DISSERTATION ON

"A CROSS SECTIONAL STUDY OF RELATION OF CREATINE PHOSPHO KINASE-MB LEVELS WITH ELECTROCARDIOGRAM PARAMETERS IN ORGANOPHOSPHOSPHORUS POISONING"

submitted to

THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY

CHENNAI, TAMIL NADU

In partial fulfilment of the regulations for the award of the degree of

M.D.BRANCH -I (GENERAL MEDICINE)

REGISTRATION NUMBER : 201911064

DEPARTMENT OF GENERAL MEDICINE

GOVERNMENT STANLEY MEDICAL COLLEGE AND HOSPITAL

CHENNAI

MAY - 2022

CERTIFICATE

This is to certify that this dissertation entitled **"A Cross sectional study of relation of Creatine Phospho Kinase-MB levels with Electrocardiogram Parameters in Organophosphosphorus poisoning"** submitted by **Dr. R. LOGESH** to the faculty of General Medicine, The Tamil Nadu Dr. M.G.R Medical University, Chennai, in partial fulfilment of the requirement for the award of M.D Degree Branch-I (General Medicine) is a bonafide research work carried out by him under direct supervision and guidance.

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DECLARATION

I solemnly declare that the dissertation titled **"A Cross sectional study of relation of Creatine Phospho Kinase-MB levels with Electrocardiogram Parameters in Organophosphosphorus poisoning"** is a bonafide work done by me at Government Stanley Medical College and Hospital, Chennai between March 2021 and September 2021 under the guidance and supervision of **Prof. Dr.S. Kalaichelvi M.D.** I also declare that this bonafide work or a part of this work was not submitted by me or any other forward degree or diploma to any other university, board either in India or abroad. This dissertation is submitted to the Tamilnadu Dr. M.G.R Medical University, towards the partial fulfilment of requirement for the award of M.D. Degree (Branch – I) in General Medicine.

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CERTIFICATE – II

This is to certify that this dissertation work titled **"A Cross sectional study of relation of Creatine Phospho Kinase-MB levels with Electrocardiogram Parameters in Organophosphosphorus poisoning"** of the candidate **Dr.R.LOGESH** with Registration Number **201911064** for the award of **M.D. DEGREE** in the branch of **BRANCH-I (GENERAL MEDICINE).** I personally verified the urkund.com website for the purpose of plagiarism check. I found that the uploaded thesis file contains, from introduction to conclusion pages and result, shows 19**%** percentage of plagiarism in the dissertation.

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SPECIAL ACKNOWLEDGEMENT

I gratefully acknowledge and thank

Prof. Dr. P. BALAJI M.S., FRCS., Ph.D., FCLS.,

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Government Stanley Medical College and Hospital, Chennai

For granting me permission to utilise the resources of this Institution for my study.

ACKNOWLEDGEMENT

I would like to express my humble gratitude to The Head of the Department of General Medicine **Prof.Dr.S.Chandrasekar M.D., and** The Head of department of cardiology **Prof.Dr.K.Kannan M.D, D.M (Cardiology)** for accepting and guiding the study.

My sincere thanks to my guide **Prof.Dr.S.Kalaichelvi M.D.,** Chief of Medicine and for her vital guidance and support for the successful completion of my dissertation.

My special thanks to my beloved unit Assistant professor **Dr.K.Lakshmi M.D** and **Dr.M.Narendran M.D, D.M (Cardiology)** and all the faculty of the Department of Medicine for their valuable support throughout the study.

I thank **Prof.Dr.M.P.Saravanan M.D**., Professor and Head of the Department of Biochemistry, Government Stanley Hospital for allowing me in utilising their laboratory facilities for getting the biochemical parameters in the thesis work which were very crucial for the study.

My sincere gratitude to the patients and their attenders for cooperation in the successful conduct of my study.

PLAGIARISM CERTIFICATE

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Document Information

Analyzed document	ECG and CPK-MB in OPC, Dr.logesh.docx (D123655304)
Submitted	2021-12-24T16:12:00.0000000
Submitted by	Logesh
Submitter email	logeshmbbs66@gmail.com
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Sources included in the report

W	URL: https://1library.net/document/9ynldx1q-biochemical-abnormalities-opc-poisoning-prognostic-significance.html Fetched: 2021-12-08T11:25:15.9800000	1
SA	**Tamil Nadu Dr. M.G.R. Medical University / karthi opc dissertation.docx** Document karthi opc dissertation.docx (D122788907) Submitted by: rkarthikeyanmbbs@gmail.com Receiver: rkarthikeyanmbbs.mgrmu@analysis.urkund.com	3
W	URL: http://repository-tnmgrmu.ac.in/13266/1/200100320yagneshwararaja.pdf Fetched: 2021-12-11T12:42:35.8600000	7

ABSTRACT

Introduction:

Organophosphorous compounds are one of the most commonly used compounds for suicides in the developing word. Raised CPK-MB levels and ECG changes are frequently observed among the OPC poisoning patients. In this study we have studied association between CPK-MB levels and ECG changes to predict prognosis in OPC poisoning patients.

Methodology:

A prospective cross-sectional study was conducted among 50 OPC poisoning patients admitted in intensive medical care unit of tertiary care hospital. Age, sex, intention of ingestion, compounds involved, POP score, ECG changes and CPK-MB levels at time of admission and 12 hours after admission were recorded.

Patients with organophosphorous compounds mixed with any other poison or patients who were chronic smokers or suffering from chronic heart diseases, myopathy, intake of drugs like statins, fibrates, dexamethasone were excluded from the study.

Results:

Mean CPK-MB levels were relatively high in OPC poisoning patients. CPK-MB levels in patients with abnormal ECG and normal ECG had significant difference. In patients with polymorphic VT and QTc Prolongation, CPK-MB levels were significantly high. The CPK-MB levels in dead patients were significantly high in

comparison to survived patients. Within each ECG parameter there was significant difference in CPK-MB levels of dead and survived patients.

Conclusion:

CPK-MB levels were frequently high among the OPC poisoning patients. On admission CPK-MB levels were significantly higher in patients with abnormal ECG as compared to normal ECG. Mortality was mainly observed in patients with QTc prolongation and polymorphic VT. Within each ECG parameter significant difference was observed in CPK-MB levels among dead and survived patients.

Keywords

CPK-MB; Organophosphorus compounds; ECG changes.

TABLE OF CONTENTS

INTRODUCTION

INTRODUCTION

Organophosphorus Compounds (OPC) are the most widely used insecticides worldwide. OPC is responsible for 50% of poisoning death in India.(1)

OPC poisoning is an important preventable public health problem in developing countries. Though accidental poisoning can occur following exposure or inhalation, serious poisoning often follows suicidal ingestion.A high incidence of mortality has been reported in past, and is attributed to delay in diagnosis and improper treatment.

Organophosphate compounds are irreversible inhibitors of the enzyme acetyl cholinesterase, binding to the esteric site of the enzyme. They inhibit both cholinesterase and pseudocholinesterase activity. This inhibition causes accumulation of acetylcholine at synapses with resultant overstimulation of neurotransmission.

The clinical features are due to excess acetylcholine at the muscarinic and nicotinic receptors which leads to initial stimulation and eventual exhaustion of cholinergic synapses. Respiratory paralysis and cardiac arrest are considered as the most common causes of death in these patients.

