

STUDY OF CLINICAL AND BIOCHEMICAL PARAMETERS IN PREDICTING THE NEED FOR VENTILATOR SUPPORT IN ORGANOPHOSPHORUS COMPOUND POISONING

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ABSTRACT: Organophosphorus compound is used for committing suicidal are on upswing in developing countries. A grading system of severity of OP poisoning suggests that most cases can be managed in the ICU³ which cannot be applied to developing countries, where facilities for ICU management are rather limited. Hence, the present study is undertaken to identify the factors both clinical and biochemical, which help in predicting the need for ventilator support and thus helping to reduce the mortality by timely institution of ventilator support. **AIMS OF THE STUDY:** To study the clinical and biochemical parameters in organophosphate poisoning, which help to predict the need for ventilator support. **MATERIAL AND METHODS:** This is a Descriptive Study done at Kempegowda Institute of Medical Sciences, Bangalore, with a sample size of 50 cases. Patients who fulfilled the inclusion criteria are assessed as per proforma specifically designed for the study. **RESULTS:** In this study population, 12 patients who reached the hospital for treatment > 4 hour of consumption, 11(91.7%) required ventilator support. In this study, 13 out of 18 (72.2%) patients with pinpoint pupils at admission required ventilator support. In this study, all 12 patients (100%) required ventilator support with a fasciculation score of more than 4 as compared to none with absent fasciculation. In this study, lower the Glasgow coma scale at admission, more vulnerable are the patients for ventilator support. In This study, patients with reduced levels of Pseudo cholinesterase i.e. 11 out of 13 patients (84%) required ventilator support. **CONCLUSION:** Clinical and biochemical parameters such as Greater the time lag from consumption of OP poison till getting specific treatment, Lower GCS scoring, Generalized Fasciculations, Low Pseudo cholinesterase levels, Larger initial dose of Atropine required for Atropinization were strong predictors for the need for Assisted Ventilation in OP poisoning. Grading of the degree of the poisoning taking the above parameters into consideration can help to identify high risk patients who may go in for Respiratory failure and require ICU admission and Ventilator support.

KEYWORDS: Organophosphorus poison, Ventilator, Pseudocholinesterase levels, Fasciculation, Atropine.

INTRODUCTION: Organophosphorus (OP) pesticide self-poisoning is estimated to kill around 200,000 people each year, largely in the Asia-Pacific region. OP poisoning is primarily a problem of the developing countries^{3, 23}.

India being predominantly an agricultural country; pesticides, insecticides are abundantly used during cultivation. Thus it has been natural to have easy access to these chemical substances by human beings. Of the various substances used for suicidal attempts in India, Organophosphorus compounds form a significant group.

The WHO estimates that each yearly nearly 1 million serious accidental and nearly 2 million suicidal attempts involving pesticides occur worldwide⁵². In developing countries, the widespread use of organ phosphorus compounds has been accompanied by an appreciable increase in incidence of poisoning with these agents, both suicidal and accidental. This is attributed mainly to their easy availability, indiscriminate handling, storage and lack of knowledge about the serious consequences of poisoning³.

OP poisoning has high inpatient mortality and many patients have cardio respiratory arrests after admission, hence the present study is undertaken to identify the factors both clinical and biochemical, which help in predicting the need for ventilator support and thus helping to reduce the mortality by timely institution of ventilator support.

AIMS AND OBJECTIVES OF THE STUDY: To study the clinical and biochemical parameters in organophosphorus poisoning, which help to predict the need for ventilator support.

MATERIAL AND METHODS: This is a Descriptive Study which had a sample size of **50** cases.

Inclusion criteria:

1. Patients with OP poisoning above 12 years of age.
2. Patients with single poisoning.
3. Patients who presented within 24 hours of poison consuming.

Exclusion criteria:

1. Patients below 12 years of age.
2. Patients with more than one type poisoning.
3. Patients with chronic lung diseases.
4. Patient with known cardiac diseases.
5. Patients with known neuromuscular junction disorders.
6. Patients already treated elsewhere.
7. Pregnancy.
8. Patients presented after 24 hours of poisoning.

Method of collection of data: A provisional diagnosis of OP poisoning was made on the basis of definite history of poisoning either by the patient himself or attendants, which was substantiated by (a) examination of the container, and or (b) typical clinical features (hyper salivation, miosis and fasciculation), and or (c) characteristic odour of stomach wash and or vomitus, and (d) levels of Pseudo cholinesterase.

Each patient enrolled for study underwent a detailed clinical examination as per proforma (specifically designed for the study), which includes examination for signs of respiratory failure, detailed assessment of central nervous system and cardiovascular system. All patients were given a stomach and body wash. Thereafter, a bolus dose of atropine was administered after correcting cyanosis till signs of Atropinization (dryness of mucosa with or without pupillary dilation >7 mm and heart rate >140 /min) appeared. This was followed by 1 gram slow IV bolus dose of P2AM. All the patients were monitored closely and continuously in the Emergency Ward/Intensive Care Unit and all clinical signs assessed 12 hourly till complete recovery.

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Ventilator support was considered in patients with - Apnea or hypoventilation, Persistent cyanosis, Persistent tachypnea (RR >30/mm) and Deranged arterial blood gases viz., PaO₂ <60 mm of Hg PCO₂ >55 mm of Hg and or Acidosis (pH < 7.2).

