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# The Potential Role Of Glial Fibrillary Acidic Protein In Evaluation of Organophosphorus- Induced Neurotoxicity: A prospective clinical study

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**Abstract**

**Background:** Organophosphorus compounds (OPC) poisoning leads to several neurotoxic disorders in humans. Glial Fibrillary Acidic Protein (GFAP) released in response to neuronal cell injury and has been used as a sensitive and specific indicator of several neurotoxic conditions, there is no human studies focused on the diagnostic and prognostic value of GFAP in OPC toxicity. Thus, there is a need for studying its role in OPC poisoning. **Objectives:** This study aimed to assess the usefulness of GFAP as early predictor of OPC related neurotoxic disorders both in acute poisoning and chronic exposure and to correlate levels of GFAP with severity of acute OPC poisoning. **Methods:** This is a prospective clinical study that was conducted in Poison Control Center, Ain Shams University Hospitals. The study included 4 groups, control group (23 healthy volunteers), group II acute moderate OPC patients (19 patients), group III acute severe OPC patients (25 patients), and group IV chronic group (41 farmers). All participants were subjected to measurement of GFAP, serum acetylcholine (ACh), serum pseudo cholinesterase (PChE), serum glucose, potassium, serum lactate ,lactate dehydrogenase (LDH), and serum creatine phosphokinase (CPK). **Results:** Serum GFAP and ACh were significantly high in all patient groups compared to the control group, but no significant difference was found between acute moderate and acute severe groups. Also serum PChE had no significant difference between patients of acute moderate and severe groups. Serum glucose, lactate, LDH and CPK were highly significant in acute severe group when compared to acute moderate group. **Conclusion:** Glial Fibrillary Acidic Protein, a biomarker of neurotoxicity, can be used in patients with acute and chronic OPC poisoning as early predictor of OP induced brain cell injury. Serum glucose, lactate, LDH and CPK could be used as simple tools in prediction of severity in acute OP poisoning.

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**Key words** organophosphorus compounds, neurotoxicity, Glial Fibrillary Acidic Protein, acetylcholine, predictor

## Introduction

Organophosphorus compounds represent a large and important class of environmental chemicals. They exert their toxicity through interfering with Ach neurotransmission resulting in accumulation of acetylcholine in cholinergic synapses with subsequent wide range of neurotoxic disorders (Nicolopoulou-Stamati et al., 2016; Jokanović, 2017).

According to the World Health Organization, 3 million cases of pesticide exposure are estimated annually; the majorities of these exposures are caused by OPC and result in more than 250,000 fatalities ( Tripathi S 2014). In 2019, Poison Control Center, Ain Shams University Hospitals (PCC-ASUH), mortality rate estimates due to OPC poisoning represented 23.8% of overall deaths that year (Abdelhamid 2021).

Organophosphate induced brain damage is a progressive damage to the brain, due to cholinergic neurons excitotoxicity resulting from OP-induced irreversible inhibition of acetylcholinesterase (AChE). This secondary neuronal damage occurs in cholinergic regions of the brain which contain dense accumulations of cholinergic neurons (Chen, 2012).

Biomarker levels can predict the degree of neurotoxicity caused by OPC and identify patients who are most likely to develop long term sequelae. These patients may benefit by being targeted for rehabilitation therapy. Elevated biomarker levels may also identify patients who are at a higher risk for secondary deterioration and who would benefit from repeated imaging, monitoring, and increased surveillance (Kochanek et al., 2008).

Glial fibrillary acidic protein (GFAP) has been used as a sensitive and specific indicator of several neurotoxic conditions as stroke and traumatic brain injury (TBI) and due to commercial availability; it had attained a growing attraction in clinical research (Lei et al. 2015; Bernal and Arranz, 2018).

## Subjects and Methods

**Subjects:**

This is a prospective clinical study that was done between the start of January 2019 and the end of February 2020 at the Poison Control Center (PCC), Ain Shams University Hospitals on 108 subjects. 44 adult patients of both sex with acute OP poisoning were included. Patients with coingestion, or those with head trauma, stroke or any neurological diseases and patients who refuse to be enrolled in the study were excluded. The diagnosis of OPC poisoning was established through history of exposure to an OP agent, clinical examination and confirmed by low pseudocholinestrase level. Patients were graded using the modified Dreisbach's classification of severity (Table1).

The studied subjects were divided into the following groups:

Group I (*Control group*): 23 healthy adult volunteers not exposed to OPC.

Group (II): *Acute moderate OPC patients group*: 19 patients moderately intoxicated by OP insecticide.

Group (III): *Acute severe OPC patients group*: 25 patients severely intoxicated by OP insecticide.

Group (IV): *Chronic OPC exposure group*: 41farmers chronically exposed to OPC during their work in the fields with duration not less than 5 years. They were selected from the outpatient laboratory of the PCC.

The classification of the studied subjects summarized in Figure (1).

**Methods**

Detailed history was taken, and then clinical examination, was done to confirm diagnosis and to grade the severity of OP poisoning in acute intoxicated patients. Samples of venous blood were collected from each subject on admission for analysis of GFAP, serum acetylcholine (ACh), serum pseudo cholinesterase (PChE), serum glucose, potassium, serum lactate, lactate dehydrogenase (LDH), and serum creatine phosphokinase (CPK).

