"STUDY OF PREDICTORS FOR VENTILATORY SUPPORT IN PATIENTS OF ORGANOPHOSPHORUS COMPOUND POISONING"

By

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IN

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UNDER THE GUIDANCE OF

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DR. VIPIN D.T.

LIST OF ABBREVIATIONS

OP	**:**	Organophosphate
REM	:	Rapid eye movement
V/Q	:	Ventilation perfusion
NMJ	**:**	Neuromuscular junction
AchE	:	Acetylcholinesterase
OPIDN	:	Organophosphate induced delayed polyneuropathy
COPIND	**:**	Chronic organophosphate induced neuropsychiatric disorder
GCS	:	Glasgow coma scale
POP	:	Peradeniya orgnosphrous poisoining scale
POM	:	paraoxonase
PAM	:	Pralidoxime
CMAPs	**:**	Compound muscle action potentials
SAPS	**:**	Simplified acute physiology score

ABSTRACT

BACKGROUND: Organophosphorus compound poisoning used most commonly for suicidal attempts which is seen frequently in farmers of younger age group of lower socio-economic status from rural areas. Identifying the factors which help in predicting the need for ventilatory support in organophosphorus compound poisoning helps to decrease in morbidity and mortality.

MATERIAL AND METHODS:A hospital based prospective cross sectional study was conducted with 100 patients to analyze the clinical profile of organophosphate compound poisoning and identify the factors which help in predicting the need for ventilatory support in organophosphorus compound poisoning.

RESULTS: Majority of the patients were in the age group of 21-30 years The mean age of the patients was 31.96 ± 14.12 years. The route of exposure was oral in all the patients. The most common organophosphorus compound consumed in our study was Malathion (28%) , 46 (46%) patients had very poor GCS score (≤7), 38 (38%) patients had low serum cholinesterase levels (≤2100 IU/L), 9 (9%) patients had amylase levels>140 U/L, 43 (43%) patients required ventilatory support while 57 (57%) patients did not require ventilator support. Among patients with fasciculations 64% were on ventilatory support. There was significant association of fasciculations and ventilatory support. 87 (87%) patients survived while 13 (13%) patients died in our study. All patients that died were on ventilatory support.

CONCLUSION: OP insecticide poisoning is a life threatening condition that needs rapid diagnosis and treatment. Since most of the patients present with respiratory failure, early initiation of mechanical ventilation plays a vital role in the treatment of such cases. Emphasis must also be given to good supportive care and monitoring for

the prevention and management of acute and delayed complications that occur during the course of stay in ICU.

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 cholinesterase levels 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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INTRODUCTION

India being an agriculture-based country, organophosphate (OP) pesticide remains the main agent for crop protection and pest control. It is therefore likely to have adverse effects on farmers who are accidentally over exposed while handling these pesticides. However, because of low cost and easy availability, it has also become an agent of choice for self poisoning.[1]

In India, majority of its population, directly or indirectly dependent on agriculture. Varieties of pesticide are widely and freely available for use in farming and other places. Deliberate self-harm in the form of consumption of toxic compounds is one of the major public health care issues in developing world including India.[2] According to National Poison Information Centre in New Delhi, India organophosphate poisoning is one of the most common agents used for suicidal poisonings.[3]

OP consumption accounts among the most cause of suicide in the world , the study done by Gunnel et al published that 258,234 would die of organophosphate poisoning and they account for 30% of the suicidal cause worldwide. OP's result in accumulation of acetylcholine as a result of phosphorylation of serine hydroxyl residue on acetylcholine esterase enzymes.[4]

Accumulation of acetylcholine leads to cholinergic features. They can be broadly divided into central and peripheral symptoms. Vomiting, diarrhea, miosis muscle fasciculations, urinary incontinence and bronchoconstriction are the peripheral symptoms where as respiratory depression and delirium are central symptoms. [5]

Respiratory failure is one of the dreaded cholinergic features of OP. Central as well as peripheral machanisms are involved in this, many centre have suggested that the

mechanism underlying respiratory failure are predominately centre in origin.Pre-bolgingen complex which is the respiratory centre located in ventrolateral medulla is composed of glutaminergic and muscarinic fibres. Significant amount of acetylcholine can suppress the respiratory activity in these areas. [6-7] Injection of dichlorous bilaterally into the pre-bolginger complex in vagally intact rats produces a decrease in respiratory rate , a decrease in volume of inspired gas, and about 2% of animals become apneic.[8]

The effect of acetylcholine related to respiratory function on the brainstem has been studied using sleep literature. During rapid eye movement (REM) sleep the concentration of acetylcholine increases in pontomedullary reticular field of brainstem which inhibits brainstem. If an exposed brainstem has been injected with acetylcholine a decrease in phrenic nerve output abd respiratory inhibition haven been observed in various studies.[9-10]

Both brain and lung are interconnected neurologically by the vagus nerve. Mechanoreceptors provide feedback via the vagus nerve. In spontaneously breathing animals , it has been observed that hypoventilation associated with OP's is blusted by vagal mechanism, vagal mechanisms are known to increase pulmonary secrections has been demonstrated following surgical vagotomy[11]

When the lungs are exposed to OP's an increase in acetylcholine at the pulmonary muscarinic receptors is observed which would result in pulmonary abnormalities. There is obstruction of airways with OP agents which increase the respiratory effort by way of increased pulmonary static and dynamic complex.[12,14] Decrease in pulmonary compliance and ventilation perfusion mismatch is observed in OP's because of interstitial edema.[15, 16]

OP poisoning can induce excitatory activity, which worsens the central hypoxia and compromises respiratory efforts.[17] Based on the time lapse from OP ingestion respiratory failure can be divide into two categories. The early one which occurs within 24hrs is because of three possible mechanisms. They include depression of central respiratory drive from the respiratory centre in the ventrolateral medulla , weekness of the muscles of respiratory and OP induced bronchospasm and bronchorea induced via local and vagal mechanism.[18-20] Prolonged stimulation of the neuromuscular junction(NMI) resulting in peripheral dysfunction is the possible explanation for late respiratory failure. [21-23]

Dangerious level of OP in blood precipitate extrapyramindal features as a result of effect OP on bilateral basal ganglia. The extrapyramindal symptoms tend tooccurs from day 4 to day 40 after exposure to OP . cortical glutamate stimulation is decreased resulting in reduced striated activity. This can result in dopamine deficiency resulting in features of parkinsonism, which include bradykinesia, rigidity resting tremors, akinesia and speech impairement. The features of parkinsonism may be mistaken for acutereactive depression or psychosis which leads to improve pharmacotherapy and pronlonged syndrome duration with increased risk of morbidity and mortility.[24]

In the above context, the fatal issue is often related to a delay in diagnosis or an improper management. Management of severe poisoning is difficult, requiring intensive care and use of atropine and oxime cholinesterase reactivators. Key to survival lies in early diagnosis followed by rapid decontamination and definitive therapy which purely lies under the expert domain of emergency medicine.

Hence the present study was done at our tertiary care centre to assess the clinical profile of organophosphate compound poisoning and identify the factors which help in predicting the need for ventilatory support in organophosphorous compound poisoning.

AIMS AND OBJECTIVES

1. To study the clinical profile of organophosphate compound poisoning.
2. To identify the factors which help in predicting the need for ventilatory support in organophosphorous compound poisoning.

REVIEW OF LITERATURE

Historical Perspectives

The first known pesticide was elemental sulphur dusting used in ancient summer about 4500 year ago in ancient Mesopotamia. By the 15th century , toxic chemical such as arsenic, mercury and lead were being applied to crops to kill pest. In the 17th century nicotine sulphate was extracted from tobacco leaves for use as an insecticide. The 19th century saw the introduction of two more natural pesticide, pyrethrum, which is derived from chrysanthemum and rotenone, which is derived from the roots of tropical vegetables. Until the 1940s arsenic based pesticides were dominant.some sources consider the 1940 and 1950s to have been start of the "pesticide era". In 1960s it was discovered that DDT has got deleterious effects on natural flora and fauna with serious threat of biodiversity. This lead to search for newer insecticidal agent and Organophosphates were introduced in markets. The agricultural use DDT is in developed nation is now banned under the Stockhollm Convention on Persistent Organic Pollutants.[25]

Organophosphorus compounds were first described as early as eighteenth century by Jean Louis Lssaigne however its effect on cholinergic nervous system were described by German Chemist Willy Lange and Gerde Von Krueger in 1932. This discovery later inspired German chemist Gerhard Schrader at company IG Farben in the 1930 to experiment with these compounds as insecticides.[25]

Classification of insecticides[26]

Insecticides are classified in several ways as follows.

1) According to chemical structure.

a) Organic insecticides-

- Organochlorine
- Organophosphates
- Carbamates
- Pyrethroids
- Nicotinoids

b) Inorganic insecticides-

- Arsenates
- Fluorides
- Sulphides
- Copper compounds

2) According to mode of action

a) Systemic insecticide

b) Contact insecticides

c) Fuming agent

3) According to source of insecticide.

a) Natural insecticide derived from plant sources Eg. neem, pyrethrum, nicotine

b) Synthetic insecticides derived from chemicals Eg. organophosphates, organochlorine, carbamate etc

4) WHO Classification as per toxicity

It is based on median lethal dose of the compounds for the rats.

Class	Toxicity	LD50 for the rat(mg/kg body weight)	
		Oral	Dermal
Ia	Extremely hazardus	≤5	≤50
Ib	Highly hazardus	5-50	50-200
II	Moderately hazardus	50-200	200-2000
III	Slightly hazardus	>2000	>2000
IV	Unlikely to present acute hazard	>5000	>5000

Classification of organophosphorus compounds:

1 By Chemical Structure:[27]

A. Alkyl phosphate

1) HETP (Hexaethyl tetra phosphate)

2) TEPP (tetraethyl pyrophosphate) tetron, fosvex etc

3) OMPA (octamethyl pyrophoramide) schardan

4) Dimefox [bis(dimethyl amino) fluorophosphine oxide]

5) Isopestox [bis (isopropylamino) fluro phosphine oxide] pestox

6) Malathion [5,(1,2 dicarbethoxyehyl) 0, o dimethyl dithiophosphate]

7) Sulfoteppa (tetra ethyl 0, dithiopyrophosphate) – dithione Asp-47 ;

8) Systox, demeton (0,0 diethyl 10-2 ehtylmercapto ethyl thionophosphate)

9) Dipterex (0,0 dimethyl 2-2-2 trichorol hydroxyl ethyl phosphateorbait

B. Aryl phosphates**:**

1. Paroxon (0,0, diethyl-o-p-nitrophenyl phosphate) –E 600-mintacol
2. Parathion (0,0, diethyl-o-p-nitrophenyl thiosulphate or diethyl thiophosphoric ester of p-nitrophenol-folidol (bayer), Eketox (sandoz), kilphos, niran, rhyntox, oriental Bug's bait etc.
3. EPN-o, ethyl-o-p nitrophenyl benzene thionophsophate, EPN 300.
4. Methyl parathion o, o-dimethyl o-p nitrophenyl thiophsophate, metacide.
5. Chlorothin-o, o-dimethyl, (o-3-chloro-4-nitrophenyl) thiophosphate
6. Diazion (o,o-diethyl-o-(2-isopropyl-6-methyl-4-pyrmidyl) thiophosphate–Tik
7. Methyl umbelliferone (o,o diethyl thiophosphate)

2.By toxicity:[28]

Highly toxic (< D50 < 50mg/kg)

1) Azinophos-methyl (Cruthion)
2) Bomyl (Swat)
3) Carbophenthion (Trithion)
4) Chlorfenvinphos (Birlane)
5) Chlormephos (Dotan)
6) Coumaphos (Co-ral)
7) Cyanofenphos (Surecide)
8) Demeton (Systox)
9) Dialifor (Torak)

10) Dicrotophos (Bidrin)

11) Disulfoton (Diasyston)

12) EPN ethyl phenylphothiate

13) Famphur (Bo-ana, warbex)

14) Phenamiphos (Nemacur)

15) Fenophos phan (Agrifox)

16) Isophenfos (Amaze, oftanol)

17) Isoflourphate

18) Mephosfolan (Cytolane)

19) Methamidophos (Monitor)

20) Methidathion (Supracide)

21) Mevinphos (Phosdrin)

22) Monocrotophos (Azodrin)

23) Parathion – ethyl

24) Parathion methyl (Penncap-M)

25) Phovate (Thimet)

26) Phostolan (Cyolane)

27) Phosphomidan (Dimecron)

28) Prothoate (Fac)

29) Sulfotep (Bladafum)

30) Tetraethylpyrophosphate (Bladan, TEPP, Tetron)

Moderate Toxicity (αD50 = 50 1000mg/kg) :

1) Acephate (Orthene)

2) Bensulide (Betasan)

3) Chloropyrofos (Durshan, Lorsban)

4) Crotoxyphos (Ciodrin)

5) Cythioate (Proban)

6) DEF (De-Green, E-Z off D)

7) Deneton-s-methyl (Metasystox)

8) Diazinon (Basudin, Spectracide)

9) Dichlorvos (DDVP, Vapona)

10) Dimethoate (Cygon)

11) Edifenphos (EDDP)

12) Ethion (Nialate)

13) Ethoprop (Mocap)

14) Fenitrothion (Accothion)

15) Fenthion (Anthio)

16) IPB (Kitazin)

17) Leptophos (Phosvel)

18) Merphos (Folex)

19) Naled (Dibrom)

20) Phosalone (Zofos)

21) Phosmet (Imidan, prolate)

22) Pirimiphos-ethyl (Dipterex, Dylox, Fernex)

23) Profenofos (Curacron, Polycron, Selecron)

24) Propetamphos (Safrotin)

25) Pyrazophos (Afugan, curamil)

26) Quinalphos (Bayrusil)

27) Sulprofos (Bolstar)

28) Thiometon (Ekatin)

29) Triazophos (Hostathion)

30) Tribufos (Butonate)

31) Trichlorfon (Tugon)

Low toxicity (αD50 = > 1000mg/kg):

1) Bromophos (Nexagan)

2) Etrimfos (Ekanet)

3) Iodofenphos (Nuvanol N)

4) Malathion (Cythion)

5) Phoxim (Baythion)

6) Prophylthiopyrophosphate (Aspon)

7) Temephos (Abate, Abathion)

8)Tetrachlorrinphos (Gardona, Rabon)(αD50 = lethal dose)

Mechanism of Action

The primary mechanism of action of organophosphate pesticides is inhibition of carboxyl ester hydrolases, particularly acetylcholinesterases (AChE). AChE is an enzyme that degrade the neurotransmitter acetylcholine into choline and acetic acid. AChE is found in the central and peripheral nervous system, neuromuscular junctions, and red blood cells. Organophosphate inactivate AChE by phosphorylating the serine hydroxyl group located at the active site of AChE.[29]

Inhibition of enzyme can be

1) Direct inhibitors – compound itself inhibit the enzyme. Eg. Malathion
2) Indirect inhibitors –compound gets converted to active form & inhibits the enzyme. Eg. Parathion which get converted to active form Paroxone.

The phosphorylation occurs by loss of an organophosphate leaving group and establishment of covalent bond with AChE. Once AChE has been inactivated, acetylcholine accumulate throughout a nervous system resulting in overstimulation of muscarinic and nicotinic receptors. Clinical effects are manifested via activation of autonomic and central nervous system and at nicotinic receptor on skeletal muscle.[30-31]

Pathophysiology:

Organophosphate compounds avidly bind to cholinesterase molecules and share a similar chemical structure. In human beings, the two principal cholinesterases are RBC, or true cholinesterase (acetylcholinesterase),and serum cholinesterase (pseudocholinesterase).[32]

Following the completion of neurochemical transmission the neurotransmitter acetylcholine is hydrolised into inactive fragments of choline and acetic acid by the cholinesterase. Acetylcholine is found in the terminal endings of all postganglalic parasympathetic nerves, myoneural junction and both sympathetic and parasympathetic ganglia. The coralent binding of phosphate radicals to the active site of cholinesterase result in dangerious amount of toxicity without the medical treatment the organophosphate cholinesterase bond is not spontoniously reversible and hence OP's behave as irreversible cholinesterase inhibitors. Following the inhibited cholinesterase activity, there is accumulation of acetylcholine at the synapses resulting in overstimulation and disruption of transmission in both the central as well as peripheral nervous system. There is interference with synaptic transmission at the peripheral at the muscarinic neuroeffector junctions and nicotinic receptors within sympathetic ganglia.[32]

Clinical features

The toxic features appears within 30 minutes to 3 hours of exposure to OP compound. The onset and severity of symptoms depends on the specific compounds , route of exposure, amount, and rate of metabolic degradation.[33]Maximum members of patients give history of accidental consumption of OP compounds. Rapid absorption through

the gastrointestinal, respiratory tract and skin resulting toxicity, specific compounds, its quality and route of entry decide the specificity of clinical signs and symptoms. Varied presentations include vomiting, diarrhea and abdominal pain, few patients are unconscious on arrival at the hospital.

A high index of suspicion is therefore needed to make an early diagnosis.[33]The clinical features can be broadly classified as secondary to the (a) Muscarinic effects (b) Nicotinic effects and (c) Central receptor stimulation.

Muscarinic receptor	Nicotinic receptor	Central receptor
Cardiovascular ▪ Bradycardia ▪ Hypotension **Respiratory** ▪ Rhinorrhea ▪ Bronchorrhea ▪ Cough **Gastrointestinal** ▪ Nausea ▪ Vomiting ▪ Abdominal cramps ▪ Diarrhea ▪ Fecal incontinence **Genitourinary** ▪ Urinary continance **Eyes** ▪ Blurred vision ▪ Increased lacrimation ▪ Glands ▪ Excessive salivation	▪ Musculoskeletal ▪ Weakness ▪ Fasciculation ▪ Cramps	▪ Headachae ▪ Giddiness ▪ Drowsiness ▪ Anxiety ▪ Coma ▪ Convulsion

Predominant parasympathetic over-activity and characteristic garlic smell are present in early cases, later , manifestations occurs in multiple system which include gastrointestinal, respiratory, cardiovascular and nervous system. There may be involvement of skeletal muscles and metaboliceffects such as hypo-hyperglycemia. Most fatalities occur within 24 hours and those who recover usually do so within 10 days.

System wise manifestation of organophosphorus poisoning includes ---

Neurological manifestations:

There are four types of neurological syndromes associated with organophosphorus poisoning.[34]

1. Cholinergic phase
2. Intermediate syndrome
3. Organophosphate induced delayed polyneuropathy (OPIDN)
4. Chronic organophosphate induced neuropsychiatric disorder (COPIND)

1. Cholinergic phase

Common manifestations are weakness, fasciculations and areflexia. This is when large numbers of both muscarinic and nicotinic receptors are occupied by acetylcholine, leading to persistent depolarization at the neuromuscular junction. They generally recover with adequate anticholinergic and cholinesterase activating agents. Symptoms are either muscarinic or the nicotinic type. The most severe manifestation in this type is respiratory failure requiring mechanical ventilation.

