EVALUATING THE USE OF *APACHE II* SCORE IN PREDICTING THE SEVERITY AND CLINICAL OUTCOMES OF ORGANOPHOSPHOROUS POISONING

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CHENNAI

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CERTIFICATE

This is to certify that the dissertation entitled, **"EVALUATING THE USE OF *APACHE II* SCORE IN PREDICTING THE SEVERITY AND CLINICAL OUTCOMES OF ORGANOPHOSPHOROUS POISONING"** submitted by **Dr. VIVEKANANDAN A** in partial fulfilment for the award of the degree of **M.D. GENERAL MEDICINE (BRANCH - I)** by the Tamilnadu Dr. M.G.R Medical University, Chennai is a Bonafide record of the work done by him in the Institute Of Internal Medicine, Madras Medical College during the academic year 2012 -15

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DECLARATION

I, **Dr. VIVEKANANDAN A** solemnly declare that dissertation titled **"EVALUATING THE USE OF *APACHE II* SCORE IN PREDICTING THE SEVERITY AND CLINICAL OUTCOMES OF ORGANOPHOSPHOROUS POISONING"** is a bonafide work done by me at Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai-3 during July 2014 to September 2014 under the guidance and supervision of my unit chief

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CONTENTS

EVALUATING THE USE OF *APACHE II* SCORE IN PREDICTING THE SEVERITY AND CLINICAL OUTCOMES OF ORGANOPHOSPHOROUS POISONING

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ABSTRACT

OBJECTIVE:

This study was done to know the efficacy of *APACHE II* score in predicting the severity and clinical outcomes of organophosphorous poisoning.

METHODOLOGY:

Patients admitted to toxicology unit of madras medical college and Rajiv Gandhi government general hospital with confirmed history of oraganophosphorous poisoning [OPC] are included in the study. Total sample size is 75. The study period is July 2014 – September 2014. All patients admitted in the toxicology ICU unit with confirmed or documented history of OPC poisoning are subjected to investigations and the APACHE II score is calculated with worst values obtained within 24 hours of admission

RESULTS:

All the patients are included in the analysis the study result showed that the difference in APACHE II score is significant among the survivors and non survivors with p value 0.0001 (<0.05).

CONCLUSION:

APACHE II score is useful in the predicting the clinical outcome in the Acute Organophosphorous poisonings in the Intensive care settings.

KEY WORDS: *OPC, Atropine, Pralidoxime, APACHE II.*

INTRODUCTION

Organic phosphorus compounds (OPC) groups of cholinesterase-inhibiting insecticides that most commonly produces toxicity in humans. In clinical practice all insecticides with a 'P' atom in their molecular structure that possesses cholinesterase inhibition are considered as OPC's, but there are other compounds also possessing the P atom in their molecule that also have property of cholinesterase inhibition (e.g.: phosphoric acids and phosphonates). Some contain thioesters (e.g.:parathion), others are vinyl esters. All those that have property of cholinesterase-inhibition (anticholinesterases) that contain phosphorus atom in their molecule will be collectively called as OPC's

OPC's act by inhibiting the enzyme acetylcholinesterase thereby increasing the acetylcholine levels in the nicotinic and muscarinic receptors. This increased Ach will produce the features of cholinergic excess syndrome[1].

The most common mode of death in OPC poisoning is respiratory failure. Most common OPC poisonings are suicidal especially in rural Indian populations. Its high mortality and easy availability for the people involved in agriculture related work which makes it ideal suicidal agent for people living in rural India.

Most of the OPC poisoned patients are managed in ICU settings. And the new advanced treatment modalities have resulted in increased survival in these patients. Such measures are also prolong the in-hospital stay and increases the hospital expenses. So there is a need of scoring system for prognostication of these patients and also for avoiding expensive procedures and treatments.

The Acute Physiology and Chronic Health Evaluation (APACHE) Score[2] is the most widely used scoring system in ICU setting. It has 12 variables and each variable's score ranges from 0-4. It includes the acute physiology score which represents the severity of present illness, the Glasgow coma scale and the chronic health status of the patients. The maximum score is 71. The score must be calculated using the worst clinical parameters obtained in the first 24 hours of ICU admission. The APACHE-II score has good discriminatory, reliability and calibration compared to other scores in many range of disease process[3].

The need of the study is based on the convergence of the following factors

1. To identify predictors of mortality in OPC poisoned patients
2. To evaluate the performance of APACHE II scoring systems for predicting severity and the outcome of patients poisoned with OPC who were admitted to the ICU.

AIMS AND OBJECTIVES

- This study was done to know the use of *APACHE II* score in predicting the severity and clinical outcome of organophosphorous poisoning.

REVIEW OF LITERATURE

Globally anti-cholinesterase insecticide kill many people than any other xeno-biotic. Estimates show about 200,000 die in rural Asia. Where intentional self-harm is very common and highly toxic OPC insecticides are widely used in agriculture. About 3000 to 6000 ventilators are constantly needed in Asia alone to provide adequate mechanical ventilation to OPC poisoned patients[4].

HISTORY:

Clermont in 1854 synthesized the first potent synthetic organo phosphorus anticholinesterase tetra-ethyl-pyrophosphate [TEPP], Clermont's report also describes the taste of the compound, and few drops of the compound proves rapidly fatal and considered as a remarkable achievement[5].

Lange and Krueger's report of blurring and choking followed the exposure to dimethyl and diethy-lphospho-flurides in 1932 inspired the Schrader and company to investigate and produce number of compounds that are used in chemical warfare. At the same time the scientists from Great Britain and other allied nations are also motivated and they produced the highly fatal compounds like di-isopropyl-phospho-fluoridate. There are about 50,000 compounds are derived after that and screened for pesticide activity.

EPIDEMIOLOGY:

OPCs are used in agriculture as an insecticide for the past 50years. Its use has declined in past 10-20 years. The reason for decline in use is partly due to carbamate group of insecticides, which has similar toxicity profile[6]

In united states there is about 890 active molecules and marketed as 20,700 different products. In India, the insecticide industry is fragmented, with about 30 -40 large manufacturers and about 400 product formulations[7].

The case fatality rate is determined by the local availability of the OPCs and the pre-hospital & hospital health care facilities available. Most patients consuming the highly toxic OPCs will die before reaching the hospital especially in developing countries like India. Hence the hospital based mortalities may be falsely low compared to actual mortality. Modes by which the people exposed to OPCs other than intentional self-harm/suicide are

1. All people are invariably exposed to OPC, through contamination of environment and/or occupational use.
2. Spraying and fogging of insecticides using the applicator causes exposures and poisoning to residents and children living in those areas.

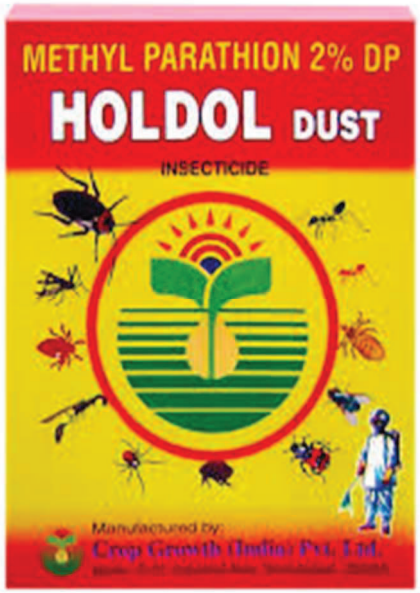
3. Occupational dermal exposures to persons working as farmers/industrial labours
4. Food poisoning due contaminated crops

WHO HAZARD SCALE OF OPCs[8]:

OPCs and other anti-cholinesterases are grouped into five classes depending upon their toxicity profiles. These estimation was based on rat's oral LD_{50}[median lethal dose in 50% test subjects].

Sl.no	class	Hazard type	LD50 for the rat (mg/kg body weight)	
			Oral	Dermal
1	Class Ia	extremely hazardous	<5	<50
2	Class Ib	highly hazardous	5-50	50-200
3	Class II	moderately hazardous	50-2000	200-2000
4	Class III	slightly hazardous	>2000	>2000
5	Class IV	unlikely to cause harm in normal doses	5000 or higher	

Class Ia **Extremely hazardous**	**Class Ib** **Highly hazardous**	**Class II** **Moderately hazardous**	**Class III** **Slightly hazardous**	**Class IV** **Harm unlikely in normal doses**
1. Methyl parathion 2. Phosphamidon 3. Phorate	1. Monocrotophos 2. Triazophos 3. Oxydemeton-methyl 4. dichlorvos	1. dimethoate 2. quinalphos 3. chlorpyriphos 4. prophenophos 5. fenthion 6. ethion 7. phenthoate	1. malathion 2. temephos	Not associated with clinically significant poisonings



Commonly available OPCs in india

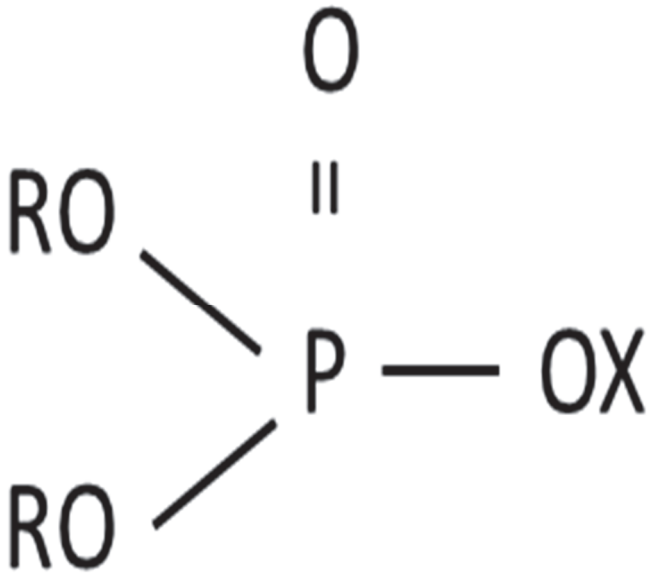
1. Monocrotophos is commonly available 36% soluble liquid
2. Methyl- parathion is commonly available as 2% dust

Commonly available OPCs in India

Chlorpyriphos, malathion and triazophos all available as emulsifiable concentrate and can be used as sprays

PHARMACOLOGY OF OPCs:

Organophosphates like any other anti-cholinesterase acts by inhibiting the enzyme acetylcholinesterase at the nicotinic and muscarinic receptors and rises the level of acetylcholine at the receptor level and producing the syndrome of cholinergic excess.



This figure shows the general structure of OPCs. ‘X’ is the leaving group and the ‘R’ may be aliphatic or aromatic ring.

The leaving group determines the nature and many chemical characteristics of OPCs and provides the way for classifying into four groups

1. Group1 or phosphoryl-chlorines have quaternary nitrogen in X position are powerful anticholinesterases and directly stimulate Ach receptors because of similarity to acetylcholine in structure. They are used as weapons of war
2. Group 2 are fluorophosphates with fluorine in X position. They are highly volatile and highly toxic. They also used for chemical warfare.
3. Group 3 is cyanophosphates or halo-phosphates other than fluorine
4. Group 4 is major group and comprises the majority of presently available OPCs. The configuration of R_1 & R_2 defines the characteristics and subgroup. They either belong to di-methoxy or di-ethoxy compounds.

Group 1: phosphorylcholines Leaving group: substituted quaternary nitrogen Echothiophate iodide
Group 2: fluorophosphates Leaving group: fluoride Dimefox, sarin, mipafox
Group 3: cyanophosphates & other halophosphates Leaving group: CN−, SCN−, OCN−, halogen other than fluoride Tabun
Group 4: multiple constituents Leaving group: Dimethoxy Azinphos-menthyl, bromophos, chlorothion, crotoxyphos, dicapthon, dichlorvos, dicrotophos, dimethoate, fenthion, malathion, mevinphos, parathion-methyl, phosphamidon, temephos, trichlorfon
Diethoxy: Carbophenothion, chlorfenvinphos, chlorpyriphos, coumaphos, demeton, diazinon, dioxathion, disulfoton, ethion, methosfolan, parathion, phorate, phosfolan, TEPP

Other dialkoxy: Isopropyl paraoxon, isopropyl parathion
Diamino: Schradan
Chlorinated and other substituted dialkoxy: Haloxon
Trithioalkyl: Merphos
Mixed substituent: Crufomate, cyanofenphos

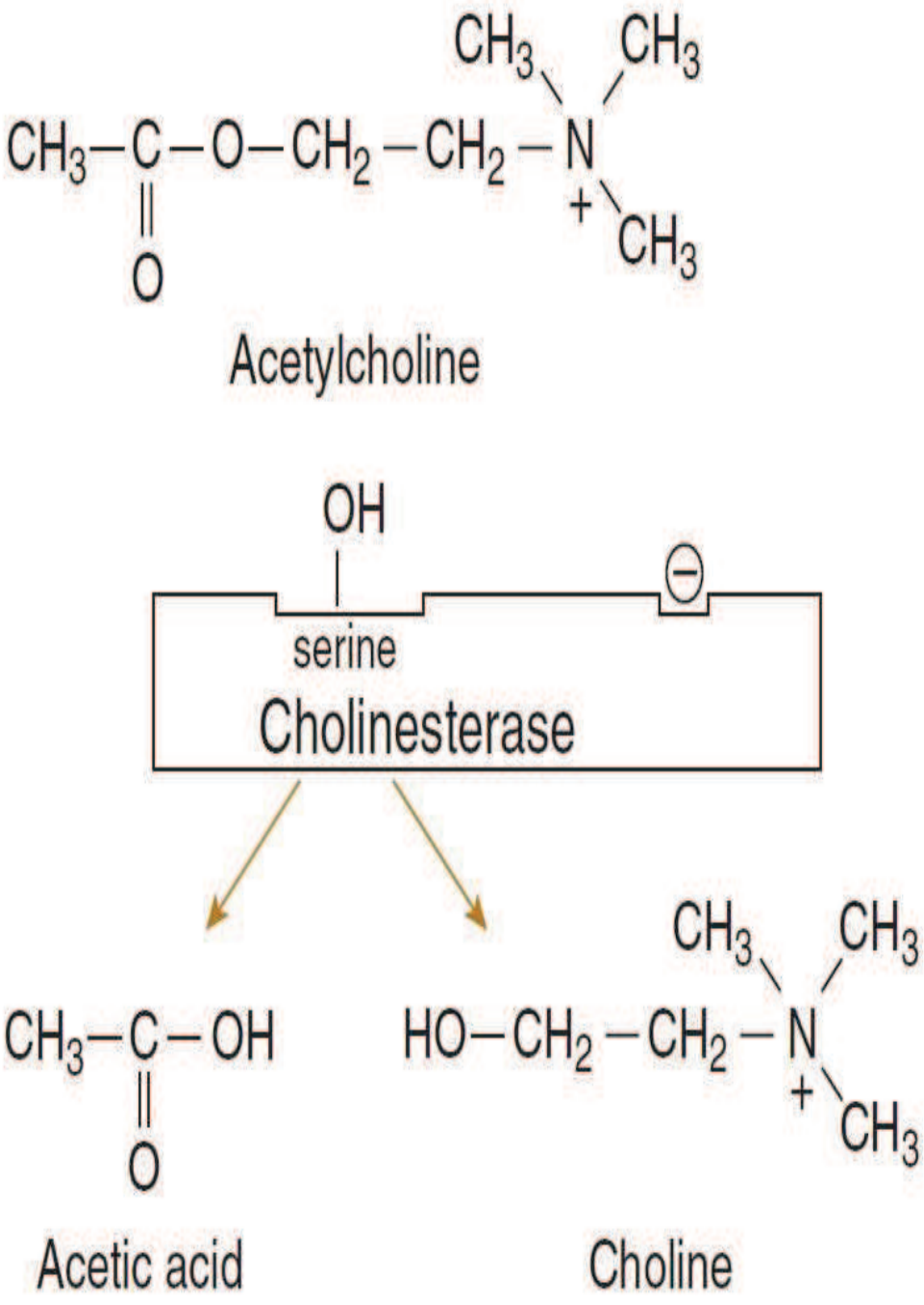
Oxons are 'directly acting' they do not need any conversion to inhibit the acetylcholinesterase but OPC_S (thions) are 'indirectly acting' [prodrug] need to be converted into active form before inhibiting acetylcholinesterase [eg: parathion→paraoxon, malathion→maloxon].

Desulfuration reaction to form oxon takes place in mucosa of intestine and liver[9].

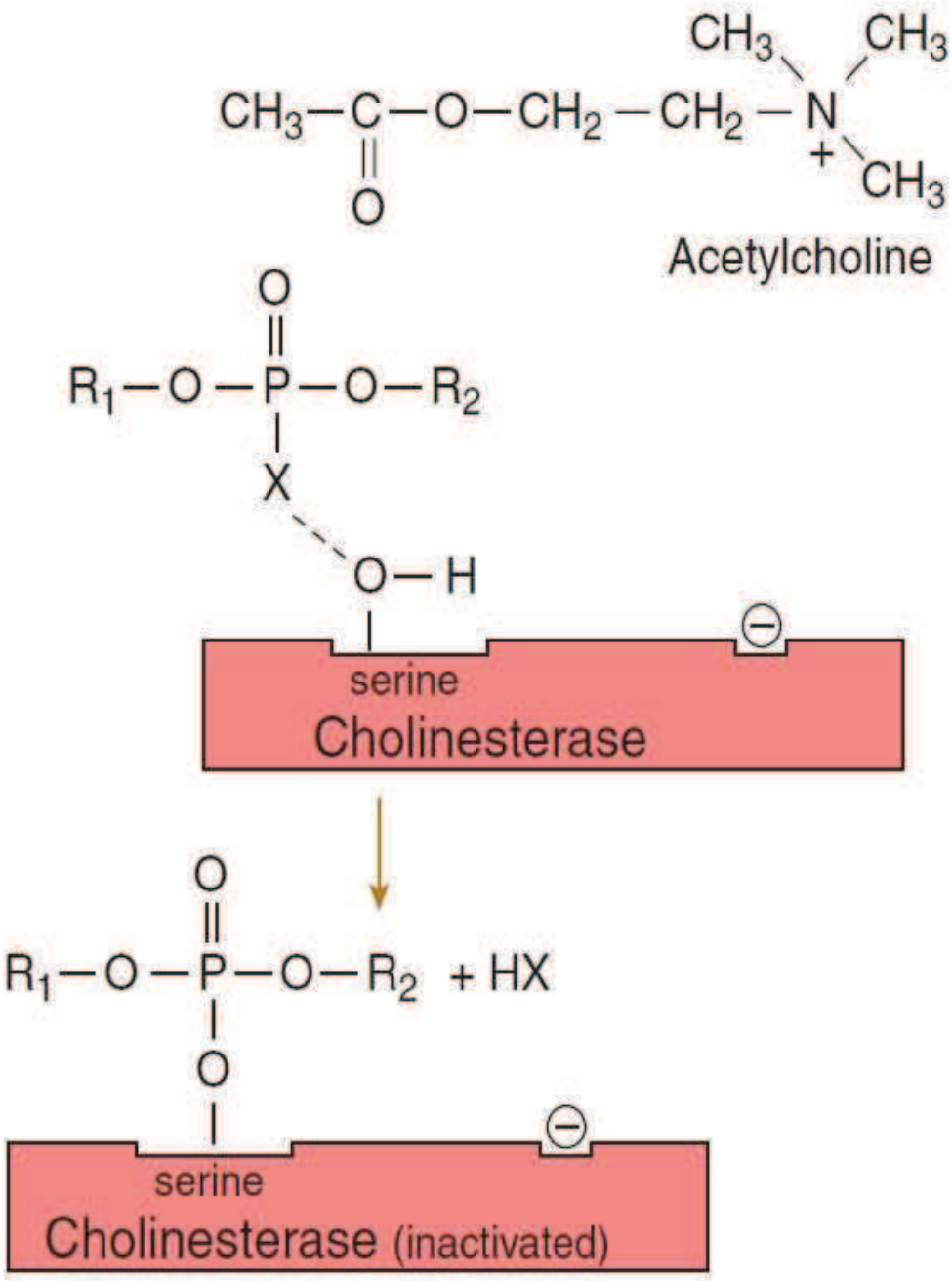
MECHANISM OF ACTION:

OPCs bind to the '–OH' group of the active site of the enzyme acetylcholinesterase. On binding, the leaving group of the OPC is split of by the acetylcholinesterase resulting in a stable but reversible bonding between the OPCs and the AChE and thereby effectively inactivating the enzyme.

The splitting of the choline-enzyme complex occurs in micro-seconds. The splitting of the OPC-enzyme complex is prolonged. The half-life depends upon the nature of the substituted phosphate. The in vitro half-life of spontaneous regeneration of enzyme by di-methoxy substituted OPC is 0.7-0.86 hour; that of di-ethoxy substituted OPC inhibition is 31-57 hours. Hence spontaneous reactivation is faster for di-methoxy OPCs.



Normal splitting of acetylcholine by the enzyme acetylcholinesterase



Mechanism of inhibition of AChE by an OPC. The X is the leaving group. A serine residue at the active site of the AChE gives up a ‘H’ atom to combine with the ‘X’(leaving group) while the active site undergoes phosphorylation and inhibition.

Oximes, like pralidoxime or obidoxime, speeds up the Rate of reactivation markedly[10]. However, if the phosphorus is remain bounded to the AChE for longer time, because of delayed or inadequate infusion of oximes, an alkyl group is non-enzymatically lost this process is called “Aging.” If the aging once occurred the AChE is no longer reactivated using Oximes and again the half-life of reaction depends upon the substituted phosphorous. In vitro half-life of human poisonings with dimethoxy OPCs is 3.7hrs while that of diethoxy OPCs is 31hrs.

PHARMACOKINETICS OF OPCs:

OPCs are absorbed well through the gastrointestinal tract, lungs, mucous membranes and conjunctiva by ingestion, inhalation and topical exposures. Absorption through the intact skin is limited but high environmental temperatures, abrasions and dermatitis can enhance the absorption through the skin. Absorption through skin and lung explains the reason for occupational exposures and some chronic cases of OPC toxicities.

The time for peak serum concentration for very low dose oral chlorpyriphos is around 6 hours but some rapidly acting ‘thions’ and some fast ‘oxons’ when ingested in large doses can attain the peak very fast and these are responsible for acute presentation within minutes in some cases.

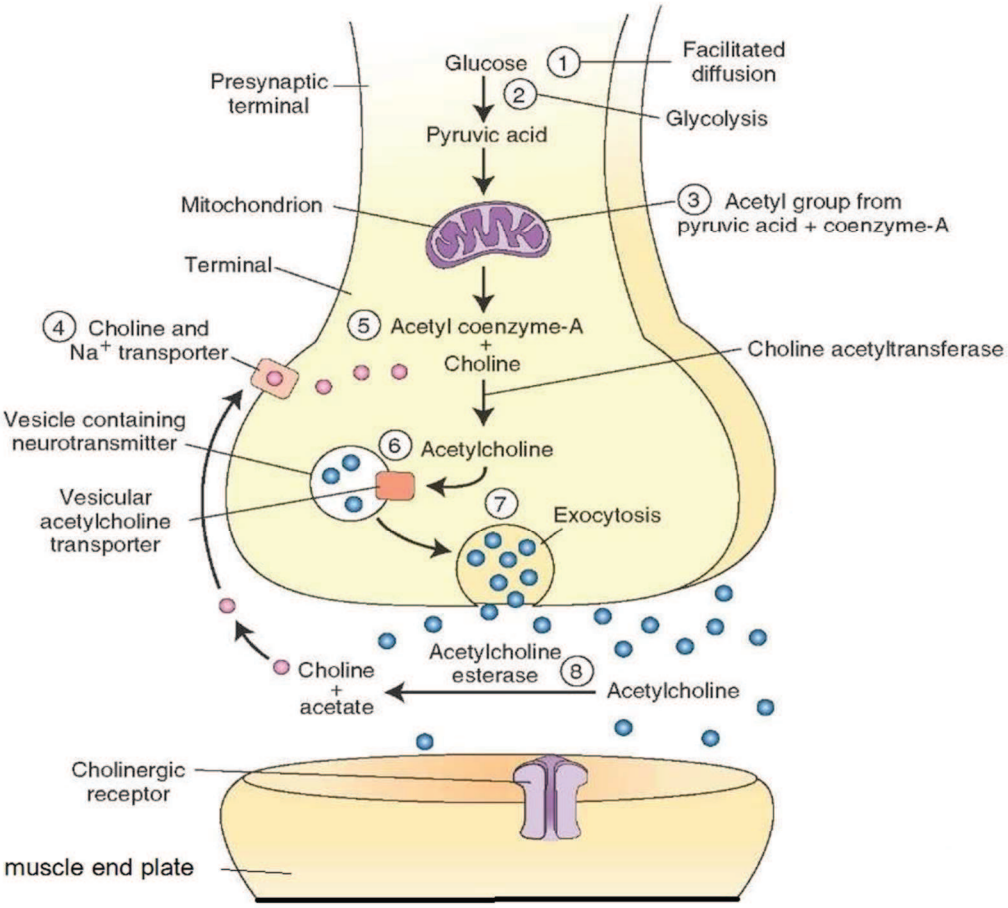
Most of the OPCs are lipophilic, after ingestion these OPCs have large volume of distribution and rapidly distributes into the adipose tissue where they are protected from the metabolism. It accumulates in highest concentration in adipose tissues, re-distribution from these stores is responsible for detection of OPCs in serum 48hrs after ingestion. Lipophilicity is more for fenthion and dichlofenthion and these compounds are notorious to cause cholinergic crisis after many days post ingestion.

