

## THE ROLE OF APACHE II SCORE IN PREDICTION OF SEVERITY AND OUTCOME OF ACUTE ORGANOPHOSPHORUS (OP) POISONING

*BY*

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### ABSTRACT

*Poisoning with organophosphorus (OP) compounds is/or may be a cause of morbidity and mortality across many countries including Egypt. The severity of OP toxicity should be assessed using scientific methods and clinical database which should be maintained so as to develop a uniform and effective management guideline. This study aimed to investigate the prognostic value of APACHE II score in predicting the severity and outcome of acute organophosphates poisoning and trying to set a cut off point for the score to help the management plan. A cross-sectional study was carried out on cases of acute OP poisoning admitted to the Poison Control Center (PCC), Ain Shams University Hospitals during the year 2010. They were divided into 2 main groups; Group I (GI): patients with acute OP poisoning not admitted to the ICU and group II (GII): patients with acute OP poisoning admitted to the ICU. Full history was taken from all patients or their relatives and they were generally examined on admission to obtain the data required for APACHE II score. This study included a total of 1553 OP poisoned cases. 1475 patients were not admitted to the ICU (GI) while 78 cases (5%) were admitted to the ICU (GII) who were subdivided into: GIIa (survivors) and GIIb (non-survivors) who included 18 cases (23%). The heart rate among cases admitted to the ICU was significantly lower (GII) than the non admitted cases (GI). The respiratory rate (RR) showed significant statistical difference between the two groups. The haematocrite value was elevated in GI and GII with significant difference between them. Cases admitted to the ICU showed a significant statistical difference regarding arterial blood gases (ABG) analysis compared to those not admitted. Serum Na<sup>+</sup> and K<sup>+</sup> were higher in the ICU group (GII) when compared with GI and the difference was statistically significant. On comparing group IIa (survivors) with group IIb (non-survivors), there were significant differences as regards age, mean arterial blood pressure (MAP) and serum K<sup>+</sup>. As regards APACHE II score results, a significant difference was found between GIIa and GIIb. The best cut off value was > 8 and this proves the importance of APACHE II score in predicting the severity of acute organophosphorus poisoning. It could be concluded that using APACHE II score facilitates the prediction of the severity and outcome of OP poisoned patients as it is simple, less time consuming and effective in emergency cases. Also, cut off point > 8 in APACHE II score may be used for ICU admission.*

**Keywords:** *Organophosphates poisoning, APACHE II score, Outcome, ICU*

## **INTRODUCTION**

Organophosphorus compounds (OPC) have been widely used throughout the world (Pore et al., 2011). They constitute a heterogeneous group of chemicals specifically designed for the control of pests (Kumar et al., 2010). Some have also been used for medical treatment of mythenia gravis, e.g., di-isopropyl phosphorofluoride (DFP). Others are still used to treat glaucoma "Ecothiophate" (Karalliedde et al., 2001).

In addition to their beneficial agricultural and medical uses, some are highly potent anti-cholinesterase including tabun, sarin and soman which have been used as nerve gases in chemical warfare (Agarwal et al., 2007). According to the WHO, worldwide especially in developing countries, two million people yearly attempt suicide using OPC and one million are exposed accidentally to these agents (Aardewa et al., 2008).

The route of exposure to OPC varies including oral, dermal and respiratory exposures (Tahir et al., 2006). Organophosphates inhibit acetyl choline esterase (AChE) and cause excessive accumulation of acetyl choline (ACh) which affects muscarinic and nicotinic receptors peripherally and centrally (Goldfrank, 2006). Combined atropine and oximes therapy is the corner stone of OP poisoning treatment

(Kang et al., 2009). The mortality rate of OPC in developing countries is high and is often related to delay in diagnosis or improper management (Eizadi-Mood et al., 2007).

Subjective assessment of the clinical status of poisoned patients by clinicians may vary in the evaluation of illness severity. Hence, various descriptive and prognostic evaluation scales have been developed to facilitate the assessment (Bilgin et al., 2005). Among the various scales, acute physiology and chronic health evaluation (APACHE) II scoring system have been used as a predictor of poisoning severity (Sungurtekin et al., 2006). The measurement of AChE often showed many controversial reports about the relationship between its level and the severity of OPC poisoning (Nelson et al., 2011 and Devanur et al., 2013).

