-144) | 142 (138-144) | Z=-0.191 | 0.849 |
| **Hemoglobin(g/dl)** | Mean ±SD | 12.181±2.138 | 12.160±1.622 | 12.174±1.95 | t=0.027 | 0.392 |
| **Total leucocytic count(x103/cmm)** | Median IQR | 7050 (4800-11250) | 11000 (6850-17000) | 11000 (6600-16240) | Z=-0.509 | 0.611 |
| **Platelet's count (x103 /cmm)** | Mean ±SD | 216000±77201.03 | 233000±59063.05 | 221483.817±71310.06 | t=-0.614 | 0.544 |

***AST: aspartate aminotransferase; ALT: alanine transaminase; n: number; IQR: interquartile range; Z: Mann-Whitney test; SD: standard deviation; T: independent samples t-test; X2: Pearson's Chi-square test for independence of observations; *significant at p<0.05***

**Table (4): Comparison between good and poor prognosis groups of acute CPF poisoned patients regarding antidote therapy and hospitalization period:**

| Variable | | Group1 (n=21) (Good prognosis) | Group2 (n=10) (Poor prognosis) | Total | Test Statistic | P-value |
|---|---|---|---|---|---|---|
| **Total amount of atropine (ampoule) 1 mg / each** | Median IQR | 0.25 (0-2) | 12 (0.6-17.5) | 2 (0-17) | Z= -3.170 | 0.002* |
| **Total amount of oximes (ampoule) 250 mg / each** | Median IQR | 3 (0-4) | 5 (1-11) | 4 (0-10) | Z=-3.173 | 0.002* |
| **Hospitalization period (hthe currents)** | Median IQR | 13.5 (11-36.75) | 41 (7- 65) | 15 (8-58) | Z=-1.906 | 0.057 |

***n: number; IQR: interquartile range; Z: Mann-Whitney test; X2: Pearson's Chi-square test for independence of observations; *significant at p<0.05***

**Table (5): Univariate and Multivariate binary logistic regression analysis for prediction of poor prognosis**

| | Univariate analysis | | Multivariate analysis | |
|---|---|---|---|---|
| | **Odd Ratio (95%CI)** | **P value** | **Odd Ratio (95%CI)** | **P value** |
| **GCS** | 0.679 (0.530-0.870) | 0.002* | 0.532 (0.284- 0.996) | 0.049* |
| **Hypotonia** | 0.083 (0.009-0.782) | 0.003* | 0.420 (0.012- 14.841) | 0.634 |
| **Fasciculation** | 0.171 (0.033-0.893) | 0.036* | 1.060 (0.091- 2809.893) | 0.293 |
| **Pulse** | 1.025 (1.003-1.046) | 0.025* | 1.016 (0.994- 1.039) | 0.029* |
| **RBS** | 1.027 (1.005-1.050). | 0.071 | 16.006 (0.990-1.135) | 0.148 |

