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ORIGINAL ARTICLE

PERADENIYA ORGANOPHOSPHORUS COMPOUND POISONING SCORE, GLYCEMIC STATUS AND ELECTROCARDIOGRAPHIC CHANGES AT THE TIME OF ADMISSION IN ORGANOPHOSPHORUS COMPOUND POISONING AND THEIR CORRELATION WITH SEVERITY AND CLINICAL OUTCOME

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Abstract

Background: *Acute organophosphorus compound (OPC) poisoning is a serious public health issue, especially in the rural areas. Peradeniya organophosphorus poisoning (POP) scale was developed to assess the severity of OPC poisoning. Although degree of choline- esterase inhibition plays a key role in the severity of OPC poisoning, some other metabolic factors like dysglycemia also has an association. Cardiovascular effects of acute OPC poisoning are also common.* ***Methods:*** *This hospital based prospective observational study was conducted at indoor of Department of Medicine, Chattogram Medical College Hospital for six months period, from January 2020 to June 2020. Fifty patients above 12 years of age with acute OPC poisoning who fulfilled the selection criteria were selected consecutively for the study. After initial resuscitation severity of poisoning was assessed by POP scale, Random blood glucose (RBS) and 12 lead ECG was documented at the time of admission. Patients were followed up till their hospital stay to observe the outcome in terms of death, need for Intensive care unit support, and length of hospital stay.* ***Results:*** *The mean age was 33.33 (±11.73) (Range: 15-65) years. Male to female ratio was 1.77:1. As per the POP score 24% had mild, 54% had moderate and 22% had severe grade of poisoning. The mean Random blood glucose level was 186.05±51.44 mg/dl (range 90-288 mg/ dl) with 21 (42 %) cases having blood glucose value above 200 mg/ dl. ECG finding was abnormal in 56% of case with ST-T changes as the most common abnormality. Mortality rate was 24%. Most of the death occur in an average of 4th day of admission. POP score at the time of admission 7.5 or more had 91.7% sensitivity and 100% specificity to predict in hospital mortality. Admission Random blood glucose level of 207.9 mg/dl had 75% sensitivity and 68.4% specificity to predict in hospital mortality and morbidity.* ***Conclusion:*** *POP scale, glycemic changes and ECG are good markers for predicting morbidity and mortality and can be used as assessment tools for severity of poisoning and also to assess the prognosis of OPC poisoning cases.*

Keywords: *Organophosphate compound poisoning, Peradeniya organophosphorus poisoning score, Random blood glucose, Electrocardiography.*

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Introduction:

Organophosphorus compounds (OPC) are pesticide that can bind and inhibit, cholinesterase enzyme making it unable to breakdown acetylcholine.[1] Acute OPC poisoning is a major clinical and public health concern across rural part of Asia.[2] Unfortunately, in most rural hospitals there is insufficient staff or inadequate equipment available to deal with patients with severe poisoning.[3] Acute OPC poisoning remains a serious problem in Bangladesh.[4] In a review Dewan et al. identified that pesticide poisoning is a cause for greater number of admission and death in Bangladesh. In his review 89.8% are due to OPC.[5] Pesticide poisoning was responsible for 72.6% of total poisoning related deaths. Approximately 0.7 deaths per 100,000 population was due to pesticide poisoning.[5] OPC poisoning are one of commonly encountered emergency situations and accounts for more than 75% of all cases of acute poisoning in hospital practice in Bangladesh and mortality rate is about 16%.[6]

As mentioned earlier, OPs compounds mainly work by inhibiting acetyl cholinesterase (AChE) enzyme. AChE is a neurotransmitter found both in central and peripheral nervous system and its normal physiological action is breakdown of acetylcholine (ACh). OPC inactivate AChE by phosphorylating the hydroxyl group located at the active site of AChE. Once AChE has been inactivated acetylcholine accumulates in the autonomic nervous system, PNS and CNS resulting in overstimulation of muscarinic and nicotinic receptors. Accumulation of acetylcholine at nerve endings has played a major part in providing a rationle for specific antidote treatment using atropine and oximes.[7]