2.Intermediate syndrome

The term intermediate syndrome was first coined by Senanayake[21] from Sri Lanka in 1987. This was first described in 1974 by Wadia et al as type II paralysis[35] and subsequently termed "The Intermediate Syndrome" by Senanayake as it appear after acute cholinergic phase but before the expected onset of delayed neuropathy. The cardinal feature of this syndrome are cranial nerve palsies, weakness of neck flexors, proximal muscle weakness and respiratory muscle paralysis which usually develop between 24 to 96 hours of ingestion of the poison.[34]

The mechanisam of intermediate syndrome is not clear. It was proposed by some authors that it may be due to the nicotinic signs of acetylcholinesterase inhibition.[36] According to the views of Gadoth and Fisher the manifestations are due to nicotinic paralysis. Despande[37] and Senanayake[36] gave a hypothesis that the down regulation of acetylcholine receptors could explain the syndrome and neurophysiological findings of intermediate syndrome. Most of the patients have weakness of neck flexor muscle as the initial manifestation followed by weakness of facial, respiratory and limb muscles. During the recovery phase, the cranial nerve palsies improves first, followed by improvement in respiratory and muscles. The deep tendon reflexes are usually depressed but involvement of pyramidal tract has been reported.

Electrophysiological study shows significant decremental response at low frequency stimulation.[39] Agents commonly causing intermediate syndrome are fenthion, monocrotophos, dimethoate, methyl parathion, dizinon, ethylparathion, malathion, and sumithion.[40] Gross reduction of serum cholinesterase in all patients with intermediate syndrome is noted. Most of the patients who developed intermediate syndrome required mechanical ventilation due to respiratory failure. In a reported

study by Singh et al[41] the incidence of intermediate syndrome was 29.4%. methyl parathion is most common compound. The time taken to recovery from the manifestation was 3-12 days.[41]

Clinical neurophysiology

In nicotinic (intermediate) syndrome there is failure of transmission at the neuromuscular junction.

Electrodiagnostic studies of neuromuscular transmission can be utilized to characterize and evaluate this disorder.

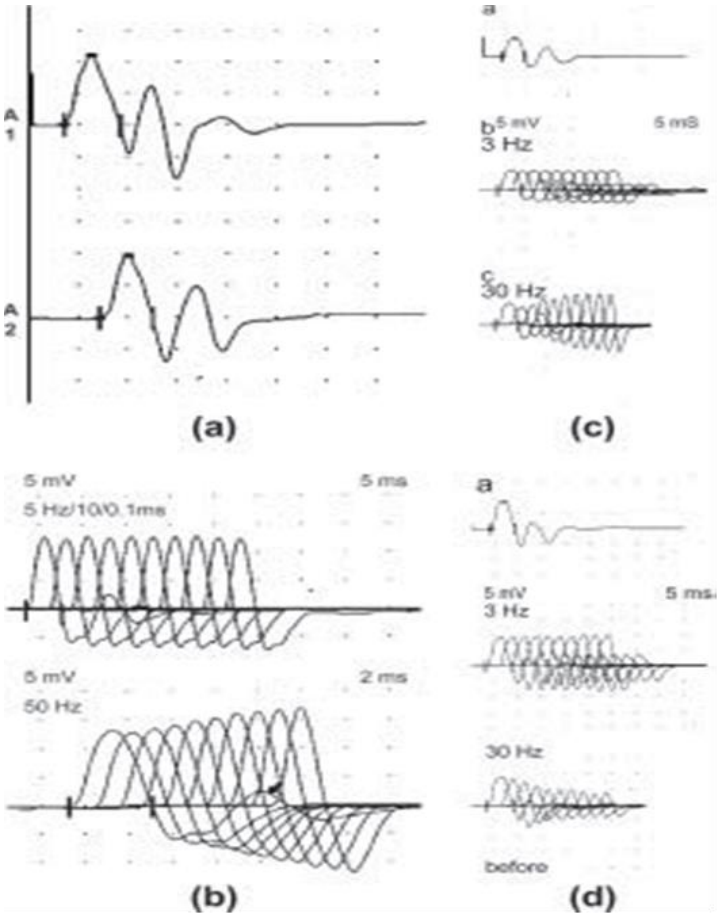
In brief, the neurophysiological abnormalities[41] include:

1. A single supramaximal electrical-stimulus-induced repetitive response
2. A decrement, increment response to high frequency(30 and 50 Hz) repetitive nerve stimulation(RNS)
3. A decremental response to high rate (30 and 50 Hz) RNS.

Repetitive response characteristically occurs in a resting muscle and disappears or decreases in amplitude after exercise and repetitive stimulation. More than one repetitive response may be seen. Repetitive action of excess acetylcholine at the motor end plates is responsible for this electrodiagnostic binding. Decrement increment response occurs at high rate (30.50 Hz) RNS and is characterized by an initial dip in the amplitude of the compound muscle action potential and then a rise in the amplitude of the subsequent compound muscle action potentials (CMAPs). In vitro microelectrode studies suggest that the decrement, Increment response represents a depolarization type of neuromuscular blockade.[42]

The decremental response is characterized by a progressive fall in the amplitude of the successive CMAPs elicitably a train of supramaximal electrical stimuli delivered to the motor nerve at 30.50 Hz. The ratio of the amplitudes of the ninth CMAP to the first CMAP (9:1 ratio) is arbitrarily taken as an objective marker of the severity of the decremental response.[43] It represents a desensitization type of neuromuscular blockade. It correlates with the presence of clinically recognizable intermediate syndrome.[44] It can be considered as an electrodiagnostic marker for the intermediate syndrome.The electrodiagnostic abnormalities of acute OP poisoning are influenced by a variety of agents including pancuronium, oximes, and magnesium sulfate. Pancuronium paradoxically ameliorates the electrodiagnostic abnormalities.[45]

The neurophysiological phenomenon is not associated with clinical improvement and can be explained by the blocking of acetyl choline receptors by pancuronium, a competitive neuromuscular blocking agent, thus preventing the OP-induced depolarization blockade.



3. Organophosphate induced delayed polyneuropathy(OPIDN)

OPIDN is common finding following exposure to organophosphate which have a weak anticholinesterase activity. Eg .triorthocrosyl phosphate. OPIDN sets in after a period of 7-21 days of exposure and causes significant morbidity.The earliest symptoms to be seen are parasthesia and calf pain. Weakness initially appears in the distal leg muscles causing foot drop, followed by small muscle of the hand. Later it may extend proximally and involve the truncal muscles. Gait ataxia is disproportionate to the motor and sensory loss. The cranial nerves and autonomic nervous system are not involved. Deep tendon jerks are absent. Clinical improvement in the corticospinal tract and the dorsal column becomes apparent when the peripheral neuropathy improves. The prognosis of the patient with mild neuropathy is good but those with severe neuropathy are usually left with persistent deficits i.e claw hand,

foot drop, persistent atrophy, spasticity and ataxia. The occurrence of OPIDN appears to follow the phosphorylation and subsequent ageing of an enzyme in axons called as neuropathy target esterase. Neuropathy only develops with compounds which are able to inhibit as well as age the neuropathy target esterase enzyme.[46]

4. Chronic organophosphorus induced neuro-psychiatric disorder (COPIND)

Follow up studies of individuals who have been exposed to high levels of organophosphorus compounds have shown that certain neuro behavioural changes may develop in them, which have been termed together as COPIND. These effects include drowsiness, confusion, lethargy, anxiety, emotional lability, depression, fatigue and irritability. Some of these symptoms could be attributed to the sequaelle of convulsion, anoxia, respiratory failure and cardiac arrhythmias that these patients might have suffered during the acute cholinergic phase. Chronic neuropsychiatric disorders like anxiety, depressions, problems with memory and concentration have been described in workers exposed to these poisons.[48]

Dystonic reactions, schizophrenia, cog-wheel rigidity, choreo athetosis and EEG changes have been reported on high dose exposure.[34] These extra pyramidal symptoms thought to be due to inhibition of the acetyl cholinesterase in human extra pyramidal area. Psychosis, delirium, aggression, hallucination and depression may also be seen during recovery from the cholinergic syndrome. Other types of delayed neuro behavioural effects are seen amongst people exposed to low dose of organophosphorus compounds for prolonged periods. Other rare neurological manifestations can be acute inflammatory demyelinating neuropathy,[49] extrapyramidal manifestation or parkinsonism.[50] Shahar et al[51] a single case report of parkinsonian features in a paediatric patient after accidental exposure to dimethoate.

Lockwood et al[52] studied 250 patients with parkinsonism and obtained detailed history regarding exposure to pesticide. Odds ratio in that study showed poor association between Parkinsonism and pesticide exposure.

Cardiovascular manifestations-

The mechanism by which organophosphates and carbamates induce is still uncertain. Ludomirsky et al described three phases of cardiotoxicity after organophosphate poisoning.[53]

- Phase 1 is brief period of increased sympathetic tone
- Phase 2 is a prolonged period of parasympathetic activity;
- Phase 3 QT prolongation is followed by torsade de pointes ventricular tachycardia and then ventricular fibrillation.

Both sympathetic and parasympathetic over activities have been shown to cause myocardial damage.[54]The cardiac toxicity associated with organophosphate and carbamate poisoning is caused by more than one mechanism. Patchy myocardial involvement as a result of direct cardiac toxicity could be one of the factors responsible for serious cardiac complications. As myocardial involvement is patchy, it may not be manifest clinically or on echocardiography. Continuous cardiac monitoring should be undertaken to detect dynamic cardiac changes.[54]Most cardiac complication occurs during first few hours after exposure. Hypoxemia, acidosis and electrolyte imbalance are major predisposing factor for development of cardiac complication.[55]

Cardiac manifestation of organophosphorus poisoning can be summarised as follows[56]

Electrocardiographic manifestations

- Prolonged QTc interval
- Elevated /depressed ST segment
- Inverted T wave
- Prolonged PR interval

Rhythm abnormality

- Sinus tachycardia
- Sinus bradycardia
- Extrasystole
- Atrial fibrillation
- Ventricular tachycardia
- Ventricular fibrillation

Other manifestations

- Noncardiogenic pulmonary edema
- Hypertension
- Hypotension

Respiratory manifestations-

It includes bronchorhea, bronchospasm, and laryngeal spasm. This is due to action of the organophosphorus compound on muscarinic receptors.

Early respiratory failure during the acute cholinergic crisis-

The mechanism of early respiratory failure during the acute cholinergic crisis in humans is unclear but is likely to involve three components: depression of central respiratory drive from the respiratory centre in the ventrolateral medulla, respiratory muscles weakness, and direct pulmonary effects (bronchospasm, bronchorrhoea)[57]

Late or peripheral respiratory failure

Not all delayed respiratory failure fitted the original clinical descriptions by Wadia and Senanayake as being separated in time from the acute cholinergic crisis. For example, delayed respiratory failure sometimes occurred at the same time as recurrent cholinergic poisoning in fenthion poisoning.[35] peripheral dysfunction was a silent features of all the respiratory failure. The patients who came out of respiratory failure later were conscious and most of them would move their arms, legs and cranial nerve innermated muscles weakly despite having inability to breathe. The presumption that central dysfunction affecting the central respiratory centre being the lone cause of respiratory failure is very unlikely. Some authors are of the opinion that peripheral dysfunction is a result of prolonged stimulation of NMJ by high synaptic concentration of Ach [57]

The molecular mechanism behind this is not well understood. It can be because of down regulation of receptors in response to continous stimulation. There is no consensus concerning whether the dysfunction is pre- and/or post-synaptic; however,

failure of the muscarinic antagonist atropine to prevent peripheral respiratory failure might favour involvement of pre- or post-synaptic nicotinic receptors over pre-synaptic muscarinic receptors. Some researchers believe that the late respiratory failure is due to direct OP toxicity to skeletal muscle.[23] presently the very little evidence exists to support such a mechanism. In animal models with OP poisoning, there is muscle necrosis but the extent of the damage to the muscle does not coincide with the degree of weakness. Pilot studies of patients with intermediate syndrome have failed to find either extensive muscle damage or increased muscle enzymes in the blood.[58]

Gastrointestinal manifestations-

Symptoms resembling gastroenteritis such as vomiting, diarrhoea and abdominal cramp are the first to occur after oral ingestion of an organophosphorus compound. Rarely severe organophosphorus poisoning may cause acute pancreatitis or parotitis.[59] Patients may develop hypoglycaemia or hyperglycemia.[60]

Ocular manifestations

It includes miosis, blurred vision, lacrimation and occasionally mydriasis.[60]

Severity assessment

Various scoring system have been tried to predict prognosis in patients of organophosphorus poisoning.[61]

1.Glasgow coma scale

Grmec et al in their study reported that group with complications due to severe organophosphorus poisoning had significantly different values of measured

parameters—a longer QTc interval and a lower GCS score and worst outcome($p<0.05$).

The two measures GCS score and QTc interval have been shown to be equally good in predicting respiratory failure and hospital mortality in patients with OP poisoning.

Eyes open	Spontaneously	4
	To speech	3
	To pain	2
	Never	1
Verbal response	Oriented	5
	Confused	4
	Inappropriate words	3
	In comprehensible sounds	2
	None	1
Best motor response	Obeys commands	6
	Localises pain	5
	Withdrawal	4
	Abnormal	3
	Extension to pain	2
	None	1
	Total	3-15

Davies et al studied 1365 patients with a history of acute OP poisoning.[5] In their study they concluded that GCS and the IPCS PSS were similarly effective at predicting

outcome. Patient presenting with GCS< 13 needs intensive monitoring and treatment. However identity of organophosphorus must be taken into account, since the half of the patient who died from fenthion poisoning only had mild symptoms at presentation.[29]

2. SAPS-2

It is calculated from 12 routine physiological measurements during the first 24 hours, information about previous health status and some information obtained at admission. SAPS-2 score has been shown to have good prognostic implications in OPP patients.[62]

3.Acid base interpretation on admission was found to be a reliable predictor of the outcome in a patient with acute OP poisoning in a study of Liu et al.[63] They reported mortality was maximum in patients with mixed acidosis before hospitalisation and minimum in a patient with normal acid base balance.[63]

4.Peradeniya organophosphorus poisoning scale which was developed by Senanayake N et al to predict outcome and to grade patient into mild, moderate and severe grades.[64]

Peradeniya organophosphorus poisoning scale

Sr.no	Parameter	Criteria	Score
1	Pupils	Normal	0
		Small	1
		Pin point	2
2	Fasciculations	None	0
		Present	1
		Generalised	2
3	Heart rate	>60	0
		40-60	1
		<40	2
4	Respiratory rate	<20	0
		>20	1
		>20 with cyanosis	2
5	Consciousness	Conscious	0
		Altered	1
		Comatose	2
6	Convulsion if present		+1

Mild 0-3

Moderate 4-7

Severe 8 or more

Biomarker for exposure to organophosphate–

Acetyl-cholinesterase level-

The activity of cholinesterase enzyme in the blood can be measured as a biomarker of effect for organophosphates. An individual with acute symptomatic exposure to organophosphate will usually have an abnormal lower level of activity of cholinesterase enzyme measured in the serum (as butyryl cholinesterase, also known as pseudocholinesterase) or in the red blood cell(as RBC cholinesterase, which is more closely related to acetyl cholinestserase activity in the nervous system).[65]

RBC cholinesterase level, measure the degree of toxicity and determine the effectiveness of antidote therapy. It better reflects CNS and motor end plate cholinesterase activity, but is costly.

Plasma (or pseudo) cholinesterase level, is easier to measure and cheap but does not correlate well with the severity of poisoning.[65]Fall in plasma cholinesterase levels more than 25% is a strong evidence of organophosphorus poisoning.[66] But studies have shown poor correlation between serum cholinesterase levels and outcome in patients of OPP. Nourie et al[67] studied correlation of severity of OPP and serum cholinesterase levels on admission in a prospective trial. And concluded in their study that serum cholinesterase level did not correlate with the total dose of atropine or with a simplified acute physiology score. Cherian et al[60] in their study published in 2005 also reported no significant difference in serum cholinesterase levels in survivors and non survivors after acute OPP.

Newer biomarker of organophosphorus poisoning

1. Paraoxonase (PON1) is an A-esterase capable of hydrolysing the active metabolites (oxons) of a number of organophosphorus (OP) insecticides such as parathion, diazinon and chlorpyrifos. PON1 activity is highest in liver and plasma, and among animal species significant differences exist, with birds and rabbits displaying very low and high activity, respectively. Human PON1 has two polymorphisms in the coding region (Q192R and L55M) and five polymorphisms in the promoter region.[68] The Q192R polymorphism imparts different catalytic activity toward some OP substrates, while the polymorphism at position -108 (C/T) is the major contributor to differences in the level of PON1 expression. Animal studies have shown that PON1 is an important determinant of OP toxicity, with animal species with a low PON1 activity having an increased sensitivity to OPs. Administration of exogenous PON1 to rats or mice protects them from the toxicity of OPs. PON1 knockout mice display a high sensitivity to the toxicity of diazoxon and chlorpyrifos oxon, but not paraoxon. In vitro assayed catalytic efficiencies of purified PON isoforms for hydrolysis of specific oxon substrates accurately predict the degree of in vivo protection afforded by each isoform. Low PON1 activity may also contribute to the higher sensitivity of newborns to OP toxicity.[68]
2. Development of rapid protocols for extraction of the target biomarker protein from a sample, digesting with the appropriate enzyme and identifiying the OP modified peptide by mass spectrometry is under evaluation.[69] And may improve diagnosis of organophosphate poisoning. Additional directions that have been underway include expressing

recombinant, active biomarker proteins in an E.coli system to provide heavy isotope labeled standards to use in quantifying the degree of modification.[70]

Factors affecting outcome in Organophosphorus Pesticide self-poisoning

• **Toxicity:** toxicity is usually rated according to the oral LD50 in rats. This scale is able to roughly differentiate between very safe and very toxic pesticides—for example parathion (LD50 13 mg/kg,40 WHO: Class IA) is highly toxic while temephos (LD50 8600 mg/kg,40 WHO: unlikely to cause acute hazard) has not been associated with deaths. However, large differences in human toxicity have been seen after poisoning with organophosphates with roughly the same animal toxicity and this classification does not account for the effects of treatment[72]

• **Impurities:** the WHO toxicity classification assesses fresh pesticide from approved manufacturers. Pesticide storage in hot conditions can result in chemical reactions that have toxic products. Such a process was blamed for the death of pesticide sprayers using malathion in Pakistan in the late 1970 and has also been noted with both diazinon and dimethoate[75]

• **Formulation:** A pesticide's toxicity will vary according to formulation, which differs according to the organophosphorus and the place of manufacture. For example, malathion is available as an 80% solution in street-side pesticide stalls in Burma, but as a 3% powder in Sri Lanka.[75]

•**Alkyl sub-groups:** Most pesticides have either two methyl groups attached via oxygen atoms to the phosphate (dimethyl organophosphorus) or two ethyl groups (diethyl organophosphates). Acetylcholinesterase ageing is much faster for dimethyl

poisoning than for diethyl poisoning, therefore to be effective, oximes must be given quickly to patients with dimethyl poisoning . A few pesticides have atypical structures, with another alkyl group (eg, propyl in profenofos) attached to the phosphate group via a sulphur atom. These organophosphorus pesticides age acetylcholinesterase even faster and oximes are probably not effective.[75]

•**Need for activation.** Many compounds are inactive thioates (with a double-bonded sulphur attached to the phosphorus atom) and have to be desulphurated to make the active oxon, via cytochrome P450 enzymes in the gut wall and liver. The P450 3A4 seems to be the most active enzyme when organophorus is present in high concentrations, as happens after self-poisoning[76]

•**Speed of activation and of AChE inhibition.** The rate of activation of thioate organophosphates varies between pesticides.[77]Large variation also exists in the rate of acetylcholinesterase inhibition between organophosphorus pesticide oxons[32]

• **Duration of effect—fat solubility and half-life.** Some fat soluble thioate organophosphorus pesticides (eg, fenthion) distribute in large amounts to fat stores after absorption. This seems to reduce the peak blood organophosphorus concentration and the early cholinergic features are usually mild. Subsequent slow redistribution and activation causes recurrent cholinergic features lasting days or weeks. Peripheral respiratory failure is common with these organophosphorus, probably due to continuing inhibition of acetylcholinesterase. Ageing only starts after acetylcholinesterase inhibition, so oximes could theoretically be beneficial for many days in such patients. By contrast, other organophosphorus (eg, dichlorvos) do not need activation, are not fat soluble, and could have a much more rapid onset of effect and shorter duration of activity. Fat solubility is graded according to the Kow

(logarithm octanol/water coefficient): less than 1•0=not fat soluble; more than 4•0=very fat soluble.[75]

The above factors have important consequences for the speed of onset of organophosphorus poisoning after ingestion. Ingestion of an oxon organophosphorus that rapidly inhibits acetylcholinesterase will result in early onset of clinical features and respiratory arrest before presentation to hospital, increasing the risk of hypoxic brain damage and aspiration. The conversion of the thioate organophosphorus parathion to paraoxon is so fast that patients can be unconscious in 20 min.[75]

Clinical features after poisoning by other thioate organophosphorus, such as dimethoate and fenthion, happen later, giving the patient more time to present to hospital needs further research.