***CI confidence interval. MAP: Mean arterial blood pressure; RBS: Random blood sugar; GCS: Glasgow coma scale.***

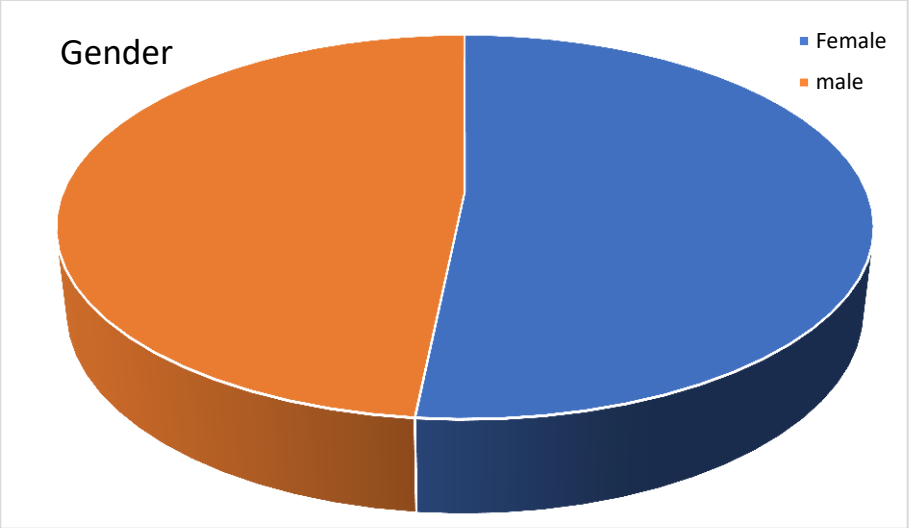


**Fig. (1): Distribution of gender among patients with chlorpyrifos intoxication**

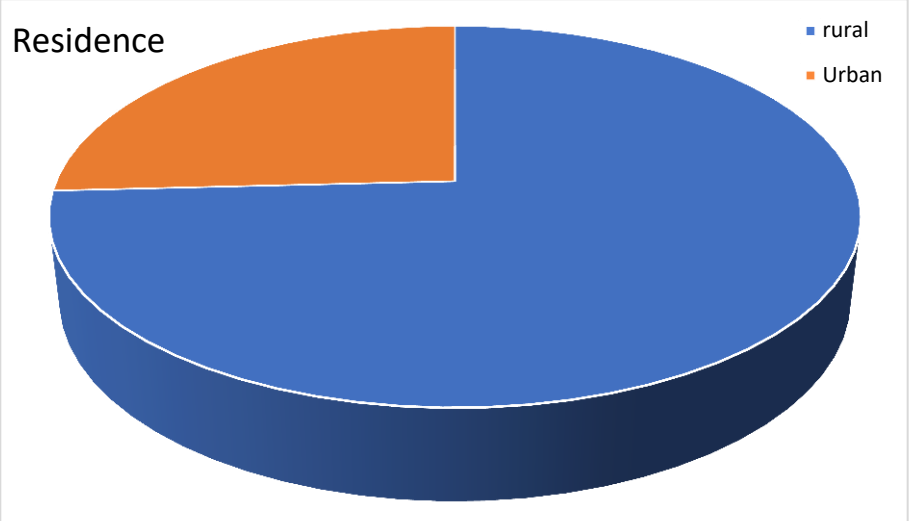


**Fig. (2): Distribution of residence among patients with chlorpyrifos intoxication**

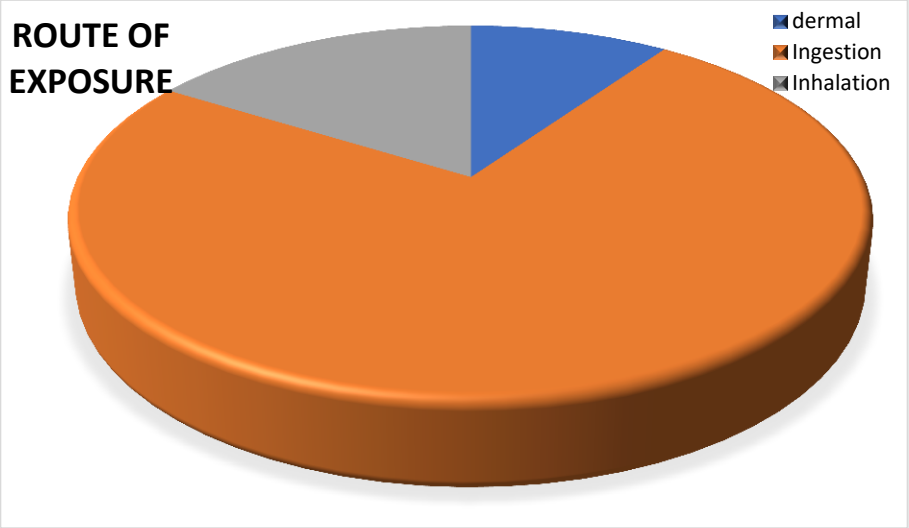


**Fig. (3): Route of exposure to chlorpyrifos in the studied patients**

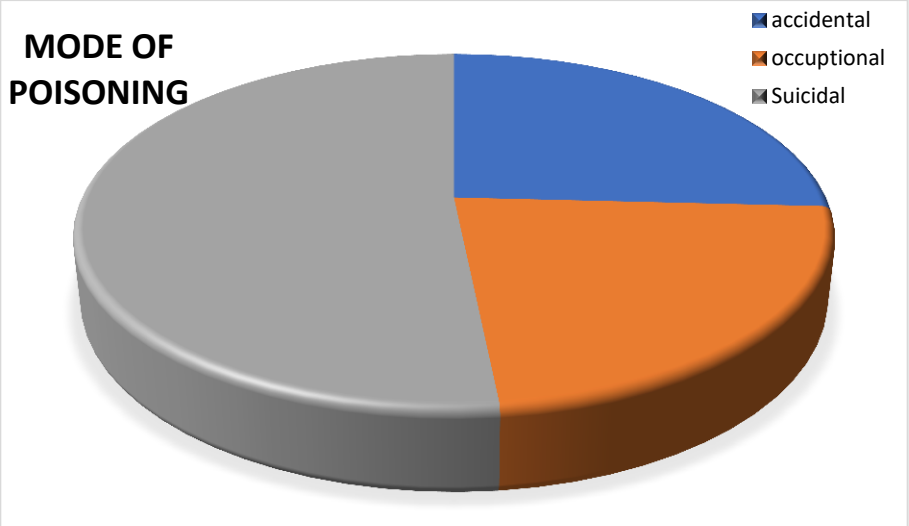


**Fig. (4): Mode of poisoning to chlorpyrifos in the studied patients**

## Discussion

Published literature has usually considered OPCs as a homogenous entity despite being a heterogenous group showing wide variations in lipophilicity, metabolism, selectivity for acetylcholinesterase over other serine esterase, speed of aging, etc…..(Eddleston et al., 2005). Thus, this study focuses on the human toxicity of acute CPF. The current study included 31 patients who presented with symptoms and signs of acute CPF poisoning. Of these patients, 10 patients required mechanical ventilation and ICU admission and 6 patients died. This study found GCS, presence of chest crepitation, hypotonia, fasciculation, diarrhea, pulse, mean arterial pressure to be predictors of prognosis in acute CPF toxicity.

The mean age of the patients in the current study was 28. The age range agrees with previous reports of acute CPF and OPCs poisoning in general (Eddleston et al., 2005, Peter et al., 2013, Rose et al., 2023). This is consistent with the fact that more than half of the patients in the current study consumed CPF intentionally. It is presently established that younger people are predisposed to various risk factors for suicide. They are more influenced by adverse life events (Abou Chahla et al., 2023). A recent online survey on the Arab world reported that younger individuals who searched for depression information online were more likely to experience suicidality compared to older individuals (Daouk et al., 2023).