The present work was designed to study the value of the different parameters included in APACHE II score in expecting the severity and outcome following OPC exposure and trying to determine a cut off value for APACHE II for decision making in management of this toxicological emergency.

## **PATIENTS & METHODS**

A clinical cross-sectional study was conducted on patients with acute organo-

phosphorus (OP) poisoning admitted to the Poison Control Center (PCC), Ain Shams University Hospitals during the year 2010.

#### **Patient's Selection Criteria :**

The selected patients were adults of both sexes with acute organophosphorus (OP) exposure. The diagnosis of OP poisoning was based on the following criteria as guided by Lee (2001):

- History of exposure to OP compounds.
- Characteristic clinical symptoms and signs of OP toxicity.
- Improvement of symptoms and signs after atropine administration.
- Low serum pseudo-cholinesterase activity.

#### **Exclusion Criteria :**

Children, patients with history of severe cardiac, pulmonary or renal disease, or severe organ insufficiency which affects the calculation of APACHE II score.

#### **Patients under study :**

Selected patients were divided into 2 main groups; Group I (GI): patients with acute OP poisoning not admitted to the ICU and group II (GII): patients with acute OP poisoning admitted to the ICU.

Group II was further subdivided into group IIa (Survivors) and group IIb (Non-survivors).

#### **Calculation of APACHE II equation:**

The following parameters were collected and APACHE II score was automatically calculated using eleven physiological parameters (William et al., 1985):

- Patient's age.
- Body temperature.
- Heart rate.
- Mean arterial blood pressure (MAP mmHg).
- Respiratory rate.
- Haematocrite (%) and WBCs ( $\times 10^3$ ), both were measured using Beckman Coulter.
- Arterial blood gas (ABG) analysis (PH, Pa  $\text{CO}_2$ , Pa  $\text{O}_2$  and  $\text{HCO}_3^-$ ) according to Kokholm (1990).
- Serum sodium (S. $\text{Na}^+$ ) level (meq/L) and serum potassium (S. $\text{K}^+$ ) level (meq/L) both after Woo (1999).
- Serum creatinine level (mg/dL) after Houout (1985).

The point score was calculated from 11 routine physiological measurements during the first 24 hours after admission and some clinical data from the history of the patient.

#### **Statistical Analysis:**

The results of the individual 11 parameters of APACHE II score were obtained, tabulated and statistically analysed using SPSS version 17, where Mean ( $\bar{X}$ ) and standard deviation (SD) were calculated as well as student t-test. Sensitivity and

specificity Roc curves were determined at the best cut off value.

### **RESULTS**

Table (1) shows the results of the different parameters of APACHE II scoring system in the two studied groups (GI & GII). The mean age of GI was 22.1 years and that of GII was 23.2 years. There was no significant statistical difference regarding the age between both groups.

No significant statistical difference was noticed between GI & GII as regards the body temperature. There was a lower mean pulse rate among cases admitted to the ICU (GII) compared to patients not admitted (GI) and the difference was statistically significant. Hypotension was present in both groups but no statistical difference was found between the two

groups concerning MAP. There was a statistically significant elevated mean respiratory rate among cases admitted to ICU (GII) compared to those not admitted (GI).

The haematocrite value was increased in both groups and the difference between them was statistically significant while WBCs count was in the normal range in GI and GII.

Lower mean pH and PaO<sub>2</sub> and higher PaCO<sub>2</sub> were found in GII and the difference was statistically significant when compared with GI. HCO<sub>3</sub><sup>-</sup> level showed non-significant difference. Serum Na<sup>+</sup> & K<sup>+</sup> was decreased in GII when compared with GI and the difference was statistically highly significant. Regarding serum creatinine level, there was no significant statistical difference between the two studied groups.