Management

Atropine-

It is commonly used agent which is available as 0.6mg per ml formulation. Atropine being lipid soluble cantrverse blood brain barrier and can cause CNS effects. Initial dose is given as 2 mg iv bolus and repeated every 5min till signs of atropinisation develop.[78]

Because atropine dries a secretions and reduces bronchospasm, its administration will improve patient oxygenation. Signs of atropinisation to be monitored are tachycardia and mydriasis, dry mucosa, warm skin and delirium. Best parameter is consider to be drying of secretions as tachycardia and mydriasis may sometime be misleading. After atropinisation regular atropine is repeated to maintain signs of atropinisation. Prior oxygenation of patient with 100% oxygen prevents ventricular dysrhythmia due to

atropine. Isolated pulmonary manifestation may respond to nebulization with atropine or ipratropium The adverse effect of atropine who receive maximum dose is anticholinergic delirium. Glycopyronium is used to treat the peripheral effects of organophosphorous without carrying confusion . however it has poor CNS penetration. A small randomized controlled trial comparing glycopyronium with atropine noted was significant difference in mortality or ventilation rates .[75]

Since extrapyramidal features are treated by hyoscine . Animal study suggests that it is more effective than atropine for control of seizures induced by op nerve agaents.[76]

Glycopyrolate

it is quaternary antimuscarinic agent with poor lipid solubility. Thus it does not cross blood brain barrier. It can be used in patients developing central anticholinergic syndrome secondary to atropine administration.[75]

Cholinesterase reactivator-

Cholinesterase reactivator i.e oximes restores cholinesterase activity by neutrophilic attack on phosphorylated enzyme, removing the bulky sterically hindering phosphate moiety thus reactivating its action. They may also prevent continued toxicity by scavenging the remaining organophosphate molecules. But they have a role only before ageing of the enzyme occurs. Ageing period for various compound differ. Treatment with 2-Pralidoxime is most effective when started early and if used in acute rather chronic poisoning.[60]

In 1950 , pralidoxime was discovered by Wilson and colleage and was introduced into practice with parathion poisoining. Oximes such as obidoxional and trimedoxime have developed but pralidoxime is commonly used . it has 2 salts: iodine chloride,

mesilate has advantages over iodide. High doses of pralidoxime iodide puta patients at risk of thyroid toxicity.[75]

Effetiveness of pralidoxime has been much debated with many asian clinicians. 2 Randomised controlled trials in vellor , india noted that low dose infusion might cause harm.[81]

Cochrane review included 2 randominised controlled trials and reported there is no clear evidence of benefit or harm, the others meta analysis combined observational studies with randomized controlled trials reducing confidence in their conclusion that oximes are harmful[86]

A randomised controlled trial in Baramati, India studied the effect of very-high-dose pralidoxime iodide (2 g loading dose, then 1 g either every hour or every 4 h for 48 h, then 1 g every 4 h until recovery) in 200 patients. Reduced case fatality was associated with high dose regimen few with pneumonia and reduced time on mechanical ventilation this study suggest that large doses of pralidoxime could have benefit if patients are treated early.[88]

Inhibited acetylcholinesterase can become aged, by loss of one of the two alkyl groups attached to the bound phosphate. Thus ageing has important consequences . 50% of the acethlcholinestherase will be alredy aged if the patient has bought to hospital after 3 hr of ingestion of dimethyl pesticide , patient carrying after 12hr will have 94% aged acetylcholinestrase and therefore unresponsive to oximes.[88]

WHO recommends that oximes can be given to all symptomatic patients who need atropine[89] For therapeutic concentration, a loading dose of pralidoxime chloride is

given, then a continuous infusion .rapidly infusion therapy causes vomiting, tachycardia and hypotension.[54]

Adverse effect of pralidoxime-

Drowsiness, diziness, disturbances of vision, nausea, tachycardia, headachae, hyperventillation and muscular weakness have been reported after the use of pralidoxime. Rapid intrvenous infusion of pralidoxime has been associated tachycardia, laryngospasm muscle regidity. Large doses of pralidoxime may cause transient neuromuscular blockade. Excitement and manic behavior immediately following recovery of consciousness have been reported in several cases. However similar behavior has occurred in cases of organophosphate poisoning that were not treated pralidoxime. When atropine and pralidoxime are used together, the signs of atropinisation may occur earlier than might be expected when atropine is used alone.[74]

Benzodiazepines

Patients with op poisoning develop agitated delusion , cause is complex like pesticide itself , atropine toxicity , hypoxia, alcohol ingestion with poison mainstay of treatment of underlying cause[76]

Diazepam is first-line therapy for seizures. Seizures are more common with organophosphorous nerve agents such as soman and tabun studies on animals suggest that diazepam reduces neural damage and prevents respiratory failure and death[76]

Other therapies

Magnesium sulphate blocks ligand-gated calcium channels, which results in reduced release of acetylcholine from pre synaptic terminals which improves function at neuromuscular junctions and reduced CNS over stimulation medicated via NMDA receptor activation. A trial in people who poisoned with op pesticide recorded reduce mortality with magnesium sulphate..[91]

Sodium bicarbonate is sometimes used for treatment of organophosphorus poisoning in Brazil and Iran, in place of oximes.[60] however a review study in Cochrane concluded that insufficient evidence exits at present to diagnose wheather sodium bicarbonate should be used in humans.

Butyrylcholinesterase scavenges organophosphorus in plasma, reduces amount to inhibit acetylcholinestherase in synapses. Military research aims to inject soldiers with op nerve gases. A study done by Turkish doctors reported use of this but this trial was not randominised and allocation decisions were unclear[75]

Decontamination: to be done in appropriate waste bags water and soap is used to wash the poision amount on person, Attention given to skin folds and underside of

finger nails. Normal saline or water is used for ocular decontamination . iv lines are to be flushed and blood samples for hematological and biochemical to be collected. ECG to be recorded.[92]

Labored breathing , pin point pupil, sweating suggest op/ carbonate poisoning . atropine should be started immediately.[94]

If clinical presentation is not evident inj atropine 0.6 to 1mg is given IV, rise in heart rate by > 25bpm should be required while observing effects of atropine normal saline 10-20 min is given to compensate fluid loss.[17]

Active cooling and sedation: - Cooling is indicated if the patient is febrile and climate is hot & humid. Inj. Diazepam 10 mg IV slowly can be given for agitated patient. It helps in reducing anxienty fascilate gastric lavage , reduce damage to CNS, diminish respiratory failure and control seizure.[95]

Gastric Decontamination:- It is indicated once patient is stabilized , calm enough for intubation and repeated after 2-3 hours. It should be done within 1-2hr of ingestion of poison aspiration of fluid is continued till fluid is colourless and odourless.[97]

Activated Charcoal: No evidence shows that single dose or multiple dose regimen of charcoal benefit a charcoal dose of 50 gm can be left in stomach.[99]

Transfer to ICU:- Resuscitation measure are continued and vitals are recorded while transferring to ICU , Patients with following criteria may need ventilator support[101]

History of intake of large dose

- Copious secretions
- Disturbed level of consciousness

- Signs of hypoventilation or respiratory obstruction by secretions

oxygen saturation are to be observed and recorded in OP/Carbamate observation sheet.

Antidote: - The antidote are anticholiregenic which reverses all muscarinic activities both in CNS and PNS, full atropination is essential part of early management. Sum of 38 regimens found in licture is to start bolus followed by boluses after a fixed time interval varying from 5-15-30 min till atropination.[102] later regimen showed improvement . there is no proven benefit of infusion therapy.[103] Although it saves time, require less observation produces less fuction in plasma atropine concentration and makes weaning easier. Low dose started (1-2mg) followed by escalation to 5mg.[104]

The peak effect of atropine is seen within three minutes of an IV injection Some authors suggest that it is better to start weaning bolus dose 1-2mg then to repeat same bolus every 5min till atropination. Atropine admistration by nebulisation also improves respiratory distress and oxygenation.[105]

Guidelines for ventilator support[94]

I. Respiratory Gas Tensions

i Direct Indices

- Arterial Oxygen Tension < 50 mm Hg on room air
- Arterial Co2 Tension > 50 mm Hg in the absence of metabolic alkalosis

ii Derived Indices

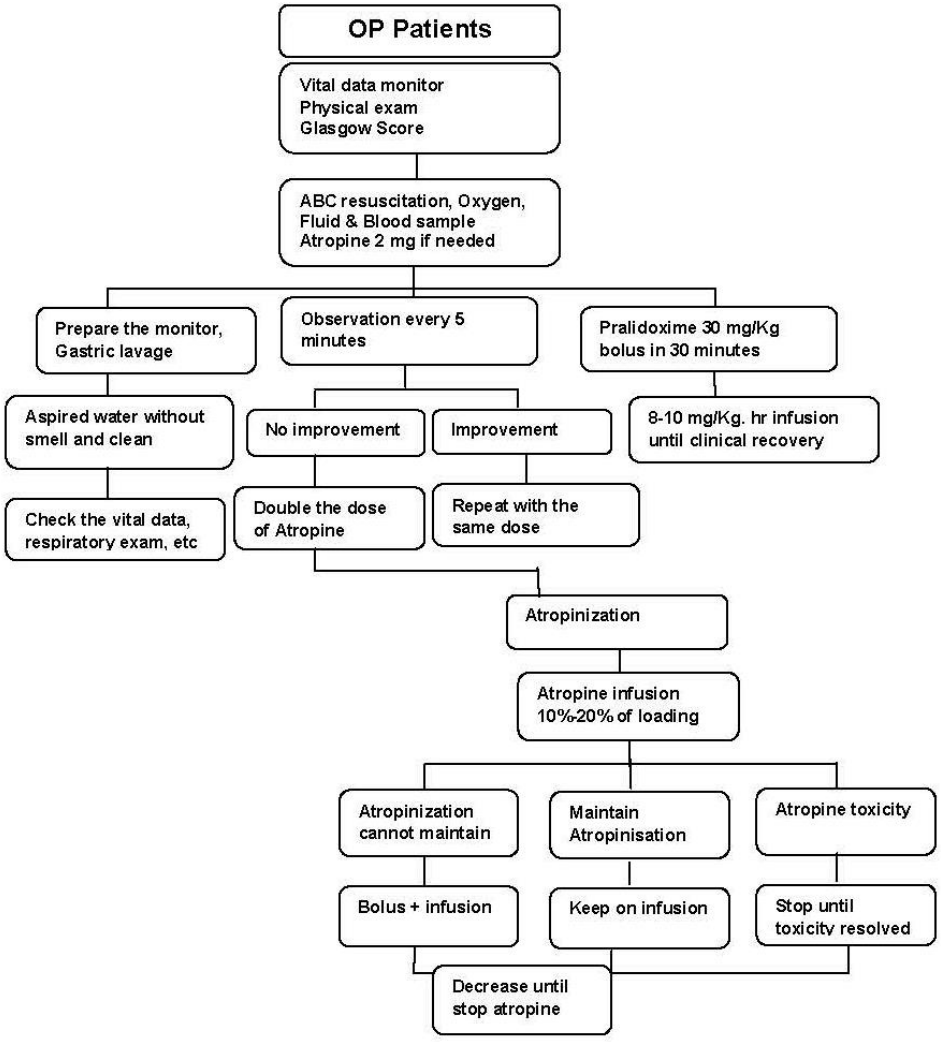
- PA o2/ Fio2 < 250 mm of Hg

- PA-aOo2 (Pulmonary arterial-alveolar O2 gradient) > 350 mm of Hg
- Vd/Vt> 0.6

II. Clinical - Respiratory Rate (RR)> 35 breaths/min

III. Mechanical Indices

- Tidal Volume 5 ml/kg
- Vital capacity < 15 ml/kg
- Maximum inspiratory force <- 25 cm of H2O



Treatment Protocol for OP Poisoned Patient[94]

Furosemide: - It is recommended if pulmonary oedema persists, even after full atropinisation.

Hydrocarbon Aspiration: - Hydrocarbon solvent aspiration causes chemical pneumonitis. These are managed as ARDS.

Antibiotics:- Broad spectrum antibiotics are to be instituted as per antibiotics policy of the institution, considering the risk of infection.

Agitation/Convulsion: - Causes of agitation which are not related to pesticide toxicity like alcohol withdrawal/full bladder unless catheterized/head injury etc are to be excluded. Diazepam, Midzolam demonstrate rapid peak control for convulsion.[94]

Injected OP poisoning: - Local tissue necrosis need surgical intervention. oily based OP are removed to avoid systemic absorption.[106]

Contraindications:-Drugs like morphine, succinylcholine, theophylline, phenothiazine and reserpine are contraindicated.[106]

Respiratory Failure Following Organophosphate Poisoning

Eddleston[57]categorized findings into early and late onset respiratory failure; however, he concluded that these syndromes overlap and it is difficulity in separation. Patients experiencing early form of respiratory failure had greater cholinergic signs and symptoms, than compared to delayed onset. longer duration of intubation is associated with greater mortality, as ventilator-associated factors contribute to morbidity and mortality.. Samuel et al. suggested that the early administration of loading 1g of pralidoxime could prevent late onset respiratory failure.[107]

Hiremanth et al.[108] formed two groups based on pseudocholinesterase (PChE) levels. Group A included patients with PChE levels greater than 1000 IU/L, whereas Group B included those having PChE levels less than 1000 IU/L. Group B patients had greater failure rates in weaning off ventilation, a higher rate of tracheostomy, a longer hospital stay, and a higher mortality rate.

APACHE II is used to measure the severity of disease in patients admitted to the intensive care unit. Kang et al.[109] suggested same for clinical outcome. Severity also related to kind of op ingested . the worst clinical outcome was associated with dimethoate poisoining which was told by eddeston et al. [57]. Burton et al. performed a study on rats; they found that atropine caused a depression of the phrenic nerve output and a depression of ventilatory output signals. Similarly, association was shown with acetylcholine.[110]

The production of secrections can be switched off with the help of atropine . the mechanism is sympathetic stimulation . Therapy for op is same 50 years back , recent advances direct the need for CNS protective stratergy for events associated with cholinerginic crisis . peripheral antagonist glycopyrolate is tried but there is no decrease in mortality rates. Gaspari et al have observed in animals with op poisoning suggest underlying central mechanisms despite oxygenation and blood pressure regulation.[17]

Patients die of complications secondary to ventilator support which include pneumonia and toxic brain injury . Respiratory failure following op ingestion carries high mortality and morbidity rates.

According to study by Davies JOJ et al in 2008,Organophosphorus pesticide poisoning kills around 200000 people each year due to self poisoning in Asia- Pacific region.[29]

Rehiman S et al in 2008[111] in their study have shown that the Peradaniya scale and serum cholineesterase at presentation are useful in assessing the severity of poisoning, particularly in terms of a higher amount of atropine needed and a prolonged duration of hospital stay required for management.

Ahmed SM et al in 2014[112] in a retrospective study assessed the outcomes and predictors of mortality in patients with acute OP poisoning requiring mechanical ventilation. The authors concluded that Mortality from OP compound poisoning is directly proportionate to the severity of poisoning, delay in starting PAM, and duration of mechanical ventilation. Death is not dependent on a single factor, rather contributory to these factors working simultaneously.

Bandy TH et al in 2015[113] described in there study that mortality was directly proportion to the lag time, amount of OP substances consumed, clinical severity, pseudocholinesterase levels, acute renal failure and duration of ventilator support. Rapid diagnosis and initiation of early and effective treatment, which may result in less complication and also decreases the mortality rates.

Coskum in 2015[114] described early initiation of atropine and pralidoxime therapy, with supportive ICU care, GCS on admission to the emergency department, can provide useful prognostic information and help predict outcomes and save life.

Soni P et al in 2016[115]predicted the need for ventilator support in organophosphate poisoning and to identify the factors which help in predicting the need for

ventilatorysupport in organophosphorous compound poisoning. The authors found with regard to grading of poisoning and its correlation of symptoms, 67% were of mild grade, 19% were of moderate grade, and 14% were of severe grade. Respiratory failure was the most common complication which may develop with 24h after exposure. Only 2 out of 67 patients required ventilatory support with mild poisoning, 4 out of 19 patients with moderatepoisoning required ventilator support, and 8 out of 14 patients with severe poisoning required ventilator support with significant($P > 0.001$) association between severity by grading system and need of ventilation. The authors concluded that grading system is developed to assess the patients at the time of admission so as to grade the severity of poisoning and deciding requirement of assisted ventilation and thereafter intensive care unit stay is to be decided. Ventilators are boon to patients with respiratory failure due to poisoning and decrease the mortality secondary to organophosphorus related respiratory failure.

Mundhe SA et al in 2017[116] in a cross-sectional observational study investigated different factors associate with morbidity and mortality in rural population that can help in identifying patients in need of intensive care and treatment to prevent deaths. The authors found 323 patients studied, 62.85% were male, 227 (70.27%) were suicides, 241 (74.61%) ingested OP compounds, 40 (12.38%) patients developed intermediate syndrome and 56 (17.34%) died. The authors concluded that OP poisoning is a life-threatening condition which requires immediate management. Early initiation of decontamination, atropine and pralidoxime therapy, with supportive ICU care, can save lives. Different demographic, exposure related parameters; some of the clinical features, treatment variables and certain laboratory findings can provide useful prognostic information and help to predict outcomes.

