AIM OF THE WORK

The aim of the present study was to investigate the validity of some indices as probable markers of severity in poisoning with cholinesterase enzyme inhibitors (CEIs) insecticides.

SUBJECTS

Sixty patients with acute cholinesterase enzyme inhibitors poisoning, admitted to the Department of Emergency Medicine or Poison Unit, Alexandria University Hospital, within 6 hours of exposure to the poison without receiving any prior treatment were included in the study. It was a prospective and observational study conducted from November 2013 to November 2014. All Subjects with any of the following criteria were excluded from the study:

1. Myopathy.
2. Chronic renal disease.
3. Epilepsy, known psychiatric illness.
4. Receiving frequent or regular intramuscular (I/M) injections.
5. Myocardial infarction, myocarditis.
6. Trauma.
7. Malignancy.
8. Autoimmune diseases.
9. Overwhelming sepsis.
10. Medications like statins, fibrates, aspirin, anticoagulants, frusemide, and dexamethasone.

METHODS

All the patients were subjected to: (Appendix)

1. Full clinical examination to assess clinical severity according to Peradeniya Organophosphorus Poisoning (POP) scale [75].
2. Serum creatine phosphokinase (CPK) levels [76].
3. Arterial blood gases including the pH [77].
4. Serum cholinesterase enzyme level [77].

All the above indices were measured on admission and then re-evaluated before discharge. All patients undergone standard treatment for CEIs inhibitors but the intramuscular injections were avoided during the course of treatment.

Informed consent was obtained from all participants who will be included in the study or from their families explaining the aim and the procedure of the study.

Complete confidentiality was insured all through the study procedure.

The approval of the local Ethical Committee of Alexandria Faculty of Medicine will be taken.

1. Assessment of the clinical severity:

Clinical severity was categorized according to Peradeniya organophosphorus poisoning (POP) scale as shown in the following **Table** [75]. Patients who had history of any kind of illnesses like myopathy, chronic renal disease, epilepsy, known psychiatric illness, receiving intramuscular (I/M) injections, myocardial infarction, myocarditis, cardiopulmonary resuscitation, trauma, malignancy, autoimmune diseases, overwhelming sepsis, or on medications like statins, fibrates, aspirin, anticoagulants, frusemide, and dexamethasone were excluded from the study.

Table (VII): The Peradeniya organophosphorus poisoning scale [75]

Parameters	Criteria	Score
Pupil size	≥2 mm <2 mm Pinpoint	0 1 2
Respiratory rate	<20/min ≥20/min ≥20/min with central cyanosis	0 1 2
Heart rate	>60/min 41–60/min <40/min	0 1 2
Fasciculation	None Present, generalized/continuous Both generalized and continuous	0 1 2
Level of consciousness	Conscious and rationale Impaired response to verbal commands No response to verbal commands	0 1 2
Seizures	Absent Present	0 1

Note: 0–3, mild poisoning; 4–7, moderate poisoning; 8–11, severe poisoning.

Sample was collected aseptically by a single prick after initial resuscitation, from a peripheral vein without tying any tourniquet. The levels of serum CPK, serum cholinesterase, and pH were measured following admission.

2. Measuring the creatine phosphokinase (CPK):[76]

a) Device used: Dimension® RXL Max, Germany, using Siemens Chemistry autoanalyzer, and Dimension® (Clinical chemistry system) Flex® reagent cartridge.

b) Test principle (Spectrophotometric assay): In a coupled enzyme reaction, the creatine kinase in patient samples catalyzes the transphosphorylation of phosphate from creatine phosphate to adenosine diphosphate (ADP) producing adenosine triphosphate (ATP). Hexokinase (HK) phosphorylates glucose from the ATP to phosphorylate glucose. The resulting glucose-6-phosphate is oxidized by glucose-6-phosphate dehydrogenase (G-6-PDH) with the simultaneous reduction of nicotinamide adenine dinucleotide phosphate (NADP). The rate of formation of NADPH is directly proportional to the CK activity in the sample and is measured bichromatically at 340 and 540 nm.

$$\text{Creatine phosphate} + \text{ADP} \xrightarrow{\text{CK}} \text{Creatine} + \text{ATP}$$

$$\text{ATP} + \text{D} - \text{glucose} \xrightarrow{\text{HK}} \text{ADP} + \text{G6P}$$

$$\text{G6P} + \text{NADP}^+ \xrightarrow{\text{G6PDH}} \text{D} - 6 - \text{phosphogluconate} + \text{NADPH} + \text{H}^+$$

CPK was measured by spectrophotometric methods [77]. The normal value of serum CPK is taken to be 39-308 U/L for males and 26-192 U/L for females [78].

Specimen collection and preparation: 3 ml of whole blood (drawn under complete aseptic conditions) was centrifugated to separate serum. Grossly hemolyzed samples were not used with the CPK method.

3. Measuring plasma cholinesterase (PchE):[79]

a) Device used: Cholinesterase BTC/DTNB, MINDRAY BS-300 analyzer (REF: PCB260), IVD, CE, Melano, Italy.

b) Test principle (Colorimetric assay):

The cholinesterase present in the serum catalyzes the hydrolysis of the butyrrilthiocholine (BTC), forming butyrate and thioholine. The thiocholine reduces the exacyanoferrate (III) to exacyanoferrate (II). The decrease of absorbance in the unit time at 405 nm is proportional at the activity of the cholinesterase in the sample.

Reference values: normal serum cholinesterase (4900 – 11900 U/L).[79]

During the course of treatment, IM injections were avoided. Patients were treated with 2-PAM (adult dose is 1–2 g intravenously followed by 0.5 g/hour infusion) and initial dose of injection atropine 2 mg followed by bolus every 5–10 min or as infusion until the

signs of "atropinization" occurred, i.e., heart rate>80/min and dilatation of initially constricted pupil.[80]

The total dose of atropine (mg) until the final clinical outcome (complete recovery or death) was calculated for each patient. Just before discharging the patients from our hospital, the levels of serum CPK was re-evaluated and the responses were tabulated. Plasma cholinesterase activity (reference range 4900-11900 U/L) was measured [80].

GraphPad QuickCalcs software (Graphpad Software Inc., La Jolla, CA, USA) and MS Excel 2007 were used for statistical analysis. For the description of data, mean values, percentages and standard deviations were used. Student's t-test and Pearson's Correlation coefficient were used for the assessment of statistical significance. Informed consent was obtained from all participants who were included in the study or from their families explaining the aim and the procedure of the study. Complete confidentiality was insured all through the study procedure.

RESULTS

The current study was conducted on sixty patients poisoned with acute cholinesterase enzyme inhibitors insecticides, admitted to the Poison Unit of Alexandria Main University Hospital, within 6 hours of exposure to the poison without receiving any prior treatment. (Carbamate cases were excluded according to the clinical presentation). The current study was conducted during a period of one year, starting from the first of November 2013 until the 31st of October 2014.

A) Demographic data:

1. Age and gender:

Table VIII and figure 6 show the age distribution of the studied patients in relation to gender, the total patients age ranged from 18 – 52 years with a mean of 31.7 ± 10.1 years. Twenty patients were in the age group of 15 – 24 years (13 males [31%], 7 females [38.9%]), 19 patients were in the age group of 25 – 34 years (15 males [35.7%], 4 females [22.2%]), 11 patients were in the age group of 35 – 44 years (7 males [16.7%], 4 females [22.2%]), 10 patients were in the age group of 45 – 54 years (7 males [16.7%], 3 females [16.7%]). There was no statistically significant difference between males and females regarding the age (χ^2 = 28.492, P = 0.33; t-test = 0.279, P = 0.78).

Table (VIII): Distribution of patients with cholinesterase inhibitors insecticides toxicity according to the age in relation to gender (n=60).

Age group (Years)	Male		Female		Total	
	No.	%	No.	%	No.	%
15 - 24	13	31.0	7	38.9	20	33.3
25 - 34	15	35.7	4	22.2	19	31.7
35 - 44	7	16.7	4	22.2	11	18.3
45 - 54	7	16.7	3	16.7	10	16.7
χ^2	28.492					
P	0.33					
Min. - Max.	19 - 52		18 - 49		18 - 52	
Mean ± SD	31.9 ± 9.7		31.1 ± 11.2		31.7 ± 10.1	
Median	30		31		30	
t-test	0.279					
P	0.78					
Total	42	70	18	30	60	100

χ^2; value of Chi-Square test. P; value of significance, considered significant if ≤ 0.05.
S.D. Standard of Deviation.

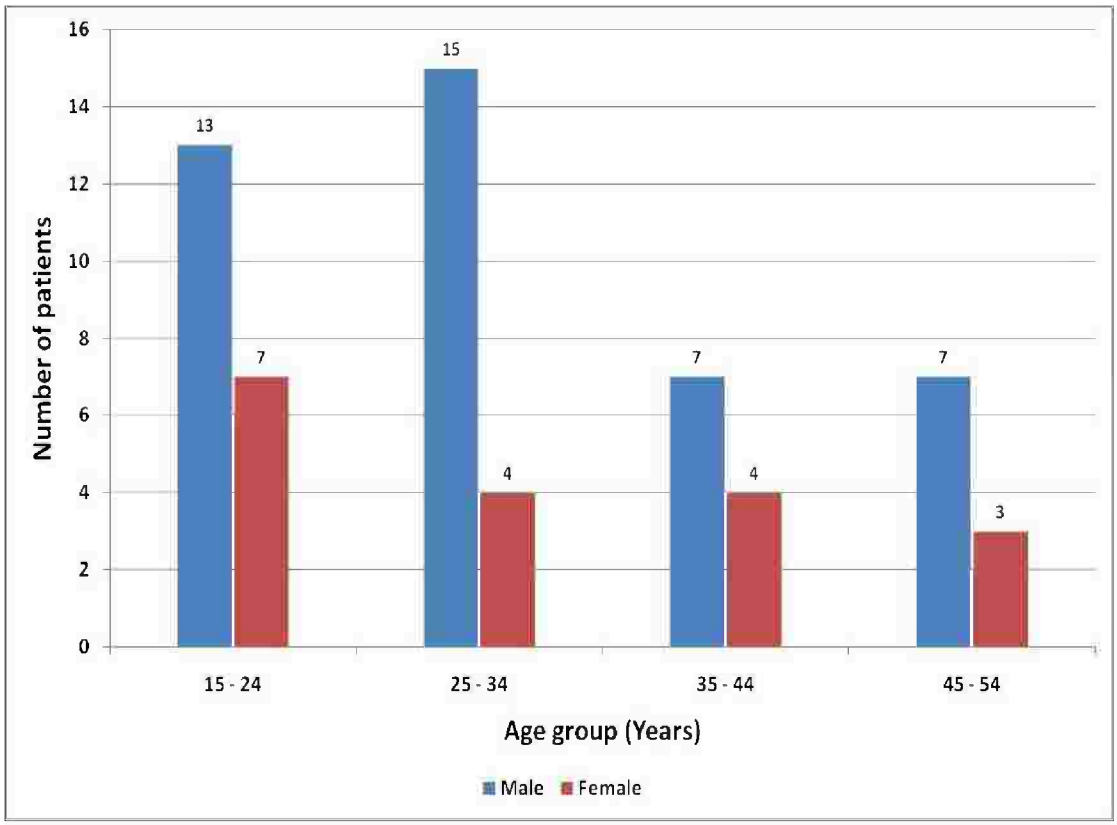

Figure 6. Distribution of patients with cholinesterase inhibitors insecticides toxicity according to the age in relation to gender (n=60).

2. Marital status:

Table IX and figure 7 show the distribution of patients with cholinesterase inhibitors insecticides toxicity according to marital status. Single patients were 18 (11 males [18.3%] and 7 females [11.7%]), married patients were 20 (16 males [26.7%] and 4 females [6.7%]) and divorced patients were 22 (15 males [25%] and 7 females [11.7%]). There was no statistically significant difference between males and females regarding the marital status ($\chi^2 = 3.215$, P = 0.20).