The enzyme called serum paraoxanase cleaves oxons in some OPCs which may be protective. Knock out mice deficient in the enzyme experiences severe toxicities when given OPCs[11]. Exogenous administration of these enzyme also found protective in some animal models. Studies have shown the relationship between human serum paraoxanase acticvity in acute and chronic OPC poisonings[12].

PATHOPHYSIOLOGY:

Acetylcholine is a neurotransmitter is found in

1. Parasympathetic and sympathetic ganglia
2. Neuro-muscular junction(NMJ)
3. Terminals of all post-ganglionic parasympathetic nerves
4. Post-ganglionic sympathetic fibres to most sweat glands
5. Some nerve endings within CNS



Mechanism at NMJ:

As the axon terminal is depolarized, ACh containing vesicles fuse with the nerve terminal, releasing acetylcholine into the synapse or NMJ. The binding of ACh to its receptors leads to activation (G proteins for muscarinic receptors and ligand-linked ion channels for the nicotinic receptors). Activation alters the flow of K^+, Na^+ and Ca^{2+} ionic currents on nerve cells, and this alters membrane potential of the postsynaptic membrane/muscle end plate, and formation of action potentials.

Normally acetylcholine released into the synaptic cleft is immediately metabolised to choline and acetate and the choline undergoes re-uptake into presynaptic terminal. Acetylcholinesterase is normally found in nervous tissue, skeletal muscle and red blood cell membrane. And the RBC AChE activity correlates well with CNS AChE activity.

COFORMULATIONS:

People mainly ingest the product formulations of OPCs and not the pure compounds. OPCs sold for agricultural purposes typically have emulsifiers like xylene or Chlorohexanone[1]. The composition of these emulsifiers for a given formulation varies across companies. These xenobiotics also causes toxicity that is different from OPCs. These organic solvents causes aspiration pneumonia once the patient loses the consciousness and it is difficult to treat.

CLINICAL MANIFESTATIONS:

The clinical features are due to Ach excess at muscarinic and nicotinic receptors

Features of muscarinic excess

1. **S**alivation,

2. **L**acrimation,
3. **U**rination,
4. **D**efecation,
5. **G**astric
6. **E**mesis,
7. **B**ronchorrhea, (can mimic acute pulmonary edema[15])
8. **B**ronchospasm,
9. **B**radycardia
10. **M**iosis.

Nicotinic features,

1. fasciculations,
2. muscle weakness
3. paralysis
4. death mostly due to respiratory failure

The symptom onset varies according to nature of the compound, route of exposure and degree of exposure. More the rapid onset of poisoning more likely the patient die en-route to the hospital. Patients can be symptomatic as quick as 5 minutes on consuming the OPCs

Oxon OPCs (eg: mevinphos and monocrotophos) doesn't need to be converted to active molecule so the patient may be symptomatic very soon. This is also true for some OPCs which are converted to their respective oxons soon.

Lipid solubility also affects the time for onset because they distribute into fat stores rapidly (eg: fenthion) and redistribute slowly for longer time and produce clinical effects for long period of time. For fenthion respiratory failure typically occurs after 24 hours of ingestion. Dichlofenthion and fenthion can cause cholinergic features for many days after ingestion due to redistribution[13,14].

CNS manifestation:

Many patients presents with awake and alert and complaining of

1. anxiety,
2. insomnia,
3. restlessness,
4. dizziness,
5. depression,
6. Blurred vision and many other non-specific symptoms.

The level of sensorium detoriates rapidly to lethargy, confusion and coma. Convulsions can occur but it is mostly due to hypoxia secondary to cholinergic syndrome.

Muscarinic symptoms though mostly emphasized, they will not be initially predominant or clinically dramatic. These parasympathetic features may initially counteracted by the excessive stimulation of

autonomic activity through stimulation of nicotinic adrenal receptors and post ganglionic sympathetic fibers[16].

1. Mydriasis,
2. urinary retention
3. Bronchodilation.
4. White blood cell de-margination and leucocytosis[15,17].
5. Metabolic effects of sympathetic activity causes glycogenolysis and hyperglycemia, ketosis and simulating ketoacidosis[18,19].

Hyperamylasemia also appears in OPC poisoning. In one study four out of 47 cases (9%) had hyperamylasemia. Malathion is mostly associated with hyperamylasemia 47(63%) out of 75 cases in one study[20]. Studies in Human poisonings shows associated pancreatic edema and necrotizing pancreatitis[21].

Excess Acetylcholine stimulate the vascular receptors and can cause hypotension. This is mostly seen with less-fat soluble OPCs like dimethoate[22]. And it is not seen with highly fat soluble OPCs like fenthion and chlorpyrifos[23]. It is also less common with other less fat soluble OPCs like methamidophos and oxydemeton-methyl.

Respiratory manifestations include bronchorrhea, bronchospasm, neuro-muscular junction failure of diaphragm and the intercostal muscles and loss of respiratory of drive. This causes severe hypoxia due to

respiratory arrest and causes death of the patient if it occurs before reaching the hospital. Atropine therapy reverses the bronchorrhea and bronchoconstriction. But it does not reverses the neuro muscular junction failure or the loss of central respiratory drive. Patient need to be ventilated until the respiratory function improves.

The formulated OPCs contain hydrocarbons as co formulation and this will cause aspiration and will eventually results in pneumonia, chemical pneumonitis and acute respiratory distress syndrome.

Skeletal muscle activity is governed by the acetylcholine through the nicotinic receptors. Excess acetylcholine at the nicotinic level will produce the features similar to the depolarizing neuro muscular blockade (eg: succinylcholine). This produces the muscle weakness and fasciculations and this is considered to be pathognomonic of the parathion poisoning. Cranial nerve abnormalities are not common during the acute presentation. But severe poisonings results in paralysis. Rigidity and choreoathetosis which are the features of extrapyramidal system is also not seen in acute presentation. But seen in patients recovering from cholinergic excess.

DELAYED SYNDROMES:

A syndrome of delayed weakness resulting in respiratory muscle weakness without fasciculations or cholinergic features it was first reported in 1974[24]. This is intermediate syndrome (IMS) defined as occurring 24-96 hours after acute OPC poisoning and following resolution of the cholinergic features[25]. Patients typically presents with proximal muscle weakness typically of neck flexors and cranial nerve palsies, respiratory failure that may last for several weeks. Consciousness is not impaired until it is not complicated by pneumonia or hypoxic encephalopathy. The first sign of IMS is patient's inability to lift the head from bed.

The exact pathophysiology of syndrome is unknown. It's clearly due to the dysfunction of neuro muscular junction with respiratory failure resulting from weakness of intercostal muscles and diaphragm. Preservation of consciousness suggests that the central respiratory drive is less likely to be involved. One more proposed mechanism is down regulation of neuro muscular junction synaptic mechanism[26]. This dysfunction is will require time to get repaired. And will persists even after the OPCs are removed from the body, and may require long periods of assisted ventilation[27].

Small case series and case reports suggests that the IMS is more common in fenthion poisoning than that of Malathion, chlorpyriphos and fenitrothion poisoning[27].

Clinical examination is the most reliable method of diagnosis of IMS. Electromyography studies shows the tetanic fade suggestive of both pre synaptic and post synaptic involvement. Recent work has suggests characteristic electro physiologic features of increment and decrement phenomenon that can be identified before neurological and respiratory paralysis[28].

A study showed that intermediate syndrome correlates best with acute cholinergic crisis. And it is continuum from the neuromuscular junction dysfunction occurring at the time of cholinergic crisis[29]. Patients acutely poisoned with dimethoate shows that patients after recovering from acute cholinergic crisis may need ventilator support. But this is short lived and the patient will improve from cholinergic crisis and regain consciousness and central respiratory drive but patient may still may need ventilator support. This matches to the classical description of IMS. But studies also showing that patient may need ventilator support before 24 hours and also after 96 hours.

Some authors suggest that IMS may be due to inadequate Oxime therapy[30]. This is suggested by a fact that the patients poisoned with OPCs

like dimethoate and fenthion have AchEs that are poorly responsive to oxime theraphy and hence have higher incidence of IMS. In contrast AChE that are inhibited by chlorpyriphos have less incidence of IMS when compared to the former. Overall the delayed NMJ dysfunction may be either due to ineffective oxime therapy or may be due to ingestion of OPCs that are poorly responsive to Oximes.

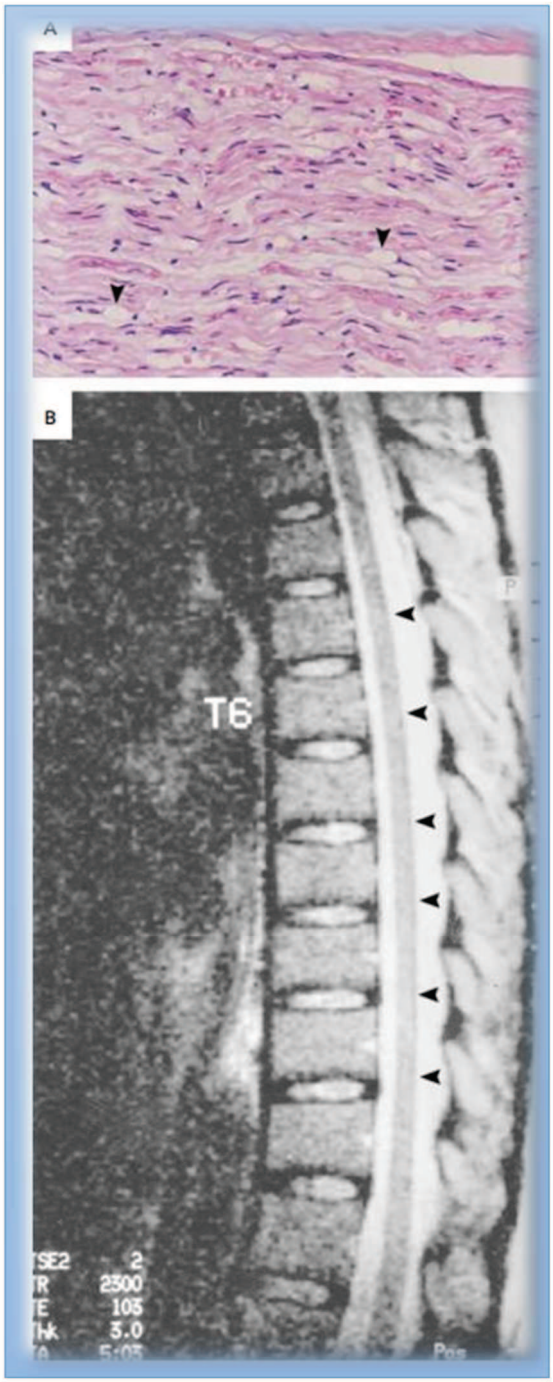
Treatment of intermediate syndrome is mainly supportive. Patient needs ventilator support and with nursing care to prevent bedsores and ventilator acquired pneumonia. Pralidoxime and atrophine are needed to control the cholinergic symptoms that occur in-between. Pralidoxime can revert the IMS when given early during its development. But once the neuro muscular dysfunction occurs the oximes are unlikely to revert it. Most of the IMS patients need ventilator support from 5-18 days[31].

OPC INDUCED DELAYED POLYNEUROPATHY:[OPIDN]

Peripheral neuropathies can occur days to weeks after acute exposure to OPCs and also can chronic exposures to OPCs like in case of occupational exposures. OPIDN is due to inhibition of phosphorylation of the enzyme called Neuropathy Targeted Esterases [NTE]. {Now known as lysophospholipase[lysoPLA]} inside the nervous tissue.

This enzyme catalyses the breakdown of endoplasmic reticulum–membrane phosphatidylcholine, it is the major phospholipid of eukaryotic cell membranes. Neuropathic OPs cause a transient loss of NTE-lysoPLA activity, putatively disrupting membrane phospholipid homeostasis, axonal transport, and glial–axonal interactions.

A second mechanism of OPIDN is imbalance in calcium homeostasis. This lead to the activation of calcium-activated neutral protease and causes increases in calcium/calmodulin-dependent protein kinases. These events can contribute to aberrant phosphorylation of cytoskeletal proteins and protein digestion occurring in the terminal axon that can proceed in same way like Wallerian-type degeneration. Many experimental studies showed improvement of the signs and symptoms of OPIDN by restoring calcium balance. Other studies have used prior administration of NTE inhibitors, such as carbamates, thiocarbamates, sulfonyl fluorides and phosphinate to prevent OPIDN[32].



Panel A: Axonal degeneration and vacuolization of sural nerve fibers in patients following an acute OPC [phosphamidon] exposure.

Panel B: T_2 weighted sagittal MRI of spine showing atrophy especially in thoracic cord.

OPIDN may result from exposure to OPCs that neither inhibit RBC cholinesterase nor produce clinical cholinergic toxicity. The commonly implicated chemicals include triaryl phosphates, such as tri-ortho-cresyl phosphate (TOCP), & di-alkyl phosphates, such as mipafox, mephosfolan, and chlorpyrifos. Pathologic findings demonstrate effects mainly on large distal neurons, with axonal degeneration followed by demyelination[33].

Contaminated foods and beverages were responsible for epidemics of OPIDP and encephalopathy. In the 1930s, thousands of individuals in the United States became weak or paralyzed after drinking a supplement containing TOCP—an outbreak named “Ginger Jake paralysis”. Contaminated mineral and cooking oils were responsible for outbreaks of delayed OPIDP in Vietnam and Sri Lanka.

Vague distal muscle weakness & pain are the usual presenting symptoms and can progress to paralysis. The administration of atropine or Oximes did not alter the onset and clinical course of these symptoms. Corticospinal tract signs can appear weeks to months after acute exposures.

Electromyographs and nerve conduction studies are helpful in diagnosing by identifying the type of neuropathy (such as myelinopathy, axonopathy, or transmission neuropathy) and differentiating it from similar presentations such as Guillain-Barre syndrome. The recovery of

these patients is highly variable, commonly with some residual deficits, and occurs over months to years.

CHRONIC TOXICITY OF OPCS:

Illness may also result from chronic exposure to excessive amounts of OPCs. Chronic exposure most commonly occurs in workers who have regular contact with these xenobiotics, but may also occur in individuals who have repeated contact with excessive amounts of insecticides in their living environments.

Exposure to cholinergic ophthalmic preparations chronically can also result in toxicity[34]. Although tolerance to acute cholinergic systemic effects of OPs (including death in rats) may be seen in long-term exposures, persons having the long term exposure to OPCs will show the symptoms after substantial length of time. These effects range from some nonspecific neurological symptoms and weakness to full blown muscarinic symptoms like miosis, diaphoresis, bronchorrhea, diarrhea and vomiting[35,36,37]. Butrylcholinesterase activity is the most sensitive measure of exposure. Persons working in those environments should have a baseline BuChE measurements done for monitoring the exposures and comparison[38,39].

Parkinson disease was associated with chronic exposure to insecticides including OPCs[40]. Some individuals have a genetic

susceptibility. Parkinsonism like movement disorders occur significant number of patients with acute OPCs exposure. They are self-limited and they resolve over months to years.

BEHAVIORAL TOXICITY:

Acute or chronic exposure to OPCs also associated with behavioural toxicity. Symptoms include confusion, anxiety, psychosis, depression, drowsiness, fatigue, and irritability. Electroencephalographic changes may be seen and lasts for weeks[41]. Morphologic changes in the basal ganglia of one child identified with single photos emission computed tomography scan (SPECT) following poisoning. Studies have shown a cognitive processing deficit after acute OPCs self-poisoning lasting for at least six months and this is not found in matched populations who had poisoned themselves with Acetaminophen[42,43]. So far there is no clear evidence for neuro-psychiatric deficiencies resulting from subclinical exposure to OPCs.

DIAGNOSTIC TESTING:

With a history of acute exposure to OPCs and the patient presenting in acute cholinergic crisis the diagnosis of OPC poisoning is straight forward.

Although many authors list a range of clinical signs for the cholinergic crisis (SLUDGE, DUMBELS), most patients with significant amount of poisoning can be identified by the presence of excessive sweating, pin point pupil and difficulty in breathing. When the history is unreliable the diagnosis must be confirmed by other means. Treatment of patient with acute cholinergic syndrome should not delayed for confirmation of diagnosis.

Most appropriate method of identifying the cholinesterase inhibition is finding the OPCs in biologic tissues or measuring the serum cholinesterase activity. Although the metabolites of the OPCs are available in the urine and serum they are rarely measured[46,47,48], and if so it takes hours to get results and the normal limits of these compounds are not established in epidemiological grounds. Moreover "normal" ranges and toxic concentrations are not established for most. Therefore at present, verifying OPC poisoning relies on measurement of plasma cholinesterase activity.

CHOLINESTERASE ACTIVITY:

The commonly measured cholinesterases are the butyrylcholinesterase and the Red cell cholinesterase. The Butyrylcholinesterase is synthesised in the liver and then it is secreted into the plasma where it will metabolize the xenobiotic like scoline and cocaine. The red cell acetylcholinesterase and neuronal

acetylcholinestearses are both product of the same gene, but the difference in mechanism is due to the mechanism of membrane attachement. The red cell acetylcholinesterase is a [GPI]glycosyl-phosphatidyl-iositol anchor linked to the red cell. Whereas the neuronal AChE is secreted in the form of tetramers or dimers and they are attached to post-synaptic membrane through other proteins.

The inhibition of red cell AChE and BuChE is the only markers of enzyme inhibition by OPCs. Their inhibition is not actually the cause for symptoms or they do not produce the symptoms per se. but the red cell acetylcholinesterase activity is accurately correlating with neuronal AChE activity in OPC poisoning[49].

There is lot of inter-individual and inter-chemical variations in the degree and the duration with which the OPCs affect the particular cholinesterases. After a significant exposure first to fall is the butyrylcholinesterase activity followed by the red cell acetylcholinesterase activity. At the time when the patients presents to the hospital both cholinesterase activity fall markedly below the baseline values though the sequence of fall may vary[15].the red cell acetylcholinesterase and butyrylcholinesterase levels vary among species to species and it will further complicate the animal studies. Human

plasma actually has very low AChE and hence papers mentioning the human plasma acetylcholinesterase activity actually means BuChE.

BUTYRYLCHOLINESTERASE:

Butyrylcholinesterase activity usually returns before the red cell acetylcholinesterase activity with mild exposures and no further exposure to the same inciting OPCs. But the BuChE activity is less sensitive than the RBC-AChE. Low butyrylcholinesterase activity is seen in patients with lot of co-morbid conditions[50] like

- iron deficiency anemia
- hepatic parenchymal disease
- malnutrition
- chronic debilitating illness
- congenital absence of the enzyme
- genetic defects

Wide ranges of normal activity make the patient to suffer a drastic fall in BuChE activity but the lab value in essentially in normal range. As high as 20% day to day variation in normal activity is seen with healthy subjects. An admission butyrylcholinesterase activity is little value in patients because it varies among the ingested OPCs and does not cause any clinical effects, but it can be used if the ingested OPCs is known and the clinical effect is specifically studied with that OPCs.

RED CELL ACETYLCHOLINESTERASE [RBC-AChE]:

Acetylcholinesterase in the RBC is true acetylcholinesterase and it correlates well with the neuronal acetylcholinesterase. As per some authors if RBC-AChE falls below 50%, clinical OPC poisoning occurs[15].and if falls below 30% NMJ dysfunction occurs[49]. Haemoglobin concentration can be related well with RBC-AChE, Reducing the variations with varying haematocrit[51].

- Mean range in many people is 600-700mU/µmol Hb
- In one study Caucasian populations had 651±18 mU/µmol Hb.

All RBCs exposed to OPC must be replaced. RBC-AChE takes longer time to recover after OPC exposure, it takes about 66 days for the RBC-AChE to recover. Animal studies shows that neuronal acetylcholinesterase activity may return to normal more rapidly than RBC-AChE. Red blood cell cholinesterase activity may be low but the patients may show no cholinergic features and have normal neuronal acetylcholinesterase and normal NMJ action. This is the demerit of measuring the RBC-AChE in case of sub-acute OPC poisoning as we cannot predict exact time or duration of exposure of poisoning.

As like BuChE the RBC-AChE is also low in conditions other than OPC poisoning they are,

1. Carbamate poisoning
2. Pernicious poisoning
3. Therapy with anti-malarial or anti-depressants

Interpreting Cholinesterase Concentrations

	Red Cell Cholinesterase	Butyrylcholinesterase
Advantage	Better reflection of synaptic inhibition	Easier to assay, declines faster
Site	RBC (reflects CNS gray matter, motor end plate)	CNS white matter, plasma, liver, pancreas, heart
Regeneration (untreated)	1%/day	25%–30% in first 7–10 days
Normalization (untreated)	35–49 days	28–42 days
Use	Unsuspected prior exposure with normal butyryl cholinesterase	Acute exposure
False depression in concentration	Pernicious anemia, hemoglobinopathies, antimalarial treatment, oxalate blood tubes	Liver dysfunction, malnutrition, hypersensitivity reactions, xenobiotics (succinylcholine, codeine, morphine), pregnancy, genetic deficiency

Collection of blood samples for RBC-AChE must not be collected with fluoride containing test tubes as it may permanently disable the enzyme. The sample is ideally collected in anti-coagulated test tube like EDTA test tube. But this problem is not there with BuChE as it is not affected by any chelators or anti-coagulants.

The OPCs and oxime can still exert their effect hence immediate dilution with saline or water in the ratio of 1:20 or 1:100 at bedside and cooled to 4ºC before rapidly freezing the test tube. This allows less variation and allows more uniform results. And again this is not a problem with BuChE as there is no rapid reactions with this enzyme.

PROTEIN ADDUCTS:

Mass spectrophometers are used to identify the protein adducts formed by the OPC with albumin, AChE and BuChE.

The OrganoTox test is a fast, point of care test capable of detecting clinically relevant OPC poisoning after low-level exposure to soman, sarin, tabun or VX chemical nerve agents[52].

ATROPINE CHALLENGE:

In a patient presenting with the syndrome of cholinergic excess but with no history suggestive OPC intake an atropine challenge can be useful to diagnose the case. Atropine at the dose of 1mg in adolescents and

adults and 0.05mg/kg in case of paediatric population must produce the features of anti-muscarinic activity particularly mydriasis, dry mucus membranes and tachycardia while the persistence of cholinergic syndrome after the atropine challenge strongly suggest the patient is poisoned with a cholinesterase inhibitor poisoning like OPC[15] . Some patients with mild doses of OPC poisoning may completely respond to this dose of atropine hence the reversal of cholinergic features will not exclude the poisoning by OPCs.

ELECTROMYOGRAM STUDIES:

Electromyogram findings show

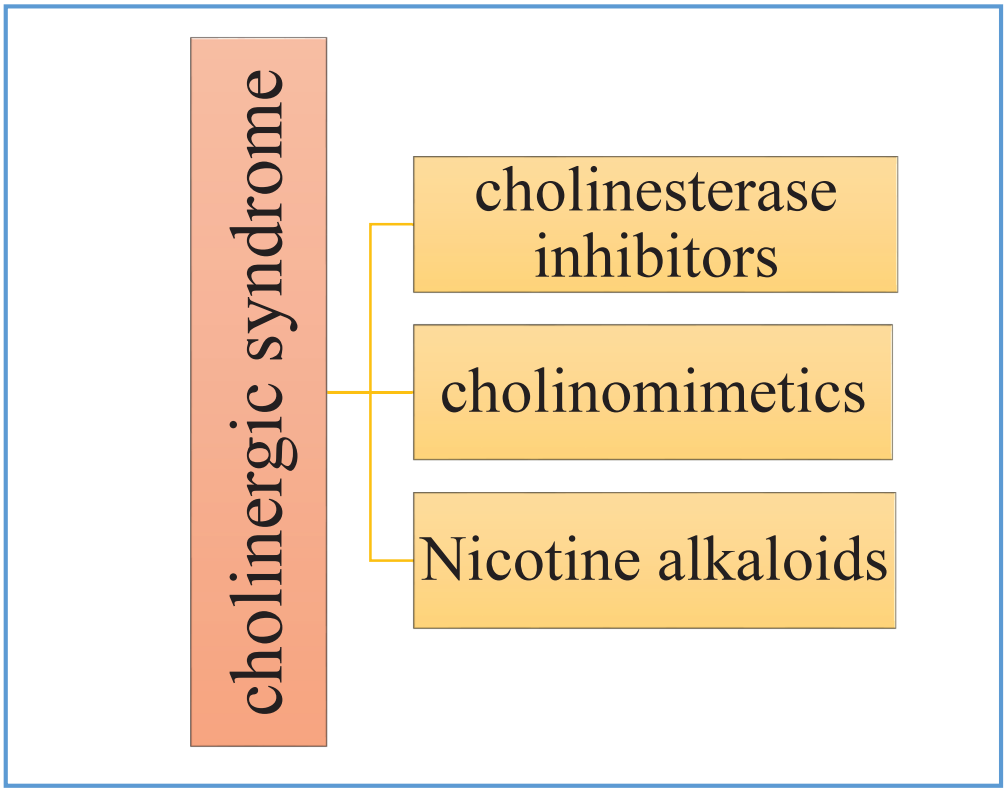
- Spontaneous repetitive potential or fasciculation following the single-nerve stimulation.