Nazima S et al in 2018[117]prospective study assessed the incidence and outcome of patients with organophosphorous poisoning with emphasis on role of intensive care management in these patients. The authors found 1258 Organophosphorous poisoning cases, males were (34.5%) and females were (65.5%).Suicidal mode of poisoning was most common in our patients and constituted 63.20%. Out of 254 Organophosphorous poisoned patients admitted in ICU, 184 survived and 70 expired. Therefore, mortality rate for Organophosphorous poisoned patients who needed mechanical ventilation was 27.55.

Harika D et al in 2018[118]prospective observational study assessing the profile of organophosphate poisoning and factors affecting the outcome. The authors found One hundred patients presented to the hospital between June 2015 to July 2016 of which 71% were males. About 59% of the patients belonged to 21-30-year group and 67% of them reached our hospital in <6 hours. Grade 1 poisoning was observed in 45% of patients, a dose of <500 units of pseudo cholinesterase was given to 40% of them. A Glasgow Coma Score >10 was found in 75% of the patients and the overall mortality of OP poisoning was 17%. The authors concluded that OP poisoning is more common among younger population, below 30 years with male preponderance. Favourable outcome determinants were younger age, female gender, being admitted to the hospital before 6 hours of OP consumption.

MATERIAL AND METHODS

A hospital based prospective cross sectional study was conducted with 100 patients to analyze the clinical profile of organophosphate compound poisoning and identify the factors which help in predicting the need for ventilatory support in organophosphorous compound poisoning.

TYPE OF STUDY- A hospital based prospective cross sectional study

Source of data:

All patients of organophosphorous compound poisoning admitted in BLDE Hospital and Research centre, Vijayapur between October 2016 to March 2018.

Sample size: 81 (≈100) Patients

Sample size was calculated using following formula with 95% confidence level, margin of error of ±10% and assuming finite population of 500 as per study of Venkataraghava BN[119]:

$$n = \frac{z^2\, p\, (1-p)}{d^2}$$

Where

z = value of z statistic at 5% level of significance = 1.96

d = margin of error = 0.1

p = anticipated prevalence rate = 0.7

$$n = \frac{(1.96)^2 \times 0.7 \times 0.3}{(0.1)^2} = 80.67$$

Hence a sample size of 100 was considered adequate for our study.

Inclusion criteria

1. Patients who have consumed organophosphorus compound poison and being admitted within 24 hours of consumption of the poison.
2. Patients with single poisoning.

Exclusion criteria

1. Patients presented after 24hrs of poisoning
2. Patients with history of chronic cardiac disease
3. Patients who consumed other poisons along with organophosphorus compound
4. Patients with chronic lung disease like pneumonia, pulmonary tuberculosis, Bronchial asthma, COPD interstitial lung disease.
5. Patients with history of neuromuscular disease.
6. Pregnancy.

METHODOLOGY

The patients included in the study were intensively monitored for any signs of respiratory insufficiency like respiratory rate of >30 breaths/minute, accessory muscles of respiration in action, O2 saturation< 90% and arterial Blood Gas analysis showing PaO2<50 mmHg or PCO2>50 mmHg. If any one or more were present, the decision for mechanical ventilation was taken. Bradycardia is defined as <60 beats/minute.

Based on the factors that influence the need for ventilatory support, the severity of organophosphorus compound poisoning was graded as mild, moderate and severe poisoning.

Mild Poisoning included

- Normal level of consciousness {score of 12-15 by Glasgow coma scale (GCS)}
- Pupil size 4mm.
- Fasciculation score 0-1.

Moderate Poisoning includes

- Mild alteration in level of consciousness (score of 8-11 by GCS).
- Pupil size 2-3mm.
- Fasciculation score 2-4.

Severe poisoning includes

- Stupor / Coma (score of 7 or less by GCS).
- Pin point pupil (1mm or less)

- Presence of convulsions
- Fasciculation score 5 or more.
- Signs of respiratory insufficiency.

Grading of fasciculation was done by giving 1 point depending on the presence of fasciculations each to the anterior chest, posterior chest, anterior abdomen, posterior abdomen, right thigh, left thigh, right leg, left leg, right arm and left arm. The total Fasciculation score was thus estimated.

All 100 patients of OPC poisoning were subjected to detailed history regarding present and past illness. Name of compound consumed, route of poisoning, nature of intention of poisoning (Accidental, suicidal, homicidal) any past history of suicidal tendency, detailed general and systemic clinical examination on admission and progress of patients subsequently till discharge. On admission, signs and symptoms of insecticidal poisoning were seen and noted in prescribed proforma, accordingly depending upon the clinical features, history given by relatives and physical verification of container showing the brand name and chemical ingredient of poison, patients were included in this study.

All the patients were also subjected for routine investigations like peripheral smear, kidney function test, liver function test, serum electrolytes, ECG, X-ray chest, bleeding time and clotting time.

All the patients were observed carefully and particular attention was paid to the progress of signs and symptoms in response to therapy.

All of them were treated with usual line of supportive treatment such as gastric lavage (repeated if needed). RT aspiration, maintaining a clear airway, i.v.fluids and antibiotics if needed. Atropine by multiple injections was given to all the patients.

STATISTICAL ANALYSIS

Quantitative data is presented with the help of Mean and Standard deviation. Comparison among the study groups is done with the help of unpaired t test as per results of normality test. Qualitative data is presented with the help of frequency and percentage table. Association among the study groups is assessed with the help of Fisher test, student 't' test and Chi-Square test. 'p' value less than 0.05 is taken as significant**.**

Pearson's chi-squared test

$$\mathrm{X}^2 = \sum_{i=1}^{n} \frac{(O_i - E_i)^2}{E_i}$$

Where X2 = Pearson's cumulative test statistic.

Oi = an observed frequency;

Ei = an expected frequency, asserted by the null hypothesis;

n = the number of cells in the table.

Results were graphically represented where deemed necessary.

Appropriate statistical software, including but not restricted to MS Excel, SPSS ver. 20 is used for statistical analysis. Graphical representation has been done in MS Excel 2010.

OBSERVATIONS AND RESULTS

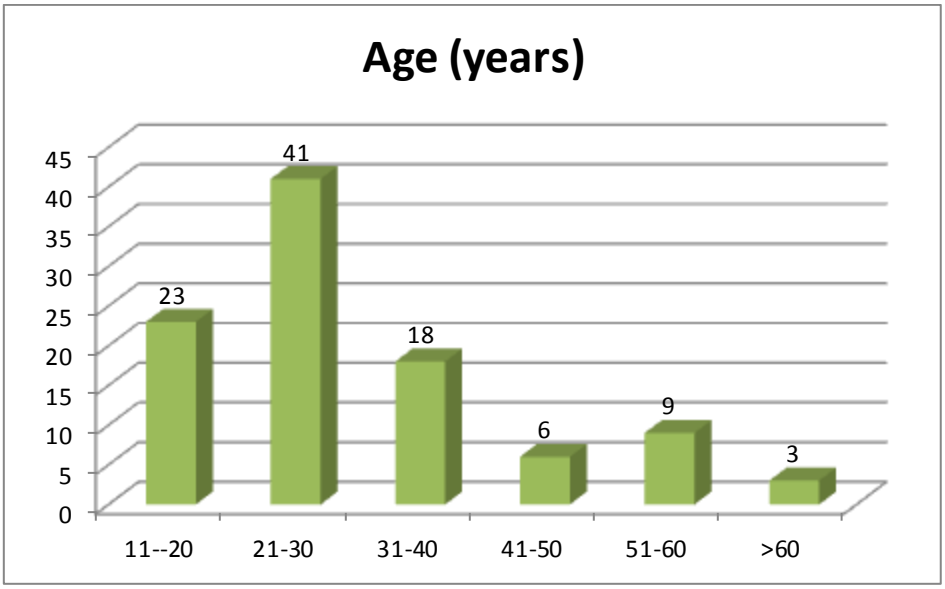
A hospital based prospective cross sectional study was conducted with 100 patients to analyze the clinical profile of organophosphate compound poisoning and identify the factors which help in predicting the need for ventilatory support in organophosphorous compound poisoning.

Distribution of patients according to Age

Majority of the patients (41%) were in the age group of 21-30 years followed by 11-20 years (23%), 31-40 years (18%), 51-60 years (9%), 41-50 years (6%) and >60 years (3%). The mean age of the patients was 31.96 ± 14.12 years.

Table 1: Distribution of patients according to Age

Age (years)	N	%
11--20	23	23
21-30	41	41
31-40	18	18
41-50	6	6
51-60	9	9
>60	3	3
TOTAL	100	100
Mean±SD	31.96 ± 14.12	



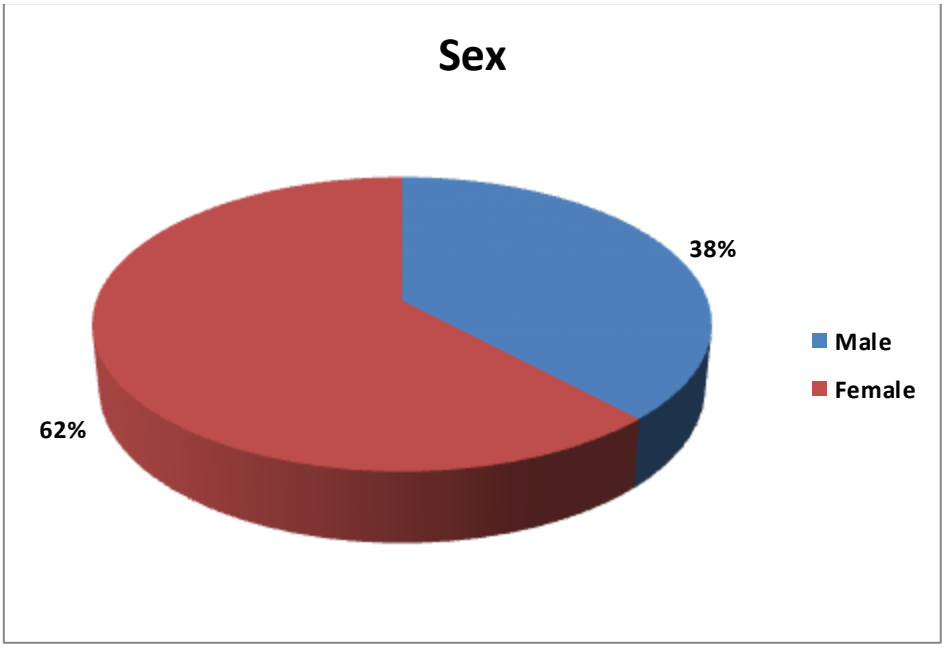
Graph 1: Distribution of patients according to Age

Distribution of patients according to Sex

In this study 38% patients were male and 62% were female. There was female preponderance in our study and the M:Fratio was 1:1.6.

Table 2: Distribution of patients according to Sex

Sex	N	%
Male	38	38
Female	62	62
Total	100	100
M:F Ratio	1:1.6	



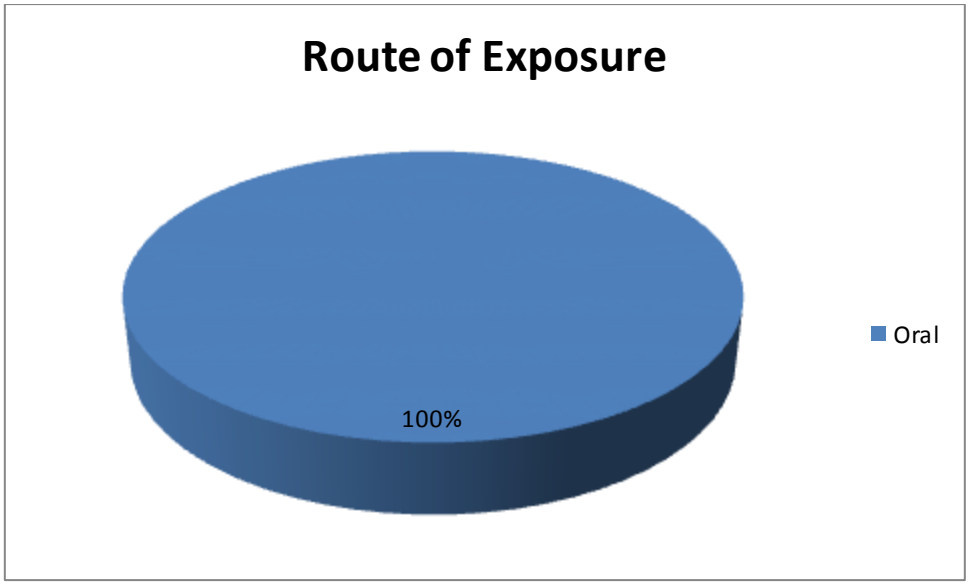
Graph 2: Distribution of patients according to Sex

Distribution of patients according to Route of Exposure

The route of exposure was oral in all the patients.

Table 3: Distribution of patients according to Route of Exposure

Route of Exposure	N	%
Oral	100	100%
Total	100	100%



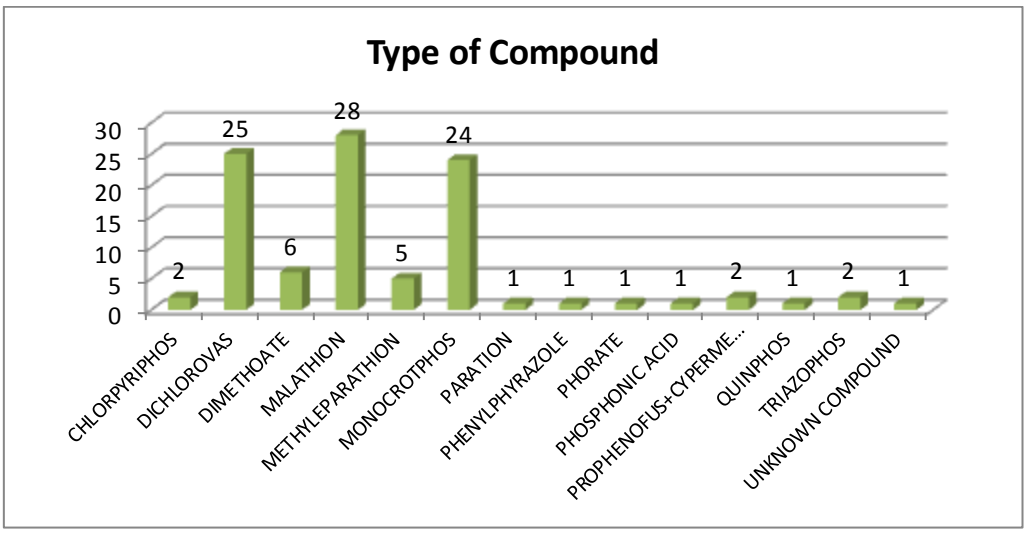
Graph3: Distribution of patients according to Route of Exposure

Distribution of patients according to Type of Compound Consumed

The most common organophosphorus compound consumed in our study was Malathion (28%) followed by Dichlorovas(25%), Monocrotphos(24%), Dimethoate (6%) and Methyleparathion (5%).

Table 4: Distribution of patients according to Type of Compound Consumed.

Type of Compound	N	%
CHLORPYRIPHOS	2	2
DICHLOROVAS	25	25
DIMETHOATE	6	6
MALATHION	28	28
METHYLEPARATHION	5	5
MONOCROTPHOS	24	24
PARATION	1	1
PHENYLPHYRAZOLE	1	1
PHORATE	1	1
PHOSPHONIC ACID	1	1
PROPHENOFUS+CYPERMETHRIN	2	2
QUINPHOS	1	1
TRIAZOPHOS	2	2
UNKNOWN COMPOUND	1	1
TOTAL	100	100



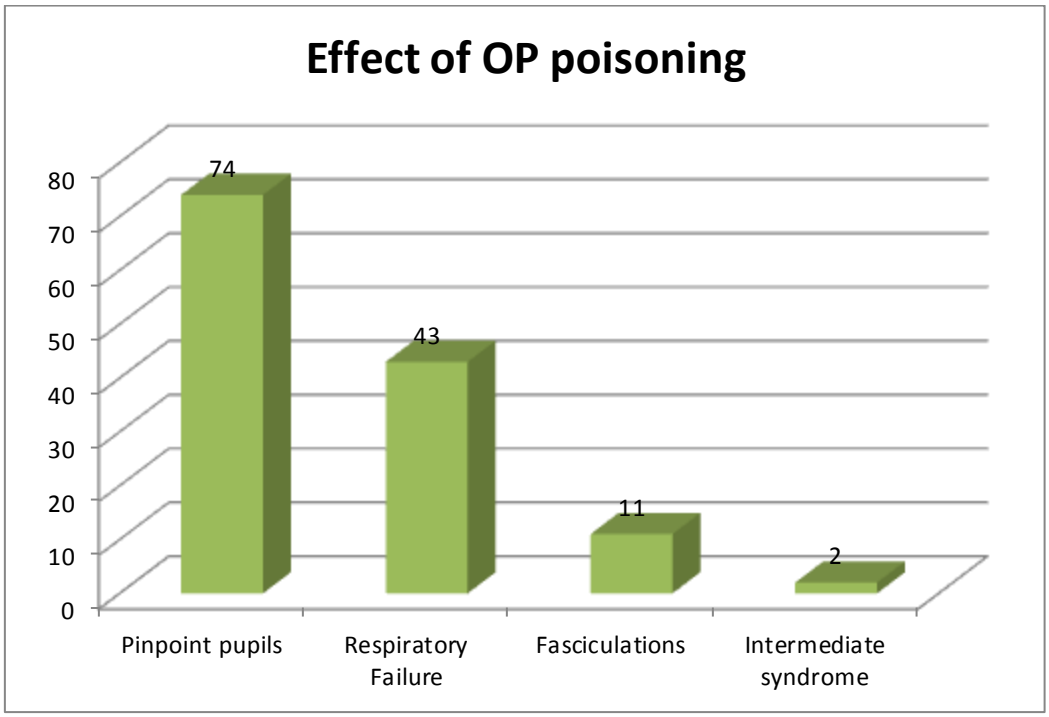
Graph4: Distribution of patients according to Type of Compound Consumed

Distribution of patients according to effect of OP poisoning

The most common effect of OP poisoning was pinpoint pupils (74%) followed by respiratory failure (42%), fasciculations (11%) and intermediate syndrome (2%).