The following biochemical investigations were done appropriately for individual cases. Blood routine, Urine routine, Blood urea, serum creatinine, Serum electrolytes, liver function tests, random blood sugars, ECG, Chest X-ray, ABG analysis, and Pseudo cholinesterase estimation.

Latter following gradings were done based on severity of poison, fasciculation, Pseudo cholinesterase, and Glasgow comma scale. -----

GRADING BASED ON SEVERITY OF POISONING¹⁶

GRADE	CRITERIA
Mild Poisoning	Normal level of Consciousness (GCS=2-15) Pupil size \geq 4 mm Fasciculation Score 0-1
Moderate Poisoning	Mild Alteration of Consciousness (GCS=8-11) Pupil Size 2-3 mm Fasciculation Score 2-4
Severe Poisoning	Stupor Coma (GCS \leq 7) Presence of Convulsions Pinpoint Pupils \leq 1mm Fasciculation Score 5 or More Signs of Respiratory Insufficiency.

GRADING OF FASCICULATIONS¹⁶: It is done by giving one point each to anterior and posterior chest, anterior and posterior abdomen, right and left thigh. Right and left arm & leg. The total Fasciculation score was is thus estimated.

GRADING OF SEVERITY BASED ON PSEUDO CHOLINESTERASE LEVELS^{44,4}

Mild poisoning	40-60% of Normal Range
Moderate poisoning	20-40% of Normal Range
Severe poisoning	less than 20% of Normal Range.

ETHICAL CLEARANCE: This study was approved by ethical committee of the institute.

RESULTS: 50 cases were included in the study who fulfilled the inclusion criteria. In this present study the maximum number of cases was in the age group of 21 - 30 years (46%), youngest patient in present study was 14 years and the oldest patient in this study was 68 years (Table 1). Out of 50 cases 33 were Males (66%) and 17 were females (34%) (Table 2). The highest number of cases affected is in student community i.e 17 (34%) followed by farmers 13 (26%), laborers 12 (24%) (Table 3). The commonest symptoms encountered were excessive salivation (66%) followed by vomiting (60%), breathlessness (26%) and altered sensorium (22%) (Table 4).

In this study population, 12 patients who reached the hospital for treatment < 1 hour of consumption, just 2 (16.7%) required ventilator support. 26 patients who reached the hospital for

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treatment between 1-4 hours of consumption, 11(42.3%) required ventilator support. 12 patients who reached the hospital for treatment > 4 hour of consumption, 11(91.7%) required ventilator support. These data are statistically significant with $P < 0.001$ (Table 5).

In this study, 13 out of 18 (72.2%) patients with pinpoint pupils at admission required ventilator support; in comparison only 11 out of 21 (52.3%) patients with pupillary size of 2 mm or more required ventilator support. Here there is no statistical significance $P > 0.05$ (Table 6).

In this present study, patients with higher the Fasciculation scoring requiring ventilator support more than patients with localized or absent Fasciculation. All 12 patients (100%) required ventilator support with a fasciculation score of more than 4 as compared to none with absent fasciculation. These data are statistically significant with $P < 0.05$ (Table 7).

In this study Methyl parathion was the commonest poisoning encountered; out of 25 cases, 15 cases (60%) required ventilator support. Among 6 cases of Dimethoate poisoning, 4 cases (66.7%) required ventilator support. (Table 8).

In this study, we noticed lower the Glassgow coma scale at admission, more vulnerable are the patients for ventilator support and there is a statistical significance ($P < 0.01$) between the two groups i.e. one with GCS scoring above 12 and the other with GCS scoring less than 11 (Table 9).

In This study, reduced levels of Pseudo cholinesterase were directly proportional to need for ventilator support; 11 out of 13 patients (84%) required ventilator support with Pseudo cholinesterase levels less than 20% of normal range. These data are statistically significant ($P < 0.001$) (Table 10).

In this study 88% of the patients who fall in the severe group of poisoning required ventilator support compared to none in mild group of poisoning, and also the more severe groups requires early ventilator support within 24 hours (66%) compared with none in milder group. Similarly four out of 18 (22%) patients required ventilator support after 24 hours while required by none in milder group. These data are statistically significant ($P < 0.001$ and $P < 0.05$ respectively) (Table 11).

In this study all the 13 (100%) patients requiring more than 60 mg of Atropine in the first 48 hours required ventilator support while 11 out 16 (68.8%) patients required ventilator support with Atropine requirement in the range of 35 and 60 mg. These data are statistically significant as shown in the table ($P < 0.001$), (Table 12).

The commonest poison encountered in this study was methyl parathion (metacid) ; 25 out of 50 (50%) cases while Fenithrothion (Tik - 20) poisoning was second commonest; 12 out of 50 (24%) cases. The survival rate after ventilator support was better with methyl parathion poisoning; 22 out of 25 (88%) patients survived while in Dimethoate poisoning where 4 out of 6 (83.3%) patients survived, (Table 13).