Since agriculture is the main occupation in tamilnadu, OPCs are widely and easily available in ordinary shops. They are often stored in an improper manner due to lack of awareness of their hazards.

Cardiac manifestations often accompany poisoning with these compounds including, hypotension, hypertension, sinus bradycardia, sinus tachycardia & ventricular tachyarrthmias.

Electrocardiographic changes reported in previous studies include Sinus tachycardia, Sinus bradycardia, QTc prolongation, ST-T changes, along with various forms of arrhythmias, which may be serious and fatal. These complications are potentially preventable, if recognised early and treated adequately.(2)

Organophosphate poisoning has been postulated both in animal and human studies to cause myocardial damage. Raised CPK-MB levels have been associated with acute OPC poisoning patients mainly due to skeletal muscle and respiratory muscle involvement. High levels of CPK-MB have been associated with mortality in acute OPC poisoning patients.

Organophosphate compound poisoning itself causes diarrhoea and vomiting which can lead to electrolyte derangements which by themselves may cause electrocardiographic changes.Thus, this study aims at studying the relation between ECG parameters and CPK MB levels in acute OPC poisoning patients which will help in predicting mortality and managing the cardiac complications.

AIM AND OBJECTIVES

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Aim

To study the relation between Electrocardiogram parameters and Creatine Phospho Kinase – MB levels in OPC poisoning to predict prognosis.

Objectives

- To study electrocardiogram parameters and Creatine Phosphokinase -MB levels in OPC poisoning patients

- To correlate electrocardiogram parameters and Creatine Phosphokinase -MB levels with outcome of OPC poisoning patients.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Sources of OPC (3)

- Crop protection sprays
- Baits for cockroaches and other insects. eg-Chlorpyrifos
- Head lice shampoos. eg-Malathion
- Pet washes
- Terrorism- Nerve Agents.eg- Tabun and Sarin

Classification (4)

The term Organophosphorus (OP) refers to any group of organic chemicals which contains phosphorus. Organophosphates are esters of phosphoric acids, in which the nature of the substituents attached to phosphorus plays a key role in determining the toxicity of the agents.

Toxicity	Examples	Applications
High toxicity	Parathion, Phorate, Monocrotophos	Agricultural insecticides
Intermediate toxicity	Chlorpyrifos, Trichorfon	Animal insecticides
Low toxicity	Malathion, Dichlorvos	Household and field sprays

Modes of exposure

- Oral (most common)
- Inhalation
- Skin

Neuromuscular physiology(4) :

Acetylcholine (Ach) :

- Acetylcholine (Ach) is one of the main neurotransmitters of the vertebrate nervous system. It is released at certain (cholinergic) nerve endings and may be excitatory or inhibitory.
- It initiates muscular contraction at neuromuscular junctions. ACh receptors fall into two main classes muscarinic and nicotinic receptors. Once ACh has been released it has only transitory effect because it is rapidly broken down by the enzyme cholinesterase.

Cholinesterase (Acetylcholinesterase) :

- An enzyme that hydrolyses the neurotransmitter acetylcholine to choline and acetate.
- Cholinesterase is secreted by nerve cells at synapses and by muscle cells at neuromuscular junctions.
- Organophosphorus insecticides act as anti-cholinesterases by inhibiting the action of cholinesterase.

Anticholinesterase :

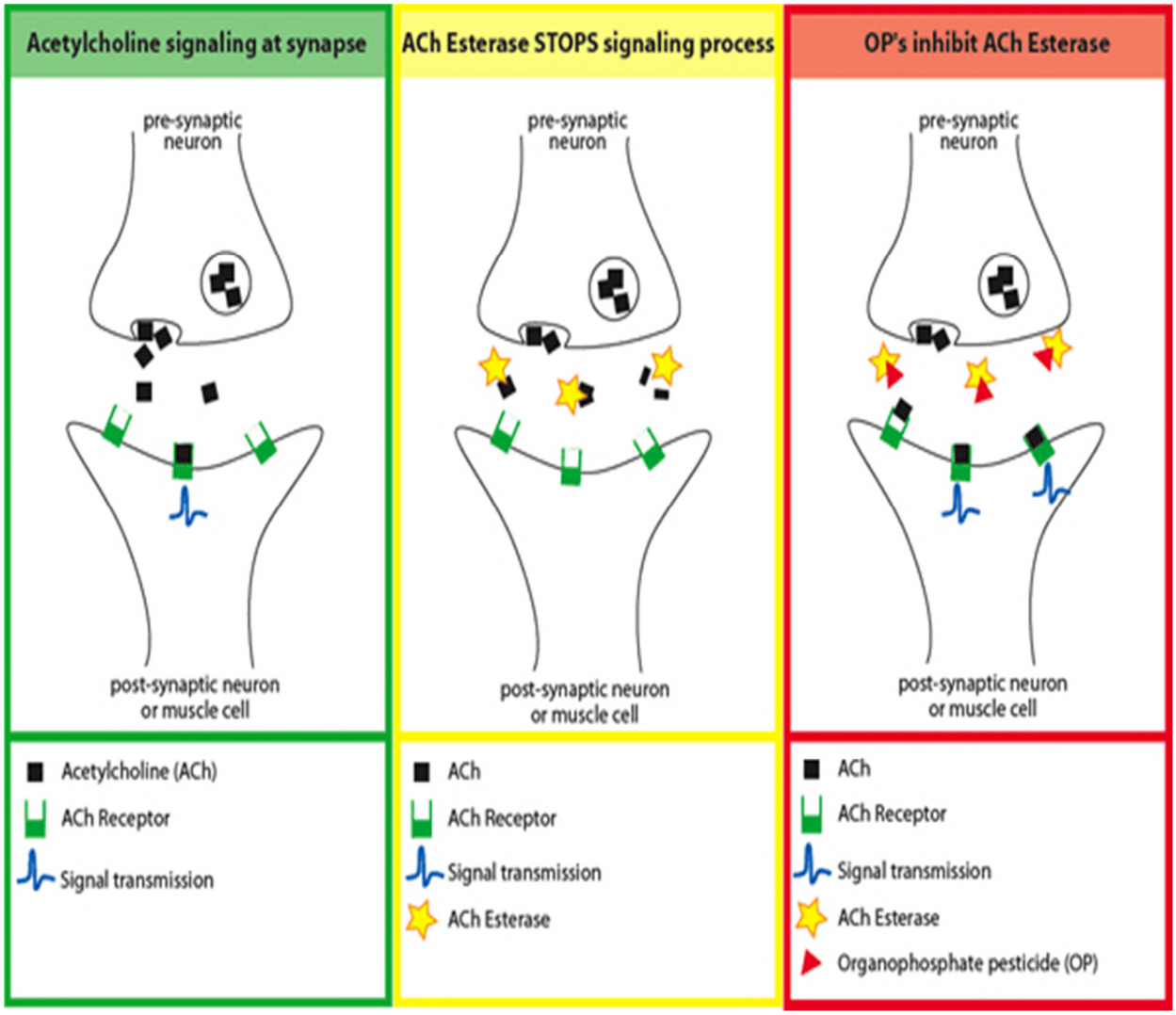
- Any substance that inhibits the enzyme cholinesterase, which is responsible for the breakdown of the neurotransmitter ACh at nerve synapses.
- Anti-cholinesterases, which include certain drugs, nerve gases, and insecticides, cause build-up of acetylcholine within the synapses, leading to disruption of nerve and muscle function.
- In vertebrates, these agents often cause death by paralysing the respiratory muscles.