This is due to persistence of Ach in the nerve terminals or AChE inhibition at the motor end plate. This test is also useful in detecting rebound cholinergic crisis that will occur due to continued absorption or re-distribution from the fat stores.

DIFFERENTIAL DIAGNOSIS:

The three important differential diagnosis of OPc poisonings are

1. Insecticides and non-insecticides in which includes medicinal AChEs like neostigmine, echothiophate and pyridostigmine [cholinergic crisis in myasthenic patients treated with these agents]
2. Second group includes the cholinomimetics they produce cholinergic syndrome without AChE or BuChE inhibition and essentially have normal AChE and BuChE levels
3. The third group is nicotinic alkaloids they produce skeletal muscle, autonomic and CNS toxicities similar to OPCs



Categories of Cholinergic Poisoning

Cholinesterase Inhibitors	Cholinomimetics	Nicotine Alkaloids
Organic phosphorus insecticides	Pilocarpine	Coniine
Organic phosphorus ophthalmic medications	Carbachol	Lobeline
Carbamate insecticides	Aceclidine	Nicotine
Carbamate medications	Methacholine	
	Bethanechol	
	Muscarine-containing mushrooms	

MANAGEMENT OF OPC POISONING

GENERAL MANAGEMENT:

1. The main cause of death in the OPC poisoned patients is the respiratory failure and resultant hypoxemia. This is due to the effect of increased Ach in the muscarinic receptors in the heart and pulmonary systems and producing increased tracheo-bronchial secretions, bronchospasm and brady cardia.
2. The nicotinic effects in the CNS and peripheral nervous system causes loss of central respiratory drive and muscular weakness due to NMJ dysfunction similar to depolarizing muscle blockade. Which ultimately leads to respiratory failure, hypoxia and death.
3. The initial treatment hence in case of OPC poisoning is assessment of airway, breathing and circulation and reversing the muscarinic effects.
4. Seizures if it is not caused by hypoxia should be treated with adequate doses of benzodiazepines.
5. Early tracheal intubation in patients who have excessive secretions and who are comatose with respiratory paralysis and cannot handle their secretions.

6. If a neuro muscular paralysis is needed for positive pressure ventilation only an agent which is not metabolised by the cholinesterase is used, because the scoline and mivacurium are metabolised by BuChE whose levels are very low in OPC poisoning. so the duration of effect of these drugs may be prolonged for hours[53,54].

ANTI-MUSCARINIC THERAPY:

Atropine an anticholinergic drug competitive antagonist of acetylcholine at muscarinic receptor and it immediately reverses the muscarinic actions like

1. Miosis
2. Bradycardia
3. Bronchospasm
4. Vomiting, diarrhoea
5. Urinary incontinence and diaphoresis

Dose:

1. For adults and adolescents i.v. dose should begin with 1-3mg depending upon the degree of symptoms
2. For children the initial starting dose is 0.05mg/kg with a minimum dose of 0.1mg

3. Atropine dose must be repeated every 2-20 minutes in the range of 1-5mg until the ‘atropinisation’ occurs or dose can be doubled every five minutes until getting the desired response.

Signs of ‘atropinisation’:

1. Dry skin and mucus membranes
2. Tachycardia
3. Decreased or absent bowel movements
4. No bronchospasm
5. Reduced secretions
6. Mydriasis

As the patient usually die from cardiovascular and respiratory compromise so it is the heart rate, blood pressure, bronchorrhea and bronchospasm that is taken as signs of atropinisation not the mydriasis and dry skin. The vital target of atropinisation must be

1. Heart rate > 80 BPM
2. Systolic blood pressure> 90mmHg
3. No bronchorrhea and no bronchospasm

Maintenance dosing:

- Once the signs of atropinisation is achieved the atropine must be given in i.v. infusion.

- The dose must be 10-20% of the initial loading dose but not exceeding the dose of 2mg/hr
- Regular periodic monitoring is necessary and further boluses or halving the dose is maintained to prevent the over or under atropinisation.
- Children need 0.025mg/kg/hr infusion.
- The atropine infusion is mainly needed for those who consume highly fat soluble OPCs as they redistribute for long time. Case reports shows that the atropine requirement may be as long as 32 days[55].

  Signs of over-atropinisation:

  1. Absent bowel sounds
  2. Marked tachycardia(>120 BPM)
  3. Mydriasis
  4. Urinary retention

The complication of atropinisation is hyperthermia, agitation and confusion. The tachycardia per se is not an absolute contraindication as it may be due to aspiration pneumonia or hypovolemia. Isolated pulmonary manifestations may respond to nebulised atropine or ipratropium bromide however their efficacy is validated in trials.

Larger dose of atropine may be required to reverse the bronchospasm, bronchorrhea and bradycardia. Slightly poisoned patients

can do that well with 1-2 mg of atropine but severely poisoned patients may need up to 40mg. case reports shows that some patients needed 1000mg within 24 hours with adequate dose of pralidoxime but without showing any anti-muscarinic effects[56]. And a total dose [over the full course of treatment] of as high as 11000mg is also reported.

Whether the higher dose is better than modest dose is not well studied but one study shows better results with infusion of 1mg/hr after the initial loading dose for adequate control of muscarinic effects[57].

Atropine does not reverse the nicotinic effects of ACh excess. And patient must be closely monitored for impending respiratory failure resulting from peripheral NMJ dysfunction. Patient must be monitored for proximal muscle weakness especially of the neck muscle and the tidal volumes must be measured at least every 6 hours as an impending signs of respiratory failure and prompt administration of positive pressure ventilation.

Atropine when given in OPC poisoning the CNS manifestations of atropinisation will be evident but the muscarinic effects like bradycardia, bronchospasm and brocnchorrhea will be present. Under these situations the glycopyrrolate which is the quaternary ammonium compound and impermeable to the blood brain barrier is used. One study compared the atropine and glycopyrrolate in OPC poisoned patients in IMCU settings and found very small difference in effects between two regimens[57].

Intravenous glycopyrrolate for adults is 1-2mg repeated as needed and the paediatric dose is 0.025mg/kg. Like atropine much higher doses of the drug is needed to control the muscarinic effects.

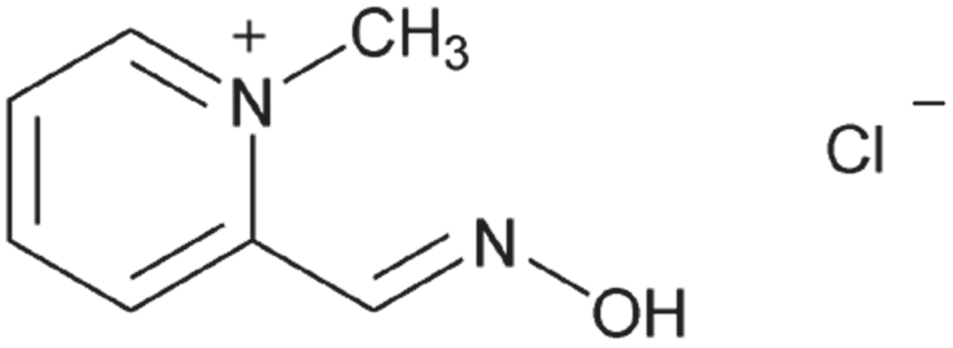
Scopolamine can also be used but it will cause much CNS effects. If the supplies of atropine is exhausted atropine ophthalmic preparation and other anti-cholinergic drugs like di-phenhydramine can also be used.

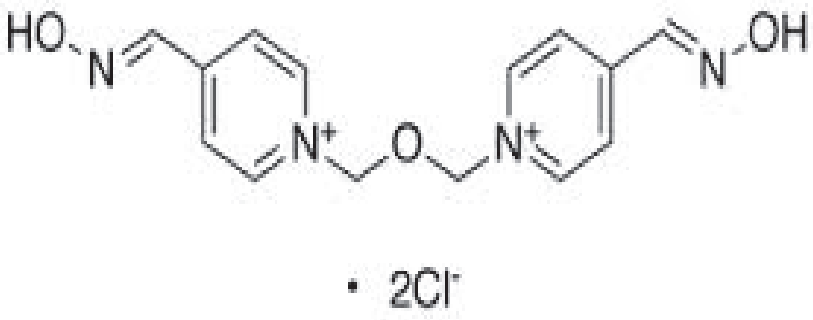
OXIMES:

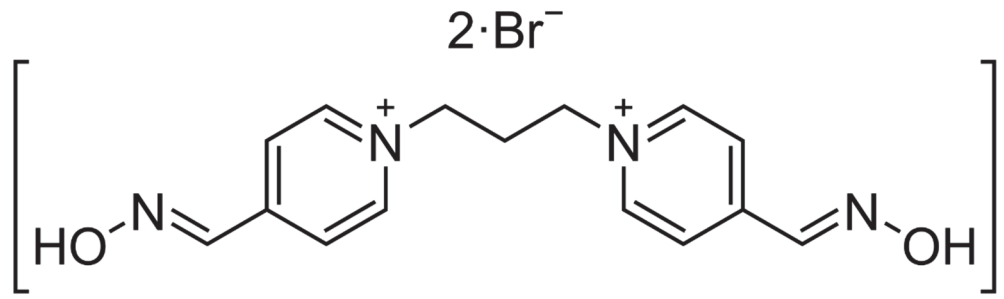
Although the phosphorylated AChE is regenerated spontaneously but the process is very slow and this process is catalysed by the presence of an oxime (2-PAM) or obidoxime. Thus decreasing the ACh levels at neuronal level and improvement in nicotinic and muscarinic symptoms. The RBC-AChE levels rises promptly following the treatment with oximes that parallels the rise in the neuronal AChE.

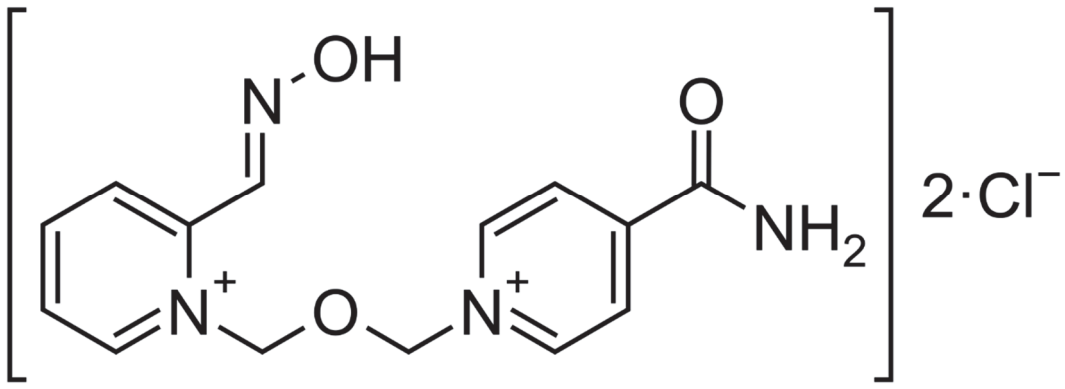
The currently available Oximes is

1. Monopyridinium Oximes
    a. Pralidoxime(2-PAM)
2. Bispyridinium Oximes
    a. Obidoxime(toxogonin)
    b. Trimedoxime(TMB-4)
    c. Asoxime(HI-6)

Pralidoxime
2-PAM


Obidoxime
Toxogonin, LuH-6


Trimedoxime
TMB-4


Asoxime
HI-6


The aging rate of OPC poisoned enzyme vary with OPCs consumed. It's early for dimethoxy compounds and relatively late for diethoxy compounds so the oxime therapy must be instituted within hours of OPC consumption and as early as possible.

The oxime therapy is particularly effective even if given late in case of fat soluble OPCs. As this compounds redistribute from the fat stores and cause new enzyme inhibition. Many case reports have validated this hypothesis by dramatically improving the weakness, reversing the paralysis and the cholinergic symptoms.

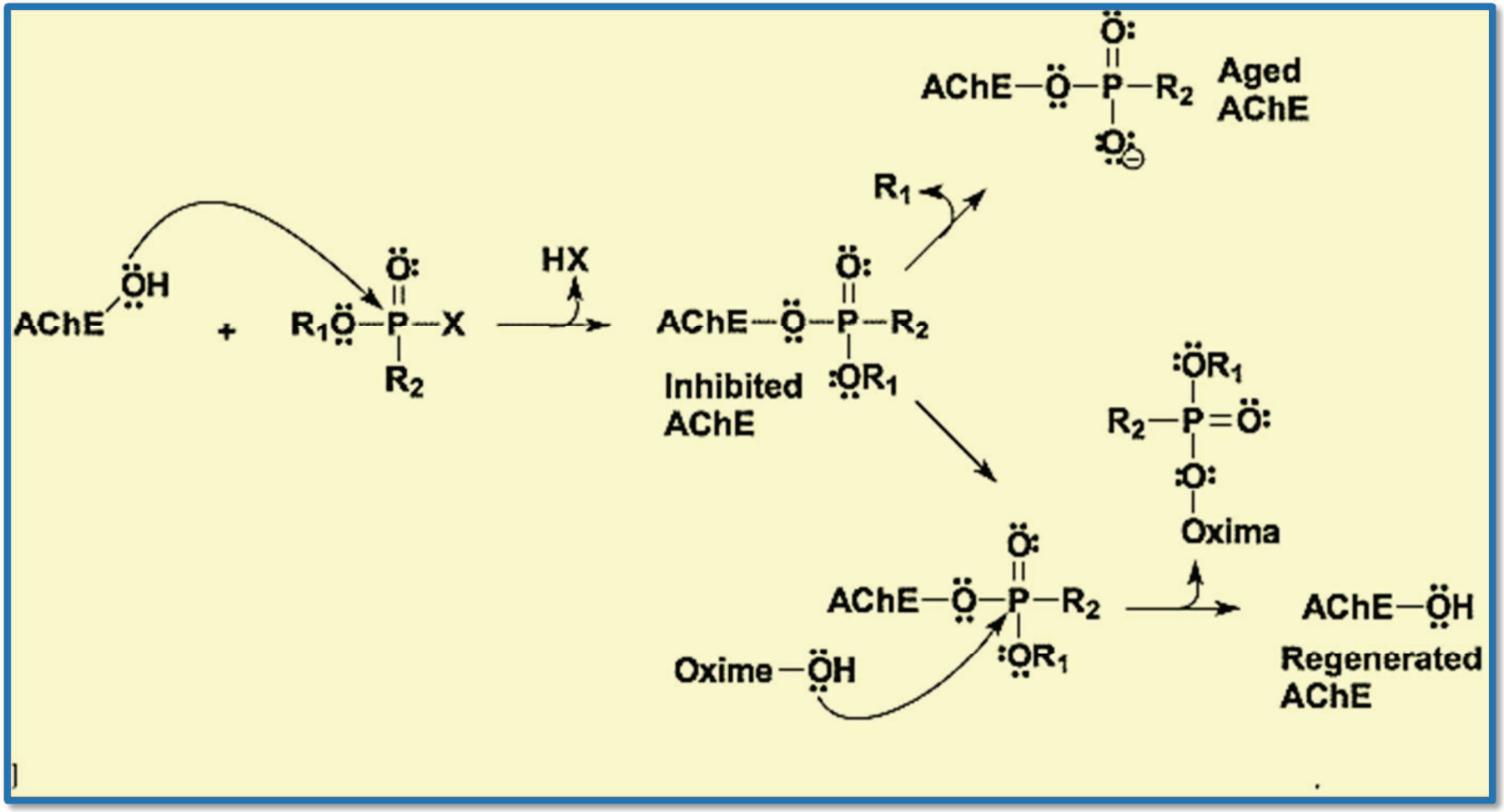


Diagram showing the mechanism of action of Oximes and regeneration of the free acetylcholinesterase

Dosing of pralidoxime:

The recent clinical trial in our country showed that very high doses of 2-PAM reduces the length of ventilation and death in moderately poisoned patients[58].

- A loading dose of 2gram pralidoxime, in 100ml of 0.9%NaCl over 30 minutes followed by 8-10mg/kg/hr of pralidoxime chloride (upto 650mg of pralidoxime chloride or 1gram of pralidoxime iodide).

Duration of treatment with Oximes:

It is recommended to continue the Oxime therapy until no atropine requirement for 12-24 hours.

Other guidelines are,

1. Measuring the serum or urinary concentration of the OP compound.
2. Measuring serial determinations of plasma cholinesterase (increasing concentrations suggests the elimination of the OP compound).
3. Incubating the patient's serum with an exogenous source of AChE or butyrylcholinesterase to look for inhibition.
4. Incubating the patient's inhibited red blood cell cholinesterase with a high concentration of oxime in vitro, checking for reactivation.

In all cases, patients should be observed for recrudescent toxicity after termination of pralidoxime. If symptoms return, therapy should be continued for at least 24 hours.

Adverse effects:

At therapeutic doses the side effects are minimal in humans

1. Transient dizziness
2. Blurred vision
3. Elevation of diastolic BP which can be reversed with i.v. phentolamine
4. Tachycardia
5. Diplopia
6. Elevated liver enzymes
7. Rapid infusions cause sudden cardiac arrest due to laryngospasm and muscle rigidity
8. Pralidoxime is pregnancy category C drug and it is used clinically to protect mother and foetus.

BENZODIAZEPINES:

In animal models it is suggested that OPCs inhibit the GABA transmission in synaptosomal preparations. Diazepam being an allosteric activator of GABA receptors is used along with atropine in OPC poisoning for neuro protection[59]. Diazepam also decreases the morphologic changes caused by OPC related seizures[60].

The dose of diazepam as per WHO is 5-10mg if there is no seizures and 10-20mg i.v. bolus if the seizure is present. And it can be continued when needed.

GACYCLIDINE[59]:

It is an anti-glutamatergic drug that inhibit seizures caused by nereve gas posonings like soman. It is also useful in conjunction with atropine, pralidoxime and diazepam.

DECONTAMINATION IN OPC POISONING:

1. Cutaneous absorption of OPCs and necessitates removal of all clothing as soon as possible.
2. Medical personnel should avoid self-contamination by wearing neoprene or nitrile gloves. Double gloving with standard vinyl gloves may be protective.
3. Skin should be triple washed with water, soap, and water, and rinsed again with water. Although alcohol-based soaps are sometimes recommended to dissolve hydrocarbons, these products can be difficult to find, and expeditious skin cleansing should be the primary goal.
4. Cutaneous absorption can also result from contact with OPCs and compounds in vomitus and diarrhoea if the initial exposure was by ingestion.

5. Oily insecticides may be difficult to remove from thick or long hair, even with repeated shampooing, hence shaving scalp hair may be necessary.
6. Exposed leather clothing or products should be discarded because decontamination is very difficult once impregnation has occurred.
7. In some military institutions the cholinesterase impregnated sponge is found to be effective in cutaneous OPCs
8. Although the Activated charcoal is useful in some studies a recent study shows that activated charcoal in multiple doses offer no benefit and hence once the risk of aspiration is ruled out the AC in a dose of 1gram/kg as a single dose is recommended[61].

SCORING SYSTEM USED IN OPC POISONING

Most of the OPC poisoned patients are managed in ICU settings. And the new advanced treatment modalities have resulted in increased survival in these patients. Such measures are also prolong the in hospital stay and increases the hospital expenses. So there is need of a scoring system for prognostication of these patients and also for avoiding expensive procedures and treatments.

Scoring systems used OPC poisoning:[62,63,64,65,66]

1. Poison severity score
2. Glasgow coma scale
3. APACHE II score
4. Sequential organ failure assessment score [SOFA]
5. Simplified acute physiology score II [SAPS]
6. Modified APACHE II score [MAS]

APACHE II SCORE

The APACHE II score is severity of disease classification system originally developed from the prototype APACHE score.

It consists of 4 components,

1. Acute physiology score
2. Age
3. Glasgow coma scale
4. Chronic health status of that patient

The APACHE II score is originally developed from the prototype scoring system APACHE score, the acute physiology score or the APS is derived from the abnormal twelve physiological variable. 12 variables are chosen in the hypothesis that detecting abnormalities in multiple physiological variables helps us to quantify the magnitude of the severity of acute disease process.

APACHE II score is objective type scoring system. The APS is calculated from the worst values obtained during the first 24 hours of ICU admission. The 24 hour time window is necessary to allow us to measure all the needed variables to calculate the APS.

Each variable is given the weightage of 0-4. The total score obtained will be in the range of 0-71.

Acute Physiology Score

Score	4	3	2	1	0	1	2	3	4
Rectal temperature, °C	≥41	39.0–40.9		38.5–38.9	36.0–38.4	34.0–35.9	32.0–33.9	30.0–31.9	≤29.9
Mean blood pressure, mmHg	≥160	130–159	110–129		70–109		50–69		≤49
Heart rate	≥180	140–179	110–139		70–109		55–69	40–54	≤39
Respiratory rate	≥50	35–49		25–34	12–24	10–11	6–9		≤5
Arterial pH	≥7.70	7.60–7.69		7.50–7.59	7.33–7.49		7.25–7.32	7.15–7.24	<7.15
Oxygenation									
If $FI_{O_2} > 0.5$, use $(A - a)\ D_{O_2}$	≥500	350–499	200–349		<200				
If $FI_{O_2} \leq 0.5$, use Pa_{O_2}					>70	61–70		55–60	<55
Serum sodium, meq/L	≥180	160–179	155–159	150–154	130–149		120–129	111–119	≤110
Serum potassium, meq/L	≥7.0	6.0–6.9		5.5–5.9	3.5–5.4	3.0–3.4	2.5–2.9		<2.5
Serum creatinine, mg/dL	≥3.5	2.0–3.4	1.5–1.9		0.6–1.4		<0.6		
Hematocrit	≥60		50–59.9	46–49.9	30–45.9		20–29.9		<20
WBC count, 10^3/mL	≥40		20–39.9	15–19.9	3–14.9		1–2.9		<1

The acute physiology score [APS] consisting of twelve physiologic variable and each given the range 0-4.

Eye opening	Verbal [Non intubated]	Verbal[intubated]	Motor activity
4 – spontaneous	5 – oriented and talks	5 – seems able to talk	6 – verbal commands
3 – verbal stimuli	4 – disoriented and talks	3 – questionable ability to talk	5 – localizes pain
2 – painful stimuli	3 – inappropriate words	1 – generally unresponsive	4 – withdraws to pain
1 – no response	2 – incomprehensible sounds		3 – decorticate posture
	1 – no response		2 – decerebrate posture
			1 – no response

Glasgow coma scale: the GCS component of APACHE II score is calculated by subtracting the Observed GCS from 15[eg: if the GCS of that patient is 12 then (15-12=3)]

Age, Years	Score
<45	0
45–54	2
55–64	3
65–74	5
≥75	6
Chronic Health (History of Chronic Conditions)[d]	**Score**
None	0
If patient is admitted after elective surgery	2
If patient is admitted after emergency surgery or for reason other than after elective surgery	5

The age and chronic health score, if the patient has chronic health history and the patient is admitted any reason other than surgery will be given 5 points

CHRONIC HEALTH HISTORY:

No.	Chronic health status
1	Biopsy proven cirrhosis and documented portal hypertension; past gastrointestinal bleeding attributed to portal hypertension; prior hepatic encephalopathy; prior hepatic failure
2	NYHA class IV angina(at rest or minimal self-care activities)
3	Chronic restrictive or obstructive or vascular lung diseases resulting in severe exercise limitation; documented hypoxemia or hypercapnia; secondary polycythemia; severe pulmonary hypertension(>40mmHg); ventilator dependence
4	Chronic renal failure needing haemodialysis
5	Immunosuppression from chemotherapy radiation therapy, long term or recent high dose steroids, immunodeficiency(e.g.: leukaemia, lymphoma, AIDS)

MATERIALS AND METHODS

SELECTION OF PATIENTS:

Patients admitted to toxicology unit of madras medical college and Rajiv Gandhi government general hospital with confirmed history of oraganophosphorous poisoning [OPC} are included in the study. On admission 10 cc of blood is withdrawn from the patient after obtaining informed consent either from the patient or the relatives. The sample is tested for complete blood count, renal function tests, liver function tests, arterial blood gases and serum electrolytes. As this study is both prospective and retrospective the lab parameters and clinical parameters of patients previously admitted are obtained from medical records department, Rajiv Gandhi government general hospital.

STUDY CENTRE:

Institute of internal medicine, IMCU & Toxicology, Madras Medical College and Rajiv Gandhi Government General Hospital, park town, Chennai-600003.

DURATION OF THE STUDY:

3 months

STUDY DESIGN:

Prospective and Retrospective observational study

SAMPLE SIZE:

75 PATIENTS

DATA COLLECTION AND METHODS:

Patients are subjected to history questioning, clinical examinations and blood sampling. Retrospective samples are obtained from case sheet records at medical records department.