Age did not show a significant statistical difference between good and poor prognosis patients in the current study. This is in agreement with a study from Taiwan on 40 CPF-poisoned patients (Liu et al., 2020). On the contrary, other studies disagree with this finding. An Indian study on acute CPF poisoning cases concluded that younger age (<40 years) was associated with better outcomes as compared to older patients (Acharya and Panda, 2022). Likewise, mortality was significantly associated with older age in other studies on acute OPCs poisoning (Noghrehchi et al., 2022, Maksimović Ž et al., 2023).

As mentioned before, intentional ingestion of CPF was the mode of poisoning in more than half the patients in the current study. This agrees with previous studies on CPF poisoning (Liu et al., 2020, Wu et al.,

2023, El-Gharbawy and Emara, 2015). This is not specific for CPF, OPCs in general are often used for self-harm. This highlights the problem of using pesticides as a convenient method of committing suicide. Governments showed control access to such compounds for non-agricultural uses (Elagamy and Gabr, 2019, Wu et al., 2023).

The median interval time between poison exposure and hospital arrival in the current study was 5 hours. This is in accordance with previous reports of CPF (Eddleston et al., 2005) and OPCs generally (Davies et al., 2008). There are two observations in the current study. First, patients with good prognosis had a higher median interval time between consumption of poison and arrival at the hospital. This could be interpreted by patients with more pronounced poisoning who tend to seek medical help and appear earlier in the hospital. Second, there was no statistically significant difference between good and bad prognosis groups regarding delay time. This disagrees with the association between early reporting to the hospital within 4 hours of poisoning and favorable outcomes reported by Acharya and Panda, (2022). However, the absence of significant difference in outcome regardless of interval time can be explained by the timely interventions and strict protocol of acute OPCs management applied in TUPCC.