Events occurring at the neuromuscular junction:

- Propagation of an action potential to a terminal button of motor neuron.
- Opening of voltage gated calcium channels
- Entry of calcium into the terminal button
- Release of ACh by exocytosis
- Diffusion of Ach across the space
- Binding of ACh to a receptor on motor end plate.

Pathophysiology of Organophosphorus compounds(5)**:**

- The effects of OPC on human physiology are multiple and complex. OPC inhibit numerous enzymes of which esterases seem to be the most clinically important.
- Inhibition of acetylcholinesterase leads to the accumulation of ACh at cholinergic synapses, interfering with the normal function of the autonomic, somatic and central nervous systems.



- This produces a range of clinical manifestations known as the acute crisis. Other esterases are also inhibited causing clinically important illnesses. (For eg., Neuropathy target esterases, producing OPC induced delayed polyneuropathy) whereas other esterases such as butrylcholine esterase (also known as pseudo cholinesterase or plasma cholinesterase) and carboxylesterase, do not cause clearly defined illness.
- Butrylcholine esterase hydrolyses exogenously administered pharmaceuticals such as lidocaine and suxamethonium, which may have an effect clinically.
- The organophosphorus-esterase complex undergoes either spontaneous reactivation allowing normal enzymatic function or irreversible inhibition.
- The rate of these competing reactions varies by more than 10 fold between individual OP compounds which influence the clinical manifestations and response to treatments.
- Although clinicians commonly think of OPC as an interchangeable class noticeable differences are observed between individual agents in the clinical manifestations of acute poisoning.
- This may result from differences in pharmacokinetics potency of enzyme inhibition, additional mechanisms of toxicity, such as oxidative stress, dynamic physiological adaptations after prolonged stimulation, difference between patients or a complex interplay of these and other unknown factors.

Acetylcholine actions on receptors and their location

	Muscarinic receptors	Nicotinic receptors
Locations	Smooth muscle, glands and cardiac muscle	N1 – ganglion- post synaptic membrane N2- skeletal muscle motor end plate
Effect	Inhibition of cardiac muscle, Excitation of smooth muscle and glands	N1- excitation of post synaptic neuron
Antagonist	Atropine	N1- hexamethonium N2- decamethonium

Clinical features(6)

Acute toxicity, intermediate syndrome, chronic toxicity

Acute toxicity

- Symptoms as early as five minutes, death within 15 minutes of ingestion can occur.
- Most patients will be symptomatic in 8 to 24 hours.
- Longest delay can occur with compounds requiring metabolic activation- malathion or very lipid soluble agent- Fenthion

Signs and symptoms of organophosphate poisoning

Muscarinic receptors	Nicotinic receptors	Central receptors
Cardiovascular • Bradycardia • Hypotension Respiratory • Rhinorrhoea • Bronchorrhoea • Bronchospasm • Cough Genito-urinary • Urinary incontinence Eyes • Blurred vision • Excessive lacrimation • Miosis Glands • Excessive salivation	Cardiovascular • Tachycardia • Hypertension Musculoskeletal • Weakness • Fasciculation • Cramps • Paralysis	General effects • Anxiety • Restlessness • Ataxia • Convulsions • Insomnia • Dysarthria • Tremors • Coma • Absent reflexes • Respiratory depression • Circulatory collapse

Effects on Cardiovascular system(7)

The mechanism by which organophosphates induce cardiotoxicity is still uncertain.

Ludomirsky et al(8) described three phases of cardiotoxicity in OPC poisoning

Phase 1 : Brief period of increased sympathetic activity

Phase 2 : Prolonged period of parasympathetic activity

Phase 3 : QTc prolongation followed by torsades de pointes ventricular tachycardia and then ventricular fibrillation.

Both these autonomic over activities have been shown to cause myocardial damage. Possible other mechanisms(9) include

- Hypoxemia
- Acidosis
- Electrolyte derangements
- Direct toxic effect of the compounds on the myocardium.

High dose atropine has also been shown to cause ventricular arrhythmias. Hypertension and sinus tachycardia are nicotinic while hypotension and sinus bradycardia are cholinergic manifestations. Though bradycardia dominate the early cholinergic phase, sinus tachycardia and hypertension was a more frequent finding in many studies and was considered as indicators of severe poisoning.

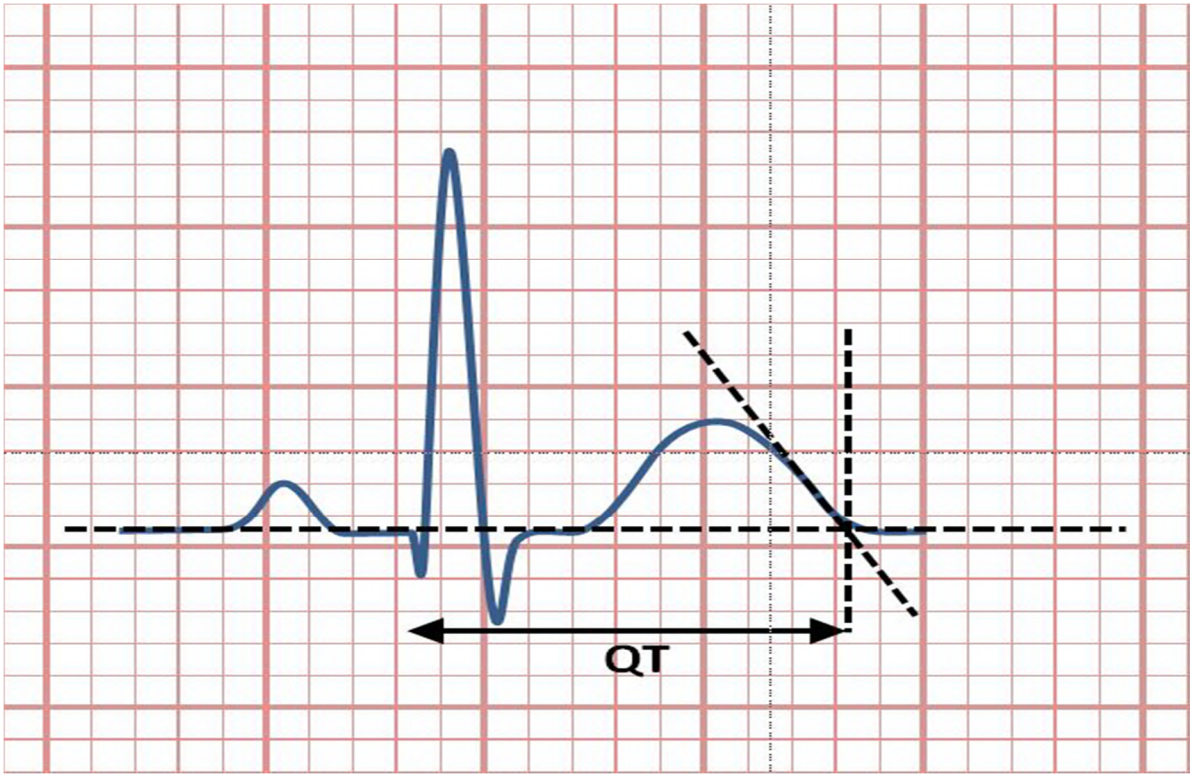
Cardiac complications of OPC poisoning are not appreciated by many physicians. Mostly they occur during early hours of poisoning for which the patient should be transferred immediately to ICU, where proper resuscitative facilities are available. Intensive supportive treatment, meticulous respiratory care, and administration of atropine in adequate doses are the keys to management of cardiac toxicity of organophosphorus compounds.