Table (IX): Distribution of patients with cholinesterase inhibitors insecticides toxicity according to marital status in relation to gender (n= 60).

Marital status	Male		Female		Total	
	No.	%	No.	%	No.	%
Single	14	23.3	4	6.7	18	30
Married	11	18.3	9	15.0	20	33.3
Divorced	17	28.3	5	8.3	22	36.7
χ^2	3.215					
P	0.20					
Total					60	100

χ^2; value of Chi-Square test. P; value of significance, considered significant if ≤ 0.05.

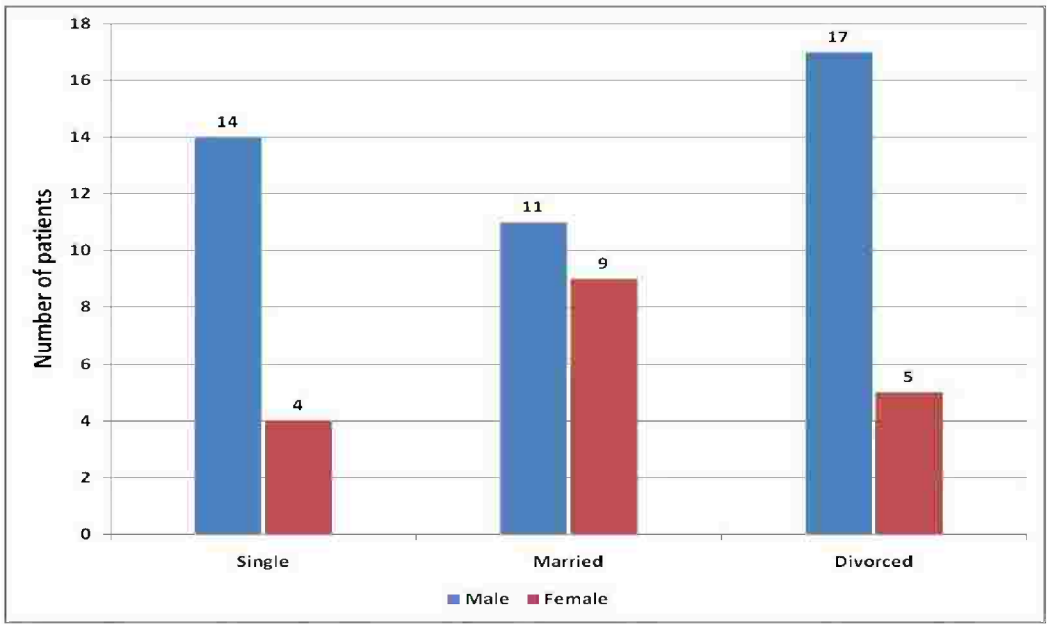

Figure 7. Distribution of patients with cholinesterase inhibitors insecticides toxicity according to marital status in relation to gender (n= 60).

3. Educational status

Table X and figure 8 show the distribution of patients with cholinesterase inhibitors insecticides toxicity by the level of education. 45% of the patients were illiterate (14 males [23.3%] and 13 females [21.7%]), 20 patients had pre-university education (17 males [28.3%] and 3 females [5%]) and 13 patients had university education (11 males [18.3%] and 2 females [3.3%]). There was no statistically significant difference between males and females regarding the educational status ($\chi^2 = 2.148$, P = 0.34).

Table (X): Distribution of patients with cholinesterase inhibitors insecticides toxicity by the level of education in relation to gender (n= 60).

Educational status	Male		Female		Total	%
	No.	%	No.	%		
Illiterate	14	23.3	13	21.7	27	45
Pre-university	17	28.3	3	5.0	20	33.3
University	11	18.3	2	3.3	13	21.7
χ^2	2.148					
P	0.34					
Total					60	100

χ^2; value of Chi-Square test. P; value of significance, considered significant if ≤ 0.05.

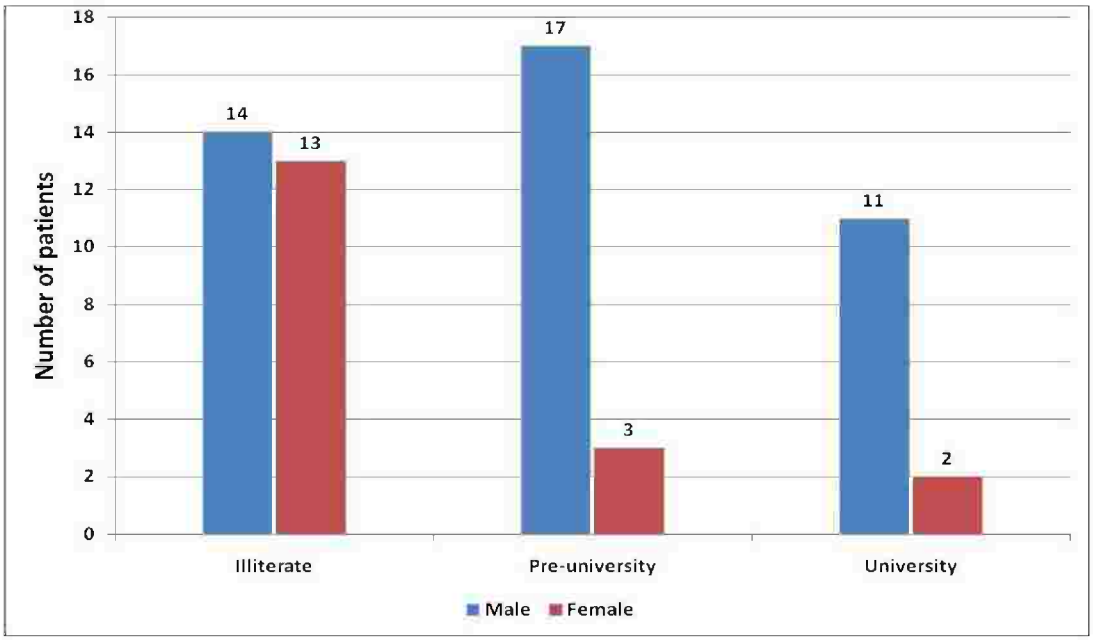

Figure 8. Distribution of patients with cholinesterase inhibitors insecticides toxicity by the level of education in relation to gender (n= 60).

4. Occupation

Table XI and figure 9 show the occupation of the studied patients, 32 patients (53.3%) were farmers, 17 patients (28.3%) were students, 3 were housewives (5%) and 8 (13.3%) were laborers. There was a statistically significant difference between males and females regarding the occupation (χ^2 = 11.821, P = 0.008).

Table (XI): Distribution of patients with cholinesterase inhibitors insecticides toxicity according to the occupation in relation to gender (n=60).

Occupation	Male		Female		Total	
	No.	%	No.	%	No.	%
Farmers	24	57.1	8	44.4	32	53.3
Students	10	23.8	7	38.9	17	28.3
Housewifes	0	0.0	3	16.7	3	5.0
Laborers	8	19.0	0	0.0	8	13.3
χ^2	11.821					
P	**0.008***					
Total					60	100

χ^2; value of Chi-Square test. * Statistically significant at P ≤ 0.05.

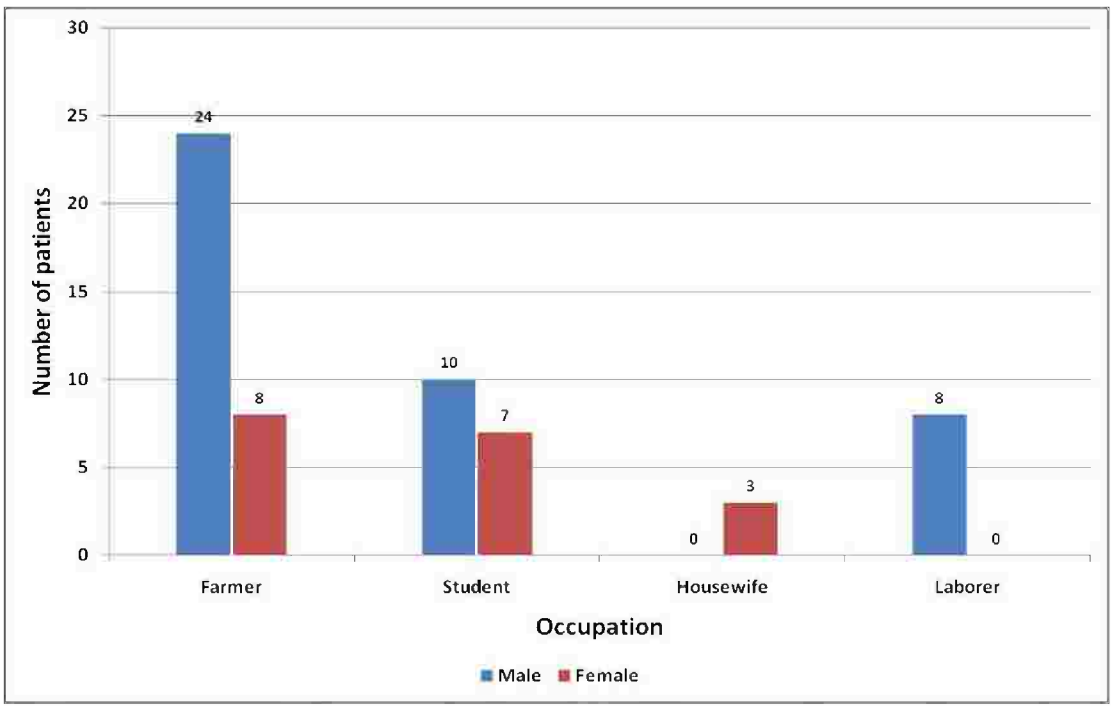

Figure 9. Distribution of patients with cholinesterase inhibitors insecticides toxicity according to the occupation in relation to gender (n=60).

5. Residency:

Table XII and figure 10 reveal that 80% of the patients (48 patients) came from rural areas (34 males 56.7% and 14 females 23.3%), while the remaining 20% came from urban areas. There was no statistically significant difference between males and females regarding the residency ($\chi^2 = 0.005$, P = 0.94).

Table (XII): Distribution of patients with cholinesterase inhibitors insecticides toxicity according to residency in relation to gender (n= 60).

Residency	Male		Female		Total	
	No.	%	No.	%	No.	%
Urban	8	13.3	4	6.7	12	20
Rural	34	56.7	14	23.3	48	80
χ^2	0.005					
P	0.94					
Total					60	100

χ^2; value of Chi-Square test. P; value of significance, considered significant if ≤ 0.05.