Most of the patients were from rural areas (74.2%). This is expected in pesticide poisoning in Gharbia-an agricultural governorate-meaning pesticides in general including CPF are more known and easily obtained in rural residences. This was pointed out in a previous study in TUPCC (El-Gharbawy and Emara, 2015).

In the current study, the poor prognosis group had a significantly higher incidence of past medical history (hypertension, diabetes mellitus, and bronchial asthma) compared to the good prognosis group. However, univariate logistic regression showed history of medical illness was not a predictor of poor outcomes. Liu et al. (2020) reported a higher hypertension history in the poor prognosis group as well. A study performed on 71 elderly patients presented with acute OPCs poisoning (1/3 of the cases were CPF) reported higher history of co-morbidities in non-survivors, with chronic kidney disease being the main comorbidity showing statistical difference (Yu et al., 2021). The association between chronic comorbidities and unfavorable outcomes in poisoning, in general, was highlighted in an Ethiopian study (Waktola et al., 2023). In a very recent animal study, CPF induced a more pronounced acute poisoning and 33 % fatality in spontaneously hypertensive rats suggesting an increased susceptibility to acute CPF toxicity in hypertension, and the possibility of hypertensive patients being a high-risk group to worse outcome (Aitken et al., 2024).

Following CPF exposure, clinical signs were typical of cholinesterase inhibition. All patients in the current study were symptomatic. Liu et al (2020) also reported acute cholinergic crises in all the studied subjects. The various manifestations are typical of cholinesterase inhibition and consistent with previous reports both of CPF and OPCs in general, especially the predominance of emesis (Acharya and Panda, 2022; Kothiwale et al., 2019).

The nervous system is the primary target of CPF (Testai et al., 2010). Patients with good prognosis had a median GCS of 15, and poor prognosis group patients had a median of 4 with a statistically significant difference between the two groups. We report low GCS as a predictor of poor outcomes in acute CPF poisoning. This is in agreement with Liu et al., (2020) who reported GCS to be a significant risk factor for mortality in acute CPF poisoning. Acharya and Panda, (2022) reported that CPF cases with the GCS $\geq$ 12 at admission had a good outcome. Several previous studies on acute OPCs poisoning asserted the role of GCS in predicting the outcome (Grmec et al., 2004; Cander et al., 2011; Acikalin et al., 2017, Sontakke and Kalantri, 2023, Oreby and El-Madah, 2017).

Eddleston et al., (2005) attempted to study the differences between different OPCs. Regarding GCS in CPF patients, despite the median for all CPF patients was 15, it was 4 for fatal cases. Davies et al., (2008) emphasized that the specific type of OPCs must be put into consideration and that the predictive power of GCS varied among OPCS. For CPF, GCS less than 13 had a sensitivity of 78% and specificity of 80% in predicting outcome.

Hypotension was significantly higher in poor prognosis patients. Shock and hypotension were reported to be associated with poor outcome in several studies of OPCs (Xu et al., 2023; Dong et al., 2021; Thakur et al., Munidasa et al., 2004). As mentioned earlier, Davies et al., (2008) studied differences between dimethoate, fenthion, and CPF. A systolic blood pressure $\leqslant$100 mmHg in dimethoate had a sensitivity of 69% and specificity 82% in predicting outcome. However, the AUC was 0.81 for dimethoate, and only 0.52 for CPF (Davies et al., 2008).