**Table (1) :** Comparison between group I and group II regarding different studied parameters.

Parameter	Group	GI (n=1475)	GII (n=78)	T	P-value
		Mean±SD	Mean±SD		
1. Age (years)		22.1 ± 14.4	23.2 ± 15.3	0.6	0.4
2. Temperature (°C)		35.8 ± 0.2	35.8 ± 0.3	0.000	1.000
3. Heart rate (beat/min)		58.4 ± 7.5	50.1 ± 6.5	10.9	0.000*
4. Mean arterial blood pressure (mmHg)		81.2 ± 11.6	83.6 ± 9.9	1.793	0.073
5. Respiratory rate (breath/min)		20.5 ± 3.9	24.0 ± 2.3	12.4	0.000*
6. Haematocrite (%)		50.7 ± 1.8	52.3 ± 1.9	7.629	0.000*
7.WBCs (×10 <sup>3</sup> )		7.4 ± 4.2	7.5 ± 2.2	0.04	0.9
<b>8.Arterial Blood gases:</b>					
PH		7.4 ± 0.1	7.34 ± 0.01	5.296	0.000*
Pa Co <sub>2</sub> (mmHg)		39.4 ±4.9	46.2 ± 2.5	12.175	0.000*
Pa O <sub>2</sub> (mmHg)		95.1 ± 4.1	87.8 ± 5.4	0.4	0.03*
HCo <sub>3</sub> <sup>-</sup> (meq/L)		24.3 ± 1.4	24.0 ± 1.1	1.2	0.2
9. Serum sodium (meq/L)		140.8 ± 3.1	133.0 ± 1.1	22.142	0.000*
10. Serum potassium (meq/L)		4.2 ± 1.7	3.3 ± 0.4	4.667	0.000*
11. Serum creatinine (mg/dL)		0.9 ± 0.6	1.0 ± 0.3	1.3	0.1
n = number; SD = Standard deviation; P>0.05 = insignificant; * P<0.05 = Significant.					
N.B: Total number of patients = 1553.					

Table (2) shows the percentage of ICU admission and the percentage of mortality among the studied patients. It shows that 5% (n = 78) of the studied patients (n = 1553) were admitted to the ICU

while 95% (n = 1475) of them had ordinary care. Also, 1.2% (n = 18) of all studied patients died while the rate of mortality among ICU patients (n = 78) was 23% (n = 18).

**Table (2) :** Percentage of ICU admission and mortality among the studied patients (n=1553).

Outcome	n	%
ICU admission	78	5.0
Mortality	18	1.2
n = number; N.B: Total number of patients = 1553.		

Table (3) shows comparison between group IIa, group IIb regarding the different parameters of APACHE II scoring system. There were no statistical significant differences between GIIa and GIIb regard-

ing all the studied parameters except for age, mean ABP and serum K level. Although bradycardia was evident in both groups but there was no statistical significant difference among them.

**Table (3) :** Comparison between group IIa (survivors) and group IIb (non-survivors) concerning different studied parameters.

Parameter	Group	GIIa (n=60) Mean±SD	GIIb (n=18) Mean±SD	t	P-value
1. Age (years)		20.4 ± 11.2	32.8 ± 12.5	2.2	0.03*
2. Temperature (°C)		36.8 ± 0.3	36.8 ± 0.2	0.04	0.9
3. Heart rate (beat/min)		51.7 ± 6.8	48.8 ± 5.0	1.675	0.098
4. Mean arterial blood pressure (mmHg)		81.9 ± 4.6	84.8 ± 3.4	2.475	0.015*
5. Respiratory rate (breath/min)		23.8 ± 2.3	24.7 ± 1.9	1.5	0.100
6. Haematocrite (%)		53.1 ± 2.9	51.8 ± 3.0	1.655	0.102
7. WBCs (×10 <sup>3</sup> )		7.6 ± 2.2	7.1 ± 2.1	1.1	0.2
<b>8. Arterial Blood gases:</b>					
PH		7.34 ± 0.2	7.33 ± 0.1	0.204	0.836
Pa CO <sub>2</sub> (mmHg)		36.5 ± 2.7	37.0 ± 2.1	0.6	0.4
Pa O <sub>2</sub> (mmHg)		87.0 ± 5.4	86.1 ± 5.3	0.6	0.5
HCO <sub>3</sub> <sup>-</sup> (meq/L)		24.0 ± 1.2	24.1 ± 0.9	0.08	0.9
9. Serum sodium (meq/L)		133.3 ± 2.2	132.2 ± 2.8	1.744	0.085
10. Serum potassium (meq/L)		3.2 ± 0.1	2.9 ± 0.4	5.349	0.000*
11. Serum creatinine (mg/dL)		0.9 ± 0.3	1.1 ± 0.3	1.7	0.09
n = number; SD = Standard deviation; P>0.05 = insignificant; * P< 0.05 = Significant. N.B: number of ICU admitted patients = 78.					