Although more than 1000 organophosphorus insecticides exist, three most common type used for self-poisoning in Sri Lanka. These three types differs in clinical features and severity.[8] The preliminary assessment of patients is mainly based on the clinical presentation of the patients.[9] However, it is complex to evaluate the severity of toxicity and the prognosis of patients with acute OPC poisoning in hospitals. A practical bed side scoring system was developed for severity assessment of OPC poisoning patients. Routine use of this scoring system could rapidly assist in identifying patients at higher risk who require more intensive care or Transfer for better management.[10]

OPC poisoning is associated with a high case fatality rate with more preventable deaths occurring in developing countries than in developed countries and yet there are no clear-cut evidence-based guidelines for the management of OPC poisoning.[11,12] Till date, many studies have been carried out to assess factors determining the severity of OPC poisoning and to predict morbidity and mortality. These include Glasgow coma scale score, Acute Physiology and Chronic Health Evaluation II score, pseudo cholinesterase level, lactate dehydrogenase level, serum immunoglobulin, circulating complements, various scoring systems, and creatinine phosphokinase.[13,14] However, there is no consensus regarding contribution of these factors and score to determine severity and also to predict morbidity and mortality. The clinical relevance of these changes to prognosis is not yet clear.[15]

As expected, the higher the level of toxins in the tissue more should be symptoms. Based on this hypothesis, a scoring system known as Peradeniya Organophosphorus poisoning (POP) scale was put forth by Senanayake et al. [16] This scale uses 6 clinical parameters to assess the severity of poisoning and graded as mild (score 0-3), moderate (score 4-7) and severe (score 8-11).[16]

POP scale has not been studied much in Bangladeshi scenario. It could be a simple and effective tool to determine the need for ventilatory support early in the course. In a recent Indian study, the POP scale showed a significant association in predicting the poor prognosis group (Intermediate syndrome, ventilatory support and mortality). Lower grade of poisoning had a better outcome whereas higher had a poorer outcome.[17]

All varieties of glycemic changes ranging from hypoglycemia to hyperglycemia and ketoacidosis have been reported in OPCs poisoning cases.[18,19] A recent prospective analytical study of 100 patients with diagnosed acute OPCs poisoning conclude that the glycemic status at the time of presentation in acute OPCs poisoning patients is a simple, cheap, reliable marker to asses the clinical severity and outcome when considered with clinical severity scores.[20]

Electrocardiographic changes in OPC poisoning have been reported along with the associated structural myocardial damage. Abnormal ST-T changes and progressive fall in voltage and or low voltage were the commonest ECG changes encountered in patients with OPC poisoning. These occurred significantly more often in patients with moderate or severe poisoning. The patients with a combination of these ECG abnormalities required higher doses of atropine and those who survived it takes longer time to normalize the ECG despite normal clinical recovery rate as compared to other cases. Other ECG abnormalities like prolongation of the QT interval, ectopic beats, conduction defects and peaked P wave were seen less frequently and had returned to normal with clinical recovery and did not correlate with prognosis.[21]

Contemplating this background this study was intended to observe the morbidity and mortality in terms of requirement of ventilation and hospital stay and time of death from admission which can be accessed from POP score, ECG findings and glycemic status at presentation. The study also tried to identify the levels of these parameters at which they indicate chances of significant morbidity and mortality.

Methods:

A hospital based prospective observational study was performed in indoor patients of documented OPC poisoning admitted in different Medicine Units of Chattogram Medical College Hospital between January 2020 to June 2020. Patients of 12 years and older irrespective of sexes who volunteered history of ingestion of OPC (irrespective of the nature of poisoning—deliberate self-harm, homicidal or otherwise and regardless of brand of OPC and whether or not a sample was provided for identification were included in this study by consecutive sampling technique. Patients who were already treated at other centers and referred to our center for further management with no details available at the time of first presentation or had consumed alcohol, drugs, mixed poisoning that could affect the glycemic status of the patients were excluded from this study. Pregnant patients or patients with Diabetes Mellitus or any cardiac co-morbidity were not included in this study. After arrival of the patients initial treatment and resuscitation was done by the ward staff. Following resuscitation the patients were assessed for eligibility in the study. When the inclusion and exclusion criteria were fulfilled, patient's attendants were invited to voluntarily participate in the study and to read and sign an informed consent statement. The data were collected by interview, and examination. Identification of the type of chemical was determined by the labels or the names of chemicals the patient was exposed. POP score, Blood sugar and bed side 12 lead ECG was done along with the initiation of appropriate treatment. Appropriate treatment of the patients was started along with atropine and pralidoxime. Atropine was given in the doses of 0.5 to 2mg atropine intravenously and double dose every 3-5 minutes interval till the signs of atropinisation appeared. Patients received the standard treatment as per hospital protocol. However, for convenience and resource limitation, finally it was possible to include 50 patients in the study within study period.

Severity of OPC poisoning was assessed by Peradeniya organophosphorus poisoning (POP) scale which is based on six cardinal manifestations of OPC poisoning (miosis, fasciculation, respiratory difficulty, bradycardia and impairment of consciousness, any history of convulsion).

The scoring system is given below-

Table I

POP scale for severity assessment of OPC poisoning

	Score
Miosis	
Pupil size >2 mm	0
Pupil size <2 mm	1
Pupil size: pin point	2
Fasciculation	
None	0
Present but not continuous	1
Genarlized and continuous	2
Respiration	
Respiratory rate d"20 min	0
Respiratory rate>20 min	1
Respiratory rate>20 min with central cyanosis	2
Bradycardia	
Pulse rate >60 min	0
Pulse rate 41-60 min	1
Pulse rate <40 min	2
Level of consciousness	
Conscious and rational	0
Impaired, respond to verbal command	1
Impaired, no respond to verbal command	2
If convulsion present, add 1	
Total:11; Mild: 0-3; Moderate: 4-7; Severe: 8-11	

A pre designed semi-structured case record form was used as a data collection tool.

After collection data were compiled in a Microsoft Office Excel Worksheet. Then they were fed into SPSS (Statistical Package for Social Science) for Windows version 23 software to process and analyze the data. Continuous variables were reported as mean values ± standard deviation (SD) while categorical variables were expressed as count and percentage. The statistical significance of intergroup differences was compared through unpaired Student's 't'-test for continuous variables and through Pearson's Chi-square test for categorical variables. The ability of the variables (POP score and CBG level) to discriminate survivors from non survivors were determined using receiver operating characteristic (ROC) curves. Correlation between CBG and POP score was assessed by correlation coefficients. Two-sided p value < 0.05 were considered to represent a statistically significant difference.

Results:

In this study, there were 50 participants who selected consecutively fulfilling the inclusion criteria. Out of them 32(64%) were male with a male to female ratio of 1.78:1. 30% of patients fall in age group of 21-30 years with mean age 33.33 ± 11.73 years. Most of the patients had educational qualification below(22%) or up to(46%) secondary level and reside in rural area(56%). Regarding occupation majority of them were either housewife(22%) or involved in business(22%).

In most of the cases nature of poisoning was suicidal and reason was domestic issues. The entire group reported to have oral exposure. Median interval for admission from exposure was 2 hours and only 14% patients received pre-hospital management (Table II).

Table II

Distribution of the patients by exposure related variables (n=50)

Poison related variable	No. of patients	Percent (%)
Nature of poisoning		
Suicidal	42	84.0
Homicidal	2	4.0
Accidental	5	10.0
Reason for poisoning		
Domestic issue	20	40.0
Financial loss	5	10.0
Marital issue	9	18.0
Educational failure	9	18.0
Not specified	7	14.0
Route of poisoning		
Oral	50	100.0
Interval between exposure to admission		
Mean ±SD, hours	2.54±1.55	
Received pre-hospital management		
Yes	7	14.0
No	43	86.0

The severity of the OPC poisoning was assessed by POP scale. The individual parameter those are used to compute POP score are described in Table III.