DISCUSSION: The leading cause of death in OP poisoning is respiratory failure^{3, 45} and various grading systems proposed³ suggests that most cases can be managed in the ICU. But this can't be applied to developing countries wherein ICU facilities are rather limited. Hence, the present study was undertaken to evaluate the clinical and biochemical factors, grading of severity of poisoning which will help in predicting the respiratory failure and the need for early ventilator support, thus reducing the mortality³.

In this present study, 23 patients were in the age group 21 30 years accounting for 46%; involving the most productive group of the society. Male patients accounted for 66% (33 out of 50

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patients) compared to females (34%) which could be due to easy accessibility to the poisons and also lack of legal stricture. These results are comparable to other studies^{6,43} where males outnumbered females and the commonest age group affected was between 21-30 years.

In present study, students formed a major group accounting for 17 out of 50 patients (34%) while farmers (26%) and laborers (24%) followed. Although the present study was conducted in an urban set up, laborers and farmers constituting 50% of the study population were encountered since our hospital is a tertiary centre with referrals from both semi urban and rural areas. The high incidence of suicidal attempts among student population in this region has to be viewed with grave alarm and concern.

In present study the most common OP poison used was methyl parathion in 25 patients (50%), followed by Fenithrothion (TIK - 20) in 12 patients (24%). These are similar to other study done by Namba et al³⁶. Field OP poisons were encountered more commonly than domestic poisons even in an urban set up. This probably indicates the easy accessibility to the poisons over the counter and lack of legal strictures.

The commonest symptoms encountered in our study were excessive salivation (66%), nausea and vomiting (60%) which correlates well with other studies done by Tsao et al⁴⁵ and Namba et al³⁶ wherein excessive salivation was encountered in 40% and 31% respectively, while nausea and vomiting were encountered in 44% and 42% respectively. A study done by Goel et al¹⁶ had vomiting as the commonest symptom (97%) and hypersalivation in 28%.

The commonest signs in this present study were miosis (60%), fasciculation's (36%) and respiratory insufficiency (40%). These are comparable to studies done by Goel et al¹⁶ where in miosis was seen in 95% and Fasciculation's were seen in 55% of cases. Also miosis was encountered in 77% of cases in a study done by Tsao et al⁵. Respiratory insufficiency was seen in 40% of cases in a study done by Tsao et al⁴⁵ and it was 42% in the study done by Goel et al¹⁶, which are quite similar to our study.

In this present study need for ventilator support was increased among patients who presented late for specific treatment. This was substantiated by the fact that 11 out of 12 patients (91.7%) required ventilator support who presented to hospital after 4 hours of poisoning while 2 out of 12 patients (16.7%) required ventilator support who presented within first hour of poisoning for specific treatment, these are statistically significant. These results are similar to a study by Sunder Ram et al wherein patients who delayed hospitalization by more than 4 hours had more death rates and also the severity of the poisoning was more. Goel et al¹⁶ study also have shown a positive relation between delay in hospitalization after consumption of poisoning to need for ventilator support; 17 out of 32 (53%) patients in their study required ventilator support who presented 4 hours or more after poisoning to specific treatment; while only 3 out of 15 patients who presented early required ventilator support accounting for 20% only. Basu et al⁵ have shown that the greater the delay in hospitalization, worse are the symptoms and outcome. A study done by Gupta et al²⁰ shows that all the deaths in the study involving 60 patients occurred following delay in treatment (more than 8 hrs) from time of consumption of poisoning.

In this present study, the pupillary size and requirement of ventilator support had a positive correlation. 13(72.2%) out of 18 patients with pinpoint pupils required ventilator support as compared to none among 11 patients with pupillary size of more than 4mm. These results are well correlated with those of Tsao et al⁴¹ wherein 43 (52%) patients with pinpoint pupils out of 83

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required ventilator support. Similarly in the study done by Goel et al¹⁶ the ventilator support was required in 11 among 17 patients (64%) with pinpoint pupils as compared to 5 among 23 patients (21%) with pupillary size of more than 2 mm. Although there was no statistical significance between the above two groups, but we can observe a clinical significance.

While common therapeutics in treatment of OP poisoning depend on pupillary size for atropine dosage, studies indicate that pupillary size alone do not form a criterion for atropine dosage⁴, Besides, the clinical features at the time of admission due to the central action of the drug, such as level of consciousness (graded by GCS scoring) and pupillary size act as a good prognostic indicators.

In the present study it was found that patients with lesser Glassgow coma scale (GCS) scoring required ventilator support as compared to patients with normal GCS. while all the 3 patients (100%) with GCS score of less than 7 required ventilator support only 21 patients out of 47 patients (44%) required ventilator support with GCS score of 8 and above. In a study Goel et al¹⁶ showed that patients with GCS score of less than 7: 6 (75%) out of 8 patients required ventilator support while 16 (21.05%) out of 76 patients required ventilator support with GCS more than 11 and these correlated well with our study both statistically and clinically.

It was found in the present study that patients with generalized fasciculation's were more prone for respiratory failure and ventilator support as compared to patients with localized or absent Fasciculation. These are quite comparable to studies done by Bardin et al³ wherein the disturbed level of consciousness / stupor and presence of fasciculation were categorized as severe Grade of poisonings.