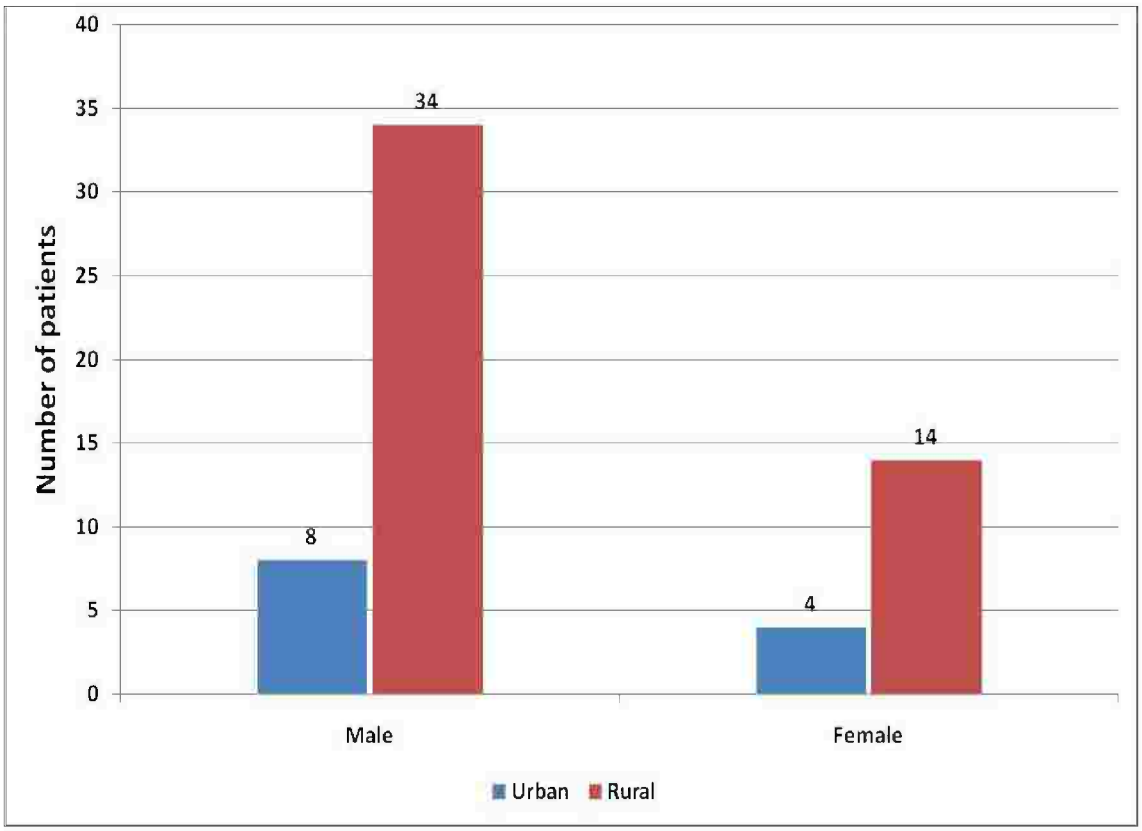

Figure 10. Distribution of patients with cholinesterase inhibitors insecticides toxicity according to residency in relation to gender (n= 60).

6. smoking:

Table XIII and figure 11 show that 51.6% of the patients were smokers (29 males [48.3%] and 2 females [3.3%]) while 48.4% patients were non-smokers (13 males [21.7%] and 16 females [26.7%]). There was no statistically significant difference between males and females regarding the habits (smoking) (χ^2 = 0.458, P = 0.0.49).

Table (XIII): Distribution of patients with cholinesterase inhibitors insecticides toxicity according to the habits of medical importance (Smoking) in relation to gender (n= 60).

Smoking status	Male		Female		Total	
	No.	%	No.	%	No.	%
Smoker	29	48.3	2	3.3	31	51.6
Non-smoker	13	21.7	16	26.7	29	48.4
χ^2	0.458					
P	0.49					
Total					60	100

χ^2; value of Chi-Square test. P; value of significance, considered significant if ≤ 0.05.

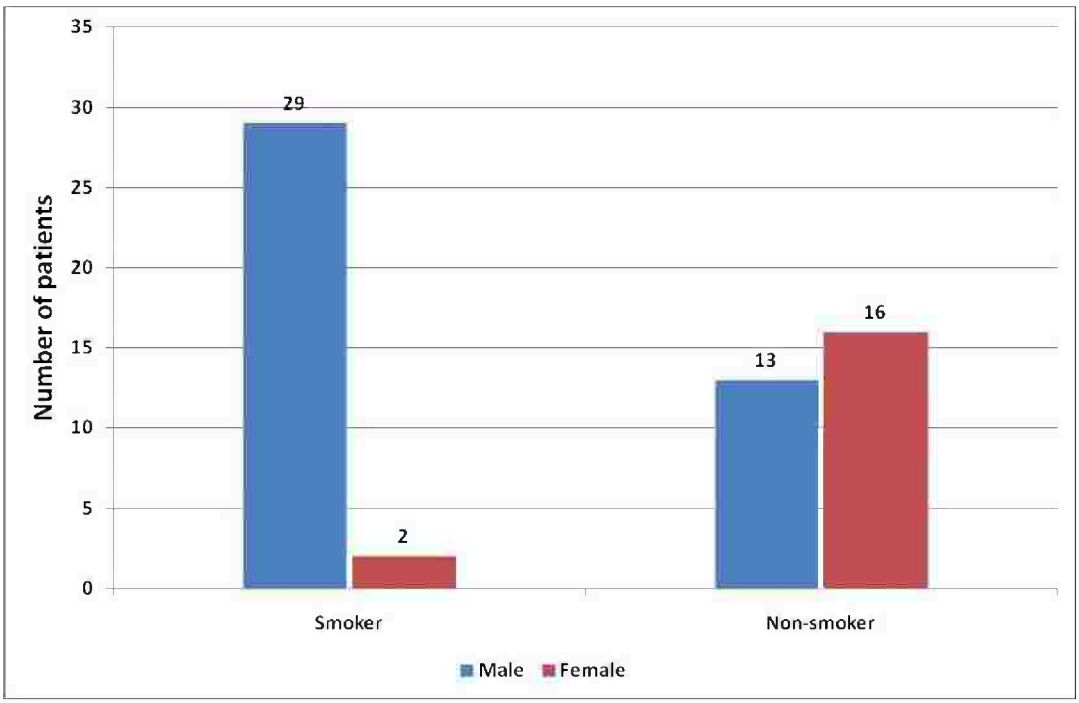

Figure 11. Distribution of patients with cholinesterase inhibitors insecticides toxicity by habits (Smoking) in relation to gender (n= 60).

7. Route of poisoning:

Table XIV and figure 12 demonstrate that the main route of poisoning was the non-oral route (inhalation, transdermal), which accounted for 70% of the cases (34 males [56.7%] and 8 females [13.3%]), while the oral route accounted for 30% of the cases (8 males [13.3%] and 10 females [16.7%]). There was a statistically significant difference between males and females regarding the route of poisoning ($\chi^2 = 6.353$, P = 0.01).

Table (XIV): Distribution of patients with cholinesterase inhibitors insecticides toxicity according to the route of poisoning in relation to gender (n= 60).

Route of poisoning	Male		Female		Total	%
	No.	%	No.	%		
Oral	8	13.3	10	16.7	18	30
Non-oral (Transdermal, Inhalation)	34	56.7	8	13.3	42	70
χ^2	6.353					
P	**0.01***					
Total					60	100

χ^2; value of Chi-Square test. * Statistically significant at P ≤ 0.05.

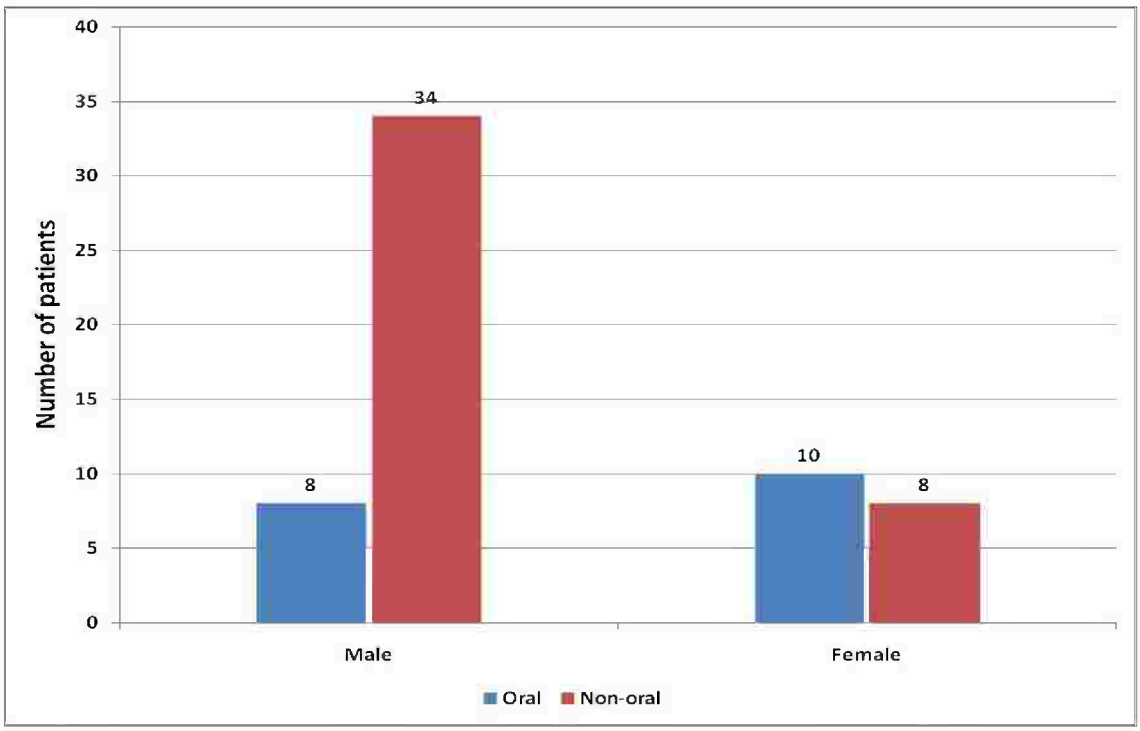

Figure 12. Distribution of patients with cholinesterase inhibitors insecticides toxicity according to the route of poisoning in relation to gender (n= 60).

8. Circumstances of poisoning:

Table XV and figure 13 show the circumstances of poisoning where accidental poisoning accounted for 86.7% of the cases (the majority were males [66.7%]). Suicidal cases were 13.3% where females predominated males. There was a statistically significant difference between males and females regarding the circumstances of poisoning (χ^2 = 6.600, P = 0.01).

Table (XV): Distribution of patients with cholinesterase inhibitors insecticides toxicity according to the circumstances of poisoning in relation to gender (n= 60).

Circumstances	Male		Female		Total	%
	No.	%	No.	%		
Accidental	40	66.7	12	20.0	52	86.7
Suicidal	2	3.3	6	10.0	8	13.3
χ^2	6.600					
P	**0.01***					
Total					60	100

χ^2; value of Chi-Square test. * Statistically significant at P ≤ 0.05.

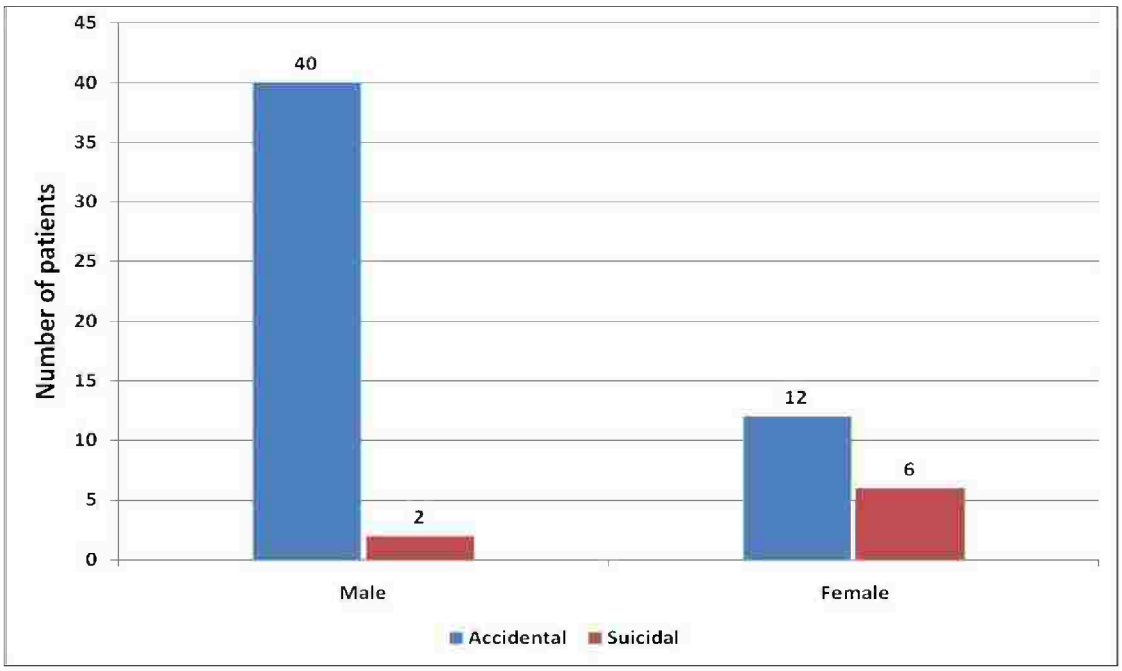

Figure 13. Distribution of patients with cholinesterase inhibitors insecticides toxicity according to circumstances of poisoning in relation to gender (n= 60).