Table 5: Distribution of patients according to effect of OP poisoning

Effect of OP poisoning	N	%
Pinpoint pupils	74	74
Respiratory Failure	43	43
Fasciculations	11	11
Intermediate syndrome	2	2



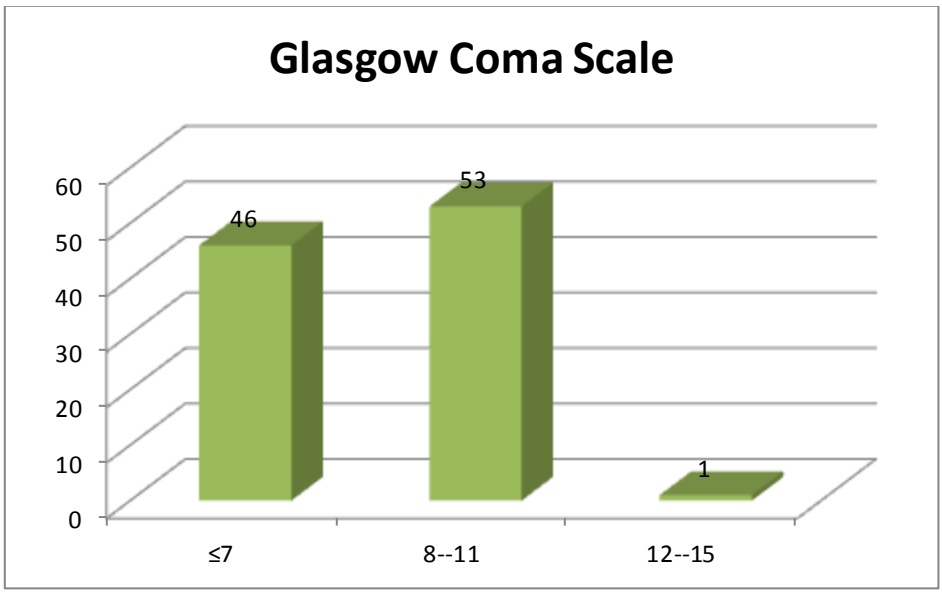
Graph5: Distribution of patients according to Effect of OP compound poisoning

Distribution of patients according to Glasgow Coma Scale (GCS)

46 (46%) patients had very poor GCS score (≤7) while 53 (53%) patients had GCS score between 8 to 11. 1 (1%) patient had good GCS score (12-15).

Table 6: Distribution of patients according to Glasgow Coma Scale (GCS)

Glasgow Coma Scale	N	%
≤7	46	46
8-11	53	53
12-15	1	1
TOTAL	100	100



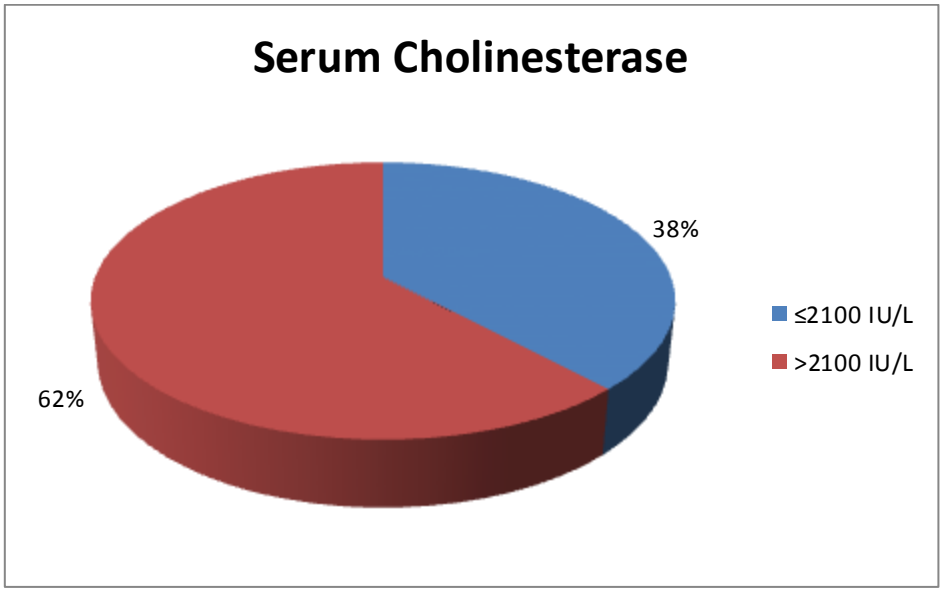
Graph6: Distribution of patients according to Glasgow Coma Scale (GCS)

Distribution of patients according to Serum Cholinesterase levels

38 (38%) patients had low serum cholinesterase levels (≤2100 IU/L) while 62 (62%) patients had serum cholinesterase levels>2100 IU/L.

Table 7: Distribution of patients according to Serum Cholinesterase levels

Serum Cholinesterase	N	%
≤2100 IU/L	38	38
>2100 IU/L	62	62
TOTAL	100	100



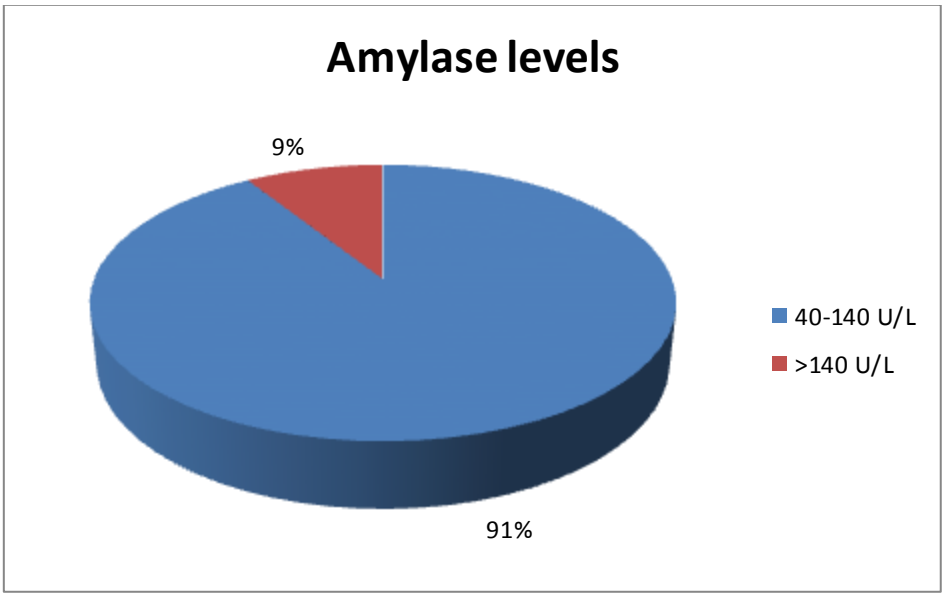
Graph7: Distribution of patients according to Serum Cholinesterase levels

Distribution of patients according to Amylase levels

91 (91%) patients had amylase levels in the normal range (40-140 U/L) while 9 (9%) patients had amylase levels>140 U/L.

Table 8: Distribution of patients according to Amylase levels

Amylase levels	N	%
40-140 U/L	91	91
>140 U/L	9	9
Total	100	100



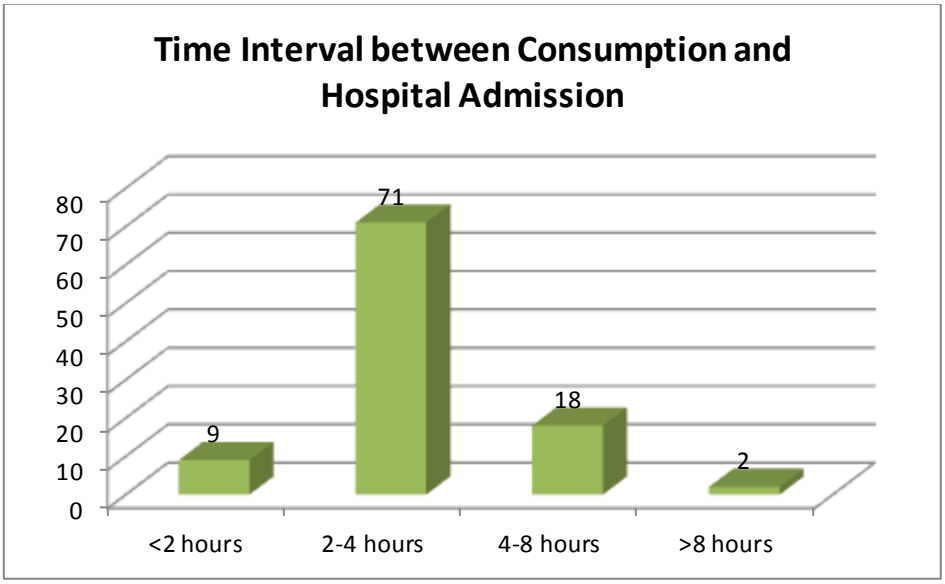
Graph8: Distribution of patients according to Amylase levels

Distribution of patients according to Time Interval between Consumption and Hospital Admission

Majority of the patients (71%) were admitted in the hospital within 2-4 hours of ingesting organophosphorus poison while 18 (18%) and 9 (9%) patients were admitted within 4-8 hours and <2 hours. 2 (2%) patients were admitted after >8 hours of ingesting organophosphorus poison.

Table 9: Distribution of patients according to Time Interval between Consumption and Hospital Admission

Time Interval	N	%
<2 hours	9	9
2-4 hours	71	71
4-8 hours	18	18
>8 hours	2	2
Total	100	100



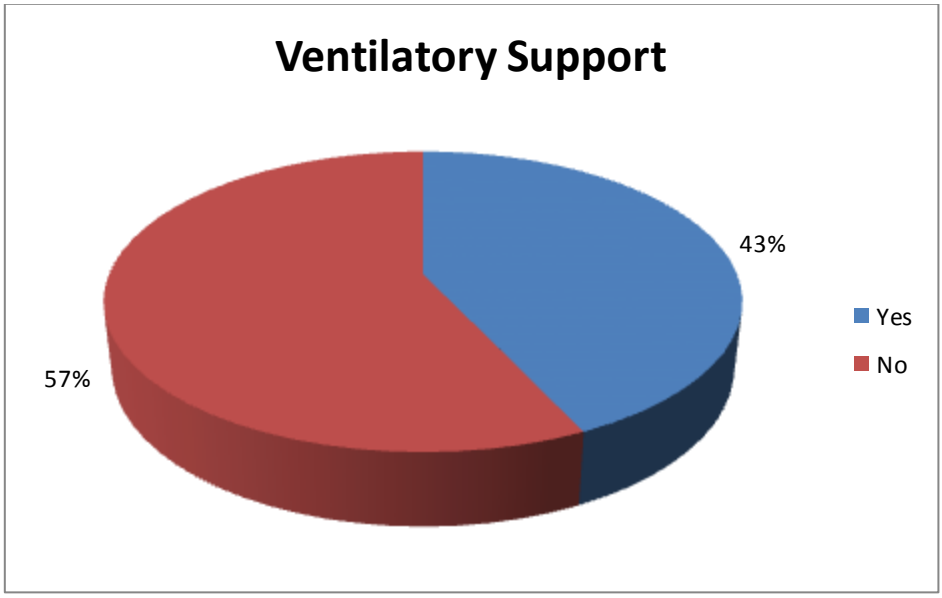
Graph9: Distribution of patients according to Time Interval between Consumption and Hospital Admission

Distribution of patients according to Requirement of Ventilatory Support

43 (43%) patients required ventilatory support while 57 (57%) patients did not require ventilator support.

Table 10: Distribution of patients according to Requirement of Ventilatory Support

Ventilatory Support	N	%
Yes	43	43
No	57	57
Total	100	100



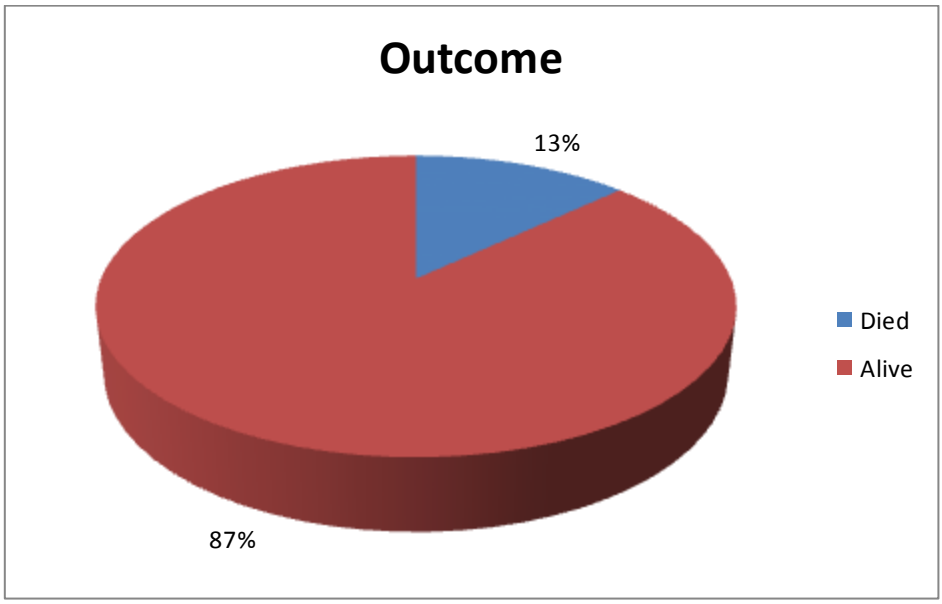
Graph10: Distribution of patients according to Requirement of Ventilatory Support

Distribution of patients according to Outcome

87 (87%) patients survived while 13 (13%) patients died in our study.

Table 11: Distribution of patients according to Outcome

Outcome	N	%
Died	13	13
Alive	87	87
Total	100	100



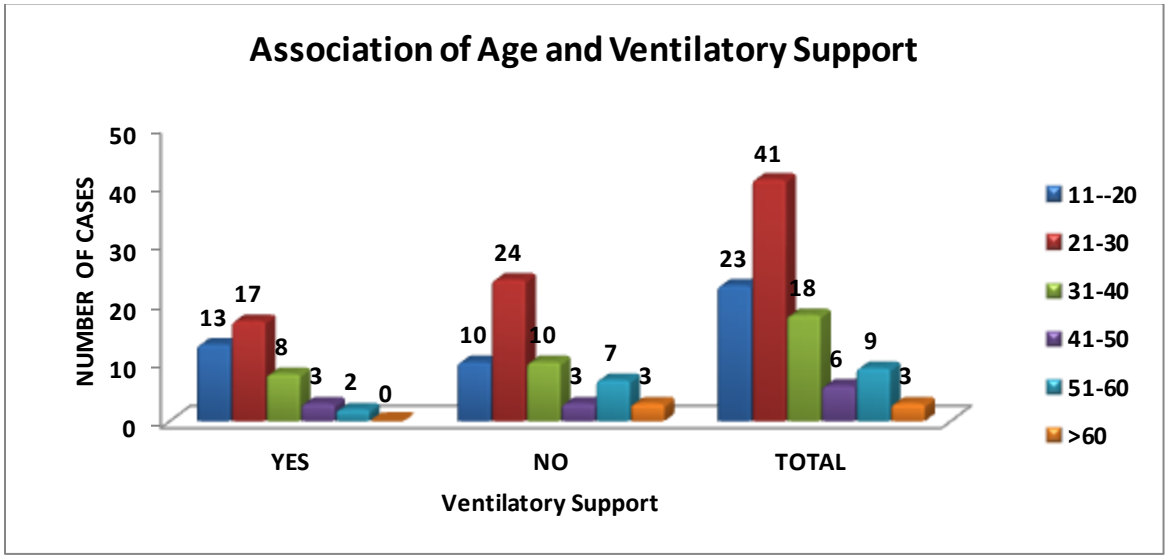
Graph11: Distribution of patients according to Outcome

Association of Age and Ventilatory Support

Majority of patients with and without ventilatory support were in the age group of 21-30 years (39.5% and 42.1% respectively). There was no significant association of age and ventilatory support as per Chi-square test (p>0.05).

Table 12: Association of Age and Ventilatory Support

Age	Ventilatory Support						p Value
	Yes		No		Total		
	N	%	N	%	N	%	
11-20	13	30.2	10	17.5	23	23.0	>0.05
21-30	17	39.5	24	42.1	41	41.0	
31-40	8	18.6	10	17.5	18	18.0	
41-50	3	7.0	3	5.3	6	6.0	
51-60	2	4.7	7	12.3	9	9.0	
>60	0	0.0	3	5.3	3	3.0	
Total	43	100.0	57	100.0	100	100.0	



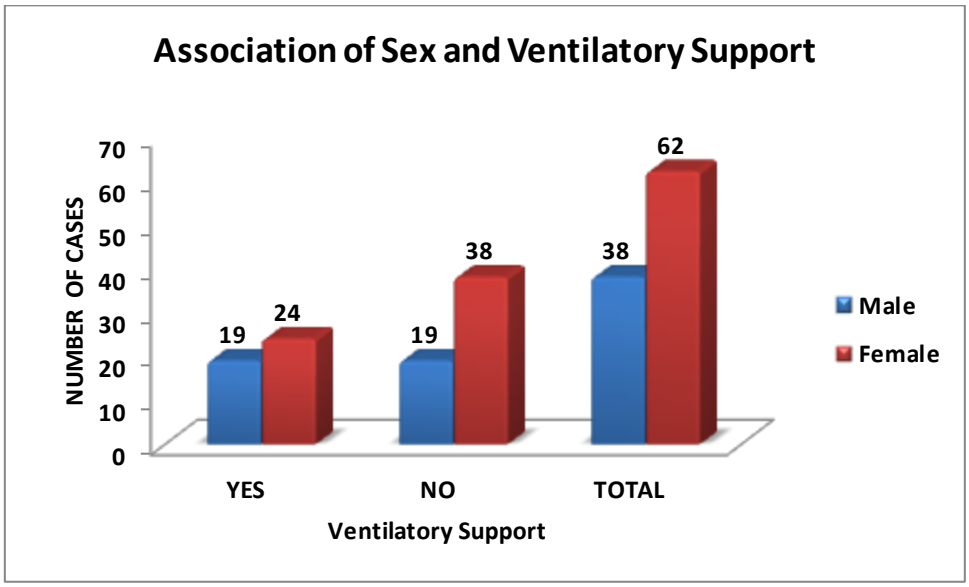
Graph 12:Association of Age and Ventilatory Support

Association of Sex and Ventilatory Support

44.2% and55.8% male and female patients respectively were on ventilatory support. There was no significant association of sex and ventilatory support as per Chi-square test (p>0.05).