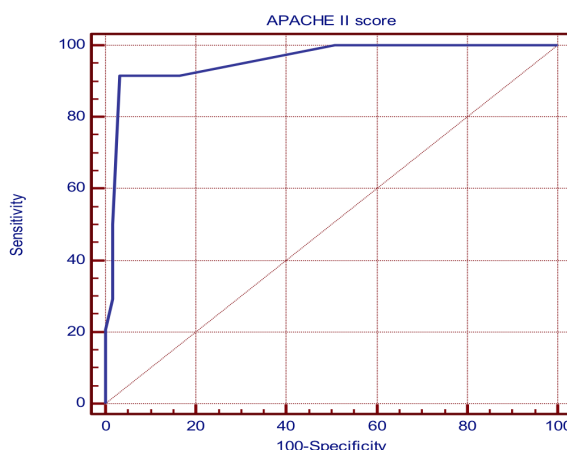
Table (4) shows the sensitivity and specificity of APACHE II score in detection of ICU admission among cases of acute organophosphorus compounds poisoning, where sensitivity represents the true positive rate and specificity repre-

sents the false positive rate and they were plotted using Receiver operating characteristic curve "ROC curve" (curve 1). In the current study, area under the curve for APACHE II score was 0.958 and the best cut off value was > 8.

**Table (4) :** Sensitivity and specificity of APACHE II score in detection of ICU admission among cases acutely poisoned with organophosphorus compounds.

Cut-off values	Accuracy	Sensitivity	Specificity	PPV	NPV
> 7	87.64	91.67	83.61	68.7	96.2
> 8 *	94.21	91.67	96.72	91.7	96.7
> 9	74.18	50.00	98.36	92.3	83.3

\*The best cut off point between survivors and non-survivors.  
 Area under the curve = 0.958; 95% confidence interval (0.89 – 0.98).  
 PPV: Positive predictive value; NPV: Negative predictive value



**Curve (1):** Receiver operating characteristic curve (Roc curve) showing sensitivity and specificity of APACHE II score in detection of ICU admission among acute organophosphorus poisoning.

Table (5) shows comparison between group IIa and group IIb as regards the APACHE II score result. APACHE II score

was higher (9.88) in GIIB when compared with GIIa (6.62) and the difference was statistically significant.

**Table (5) :** Comparison between group IIa & group IIb as regards results of APACHE II score.

Group	GIIa (n = 60)	GIIb (n=18)	T	P-value
	Mean ± SD	Mean ± SD		
APACHE-II score	6.62±1.11	9.88±1.54	10.828	0.000*

n = Number; SD = Standard Deviation, \*p < 0.05= Significant.

### **DISCUSSION**

Acute organophosphorous (OP) poisoning is a serious clinical entity that cause considerable mortality and morbidity especially polyneuropathy in survivors. The estimated mortality following OP exposure ranges from 20-50% all over the world (Munidasa et al., 2004).

The results of the current study showed that the most commonly affected age group ranged from 22.1 to 23.2 years and these findings were similar to those recognized by Murali et al. (2009) and Devanur et al. (2013). They revealed that the mean age in a retrospective study about acute OP poisoning was 23.5 years. This result is also comparable to the study of Shaikh et al. (2008). They observed that 88% of the patients in their study were in the age limit of 22-30 years.

Regarding the mean body temperature recorded in this study, there was hypothermia in both groups (GI & GII) and this coincides with that reported by Ali et al. (2012), who found rapid drop in body temperature within one hour post OP exposure. Similar results were noticed by Houze et al. (2011), who recorded a decrease in body temperature after 30 minutes from OP ingestion. This hypothermia is a common response in acute OP toxicity which is mediated by cholinergic stimulation of heat loss. It could be also attributed

to excessive sweating (Gordon and Ward, 2009), yet, there were no significant statistical differences between GI and GII regarding age and the temperature recorded in the current study. These results are in accordance with the work of Sugunadevan et al. (2009), who stated that acute OP poisoning is a serious condition and ICU admission depends on HR, RR and other important physiological parameters rather than age or body temperature.

The cardiac manifestations of acute OP toxicity in this work were in the form of bradycardia and hypotension in both groups (GI & GII). Nevertheless, there was a significant difference regarding the HR between both groups, while regarding MAP no significant difference was noticed between GI and GII. Paul and Bhattachavyya (2012) postulated that there are many mechanisms to explain OP induced bradycardia and hypotension including muscarinic effect, acidosis and electrolyte derangement. Ali et al. (2012) reported that 32% of cases in their study had cardiac manifestations. The same was recorded by Anand et al. (2009), and added that hypotension and sinus bradycardia are cholinergic in origin.