B) Clinical examination and scoring:

1. Vital signs:

Table XVI shows that the mean arterial blood pressure was 100 ± 14 mmHg, with a minimum of 71 mmHg and a maximum of 120 mmHg. All of the patients were hypotensive except for one patient, who was hypertensive.

The mean respiratory rate was 17 ± 5 cycles per minute with a minimum of 9 and a maximum of 30 cycles. Respiratory manifestations of the studied patients encompassed changes in respiratory rate; tachypnea in 38.3% of cases and bradypnea in 5% of cases, while 56.7% of patients were presented with normal respiratory rate at admission, bronchorrhea was found in all cases with variant degrees of wheezes.

The mean pulse rate for the whole patients was 51 ± 8 beats/minute, with a minimum of 35 beats/minute and a maximum of 66 beats/minute.

The total sample had a mean temperature of 35.5 ± 0.8 °C, with a minimum of 36 °C and a maximum of 37.1 °C.

Arrhythmias were recorded in 81.6% of the cases (forty-nine patients) where sinus bradycardia was present in 73.33%, tachycardia in 5% and conduction defect (prolonged QTc interval) in 3.33% of the patients. The rest of the patients (18.33%) were presented with normal rhythm.

Table (XVI): Vital signs in patients with cholinesterase inhibitors insecticides toxicity (n= 60).

Vital signs	Mean ± SD
Mean arterial blood pressure (mmHg)	100 ± 14
Respiratory rate (breath/minute)	17 ± 5
Pulse rate (beats/minute)	51 ± 8
Temperature (◦C)	36.1 ± 0.7

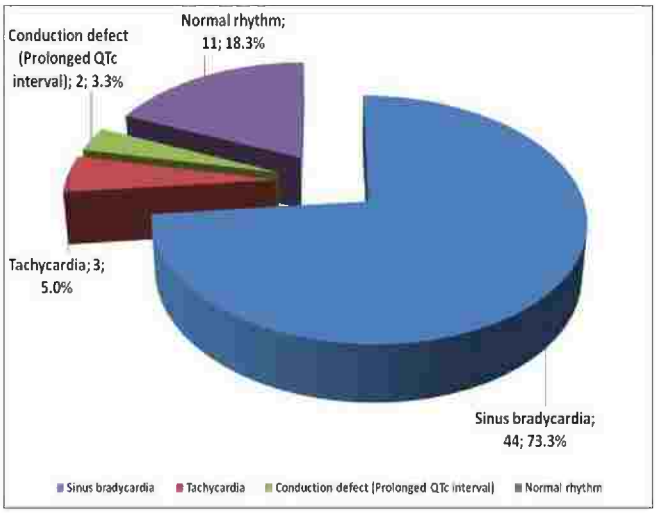

Figure 14. Distribution of patients with cholinesterase inhibitors insecticides toxicity by arrhythmia (n= 60).

2. General examination:

a. Pupil size:

Examination of the pupil revealed that pupils were constricted in 50%, pinpoint in 18.3% and normal in 31.7% of the patients.

Table XVII. Distribution of patients with cholinesterase inhibitors insecticides toxicity according to the pupil size (n=60).

Pupil size	No.	%
Normal	19	31.7
Miosis	30	50
Mydriasis	0	0
Pinpoint	11	18.3
Total	60	100

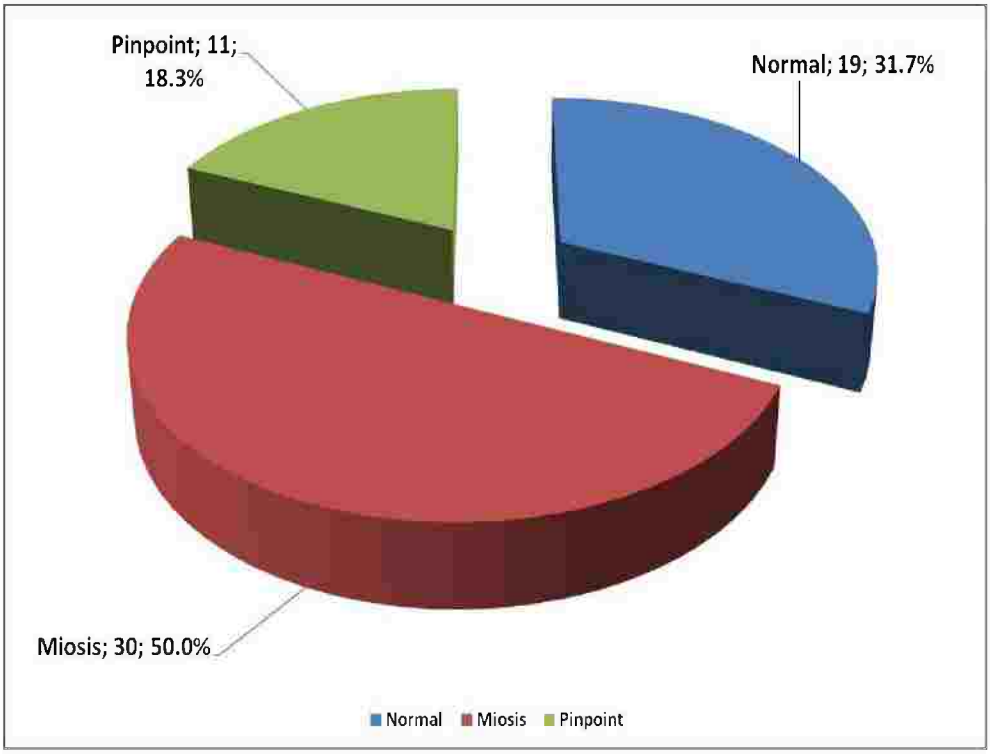

Figure 15. Distribution of patients with cholinesterase inhibitors insecticides toxicity according to the pupil size (n=60).

b. Clinical manifestations

Table XVIII and figure 16 show that the most prevalent symptoms in the studied patients were muscarinic manifestations: vomiting (55 patients; 91.6%), followed by the most prevalent sign, bradycardia 44 patients (73.33%), salivation in 41 patients (68.3%), sweating 36 patients (60%), followed by miosis in 30 patients (50%), followed by bradypnea in 3 patients (5%) and the least represented symptom was tachycardia 3 patients (5%). There was no statistically significant difference between the total sample regarding the presenting symptoms ($\chi^2 = 0.036$, P = 0.45).

Table (XVIII): Distribution of patients with cholinesterase inhibitors insecticides toxicity according to the presenting symptoms (n=60).

Symptoms	No.	%
Muscarinic manifestations		
Vomiting	55	91.6
Bradycardia	44	73.3
Salivation	41	68.3
Sweating	36	60
Miosis	30	50
Bradypnea	3	5
Nicotinc manifestations		
Altered sensorium	31	51.6
Tachypnea	23	38.3
Fasiculation	16	26.6
Tachycardia	3	5
χ^2		0.036
P		0.45

χ^2; value of Chi-Square test. P; value of significance, considered significant if ≤ 0.05.

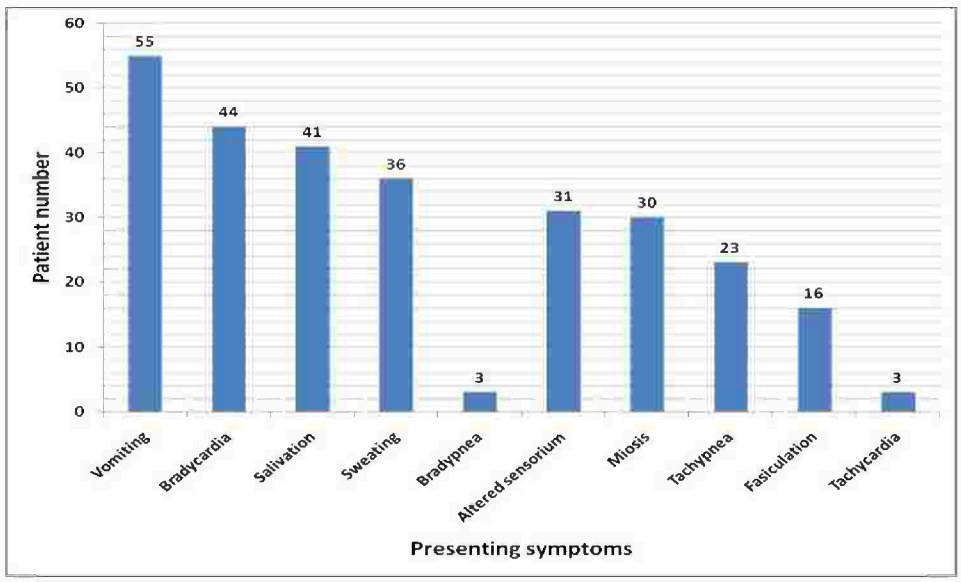

Figure 16. Distribution of patients with cholinesterase inhibitors insecticides toxicity according to the presenting symptoms (n=60).

c. POP score:

Table XIX, figure 17 and figure 18 show POP score distribution in relation to gender among the studied patients. They reveal that about half of the patients (53.3%) had moderate toxicity and scored from 4 to 7, 28.3% had mild toxicity and scored from 0 – 3 all of which were males and 18.4% had severe toxicity and scored from 8 – 11 all of which were females. There was a statistically significant difference between males and females regarding the severity of poisoning (χ^2 = 33.958, P = 0.0001).

Table (XIX): Distribution of patients with cholinesterase inhibitors insecticides toxicity according to the POP score in relation to gender (n=60).

POP Score	No.	%	Male	Female	Total	%
Mild (0-3)	17	28.3	17	0	17	28.3
Moderate (4-7)	32	53.3	25	7	32	53.4
Severe (8-11)	11	18.4	0	11	11	18.3
χ^2			33.958			
P			**0.0001***			
Total					60	100

χ^2; value of Chi-Square test. * Statistically significant at P ≤ 0.05.

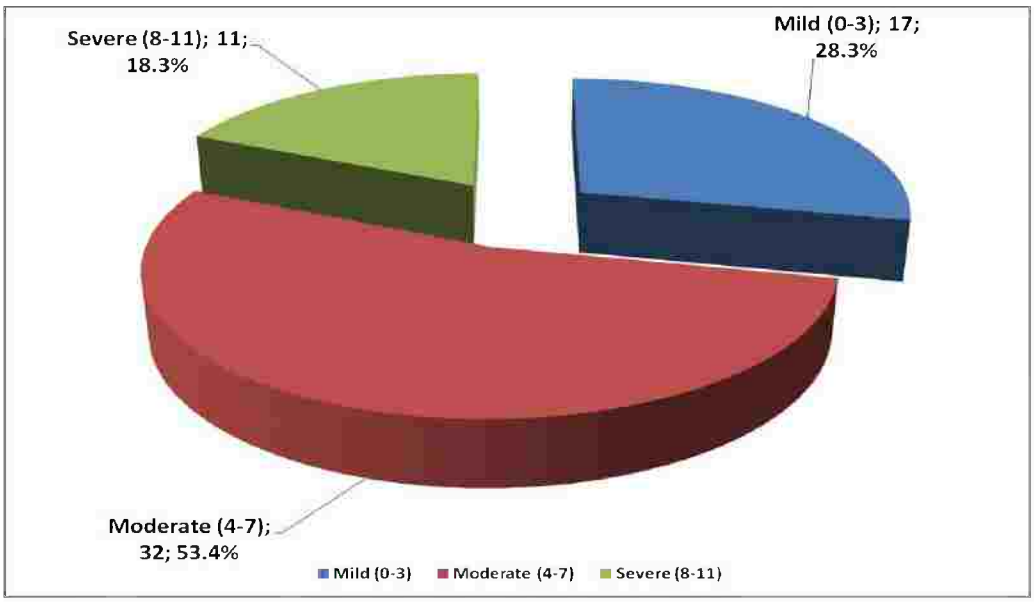

Figure 17. Distribution of patients with cholinesterase inhibitors insecticides toxicity according to the POP score (n=60).