An observation sheet was designed for acute OP intoxicated patients; it included demographic data (age, sex, and residence), intoxication data (route, mode of poisoning and delay time), and clinical data in addition to investigational data, and outcome. Patients were observed till recovery, or death.

**Ethical consideration**

A written informed consent was taken from subjects or their guardians for participation in this study. Permission was obtained from institutional ethical committee and the director of PCC-ASU hospitals. Confidentiality of records was maintained through coding numbers,

**Statistical analysis:**

In the present study, all data were statistically analyzed by SPSS software version (21.0). Results were expressed as Mean± standard deviation (SD) Statistical analysis was performed using parametric analysis (ANOVA one-way - Spearman correlation and Chi-Square Test). Significant values were $P< 0.05$ and highly significant at $P < 0.01$.

## Results

In this study, the mean age of patients with acute OP poisoning was 31.68 ± 14.401. Among the 44 patients, 23 were males and 21 females. The majority of patients (50%) were from Cairo followed by Qalioubya 22.7% (Table 2).

Oral route was the commonest (97.7%) and only one patient inhaled OPC, the mode of poisoning was mainly suicidal (95.5%). the mean delay time was 5.28±5.15 hours. There was no significant relation between route, or mode and severity of OP poisoning but delay time had significant relation with severity of OP poisoning (Table 3).

In chronic exposure group the 41farmers were 28-40 years age and all were males. Most of them came from Dakahlia for Agricultural Development Company and the exposure was mainly through inhalation.

The most frequent clinical manifestations among acute OPP patients were small pupils (in 79.5%), vomiting (70.5%), and chest creapitations (54.5%), and the least frequent manifestation was abdominal pain (36.4%). Coma had high significant association with severity of acute OPP, also the presence of fasiculations and chest crepitations showed significant difference between acute moderate and acute severe OPP groups (Table 4).

Serum GFAP and ACh exhibited a significant increase in all patient groups as compared to control group. On the other hand, there was significant low serum pseudo cholinesterase (PChE) level among patient of acute severe and acute moderate groups compared to both control and chronic groups. But no significant difference was detected between acute moderate and acute severe groups as regards serum GFAP, ACh and pseudo cholinesterase level, as shown in (table 5).

Table (6): showed statistically significant low $K^+$ levels among patient of acute moderate and acute severe groups compared to both control and chronic groups but no significant difference was noted between acute moderate and acute severe groups.

Furthermore, markers for systemic functions showed results of serum glucose, lactate, LDH and CPK exhibited significant increase in acute OPs groups when compared to both control and chronic groups. Also high significant differences were found between acute moderate and acute severe groups, as shown in table (6).

As regards GFAP, strong positive correlations were detected between GFAP and acetylcholine as well as CPK and LDH. While strong negative correlations were detected between pseudocholinesterase and the following parameters: GFAP, Lactate, LDH and CPK Figures (2, 3, 4, 5, 6, 7, 8).

Regarding mortality rate it was high, out of 44 cases of acute poisoning groups 18 patient died (40.9%), as shown in table (7).

**Table (1): The severity of poisoning was graded using the modified Dreisbach's classification (Cited in Shaikh et al., 2008).**

| Grade | Manifestation |
|---|---|
| Mild | Nausea, vomiting, diarrhea, sweating |
| Moderate | Salivation, Miosis, Fasciculation,weekness |
| Severe | Incontinence, apneic spells, moist rales,Acute respiratory distress syndrome (ARDS), seizures, coma |

**Table (2): Distribution of demographic variables (age, sex and residence) in the studied patients with acute OP poisoning.**

| **Sociodemographic data** | | Acute OP intoxicated patients |
|---|---|---|
| **Age (year) Mean ± SD** | | 31.68 ± 14.401 |
| | | **No. (%)** |
| **Sex** | **Male** | 23(52.3%) |
| | **Female** | 21(47.7%) |
| **Residence** | **Cairo** | 22(50.0%) |
| | **Fayioum** | 2(4.5%) |
| | **Giza** | 6(13.6%) |
| | **Ismailia** | 1(2.3%) |
| | **Mania** | 1(2.3%) |
| | **Menoufyia** | 1(2.3%) |
| | **Qalioubya** | 10(22.7%) |
| | **Suez Canal** | 1(2.3%) |

**Table (3): The relation between intoxication data and severity in the studied patients with acute OP poisoning.**

| **Intoxication data** | | **Group II** (19 patients) | **Group III** (25 patients) | **P-value** |
|---|---|---|---|---|
| | | **No. (%)** | **No. (%)** | |
| **Mode of poisoning** | Suicidal | 18 (94.7%) | 24 (96%) | 0.842 |
| | Accidental | 1 (5.3%) | 1 (4%) | |
| **Route of exposure** | Oral | 19(100%) | 24(96%) | 0.378 |
| | Inhalation | 0 (0.0%) | 1 (4%) | |
| **Delay time (hours) Mean ± SD** | | 4.4± 2.4 | 5.9 ± 6.5 | 0.040* |