PROCEDURE / INVESTIGATION DETAILS:

1. Complete blood count
2. Renal function test – urea, creatinine
3. Serum sodium
4. Serum potassium
5. Arterial blood gas assessment for pH, paO2
6. Vital parameters including rectal temperature, oxygen saturation, respiratory rate, pulse rate and blood pressure.

INCLUSION CRITERIA:

1. Age: above 18 years.
2. Sex-both genders.
3. Patients presenting with confirmed consumption of organophosphorous compounds.
4. Patients willing to give written informed consent.

EXCLUSION CRITERIA:

1. Age less than 18 years.
2. Patients who consumed substances other than organophosphates and mixed compound poisonings.

STATISTICAL METHODS:

The statistical analysis is done using SPSS software. 'p' value obtained is analysed using the SPSS software.

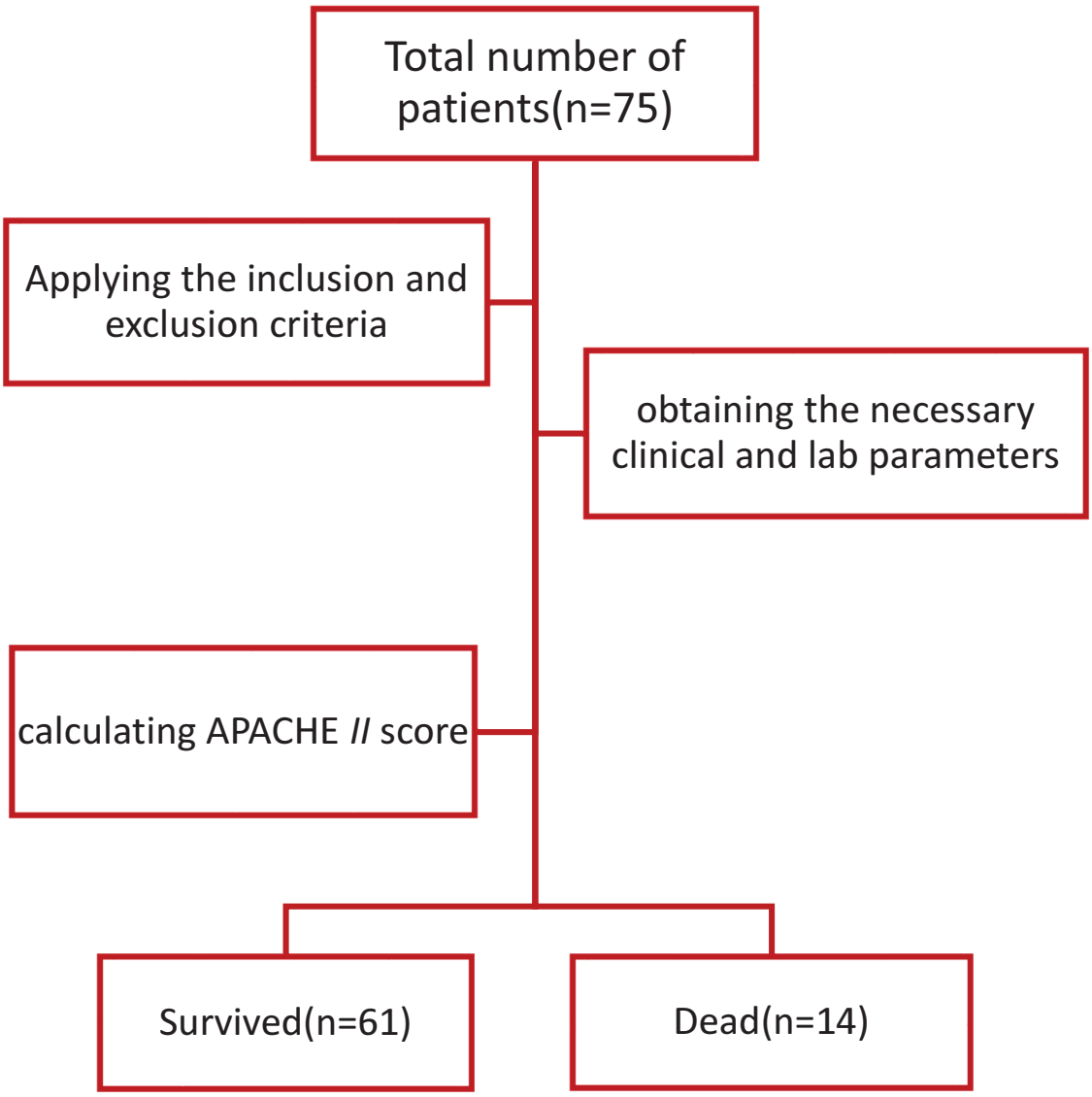
SPONSORSHIP:

NO

CONFLICT OF INTEREST:

NONE

OBSERVATION AND RESULTS

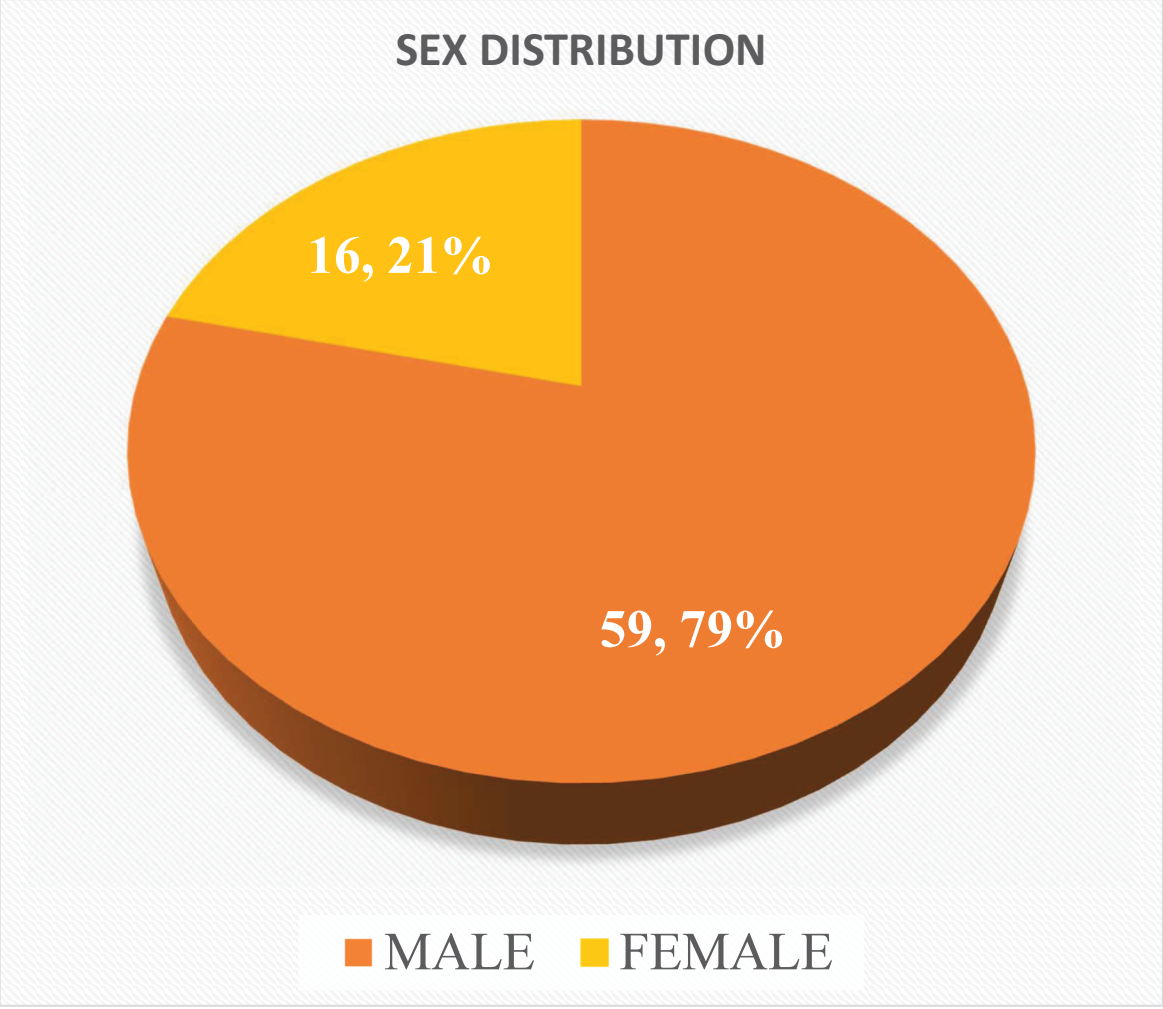


Flow chart depicting the process of the study

SEX WISE DISTRIBUTION

Total number of cases: 75

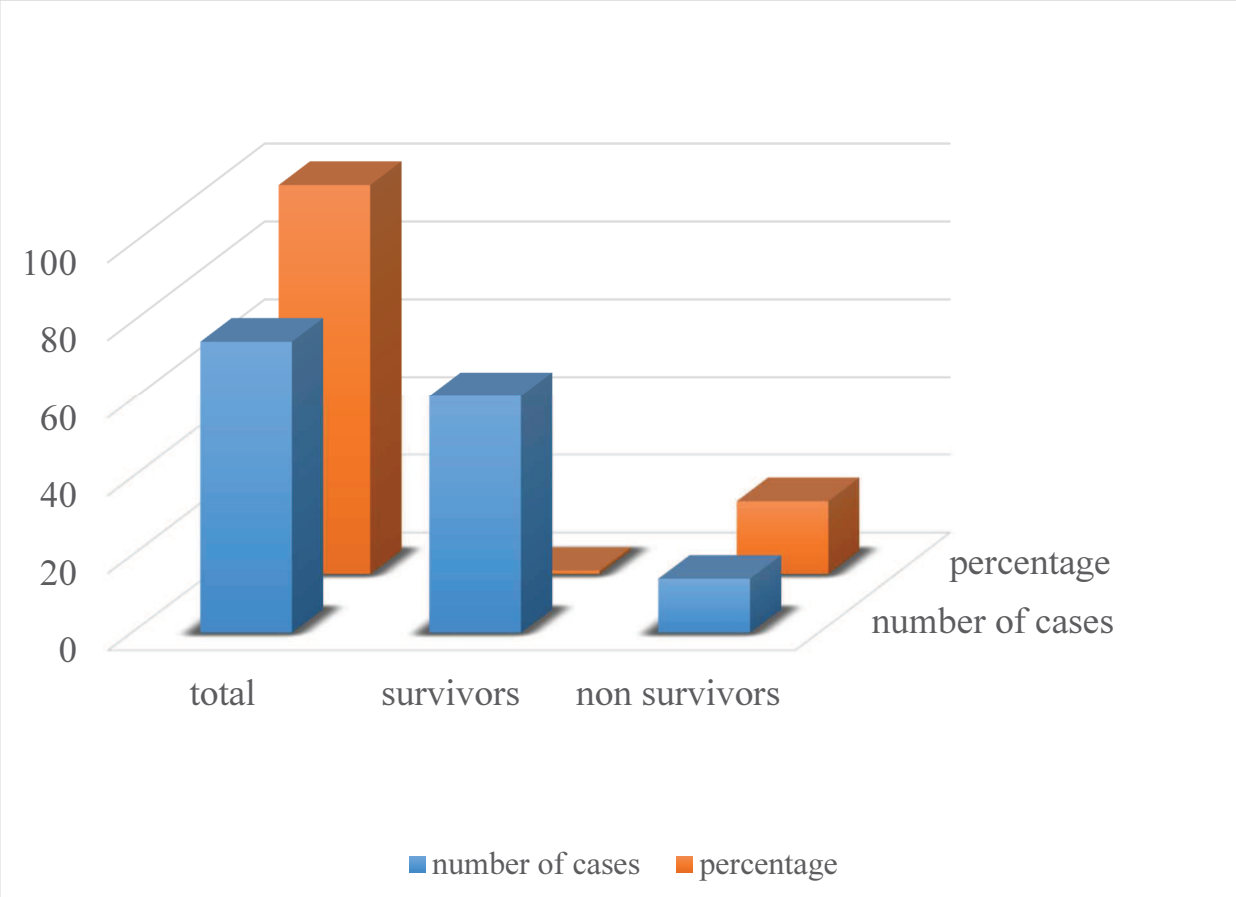
SL. NO	MALE	FEMALE	TOTAL
NUMBER	59	16	75
PERCENTAGE	78.6	21.4	100%



SURVIVAL AND MORTALITY:

Total number of cases	75
survivors	61
Non survivors	14
percentage of survivors	81.33
Percentage of non survivors	18.66

Bar diagram comparing the survivors and non survivors and their percentage



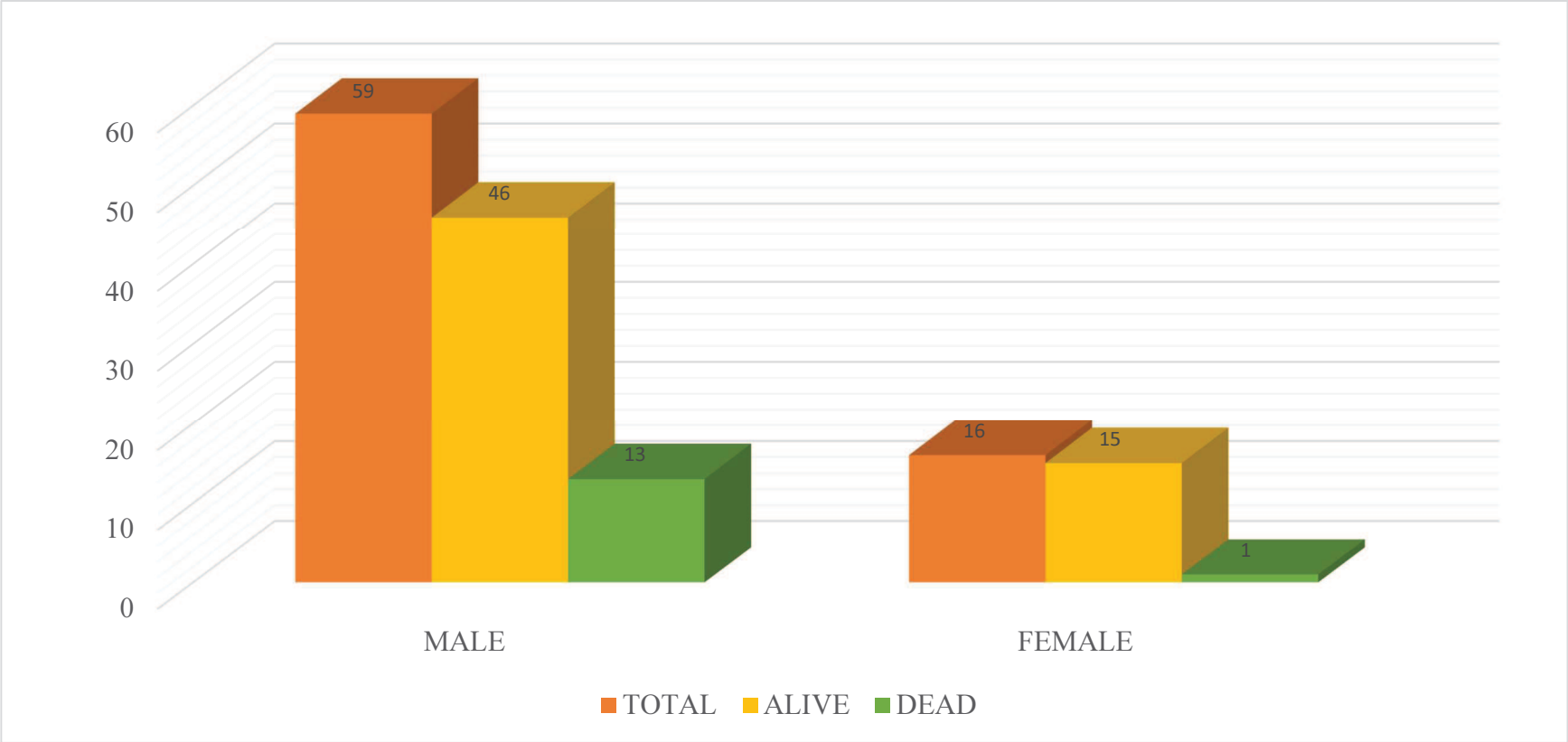
SEX WISE MORTALITY

Table: showing mortality among males and females

	MALE	FEMALE
TOTAL	59	16
ALIVE	46	15
DEAD	13	1
PERCENTAGE LIVE	77.96%	93.75%
PERCENT DEAD	22.03%	6.25%

THE MEAN OF AGE DEATH IN MALES IS : 46

THE MEAN AGE OF DEATH IN FEMALES IS : 66

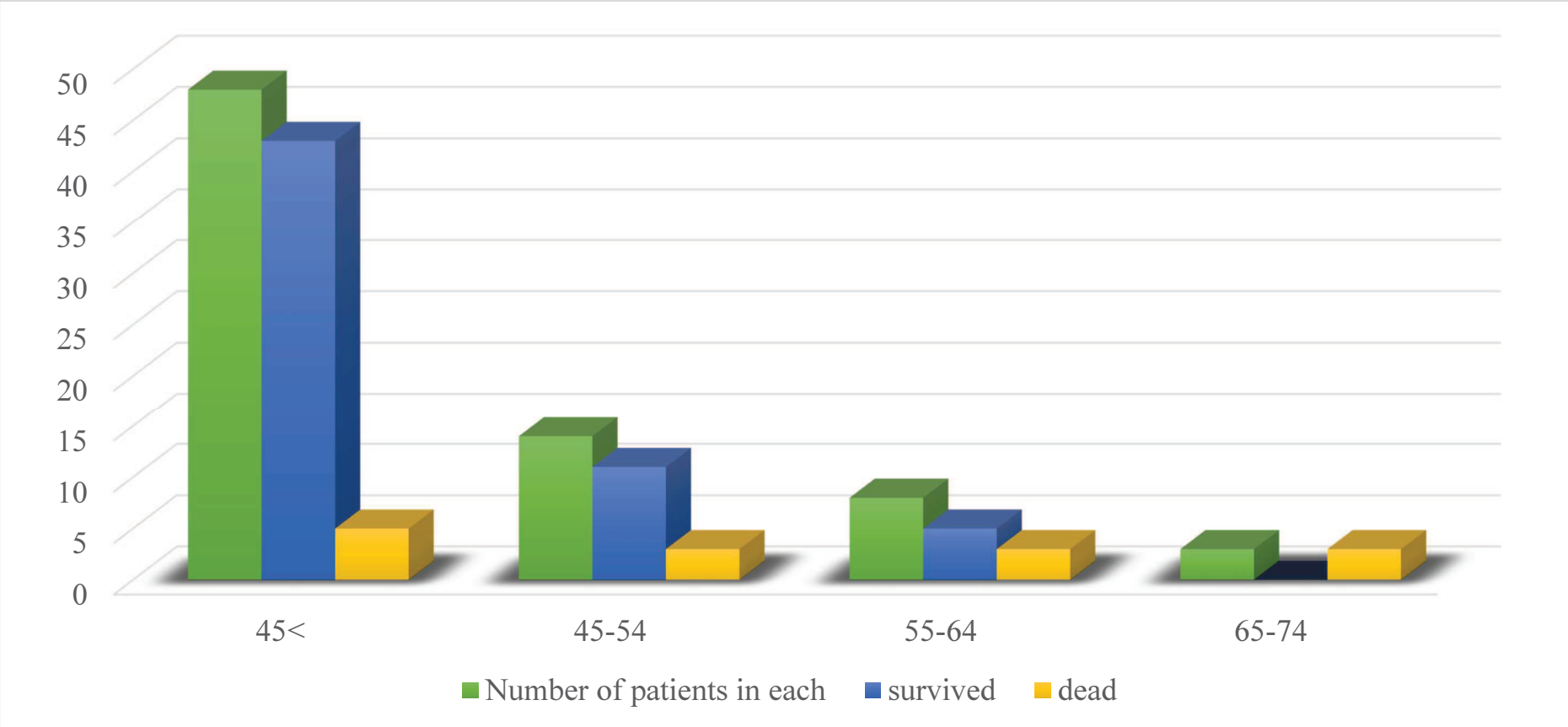


Bar diagram comparing the age wise and sex wise survived and dead patients

Table : showing patient numbers according to the age group

Age group	Number of patients in each	survived	dead	Mortality percentage
45<	48	43	5	10.41%
45-54	14	11	3	21.42%
55-64	8	5	3	37.5%
65-74	3	0	3	100%

In our study 64% of the patients belong to the group of less than 45 years of age



Bar diagram to compare the age group wise survivors and non survivors

AGE:

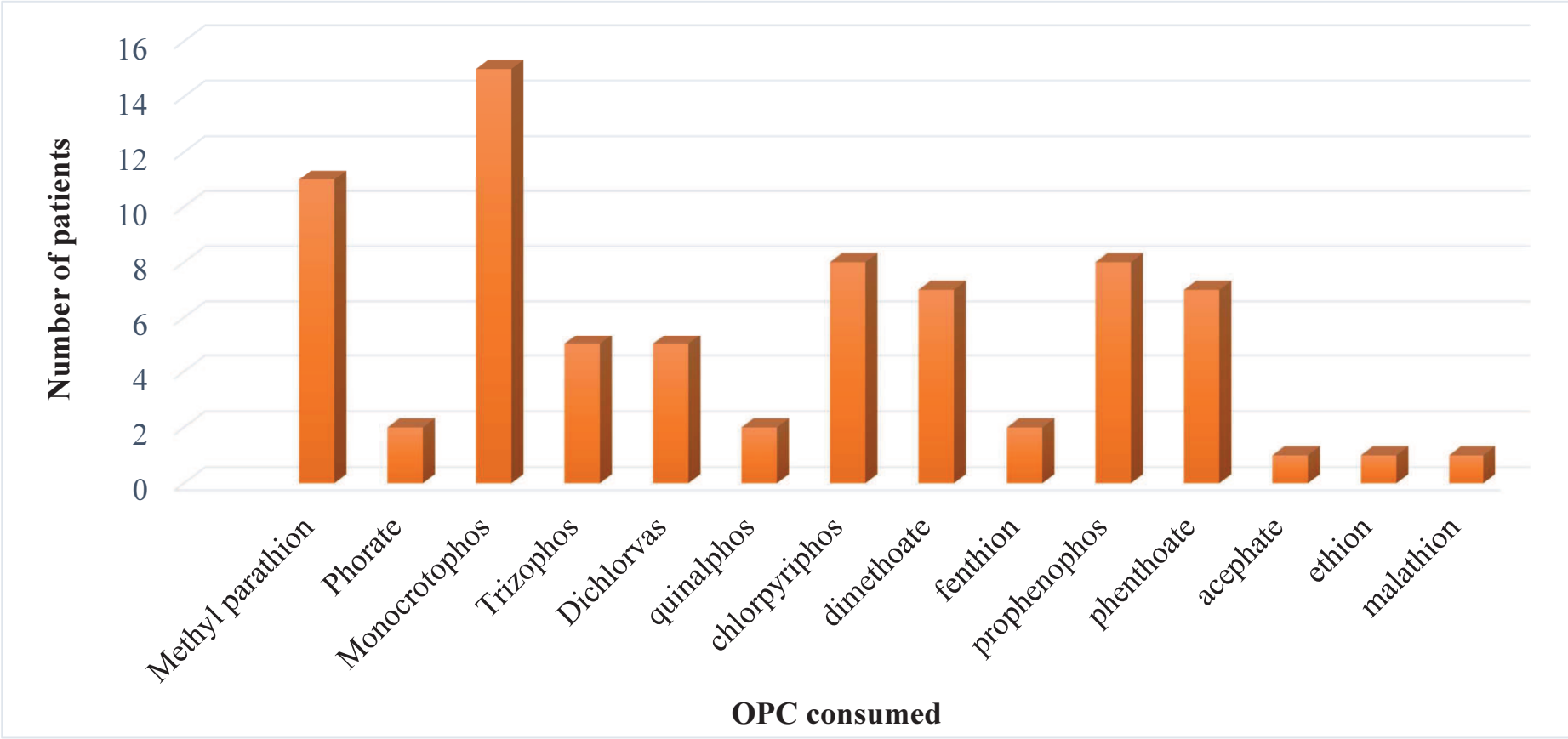
Variable	Survivors	Non-survivors	*p* value
Age	37.18 ± 12.92	47.28 ± 15.3	0.001

± Standard deviation, the p value is calculated using the t-test for two independent samples.

In our study the difference in age among the survivors and non survivors is **significant** p value 0.001(<0.05).