The management of ventricular arrhythmias in OPC poisoning is difficult and therapy has included, electrical cardioversion, lidocaine, bretylium for tachycardias and atropine, intravenous isoproterenol, magnesium sulphate and pacing for bradycardia.

QT prolongation(8)

QT interval is the time interval between the start of the Q wave and the end of the T wave. In general, the QT interval represents electrical depolarisation and repolarization of ventricles. A prolonged QT interval is a risk factor for ventricular tachyarrhythmias like torsades de pointes VT and a risk factor for sudden cardiac death.

QT interval



The QT interval is dependent on the heart rate (the faster the heart rate the shorter the QT interval and vice versa) and may be adjusted to improve the detection of patients at increased risk of ventricular arrhythmia. A quick but rough assessment to find QT prolongation is that, if QT is more than half of the RR interval, it is supposed to be prolonged but it is not always true.

The standard correction is to use Bazett's formula,

$QTc = QT/\sqrt{RR}$

where QTc is the QT interval corrected for heart rate

RR is the interval from onset of one QRS complex to onset of the next QRS complex, measured in seconds.

Normal QT duration is 0.35 to 0.450 milli Seconds, adjusted to a heart rate.

Prolongation of the QT interval can be categorised into primary and secondary forms. Primary (Congenital) QT prolongation includes underlying gene mutations that result in ion channel malfunction and congenital long QT syndromes.

Based on the malfunction, the long QT syndromes (LQTS) can be due to either excessive sodium inflow or inadequate potassium outflow, resulting in excessive positive intracellular ions and delayed ventricular depolarisation.

Secondary (acquired) QT prolongation can be attributed to

- Electrolyte disturbances (hypokalemia, hypomagnesemia, hypocalcemia)
- Drugs (like Amiodarone, Chloroquine, Macrolides, Fluroquinolones, etc)
- Cerebrovascular disease (intracranial and subarachnoid hemorrhage, stroke)
- Cardiomyopathies (dilated or hypertrophic)
- Altered nutrition (anorexia nervosa, starvation, alcoholism)
- Bradycardia (< 50 beats/min)
- Myocardial ischemia or infarction
- Diabetes mellitus
- Elderly age
- Deep sleep
- Hypertension
- Hypoglycaemia
- Hypothermia
- Hypothyroidism
- Obesity

- Poisoning (arsenic, organophosphates compounds)
- Pituitary insufficiency

Low Voltage Complexes

Diagnostic Criteria

Low QRS voltage is said to be present when the total amplitude of the QRS complexes in each of the six extremity leads is 5 mm or less, or 10 mm or less in the chest leads

Differential Diagnosis

1.Increased Distance

- Pericardial effusion
- Obesity
- COPD with hyperinflation
- Left sided Pleural effusion

2.Constrictive pericarditis

3.Infiltrative Heart Disease

- Scleroderma
- Hemochromatosis
- Amyloidosis

4.Metabolic Abnormality

- Myxoedema

Causes of Inverted T Waves(10)

- T wave inversion in lead III is a normal variant.
- Normal finding in children
- Persistent juvenile T wave pattern.
- Myocardial ischaemia and infarction(11)
- Bundle branch block
- Ventricular hypertrophy (strain pattern)
- Pulmonary embolism
- Hypertrophic cardiomyopathy
- Raised intracranial pressure

- New T-wave inversion (compared with prior ECGs) is always abnormal.

Pathological T wave inversion is usually symmetrical and deep (>3mm).

Studies on ECG changes in OPC poisoning

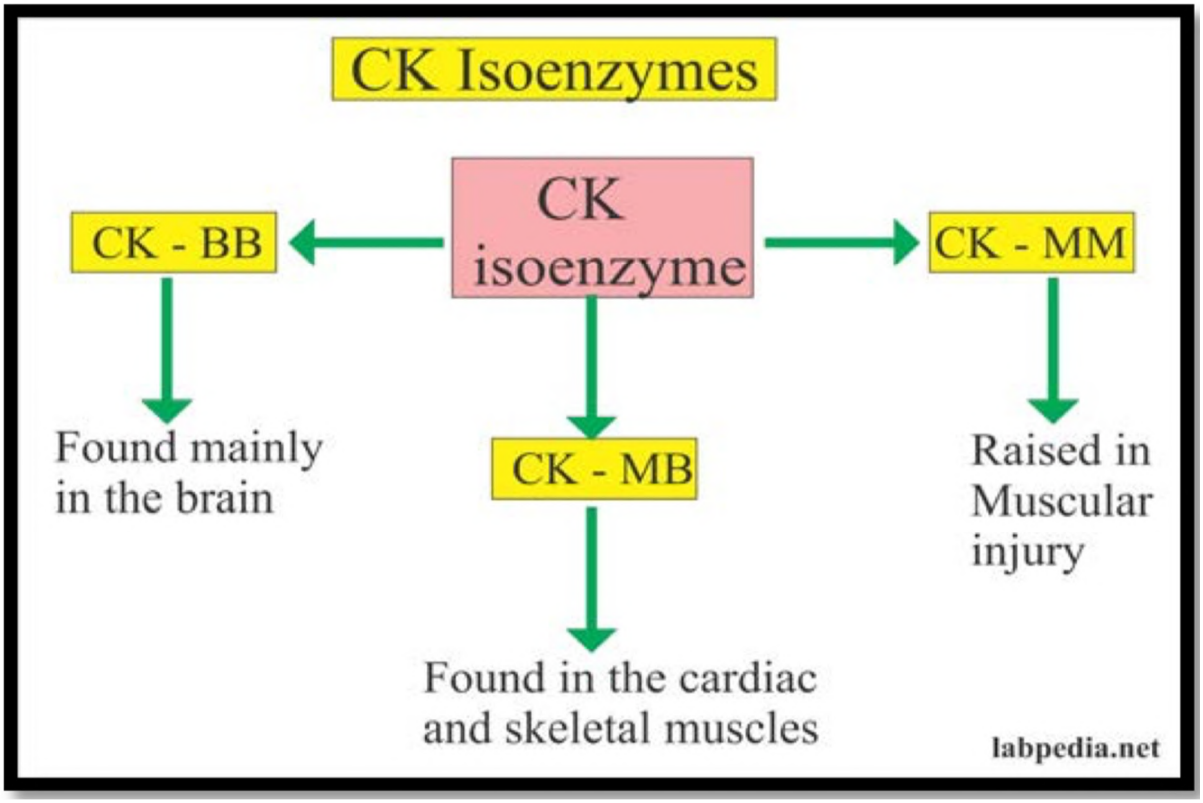
- *SC Chatterjee* et al(12) observed QTc prolongation (63.5%) followed by sinus tachycardia (37.5%) were the most common ECG changes.
- Mathur et al reported sinus tachycardia was the most common abnormality (99.33%) followed by ST-T changes (91.66%), QTc prolongation (35%) and conduction blocks (8.88%).
- Another study from Taiwan by Chuang et al (1996), in 223 cases of organophosphate compound poisoning over 12 years reported the electrocardiographic changes which included, QTc prolongation in 43.5%

patients. These patients had higher mortality (19.6%) and higher incidence of respiratory failure. QTc prolongation also correlated with severity of poisoning.