***Group II: acute moderate Group III acute severe, P-value > 0.05: Non-significant; * P-value < 0.05: Significant.***

**Table (4): Chi-Square statistical analysis test comparing clinical manifestations among moderate and severe patients in the present study.**

| **Clinical manifestation** | | **Groups** | | | | | | **Chi-Square** | |
|---|---|---|---|---|---|---|---|---|---|
| | | **Overall patients (No=44)** | | **Group II (No=19)** | | **Group III (No=25)** | | | |
| | | **No** | **%** | **No** | **%** | **No** | **%** | **$X^2$** | **P-value** |
| **Coma** | **No** | 23 | 52.3% | 19 | 100 | 4 | 16 | 30.532 | **0.00**** |
| | **Yes** | 21 | 47.7 | 0 | 0.0 | 21 | 47.7 | | |
| **Fasciculations** | **No** | 24 | 54.5 | 7 | 36.8 | 17 | 68 | 4.227 | **0.040*** |
| | **Yes** | 20 | 45.5 | 12 | 63.2 | 8 | 32 | | |
| **Crepitations** | **No** | 20 | 45.5 | 12 | 63.2 | 8 | 32 | 4.227 | **0.040*** |
| | **Yes** | 24 | 54.5 | 7 | 36.8 | 17 | 68 | | |
| **Weakness** | **No** | 24 | 54.5 | 8 | 42.1 | 16 | 64 | 2.087 | 0.149 |
| | **Yes** | 20 | 45.5 | 11 | 57.1 | 9 | 36 | | |
| **Pupils** | **constricted** | 10 | 22.7 | 6 | 31.6 | 7 | 28 | 3.650 | 0.302 |
| | **normal** | 6 | 13.6 | 3 | 15.8 | 3 | 12 | | |
| | **PPP** | 25 | 56.8 | 10 | 52.6 | 15 | 60 | | |
| **Vomiting** | **No** | 13 | 29.5 | 3 | 15.8 | 10 | 40 | 3.040 | 0.081 |
| | **Yes** | 31 | 70.5 | 16 | 84.2 | 15 | 60 | | |
| **Diarrhea** | **No** | 23 | 52.3 | 9 | 47.4 | 14 | 56 | 0.322 | 0.570 |
| | **Yes** | 21 | 47.7 | 10 | 52.6 | 11 | 44 | | |
| **abdominal pain** | **No** | 28 | 63.6 | 9 | 47.4 | 19 | 76 | 3.824 | 0.051 |
| | **Yes** | 14 | 36.4 | 10 | 52.6 | 6 | 24 | | |

***Group II: acute moderate***
***Group III: acute severe***

***-X2: Chi-square statistical analysis test, No: number, P-value > 0.05: Non-significant, * P-value < 0.05: Significant, **P-value < 0.01: Highly significant***

**Table (5): Differences in the studied parameters (GFAP, Acetylcholine, Pseudo cholinesterase) among all groups.**

| | | Control group | Acute moderate | Acute severe | Chronic | Test value• | P-value | Sig. |
|---|---|---|---|---|---|---|---|---|
| | | No.= 23 | No.= 19 | No.= 25 | No.= 41 | | | |
| GFAP (ng/ml) | Mean±SD<br>Range | 2.35±0.49<br>1.5 – 3 | 10.68±3.71<br>6.1 – 20 | 12.25±4.93<br>5.5 – 23 | 13.44±3.79<br>6.51 – 22 | 48.011 | 0.000 | HS |
| Acetylcholine (ug/dl) | Mean±SD<br>Range | 6.10±0.82<br>4.6 – 8 | 21.42±8.36<br>6 – 35 | 22.18 ± 6.82<br>10.5 – 40 | 27.27±4.96<br>14.5 – 36 | 69.231 | 0.000 | HS |
| Pseudochol (U/L) | Mean±SD<br>Range | 8618.35±1446.79<br>6100 – 11200 | 636.58±158.54<br>338 – 950 | 688.40±228.33<br>300 – 1230 | 8332.80±1544.37<br>5349 – 11488 | 381.438 | 0.000 | HS |

**Post hoc analysis using LSD test**

| Parameters | P1 | P2 | P3 | P4 | P5 | P6 |
|---|---|---|---|---|---|---|
| GFAP | 0.000 | 0.000 | 0.000 | 0.164 | 0.008 | 0.208 |
| Acetylcholine | 0.000 | 0.000 | 0.000 | 0.662 | 0.000 | 0.001 |
| Pseudochol | 0.000 | 0.000 | 0.352 | 0.885 | 0.000 | 0.000 |

***P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant (HS), •: One Way ANOVA followed by post hoc analysis using LSD test, P1: Control vs Acute moderate, P2: Control vs Acute severe, P3: Control vs chronic, P4: Acute moderate vs Acute severe, P5: Acute moderate vs chronic, P6: Acute severe vs chronic, GFAP: Glial fibrillary acidic protein, Pseudocho.: pseudo cholinesterase No.: Number, Sig.: significant, HS: highly significant***