Table: showing the number of patients who consumed each OPCs

OPC	Number of patients
1. Methyl parathion	11
2. Phorate	2
3. Monocrotophos	15
4. Trizophos	5
5. Dichlorvas	5
6. quinalphos	2
7. chlorpyriphos	8
8. dimethoate	7
9. fenthion	2
10.prophenophos	8
11.phenthoate	7
12.acephate	1
13.ethion	1
14.malathion	1

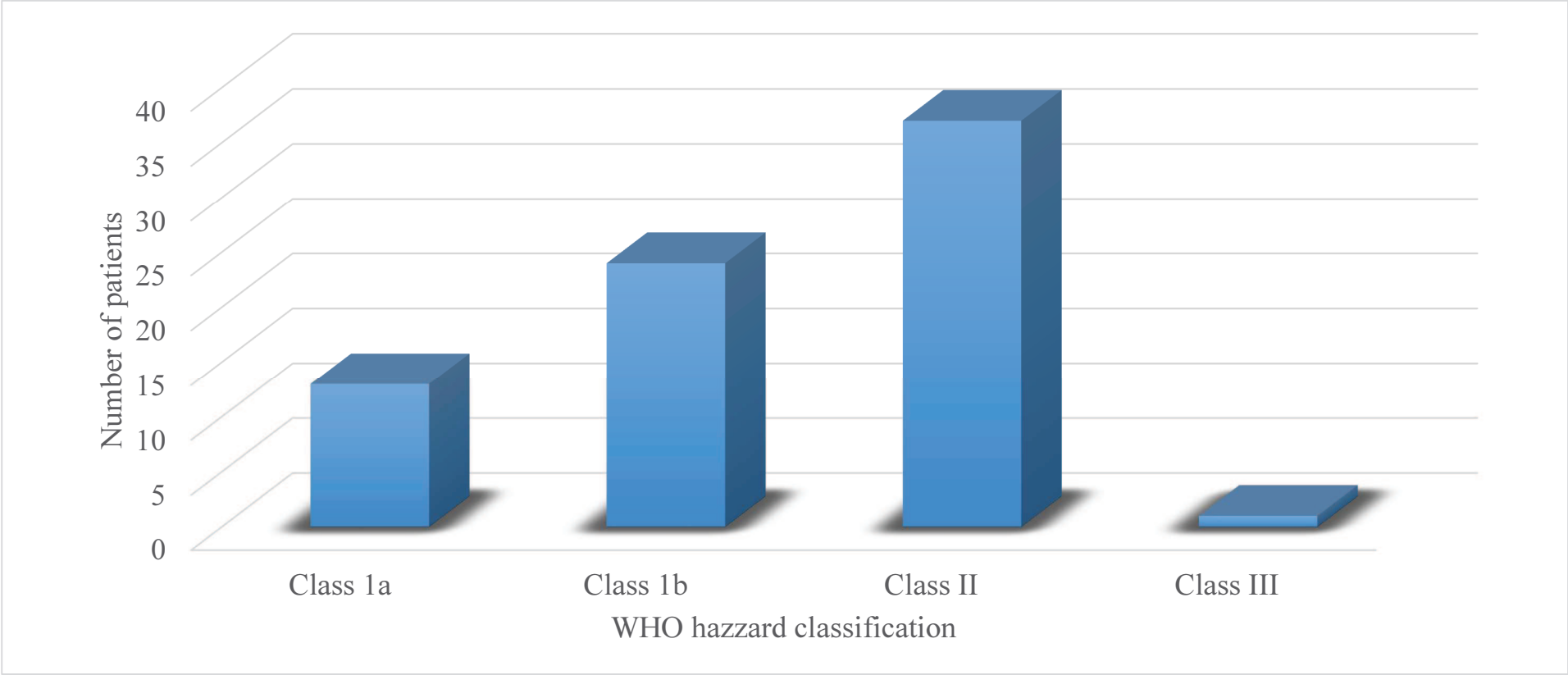


Bar diagram to show the number of cases in each organophosphorous compounds

Table: Patients who consumed as per WHO class

Class of poison	Number of patients
Class Ia	13
Class Ib	24
Class II	37
Class III	1

As per WHO class about 50% of the poisonings belong to classs II group, 33% belong to class Ib group. And only one patient in class III group.

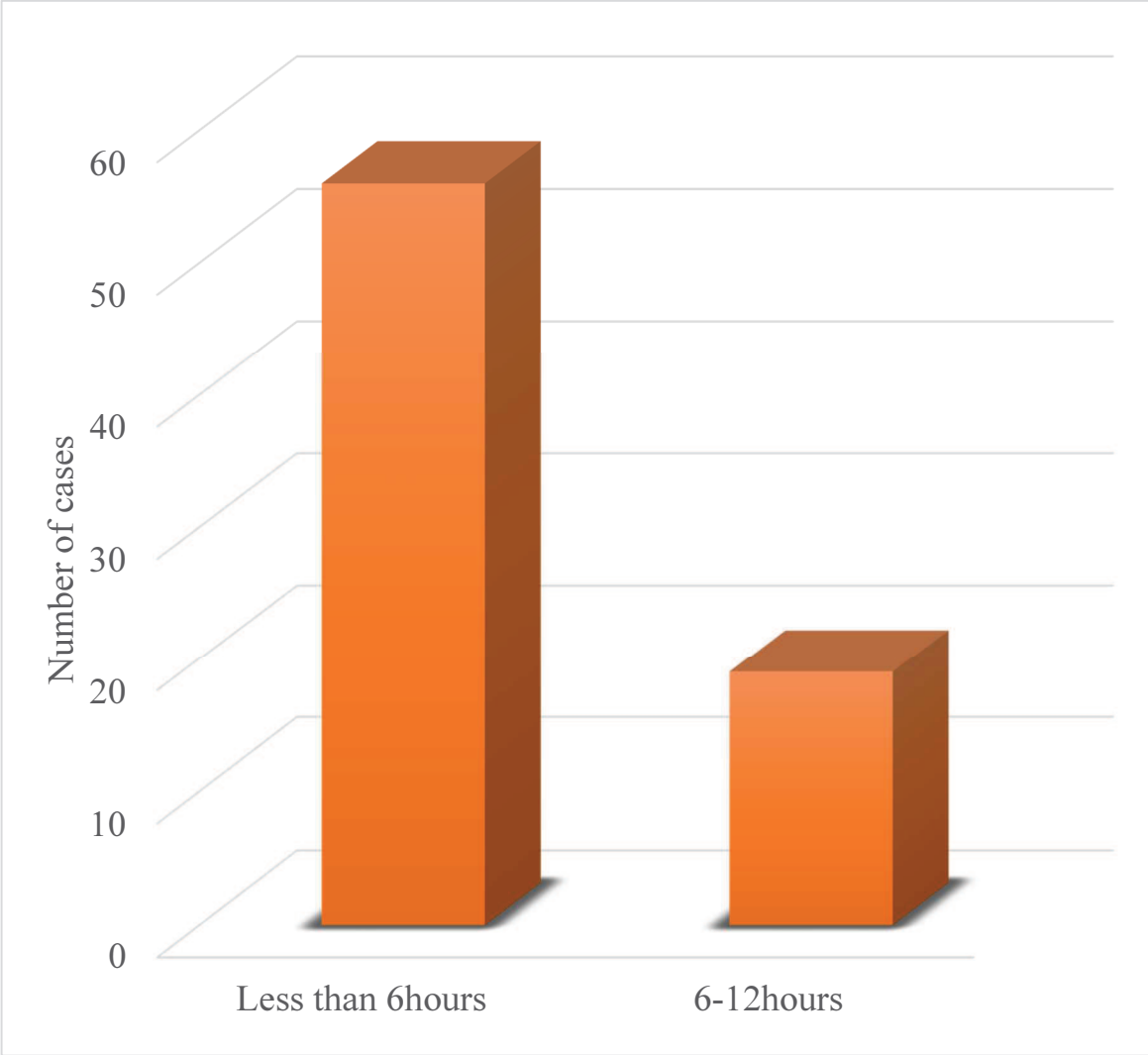


Bar diagram showing the number of patients consumed poison as per WHO class

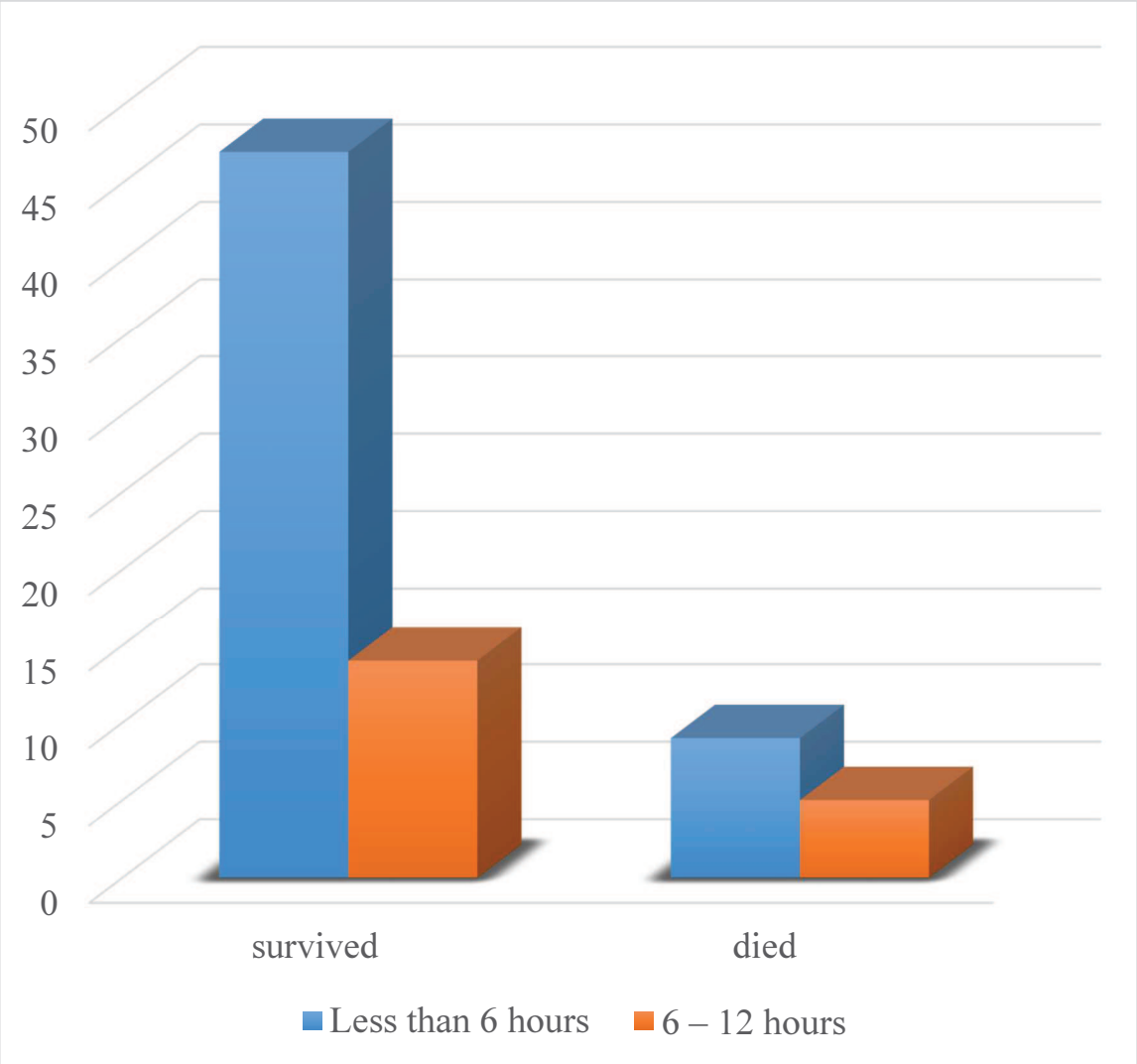
Table: showing number of patients classified with time of presentation

Time elapsed	Number of cases
Less than 6hours	56
6-12hours	19

Bar diagram showing number of patients classified with time of presentation



Bar diagram comparing the significance of time elapsed till admission and mortality



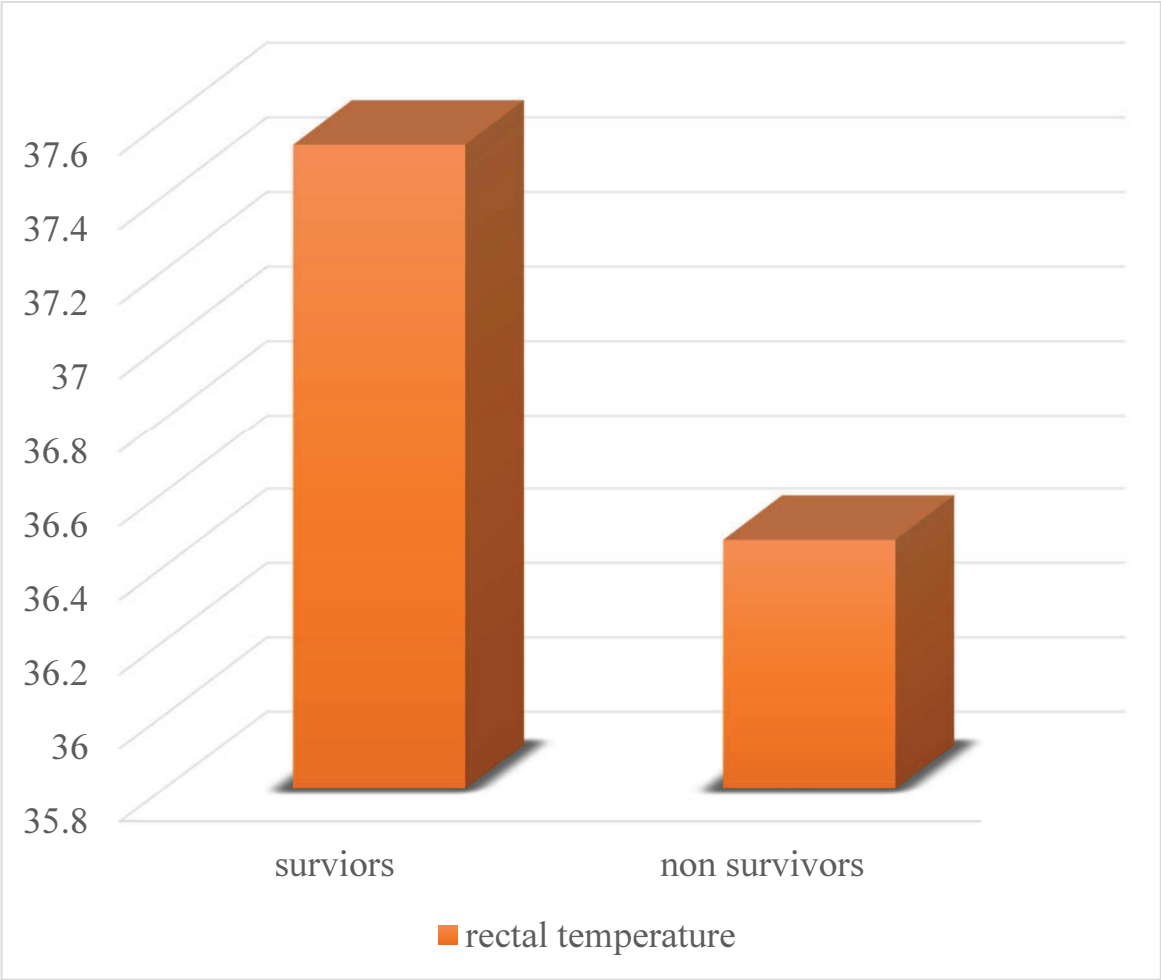
RECTAL TEMPERATURE:

Variable	Survivors	Non survivors	P value
Rectal temperature	37.53±0.76	36.47±0.72	<0.0001

± Standard deviation, the p value is calculated using the t-test for two independent samples.

In our study the difference in rectal temperature among survivors and non survivors is **significant** with p value <0.0001.

Bar diagram showing the comparison between the average rectal temperature (ºC) among the survivors and non survivors



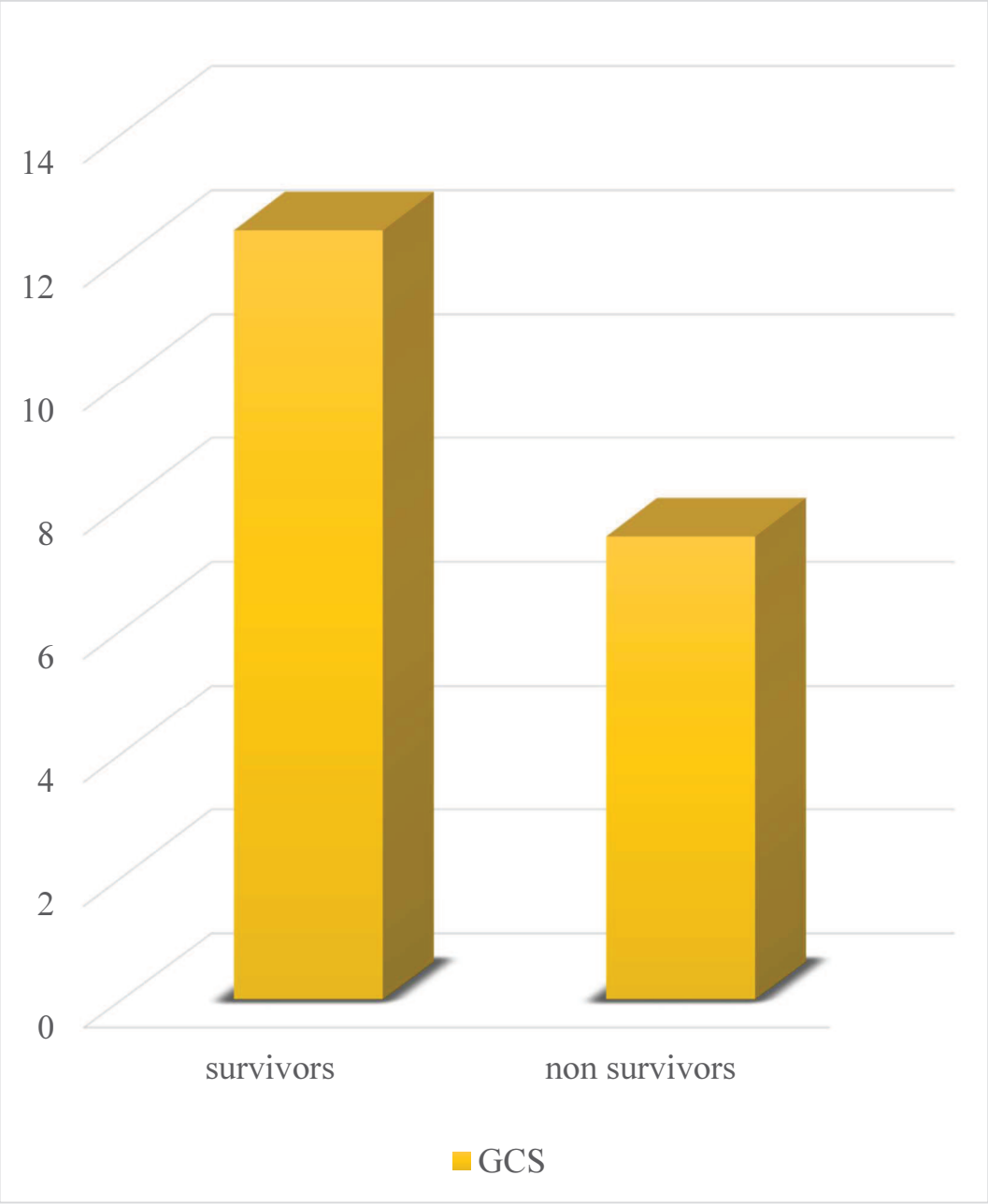
GLASGOW COMA SCALE:

variable	survivors	Non survivors	*p* value
GCS	12(8-15) ± 1.576	8(6-12) ± 1.557	<0.0001

± is standard deviation, the values in parantheses are the range of score obtained in each group. The p value is calculated using the t-test for two independent samples.

In our study the difference in Glasgow coma scale among survivors and non survivors is **significant** with p value <0.0001.

Bar char representing the comparison of Glasgow coma scale among the survived and dead.



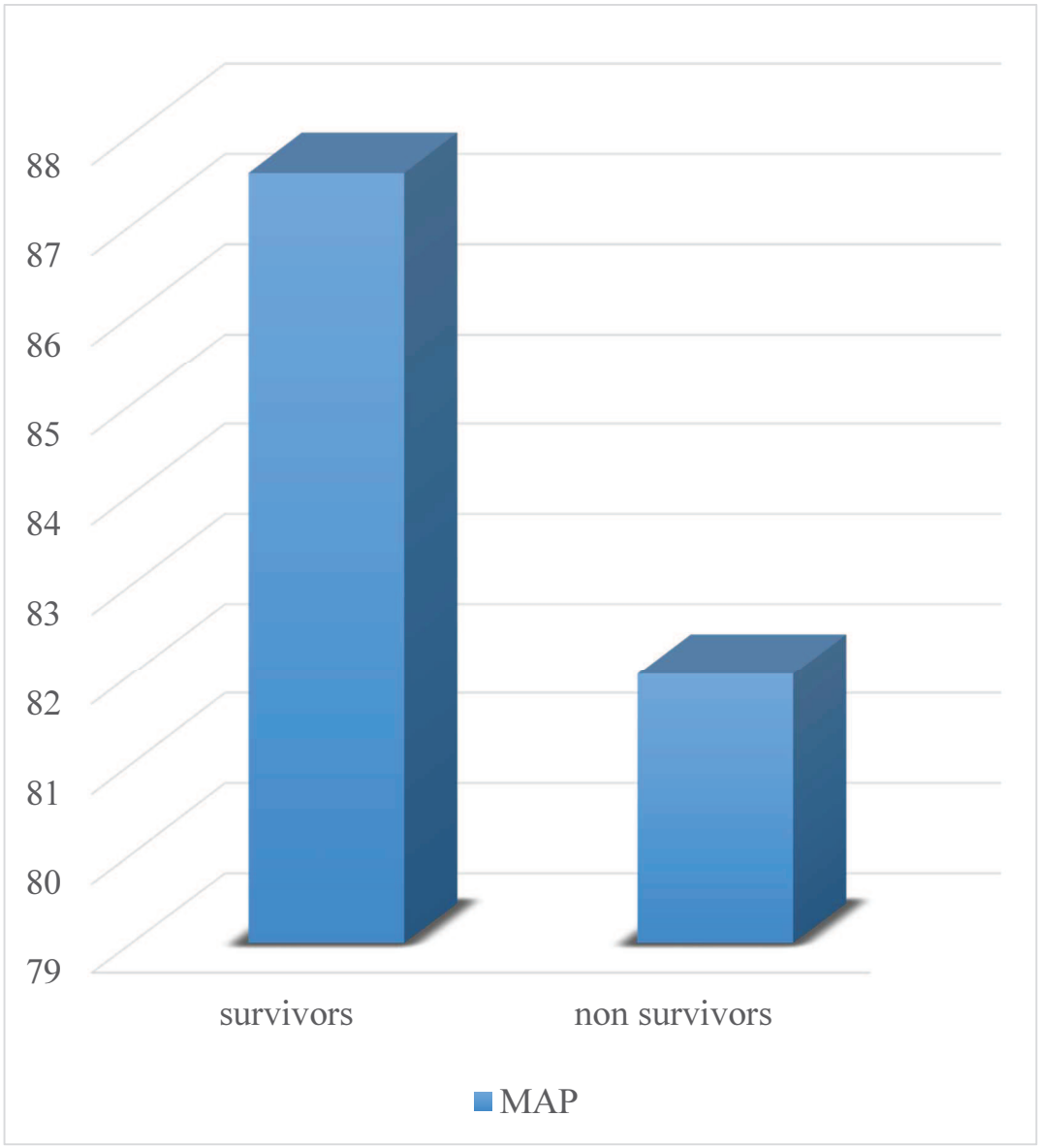
MEAN ARTERIAL PRESSURE:

Variable	Survivors	Non survivors	P value
MAP	87.57±15.76	82±26.70	0.30

± is standard deviation, the p value is calculated using the t-test for two independent samples.

In our study the difference in mean arterial pressure among the survivors and non survivors is **not significant** p value 0.30(>0.05).