In the present study, both groups (GI & GII) showed increase in the respiratory rate. Alarcon et al. (2005) and Rehiman et al. (2008) reported tachypnea in all patients included in their study on acutely

intoxicated OP patients. This tachypnea could be due to respiratory distress which is one of the signs of severity in acute OP intoxication (Shaikh et al., 2008).

Regarding the haematocrite value, it showed elevation in GI and GII, and the difference between them was statistically significant, while WBCs showed non-significant changes. The elevation in the haematocrite value could be explained after Murray et al. (2008), who stated that excessive muscarinic cholinergic stimulation leads to severe gastrointestinal manifestation in the form of severe vomiting and diarrhea which may lead to dehydration with subsequent elevation of the haematocrite level especially in severe cases with acute OP poisoning.

Considering ABG values, there was significant decrease in pH and PaO<sub>2</sub> and significant increase in PaCO<sub>2</sub> among cases admitted to ICU (GII) and the difference between this group and GI was significant statistically, while HCO<sub>3</sub><sup>-</sup> level showed non-significant differences between both groups. Liu et al. (2008) postulated that acute OP poisoning causes alteration in the acid-base equilibrium in the form of acidosis and they concluded that acidosis is a major predisposing factor that influences the outcome of patients with OP intoxication. These changes in ABG values could be due to inadequate oxygenation as a result of hypotension and respiratory

distress which are criteria of severity in patients with OP poisoning (Khan et al., 2006). Setlur and Sharma (2005) concluded that ABG monitoring remains a useful parameter in assessing the clinical care of acute OP poisoning.

As regards serum Na<sup>+</sup> and K<sup>+</sup> levels, there was significant decrease in GII (cases admitted to ICU). This result is in accordance with those of Sugunadevan et al. (2009), who found a decrease in serum Na<sup>+</sup> and K<sup>+</sup> in cases with acute OP poisoning admitted to the ICU and considered serum Na<sup>+</sup> and K<sup>+</sup> to be included in the criteria for cases requiring ICU admission. They stated that careful monitoring of serum electrolytes may decrease the mortality among these patients.

Regarding the percentage of mortality in (GIIb), it was 23% of cases admitted to ICU which is considered a high percentage and this group showed higher APACHE II score than GIIa (survivors). Correlation between APACHE II score and the severity and as well as outcome in the current study were similar to the results observed by Pore et al. (2011); Vaidyanathan et al. (2012) and Hrabetz et al. (2013).

Kang et al. (2009) reported that APACHE II score was higher in ICU admitted cases. Hsien et al. (2009) concluded that the higher the APACHE II score the

poorer the outcome and added that APACHE II score together with cholinesterase level are reliable and useful in evaluating patients with OP poisoning admitted to the ICU because it essentially shows the degree of physiological derangement and is closely correlated with the outcome in critically ill patients.

Sam et al. (2009) said that APACHE II score is a simplified physiological score predicting and assessing the severity and mortality of OP poisoning. This score is simple and effective when applied for young patients (15-22 years) and is considered one of the ICU scoring systems which can be used to measure the severity of the situation and to describe and predict the probability of mortality among OP poisoned patients. Sungurtekin et al. (2006) and Bilgin (2005) stated that APACHE-II score is a good score for predicting the outcome among OP intoxicated patients.

In the present study, the results of the role of APACHE II score in detection of OP poisoning cases requiring ICU admission (Table 4 & Curve 1) showed that the best cut off value was  $> 8$  which coincides with the work done by Kang et al. (2009). Eizadi-Mood et al. (2007) observed that the best cut off value for APACHE II score was 7 and that the severity and prognosis of OP poisoning differed significantly below and above this point.

From the results of the current work, it can be concluded that APACHE II score is a useful prognostic indicator in cases of acute OP poisoning due to its simplicity, less time consumption and effectiveness in emergency cases.

It is recommended to calculate APACHE II score on admission as it has a significant value in predicting not only the severity of OPP but also the outcome.

There were some limitations in our study as the exact type of OPC and amount consumed were not known and this must be considered as different compounds may have different clinical syndromes and outcomes. Yet, the findings in this study highlighted the usefulness of APACHE II score as a reliable index for predicting the outcome of acute OP intoxicated cases which may reduce the mortality rate among them. Furthermore, it sets an APACHE II score that can be used for decision making for ICU admission and close clinical monitoring for patients with score  $> 8$ .