**Table (6): Differences in the studied parameters (Glucose, K, Lactate, LDH, CPK) among all groups.**

| | | Control group | Acute moderate | Acute severe | Chronic | Test value• | P-value | Sig. |
|---|---|---|---|---|---|---|---|---|
| | | No.= 23 | No.= 19 | No.= 25 | No.= 41 | | | |
| Glucose (mg/dl) | Mean±SD<br>Range | 107.70 ± 21.17<br>78 – 153 | 158.42 ± 16.77<br>130 – 190 | 205.72 ± 86.69<br>94 – 418 | 108.41 ± 27.69<br>75 – 220 | 27.511 | 0.000 | HS |
| $K^+$ (mEq/L) | Mean±SD<br>Range | 4.31 ± 0.43<br>3.8 – 5 | 3.32 ± 0.50<br>2.6 – 4.2 | 3.48 ± 0.59<br>2.3 – 4.6 | 4.22 ± 0.37<br>3.6 – 4.9 | 29.333 | 0.000 | HS |
| Lactate (mg/dl) | Mean±SD | 1.60 ± 0.35 | 3.06 ± 1.60 | 4.64 ± 0.92 | 1.72 ± 0.54 | 70.022 | 0.000 | HS |
| | Range | 0.9 – 2.1 | 0.9 – 5.8 | 3.1 – 6.7 | 0.8 – 3.3 | | | |
| LDH (U/L) | Mean±SD | 302.39 ± 48.93 | 495.05 ± 171.37 | 873.68 ± 335.22 | 323.49 ± 65.42 | 56.354 | 0.000 | HS |
| | Range | 226 – 396 | 309 – 890 | 448 – 1823 | 166 – 492 | | | |
| CPK (U/L) | Mean±SD | 118.09 ± 31.47 | 200.95 ± 32.88 | 254.64 ± 81.02 | 151.32 ± 32.99 | 38.407 | 0.000 | HS |
| | Range | 84 – 224 | 150 – 273 | 165 – 487 | 85 – 210 | | | |

**Post hoc analysis using LSD test**

| Parameters | P1 | P2 | P3 | P4 | P5 | P6 |
|---|---|---|---|---|---|---|
| Glucose | 0.001 | 0.000 | 0.953 | 0.001 | 0.000 | 0.000 |
| K | 0.000 | 0.000 | 0.452 | 0.249 | 0.000 | 0.000 |
| Lactate | 0.000 | 0.000 | 0.602 | 0.000 | 0.000 | 0.000 |
| LDH | 0.001 | 0.000 | 0.657 | 0.000 | 0.001 | 0.000 |
| CPK | 0.000 | 0.000 | 0.010 | 0.000 | 0.000 | 0.000 |

***P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant, •: One Way ANOVA followed by post hoc analysis using LSD test, P1: Control vs Acute moderate, P2: Control vs Acute severe, P3: Control vs chronic, P4: Acute moderate vs Acute severe, P5: Acute moderate vs chronic, P6: Acute severe vs chronic, Na: Sodium, K: Potassium, No.: Number, Sig.: significant***

**Table (7): The outcome in the studied patients with acute OP poisoning.**

| Outcome | No. | % |
|---|---|---|
| **Survival** | 26 | 59.1% |
| **Death** | 18 | 40.9% |