Another important parameter, which strongly influenced ventilator assistance, was the initial bolus atropine requirement to produce signs of Atropinization. Patients requiring more than 60 mg of atropine were more prone (all 13 patients -100 %) for ventilator support as against none among 21 patients with Atropine requirement of less than 35 mg. These are quite comparable to studies done by Singh et al⁴², who showed that aggressive Atropinization improves survival in patients with OP poisoning. Sunder ram et al have shown that earlier the Atropinization better is the survival rate. Also the results of the present study are comparable to the study done by Goel et al¹⁶ wherein 90% of patients required ventilator support with 60mg and more of initial atropine requirement as compared to 47% with requirement less than 36 mg.

In the present study, the levels of Pseudo cholinesterase at admission correlated well with the need for ventilator assistance. 11 out of 13 patients (84%) required ventilator support with levels less than 20% of normal, while 9 out of 31(29%) patients required ventilator support with levels between 40 60%. In the study by Sunder Ram et al⁴⁴ the mortality was high in patients with Pseudo cholinesterase levels less than 20% as compared to patients with 40 60% of normal levels.

In the present study, A new modified grading system for severity of OP poisoning suggested by Goel et al¹⁶ was used and based on this grading the need for ventilator support was evaluated in the present study. In the severe grade of poisoning group - out of 18 patients 12 (66%) required early ventilator support (with in 24 hrs) while 4 (22%) required late ventilator support. In the moderate grade of poisoning group - out of 12 patients 6 (50%) required early and 2 (16%) late ventilator support. The data are statistically significant when compared between two groups. Though the suggested modified grading has a positive correlation to requirement of ventilator support both clinically and statistically, further large independent hospital based studies are required, so as to

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find routine clinical application in terms of predicting the severity and hence the need for ICU monitoring and ventilator support.

Apart from the above factors which help in predicting the need for ventilatory support; Severity of OP poisoning and need for ventilator support was also studied in relation to nature of poisoning. Although some OP compounds required an increased ventilatory assistance, especially Dimethoate (66%) when compared to Methyl Parathion (60%), the values were statistically insignificant. Further larger studies are required to delineate the same.

Mortality in the present study was 16% (4 out of 24 Ventilated patients) and causes of death were acute renal failure (ARF), refractory circulatory failure and status epilepticus with Anoxic encephalopathy.

CONCLUSION: Clinical and biochemical parameters such as Greater the time lag from consumption of OP poison till getting specific treatment, Lower GCS scoring, Generalized Fasciculation's, Low Pseudo cholinesterase levels, Larger initial dose of Atropine required for Atropinization were strong predictors for the need for Assisted Ventilation in OP poisoning. Grading of the severity of the OP compound poisoning taking the above parameters into consideration can help to identify high risk patients who may go in for Respiratory failure and require ICU admission and Ventilator support.

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LIST OF ABBREVIATIONS USED

OP	Organophosphorus
WHO	World Health Organization

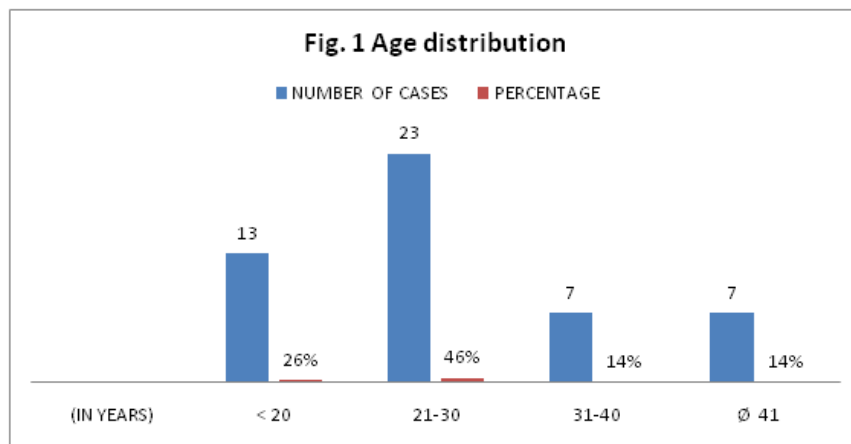
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GCS
ABG
KIMS
ICU

Glasgow Comma Scale
Arterial Blood Gas
Kempegowda Institute Of Medical Science
Intensive Care Unit

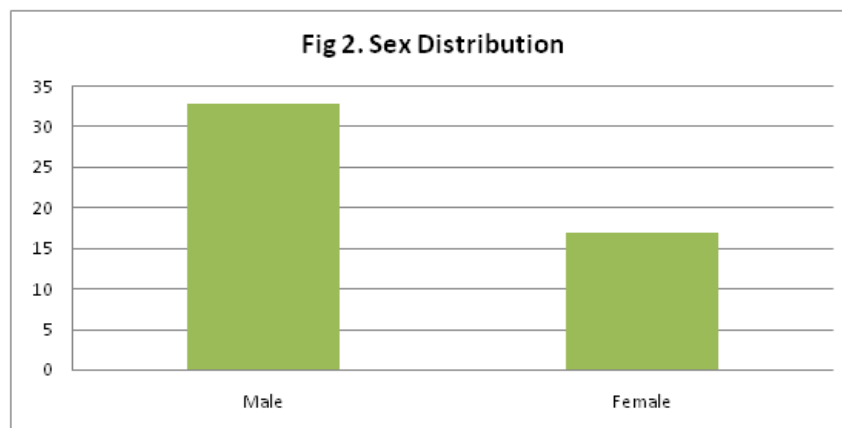
AGE GROUPS (IN YEARS)	NUMBER OF CASES	PERCENTAGE
< 20	13	26%
21-30	23	46%
31-40	7	14%
➤ 41	7	14%