Table 13: Association of Sex and Ventilatory Support

Sex	Ventilatory Support						p Value
	Yes		No		Total		
	N	%	N	%	N	%	
Male	19	44.2	19	33.3	38	38.0	>0.05
Female	24	55.8	38	66.7	62	62.0	
Total	43	100.0	57	100.0	100	100.0	



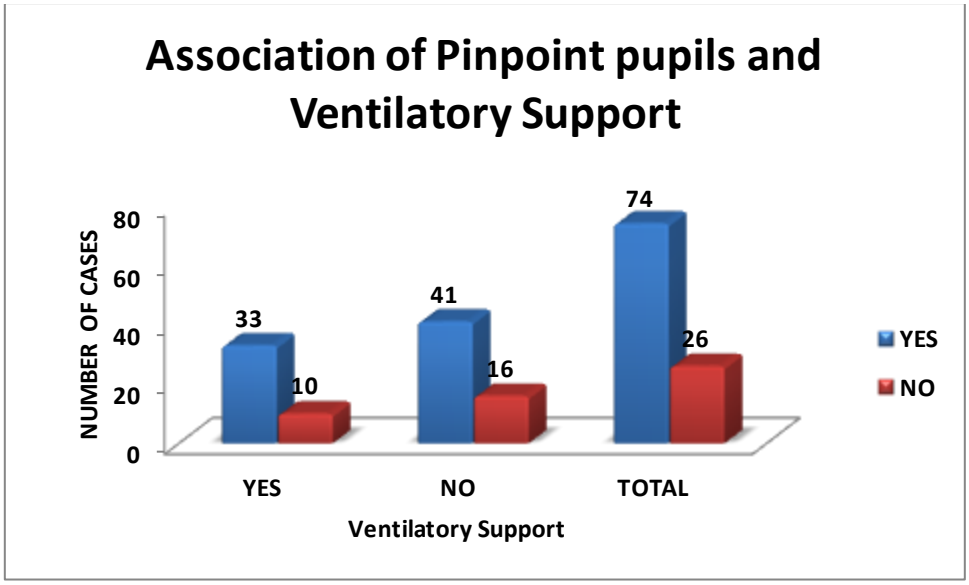
Graph 13:Association of Sex and Ventilatory Support

Association of Pinpoint pupils and Ventilatory Support

Among patients with pinpoint pupils 41(55.4%) were not on ventilatory support however there was no significant association of pinpoint pupils and ventilatory support as per Chi-square test (p>0.05).

Table 14: Association of Pinpoint pupils and Ventilatory Support

Pinpoint pupils	Ventilatory Support						p Value
	Yes		No		Total		
	N	%	N	%	N	%	
YES	33	44.6	41	55.4	74	74.0	>0.05
NO	10	38.5	16	61.5	26	26.0	
Total	43	43.0	57	57.0	100	100.0	



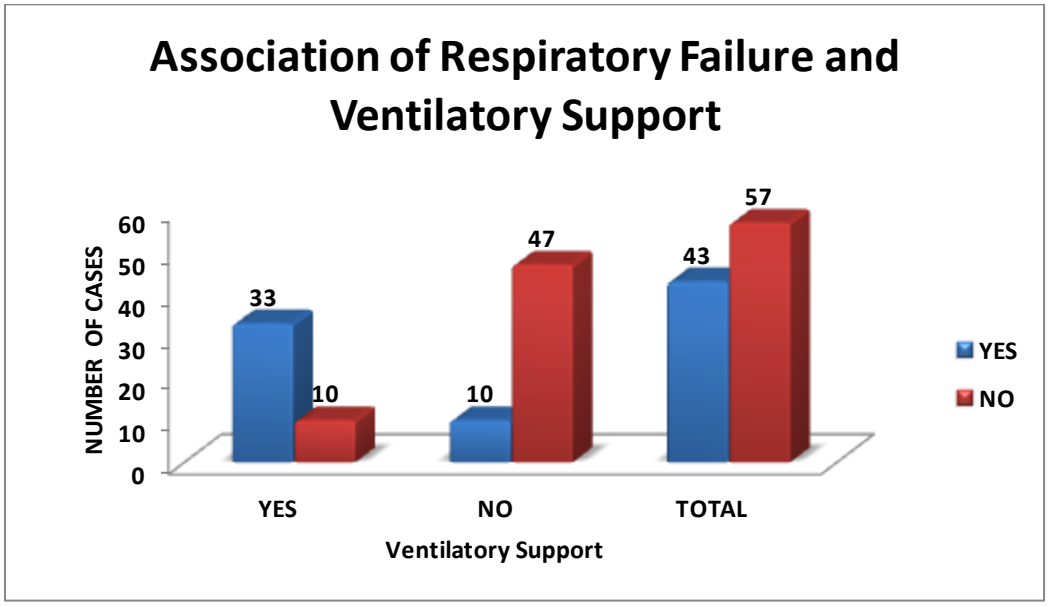
Graph 14:Association of Pinpoint pupils and Ventilatory Support

Association of Respiratory Failure and Ventilatory Support

Among all patients 33 were on ventilatory support with respiratory failure, while 10 were not on ventilatory support with respiratory failure. There was significant association of respiratory failure and ventilatory support as per Chi-square test (**p<0.05**).

Table 15: Association of Respiratory Failure and Ventilatory Support

Respiratory Failure	Ventilatory Support						p Value
	Yes		No		Total		
	N	%	N	%	N	%	
YES	33	76.7	10	23.3	43	43.0	
NO	10	17.5	47	82.5	57	57.0	**<0.05**
Total	43	43.0	57	57.0	100	100.0	



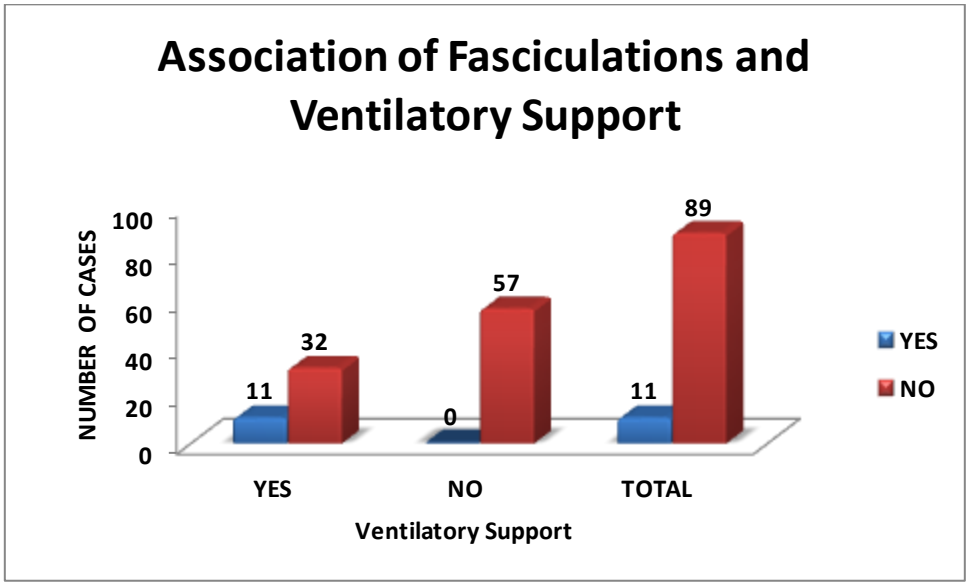
Graph 15:Association of Respiratory Failure and Ventilatory Support

Association of Fasciculations and Ventilatory Support

Among all patients 11 were on ventilatory support with fasciculations, while there was no case without ventilatory support with fasciculations. There was significant association of fasciculations and ventilatory support as per Chi-square test (**p<0.05**).

Table 16: Association of Fasciculations and Ventilatory Support

Fasciculations	Ventilatory Support						p Value
	Yes		No		Total		
	N	%	N	%	N	%	
YES	11	100.0	0	0.0	11	11.0	<0.05
NO	32	36.0	57	64.0	89	89.0	
Total	43	43.0	57	57.0	100	100.0	



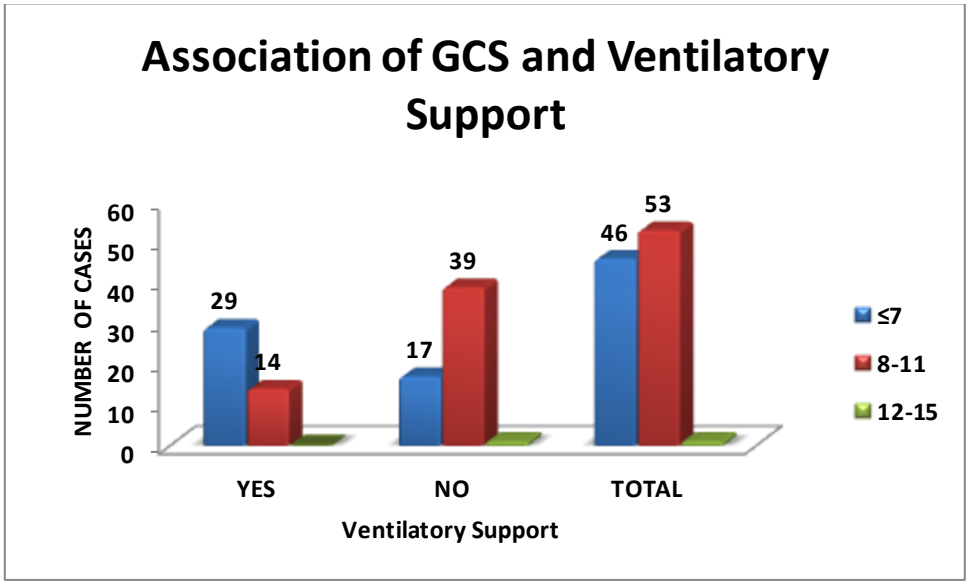
Graph 16:Association of Fasciculations and Ventilatory Support

Association of Glasgow Coma Scale (GCS) and Ventilatory Support

Majority of patients with very poor GCS score (67.4%) were on ventilatory support. There was significant association of Glasgow Coma Scale (GCS) and ventilatory support as per Chi-square test (**p<0.05**).

Table 17: Association of GCS and Ventilatory Support

GCS	Ventilatory Support						p Value
	Yes		No		Total		
	N	%	N	%	N	%	
≤7	29	67.4	17	29.8	46	46.0	<0.05
8-11	14	32.6	39	68.4	53	53.0	
12-15	0	0.0	1	1.8	1	1.0	
Total	43	100.0	57	100.0	100	100.0	



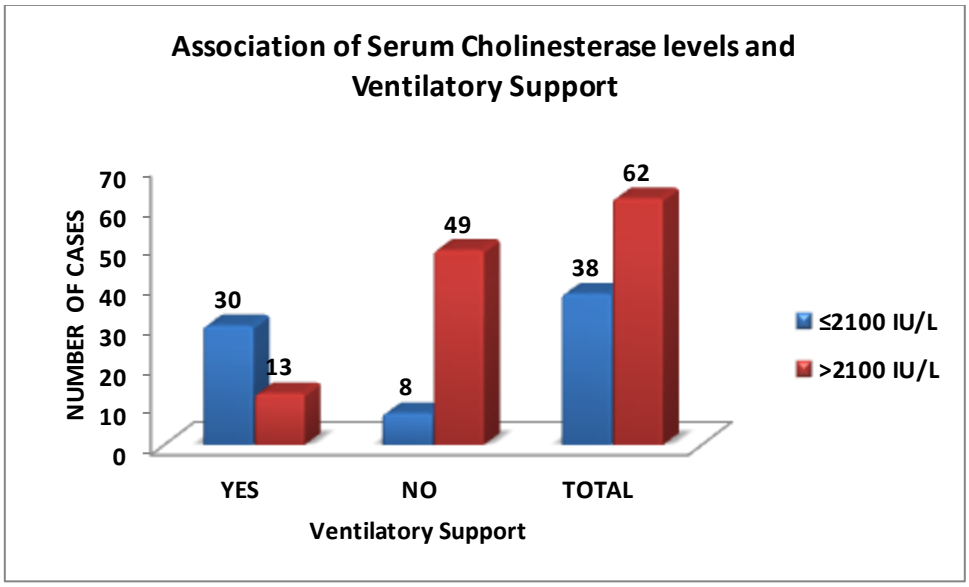
Graph 17:Association of GCS and Ventilatory Support

Association of Serum Cholinesterase levels and Ventilatory Support

Majority of the patients on ventilatory support had low serum cholinesterase levels (69.8%). There was significant association of serum cholinesterase levels and ventilatory support as per Chi-square test (**p<0.05**).

Table 18: Association of Serum Cholinesterase levels and Ventilatory Support

Serum Cholinesterase levels	Ventilatory Support						p Value
	Yes		No		Total		
	N	%	N	%	N	%	
≤2100 IU/L	30	69.8	8	14.0	38	38.0	<0.05
>2100 IU/L	13	30.2	49	86.0	62	62.0	
Total	43	100.0	57	100.0	100	100.0	



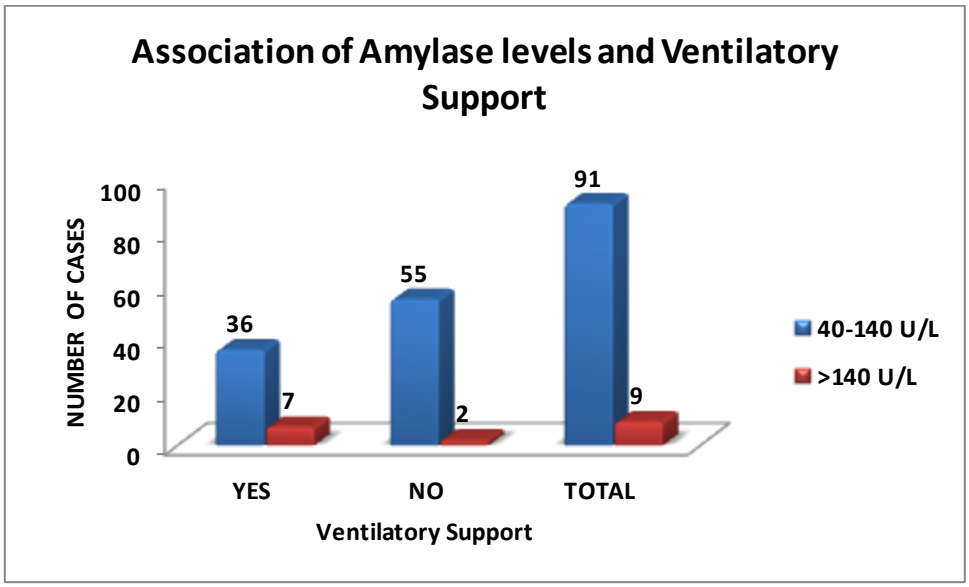
Graph 18:Association of Serum Cholinesterase levels and Ventilatory Support

Association of Amylase levels and Ventilatory Support

Among patients with high amylase levels, 7 (16.3%) patients were on ventilatory support while 2 (3.5%) patients were not on ventilatory support. There was significant association of amylase levels and ventilatory support as per Chi-square test (**p<0.05**).

Table 19: Association of Amylase levels and Ventilatory Support

Amylase levels	Ventilatory Support						p Value
	Yes		No		Total		
	N	%	N	%	N	%	
40-140 U/L	36	83.7	55	96.5	91	91.0	**<0.05**
>140 U/L	7	16.3	2	3.5	9	9.0	
Total	43	100.0	57	100.0	100	100.0	



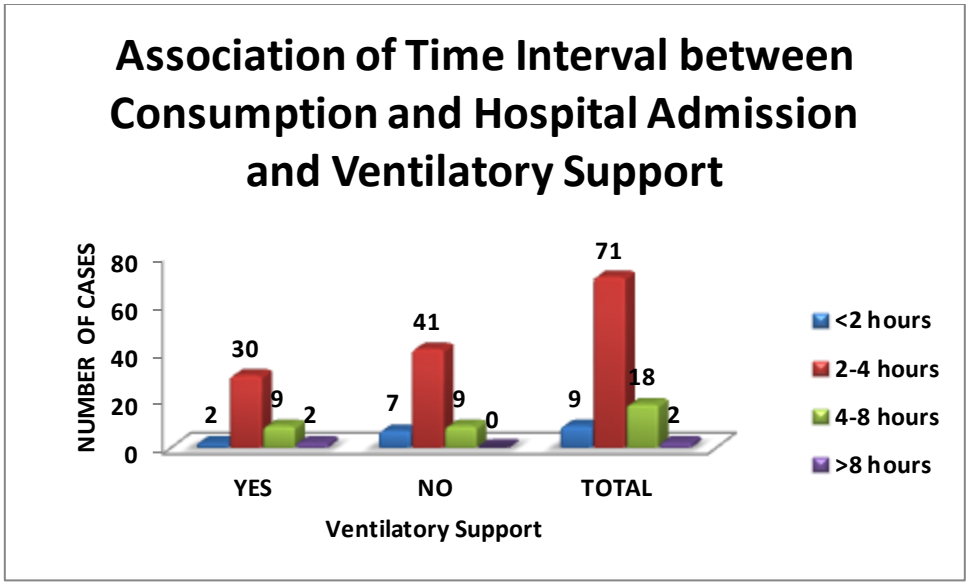
Graph 19:Association of Amylase levels and Ventilatory Support

Association of Time Interval between Consumption and Hospital Admission and Ventilatory Support

Among patients admitted with less than 2 hours of OP poisoning, out of total 9 cases, 2 (22.2%) were on ventilatory support. Patients admitted with 2-4 hours of OP poisoning, out of total 71 cases, 30 (42.3%) required ventilatory support while patients admitted with 4-8 hours, out of 18 cases, 9 (50%) required ventilatory support. Whereas 2 patients admitted with more than 8 hours of time interval and all were on ventilatory support. There was significant association of time interval between consumption and hospital admission and ventilatory support as per Chi-square test (**p<0.05**).

Table 20: Association of Time Interval between Consumption and Hospital Admission and Ventilatory Support

Time Interval	Ventilatory Support						p Value
	Yes		No		Total		
	N	%	N	%	N	%	
<2 hours	2	22.2	7	77.8	9	9.0	<0.05
2-4 hours	30	42.3	41	57.7	71	71.0	
4-8 hours	9	50.0	9	50.0	18	18.0	
>8 hours	2	100.0	0	0.0	2	2.0	
Total	43	43.0	57	57.0	100	100.0	



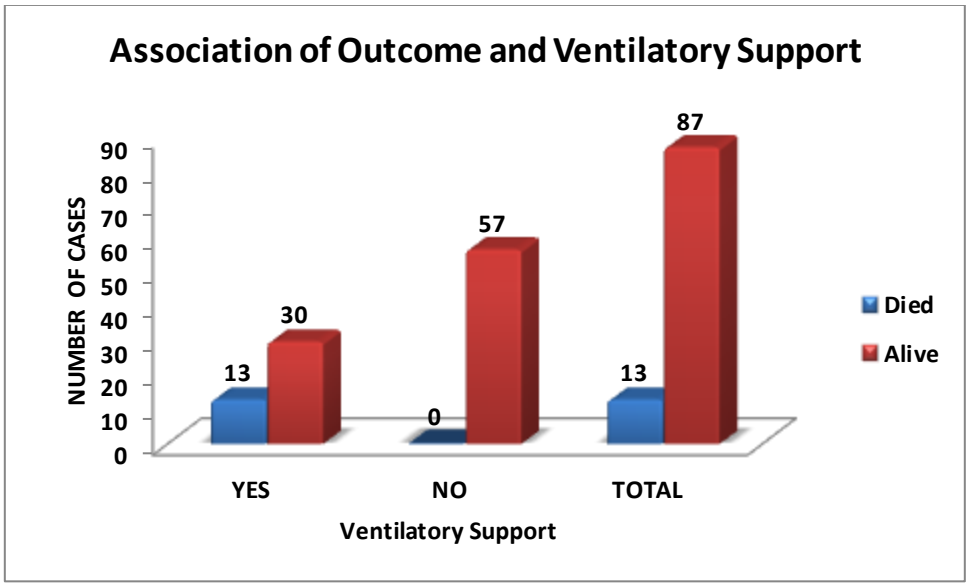
Graph 20:Association of Time Interval between Consumption and Hospital Admission and Ventilatory Support

Association of Outcome and Ventilatory Support

All patients that died were on ventilatory support. There was significant association of outcome and ventilatory support as per Chi-square test (**p<0.05**).