- Paul, Uttam Kumar, and Anup Kumar Bhattacharyya et al(10) reported ECG changes in 107 patients, prolonged QTc interval was seen in 62.6% patients followed by sinus tachycardia in 33.6% patients. The cause of death was ventricular fibrillation in 5 patients and non-cardiogenic pulmonary oedema in others.

CPK-MB in OPC Poisoning (9,13)

Raised CPK-MB levels have been associated with acute OPC poisoning patients mainly due to skeletal muscle and respiratory muscle involvement.



High levels of CPK-MB have been associated with mortality in acute OPC poisoning patients.

CPK-MB is elevated in many conditions in the absence of cardiac injury such as

- renal failure,
- non cardiac surgery,
- chest trauma,
- asthma,
- pulmonary embolism,
- chronic and acute muscle disease,
- head trauma,
- hyperventilation,
- hypothyroidism.

Ageing of enzyme

- OPC-ACh esterase complex is irreversibly bound for 24 to 72 hours.
- When one of the R group leaves the phosphate molecule, this step is called ageing.
- Denovo synthesis of ACh esterase is required to replenish the supply once ageing has occurred.
- Ageing can not occur in carbamates.
- ACh esterase is spontaneously hydrolysed in 24 hour.
- Ach esterase ageing is rapid with dimethyl compounds such as Malathion, Fenthion, Methyl Parathion, Dichlorvos, etc

- Ageing is slow with diethyl compounds as Parathion, Phorate, Chlorpyriphos, etc will benefit from pralidoxime.
- As a result, it may not be possible to reactivate ACh esterase inhibited by Dimethylated OPs after 12 hour.
- While ACh esterase inhibited by Diethylated Ops may be reactivated for several days after the poisoning.
- Antidotal treatment with an oxime prolong the half life of ageing, early administration of oximes is therefore likely to be valuable.

Pharmacokinetics

- Most OPCs are lipophilic, so adipose tissue accumulation is highest.
- Cholinergic crisis may occur when unmetabolised OPC are mobilised from fat store.
- Prolonged absorption from intestine and reabsorption from fat store may allow the insecticide concentration for up to 48 hours.

Diagnosis(14)

- Diagnosis is based on the history of exposure and the presence of characteristic muscarinic, nicotinic and CNS manifestations of ACh excess.
- There may be a solvent odour and some agents have a strong garlicky odour.

- Laboratory evidence of poisoning maybe obtained by measuring decreases in the plasma pseudocholinesterase (PChE) and red blood cell cholinesterase activities.
- However, because of wide inter-individual variability, significant depression of enzyme activity may occur but still fall within the normal range.
- It is most helpful if the patient had a pre-exposure baseline measurement for comparison.
- PChE activity is a sensitive indicator of exposure but is not as specific as AChE activity. (PChE maybe depressed owing to genetic deficiency, medical illness or chronic organophosphorus exposure).
- PChE activity usually recovers within weeks after exposure, whereas AchE recovery may take several months.

Identification of pesticides

- Identify pesticide at admission to know the patients at risk of developing respiratory failure.
- Monocrotophos and Diamethoate present with early and rapid onset of respiratory paralysis within few hours of ingestion.
- Identify pesticides by history given by patient, container of pesticide and clinical presentation.
- Ask patient to identify pesticide by showing photographs.

Severity assessment: (symptom wise)(15)

Normal serum acetylcholinesterase/RBC cholinesterase level is 8-20 u/l.

Mild	Moderate	Severe
Walks and talks	Cannot walk	Unconscious
Headache, Dizzy Nausea,Vomiting Abdominal pain Sweating, Salivation Rhinorrhea.	Soft voice, Muscle twitching (fasciculations), anxiety, restlessness, small pupils (miosis).	No pupillary reflex, muscle twitching, flaccid paralysis, increased bronchial secretions, Dyspnoea and crackles/wheeze, possible convulsions, respiratory failure.
Serum AchE Results: 1.6- 4.0 u/l	Serum AchE Results: 0.8- 2.0 u/l	Serum AchE Results: < 0.8 u/l

Patient received in emergency department should be classified according to severity, based on symptoms and based on clinical examination so as to predict the outcome and intensity of treatment.

Paredeniya OPC severity scoring (clinical)(16)

Parameter	Criteria	Score
Pupil size	>2 mm	0
	<2 mm	1
	Pinpoint	2
Respiratory rate	<20/min	0
	>20/min	1
	>20/min with central cyanosis	2
Heart rate	>60/min	0
	41-60/min	1
	<40/min	2
Fasciculation	None	0
	Present, generalised/continuous	1
	Both generalised and continuous	2
Level of consciousness	Conscious and rationale	0
	Impaired response to verbal commands	1
	No response to verbal comments	2
Seizures	Absent	0
	Present	1

0-3 : mild poisoning; 4-7 : moderate poisoning; 8-11 : severe poisoning

Management(17)

Unknown poisoning/suspected OPC poisoning

- Use a “atropine test” if you are not sure if the patient has consumed organophosphorus.

- Inject 0.6 – 1 mg iv atropine. If pulse rate goes up by 25 per minute or skin flushing develops patient has mild or no toxicity.

Decontamination

- Skin decontamination- medical personals should use apron or nitrile gloves or double gloves (standard vinyl gloves).
- Skin should be triple washed with soap and water.
- Irrigate exposed eyes with copious tepid water or saline.