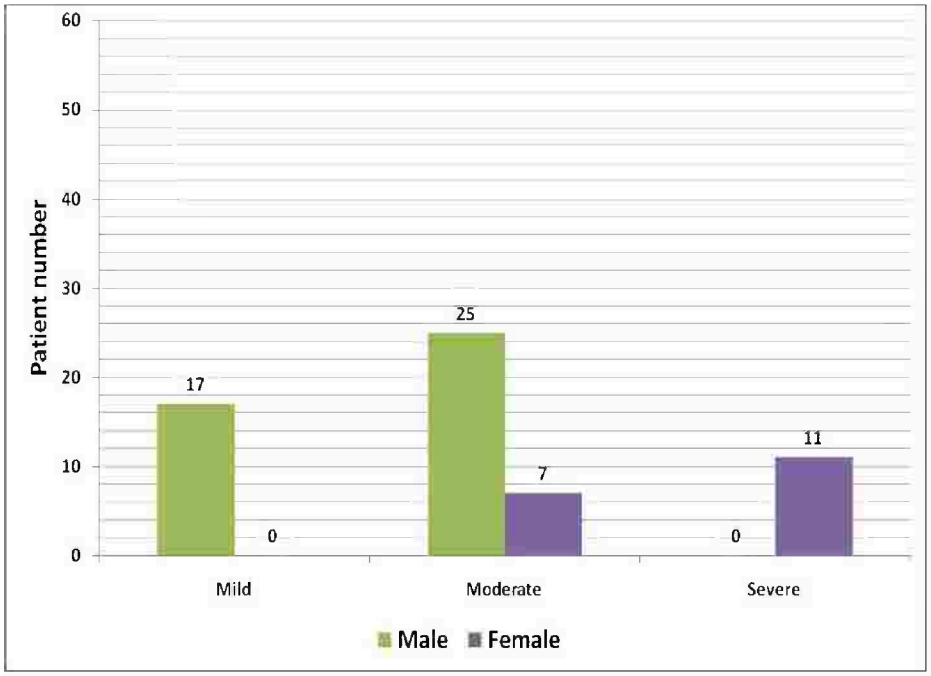

Figure 18. Distribution of patients with cholinesterase inhibitors insecticides toxicity according to the POP score in relation to gender (n=60).

C) Laboratory investigations:

Table XX shows the laboratory investigations values on admission (initial) and on discharge (final), the distribution of patients with cholinesterase inhibitors insecticides toxicity according to the mean laboratory investigations. The total sample had a mean initial creatine phosphokinase level of 514 ± 278.3 U/L, while they had a mean final creatine phosphokinase level of 992.9 ± 11268 U/L, both mean initial and final CPK levels are higher than the normal range (39-308 U/L males; 26-192 U/L females), the comparison between the initial and the final levels of CPK was statistically significant ($p < 0.05$).

The total sample had a mean initial plasma cholinesterase level of 4140.7 ± 1099.3 U/L, which is lower than the normal range of (4900 – 11900 U/L), while they had a mean final plasma cholinesterase level of 8430 ± 2002 U/L, which is within the normal range. The comparison between the initial and the final levels of PchE was statistically significant ($p < 0.05$).

As regards the arterial blood gases analysis, the total sample had an initial mean partial carbon dioxide tension of 47.3 ± 8 mmHg, while they had a final mean partial carbon dioxide tension of 39.9 ± 2.2. The sample had an initial mean bicarbonate level of 23.4 ± 1.9 mEq/L, while they had a final mean bicarbonate level of 24.1 ± 1.2 mEq/L. The initial mean pH level of the total sample was 7.31 ± 0.05, while the finial mean was 7.40 ± 0.02. The comparison between the initial and the final levels of all arterial blood gases was statistically significant ($p < 0.05$).

Table (XX): Distribution of patients with cholinesterase inhibitors insecticides toxicity according to the mean laboratory investigations (n= 60).

Laboratory Investigations	On admission (Initial)		At discharge (Final)		t-test	P
CPK (U/L) [39-308 U/L; males] [26-192 U/L; females]	514 ± 278		992.9 ± 1126.8		**4.247**	**0.001***
PchE (U/L) [4900-11900 U/L]	4140.7 ± 1099.3		8430 ± 2002		**15.277**	**0.0001***
Arterial blood gases						
PCO_2 [36-44 mmHg]	47.3 ± 8		39.9 ± 2.2		**6.909**	**0.0001***
	No.	**%**	**No.**	**%**		
<36	4	6.7	2	3.3		
36-44	50	83.3	58	96.7		
>44	6	10	0	0.0		
HCO_3 [22-26 mEq/L]	23.4 ± 1.9		24.1 ± 1.2		**2.052**	**0.04***
	No.	**%**	**No.**	**%**		
<22	12	20.0	3	5		
22-26	40	66.7	57	95		
>26	8	13.3	0	0		
pH [7.36-7.44]	7.31 ± 0.05		7.40 ± 0.02		**12.312**	**0.0001***
	No.	**%**	**No.**	**%**		
<7.36	47	78.3	1	1.7		
7.36-7.44	13	21.7	59	98.3		
>7.44	0	0.0	0	0.0		

t-test; value of Chi-Square test. * Statistically significant at $P \leq 0.05$.

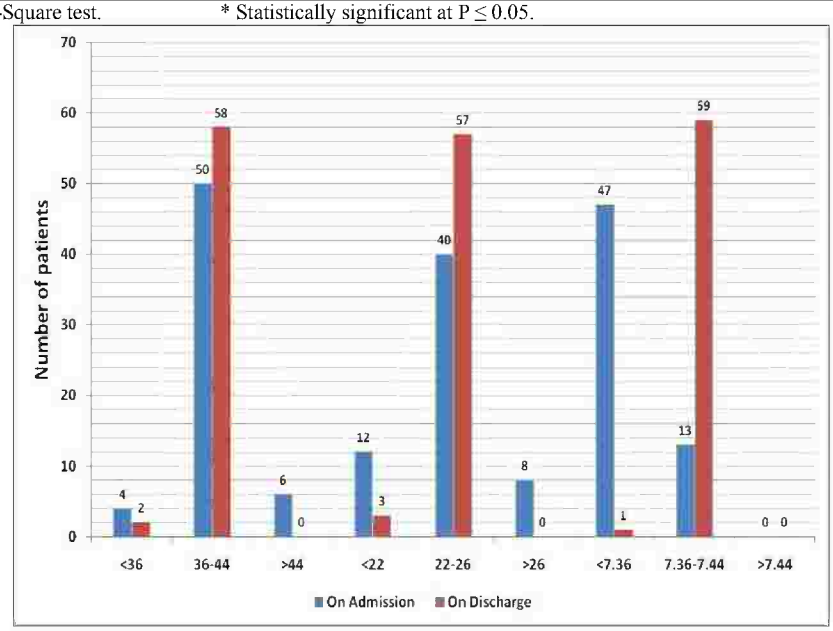

Figure 19. Distribution of patients with cholinesterase inhibitors insecticides toxicity according to the arterial blood gases initial and final levels (n=60).

D) Interventions and treatment:

Table XXI and figure 20 show the distribution of patients with cholinesterase inhibitors insecticides toxicity according to the mean total amount of atropine used in relation to the severity, the mean dose of atropine used for the mild toxicity patients (n= 17, 28.3%) was 12.8 ± 1.4 mg, while the mean dose was 17.3 ± 1.3 for the moderate toxicity patients (n= 32, 53.3%), however, patients with severe toxicity had a mean dose of atropine of 20.7 ± 1.1 mg.

General management of all patients was done in the form of: airway control and adequate oxygenation. Intubation was done in cases of respiratory distress due to laryngospasm, bronchospasm, bronchorrhea, or seizures. Central venous access and arterial lines were done. Continuous cardiac monitoring and pulse oximetry were established; an electrocardiogram (ECG) was performed.

All clothing were removed and patients were cleansed with soap and water because organophosphates are hydrolyzed readily in aqueous solutions with a high pH. The eyes of patients who have had ocular exposure were irrigated using isotonic sodium chloride solution or lactated Ringer's solution.

During the course of treatment, I/M injections were avoided. Patients were treated with 2-PAM (adult dose is 1–2 g intravenously followed by 0.5 g/hour infusion) and initial dose of injection atropine 2 mg followed by bolus every 5–10 min or as infusion until the signs of "atropinization" occurred, i.e., heart rate>80/min and dilatation of initially constricted pupil.

Table (XXI): Distribution of patients with cholinesterase inhibitors insecticides toxicity according to the mean total amount of atropine used in relation to the severity (n=60).

Severity (POP Score)	Mild (n= 17)	Moderate (n= 32)	Severe (n= 11)	Total (n= 60)
Mean ± SD	12.8 ± 1.4	17.3 ± 1.3	20.7 ± 1.1	16.5 ± 2.9

Intergroup comparison between the three groups:
P1 < 0.001 (Mild vs. Moderate).
P2 < 0.001 (Mild vs. Severe).
P3 < 0.001 (Moderate vs. Severe).

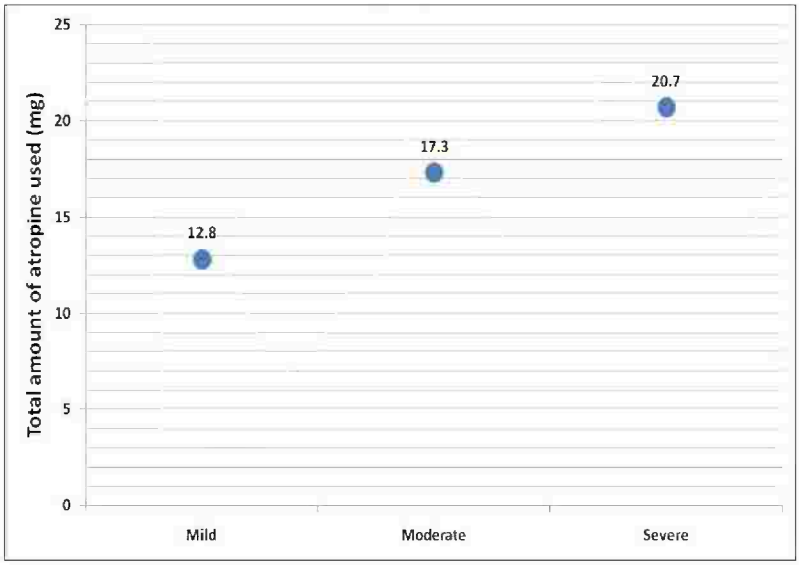

Figure 20. Distribution of patients with cholinesterase inhibitors insecticides toxicity according to the mean total amount of atropine used in relation to the severity (n=60).

E) Comparisons (between pre & post treatment levels)

Table XXII show the comparisons between the mean initial and final levels of the different laboratory investigations in relation to the severity (POP Score), the comparison between the pre- and post- treatment levels.

Regarding the creatine phosphokinase the mild group had a mean initial CPK level of 277.2 ± 91.9 U/L compared to a final level of 206.3 ± 31.5 U/L, the moderate group had a mean initial level of 460 ± 80.5 U/L compared to a final level of 611.4 ± 79.7 U/L, while the severe group had a mean initial CPK level of 1036.7 ± 1347 U/L compared to a final level of 3318.2 ± 63.7 U/L. The noted trend of the CPK levels is that in cases of mild toxicity, it mildly increases and then returns to normal, while in cases of moderate and sever toxicity the CPK increases and stays increased at the final level, this may be explained by the fact that in increased levels of severity, CPK normalizes after 5 – 6 days.