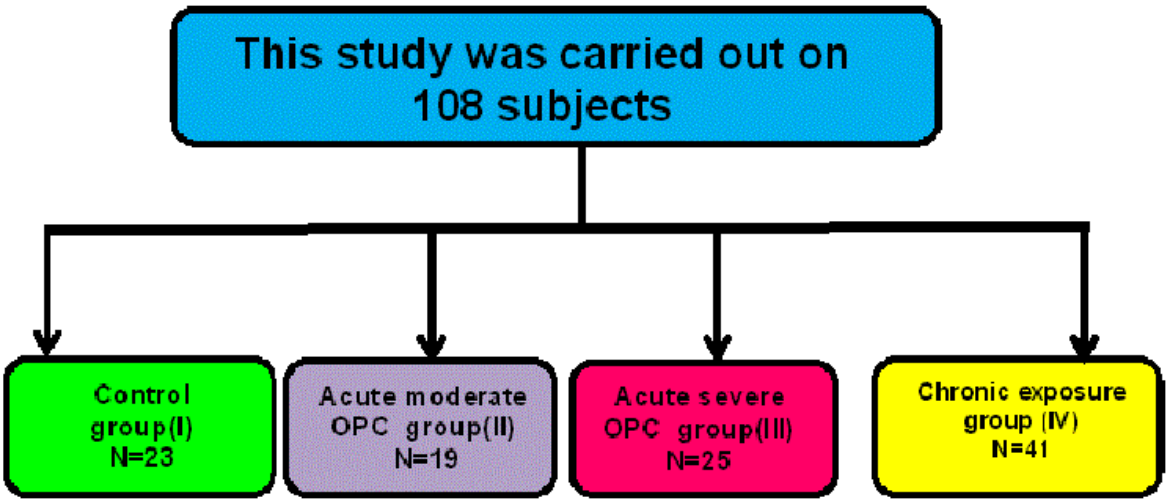


**Figure (1): The classification of the studied subjects.**

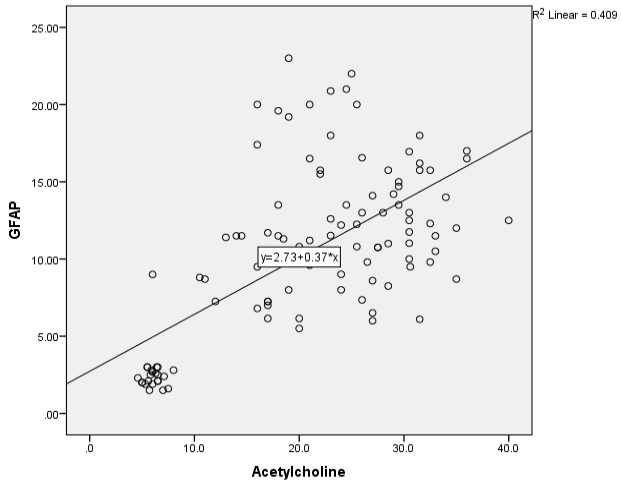


**Figure (2): Strong positive correlation between serum GFAP and Acetylcholine in all patient groups.**

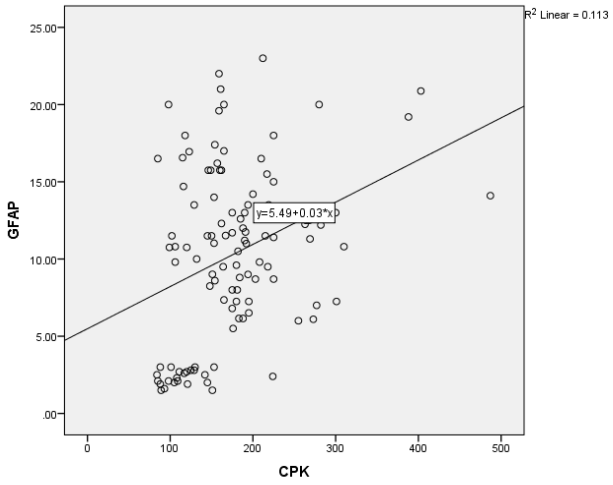


**Figure (3): Strong positive correlation between serum GFAP and CPK in all patient groups**

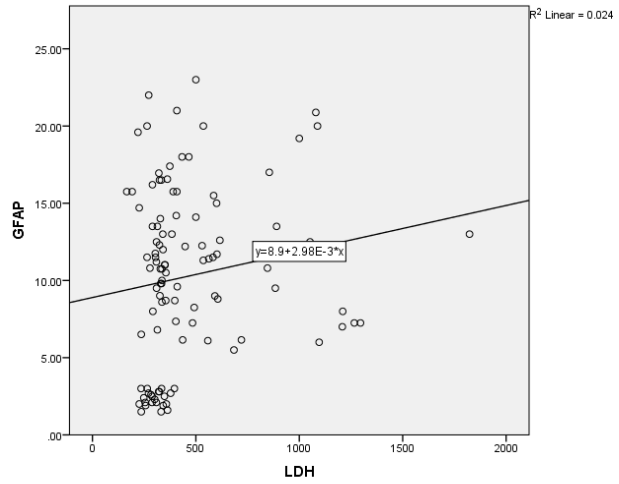


**Figure (4): Strong positive correlation between serum GFAP and LDH in all patient groups.**

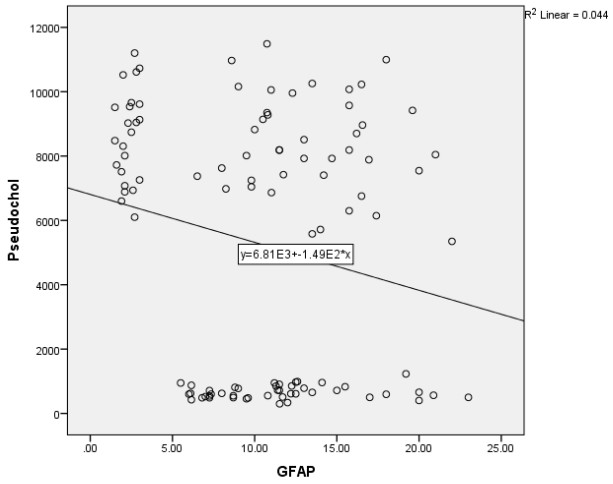


**Figure (5): Strong negative correlation between serum PChE and GFAP in all patient groups**

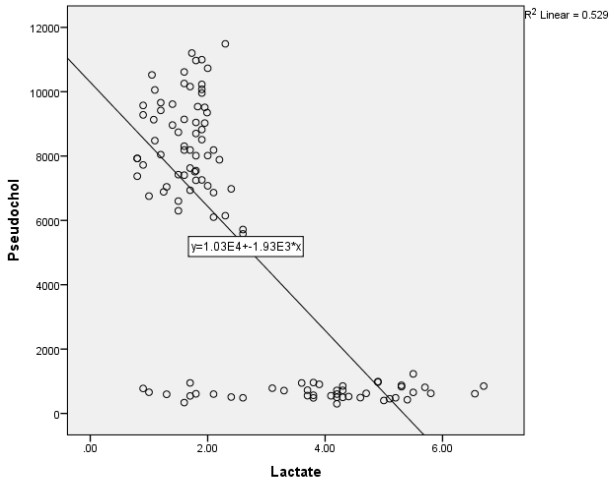


**Figure (6): Strong negative correlation between serum PChE and Lactate in all patient groups.**

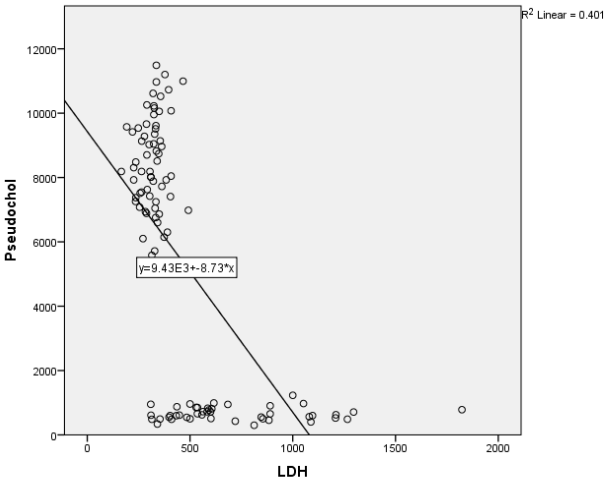


**Figure (7): Strong negative correlation between serum PChE and LDH in all patient groups.**

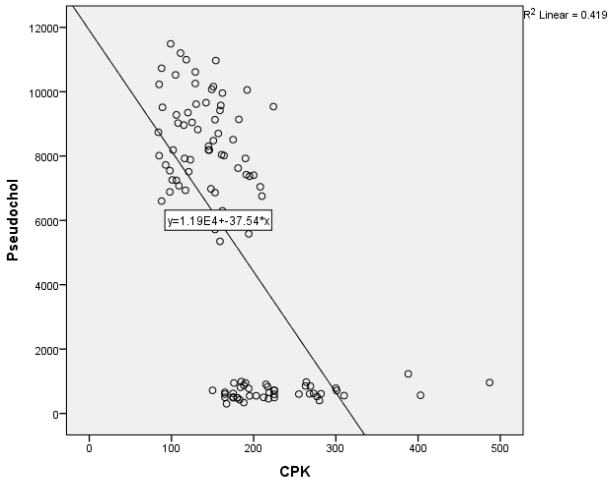


**Figure (8): Strong negative correlation between serum PChE and CPK in all patient groups.**

## Discussion

Organophosphorus compounds, the most widely used insecticides, may cause serious poisoning and even death especially in developing countries. There effects are primarily neurotoxic, AChE inhibition is the main mechanism of toxicity resulting in accumulation of Ach which cause overstimulation of muscarinic and nicotinic receptors with subsequent disruption of transmission of nerve impulse in both central and peripheral nervous systems (Joshi et al.,2005).

In the present study the mean age for the patients was 31.68±14.40. Similar finding was reported by Ahmed et al., (2014) and Banday et al., (2015) In this study males were affected more than females. This was in agreement with many other studies (Jayawardane et al., 2012; Ahmed et al., 2014 & Sumathi et al., 2014).

Half of patients in the current study were from Cairo followed by Qalioubya (22.7%). This could be attributed to near distance to PCC-ASU and presence of toxicologists in other governorate.

In this study majority of patients (97.7%) were exposed to the OPC through ingestion, while only one patient through inhalation. This was similar to results of Bilal et al., (2014), ÇOLAK et al., (2014), and Priyadarsini et al., (2015). This is could be due to easy ingestion of poison especially with liquid form of OPC (Coskun et al, 2015).