Pulse and blood pressure abnormalities reflect mixed effects of OPCs on the autonomic nervous system, hypoxia, and hypovolemia. Tachycardia and bradycardia were reported with different predominance in OPCs poisoning in several studies. Bradycardia was reported to predominate by (El-Sheikh et al., 2017) , while tachycardia was the main pulse abnormality in other studies Elmadah et al., Moussa et al., (2018). The current results report pulse as a predictor of outcome, with bradycardia being significantly higher in poor prognosis patients. This is in agreement with a Turkish study reporting bradycardia as an independent predictor for mortality in OPCs patients (Gündüz et al., 2015). On the other hand, the current result disagree with pulse having little value in predicting outcome reported by Davies et al., (2008) even though bradycardia was significantly higher in non-survivors, but pulse exhibited little sensitivity in predicting outcome. It is also important to be careful when interpreting pulse on admission because of prehospital atropine administration. This also applies to pupils. The current results report no significant difference between pupils in both groups agreeing with Davies et al., (2008).

Poor prognosis group patients had a higher median respiratory rate in the current study, but the difference was not statistically significant. This disagrees with the results of Moussa et al., (2018) who reported a statistical difference between respiratory rates in dead and improved patients of acute OPCs. The variable results could be attributed to the cause of tachypnea in patients. Tachypnea resulting from bronchorrhea responds to adequate atropine therapy unlike respiratory abnormalities resulting from neuromuscular junction failure or central respiratory depression that usually requires mechanical ventilation (Eddleston, 2019).

Random blood sugar levels were significantly higher in poor prognosis patients. However, univariate logistic regression revealed that RBS was not a predictor of outcome. Sagah and Elhawary, (2021) recorded a significant positive correlation between hyperglycemia and severity of acute OPCs poisoning, a significant association with intubation, mechanical ventilation and death. The role of acute CPF poisoning on glucose levels needs further studying. Animal studies supported CPF effect on glucose levels. In one study, a single acute administration of CPF caused hyperglycemia (Acker and Nogueira, 2012). However, a meta-analysis of 7 animal studies showed that CPF affected glucose level in a dose-dependent manner. Low doses of CPF caused significant hyperglycemia, and high doses markedly decreased blood glucose levels (Farkhondeh et al., 2020).

Regarding ABG analysis, although serum bicarbonate levels were significantly lower in poor prognosis patients, pH values were not significantly different. This is in disagreement with (Gündüz et al., 2015) who concluded acidosis was an independent predictor of mortality.

Neither urea, creatinine levels, nor CBC analysis showed statistically significant differences between good and poor prognosis patients. Liu et al. reported high blood urea as a significant risk for poor prognosis of CPF. Blood urea nitrogen was not included in the current study since it is not routinely performed taking into consideration the retrospective nature of the current study (Liu et al., 2020).

The mortality rate in the current study was 19.4%. Several studies reported comparable ranges of mortality in CPF (Liu et al., 2020) and OPCs (Peter et al., 2013; Lin et al.; 2007, Ibrahim et al.; 2011, Kothiwale et al., 2019). Wu et al., (2023) reported an overall mortality rate of 14% in all studied patients, 17% mortality of cases of CPF. On the other hand, Eddleston et al., (2005) reported a lower mortality rate for CPF (5.8-10%). There are different reasons for the variable mortality rate in different studies, including time taken for arrival in the hospital, whether any treatment was received prior to arrival at hospital, the degree of awareness regarding the appropriate management of OP poisoning, availability of antidotes, ICU beds, etc.…

In the current study, 32.3 % of the cases needed mechanical ventilation and ICU admission. It is comparable with the results reported in acute CPF poisoning by Acharya and Panda, (2022). Poor prognosis patients consumed significantly higher amounts of atropine and oximes. A study of 50 acute OPCs patients (3 of which were CPF) highlighted the significant difference in amount of oximes too (Lin et al., 2007).

We hope the current study adds to the existing pool of literature regarding the acute poisoning of CPF.

## Conclusion

Acute CPF intoxication can lead to serious morbidity and mortality. The most common presentation among the current patients was vomiting. We report Glasgow coma scale and pulse to be predictors of prognosis in acute CPF toxicity.

## Recommendations

Based on the findings presented in this study, the following recommendations are proposed:

1. Implement protocols to rapidly assess GCS and vital signs in suspected CPF poisoning cases to initiate appropriate and timely interventions. Regular monitoring of GCS and vital signs is crucial to detect any deterioration in the patient's condition early.
2. Strategies to reduce the time between exposure and medical care should be prioritized, including improving transportation and emergency response services in rural areas.
3. Tailored management plans for patients with comorbidities should be developed to mitigate additional risks posed by their underlying health conditions.