Regarding the plasma cholinesterase, the mild group had a mean initial level of 5523.7 ± 416.6 U/L compared to a final level of 8420.1 ± 2112.5 U/L, the moderate group had a mean initial level of 3968.2 ± 392.9 U/L compared to a final level 8608.5 ± 1979.1 U/L, while the severe group had a mean initial level of 2505.1 ± 304.1 U/L compared to a final level of 7925.9 ± 1996.1 U/L. On contrary to the CPK, the PchE levels tend to decrease with toxicity and increase back to normal once the condition is reversed and the patient is managed.

Regarding the carbon dioxide partial tension, the mild group had a mean initial level of 43.3 ± 7.7 mmHg compared to a mean final level of 40.1 ± 2.3 mmHg, the moderate group had a mean initial level of 41.5 ± 6.8 mmHg compared to a final level of 39.6 ± 2.4 mmHg, while the severe group had a mean initial level of 42.5 ± 7.1 mmHg compared to a final level of 40.4 ± 1.8.

Regarding the bicarbonate level, the mild, moderate and severe groups had mean normal levels for both initial and final levels.

Regarding the pH, the mild group had a mean initial level of 7.37 ± 0.02 compared to a mean final level of 7.40 ± 0.03, the moderate group had a mean initial level of 7.31 ± 0.02 compared to a final level of 7.40 ± 0.02, while the severe group had a mean initial level of 7.23 ± 0.01 compared to a final level of 7.40 ± 0.03.

The trend of the arterial blood gases (increased levels of PCO_2, normal levels of HCO_3 and low levels of pH), indicate the picture of the respiratory acidosis (uncompensated).

Table (XXII): Comparison between the mean initial and final levels of the different laboratory investigations in patients with cholinesterase inhibitors insecticides toxicity in relation to severity by POP Score (n= 60).

	Mild (0-3)	**Moderate (4-7)**	**Severe (8-11)**
CPK (U/L)			
Initial	277.2 ± 91.9	460 ± 80.5	1036.7 ± 1347
Final	206.3 ± 31.5	611.4 ± 79.7	3318.2 ± 63.7
t-test	3.009	7.560	5.611
P	**0.005***	**0.0001***	**0.0001***
PchE			
Initial	5523.7 ± 416.6	3968.2 ± 392.9	2505.1 ± 304.1
Final	8420.1 ± 2112.5	8608.5 ± 1979.1	7925.9 ± 1996.1
t-test	10.420	17.814	20.796
P	**0.0001***	**0.0001***	**0.0001***
Arterial blood gases			
PCO_2			
Initial	43.3 ± 7.7	41.5 ± 6.8	42.5 ± 7.1
Final	40.1 ± 2.3	39.6 ± 2.4	40.4 ± 1.8
t-test	1.642	1.490	0.951
P	0.1	0.1	0.3
HCO_3			
Initial	23.8 ± 1.8	23.3 ± 2	23.3 ± 1.9
Final	24.5 ± 1	23.8 ± 1.2	24.2 ± 1.5
t-test	1.402	1.213	1.233
P	0.4	0.2	0.2
pH			
Initial	7.37 ± 0.02	7.31 ± 0.02	7.23 ± 0.01
Final	7.40 ± 0.03	7.40 ± 0.02	7.40 ± 0.03
t-test	3.431	18.001	17.830
P	**0.001***	**0.0001***	**0.0001***

t-test; value of Chi-Square test. * Statistically significant at $P \leq 0.05$.

F) Correlations:

a) Laboratory investigations and POP Score

1. Plasma cholinesterase and POP Score

Table XXIV and figure 21 show the correlation between the on admission plasma cholinesterase levels (U/L) and POP score categorization. Patients with mild toxicity (0-3) had a mean PchE level of 5523.7 ± 416.6 U/L (range 4951.4 – 6351.3 U/L), patients with moderate toxicity (4-7) had a mean PchE level of 3968.2 ± 392.9 U/L (range 3156.4 – 4649.9 U/L), and patients with severe toxicity (8-11) had a mean PchE level of 2505.1 ± 304.1 U/L (range 1940.7 – 2983.9 U/L), with a Pearson's correlation coefficient of -0.87 (high degree of negative correlation), and a highly significant P value of < 0.0001.

Table (XXIII): Correlation between the initial PchE levels (U/L) and POP Score categorization among the studied patients (n=60).

POP Score	Initial (On admission) PchE (Mean ± SD)	Pearson correlation-coefficient (r)	95% CI	P value
Mild (0-3)	5523.7 ± 416.6	-0.87	-0.91 to -0.78	**< 0.0001***
Moderate (4-7)	3968.2 ± 392.9			
Severe (8-11)	2505.1 ± 304.1			

* Statistically significant at P ≤ 0.05.

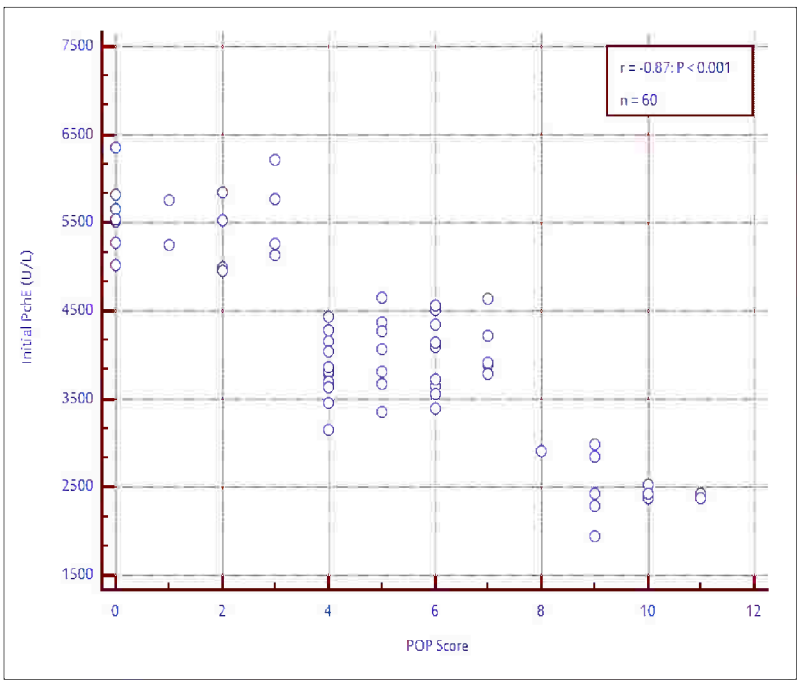

Figure 21. Correlation between the initial PchE levels (U/L) and POP Score categorization among the studied patients (n=60).

2. CPK and POP Score

Table XXIV and figure 22 show the correlation between the initial CPK levels (U/L) and POP score categorization among the studied patients. Patients with mild toxicity (0-3) had a mean CPK level of 277.20 ± 91.87 U/L (range 109 – 454 U/L), patients with moderate toxicity (4-7) had a mean CPK level of 460.04 ± 80.52 U/L (range 269 – 618 U/L) and patients with severe toxicity (8-11) had a mean CPK level of 1036.71 ± 134.69 U/L (range 832 – 1259 U/L), with a Pearson's correlation coefficient of 0.82 (high degree of positive correlation), and a highly significant P value of < 0.001.

Table (XXIV):Correlation between the initial CPK levels (U/L) and POP Score categorization among the studied patients (n=60).

POP Score	Initial (On admission) CPK (Mean ± SD)	Pearson correlation-coefficient (r)	95% CI	P value
Mild (0-3)	277.20 ± 91.87	0.82	0.71 - 0.88	**< 0.001***
Moderate (4-7)	460.04 ± 80.52			
Severe (8-11)	1036.71 ± 134.69			

CI; Confidence Interval.
* Statistically significant at P ≤ 0.05.

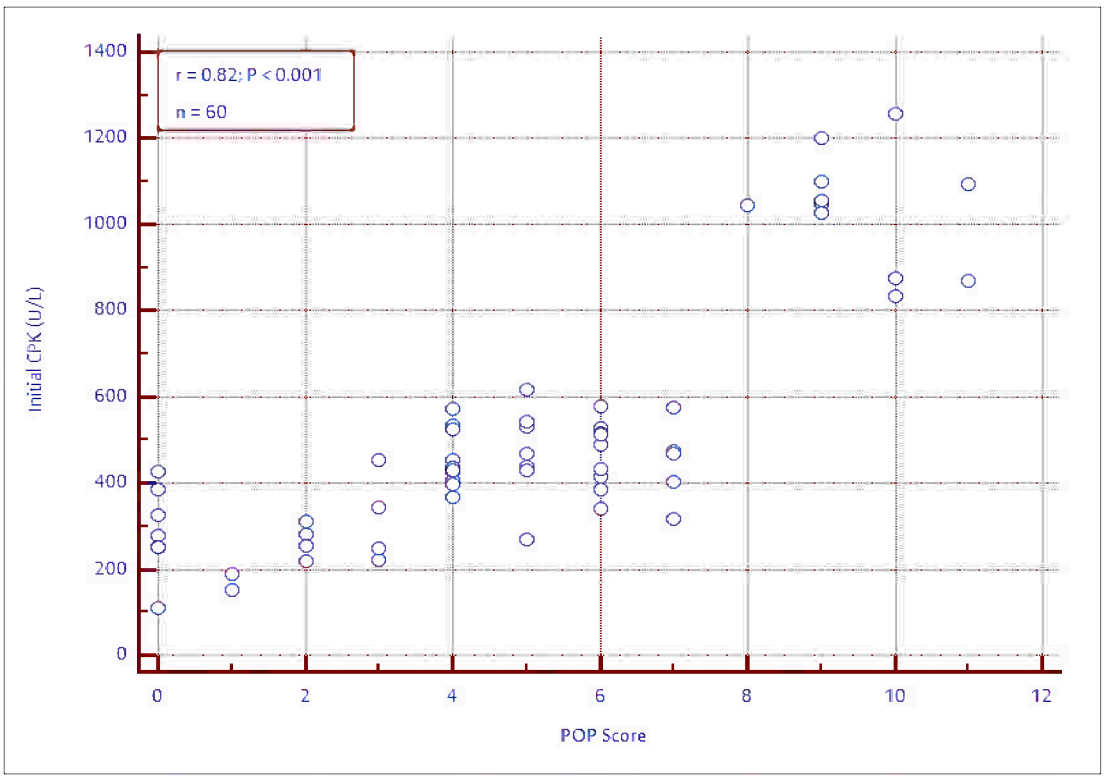

Figure 22. Correlation between the initial CPK levels (U/L) and POP Score categorization among the studied patients (n=60).

3. pH and POP Score

Table XXV and figure 23 show the correlation between the initial pH levels and the POP score categorization among the studied patients. Patients with mild toxicity (0-3) had a mean pH level of 7.37 ± 0.02, patients with moderate toxicity (4-7) had a mean pH level of 7.31 ± 0.02 and patients with severe toxicity (8-11) had a mean pH level of 7.23 ± 0.01, with a Pearson's correlation coefficient of – 0.86 (high degree of negative correlation), and a highly significant P value of < 0.001.

Table (XXV): Correlation between the initial pH levels and the POP score categorization among the studied patients (n= 60).