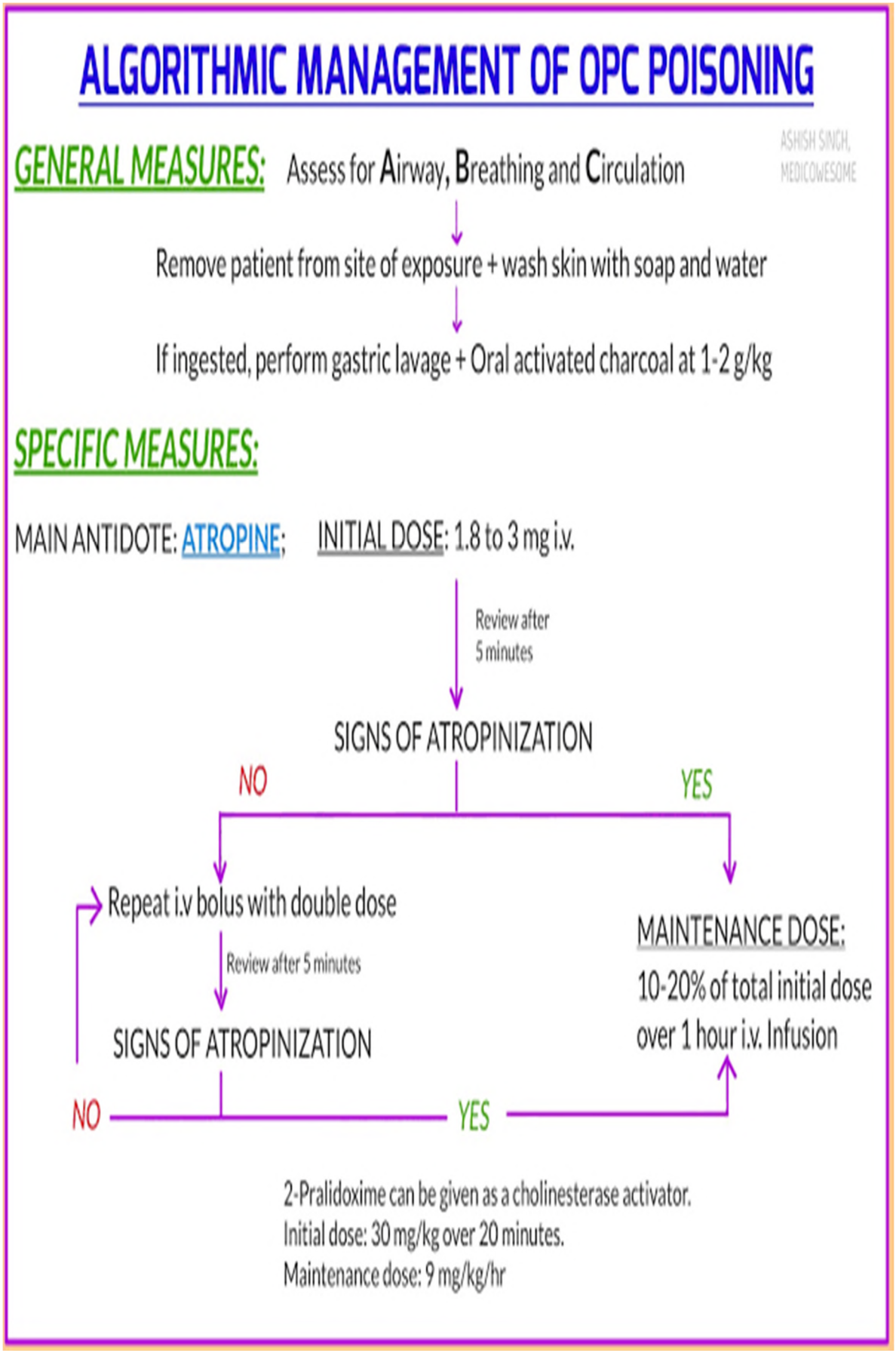
Gastric lavage

- Consider gastric lavage if patient has taken a large amount of highly toxic pesticide.
- Reaches hospital within 1 to 2 hours .
- Larger volumes (more than 300 ML) of fluid may push the poison into the intestines.

Activated charcoal (gut dialysis)

- Effective in preventing the absorption of poison from GIT.
- Dose 1 g/Kg within one hour; repeat the dose every 4 to 6 hourly for 24 hours until it appears in the stools.

ALGORITHMIC MANAGEMENT OF OPC POISONING



Drugs

1) Atropine(18)

- Inject 1.8-3 mg (3-5 ml) of atropine, as bolus.
- Check whether targets are achieved
- Aim for heart rate of > 80 bpm; SBP >80 mm hg or a clear chest (atropine won't dry focal areas of aspiration).
- Double the atropine dose every five minutes, if you have not achieved these targets.
- Review patient every five minutes.
- Once these parameters start improving, repeat last same or small dose of atropine.
- If improvement in these parameters is persistent and satisfactory after five minutes, you can plan for atropine infusion.

Atropine infusion(17,19)

- Calculate total dose of atropine required for rapid atropinisation.
- Start hourly atropine infusion at 20% of total dose of atropine required for atropinisation.
- Most patients do not need >3 to 5 mg/h of atropine infusion.
- Use targets checklist to reduce infusion rate by 20% every 4 hourly once patient is stable.
- Do not use oral secretions to guide therapy in patients who are intubated or unconscious, having oropharyngeal airway and with intermediate syndrome.

- Ignore sweating to adjust atropine dose.
- Stable patients with clear chest but heart rate just below target do not need further more atropine.
- Bronchorrhoea is the most important sign for titrating dose of atropine once patient is stable.
- Atropine toxicity = absent bowel sounds + fever + confusion.
- Stop atropine infusion for 60 minutes, if patient has developed atropine toxicity.
- When features of atropine toxicity like delirium, are confused with CNS effects of the poison or when atropine is not available , glycopyrrolate can be used.
- $MgSO_4$ in addition to atropine and oximes has been found to be beneficial. The mechanism appears to be inhibition of ACh esterase and organophosphorus compound antagonism.
- Diphenhydramine can be an alternative centrally acting anticholinergic agent if atropine is not available.

1) Pralidoxime (PAM)(20,21)

- The main difference in the mechanism of action between OPCs and carbamates is that carbamates spontaneously hydrolyse from the AchE within 24 hours, whereas OPCs undergo ageing.
- Ageing occurs when the phosphorylated AchE non-enzymatically loses an alkyl side chain, becoming irreversibly inactivated.

- Carbamates, however reversibly bind to the active site and do not undergo ageing.
- Organophosphorus binds to the hydroxy component (the esteric site) of the active site of the AchE, thereby blocking its activity. Pralidoxime binds to the other half (the unblocked, anionic site) of the active site and then displaces the phosphate.

How much ?

- Bolus dose: 30 mg/kg pralidoxime over 30 minutes (1-2 g in 100 ml NS over 20 minutes)
- Maintenance dose: continuous infusion of 8 mg/kg/hour (500 mg/hour for 24 hours) until clinical recovery.
- When obidoxime is available a loading dose of 250 mg followed by 0.5 mg/kg per hour infusion.
- Pralidoxime use longer than 24 hours might be indicated when unaged OPCs are redistributed from fat. In such cases it should be continued until patient will become symptoms free.
- It is more useful for diethyl OPCs which undergoes slow ageing than the dimethyl OPCs which undergoes faster ageing.
- The use of pralidoxime is depends on the treating physicians discretion.

How ?

- Pralidoxime must be given as infusion. Go slow for both bolus and maintenance. A fast infusion can cause vomiting, hypertension, cardiac arrhythmia or a cardiac arrest.
- Effectiveness of pralidoxime differs according to the class of organophosphorus compounds. Example in Profenofos, Pralidoxime is not effective.
- Pralidoxime is effective in dimethyl OPCs up to 12 hours and in diethyl OPCs up to 5 days.
- PAM is not generally recommended for carbamate intoxication.
- Because in such cases the cholinesterase inhibition is spontaneously reversible and short lived.
- However, if the exact agent is not identified and the patient has significant toxicity, PAM may be given empirically.

Intermediate syndrome(22–24)

- It usually presents 12 to 96 hours after exposure.
- Early signs of intermediate syndrome are action tremors and pharyngeal weakness (difficulty in deglutition or pooling of secretions in pharynx).
- Later patient develops inability to flex neck, deep tendon jerks are lost, develop cranial neuropathies, proximal muscle weakness and respiratory muscle paralysis.