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## دور مجموع نقاط أباتشي II في التنبؤ بشدة ونتيجة التسمم الحاد بالمبيدات الفوسفورية العضوية

المشتركون في البحث

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يعد التسمم بالمركبات الفوسفورية العضوية سبباً للحالات المرضية والوفيات في بلدان كثيرة بما فيها مصر. لذا فإنه من الضروري تقييم خطورة التسمم بالمبيدات الفوسفورية العضوية باستخدام طرق علمية والحفاظ على قاعدة بيانات سريرية للتمكن من إرساء طرق منظمة وفعالة علاجياً لهذه الحالات. وتهدف هذه الدراسة لبحث القيمة التنبؤية لنقاط أباتشي II في التوقع بخطورة ونتيجة التسمم الحاد بمختلف المبيدات الفوسفورية العضوية ومحاولة وضع نقطة تقاطع لمجموع النقاط حتى تساعد على خطة العلاج. تم إجراء هذه الدراسة على حالات التسمم الحاد بالمبيدات الفوسفورية العضوية والذين تم دخولهم مركز علاج التسمم جامعة عين شمس خلال عام ٢٠١٠. وقد تم تقسيمهم إلى مجموعتين أساسيتين. المجموعة الأولى: حالات التسمم الحاد بالمبيدات الفوسفورية العضوية والتي لم تدخل العناية المركزة. والمجموعة الثانية: حالات التسمم الحاد بالمبيدات الفوسفورية العضوية والتي دخلت العناية المركزة وقد تم تقسيم هذه المجموعة إلى مجموعتين فرعيتين، المجموعة الثانية أ: الناجين والمجموعة الثانية ب: الغير ناجين. تم أخذ التاريخ الطبي كاملاً من كل المرضى أو أقاربهم وتم عمل فحص عام عند الدخول للحصول على البيانات اللازمة لنقاط أباتشي II.

وقد أظهرت الدراسة أنه من إجمالي ١٥٥٣ حالة تم دخول ٧٨ حالة (٥٪) الرعاية المركزة (المجموعة الثانية) وتوفى ١٨ حالة (٢٣٪) منهم (المجموعة الثانية ب). وجد نقص في ضربات القلب في المجموعة التي تم دخولها الرعاية المركزة (المجموعة الثانية) مقارنة بالمجموعة التي لم يتم دخولها (المجموعة الأولى) وكانت الاختلافات ذات دلالة إحصائية. كذلك أظهر معدل التنفس اختلافات ذات دلالة إحصائية بين المجموعتين. كانت قيمة الهيماتوكريت مرتفعة في المجموعة الأولى والثانية وكانت الإختلافات بينهما ذات دلالة إحصائية. أظهرت الحالات التي تم دخولها الرعاية المركزة اختلافاً ذي دلالة إحصائية بالنسبة لتحليل الغازات بالدم الشرياني مقارنة بهؤلاء الذين لم يتم دخولهم. كان مستوى الصوديوم والبوتاسيوم أعلى في مجموعة الرعاية المركزة (المجموعة الثانية) عند المقارنة بالمجموعة الأولى وكان الاختلاف ذا دلالة إحصائية. عند مقارنة المجموعة الثانية أ (الناجين) مع المجموعة الثانية ب (الغير ناجين) كانت هناك فروق ذات دلالة إحصائية لكل من العمر، متوسط ضغط الدم ومستوى البوتاسيوم بين المجموعتين. وبالنسبة لنتائج نقاط أباتشي II فقد وجد فرقاً ذو دلالة إحصائية بين المجموعتين الفرعيتين (المجموعة الثانية أ و المجموعة الثانية ب) وأفضل نقطة تقاطع كانت أقل من ٨ وتدل هذه النتيجة على أهمية نقاط أباتشي II في التنبؤ بخطورة التسمم الحاد بالمبيدات الفوسفورية العضوية وبالتالي تحديد خطة العلاج الفوري. وتخلص الدراسة إلى أنه يمكن استخدام نقاط أباتشي II في التنبؤ بخطورة ونتيجة التسمم بالمبيدات الفوسفورية العضوية في المرضى وذلك لسهولته وسرعته وفاعليته في حالات الطوارئ ونقطة التقاطع أقل من ٨ في مجموع نقاط أباتشي II يمكن أن تستخدم لدخول العناية المركزة.