Bar diagram showing the average mean arterial pressure (mm Hg) among the survivors and non survivors



HEART RATE:

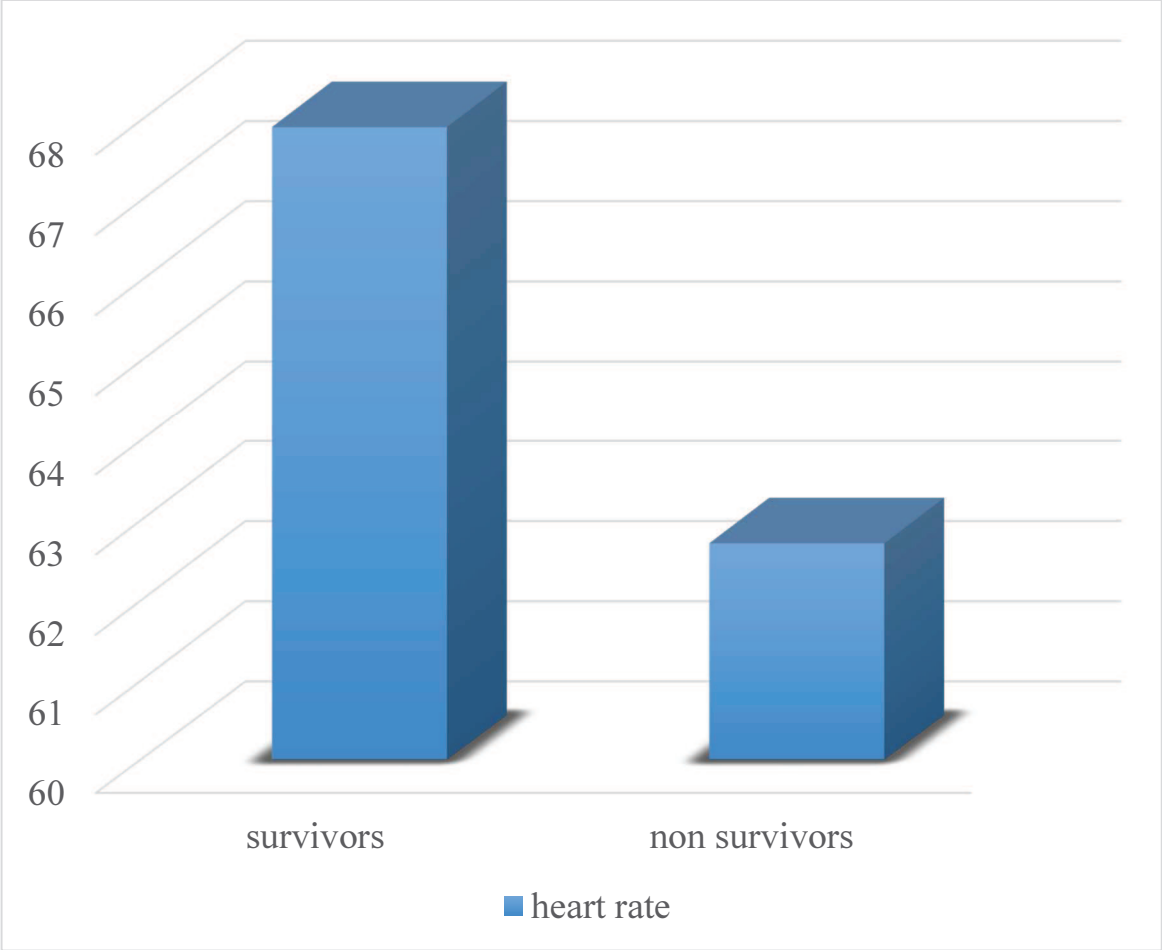
Variable	Survivors	Non survivors	P value
Heart rate	67.91±13.62	62.71±22.30	0.262

± is standard deviation, the p value is calculated using the t-test for two independent samples

In our study the difference in heart rate among the survivors and non survivors is **not significant** p value 0.262(>0.05).

Though the initial rate is normal in OPC poisoned patients. They develop bradycardia at some point of time during the first 24 hours of hospital admission. As our patients are not maintained in atropine infusion and atropine is given as per the atropine requirement chart.

Bar diagram showing the comparison of average heart rate (per minute) among the survivors and non survivors



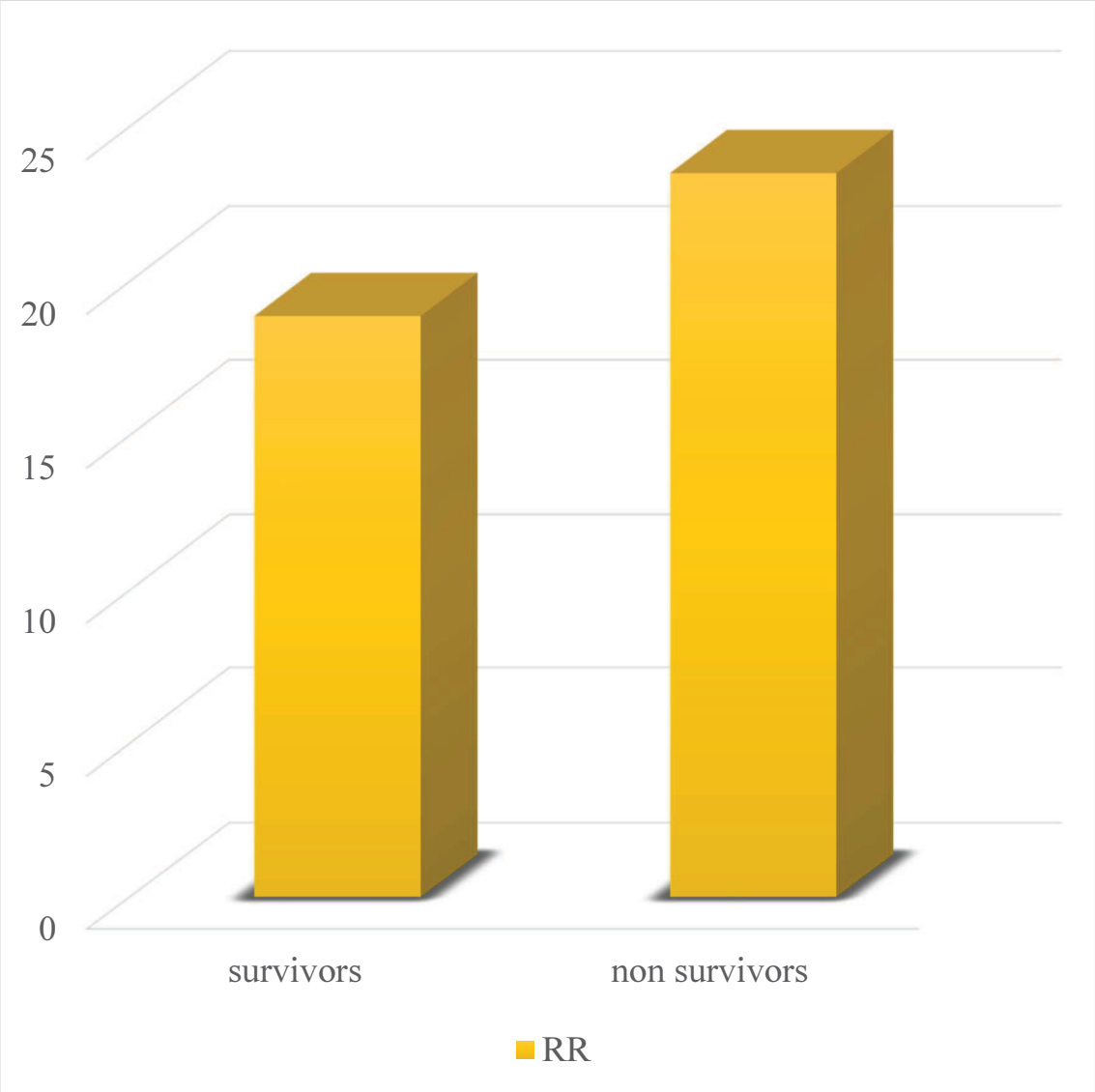
RESPIRATORY RATE:

Variable	Survivors	Non survivors	P value
Respiratory rate	18.88±4.15	23.50±7.37	0.002

± is standard deviation, the p value is calculated using the t-test for two independent samples

In our study the difference in respiratory rate among the survivors and non survivors is **significant** p value 0.002(<0.05).

Bar diagram showing the comparison of average respiratory rate (per minute) among the survivors and non survivors



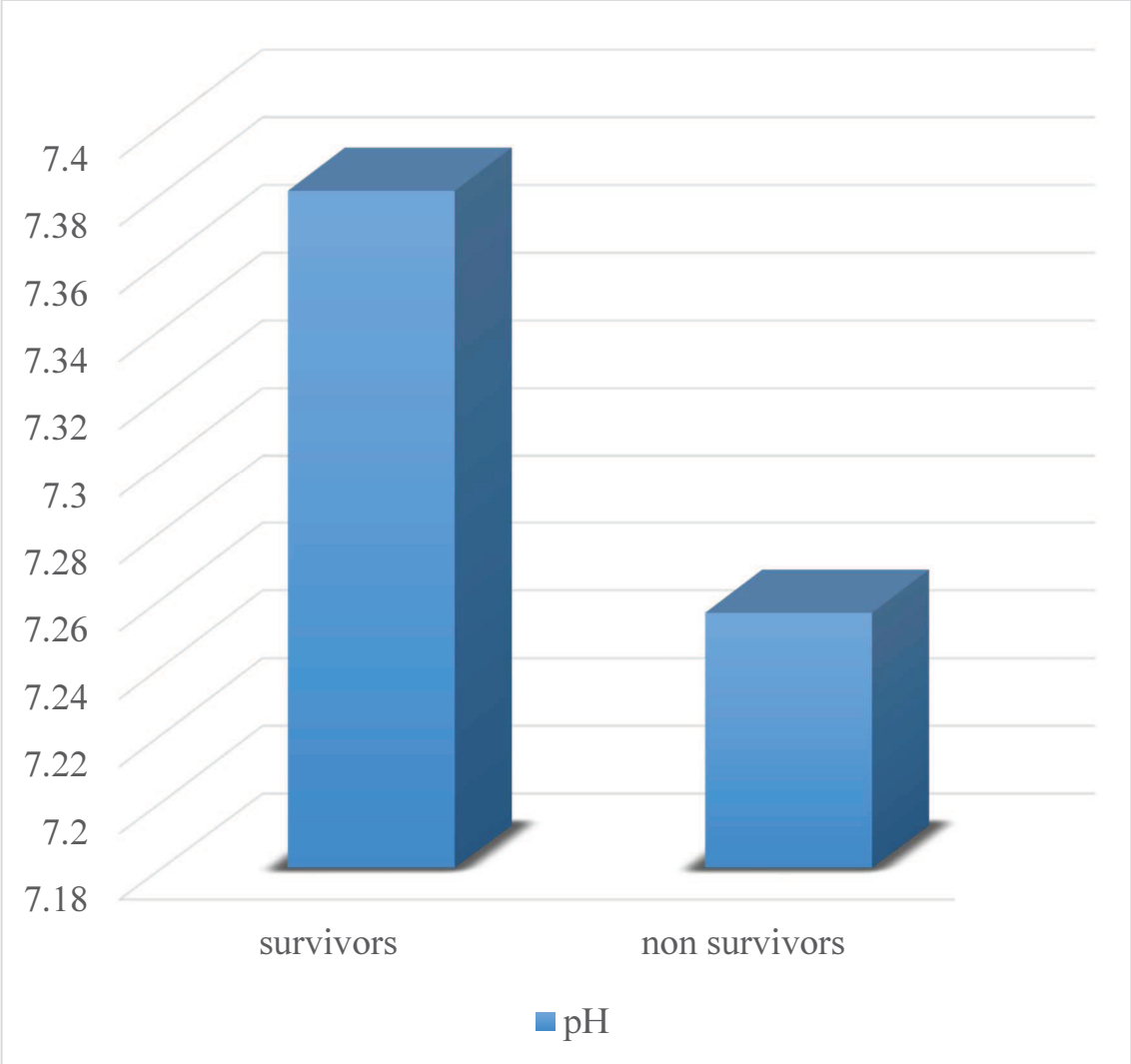
pH:

Variable	Survivors	Non survivors	P value
pH	7.381±0.05	7.25±0.04	<0.0001

± is standard deviation, the p value is calculated using the t-test for two independent samples

In our study the difference in pH among the survivors and non survivors is **significant** p value 0.0001(<0.05).

Bar diagram showing the comparison of average respiratory rate among the survivors and non survivors



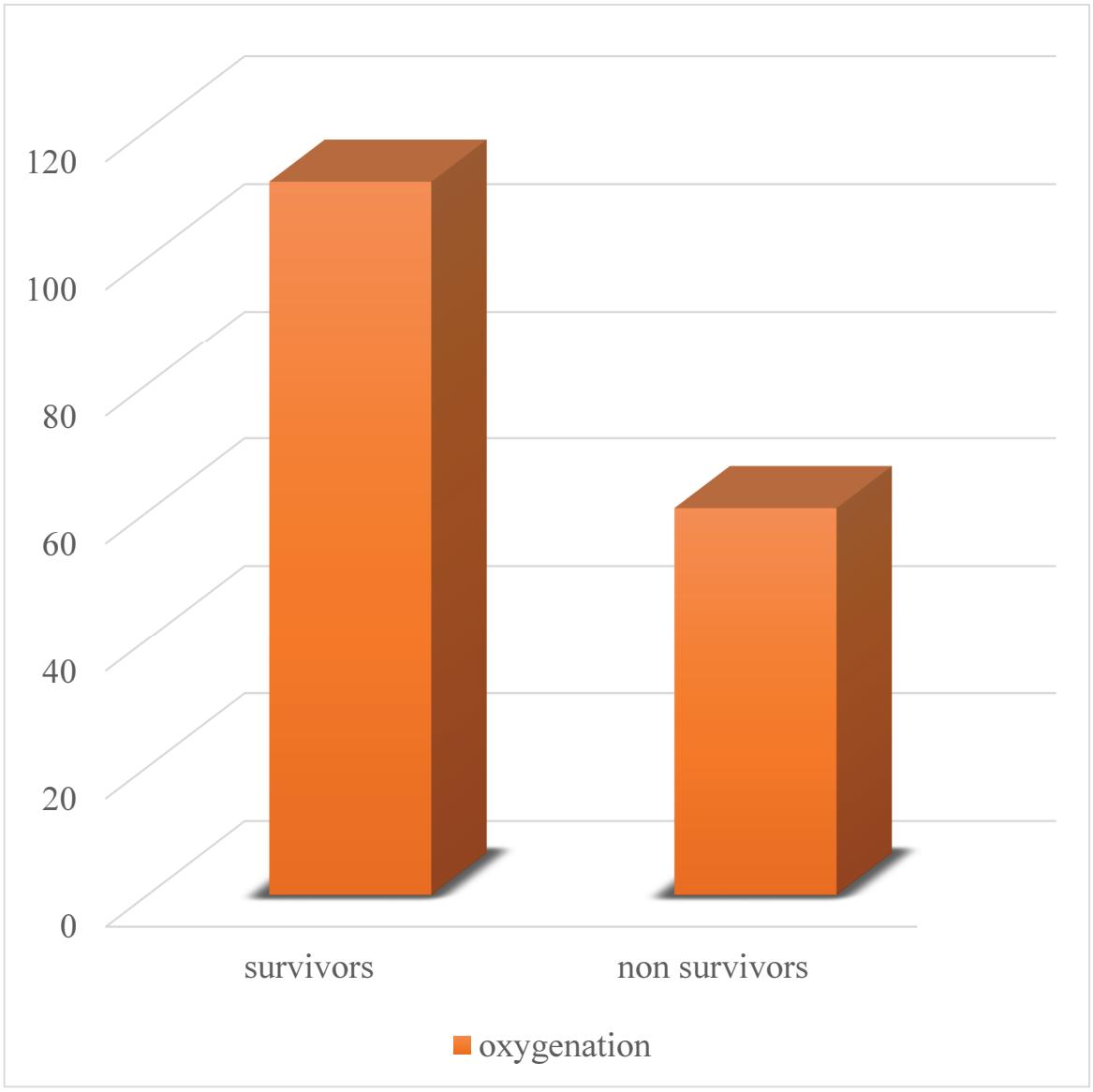
OXYGENATION:

Variable	Survivors	Non survivors	P value
Oxygenation	111.88±28.66	60.57±26.78	<0.0001

± is standard deviation, the p value is calculated using the t-test for two independent samples

In our study the difference in oxygenation among the survivors and non survivors is **significant** p value 0.0001(<0.05).

Bar diagram showing the comparison of average oxygenation (mm Hg) among the survivors and non survivors



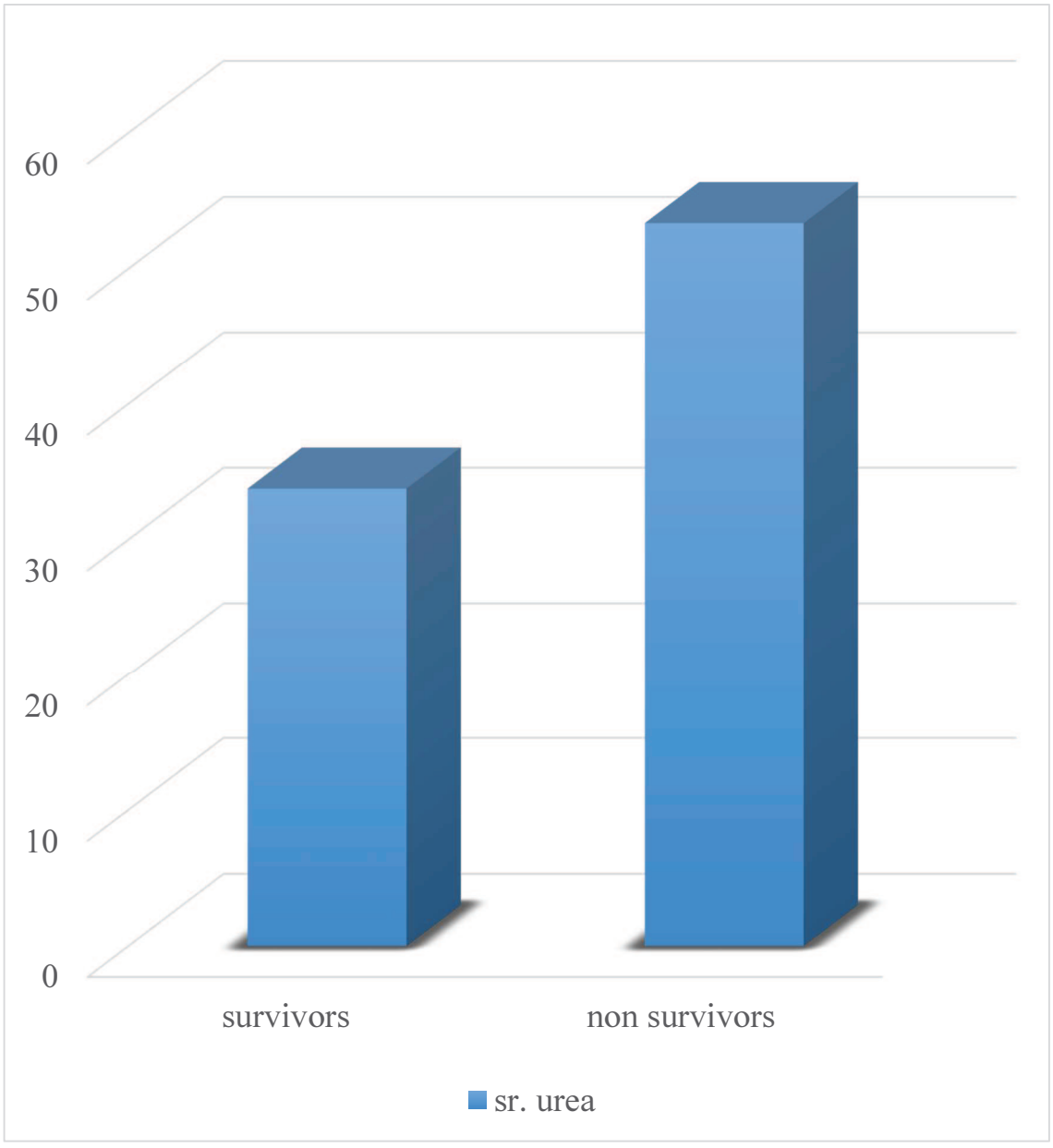
SERUM UREA:

Variable	Survivors	Non survivors	P value
Serum urea	33.75±7.99	53.35±18.40	<0.0001

± is standard deviation, the p value is calculated using the t-test for two independent samples

In our study the difference in serum urea among the survivors and non survivors is **significant** p value 0.0001(<0.05).

Bar diagram showing the comparison of average serum urea (mg/dl) among the survivors and non survivors



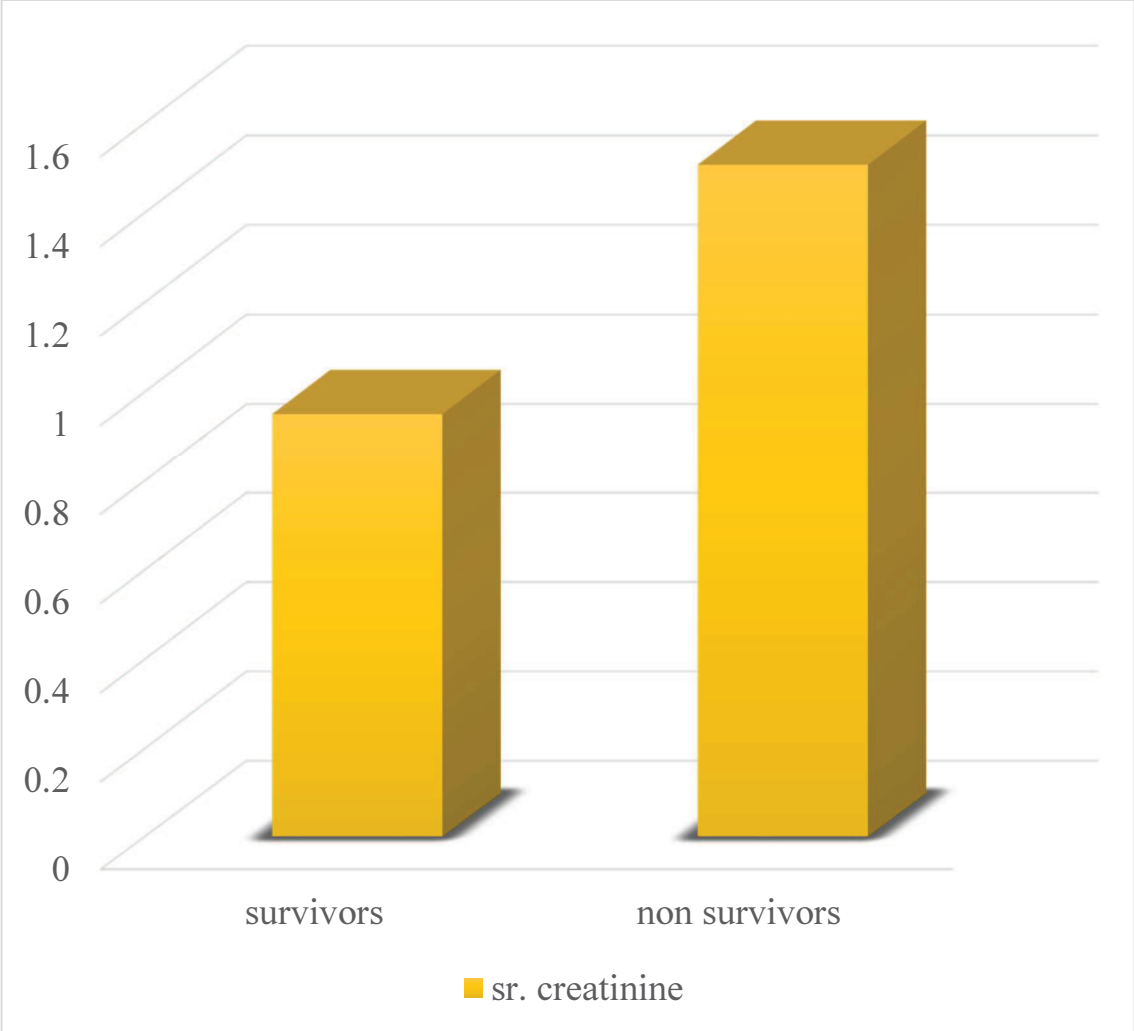
SERUM CREATININE:

Variable	Survivors	Non survivors	P value
Serum creatinine	0.95±0.19	1.50±0.59	<0.0001

± is standard deviation, the p value is calculated using the t-test for two independent samples

In our study the difference in serum creatinine among the survivors and non survivors is ***significant*** p value 0.0001(<0.05).