Table III

Distribution of POP scale parameters of the patients (n=50))

Parameters	No of patients	Percent (%)
Pupil size		
>2 mm	5	10.0
<2 mm	23	46.0
Pin point	22	44.0
Fasciculation		
None	19	38.0
Present but not continuous	25	50.0
Generalized and continuous	6	12.0
Respiratory rate		
Respiratory rate d”20 min	11	22.0
Respiratory rate>20 min	31	62.0
Respiratory rate>20 min with central cyanosis	8	16.0
Hear rate		
Pulse rate >60 min	15	30.0
Pulse rate 41-60 min	26	52.0
Pulse rate <40 min	9	18.0
Level of consciousness		
Conscious and rational	14	28.0
Impaired, respond to verbal command	24	48.0
Impaired, no respond to verbal command	12	24.0
Convulsion		
None	44	88.0
Present	6	12.0

Based on POP score the severity form was classified as mild: score 0-3; moderate: score 4-7 and severe: score 8-11 which is shown in Figure 1.

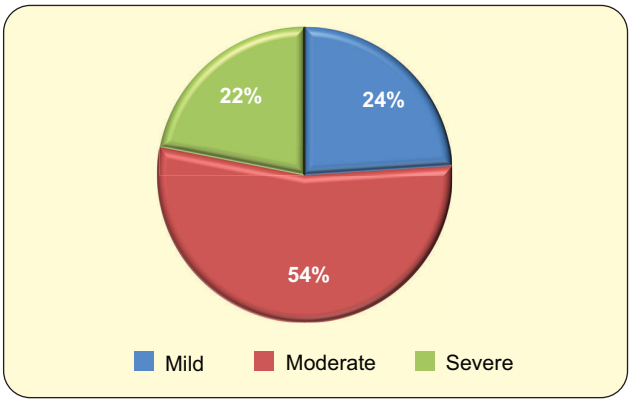

Fig.-1: *Distribution of the study population based on the severity of OPC poisoning by using the POP scale*

The present study group comprised of non-diabetic patients. At the time of admission of a OPC poisoning patient average blood sugar level was 186.05±51.44 mg/dl mg/dl (range 90-288 mg/). 21 (42 %) patients having RBS value above 200 mg/ dl.

ECG finding was normal in 44% cases. The most common ECG abnormality was ST-T change (ST elevation/depression and isolated T inversion) observed in 30% patients followed by QT prolongation (12%) and conduction defect (4%).

In- hospital outcome of the patients is shown in Table IV.

Table IV

In-hospital outcome of the patients (n=50)

Outcome parameters	Frequency	Percent (%)
Develop IMS	4	8.0
Death	12	24.0
ICU referral	11	22.0
Length of hospital stay (days)		
Mean ± SD	5.58±1.42	
Range	2-8	

IMS: Intermediate syndrome

Figure 2 shows that, earliest death was recorded in 2nd day after admission and last death at 8th day after admission. Most of the death (33.33%) was recorded on day 4.

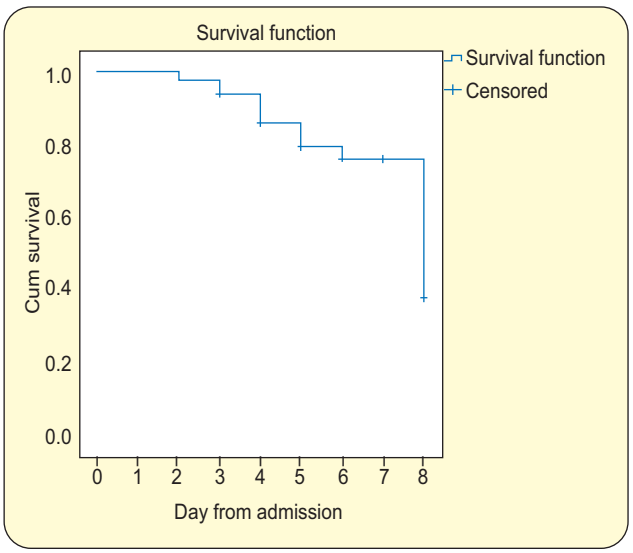

Fig.-2: *In-hospital survival analysis among OPC poisoning patients*

In the present study, 12 (24%) patients died out of 50 included patients. All patients with severe poisoning as per POP score at admission died in hospital. Regarding admission RBS glucose level >200 mg/dl were associated with mortality and morbidity in the study. Admission ECG finding had no significant association with the in-hospital mortality in the study. All these associations are shown in Table 5 and Figure 3.