TABLE 1: AGE DISTRIBUTION OF PATIENTS



SEX	NUMBER OF CASES	PERCENTAGE
Male	33	66%
Female	17	34%

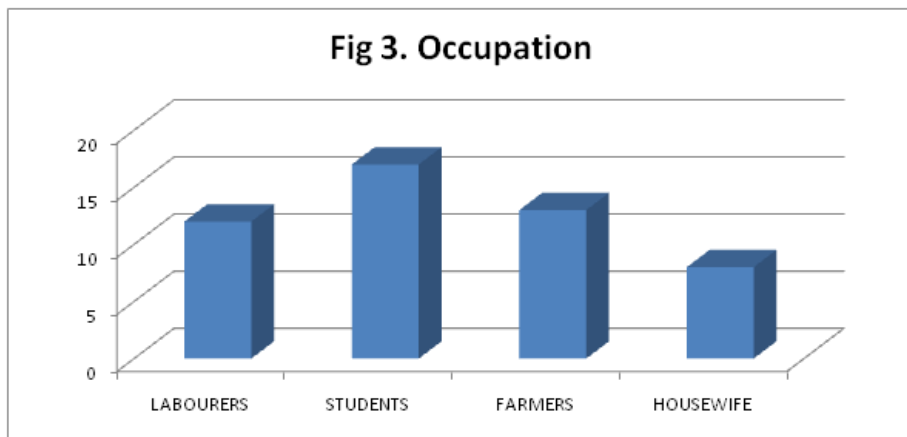
TABLE 2: SEX DISTRIBUTION OF PATIENTS



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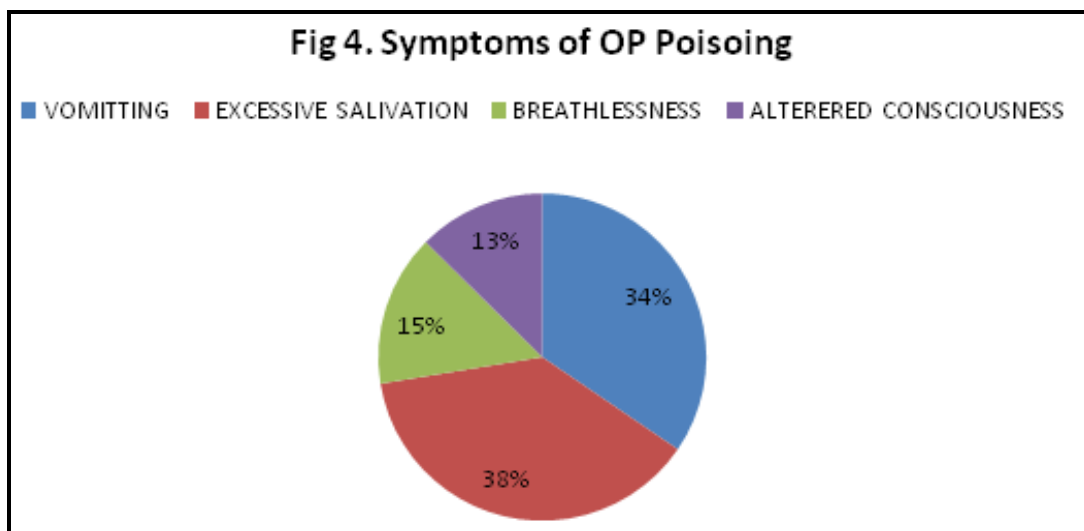
OCCUPATION	NUMBER OF CASES	PERCENTAGE
LABOURERS	12	24%
STUDENTS	17	34%
FARMERS	13	26%
HOUSEWIFE	08	16%

TABLE 3: OCCUPATION OF PATIENTS



SYMPTOM	NUMBER OF CASES	PERCENTAGE
VOMITTING	30	60%
EXCESSIVE SALIVATION	33	66%
BREATHLESSNESS	13	26%
ALTERERED CONSCIOUSNESS	11	22%