Majority of patients in the current study (95.5%) were intoxicated intentionally. These results similar to Ali et al., (2012), Hassan and Madboly, (2013), Banday et al., (2015). It could be due to easy availability, low cost, lack of rules regarding usage and sale of these compounds.

In the current study there was no significant relation between route and mode of intoxication as regard the severity of cases. In contrast Amir et al., (2020) who stated that mortality in OP toxicity, depend upon route of poisoning. This could be attributed to that almost all of acute patients in this study had the same route and mode of poisoning.

In this study there was significant relation between the delay time and severity of OP poisoning. Parate et al., (2016), also found significant relation between the delay time and the outcome.

In the present study the most frequent clinical manifestations were small pupils in 79.5% which

include pin point pupil in 56.8% and constricted pupil in 22.7% followed by vomiting in 70.5% and chest crepitation in 54.5%.

This was in agreement with Banday et al., (2015) who found that miosis was the most presenting manifestation .Also in studies by Banerjee et al.,(2012) & rehiman et al., (2008) the vomiting was the most common symptom and miosis was the most common sign in acute organophosrous intoxicated patient.

There was significant relation between severity and clinical features of coma, fasciculation and chest crepitations. This was in accordance with Amir et al., (2020) who reported that development of fasciculation or impaired consciousness in organophosphrous poisoned patient carried a poor prognosis.

Previous studies highlight the neurotoxic consequences of acute pesticide exposure which associated with a wide range of symptoms as well as abnormalities in nerve function and deficits in neurobehavioral performance and may be accompanied by increased risk of neurodegenerative diseases (Kamel and Hoppin, 2004).

The present study showed serum mean GFAP was significantly high in all patient groups compared to the control group. Similarly, Lim et al. (2011) found significant increase in GFAP expression in hippocampus of albino rats exposed to chronic chlorpyrifos administration without inhibiting serum cholinesterase.