- Not all patients will develop the full intermediate syndrome requiring intubation and mechanical ventilation, but patients with tremors and pharyngeal weakness are at risk.
- Treatment of intermediate syndrome totally symptomatic.
- Patients will require ventilator support if he develops respiratory muscle paralysis.
- Do not use atropine and unless signs of cholinergic excess are present.
- Common cause of death in organophosphorus poisoning is respiratory failure and complication in management of respiratory failure.

Seizures/sedation

- Agitation and seizures: diazepam 10 mg slow iv, repeated as necessary.
- Up to 30 to 40 mg diazepam for 24 hours can be given.
- Use diazepam infusion for status epilepticus.
- General anaesthetic agents (propofol, midazolam) may be used, if seizures are not controlled by diazepam. Do not use phenytoin, haloperidol or atracurium.

Ventilation(25,26)

- The average respiratory rate of these patients increased from 22 to 38 breaths per minute, which is an important sign of respiratory distress.
- Early recognition of respiratory failure resulting in intubation and mechanical ventilation is a life-saving intervention for patients with OPC poisoning.

- Respiratory failure is the most troublesome complication, which was observed in OPC poisoning patients.
- Patients with OPC poisoning may have respiratory failure for many reasons, including aspiration of gastric content, excessive secretions, pneumonia and sepsis complicated by acute respiratory distress syndrome.

Weaning

- Follow weaning protocols for mechanically ventilated patients.
- Patients develop respiratory failure in intermediate syndrome because of respiratory muscle weakness.
- Assess respiratory muscle performance before weaning off patient from mechanical ventilator.

Indices for respiratory muscle performance(27)

PARAMETER	WEANING THRESHOLD
PaCO2	<50 mm hg
Minute ventilation	<10-15 L/min
Tidal volume	>5 ml/kg
Maximum voluntary ventilation	>20 L/min
Respiratory frequency	<35 breaths/min >6/min

Complications(11,28,29)

Complications resulting from organophosphorous poisoning occur in about 43% of cases with acute intoxication. Death can often occur early (within 24 hours) in untreated cases and upto 10 days in hospital with optimal management.

Early deaths are due to CNS depression, seizures, and ventricular arrhythmias (Eg. Torsades de pointes) or respiratory failure due to excessive bronchial secretions, pulmonary edema, aspiration pneumonia, respiratory muscle paralysis or respiratory center depression.

Late mortality is caused by respiratory failure associated with infection (pneumonia, sepsis) or ventilator related complications.

The pathogenesis is multifactorial and related to aspiration of gastric contents, excessive secretions in the airways, pulmonary infections, pneumonia, sepsis and development of ARDS.

Respiratory consequences of muscarinic overstimulation including rhinorrhoea, bronchorrhea, bronchoconstriction and laryngeal spasm may contribute to respiratory failure. These are often combined with nicotinic effects such as respiratory muscle weakness and paralysis (including paralysis of tongue and nasopharynx).

Central depression of respiratory centre occurs following cholinergic overstimulation of synapses in the brain stem and is a prominent cause of hypoxia, respiratory failure and death in the early period of acute organophosphorous poisoning.

Peripheral neuromuscular block producing respiratory muscle weakness and paralysis as well as intermediate syndrome contributes to the development of respiratory insufficiency at a later stage.

Sudden cardiovascular collapse is often the first indication of unsuspected or incipient respiratory failure, a presentation that is associated with a high mortality.

The development of pneumonia is the most important cause of delayed respiratory failure after organophosphorous poisoning and this occurs in upto 43% of the patients. Upto 80% of patients with pneumonia had respiratory failure; majority of these could be diagnosed within 96 hours of poisoning.

Inadequate or delayed atropinisation appears to be one of the principle reasons for the development of pneumonia and emphasis the importance of skilled medical assessment and treatment at an early stage after poisoning.

Prevention: (30)

Preventive measures should be considered at all the levels of the chain of insecticide movement through the environment-formulation manufacture, mixing application and disposal.

Psychiatric counselling for prevention of second episode should always be given. General counselling and drug therapy for depression should be added. Strict guidelines should be adopted during transport and storage to prevent contamination of food, clothing, drugs, toys, cosmetics and furnishing

Chronic toxicity

- Peripheral neuropathy is common with TOCP (Triorthocresyl phosphate) and chlorpyrifos, primarily affects large distal neurons.
- Pyramidal tract may get affected after months.
- Some of the OPC resemble MPTP chronic toxicity lead on to Parkinsonism.

Chronic organophosphate induced neuropsychiatric disorder (COPIND)(30,31)

- Individuals who have been exposed to high levels of organophosphorus compounds have shown that certain neuro behavioural changes may develop in them, which have been termed together as COPIND.
- These effects include, drowsiness, confusion, lethargy, anxiety, emotional liability, depression, fatigue and irritability.
- Many of the studies of long-term effects of high-dose organophosphorus compounds exposure, are limited by the non-specific nature of these symptoms and by the low sensitivity and specificity of neuro psychological scoring systems.
- On the other hand, some of these symptoms could be attributed to the sequelae of convulsions, anoxia, respiratory failure and cardiac arrhythmias that these patients might have suffered during the acute cholinergic syndrome.
- Chronic neuro-psychiatric disorders like anxiety, depression, problems with memory and concentration have been described in workers exposed to organophosphorus compounds. In addition, dystonic reactions, schizophrenia,

cog-wheel rigidity, choreoathetosis and EEG changes have been reported on high dose exposure.

- These extrapyramidal symptoms are thought to be due to the inhibition of acetylcholinesterase in the human extrapyramidal area. Psychosis, delirium, aggression, hallucinations and depression, may also be seen during recovery from the cholinergic syndrome.
- Other types of delayed neuro-behavioural effects are seen amongst people exposed to low dose of organ of phosphorus compounds for prolonged periods. Levin et al found high level of anxiety in commercial sprayers of insecticides but not in farmers.

OPC induced delayed polyneuropathy (OPIND)(32,33)

OPIND is unrelated to acetylcholinesterase inhibition and occurs because of inhibition of other enzymes, in particular neurotoxic agent esterase. It is characterised by demyelination of long nerves, when neurological dysfunction occurs 1-3 weeks after an acute exposure, particularly motor dysfunction but also sensory dysfunction, which may be chronic or recurrent.

METHODOLOGY

METHODOLOGY

Study setting:

Intensive Medical Care Unit, Department of General Medicine, Government Stanley Medical College Hospital.

Study design :

Cross sectional Study.

Study population :

Patients who have consumed OPC Poison

Inclusion criteria :

Patients with OPC Poisoning who are above 12 yrs of age and above.

Exclusion criteria :

OPC Poisoning mixed with any other poison

Chronic smokers

Chronic heart diseases

Myopathy

Patients taking drugs like statins, fibrates, dexamethasone

Sampling method :

Convenient sampling.

Duration of study :

6 months (April 2021 - September 2021)

Sample size :

Based on the reference study done by sharma et al(9), Rajasthan

Formula:

$n = 2(Z_a+Z_B)^2SD^2/(M_1-M_2)^2$

Where $Z_a = 1.96$ (statistical significant constant for 95% CI)

$Z_B = 0.84$ (80% power)

SD = 75 (Average Standard deviation of Creatine phosphokinase -MB among patients admitted with Organophosphorous poisoning from previous study.)