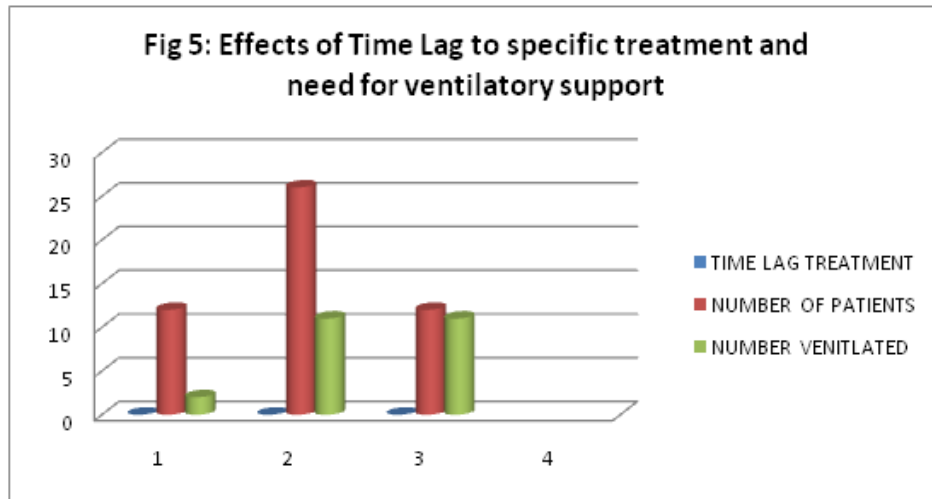
TABLE 4: SYMPTOMS OF O.P POISONING AT ADMISSION



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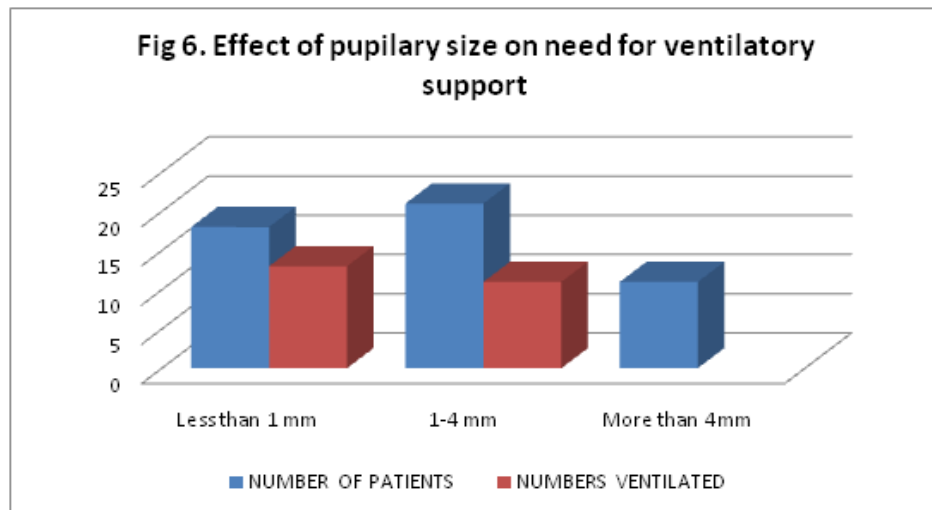
TIME LAG TREATMENT	NUMBER OF PATIENTS	NUMBER VENTILATED	PERCENTAGE
≤ 1 Hour	12	2	16.7%
1 – 4 Hrs	26	11	42.3%
≥ 4 Hrs	12	11	91.7%

TABLE 5: EFFECTS OF TIME LAG TO SPECIFIC TREATMENT AND NEED FOR VENTILATOR SUPPORT



SIZE OF PUPIL	NUMBER OF PATIENTS	NUMBERS VENTILATED	PERCENTAGE
Less than 1 mm	18	13	72.2%
1-4 mm	21	11	52.3%
More than 4mm	11	0	0

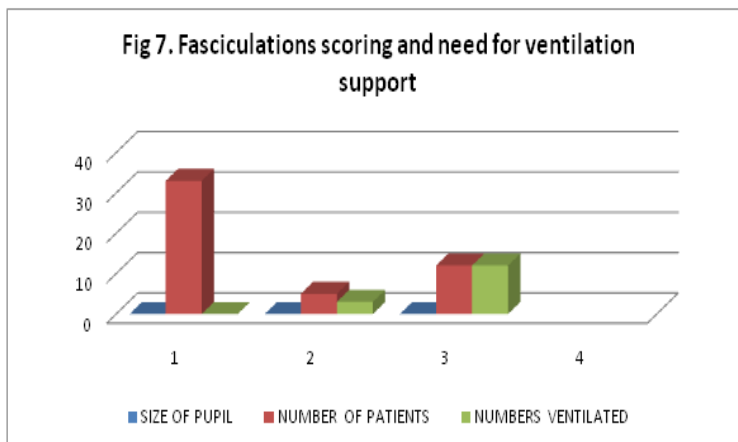
Table 6: EFFECT OF PUPILARY SIZE ON NEED FOR VENTILATOR SUPPORT



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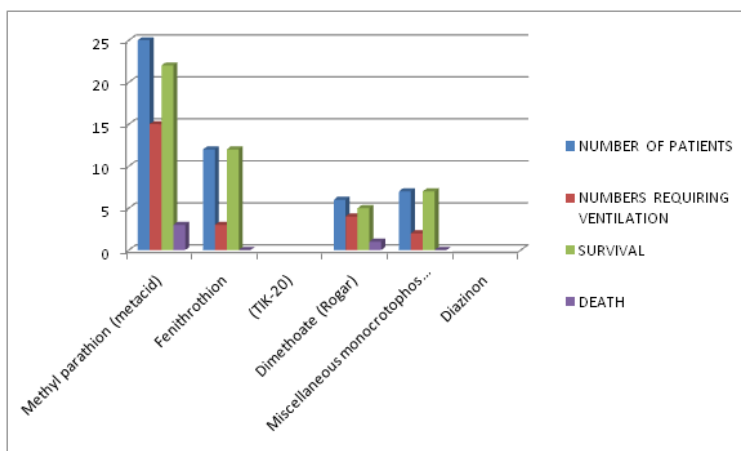
FASCICULATIONS SCORING	NUMBER OF PATIENTS	NUMBERS VENTILATED	PERCENTAGE
0	33	0	0
1-3	05	03	60%
4-6	12	12	100%

TABLE 7: FASCICULATIONS SCORING AND NEED FOR VENTILATOR SUPPORT.