Various clinical investigation in other studies clarified that level of GFAP was considered as informative biomarker for brain injury (Borg et al. 2012 Akdemir et al., 2014, Di Battista et al., 2015).

GFAP is a cytoplasmic filament protein released in response to neuronal cell injury, it is expressed by several cells in central nervous system (CNS) as astrocytes and ependymal cells (Akdemir et al., 2014). In the CNS, astrocytes become reactive due to trauma, infection, and chemical insults. Since GFAP is a marker protein of astrocytes, it is upregulated in many neurological diseases such as ischemic stroke, neuroinflammation, TBI, neurodegeneration and other diseases in the CNS (Li et al., 2020). Reactive astrogliosis, a process by which astrocytes respond to all CNS insults, has emerged as a pathological hallmark of CNS lesions (Sofroniew, 2009). This coincide with the findings of Liu et al. (2012) who discovered that astroglial activation, characterized by elevated GFAP protein within 24 hours and sustained for up to 7 days, preceded OP-induced brain injury.

An experimental study done by Badawy et al. (2017), which demonstrated the histopathological effects of OPC on the brains of albino rats. They found longer and more numerous astrocytic processes in the brain tissues of OP-treated albino rats with high levels of GFAP compared to controls.

Fodale et al., (2006) reported that accumulation of Ach in acute OP poisoning evokes the muscarinic and nicotinic receptors lead to increase in the oxidative stress and free radicals generation. This process exhausted the nervous cells and may even degenerate them or increase cell membrane permeability causing damage of blood brain barrier (BBB). Leakage of GFAP from astrocytes to the interstitial fluid then to blood may be helpful in detecting the degree of degeneration in CNS.

The present study showed serum acetylcholine was significantly elevated in all patient groups compared to controls. Once acetylcholinesterase (AChE) has been inactivated by OPC, ACh accumulates throughout the nervous system, resulting in over stimulation of muscarinic and nicotinic receptors (Hundekari et al., 2012, Prabodh et al., 2012 and Cupic Miladinovic et al., 2018).

The present study showed significant low serum pseudo cholinesterase level (PChE) among patient of acute OPP groups compared to control and chronic groups. But no significant difference was detected between acute moderate and acute severe groups as regards pseudo cholinesterase level.

Abd Alkareem M., et al., (2019) agreed with the current study as regard no significant correlation to the grade of severity. Similarly. Singh (2004) and Cherian et al. (2005) found that pseudocholinesterase level is a marker of OP exposure, however not an indicator of OP toxicity severity.

In contrast, Muley etal. (2014) and Tripathi (2014), concluded that low PChE level was associated with both higher mortality and higher degree of severity.

The present study showed serum glucose was significantly high in acute OP groups compared to controls. Similarly, serum glucose was significantly high in acute severe group compared to acute moderate group.

Panda et al., (2014) agreed with the current study regarding the correlation between the severity of OPC and high glucose levels. At the time of admission, a patient's glycemic status may help determine the severity of OPC. Also Rao and Raju, (2016) discovered that levels of glucose greater than 200 mg/dl were reliable parameters for predicting mortality and the need for ventilator support, and that hyperglycemia on admission was correlated with the severity of the cases.

Hyperglycemia induced by insecticide poisoning could be explained by elevation of counter-regulatory hormones (catecholamine and cortisol), which reduces a person's sensitivity to insulin and results in elevated blood sugar, which is further exacerbated by excessive adrenergic influence on glycogenolysis leading to hyperglycemia (Amanvermez et al., 2010).

In the current study, patients in the acute severe and acute moderate groups had significantly lower K+ levels than those in the control and chronic groups; however, no significant difference was found between the acute moderate and acute severe groups.

Hypokalemia and paralysis are potentially reversible medical emergencies. In addition, hypokalemia may aggravate muscular weakness due to inhibition of AChE by OP poisoning (Tripathy et al., 2018).

These results were in a good agreement with Salameh et al. (2008) who found a decrease in serum potassium level in acute OPP. Hypokalemia could be

attributed to sympathetic over activity in OPP or as a result of pancreatitis. Also, severe vomiting and diarrhea can lead to hypokalemia.

In the current study, serum lactate was significantly high in both acute moderate and acute severe groups when compared to control group as well as chronic group. In addition, high significant difference was noted between acute moderate and acute severe groups.

This was in agreement with Maignan et al. (2014), who stated that, some indicators such as toxicological history and serum lactate level, proved to be useful to distinguish between low and high acuity poisoned patients with deliberate poisoning, in order to avoid excessive morbidity.

Similarity, Blood lactate levels were considered as a high-risk factor that affect the prognosis of acute OPP (Tang et al., 2016; Wu, Xie, Cheng, & Guan, 2016). Also, Arafa et al. (2017) who correlated lactate levels with severity of acute OPC poisoning. They found that strong positive correlation between serum lactate and severity of poisoning.

In the present study, the mean serum LDH was significantly high in acute moderate group as well as acute severe group when compared to chronic group and controls. Also, there was highly significant difference between acute moderate and acute severe groups.

This was similar to Panda et al., (2014), Coskun et al., (2015) and Gündüz et al., (2015) who found that LDH levels positively correlated with severity of poisoning and can be used as a predictor of severity and mortality.