Table 21: Association of Outcomeand Ventilatory Support

Outcome	Ventilatory Support						p Value
	Yes		No		Total		
	N	%	N	%	N	%	
Died	13	30.2	0	0.0	13	13.0	**<0.05**
Alive	30	69.8	57	100.0	87	87.0	
Total	43	100.0	57	100.0	100	100.0	



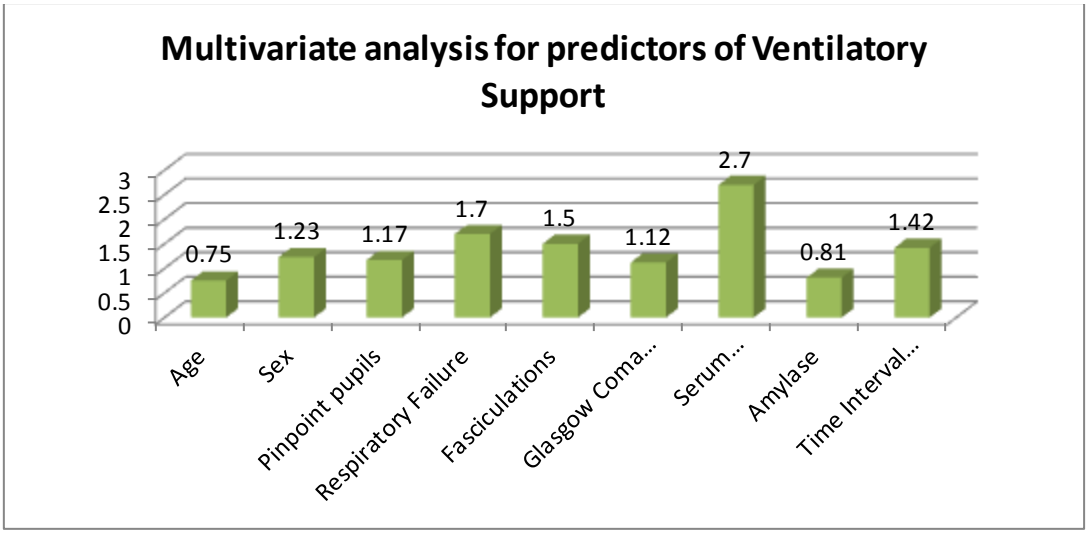
Graph 21:Association of Outcome and Ventilatory Support

Multivariate analysis for predictors of Ventilatory Support

Logistic regression analysis was used to evaluate predictors of ventilatory support. The logistic regression analysis showed that respiratory failure, fasciculations, Glasgow Coma Scale, serum cholinesterase and time interval between consumption and hospital admission were independently associated with ventilatory support.

Table 22: Multivariate analysis for predictors of Ventilatory Support

Parameters	OR	95% CI	p Value
Age	0.75	0.54–1.03	p>0.05
Sex	1.23	1.00–1.51	p>0.05
Pinpoint pupils	1.17	0.45–2.85	p>0.05
Respiratory Failure	1.70	1.15–2.50	**p<0.05**
Fasciculations	1.50	1.28–1.75	**p<0.05**
Glasgow Coma Scale	1.12	1.01–1.25	**p<0.05**
Serum Cholinesterase	2.70	2.33–3.13	**p<0.05**
Amylase	0.81	0.61–1.09	p>0.05
Time Interval between Consumption and Hospital Admission	1.42	1.26–1.60	**p<0.05**



Graph 22: Multivariate analysis for predictors of Ventilatory Support

DISCUSSION

A hospital based prospective cross sectional study was conducted with 100 patients to analyze the clinical profile of organophosphate compound poisoning and identify the factors which help in predicting the need for ventilatory support in organophosphorus compound poisoning.

Various forms of poisoning cases are seen in tertiary care hospitals. In rural parts of India, especially in the agricultural belt, there has been the highest prevalence of poisoning cases. Among the poisoning cases the pesticide consumption is a common phenomenon. In rural areas it is very common to find the OPP poisoning cases due to various reasons. Among these, suicidal attempt is the commonest cause. The main rreason for selecting these drugs is; these are cheap, easily available over the counter and used as a major pesticide during farming, so readily available at homes of the farmers.

OP compounds were synthesized by von Hoffman. OP pesticide poisoning is common in developing worlds[120]. The highest incidence is seen in India[121]. Suicidal and non-suicidal organophosphate poisoning is a major problem in rural areas of India, with rapidly increasing incidence rate[122].

Banday TH et al[113] prospective study reported incidence of suicidal poisoning is 98.6%, probably because it is cheap, easily available and used as a major pesticide in agricultural farming throughout India. And in our study incidence of suicidal poisoning was 100%.

The leading cause of death in OP poisoning is respiratory failure[123,124] and various grading systems proposed suggests that most cases can be managed in the ICU. But

this can't be applied to developing countries where in 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 mortality[123].

In the present study, Majority of the patients (41%) were in the age group of 21-30 years followed by 11-20 years (23%), 31-40 years (18%), 51-60 years (9%), 41-50 years (6%) and >60 years (3%). The mean age of the patients was 31.96 ± 14.12 years. In this study 38% patients were male and 62% were female. There was female preponderance in our study and the M:F ratio was 1:1.6. This is similar to the studies of Banday TH et al[113], Shetti AN et al[125], Chethan Kumar RAN et al[126] and Rajeev H et al[127].

The route of exposure was oral in all the patients. The most common organophosphorus compound consumed in our study was Malathion (28%) followed by Dichlorovas (25%), Monocrotphos (24%), Dimethoate (6%) and Methyleparathion (5%). This is comparable to the studies of Chethan Kumar RAN et al[126] and Rajeev H et al[127].

The most common effect of OP poisoning was pinpoint pupils (74%) followed by respiratory failure (42%), fasciculations(11%) and intermediate syndrome (2%). This is concordant to the studies of Chethan Kumar RAN et al[126] and Rajeev H et al[127].

In our study, 46 (46%) patients had very poor GCS score (≤7) while 53 (53%) patients had GCS score between 8 to 11. 1 (1%) patient had good GCS score (12-15). 38 (38%) patients had low serum cholinesterase levels (≤2100 IU/L) while 62 (62%) patients had serum cholinesterase levels>2100 IU/L. 91 (91%) patients had amylase

levels in the normal range (40-140 U/L) while 9 (9%) patients had amylase levels>140 U/L. It was similar to the study conducted by chethan kumar et al[126]

It was observed in our study that majority of the patients (71%) were admitted in the hospital within 2-4 hours of ingesting organophosphorus poison while 18 (18%) and 9 (9%) patients were admitted within 4-8 hours and <2 hours. 2 (2%) patients were admitted after >8 hours of ingesting organophosphorus poison. Similar observation were made in the study by chethan kumar et al[126]

.In the present study, 43 (43%) patients required ventilatory support while 57 (57%) patients did not require ventilator support. This finding was consistent with the studies of Banday TH et al[113], Patil SL et al[128] and Rajeev H et al[127].

.It was observed in the present study that 87 (87%) patients survived while 13 (13%) patients died in our study. This is in concordance to the studies of Shetti AN et al[125] and Rajeev H et al[127].

In our study, majority of patients with and without ventilatory support were in the age group of 21-30 years (39.5% and 42.1% respectively). There was no significant association of age and ventilatory support as per Chi-square test ($p>0.05$). which was similar to the study of Rajeev H et al[127] and Shetti AN et al[125]

44.2% and 55.8% male and female patients respectively were on ventilatory support. There was no significant association of sex and ventilatory support as per Chi-square test ($p>0.05$).which was similar to the study of Rajeev H et al[127] and Shetti AN et al[127]

Among patients with pinpoint pupils 41(55.4%) were not on ventilatory support however there was no significant association of pinpoint pupils and ventilatory

support as per Chi-square test (p>0.05). Which was similar to the study of Rajeev H et al[127]

It was observed in our study that among all patients 33 were on ventilatory support with respiratory failure, while 10 were not on ventilatory support with respiratory failure. There was significant association of respiratory failure and ventilatory support as per Chi-square test (**p<0.05**). Similar observation was done in the study of Rajeev H et al[127]

Among all patients 11 were on ventilatory support with fasciculations, while there was no case without ventilatory support with fasciculations. There was significant association of fasciculations and ventilatory support as per Chi-square test (**p<0.05**). Similar observation was done in study of Rajeev H et al[127]

In the present study, Majority of patients with very poor GCS score (67.4%) were on ventilatory support. There was significant association of Glasgow Coma Scale (GCS) and ventilatory support as per Chi-square test (**p<0.05**). Similar observation was done in study of Rajeev H et al[127.]

It was observed in the present study that majority of the patients on ventilatory support had low serum cholinesterase levels (69.8%). There was significant association of serum cholinesterase levels and ventilatory support as per Chi-square test (**p<0.05**).Similar observations were noted in the studies of Shetti AN et al[125], Chethan Kumar RAN et al[126] and Rajeev H et al[127].

Among patients admitted with less than 2 hours of OP poisoning, out of total 9 cases, 2 (22.2%) were on ventilatory support. Patients admitted with 2-4 hours of OP poisoning, out of total 71 cases, 30 (42.3%) required ventilatory support while

patients admitted with 4-8 hours, out of 18 cases, 9 (50%) required ventilatory support. Whereas 2 patients admitted with more than 8 hours of time interval and all were on ventilatory support. There was significant association of time interval between consumption and hospital admission and ventilatory support as per Chi-square test (**p<0.05**). similar observation was done in study of Banday TH et al[113]

.It was observed in our study that all patients that died were on ventilatory support. There was significant association of outcome and ventilatory support as per Chi-square test (**p<0.05**).Banday TH et al[113] and Rajeev H et al[127]noted similar observations in their studies. Which was similar to the study of Banday TH et al[113.]

In the present study, logistic regression analysis was used to evaluate predictors of ventilatory support. The logistic regression analysis showed that respiratory failure, fasciculations, Glasgow Coma Scale, serum cholinesterase and time interval between consumption and hospital admission were independently associated with ventilatory support.

SUMMARY

A hospital based prospective cross sectional study was conducted with 100 patients to analyze the clinical profile of organophosphate compound poisoning and identify the factors which help in predicting the need for ventilatory support in organophosphorous compound poisoning. The following observations were noted:

1. Majority of the patients (41%) were in the age group of 21-30 years followed by 11-20 years (23%), 31-40 years (18%), 51-60 years (9%), 41-50 years (6%) and >60 years (3%). The mean age of the patients was 31.96 ± 14.12 years.
2. In this study 38% patients were male and 62% were female. There was female preponderance in our study and the M:F ratio was 1:1.6.
3. The route of exposure was oral in all the patients.
4. The most common organophosphorus compound consumed in our study was Malathion (28%) followed by Dichlorovas (25%), Monocrotphos (24%), Dimethoate (6%) and Methyleparathion (5%).
5. The most common effect of OP poisoning was pinpoint pupils (74%) followed by respiratory failure (42%), fasciculations(11%) and intermediate syndrome (2%).
6. 46 (46%) patients had very poor GCS score (≤7) while 53 (53%) patients had GCS score between 8 to 11. 1 (1%) patient had good GCS score (12-15).
7. 38 (38%) patients had low serum cholinesterase levels (≤2100 IU/L) while 62 (62%) patients had serum cholinesterase levels>2100 IU/L.
8. 91 (91%) patients had amylase levels in the normal range (40-140 U/L) while 9 (9%) patients had amylase levels>140 U/L.
9. Majority of the patients (71%) were admitted in the hospital within 2-4 hours of ingesting organophosphorus poison while 18 (18%) and 9 (9%) patients were admitted within 4-8 hours and <2 hours. 2 (2%) patients were admitted after >8 hours of ingesting organophosphorus poison.
10. 43 (43%) patients required ventilatory support while 57 (57%) patients did not require ventilator support.
11. 87 (87%) patients survived while 13 (13%) patients died in our study.

12. Majority of patients with and without ventilatory support were in the age group of 21-30 years (39.5% and 42.1% respectively). There was no significant association of age and ventilatory support as per Chi-square test ($p>0.05$).
13. 44.2% and 55.8% male and female patients respectively were on ventilatory support. There was no significant association of sex and ventilatory support as per Chi-square test ($p>0.05$).
14. Among patients with pinpoint pupils 41(55.4%) were not on ventilatory support however there was no significant association of pinpoint pupils and ventilatory support as per Chi-square test ($p>0.05$).
15. Among all patients 33 were on ventilatory support with respiratory failure, while 10 were not on ventilatory support with respiratory failure. There was significant association of respiratory failure and ventilatory support as per Chi-square test (**$p<0.05$**).
16. Among all patients 11 were on ventilatory support with fasciculations, while there was no case without ventilatory support with fasciculations. There was significant association of fasciculations and ventilatory support as per Chi-square test (**$p<0.05$**).
17. Majority of patients with very poor GCS score (67.4%) were on ventilatory support. There was significant association of Glasgow Coma Scale (GCS) and ventilatory support as per Chi-square test (**$p<0.05$**).
18. Majority of the patients on ventilatory support had low serum cholinesterase levels (69.8%). There was significant association of serum cholinesterase levels and ventilatory support as per Chi-square test (**$p<0.05$**).
19. Among patients with high amylase levels, 7 (16.3%) patients were on ventilatory support while 2 (3.5%) patients were not on ventilatory support. There was significant association of amylase levels and ventilatory support as per Chi-square test (**$p<0.05$**).
20. Among patients admitted with less than 2 hours of OP poisoning, out of total 9 cases, 2 (22.2%) were on ventilatory support. Patients admitted with 2-4 hours of OP poisoning, out of total 71 cases, 30 (42.3%) required ventilatory support while patients admitted with 4-8 hours, out of 18 cases, 9 (50%) required ventilatory support. Whereas 2 patients admitted with more than 8 hours of time interval and all were on ventilatory support. There was

significant association of time interval between consumption and hospital admission and ventilatory support as per Chi-square test (**p<0.05**).

21. All patients that died were on ventilatory support. There was significant association of outcome and ventilatory support as per Chi-square test (**p<0.05**).
22. Logistic regression analysis was used to evaluate predictors of ventilatory support. The logistic regression analysis showed that respiratory failure, fasciculations, Glasgow Coma Scale, serum cholinesterase and time interval between consumption and hospital admission were independently associated with ventilatory support.

CONCLUSION

OP insecticide poisoning is a life threatening condition that needs rapid diagnosis and treatment. Since most of the patients present with respiratory failure, early initiation of mechanical ventilation plays a vital role in the treatment of such cases. Emphasis must also be given to good supportive care and monitoring for the prevention and management of acute and delayed complications that occur during the course of stay in ICU.

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 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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ANNEXURE I

ETHICAL CLEARANCE CERTIFICATE

6/1/2016
06/10/16

B.L.D.E. UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103
INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 04-10-2016 at 3-00 pm to scrutinize the Synopsis of Postgraduate Students of this college ~~from~~ Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis has been accorded Ethical Clearance.

Title "Study of predictors for ventilatory support in patients of organophosphorous compound - poisoning"

Name of P.G. student Dr Vipin S. Thakur
Dept of Medicine.

Name of Guide/Co-investigator Dr S.M. Biradar
Assoc prof of Medicine

DR.TEJASWINI. VALLABHA
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDEU'S, SHRI.B.M.PATIL
MEDICAL COLLEGE, BIJAPUR.

Following documents were placed before E.C. for Scrutinization
1) Copy of Synopsis/Research project.
2) Copy of informed consent form
3) Any other relevant documents.

ANNEXURE II

INFORMED CONSENT FORM

BLDEU'S SHRI B. M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, VIJAYAPUR- 586103

TITLE OF THE PROJECT STUDY OF PREDICTORS FOR VENTILATORY SUPPORT IN PATIENTS OF ORGANOPHOSPHORUS COMPOUND POISOINING

PRINCIPAL INVESTIGATOR - Dr .VIPIN D.T

P.G. GUIDE NAME - Dr. SIDDANAGOUDA.M.BIRADAR
ASSOCIATE PROFESSOR OF MEDICINE

CHAIRMAN ETHICAL COMMITTEE

All aspects of this consent form are explained to the patient in the language understood by him/her.

I) **INFORMED PART**

1) PURPOSE OF RESEARCH:

I have been informed about this study. I have also been given a free choice of participation in this study.

2) PROCEDURE:

I am aware that in addition to routine care received I will be asked series of questions by the investigator. I have been asked to undergo the necessary investigations and treatment, which will help the investigator in this study.

3) RISK AND DISCOMFORTS:

I understand that I may experience some pain and discomfort during the examination or during my treatment. This is mainly the result of my condition and the procedure of this study is not expected to exaggerate these feelings that are associated with the usual course of treatment

4) BENEFITS:

I understand that my participation in this study will help to patients survival and better outcome.

5) CONFIDENTIALITY:

I understand that the medical information produced by this study will become a part of Hospital records and will be subject to the confidentiality and privacy regulation. Information of a sensitive personal nature will not be a part of the medical records, but will be stored in the investigator's research file and identified only by a code number. The code-key connecting name to numbers will be kept in a separate location.

If the data are used for publication in the medical literature or for teaching purpose, no name will be used and other identifiers such as photographs and audio or videotapes will be used only with my special written permission. I understand that I may see the photographs and videotapes and hear the audiotapes before giving this permission.

6) REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at anytime .Dr.VIPIN D.T is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of the study, which might influence my continued participation.

If during the study, or later, I wish to discuss my participation in or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me. A copy of this consent form will be given to me to keep for careful reading.

7) REFUSAL OR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and that I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital. I also understand that Dr..VIPIN D.T may terminate my participation in the study after he has explained the reasons for doing so and has helped arrange for my continued care by my own physician or physical therapist, if this is appropriate.

8) INJURY STATEMENT:

I understand that in the unlikely event of injury to me resulting directly from my participation in this study, if such injury were reported promptly, the appropriate treatment would be available to me, but no further compensation would be provided. I understand that by my agreement to participate in this study I am not waiving any of my legal rights.

I have explained to _____the purpose of the research, the procedures required and the possible risks and benefits to the best of my ability in patient's own language.