NAME OF COMPOUND	NUMBER OF PATIENTS	NUMBERS REQUIRING VENTILATION	PERCENTAGE REQUIRING VENTILATION
Methyl parathion (metacid)	25 (50%)	15	60%
Fenithorothion Dimethoate (Rogar)	6 (12%)	4	66%
Miscellaneous Monocrotophos Dichlorovas, Diazinon	7 (14%)	2	28%

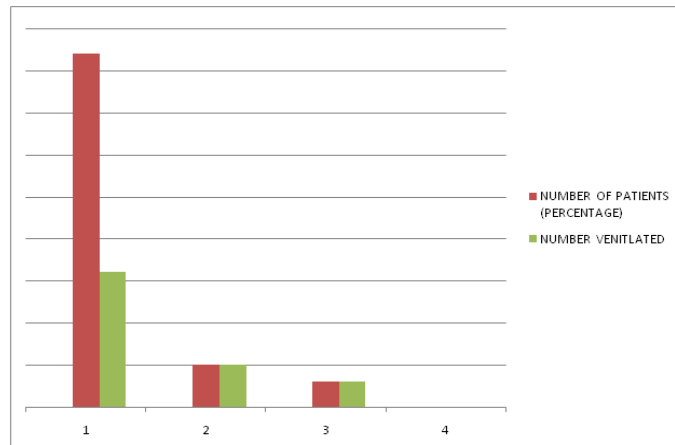
TABLE 8: TYPE OF ORGANOPHOSPHORUS COMPOUND & ITS RELATIONSHIP TO NEED FOR VENTILATOR SUPPORT



ORIGINAL ARTICLE

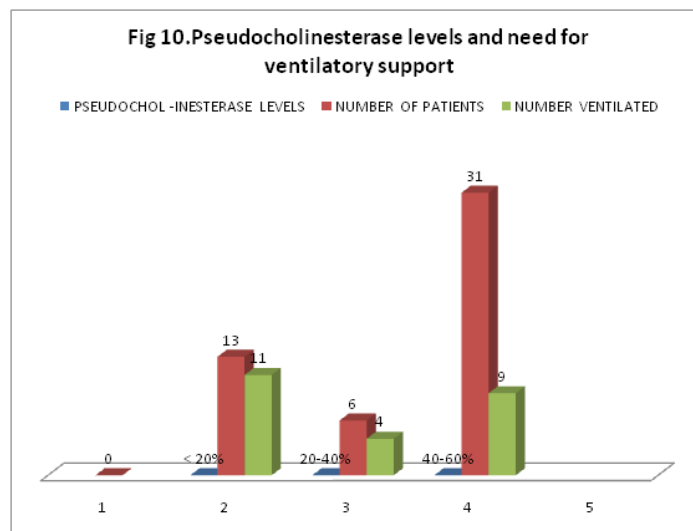
GLASSGOW COMA SCALE	NUMBER OF PATIENTS (PERCENTAGE)	NUMBER VENTILATED	PERCENTAGE
12-15	42	16	38%
8-11	5	5	100%
Less than 7	3	3	100%

TABLE 9: ASSOCIATION OF GLASSGOW COMA SCALE SCORING AND NEED FOR VENTILATOR SUPPORT.



PSEUDOCHOL -INESTERASE LEVELS	NUMBER OF PATIENTS (PERCENTAGE)	NUMBER VENTILATED	PERCENTAGE
Less than 20%	13	11	84.4%
20-40%	6	4	66.7%
40-60% of normal levels	31	9	29%

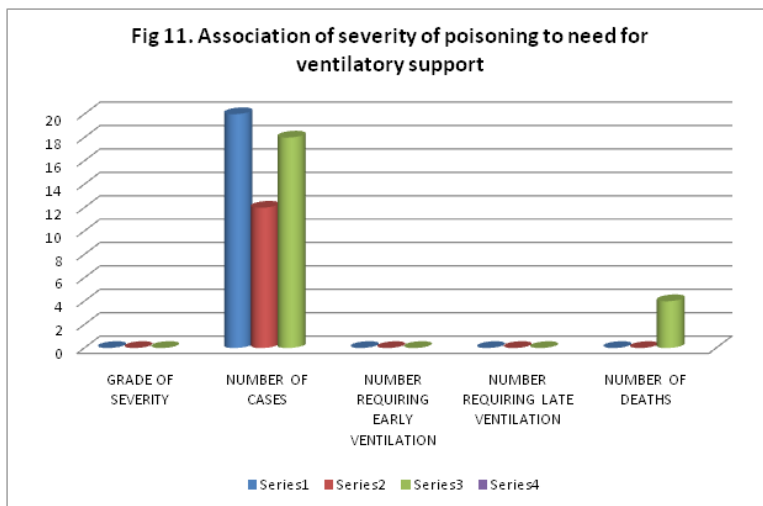
TABLE 10: ASSOCIATION OF PSEUDOCHELINESTERASE LEVELS TO NEED FOR VENTILATOR SUPPORT