Table V

Association between baseline POP score, ECG findings and glycemic status with outcome of the patients

Parameters	Level	Outcome of the patients		P value*
		Survived (n=38)	Died (n=12)	
	Mild (0-3)	11 (28.9)	1 (8.3)	
POP	Moderate (4-7)	27 (71.1)	0 (0)	<0.001
	Severe (8-11)	0 (0)	11 (91.7)	
RBS level	<140 mg/dl	7 (18.4)	2 (16.7)	
	140-200 mg/dl	19 (50.0)	1 (8.3)	0.001
	>200 mg/dl	12 (31.6)	9 (75.0)	
ECG	Normal	19 (50.0)	3 (25.0)	0.128
	Abnormal	19 (50.0)	9 (75.0)	

*P values are derived from Fishers exact test.

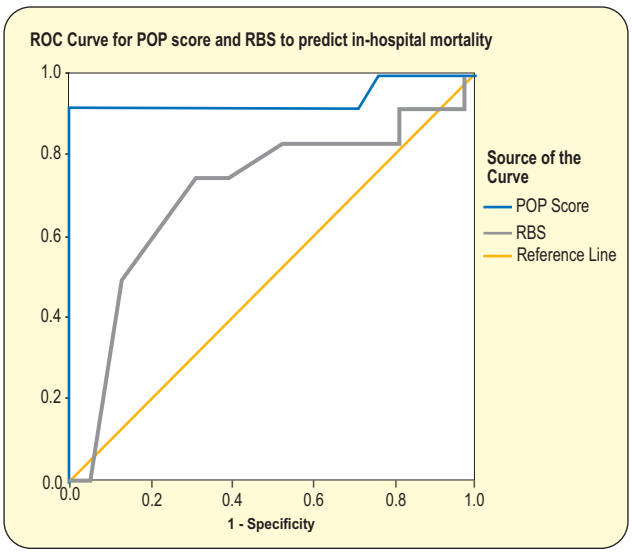

Fig.-3: *Receiver operating characteristic curve showing discrimination of the POP score and admission RBS for the prediction of in-hospital mortality*

Correlation between POP score and admission RBS levels of the patients were assess by Pearson correlation coefficient and presented as a scatter diagram in Figure 4.

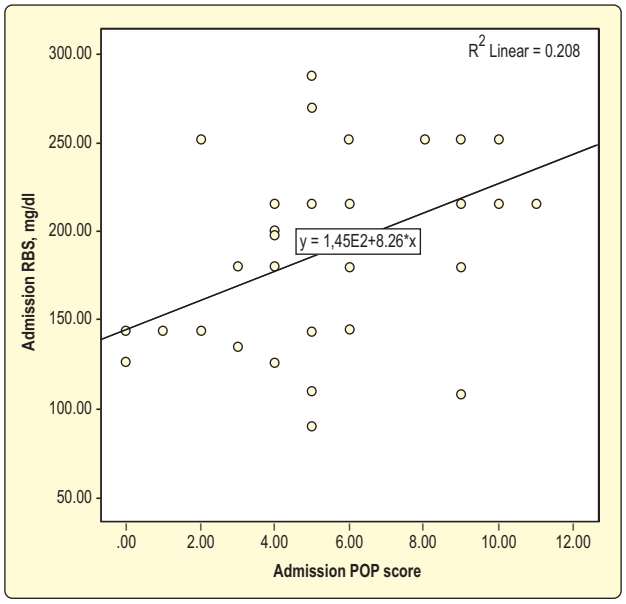

Fig.-4: *Scatter diagram showing correlation of POP score with admission RBS.*

Discussion:

OPC poisoning has been diagnosed as a prime problem in developing countries like Bangladesh because of its predominant use in pest control and crop protection. The diagnosis of OPC poisoning is mainly based on the history of ingestion or exposure, clinical features, low serum cholinesterase levels and therapeutic response to atropine.[9] Present study was conducted to determine and correlate the outcome with the severity of acute OPC poisoning assessed by POP score, admission RBS and ECG findings. Fifty OPC poisoning cases admitted in the medicine ward of CMCH were enrolled for this purpose.

OPC poisoning is mostly common in young, affecting both genders equally.[22-35] which correlates with the current study. The mean age of the patients was 33.26 (±13.13) years. Half of the patients were younger than 30 years. The most predominant age was 21-30 years with 30% cases. Of the entire study subjects males were more in numbers than the females. In the present study majority of patients were housewives or engaged in business. Majority of the patients were from rural area and had education up to or below SSC. This finding was expected because our hospital is a Government level tertiary care hospital usually provides health services mostly to lower to lower middle class patients. These observations with respect to demographic data were in line with observations of other studies conducted in and around our country.[22-37]

Majority of the patients in the present study were in the second or third decade who could contribute to the economic status of the family. Most common reasons identified for consuming the poison was suicidal and reason was domestic issues. Other reasons for suicidal attempt were financial loss, and stress and a similar type of result was quoted by a study done by Mundhe et al.[30] Moreover, individuals in this age group are active physically, mentally and socially and thus more prone to various stresses.

In the present study, out of 50 OPC poisoning cases, 11 patients required ventilation support for respiratory failure. Unfortunately all of them were expired with an overall mortality of 12 (24%). The mortality rates of the current study compares well with another recent study from India where the overall mortality rate was 22%.[38] However, reported mortality rates in OPC poisoning patients widely varied among studies from 61.9% to 11.5%.[39,40] It should be noted that all of the mentioned studies including the current one were single center study with small sample size, which might be attributable for these wide variation in the mortality rate.

The initial evaluation of the severity of acute OPC poisoning remains critical, and this is because severe cases usually need intensive care and ventilator support, which are not available in rural areas. Currently, no widely accepted criteria are present for classifying the severity of such poisoning cases. The

preliminary evaluation is mainly based on the presentation of clinical symptoms.[9] In the current study admission POP score, admission RBS and ECG parameters were evaluated and correlated with the mortality.

The present study demonstrated that, glycemic variability was a marker of poor prognosis. Out of 12 expired patients 9 (75%) had admission RBS level >200 mg/dl. This finding indicated that, hyperglycemia at the time of presentation may be a harbinger of greater in-hospital mortality. Excess activation of nicotinic-N receptors resulting in excess catecholamine release (from sympathetic ganglia) and ACTH (from anterior pituitary)which causes stress hyperglycemia and reduction in glucose induced insulin secretion by beta cells of Langerhans that might be attributable for this association between glucose level and mortality.[33] Raveendra et al.[33] reported a overall mortality of 9%, with highest percentage of deaths occurred among hyperglycemic [3 out of 15(20%)] and a similar trends was also observed in the study conducted by Raghapriya et al.[20] Mir et al.[24] .In this study the patient whose blood glucose levels were 216±61 mg/dl had increased mortality as compared to patients who survived in whom blood glucose levels were 136±88 mg/dl.

In the current study glycemic status as measured by RBS at admission significantly correlated with the severity of the patients as assessed by POP score. In the study of Raveendra et al.[33] observed that, 16% of euglycemic, 30% of hypoglycemic and 60% of hyperglycemic had severe grade of poisoning based on POP scoring and which was statistically significant. Sudhir et al.[22] also assessed glycemic changes in acute anticholinesterase insecticide poisoning and correlate with the severity of poisoning. Similar to our results they concluded that a positive correlation exists between the glycemic changes and the severity of OPC poisoning.