POP Score	Initial (On admission) pH levels (Mean ± SD)	Pearson correlation-coefficient (r)	95% CI	P value
Mild (0-3)	7.37 ± 0.02	-0.86	-0.91 to 0.78	**< 0.001***
Moderate (4-7)	7.31 ± 0.02			
Severe (8-11)	7.23 ± 0.01			

*** Statistically significant at P ≤ 0.05.**

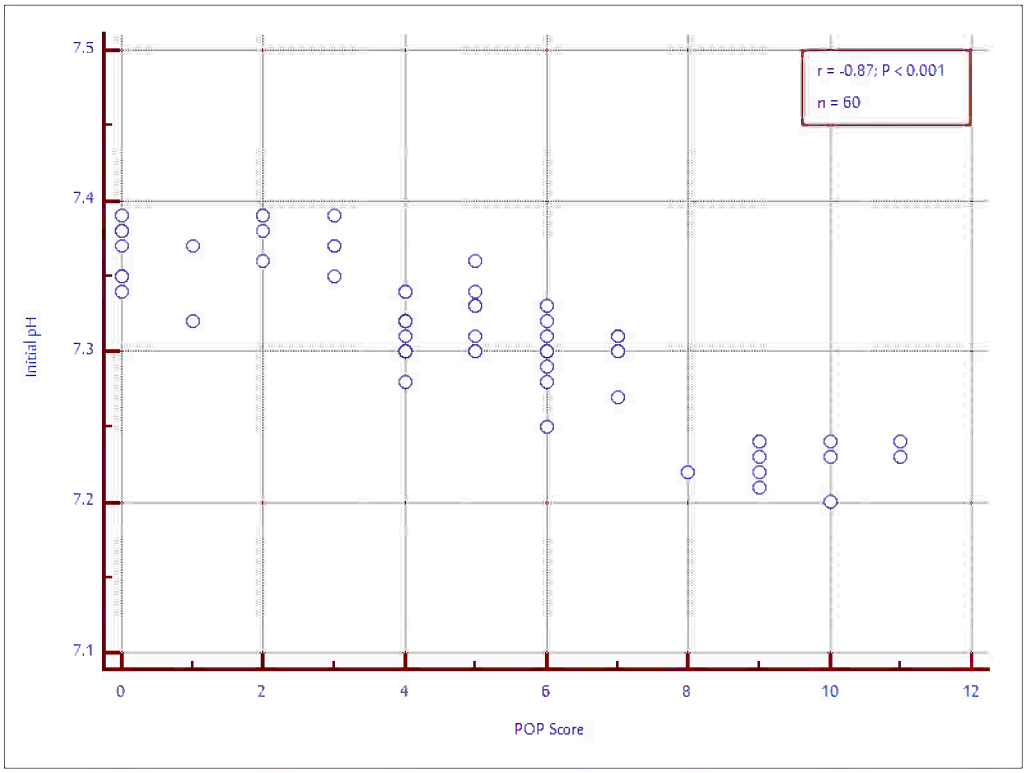

Figure 23. Correlation between the initial pH levels and POP Score categorization among the studied patients (n=60).

4. PCO_2 and POP Score

Table XXVI and figure 24 show the correlation between the initial PCO_2 levels (mmHg) and the POP score categorization among the studied patients. Patients with mild toxicity (0-3) had a mean PCO_2 level of 43.3 ± 7.7 mmHg, patients with moderate toxicity (4-7) had a mean PCO_2 level of 41.5 ± 6.8 mmHg and patients with severe toxicity (8-11) had a mean PCO_2 level of 42.5 ± 7.1 mmHg, with a Pearson's correlation coefficient of -0.11 (low degree of negative correlation), and a non significant P value of 0.3.

Table (XXVI): Correlation between the initial PCO2 levels (mmHg) and the POP score categorization among the studied patients (n= 60).

POP Score	Initial (On admission) PCO_2 levels (Mean ± SD)	Pearson correlation-coefficient (r)	95% CI	P value
Mild (0-3)	43.3 ± 7.7	-0.11	-0.36 to 0.13	0.3
Moderate (4-7)	41.5 ± 6.8			
Severe (8-11)	42.5 ± 7.1			

P; value of significance, considered significant if ≤ 0.05.

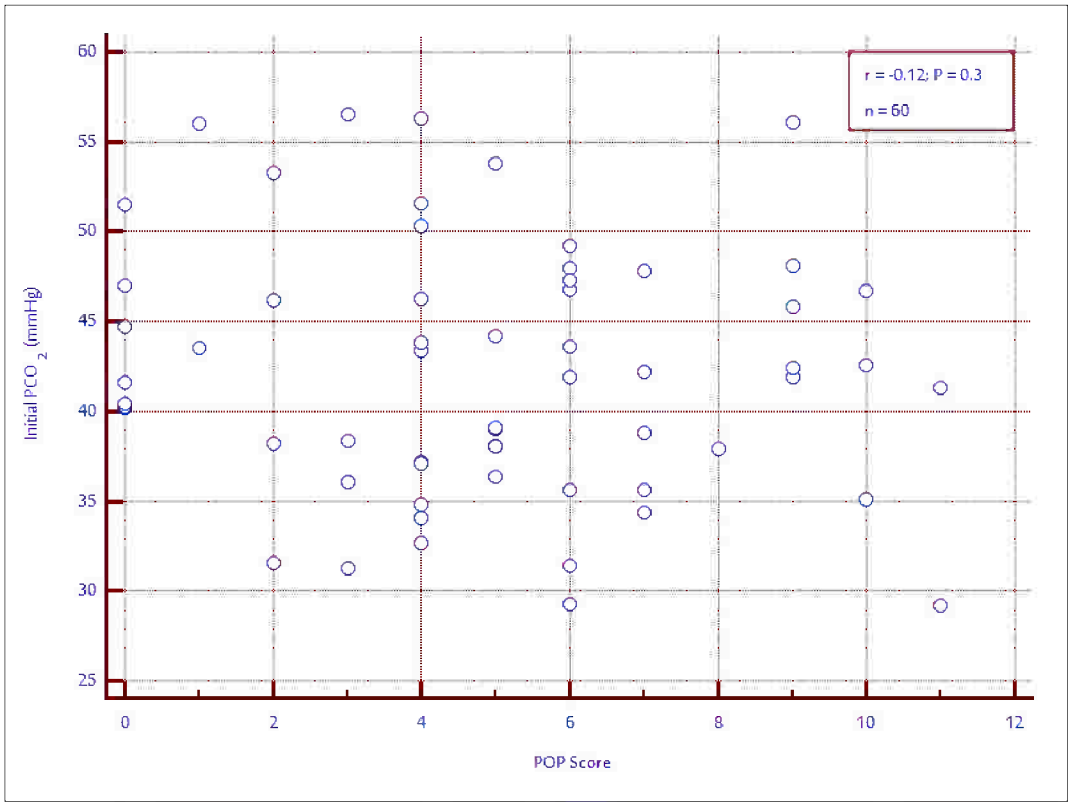

Figure 24. Correlation between the initial PCO2 levels (mmHg) and the POP score categorization among the studied patients (n= 60).

5. HCO_3 and POP Score:

Table XXVII and figure 25 show the correlation between the initial HCO_3 levels (mEq/L) and the POP score categorization among the studied patients. Patients with mild toxicity (0-3) had a mean HCO_3 level of 23.8 ± 1.8 mEq/L, patients with moderate toxicity (4-7) had a mean HCO_3 level of 23.3 ± 2 mEq/L and patients with severe toxicity (8-11) had a mean HCO_3 level of 23.3 ± 1.9 mEq/L, with a Pearson's correlation coefficient of -0.11 (low degree of negative correlation), and a non significant P value of 0.3.

Table (XXVII): Correlation between the initial HCO3 levels (mEq/L) and the POP score categorization among the studied patients (n= 60).

POP Score	Initial (On admission) HCO_3 levels (Mean ± SD)	Pearson correlation-coefficient (r)	95% CI	P value
Mild (0-3)	23.8 ± 1.8	-0.11	-0.35 to 0.14	0.3
Moderate (4-7)	23.3 ± 2			
Severe (8-11)	23.3 ± 1.9			

P; value of significance, considered significant if ≤ 0.05.

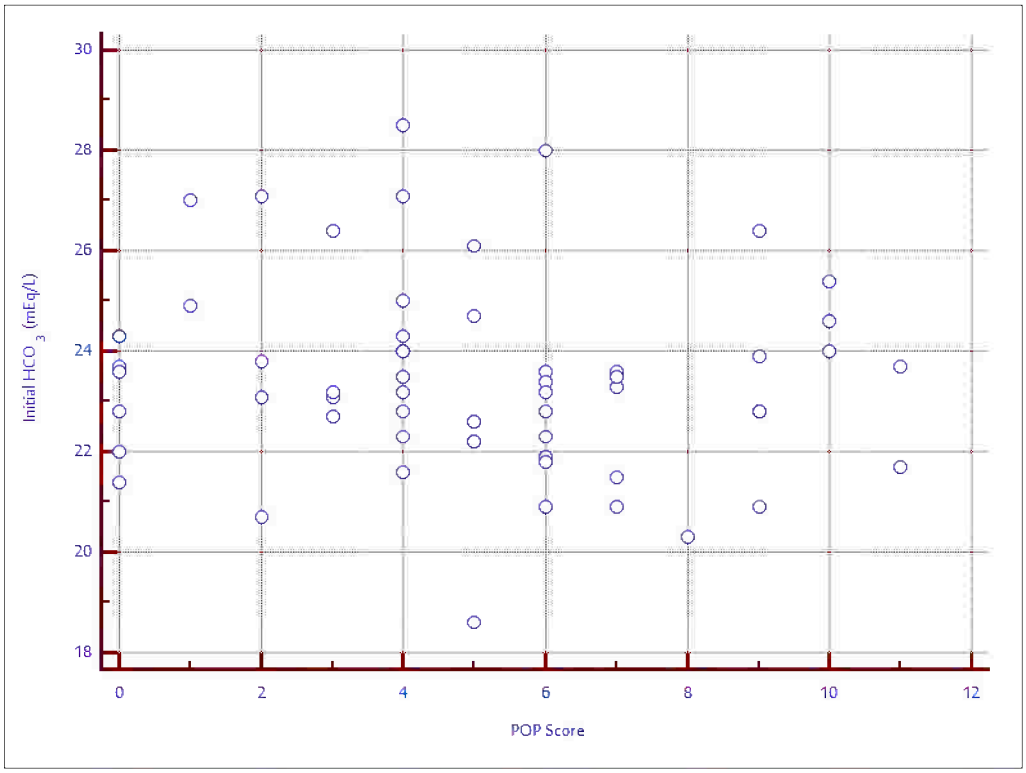

Figure 25. Correlation between the initial HCO3 levels (mEq/L) and the POP score categorization among the studied patients (n= 60).

b) Arterial blood gases with plasma cholinesterase

1. Plasma cholinesterase and PCO_2

Table XXVIII and figure 26 show the correlation between the initial plasma cholinesterase levels (U/L) and the initial PCO_2 levels (mmHg) among the studied patients. Patients with mild toxicity had a mean PchE level of 5523.7 ± 416.6 U/L *vs.* a mean PCO_2 of 43.3 ± 7.7 mmHg, patients with moderate toxicity had a mean PchE level of 3968.2 ± 392.9 U/L *vs.* a mean PCO_2 of 41.5 ± 6.8 mmHg and patients with severe toxicity had a mean PchE level of 2505.1 ± 304.1 U/L *vs.* a mean PCO_2 of 42.5 ± 7.1, with a Pearson's correlation coefficient of –0.01 (low degree of negative correlation), and a non-significant P value of 0.9.

Table (XXVIII): Correlation between the initial PchE levels (U/L) and PCO2 (mmHg) among the studied patients (n= 60).

POP Score	Initial (On admission) PchE (Mean ± SD)	Initial (On admission) PCO_2 (mmHg) (Mean ± SD)	Pearson correlation-coefficient (r)	95% CI	P value
Mild	5523.7 ± 416.6	43.3 ± 7.7	-0.01	-0.26 to 0.24	0.9
Moderate	3968.2 ± 392.9	41.5 ± 6.8			
Severe	2505.1 ± 304.1	42.5 ± 7.1			

P; value of significance, considered significant if ≤ 0.05.