_____ _____

Dr.Vipin D.T

(Investigator) Date :

APPENDIX –III

BLDEDU'S SHRI B.M. PATIL MEDICAL COLLEGE

HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA

Name: CASE NO:

Age: IP NO:

Sex: DOA:

Religion: DOD:

Past Occupation:

Present Occupation:

Residence:

Chief complaints:

History of present illness:

Given by patient or patient attender

Time of consumption of op compound

Name of the compound

Time of onset of symptoms

Has patient received first aid

Time when patient became unconscious

History of convulsions

Mode of exposure

History of presenting symptoms like vomiting, excess salivation, breathlessness, altered sensorium, bladder incontinence , loss of consciousness

Past history: past history , neurological disorder, hypertension and type 2 diabetes mellitus

Personal history:

Diet

Appetite

Sleep

Bowel and bladder

Family history:

General physical examination

Height :

Weight:

Body Mass Index :

Vitals

PR:

BP:

RR:

Temp:

Head to toe examination

SYSTEMIC EXAMINATION

Respiratory System

Cardiovascular System

Central Nervous System

Per abdomen

PREDICTORS:

STUPOR COMA

PRESENCE OF CONVULSION

PIN POINT PUPIL

HYPERSALIVATION

FASCICULATION SCORE 5 OR MORE

INTERMEDIATE SYNDROME

OP INDUCED POLYNEUROPATHY

LEVELS OF CHOLINESTERASE

LEVELS OF SERUM AMYLASE

TIME INTERVAL FROM CONSUMPTION TO TREATMENT

INVESTIGATIONS

HAEMATOLOGY –

Hemoglobin	gm. %
Total WBC counts	Cells/mm^3
Differential counts -	
Neutrophils	%
Lymphocytes	%
Eosinophils	%
Monocytes	%
Basophils	%
ESR	mm after 1 hour

ABG:

BLOOD SUGAR

URINE ROUTINE

SERUM CHOLINESTERASE

SERUM AMYLASE

SERUM ELECTROLYTES

SGPT / SGOT

Chest X-ray:

ECG:

FINAL DIAGNOSIS

TREATMENT

MASTER CHART

Sl. No	IP NO	D.O.A	NAME	AGE	SEX	ROUTE OF EXPOSURE	COMPOUND	SCE(IU/L)	sc amylse	GCS	FASCULATION	CONVULSION	RS FAILURE	INTEMIDATE SYNDROME	PIN POINT PUPIL	TIME INTERVAL	OP DETECTED	D.O.D	CLINICAL OUTCOME
1	38640	21.11.16	kasturibai	32	F	ORAL	MONOCROTPHOS	505	741	4	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	1 HOUR	Y	6.12.16	survived without ventilatory support
2	38940	26.11.16	TIPPANNA B PUJARI	85	M	ORAL	MONOCROTPHOS	6406	54	13	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	2 HOUR	Y	5.12.16	survived without ventilatory support
3	39188	26.11.16	YALLAPPA	19	M	ORAL	DICHLOROVAS	261	41	4	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	48 HOUR	Y	27.11.16	death with ventilatory support
4	39233	26.11.16	ASHWINI	20	F	ORAL	DICHLOROVAS	68	270	4	PRESENT	ABSENT	PRESENT	PRESENT	PRESENT	6 HOUR	Y	15.15.16	death with ventilatory support
5	40086	4.12.16	PREM SINGH	55	M	ORAL	PHOSPHONIC ACID	600	98	4	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	4 hour	Y	16.12.16	survived with ventilatory support
6	39920	2.12.16	NINGAMMA	25	F	ORAL	CHLORPYRIPHOS	102	177	4	ABSENT	ABSENT	present	ABSENT	PRESENT	5 hour	Y	15.12.16	survived with ventilatory support
7	3503	31.1.17	kusuppa	20	M	ORAL	MONOCROTPHOS	5188	91	7	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	2 HOUR	Y	8.2.17	survived without ventilatory support
8	42789	28.12.16	SUGHANDHA	36	F	ORAL	PARATION	6343	78	8	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	6 HOUR	Y	10.1.17	survived without ventilatory support
9	41784	19.12.16	SHALAWWA	35	F	ORAL	MONOCROTPHOS	2928	46	7	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	3 HOUR	Y	29.12.18	survived without ventilatory support
10	41903	20.12.16	RAVAT	21	M	ORAL	MONOCROTPHOS	228	96	4	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	4 HOUR	Y	20.1.17	survived with ventilatory support
11	40811	10.12.16	GURAPPA	44	M	ORAL	TRIAZOPHOS	4219	66	7	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	3 HOUR	Y	25.12.16	survived without ventilatory support
12	1332	12.1.17	RENUKA	35	F	ORAL	MALATHION	125	225	6	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	4 HOUR	Y	25.1.17	survived with ventilatory support
13	2055	19.1.17	DUNDAPPA	32	M	ORAL	MALATHION	7479	172	7	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	3 HOUR	Y	26.1.17	survived without ventilatory support
14	41989	21.12.16	SHIVANGAPPA	35	M	ORAL	DIMETHOATE	6611	83	7	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	1 HOUR	Y	30.12.16	survived with ventilatory support
15	4668	10.2.17	SHIVANAND	35	M	ORAL	MALATHION	6087	67	7	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	2 HOUR	Y	20.2.17	survived without ventilatory support
16	6928	3.3.17	SHANTAVVA	58	F	ORAL	MALATHION	4078	49	7	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	2 HOUR	Y	10.3.17	survived without ventilatory support
17	6242	24.2.17	MANGALA	47	F	ORAL	PHORATE	4179	67	8	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	2 HOUR	Y	3.3.17	survived without ventilatory support
18	7150	4.3.17	PRABHU	24	M	ORAL	TRIAZOPHOS	4787	70	8	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	1 HOUR	Y	14.3.17	survived without ventilatory support
19	11377	23.4.16	AKSHAY	60	M	ORAL	MONOCROTPHOS	9857	88	8	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	2 HOUR	Y	20.4.17	survived without ventilatory support
20	11849	13.4.17	MAHANTESH	28	M	ORAL	METHYLEPARATHION	2800	86	4	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	3 HOUR	Y	28.4.17	survived with ventilatory support
21	9664	26.3.17	SHAKIL	35	M	ORAL	DICHLOROVAS	1176	161	4	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	4 HOUR	Y	15.4.17	survived with ventilatory support
22	7453	7.3.17	DADASHEB	30	M	ORAL	MALATHION	4983	50	9	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	2 HOUR	Y	15.3.17	survived without ventilatory support
23	7980	10.4.17	BHIMANNA	65	M	ORAL	MALATHION	4983	50	9	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	1 hour	Y	20.4.17	survived without ventilatory support
24	7892	10.3.17	mounesh	17	M	ORAL	MONOCROTPHOS	4262	204	5	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	7 hour	Y	11.3.17	death with ventilatory support
25	14505	6.5.17	BHAVANA	16	F	ORAL	PROPHENOFUS+CYPERMETHRIN	158	70	5	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	3 HOUR	Y	20.5.17	survived with ventilatory support
26	14634	8.5.17	GEETHA	26	F	ORAL	METHYLPARATHION	244	80	4	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	3 HOUR	Y	28.5.17	survived with ventilatory support
27	15079	11.5.17	PARVATI	36	F	ORAL	METHYLPARATHION	818	70	6	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	3 HOUR	Y	25.5.17	survived with ventilatory support
28	15240	13.5.17	SUBHASCHNADRA	30	M	ORAL	MALATHION	244	80	4	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	24 HOUR	Y	15.5.17	death with ventilatory support
29	15079	11.5.17	PARVATI	36	F	ORAL	MONOCROTPHOS	316	86	4	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	2 HOUR	Y	20.5.17	survived without ventilatory support
30	15678	26.5.17	IRANGOUDA	26	M	ORAL	CHLORPYRIPHOS	4458	100	8	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	1 HOUR	Y	6.6.17	survived without ventilatory support

31	15140	12.5.17	VIDYASHREE	22	F	ORAL	MONOCROTPHOS	2385	489	4	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	2 HOUR	Y	28.5.17	survived with ventilatory support
32	15702	17.5.17	SUREKHA	25	F	ORAL	MALATHION	4635	80	6	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	2 HOUR	Y	27.5.17	survived without ventilatory support
33	15731	17.5.17	SANTOSH	20	M	ORAL	DICHLOROVAS	1300	86	5	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	1 HOUR	Y	28.5.17	survived with ventilatory support
34	17017	27.5.17	POOJA	23	F	ORAL	MALATHION	1200	90	7	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	3 HOUR	Y	6.6.17	survived without ventilatory support
35	18210	6.6.17	AKSHATA	20	F	ORAL	DICHLOROVAS	2000	86	7	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	2 HOUR	Y	15.6.17	survived without ventilatory support
36	18485	8.6.17	VAISHALI	19	F	ORAL	MONOCROTPHOS	250	84	4	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	3 HOUR	Y	18.6.17	survived with ventilatory support
37	19152	14.6.17	MACHANDRA	18	M	ORAL	DICHLOROVAS	414	90	5	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	2 HOUR	Y	26.6.17	survived with ventilatory support
38	25034	30.7.17	GEETHA	19	F	ORAL	MONOCROTPHOS	4257	69	7	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	3 HOUR	Y	6.8.17	survived without ventilatory support
39	24446	25.7.17	POORNIMA	18	F	ORAL	MONOCROTPHOS	4817	70	8	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	2 HOUR	Y	6.8.17	survived without ventilatory support
40	21855	4.7.17	ROOPASHREE	25	F	ORAL	DICHLOROVAS	2356	70	8	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	2 HOUR	Y	6.7.17	death with ventilatory support
41	21893	5.7.17	SAPNA	18	F	ORAL	DICHLOROVAS	6058	78	8	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	3 HOUR	Y	16.7.17	survived with ventilatory support
42	19593	17.6.17	BASAVANTH	24	M	ORAL	MONOCROTPHOS	82	90	4	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	3 HOUR	Y	20.6.17	death with ventilatory support
43	4637	6.2.18	IMTAZ	38	M	ORAL	MALATHION	8320	70	8	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	2 HOUR	Y	16.2.18	survived without ventilatory support
44	3734	30.1.18	JAGADEVI	33	F	ORAL	DICHLOROVAS	200	70	4	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	2 HOUR	Y	16.2.18	survived with ventilatory support
45	3686	30.1.18	GANGA BAI	27	F	ORAL	MONOCROTPHOS	530	70	8	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	3 HOUR	Y	6.2.18	survived without ventilatory support
46	3548	29.1.18	PRAKASH	28	M	ORAL	MONOCROTPHOS	420	80	4	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	3 HOUR	Y	16.2.18	survived with ventilatory support
47	1276	11.1.18	RAMAPPA	50	M	ORAL	MALATHION	320	90	5	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	3 HOUR	Y	30.1.18	survived with ventilatory support
48	2865	23.1.18	NAGAMMA	60	F	ORAL	MALATHION	3920	80	5	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	2 HOUR	Y	5.2.18	survived without ventilatory support
49	6938	31.1.18	KIRAN	32	M	ORAL	MALATHION	200	80	5	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	3 HOUR	Y	20.2.18	survived with ventilatory support
50	3084	25.1.18	KALPANA	25	F	ORAL	MALATHION	200	86	5	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	2 HOUR	Y	16.2.18	survived with ventilatory support
51	5264	12.2.17	SARASVATHI	27	F	ORAL	MALATHION	8320	90	5	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	3 HOUR	Y	24.2.18	survived without ventilatory support
52	7737	4.3.18	SUREKHA	32	F	ORAL	MONOCROTPHOS	5523	70	8	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	2 HOUR	Y	15.3.18	survived without ventilatory support
53	16710	17.5.18	MAHANANDA	30	F	ORAL	MALATHION	1771	80	8	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	3 HOUR	Y	25.5.18	survived without ventilatory support
54	5579	10.4.18	GOURESH	25	M	ORAL	MONOCROTPHOS	5000	80	8	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	2 HOUR	Y	16.5.18	survived without ventilatory support
55	5759	7.4.18	RESHMA	20	F	ORAL	DICHLOROVAS	400	96	4	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	3 HOUR	Y	8.4.18	survived with ventilatory support
56	5992	10.4.18	KAMALA	55	F	ORAL	MONOCROTPHOS	6000	90	5	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	2 HOUR	Y	16.4.18	survived without ventilatory support
57	6242	13.4.18	SAGAMA	40	F	ORAL	MALATHION	500	86	9	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	2 HOUR	Y	18.4.18	survived with ventilatory support
58	6928	16.4.18	SHANTABAI	60	F	ORAL	DIMETHOATE	518	68	8	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	3 HOUR	Y	25.4.18	death with ventilatory support
59	7453	16.4.18	HANMANTH	28	M	ORAL	DICHLOROVAS	4903	86	8	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	2 HOUR	Y	26.4.18	survived without ventilatory support
60	7706	20.4.18	POOJA	18	F	ORAL	PROPHENOFUS+CYPERMETHRIN	5956	85	8	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	2 HOUR	Y	28.4.18	survived without ventilatory support
61	7892	20.4.18	SOUJANAYA	18	F	ORAL	MALATHION	3562	90	8	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	1 HOUR	Y	26.4.18	survived without ventilatory support
62	14505	21.4.18	savita	30	F	ORAL	MALATHION	4262	96	6	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	1 HOUR	Y	26.4.18	survived without ventilatory support
63	14634	22.4.18	YASHODA	26	F	ORAL	DICHLOROVAS	1989	86	6	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	2 HOUR	Y	23.4.18	death with ventilatory support
64	14950	22.4.18	RAJKUMAR	40	M	ORAL	MALATHION	5619	80	8	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	3 HOUR	Y	28.4.18	survived without ventilatory support
65	15040	26.4.18	SANGEETA	28	F	ORAL	MALATHION	4458	85	8	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	2 HOUR	Y	30.4.18	survived without ventilatory support
66	15079	29.4.18	SAVITRI	23	F	ORAL	QUINPHOS	244	191	4	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	2 HOUR	Y	6.4.18	death with ventilatory support
67	15140	2.5.18	SRIDEVI	22	F	ORAL	MALATHION	2385	60	8	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	2 HOUR	Y	10.5.18	survived without ventilatory support
68	18503	1.6.18	SAVITA	31	F	ORAL	DICHLOROVAS	5100	95	8	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	3 HOUR	Y	8.6.18	survived without ventilatory support
69	16061	12.5.18	SHILPA	25	F	ORAL	DIMETHOATE	4635	63	9	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	4 HOUR	Y	18.5.18	survived without ventilatory support
70	16868	18.5.18	ANITA	23	F	ORAL	MONOCROTPHOS	200	70	4	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	4 HOUR	Y	20.5.18	death with ventilatory support
71	16730	17.5.18	SHEEVALEELA	25	F	ORAL	UNKNOWN COMPOUND	6446	86	9	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	3 HOUR	Y	27.5.18	survived without ventilatory support
72	16114	13.5.18	PAVITRA	22	F	ORAL	DIMETHOATE	7221	70	8	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	2 HOUR	Y	18.5.18	survived without ventilatory support

73	16710	17.5.18	MAHANANDA	30	F	ORAL	PHENYLPHYRAZOLE	1771	65	9	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	1 HOUR	Y	23.5.18	Survived without ventilatory support
74	16578	16.5.18	ROOPA	16	F	ORAL	DICHLOROVAS	5523	70	8	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	3 HOUR	Y	26.5.18	survived without ventilatory support
75	8520	10.3.18	SANGAWWA	60	F	ORAL	MONOCROTPHOS	5638	101	8	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	2 HOUR	Y	21.3.18	survived without ventilatory support
76	8678	11.3.18	kusuppa	62	M	ORAL	DICHLOROVAS	1648	80	8	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	2 HOUR	Y	21.3.18	survived without ventilatory support
77	23989	16.7.18	bouramma	22	F	ORAL	DICHLOROVAS	200	100	6	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	4 hour	Y	18.7.18	death with ventilatory support
78	23876	15.7.18	KAMALA	25	F	ORAL	DICHLOROVAS	6020	86	8	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	2 HOUR	Y	22.7.18	survived without ventilatory support
79	22611	4.7.18	BEEMU	55	M	ORAL	DICHLOROVAS	6490	84	8	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	3 HOUR	Y	15.7.18	survived without ventilatory support
80	20708	19.6.18	gangaram	45	M	ORAL	DICHLOROVAS	200	90	9	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	6 HOUR	Y	20.6.18	death with ventilatory support
81	22072	30.6.18	SANGU	19	M	ORAL	DICHLOROVAS	5730	86	9	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	2 HOUR	Y	10.1.17	survived without ventilatory support
82	25833	1.8.18	siddanagouda	22	M	ORAL	DICHLOROVAS	6000	84	8	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	3 HOUR	Y	10.8.18	survived with ventilatory support
83	25884	1.8.18	AYASHU	16	F	ORAL	MONOCROTPHOS	4000	80	9	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	4 hour	Y	11.8.18	survived with ventilatory support
84	25614	30.7.18	AMBIKA	22	F	ORAL	DICHLOROVAS	7000	74	8	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	6 HOUR	Y	9.8.18	survived without ventilatory support
85	25344	27.7.18	AKSHATA	18	F	ORAL	MALATHION	5000	78	9	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	5 hour	Y	9.8.18	survived with ventilatory support
86	25103	25.7.18	UMABAI	50	F	ORAL	MALATHION	6000	82	8	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	6 HOUR	Y	5.8.18	survived without ventilatory support
87	224796	24.7.18	RAJESWARI	23	F	ORAL	DIMETHOATE	4000	84	9	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	4 hour	Y	6.8.18	survived without ventilatory support
88	24435	19.7.18	PRAVEEN	20	M	ORAL	MALATHION	2000	94	8	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	5 hour	Y	29.7.18	survived with ventilatory support
89	24246	18.7.18	MAHANTESH	25	M	ORAL	DICHLOROVAS	4000	89	7	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	6 HOUR	Y	28.7.18	survived without ventilatory support
90	23989	16.7.18	bouramma	22	F	ORAL	METHYLEPARATHION	6000	84	9	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	5 hour	Y	26.7.18	survived without ventilatory support
91	23876	15.7.18	KAMALA	25	F	ORAL	DICHLOROVAS	5000	94	9	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	6 HOUR	Y	26.7.18	survived without ventilatory support
92	23252	10.7.18	GIRIJA	25	F	ORAL	MALATHION	4000	97	9	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	5 hour	Y	20.7.18	survived without ventilatory support
93	22611	5.7.18	BEEMU	55	M	ORAL	MONOCROTPHOS	6000	95	9	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	4 hour	Y	15.7.18	survived without ventilatory support
94	22333	3.7.18	POOJA	23	F	ORAL	METHYLPARATHION	5000	85	9	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	6 HOUR	Y	15.7.18	survived with ventilatory support
95	22099	1.7.18	POORNIMA	14	F	ORAL	MALATHION	4000	78	8	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	5 hour	Y	10.7.18	survived without ventilatory support
96	22072	30.6.18	SANGAMESH	19	M	ORAL	DIMETHOATE	400	108	8	ABSENT	ABSENT	PRESENT	PRESENT	ABSENT	6 HOUR	Y	15.7.18	death with ventilatory support
97	212802	19.6.18	SUPRIYA	16	F	ORAL	MONOCROTPHOS	5000	90	8	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	5 HOUR	Y	27.6.18	survived without ventilatory support
98	20708	19.6.18	gangaram	45	M	ORAL	DICHLOROVAS	6000	86	9	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	4 hour	Y	29.6.18	survived with ventilatory support
99	18503	1.6.18	SAVITA	31	F	ORAL	MALATHION	4000	90	8	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	6 HOUR	Y	10.8.18	survived with ventilatory support
100	149402	26.6.18	SANGEETA	28	F	ORAL	MONOCROTPHOS	3000	78	9	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	4 hour	Y	5.7.18	survived with ventilatory support