Bar diagram showing the comparison of average serum creatinine (mg/dl) among the survivors and non survivors



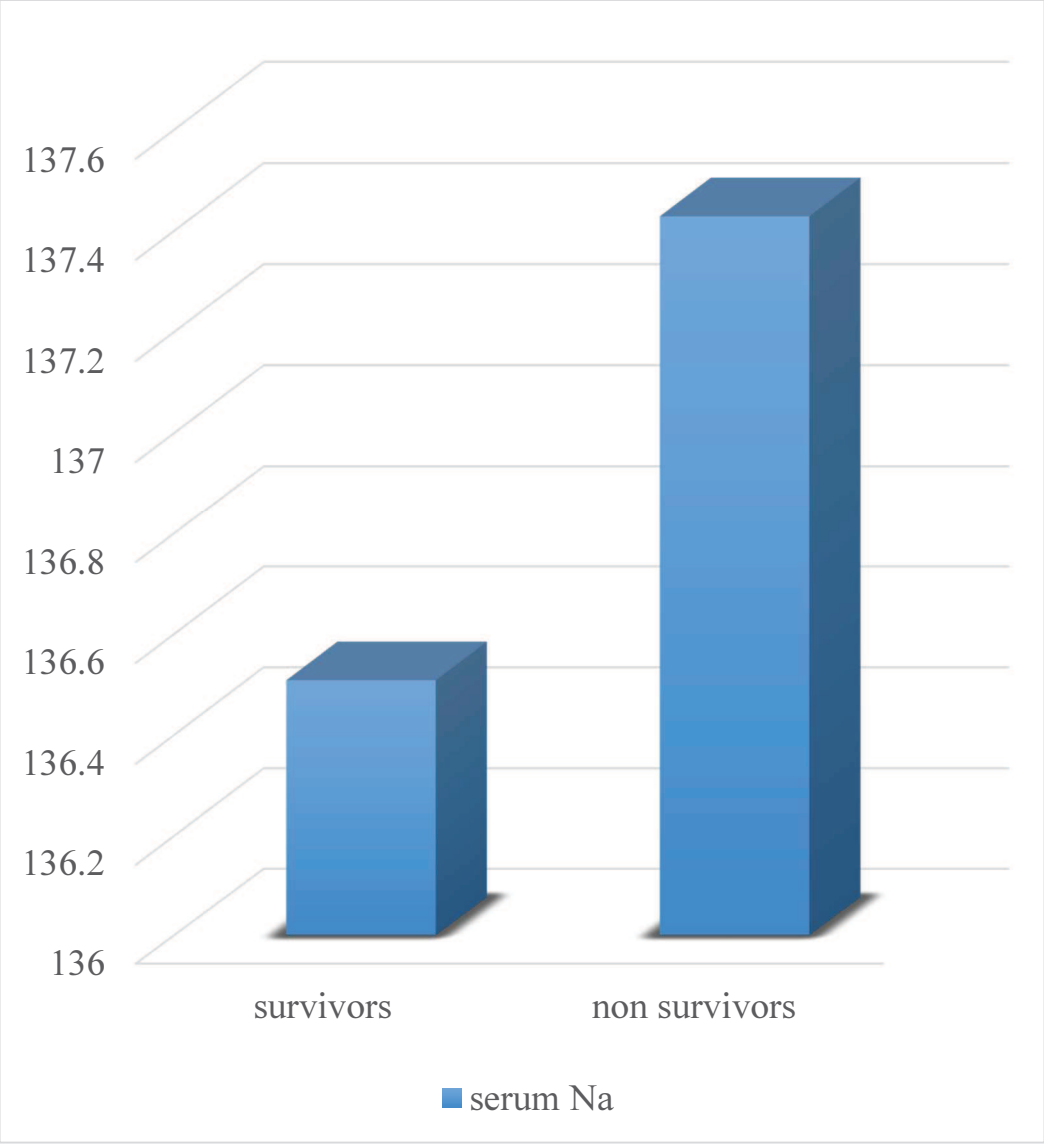
SERUM SODIUM:

Variable	Survivors	Non survivors	P value
Serum sodium	136.50±5.91	137.42±4.41	0.586

± is standard deviation, the p value is calculated using the t-test for two independent samples

In our study the difference in serum sodium among the survivors and non survivors is ***not significant*** p value 0.586(>0.05).

Bar diagram showing the comparison of average serum sodium (mEq/L) among the survivors and non survivors



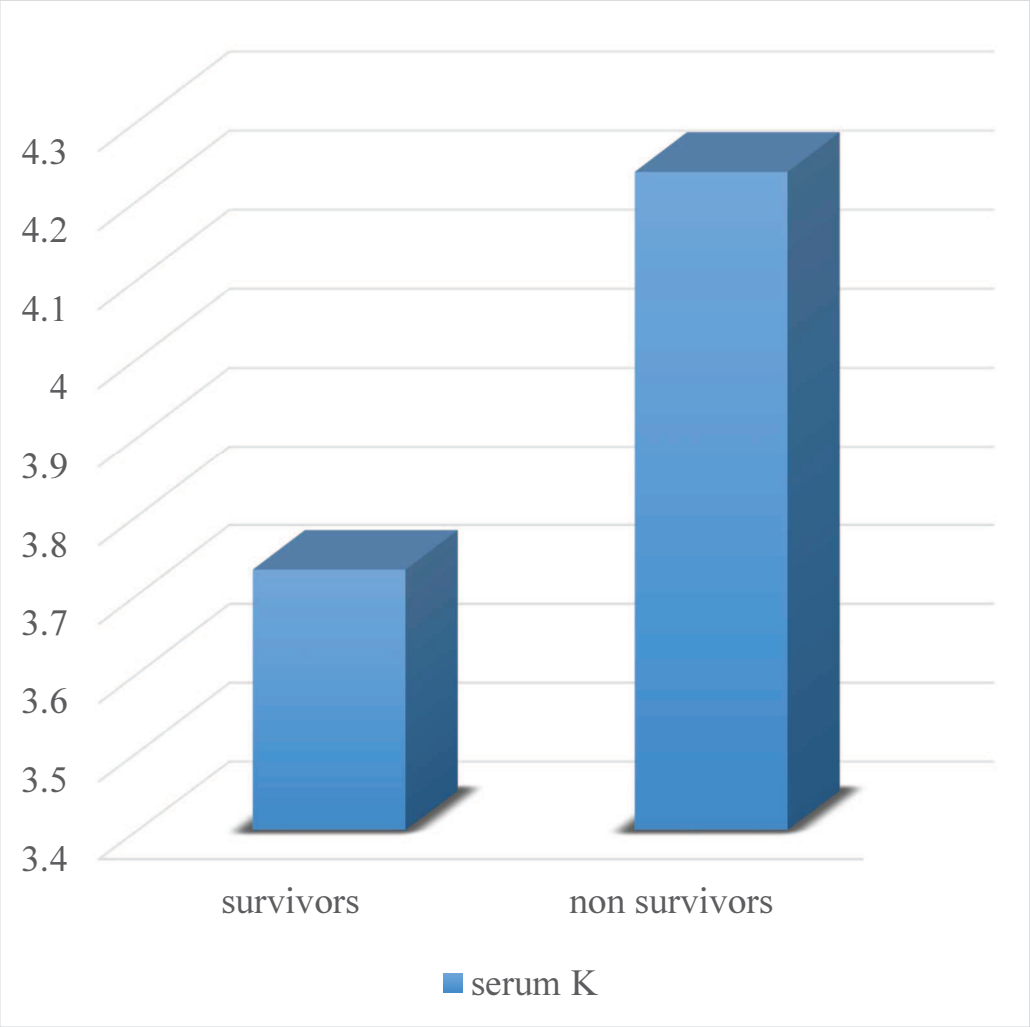
SERUM POTASSIUM:

Variable	Survivors	Non survivors	P value
Serum potassium	3.73±0.53	4.23±0.79	0.005

± is standard deviation, the p value is calculated using the t-test for two independent samples

In our study the difference in serum potassium among the survivors and non survivors is ***significant*** p value 0.005(<0.05).

Bar diagram showing the comparison of average serum potassium (mEq/L) among the survivors and non survivors



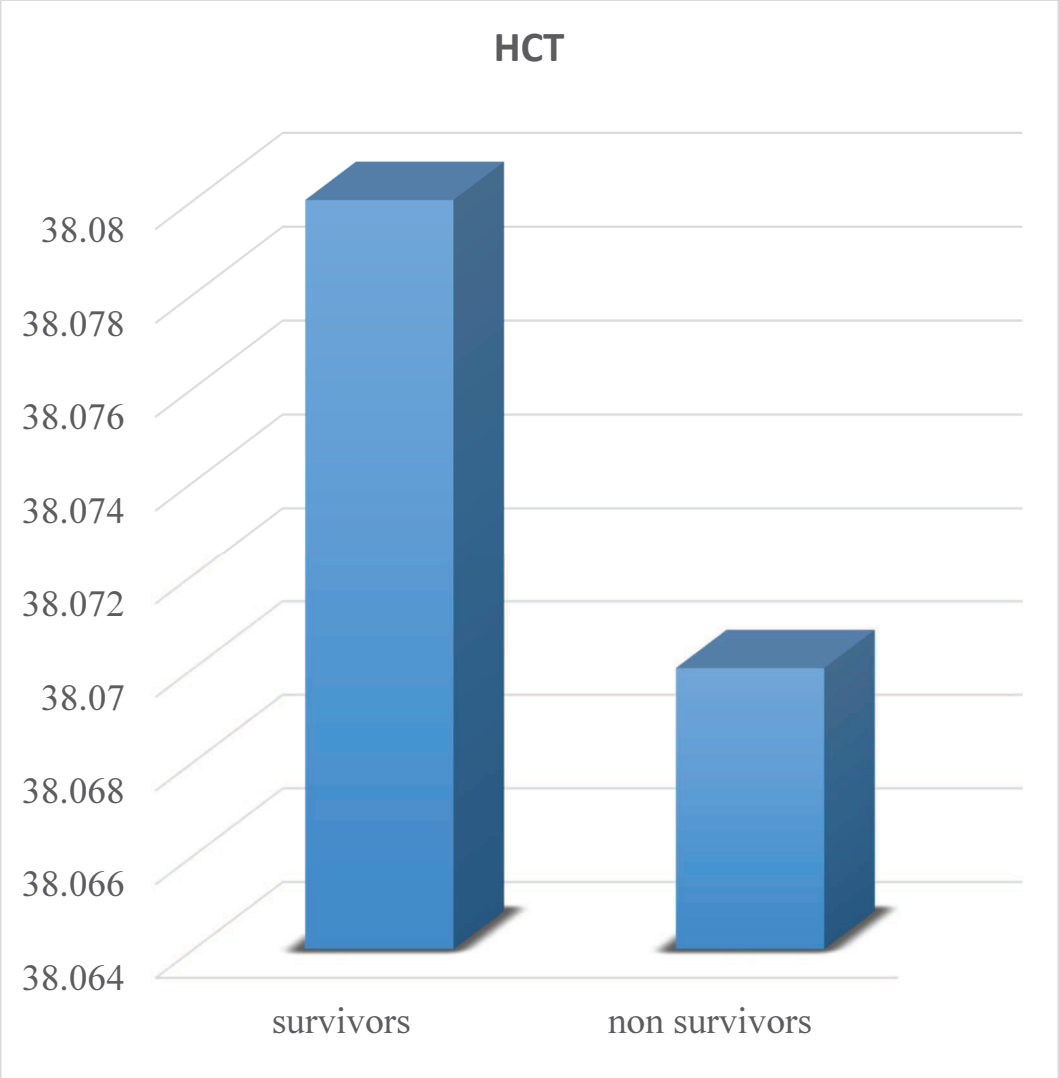
HAEMATOCRIT:

Variable	Survivors	Non survivors	P value
Haematocrit	38.08±5.01	38.07±4.25	0.994

± is standard deviation, the p value is calculated using the t-test for two independent samples

In our study the difference in haematocrit among the survivors and non survivors is ***not significant*** p value 0.994(>0.05).

Bar diagram to compare the haematocrit among the survivors and non survivors



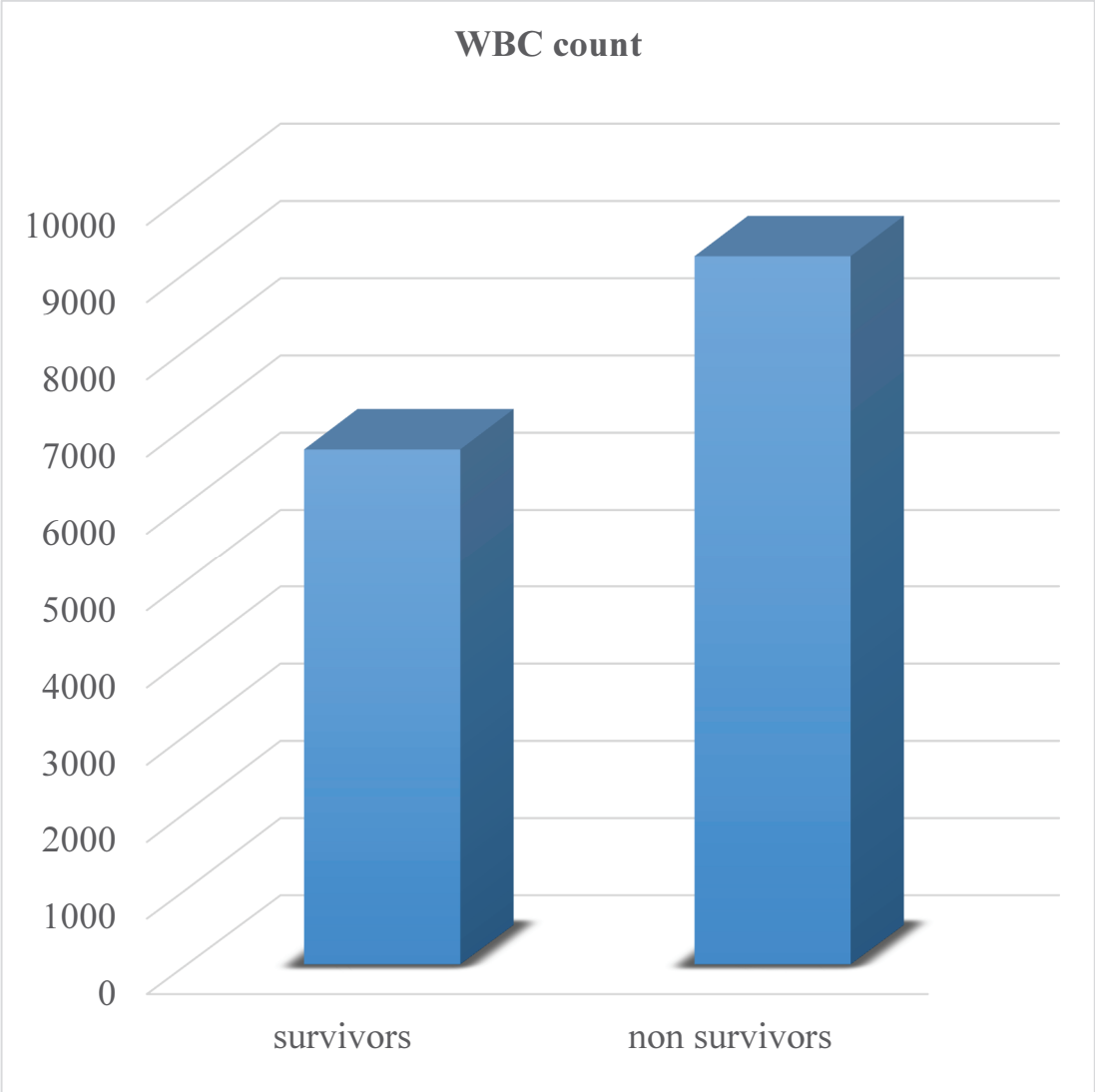
WBC COUNT:

Variable	Survivor	Non survivor	P value
WBC count	6667.21±2171.23	9228.57±2893.42	1.993

± is standard deviation, the p value is calculated using the t-test for two independent samples

In our study the difference in WBC count among the survivors and non survivors is ***not significant*** p value 1.993(>0.05).

Bar diagram to compare the WBC count among the survivors and non survivors



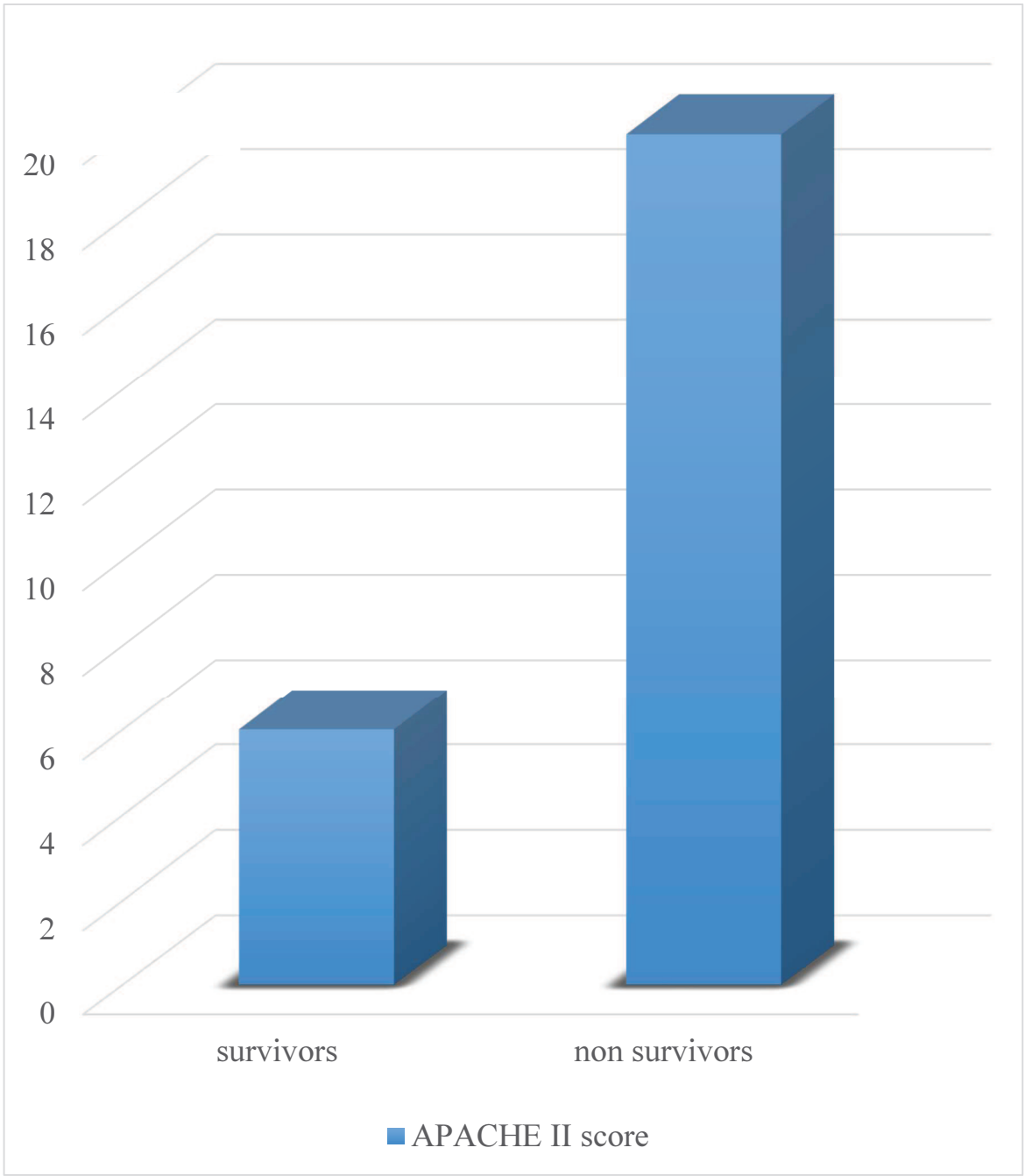
APACHE *II* SCORE:

Variable	Survivors	Non survivors	*p* value
APACHE II	5.70 ± 3.01	19.57 ± 3.93	<0.0001

± is standard deviation, the p value is calculated using the t-test for two independent samples

In our study the difference in APACHE *II* score among the survivors and non survivors is ***significant*** p value 0.0001(<0.05).

Bar diagram to compare the APACHE *II* score among the survivors and non survivors



DISCUSSION

This study is a prospective and retrospective observational study and was done in toxicology unit of madras medical college and Rajiv Gandhi government general hospital. 75 patients with confirmed history or documented OPC poisoning is taken for study. Most of the severely poisoned patients are referred cases from nearby government hospitals in the view of respiratory failure or impending failure. Informed consent is obtained from the prospective samples. The necessary parameters from the retrospective samples obtained from the case records of medical records department of Rajiv Gandhi government general hospital.

The organophosphate compounds are the most common mode of suicidal poisonings in India. The most common mode of death in OPC poisoning is due to respiratory failure. Most of the severely poisoned patients need to intubation and mechanical ventilation and must be closely monitored in ICU settings. Multiple organ system involvement is common in OPC poisoning as this muscarinic and nicotinic receptors are virtually present in almost all organ systems.

The APACHE *II* score is objective type scoring system. The score is calculated from the worst values obtained during the first 24 hours of ICU admission

APACHE II score = APS+ GCS +Age+ chronic health status

Many studies[62,63,64,65] shown the discriminative value of APACHE *II* score in the assessment of outcomes of OPC poisoning. The APACHE *II* score is useful especially in patients with multiple organ dysfunction due to acute insult like OPC poisoning.

The minimum APACHE *II* score obtained in our study is 0 and the maximum score obtained in our study is 27. The mean APACHE II score in survivors is 5.70 with standard deviation of 3.01 and in non survivors is 19.57 with standard deviation of 3.93. No one patient survived with APACHE *II* score of more than 15.

The difference in APACHE *II* score is statistically significant among the survivors and non survivors. All the statistical analysis are done using the t-test for two independent samples

Other parameters which are shown to be statistically significant [$p<0.05$] in our study are age, Glasgow coma scale, rectal temperature, respiratory rate, pH, oxygenation, serum urea, serum creatinine and serum potassium. Though insignificant the WBC count is increased in non survivors group may be due to aspiration pneumonia.

Parameters thet are responsible for increased APACHE II score in non survivors group is age, GCS, oxygenation and pH.

The chronic health history is present in only two of our patients. Both have immunodeficiency one due to retroviral disease and the other had an active malignancy and was on chemotherapy and both patients expired.

APACHE II score predicts the severity of acute physiological dysfunction due to multi organ involvement in OPC poisoning and can be recommended as a useful scoring system in OPC poisonings in ICU settings

Limitations of the study:

1. Further studies with large sample size and multicentre studies with different population are needed to conform the use of *APACHE II* score in predicting the severity and clinical outcomes of organophosphorous poisoning.

CONCLUSION

- APACHE II score is an objective scoring system and it is useful in the predicting the clinical outcome in the Acute Organophosphorous poisonings in the Intensive care settings.

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ABBREVATIONS

OPC	:	Organo phosphorous compound
WHO	:	world health organization
PAM	:	pralidoxime
APACHE	:	acute physiology and chronic health evaluation
GCS	:	glassgow coma scale
AChE	:	Acetylcholinesterase
ACh	:	Acetylcholine
BuChE	:	Butyrylcholinesterase
NMJ	:	neuro muscular junction
RBC-AChE	:	red blood cell Acetylcholinesterase
Hb	:	Haemoglobin
HCT	:	haematocrit
WBC	:	white blood cell
Sr.	:	Serum

STUDY PROFORMA SHEET

1. Name :
2. Patient ID No:
3. Age/Sex :
4. Contact No:
5. Address:
6. Date of admission with time:
7. Date of discharge:
8. Occupation:
9. Substance consumed:
10. Time of consumption:
11. Place of consumption:
12. Time elapsed since consumption to admission:
13. WHO hazard scale of the consumed Substance?
14. Chronic health history(any of the following):
    I. Liver: Cirrhosis with portal hypertension or encephalopathy
    II. CVS: class IV angina
    III. Pulmonary: chronic hypoxia, hypercapnea, polycythemia,
    IV. Kidney: chronic peritoneal or haemodialysis
    V. Immune status: immunocompromised host
15. Glasgow coma scale:

VITAL PARAMETERS:

- BLOOD PRESSURE (SYS/DIA):
- PULSE RATE:
- RESPIRATORY RATE:
- Spo2:
- RECTAL TEMPERATURE:

INVESTIGATIONS:

1. COMPLETE BLOOD COUNT
2. RENAL FUNCTION TESTS
    a. UREA(mg/dl):
    b. Creatinine (mg/dl):
3. SERUM ELECTROLYTES
    a. Serum sodium (mEq/L):
    b. Serum potassium (mEq/L):
4. Arterial blood gases:

OUTCOME OF THE PATIENT (tick in appropriate boxes):

1. survived ☐
2. Not survived ☐

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-3

EC Reg No.ECR/270/Inst./TN/2013
Telephone No : 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr. Vivekanandan A,
Post Graduate, MD (General Medicine)
Institute of Internal Medicine,
Madras Medical College,
Chennai – 600003.

Dear Dr. Vivekanandan .A,

The Institutional Ethics Committee has considered your request and approved your study titled **"EVALUATING THE USE OF APACHE II SCORE IN PREDICTING THE SEVERITY AND CLINICAL OUTCOMES OF ORGANOPHOSPHOROUS POISONING"** No. 55072014.

The following members of Ethics Committee were present in the meeting held on 01.07.2014 conducted at Madras Medical College, Chennai-3.