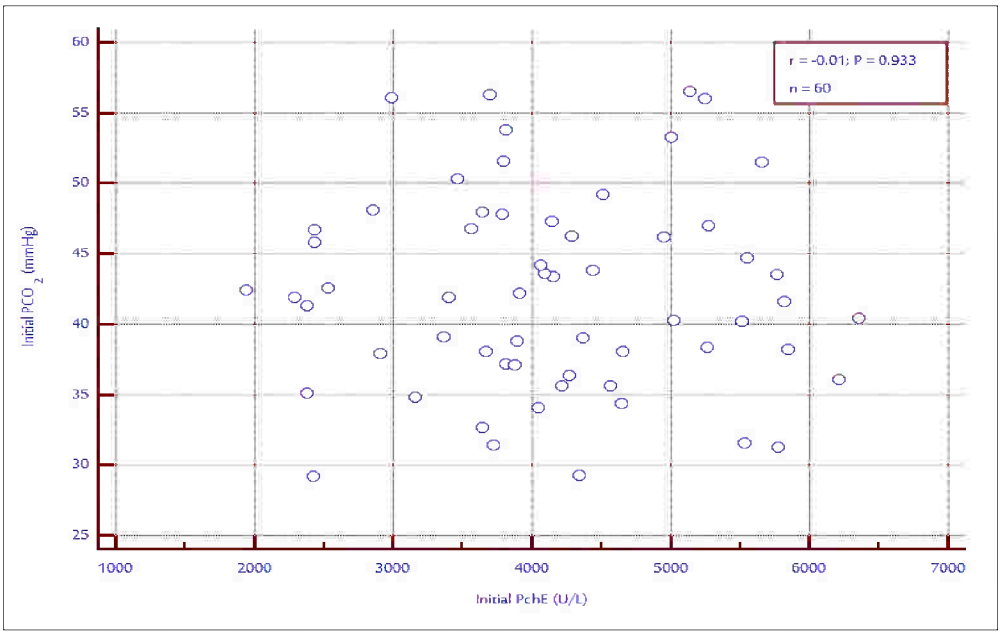

Figure 26. Correlation between the initial PchE levels (U/L) and the initial PCO2 levels (mmHg) among the studied patients (n= 60).

2. Plasma cholinesterase and HCO_3:

Table XXIX and figure 27 show the correlation between the initial plasma cholinesterase levels (U/L) and the initial HCO_3 levels (mEq/L) among the studied patients, patients with mild toxicity had a mean PchE level of 5523.7 ± 416.6 U/L *vs.* a mean HCO_3 of 23.8 ± 1.8 mmol/L, patients with moderate toxicity had a mean PchE level of 3968.2 ± 392.9 U/L *vs.* a mean HCO_3 of 23.3 ± 2 mmol/L and patients with severe toxicity had a mean PchE of 2505.1 ± 304.1 U/L *vs.* a mean HCO_3 of 23.3 ± 1.9 mmol/L, with a Pearson's correlation coefficient of 0.02 (positive correlation), and a non significant P value of 0.8.

Table (XXIX): Correlation between the initial PchE levels (U/L) and the initial HCO3 levels (mEq/L) among the studied patients (n= 60).

POP Score	Initial (On admission) PchE (Mean ± SD)	Initial (On admission) HCO_3 (mEq/L) (Mean ± SD)	Pearson correlation-coefficient (r)	95% CI	P value
Mild	5523.7 ± 416.6	23.8 ± 1.8	0.02	-0.23 to 0.27	0.8
Moderate	3968.2 ± 392.9	23.3 ± 2			
Severe	2505.1 ± 304.1	23.3 ± 1.9			

P; value of significance, considered significant if ≤ 0.05.

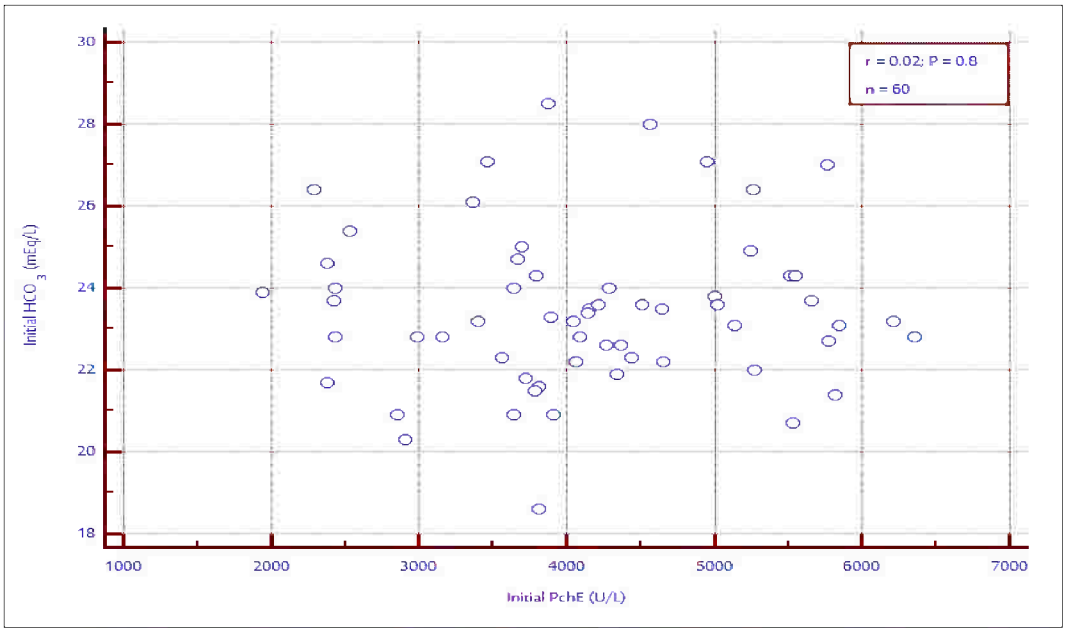

Figure 27. Correlation between the initial PchE levels (U/L) and the initial HCO3 (mEq/L) among the studied patients (n= 60).

3. CPK, PchE and pH

Table XXX figure 28 and figure 29 show the correlation between the initial CPK levels (U/L) and PchE (U/L) and pH among the studied patients. Inverse relationship was found between the initial CPK levels and both the plasma cholinesterase and the pH, both inverse relations were statistically significant.

Table (XXX): Correlation between the initial CPK levels (U/L) and PchE (U/L) and pH among the studied patients (n=60).

Correlation between	Pearson's co-efficient	P value	Comments
CPK & PchE	-0.82	**0.0001***	High degree of negative correlation
CPK & pH	-0.85	**0.0001***	High degree of negative correlation

P; value of significance, considered significant if ≤ 0.05.

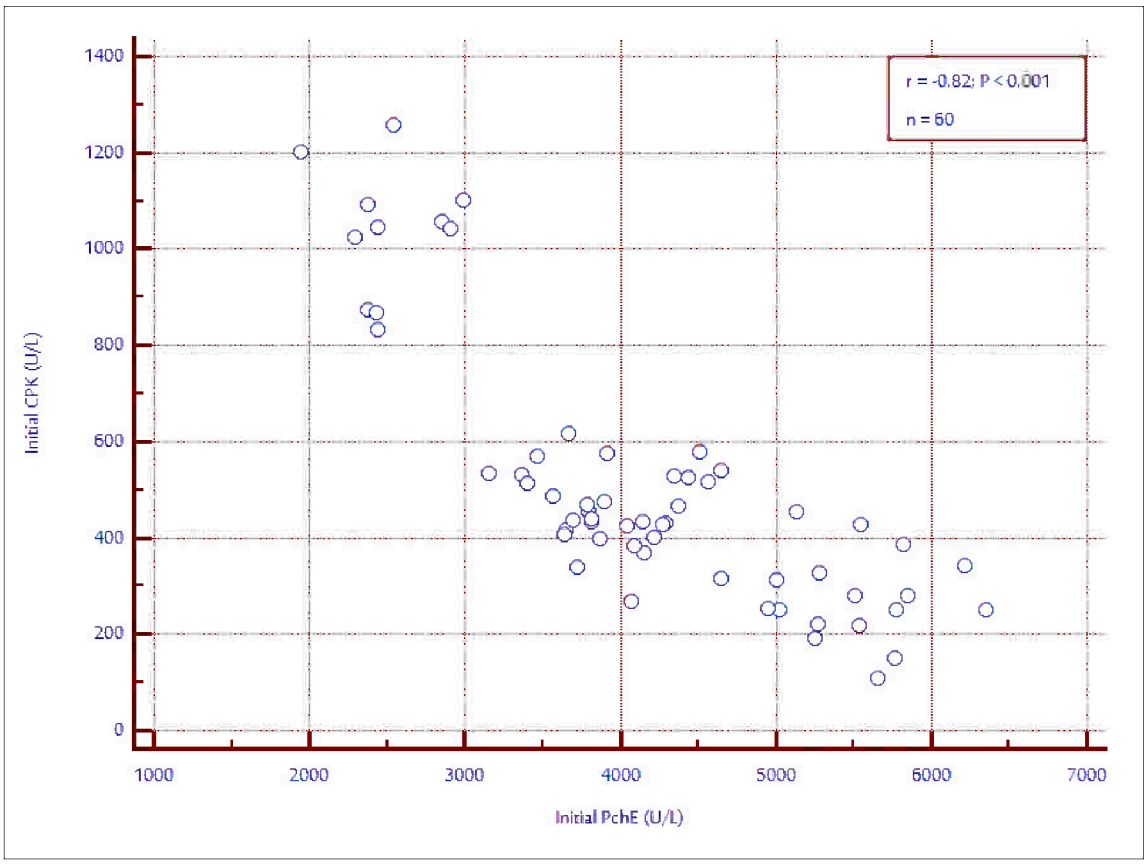

Figure 28. Correlation between the initial CPK levels (U/L) and Plasma Cholinesterase levels (U/L).

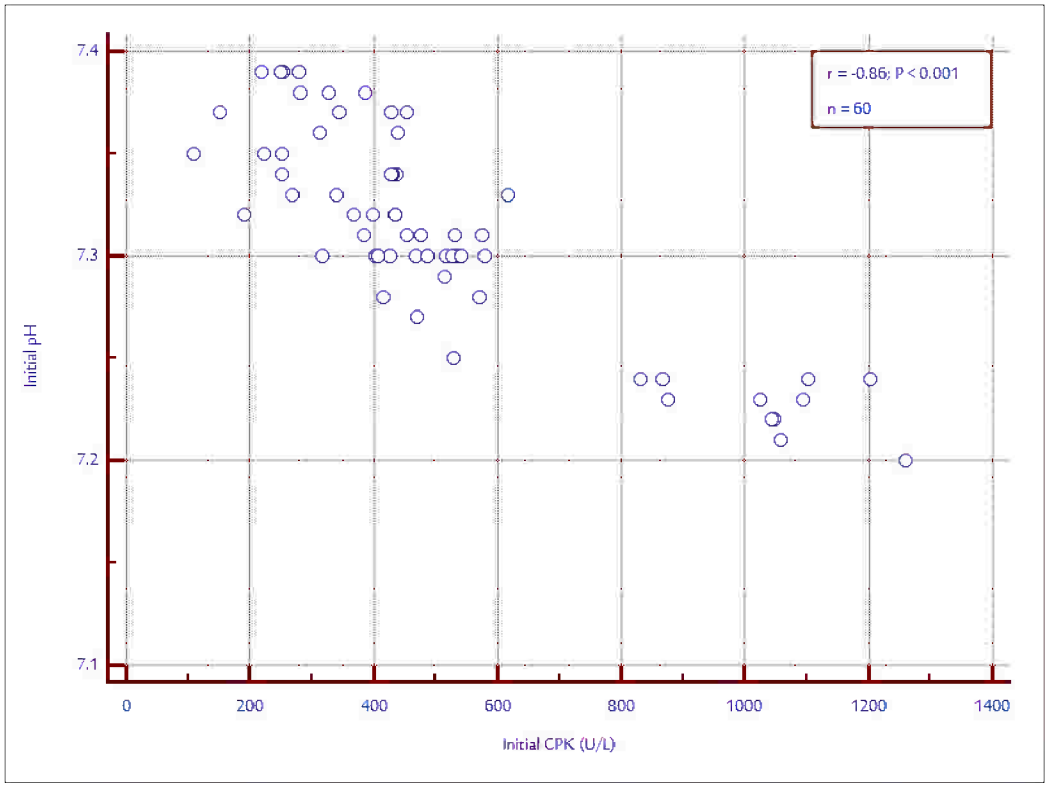

Figure 29. Correlation between the initial CPK levels (U/L) pH levels.