Further research is needed to explore the specific mechanisms by which CPF affects different physiological systems and to validate the predictive factors for poor outcomes identified in this study.

## Study Limitation

This study was subject to some limitations. Being a single-center study, the sample size was small. We included patients of CPF poisoning only when it was mentioned in the history taken, or the container brought by the patient or relatives, and when that was documented by the attending physician in the retrieved records.

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# التنبؤ بالنتائج المختلفة عند مرضي التسمم الحاد بالكلوروبيريفوس

فاطمة صبيح[١] و هبه خليفة[١] و يارا عبد الدايم[١]

**الملخص العربي**

**المقدمة**: مركبات الفوسفور العضوية مثل الكلوربيريفوس هي مثبطات قوية لإنزيم الكولينستراز. الكلوربيريفوس هو فوسفات عضوي كلورى واسع النطاق تم طرحه لأول مرة في الأسواق في عام ١٩٦٥.

**الأهداف**: تهدف هذه الدراسة إلى تقييم الخصائص الأساسية والمظاهر السريرية والعوامل النذير للمرضى الذين يعانون من التسمم الحاد بالكلوربيريفوس والتمييز بين أولئك الذين يعانون من نتائج جيدة او سيئة للتسمم وهذه التوقعات بنتائج التسمم تعتمد على الحاجة إلى التهوية الميكانيكية، ودخول وحدة العناية المركزة، والوفيات.

**طريقة البحث**: أجرينا دراسة استرجاعية (بأثر رجعى) من ٣١ مريضا يعانون من التسمم الحاد بالكلوربيريفوس وتم تقسيم المرضى إلى مجموعات ذات نتائج جيدة (ن = ٢١، ٦٧.٨%) ومجموعات ذات نتائج سيئة (ن = ١٠، ٣٢.٢%). تم جمع وتحليل البيانات المتعلقة بالتركيبة السكانية وتفاصيل التعرض والأعراض السريرية والنتائج المختبرية ونتائج العلاج.

**النتائج**: كان متوسط عمر المرضى ٢٨ عامًا، مع غلبة طفيفة للإناث (٥١.٦٪). سريرياً كانت الأعراض الأكثر شيوعاً هي القيء (٨٧.١%)، الإسهال (٨٣.٩%)، زيادة افرازات الصدر (٨٠.٦%)، وهن في العضلات (٥٨.١%)، ضيق إنسان العين (٥٤.٨%). ارتبط سوء التشخيص بشكل كبير بوهن في عضلات الجسم (ع = ٠.٠١٣)، ورعشات طفيفة بالعضلات في الجسم (ع = ٠.٠٢٩)، وانخفاض ضغط الدم (ع = ٠.٠٠١)، وبطء القلب (ع <٠.٠٠١)، وانخفاض درجات مقياس غلاسكو للغيبوبة (ع <٠.٠٠١). كان متوسط مقياس جلاسكو في الحالات هو ٦، مع تناقض شديد بين التشخيص الجيد حيث متوسط مقياس جلاسكو ١٥ ومجموعات التشخيص الضعيفة حيث متوسط مقياس جلاسكو٤ و ظهرت النتائج المختبرية انخفاض مستويات بيكربونات الصوديوم في الدم (ع = ٠.٠٣٠) وارتفاع مستويات السكر في الدم العشوائي (ع = ٠.٠٤١) في المجموعة ذات التشخيص السيئ. كشف تحليل العلاج أن المرضى الذين يعانون من سوء التشخيص يحتاجون إلى كمية أكبر بكثير من الأتروبين والأوكسيمات (قيمة الاحتمال = ٠.٠٠٢ لكل منهما).

**الاستنتاج**: كان مقياس جلاسكو والنبض منبئين هامين بالنتائج لدى المرضى الذين يعانون من التسمم الحاد بالكلوربيريفوس يمكن أن يؤدي التحديد المبكر والعلاج بشكل سريع و فعال لهذه المتنبئات إلى تحسين نتائج المرضى.

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