1.	Dr. C. Rajendran, M.D.	-- Chairperson
2.	Dr. R. Vimala, M.D., Dean, MMC, Ch-3.	-- Deputy Chair Person
3.	Prof. Kalaiselvi, MD., Vice-Principal, MMC, Ch-3	-- Member Secretary
4.	Prof. Nandhini, M.D. Inst. of Pharmacology, MMC, Ch-3.	-- Member
5.	Dr. G. Muralidharan, Director Incharge , Inst. of Surgery	-- Member
6.	Prof. Md Ali, MD., DM., Prof & HOD of MGE, MMC, Ch-3.	-- Member
7.	Prof. Ramadevi, Director i/c, Biochemistry, MMC,Ch-3.	-- Member
8.	Prof. Saraswathy, MD., Director, Pathology, MMC, Ch-3.	-- Member
9.	Prof. Tito, Director, i/c. Inst. of Internal Medicine, MMC	-- Member
10.	Thiru. Rameshkumar, Administrative Officer	-- Lay Person
11.	Thiru. S. Govindasamy, BABL, High Court, Chennai-1.	-- Lawyer
12.	Tmt. Arnold Saulina, MA MSW	-- Social Scientist

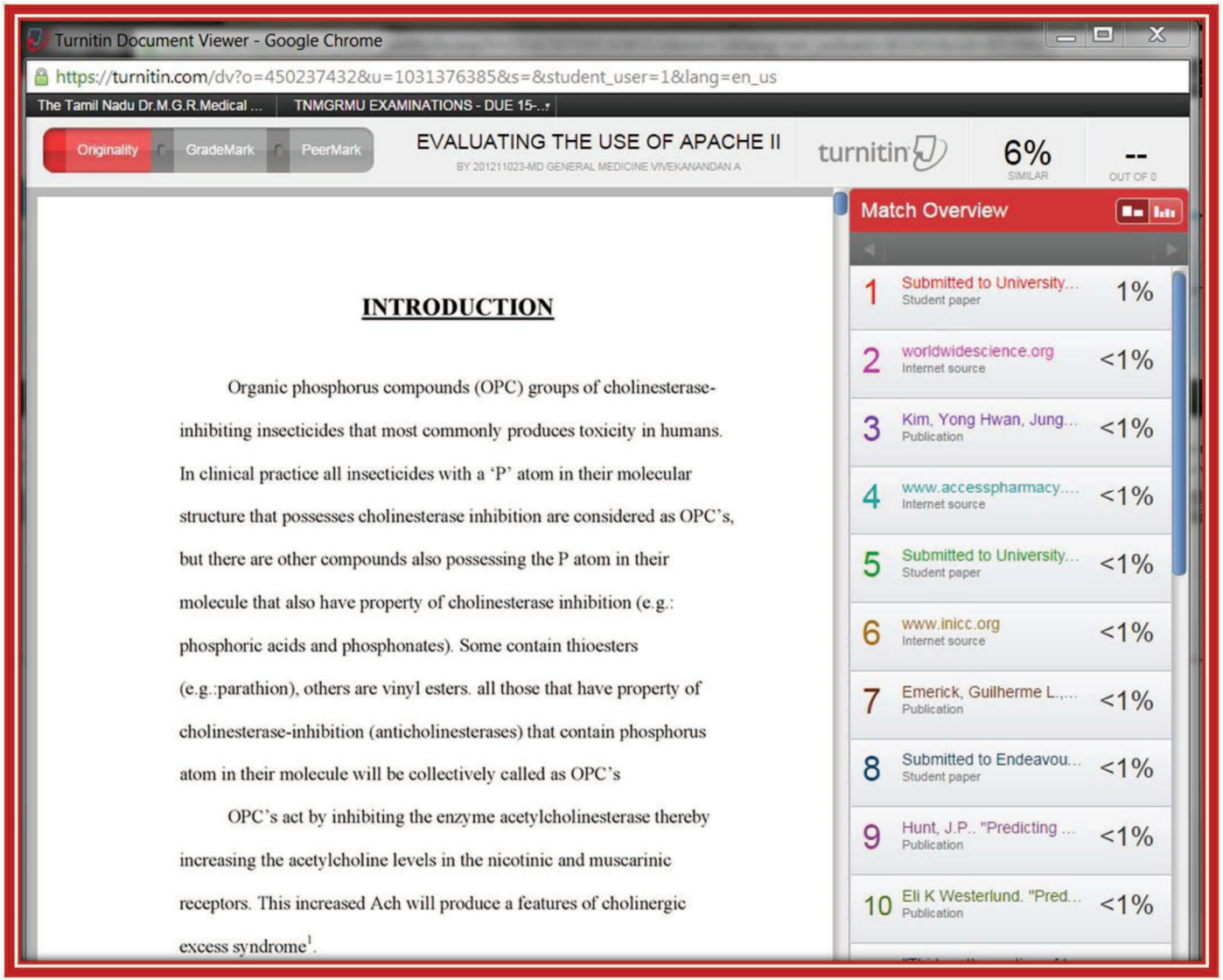
We approve the proposal to be conducted in its presented form.

Sd/Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003



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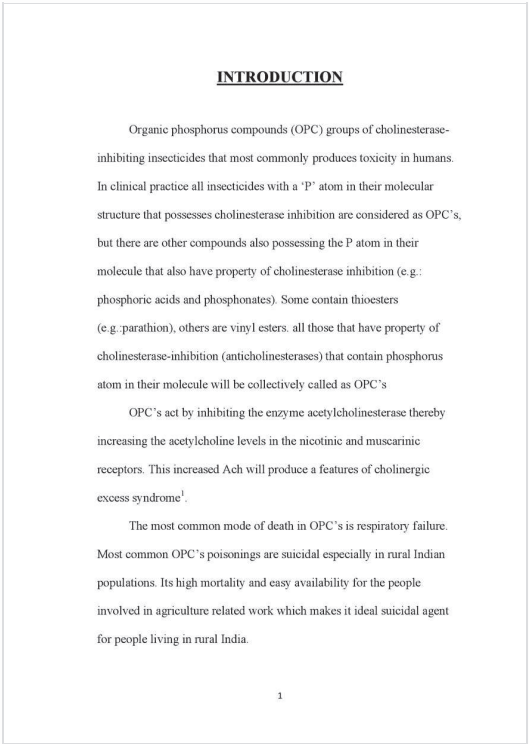

INTRODUCTION

Organic phosphorus compounds (OPC) groups of cholinesterase-inhibiting insecticides that most commonly produces toxicity in humans. In clinical practice all insecticides with a 'P' atom in their molecular structure that possesses cholinesterase inhibition are considered as OPC's, but there are other compounds also possessing the P atom in their molecule that also have property of cholinesterase inhibition (e.g.: phosphoric acids and phosphonates). Some contain thioesters (e.g.:parathion), others are vinyl esters. all those that have property of cholinesterase-inhibition (anticholinesterases) that contain phosphorus atom in their molecule will be collectively called as OPC's

OPC's act by inhibiting the enzyme acetylcholinesterase thereby increasing the acetylcholine levels in the nicotinic and muscarinic receptors. This increased Ach will produce a features of cholinergic excess syndrome[1].

The most common mode of death in OPC's is respiratory failure. Most common OPC's poisonings are suicidal especially in rural Indian populations. Its high mortality and easy availability for the people involved in agriculture related work which makes it ideal suicidal agent for people living in rural India.

1

INFORMATION SHEET

We are conducting a study on "**EVALUATING THE USE OF *APACHE II* SCORE IN PREDICTING THE SEVERITY AND CLINICAL OUTCOMES OF ORGANOPHOSPHOROUS POISONING**" among patients attending Rajiv Gandhi Government General Hospital, Chennai and for that your specimen may be valuable to us.

The purpose of this study is to assess the efficacy of the APCHE II score in guiding prognosis of organophosphorous poisoning.

We are selecting certain cases and if you are found eligible, after filling up the questionnaire, 10 ml blood will be collected from you. You will also undergo ECG, Biochemistry, and arterial blood gas measurement. These tests and special studies do not affect your final report or management.

The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.

The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of the investigator

Signature of the Participant/impartial witness

Date:

Date:

ஆராய்ச்சி தகவல் தாள்

ஆராய்ச்சி தலைப்பு:

ஆர்கனோ பாஸ்பரஸ் நச்சு பொருள் உட்கொள்வதால் ஏற்படும் விளைவு மற்றும் தீவிரத்தன்மையை அளவிடுதலில் அப்பாச்சி-II அளவீட்டின் (APACHE II SCORE) பயன்பாட்டினை ஆராய்தல்.

இந்த ஆராய்ச்சி ராஜிவ் காந்தி அரசு பொது மருத்துவமனையில் நடைபெற உள்ளது.

இது ஆர்கனோ பாஸ்பரஸ் நச்சு பொருள் உட்கொள்வதால் ஏற்படும் விளைவு மற்றும் தீவிரத்தன்மையை அளவிடுதலில் அப்பாச்சி-II அளவீட்டின் பயன்பாட்டினை ஆராயும் பொருட்டு மேற்கொள்ளபடுவது.

நீங்களும் இந்த ஆராய்ச்சியில் பங்கு கொள்ள நாங்கள் விரும்புகிறோம். இதற்காக உங்கள் உடலில் இருந்து 10 மி.லி. இரத்தம் மட்டும் எடுக்கப்படும்.

முடிவுகளை அல்லது கருத்துக்களை வெளியிடும் போது உங்கள் பெயரயோ, அடையாளங்களையோ வெளியிடமாட்டோம்.

இந்த ஆராய்ச்சியில் பங்கு கொள்வது உங்கள் விருப்பத்தின் பேரில் மட்டும் தான் இருக்கிறது. இதிலிருந்து எந்த நேரமும் நீங்கள் பின்வாங்கலாம். இதிலிருந்து நீங்கள் பின்வாங்கினாலும் உங்கள் சிகிச்சை எந்த வகையிலும் பாதிக்கப்படாது.

இந்த பரிசோதனை முடிவுகளை ஆராயச்சியின் போதோ அல்லது ஆராய்ச்சி முடிவின் போதோ உங்களுக்கு அறிவிப்போம் என தெரிவித்து கொள்கிறோம்.

ஆராய்ச்சியாளர் கையொப்பம்

பங்கேற்பாளர்/ பாதுகாவலர் கையொப்பம்

தேதி:

PATIENT CONSENT FORM

Study Title	:	Evaluating the use of *APACHE II* score in predicting the severity and clinical outcomes of organophosphorous poisoning
Study Centre	:	Rajiv Gandhi Government General Hospital, Chennai.
Name	:	
Age/Sex	:	
Identification Number	:	

Patient may check (☑) these boxes

- The details of the study have been provided to me in writing and explained to me in my own language ❑
- I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected. ❑
- I understand that investigator of the clinical study, others working on the investigators's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study. ❑
- I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well being or any unexpected or unusual symptoms. ❑
- I hereby consent to participate in this study. ❑
- I hereby give permission to undergo complete clinical examination and diagnostic tests including hematological and biochemical tests. ❑

Signature/thumb impression of Patient/impartial witness
Name:
Address:

Signature of Investigator
Study Investigator's Name:
Dr. VIVEKANANDAN A

சுய ஒப்புதல் படிவம்

***<u>ஆராய்ச்சி தலைப்பு</u>*:**

ஆர்கனோ பாஸ்பரஸ் நச்சு பொருள் உட்கொள்வதால் ஏற்படும் விளைவு மற்றும் தீவிரத்தன்மையை அளவிடுதலில் அப்பாச்சி-II அளவீட்டின் (APACHE II SCORE) பயன்பாட்டினை ஆராய்தல்.

பெயர்: *தேதி:*

வயது: *உள்நோயாளி எண்:*

பால்: *ஆராய்ச்சி சேர்க்கை எண்:*

இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கங்களும் முழுமையாகவும் தெளிவாகவும் எனக்கு விளக்கப்பட்டது. எனக்கு விளக்கப்பட்ட விஷயங்களை நான் புரிந்து கொண்டு நான் எனது சம்மதத்தை தெரிவிக்கிறேன்.

மேற்கொண்ட பரிசோதனையின் போது ஏற்படக்கூடிய பின்விளைவுகளை முழுவதும் உணர்ந்து இந்த பரிசோதனைக்கு மனமார சம்மதிக்கிறேன்.

இந்த ஆய்விற்கான பரிசோதனை செய்துகொள்ள சம்மதிக்கிறேன். *இந்த ஆராய்ச்சியின் விளக்கத்தாளை பெற்றுக்கொண்டேன் இந்த ஆய்வை முழு சுதந்திரத்துடன் மற்றும் சுய நினைவுடன் பங்கு கொள்ள சம்மதிக்கிறேன்*

பங்கேற்பாளர்/ பாதுகாவலர் கையொப்பம்

தேதி:

SL. NO	IP NO	AGE	AGE GROUP	SEX	SUBSTANCE CONSUMED	TIME ELAPSED SINCE CONSUMPTION TO ADMISSION	WHO SCALE OF POISON	CHRONIC HEALTH HISTORY	RECTAL TEMPERATURE	GCS	MAP	HEART RATE	RR	PH	OXYGENATION	SR. UREA	SR. CREATININE	SERUN NA	SERUM K	HCT	WBC COUNT	OUTCOME	APACHE II SCORE
1	85113	37	1	M	12	1	3	2	38.2	15	70	56	28	7.14	230.8	36	1.4	146	2.2	38	11300	1	9
2	82778	48	2	M	1	1	1	2	37.4	15	80	124	25	7.39	75	49	1.3	143	3.2	42	14200	1	6
3	85363	24	1	M	9	1	3	2	37.9	7	123	102	29	7.24	147	52	1.7	135	3.5	46	15800	2	19
4	82239	58	3	M	1	1	1	2	37	9	68	124	32	7.18	56	50	1.9	135	4.1	43	11200	2	27
5	85202	41	1	M	4	2	2	2	38	15	83	100	18	7.38	154	23	0.8	139	4	46	9200	1	0
6	84331	24	1	M	8	1	3	2	37.1	15	69	110	20	7.42	132	35	0.9	134	3.6	45	8400	1	2
7	81570	48	2	F	9	1	3	2	38.3	15	106	80	14	7.36	118	24	0.8	134	3.1	38	6800	1	3
8	81427	24	1	M	5	2	2	2	37.1	12	80	65	18	7.35	145	35	1	134	3.2	42	8400	1	6
9	80241	50	2	M	8	1	3	2	37.8	11	105	54	22	7.37	110	41	1.1	139	3	38	6600	1	10
10	79086	55	3	M	9	2	3	2	37.9	12	120	70	16	7.41	98	56	1.4	140	4.5	32	5800	1	8
11	78701	55	3	M	12	2	3	2	37.4	13	118	54	19	7.46	101	61	1.6	142	4.5	40	9200	1	12
12	77371	24	1	F	4	1	2	2	40.2	12	80	57	24	7.48	121	28	1.2	129	3.7	35	10500	1	10
13	77327	23	1	M	1	2	1	2	38.7	11	83	64	28	7.31	118	18	1	138	3.5	46	6300	1	11
14	75744	20	1	M	4	2	2	2	39	10	93	78	20	7.38	159	29	0.9	136	2.9	44	7100	1	10
15	72688	24	1	F	15	1	3	2	39.1	15	93	50	21	7.39	117	31	0.8	145	3	30	7900	1	6
16	72736	24	1	M	12	1	3	2	37.4	13	83	60	20	7.42	101	34	0.8	134	3.9	41	7300	1	4
17	72688	55	3	M	4	2	2	1	36.2	8	60	49	18	7.29	61	54	1.4	142	4.9	43	11200	2	22

SL. NO	I.P. NUMBER	AGE	AGE GROUP	SEX	SUBSTANCE CONSUMED	TIME ELAPSED SINCE CONSUMPTION TO ADMISSION	WHO SCALE OF POISON	CHRONIC HEALTH HISTORY	RECTAL TEMPERATURE	GCS	MAP	HEART RATE	RR	PH	OXYGENATION	SR. UREA	SR. CREATININE	SERUN NA	SERUM K	HCT	WBC COUNT	OUTCOME	APACHE II SCORE
18	72226	18	1	F	1	2	1	2	37.2	12	70	50	28	7.33	89	36	1	136	4.1	34	5400	1	6
19	71900	53	2	M	12	1	3	2	39.2	11	128	57	17	7.34	126	32	0.9	143	4.4	39	4600	1	13
20	71047	27	1	F	4	1	2	2	37	12	83	64	24	7.4	156	29	0.8	140	4	43	4900	1	5
21	70644	55	3	M	9	1	3	2	38	10	100	59	24	7.42	160	38	1.2	144	4.9	37	4700	1	7
22	69946	65	4	M	4	1	2	2	36	7	103	49	11	7.24	65	44	1.6	144	5.1	40	8900	2	18
23	69921	18	1	M	11	1	3	2	37.4	13	83	74	16	7.34	121	28	0.8	139	4.2	44	5600	1	2
24	69743	35	1	F	12	1	3	2	37.1	12	80	59	18	7.3	70	40	1.1	141	4.6	32	7200	1	7
25	67282	34	1	M	11	2	3	2	38	10	100	60	14	7.34	89	45	1.4	132	3.6	28	8100	1	9
26	66421	26	1	M	4	1	2	2	37.2	11	90	54	16	7.35	90	40	1.1	137	3.5	45	7300	1	7
27	65310	18	1	M	5	1	2	2	38.6	10	80	64	28	7.34	66	35	1	132	3.1	38	7700	1	10
28	65100	20	1	M	1	1	1	2	38.4	11	90	78	16	7.36	178	28	0.9	137	3.6	39	4900	1	4
29	64071	46	2	M	6	2	2	2	37.8	10	106	62	21	7.38	144	40	1.1	145	5	33	6700	1	7
30	63018	26	1	M	1	1	1	2	36.7	7	63	56	29	7.3	54	45	1.2	141	4.7	39	7100	2	19
31	59524	35	1	M	4	2	2	2	36.1	6	70	50	26	7.28	58	40	0.9	143	4.2	37	8900	2	18
32	57685	22	1	M	4	1	2	2	37.1	11	80	64	20	7.34	129	41	1.1	142	4.6	39	15600	1	6
33	56338	50	2	M	12	1	3	2	36.8	12	133	69	17	7.36	144	39	1.2	144	4.1	38	7300	1	5
34	55044	19	1	F	8	1	3	2	37.4	12	70	71	22	7.37	138	27	0.8	138	3.9	28	5400	1	5
35	58037	24	1	M	4	1	2	2	37.8	12	70	64	21	7.35	114	32	0.9	135	3.5	42	5900	1	5
36	54548	45	2	M	8	1	3	2	37.7	11	70	62	18	7.38	98	42	1.1	129	3.6	38	5200	1	6
37	54588	65	4	M	11	2	3	2	36.9	8	123	52	14	7.28	62	41	0.9	134	4.6	36	9400	2	15

SL. NO	IP NO	AGE	AGE GROUP	SEX	SUBSTANCE CONSUMED	TIME ELAPSED SINCE CONSUMPTION TO ADMISSION	WHO SCALE OF POISON	CHRONIC HEALTH HISTORY	RECTAL TEMPERATURE	GCS	MAP	HEART RATE	RR	PH	OXYGENATION	SR. UREA	SR. CREATININE	SERUN NA	SERUM K	HCT	WBC COUNT	OUTCOME	APACHE II SCORE
38	54889	21	1	M	4	1	2	2	38.1	13	83	61	20	7.36	102	35	0.8	139	4	42	8400	1	4
39	54555	47	2	M	8	1	3	2	37.6	14	96	74	18	7.38	124	32	0.9	140	3	39	6200	1	2
40	54069	52	2	F	1	1	1	2	38.1	11	83	64	26	7.37	102	39	1	141	3.5	28	7300	1	8
41	53705	32	1	M	6	2	2	2	37.2	13	80	70	18	7.38	110	32	0.9	129	3.2	36	6600	1	5
42	52900	22	1	F	1	1	1	2	36.4	11	70	82	21	7.39	95	29	0.8	131	3.7	33	5600	1	4
43	51603	38	1	M	6	2	2	2	36.8	13	80	68	22	7.35	84	35	0.7	139	3.8	40	7400	1	4
44	51423	23	1	M	9	2	3	2	37	13	93	70	16	7.41	100	31	0.8	132	3.6	42	5400	1	2
45	51402	44	1	M	13	1	3	2	37.2	15	83	78	14	7.43	138	30	0.7	129	3.7	44	5100	1	2
46	51063	60	3	M	7	2	3	2	35.2	7	60	54	24	7.22	50	59	1.8	140	5.2	38	12600	2	25
47	50713	30	1	M	5	1	2	2	36.8	15	83	82	14	7.42	98	34	1.1	134	3.1	43	4600	1	1
48	50588	30	1	M	8	1	3	2	37.6	13	83	84	16	7.4	119	31	0.9	138	3.6	39	4900	1	2
49	49425	27	1	F	4	1	2	2	37.4	13	70	61	19	7.35	94	37	0.8	136	3.9	30	7100	1	4
50	48747	25	1	M	1	1	1	2	38.1	14	80	79	14	7.38	101	25	0.8	133	3.6	43	6200	1	1
51	43665	38	1	M	11	1	3	2	37.2	13	106	68	17	7.34	123	40	1	128	3.1	36	5800	1	7
52	48669	35	1	M	10	1	3	2	37.8	14	103	74	13	7.37	97	36	0.8	132	3.7	39	4700	1	1
53	48599	26	1	M	11	1	3	2	36.9	13	83	78	17	7.39	88	33	0.7	137	3.4	44	5600	1	3
54	48763	22	1	F	4	1	2	2	36.3	12	80	82	24	7.42	98	31	0.9	138	3.6	33	4800	1	3
55	48323	55	3	M	3	1	1	2	36.1	10	73	52	23	7.4	75	42	1.1	141	3.8	35	6900	1	8
56	45008	44	1	M	12	2	3	2	37.2	13	83	78	19	7.4	98	36	0.9	134	3.2	39	7200	1	3
57	45745	45	2	M	5	2	2	2	36.1	6	70	50	29	7.24	62	59	1.5	130	3.3	36	9000	2	17
58	45350	34	1	M	9	1	3	2	35.4	7	63	66	25	7.21	50	110	3.2	138	5.6	39	7800	2	24
59	45000	48	2	M	8	1	3	2	36.8	8	126	58	21	7.3	65	40	1	134	3.6	34	5600	2	12

SL. NO	IP NO	AGE	AGE GROUP	SEX	SUBSTANCE CONSUMED	TIME ELAPSED SINCE CONSUMPTION TO ADMISSION	WHO SCALE OF POISON	CHRONIC HEALTH HISTORY	RECTAL TEMPERATURE	GCS	MAP	HEART RATE	RR	PH	OXYGENATION	SR. UREA	SR. CREATININE	SERUN NA	SERUM K	HCT	WBC COUNT	OUTCOME	APACHE II SCORE
60	44964	66	4	F	4	1	3	1	36.2	6	63	55	36	7.35	30	35	1	137	3.8	30	7800	2	19
61	43675	52	2	M	11	1	3	2	36.8	13	110	56	16	7.41	100	30	0.9	129	3.5	36	4600	1	10
62	43244	53	2	M	6	1	2	2	37.2	7	100	51	21	7.21	40	54	1.4	131	3.7	33	4300	2	20
63	43204	55	3	M	7	1	3	2	38	14	103	54	14	7.36	92	28	1	137	4.1	35	5700	1	7
64	42458	58	3	M	6	1	2	2	38.2	12	123	62	18	7.4	117	27	0.9	134	4.6	38	5900	1	10
65	41693	19	1	M	10	1	3	2	37.1	13	83	63	13	7.33	92	18	0.9	135	4.5	42	7000	1	4
66	41234	47	2	M	11	1	3	2	37.4	13	80	65	19	7.41	104	34	0.8	133	4.2	39	3600	1	6
67	40193	18	1	M	1	1	1	2	36.8	12	80	69	21	7.45	90	39	0.9	134	4	44	4800	1	5
68	40168	24	1	F	14	1	3	2	36.6	13	93	61	14	7.41	88	40	1	141	3.7	33	5500	1	4
69	39593	45	2	M	11	1	3	2	37.1	14	93	50	12	7.49	113	23	0.7	145	3.8	38	4900	1	6
70	39344	18	1	F	4	1	2	2	37	13	63	57	16	7.47	96	29	0.8	111	3.5	35	7200	1	9
71	37690	22	1	M	8	2	3	2	38.2	13	73	60	18	7.44	80	25	0.7	130	4.1	44	5700	1	4
72	36788	38	1	M	9	1	3	2	36.4	13	93	64	11	7.41	79	40	0.9	142	4	36	3700	1	5
73	35894	28	1	M	1	1	1	2	36.9	12	56	62	14	7.24	48	64	1.6	140	3	39	9600	2	19
74	35385	27	1	F	3	1	1	2	37	8	70	70	17	7.36	124	19	0.7	132	3.6	24	7500	1	9
75	35008	44	1	M	5	1	2	2	37	11	70	74	19	7.38	112	27	0.8	146	3.5	40	5300	1	4

KEY TO MASTER CHART

AGE GROUP:

<45	:	1
45 – 54	:	2
55 – 64	:	3
>75	:	4

SUBSTANCE CONSUMED:

Methyl parathion	:	1
Phosphamidon	:	2
Phorate	:	3
Monocrotophos	:	4
Triazophos	:	5
Dichlorvas	:	6
Quinalphos	:	7
Chlorpyriphos	:	8
Dimethoate	:	9
Fenthion	:	10
Prophenophos	:	11
Phenthoate	:	12
Acephate	:	13
Ethion	:	14
Malathion	:	15
Temephos	:	16
Tetra chlorinphos	:	17

WHO CLASS:

Class Ia	:	1
Class Ib	:	2
Class II	:	3
Class III	:	4

TIME ELAPSED:

<6hr	:	1
6 – 12 hours	:	2
13 – 24 hours	:	3
>24 hours	:	4

CHRONIC HEALTH STATUS:

Yes	:	1
No	:	2

OUTCOME:

Survivor	:	1
Non survivor	:	2