Regarding ECG changes in most of the cases (44%) ECG finding was normal. The most common ECG abnormality was ST-T change (ST elevation/depression and isolated T inversion) observed in 30% patients followed by QT prolongation (12%) and conduction defect (4%). Cha et al.[26] observed that, sinus tachycardia was the most common ECG abnormality and 11.1% had ST change. Some investigators have described a polymorphic ventricular tachycardia of the torsade de pointes type attributed to a prolongation of the Q-Tc interval associated with OPC poisoning.[41-43] In spite of the presence of a prolonged Q-Tc interval in 12% patients in the current study none of them had this type of arrhythmia. For the absences of such grave ECG changes present study failed to determine any association between ECG changes and mortality. Small sample size might be the limited factor for the absence of different ECG changes and their association with mortality in the current study.

In present study, according to POP scale, out of 50 patients, 24% were in mild category, 54% in moderate category and 22% patients fell in severe category. A total of 24% of the patients died, of which none patients belonged to moderate and 11 out of 12 patients belonged to severe group. So, POP scale correlated, directly and significantly, with mortality. Other studies also showed increased mortality and need of ventilator support was more in patients with high POP scale.[28,30]

The clinical significance of the present study was that, POP scale was found to be valid for our patients for prediction of adverse outcome following OPC poisoning. The POP applied at admission was able to predict the outcome of the subjects in terms of mortality and morbidity. The results of the present study agreed with other study done, which had similar results and hence it is safe to assume that POP score which is an easy, quick and inexpensive method can be used on all patients presenting with OP poisoning as a predictor of outcome. The routine use of this scoring system and also the assessment of blood sugar could rapidly assist in identifying patients at higher risk who require more intensive care or transfer to a larger better-equipped hospital. The patients with evidence of moderate and severe degrees of poisoning and high blood sugar need close monitoring, as respiratory failure is the prime cause. However the studies to understand the OPC induced glycemic variability and its role on the severity and outcomes are very few. Prospective studies regarding the same in a large cohort are desirable with focus on mechanistic association between the glycemic status and outcomes. Also the importance of continuous glucose monitoring and the management of the fluctuations in critical care settings need to be investigated and emphasized.

Though from the findings of the present study it can be concluded that initial assessment by POP scale and blood sugar level at presentation in OPC poisoning cases is useful in assessing the severity and at the same time being important indicators of mortality, the methodological limitations specially the small sample size need to be considered during generalizing the study results.

Conclusion:

In conclusion, 22% of the patients had severe grade of poisoning as per POP score, 42% of the patients had blood glucose value above 200 mg/ dl, and ECG finding

was abnormal in 56% of case with ST-T changes as the most common abnormality. POP score at the time of admission 7.5 or more had 91.7% sensitivity and 100% specificity to predict in hospital mortality. Admission Random blood glucose level of 207.9 mg/dl had 75% sensitivity and 68.4% specificity to predict in hospital mortality and morbidity.

Limitations:

This study has some methodological limitations which must be considered in the analysis of the results. Due to the COVID-19 situation and limited resource sample size was relatively small. Moreover, it was a single center study and the samples were collected conveniently which might limit its ability to generalize the results. Toxicological analysis was not possible. The study did not record or analyze the dose of the ingested OPC. Patient follow-up period was short. Admission RBS > 208 mg/dl along with POP score >7 can be considered as a useful factor in predicting the need for ventilator support and as well as mortality of OPC poisoning. Further prospective studies with greater number of patients are needed taking into consideration of various aspects of poisoning like intake of different OPC compounds, the amount of exposure, the type and dose of the drug, time lag between the intake of poison and initiation of treatment as well as the type of treatment to support the current observation as the current study was conducted with a relatively small number of patients, and in only one center of Bangladesh.

Conflicts of interest:

The authors report no conflict of interest.

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Ethical consideration:

The study was approved by the Ethical Review Committee of Sir Salimullah Medical College Mitford Hospital (SSMCMH) Dhaka, Bangladesh. Informed consent was obtained from each participant or caregivers of the patients.

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