The LDH elevation in case of cholinesterase inhibitors poisoning may be attributed to muscle injury or to insecticide induced oxidative tissue injury that lead to functional impairment in cardiac and skeletal muscle, liver, kidney and red blood cells (Panda et al., 2014 and Coskun et al., 2015).

Regarding results of serum CPK in different groups. A significant difference was observed in chronic group when compared to the control group. High significant differences were observed in acute moderate group and acute severe group when compared to the control group. Acute moderate group and acute severe group displayed highly significant differences when compared with the chronic group. The mean serum CPK in acute severe group was significantly high when compared with acute moderate group.

These results are in good agreement with Arafa et al. (2017) who discovered a positive correlation between initial CPK levels and the severity of the OP poisoning, with CPK levels rising in tandem with severity. Similarly, a study done by Bhattacharyya et al. (2011) on acute OPP patients who found that serum CPK was significantly increased with the increase in the severity grade of OPP compared to control group.

On the other hand, Khan et al., (2016) and Gündüz et al., (2015) discovered that there was no significant correlation between CPK levels and patients' severity or mortality.

Regarding outcome, the mortality rate in this study was 40.9%, this high mortality rate could be due to that patients with severe OP poisoning was the largest group in acute intoxication. Mortality rate estimates in OP toxicity range from 5%-35% but severe OP toxicity had mortality rate of about 50% even in young cases (Amir et al., 2020).

## Conclusion

The study clarified that Glial fibrillary acidic protein (GFAP), a biomarker of neurotoxicity, was significantly high in both acute OP poisoning and chronic OP exposure, and can serve as predictor of OPC related neurotoxic disorders. Glucose, lactate, LDH and CPK are easily available simple tools that can be used as markers of severity in acute OP intoxicated patients.

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# الدور المحتمل للبروتين الحمضي الليفي الدِبقي في تقييم السمية العصبية للمبيدات الفسفوريه العضوية

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## الملخص العربى

**الخلفيه العلمية:** يؤدي التسمم بالمركبات الفوسفورية العضويه الى العديد من الاضطرابات السمية العصبية لدى الانسان. ولقد تم استخدام البروتين الحمضي الليفي الدبقي كمؤشر حساس ومتخصص للعديد من الامراض العصبية ولا توجد دراسات بشريه للقيمه التشخيصيه والتنبؤيه للبروتين الحمضي الليفي الدبقي في التسمم بالمركبات الفوسفورية العضويه لذا تزداد الحاجه لدراسه دوره في السميه بالمركبات الفوسفورية العضويه.

**الهدف من البحث:** تقييم فائدة البروتين الحمضي الليفي الدبقي كأداة للتنبؤ المبكر باضطرابات السمية العصبية الناتجه عن المركبات الفوسفورية العضويه في كل من التسمم الحاد والمزمن وعلاقه مستويات البروتين الحمضي الليفي الدبقي بشدة التسمم الحاد لمركبات الفوسفوريه العضويه

**طُريقه البحث:** دراسه اكلينيكيه مستقبليه أجريت بمركز علاج التسمم بمستشفيات جامعة عين شمس. تضمنت الدراسه اربع مجموعات. المجموعة الأولى المجموعه الضابطة التى ضمت ٢٣ متطوعًا صحيًحا والمجموعة الثانية الحادة المعتدلة و ضمت ١٩ مريضاًوالمجموعة الثالثة الحادة الشديده و ضمت ٢٥ مريضاً. بالإضافة الى المجموعة الرابعة التى ضمت ٤١ مزارع من المعرضين لمركبات الفسفور العضوي بشكل مزمن . وقد تم سحب عينات الدم من جميع الافراد عند حجزهم بالمركز لقياس مستوي البروتين الحمضي الليفي الدبقي، أسيتيل كولين ا انزيم السودو كولين، الكرياتين فسفوكيناز، اللاكتات ديهدروجيناز ولاكتات فى الدم بالإضافة الى الجلكوز والبوتاسيوم

**نتائج البحث:** وكشفت الدراسة عن وجود فروق ذات دلالة إحصائية عالية بين البروتين الحمضي الليفي الدبقي والأستيل كولين في جميع مجموعات المرضى عند مقارنتها بالمجموعة الضابطة ومن ناحية أخرى، لم يظهر انزيم السودو كولين اى فرق احصائي بين المجموعات الحادة الشديده والحادة المعتدلة. كما زادت ارتفاع مستويات (الاكتات ومستوي الجلوكوز ومستوى اللاكتات ديهدروجيناز ومستوى الكرياتين فسفوكيناز) في الدم في المجموعة الحادة الشديده بشكل احصائي ملحوظ مقارنة بالمجموعة الحادة المعتدلة.

**الاستنتاج:** لقد تم استنتاج أن البروتين الحمضي الليفي الدبقي ذو الدلاله للتسمم العصبى يمكن استخدامه في مرضى التسمم الحاد والمزمن بالمركبات الفوسفوريه العضويه كعلامه مبكرة في إصابة الخلايا العصبية ووجد أن الجلوكوز واللاكتيت والاكلات ديهدروجينيز والكراتين فسفوكينيز في الدم علامات مختبرية بسيطه وجيدة لتشخيص شدة التسمم بمركبات الفوسفورية العضويه في مرضى التسمم الحاد.

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