ORIGINAL ARTICLE

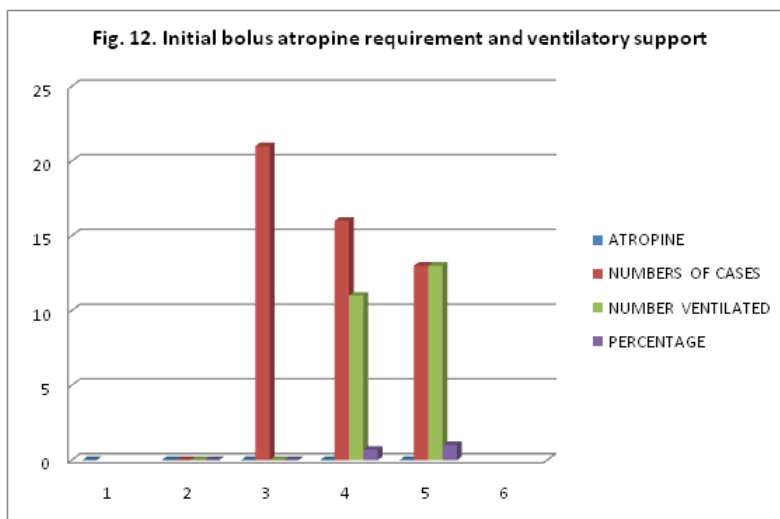
GRADE OF SEVERITY	NUMBER OF CASES	NUMBER REQUIRING EARLY VENTILATION	NUMBER REQUIRING LATE VENTILATION	NUMBER OF DEATHS
Mild	20	0	0	0
Moderate	12	6 (50%)	2 (16.67%)	0
Severe	18	12 (66.7%) P<0.001	4 (22.23%) P<0.05	4 p>0.5 (NS)

TABLE 11: ASSOCIATION OF SEVERITY OF POISONING TO NEED FOR VENTILATOR SUPPORT



ATROPINE (IN MG)	NUMBERS OF CASES	NUMBER VENTILATED	PERCENTAGE
Less than 10	0	0	0
10-35	21	0	0
35-60	16	11	68.8%
More than 60	13	13 P<0.001	100%

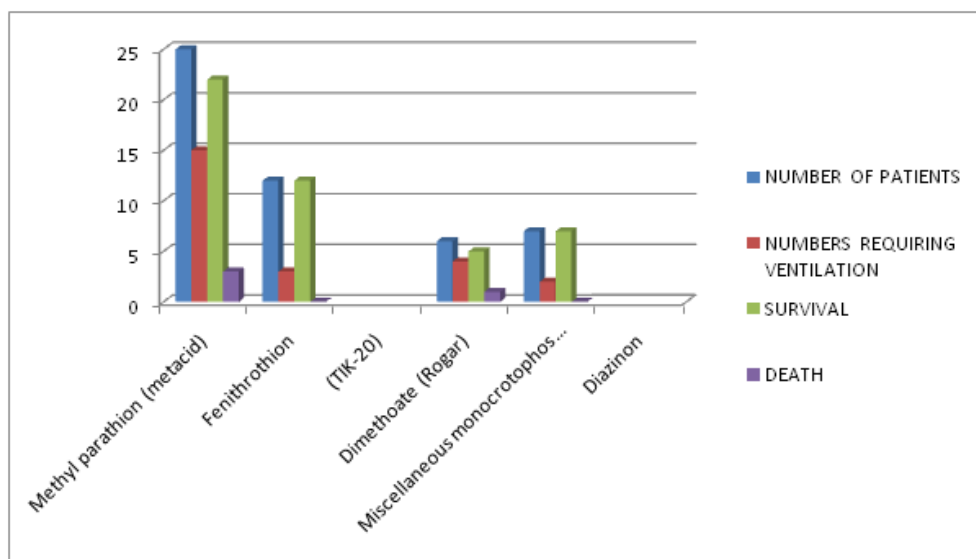
TABLE 12: INFLUENCE OF INITIAL BOLUS DOSE OF ATROPINE AND NEED FOR VENTILATOR SUPPORT



ORIGINAL ARTICLE

NAME OF COMPOUND	NUMBER OF PATIENTS	NUMBERS REQUIRING VENTILATION	SURVIVAL	DEATH
Methyl parathion (metacid)	25 (50%)	15 (60%)	22 *88%)	3
Fenithrothion (TIK-20)	12(24%)	3 (25%)	12 (100%)	0
Dimethoate (Rogar)	6 (12%)	4 (66%)	5 (83.3%)	1 (16.67%)
Miscellaneous monocrotophos Dichlorovas Diazinon	7 (14%)	2 (28%)	7 (100%)	0

TABLE 13: TYPE OF ORGANOPHOSPHORUS COMPOUND & ITS RELATIONSHIP TO NEED FOR VENTILATOR SUPPORT & ITS OUTCOME



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