M_1 =78.45 (Mean Creatine phosphokinase -MB among patients admitted with Organophosphorous poisoning with abnormal ECG from previous study.)

M_2 = 29.25 (Mean Creatine phosphokinase -MB among patients admitted with Organophosphorous poisoning with normal ECG from previous study.)

$(M_1-M_2)^2$ = 2421 (49.2 x 49.2)

On substituting in the formula

n = 15.6 x 75 x 75 / 2421

n = 37

Adding 10% non response rate (ie 10% of 37= 4)

n = 41 (minimum sample size)

Therefore Sample size n = 50 (1 group)

STUDY TOOLS :

•Detailed history, clinical examination, biochemical examinations

•CPK-MB, ECG.

Ethical Clearance :

Institutional Ethical Committee (IEC) permission was obtained.

Data collection :

All patients above the age of 12 years with clinical toxidome suggestive of acute organophosphorous compound poisoning admitted in the intensive care unit of the hospital was included in the study.

On admission the patient was assessed for features of OPC poisoning like pin point pupils, depressed mental status assessed by GCS, secretions, presence of fasciculations, heart rate and respiratory failure evidenced by SPO2<94%.

The following details was obtained in the proforma like age, gender, socio economic status, occupation, accidental or suicidal, name and quantity of the compound and route of exposure.

Serum CPK-MB levels and ECG was recorded on admission and 12 hours after admission.

In ECG rate, rhythm, Axis, PR-Interval, QT- Interval, ST segment and T wave changes was noted.

All patients had routine investigations like CBC, RFT, LFT, serum electrolytes done on the day of admission. Patients clinical parameters was followed up to discharge or death. Complications and outcome was recorded and correlated with the serum CPK-MB and ECG.

ECG was recorded in each case as soon as possible (usually within 15 minutes) after admission. Treatment was not withheld in any case for the purpose of study.

ECG analysis included the rate, rhythm, ST-T abnormalities, conduction defects and measurement of PR and QT interval.

The QT interval was corrected (QTc) according to the formula of Bazett

$$QTc = QT / \sqrt{RR}$$

where QTc is the QT interval corrected for heart rate, and RR is the interval from the onset of one QRS complex to the onset of the next QRS complex, measured in seconds.

The final outcome was registered as death or survival.

Statistical Tools

The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer using Epidemiological Information Package (EPI 2010) developed by Centre for Disease Control, Atlanta.

Using this software range, frequencies, percentages, means, standard deviations, chi square and 'p' values were calculated.

Kruskal Wallis chi-square test was used to test the significance of difference between quantitative variables and Yate’s chi square test for qualitative variables.

A 'p' value less than 0.05 was taken to denote significant relationship

INFORMED CONSENT

NAME :

AGE : SEX :

ADDRESS :

CONTACT :

PRINCIPAL INVESTIGATOR :

GUIDE :

The details of the study have been provided to me in writing in my own language. I confirm that I have understood the above study and had the opportunity to ask questions. I am willing for blood investigations and ECG during the course of study. I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s). I fully consent to participate in the above study.

SIGNATURE OF PARTICIPANT SIGNATURE OF INVESTIGATOR

PLACE:

DATE:

ஆராய்ச் சிஓப்புதல் படிவம்

பெயர்:

வயது: பாலினம்: ஆண் / பெண்

பங்கு பெறுபவர் அடையாள எண்:

இந்த ஆராய்ச் சியின் விவரங்களும் அதன் நோக்கமும் முழுமையாக எனக்கு தெளிவாக விளக்கப்பட்டது.

இந்த சோதனையில் நான் கலந்து கொண்டு ரத்த பரிசோதனைக்ககும் இசிஜி பரிசோதனைக்ககும் சம்மதிக்கிறேன்.

எனக்கு விளக்கப்பட்ட விஷயங்களை புரிந்து கொண்டு நான் எனது சம்மதத்தை தெரிவிக்கிறேன்.

நான் என்னுடைய சுய நினைவுடன் மற்றும் முழு சம்மதத்துடன் இந்த ஆராய்ச் சிக்கு என்னை பரிசோதிக்க சம்மதிக்கிறேன்.

பங்கேற்ப்பாளர் கையொப்பம் ஆராய்ச் சியாளர்கையொப்பம்

இடம் :

நாள் :

ஆராய்ச் சிதகவல் தாள்

பூச்சி மருந்து குடிப்பவர்களுக்கு இருதய பாதிப்பு ஏற்பட வாய்ப்பு உள்ளது. இதனை இரத்தம் மற்றும ECG பறிசோதனை மூலம் கண்டறியலாம. இதனால் தங்களது ஆய்வறிக்கையோ, அன்றாட செயல்பாடுகளோ பாதிக்கப்படாது என்று தெரிவித்துக் கொள்கிறோம்.

ஆராய்ச் சியின் முடிவுகளை அல்லது கருத்துக்களை வெளியிடும் போதோ தங்கள் பெயரையோ அல்லது அடையாளங்களையோ வெளியிட மாட்டோம் என்பதையும் தெரிவித்து கொள்கிறோம்.

இந்த சிறப்பு பரிசோதனைகளின் முடிவுகளை ஆராய்ச் சியின் போது அல்லது அதன் முடிவில் அறிவிக்கப்படும் என்பதையும் தெரிவித்துக்கொள்கிறோம்.

இந்த ஆராய்ச் சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின் பேரில் தான் இருக்கிறது .மேலும் நீங்கள் எந்த நேரமும் இந்த ஆராய்ச் சியிலிருந்து பின் வாங்கலாம் என்பதையும் தெரிவித்துக்கொள்கிறோம்.

பங்கேற்ப்பாளர் கையொப்பம் ஆராய்ச் சியாளர்கையொப்பம்

இடம் :

நாள் :

PROFORMA

Name :

Age : Sex : IP NO: Outcome: Survival / Death

Presenting Complaints :

Compound :

Route of exposure:

Amount ingested :

Time since ingestion :

Altered sensorium :

Increased Salivation:

Increased Lacrimation:

Loose stools:

Vomiting:

Abdominal pain:

Breathing difficulty:

Past history :

DM/SHT/CAD/CVA/CKD/CLD/COPD

Clinical examination

Sensorium

Vitals

BP	
PR	
SPO2	
RR	

CVS

RS

P/A

CNS

POP Score :

INVESTIGATIONS

CPK-MB level On admission: 12 hours after admission :

ECG On admission 12 hours after admission

CBC :

RFT			LFT		
RBS		mg/dl	T.B		mg/dl
UREA		mg/dl	D.B		mg/dl
CREATININE		mg/dl	SGOT		U/l
Na+		mEq/l	SGPT		U/l
K+		mEq/l	ALP		U/l
			T. PROTEIN		g/dl
			ALBUMIN		g/dl

STATISTICAL ANALYSIS

Age distribution of the participants

The mean age of the participants is 37.1 years (S.D=11.5 years).

	AGE
Mean	37.080
Median	35.500
Std. Deviation	11.4835
Minimum	18.0
Maximum	60.0

Table 1: Age distribution of the participants

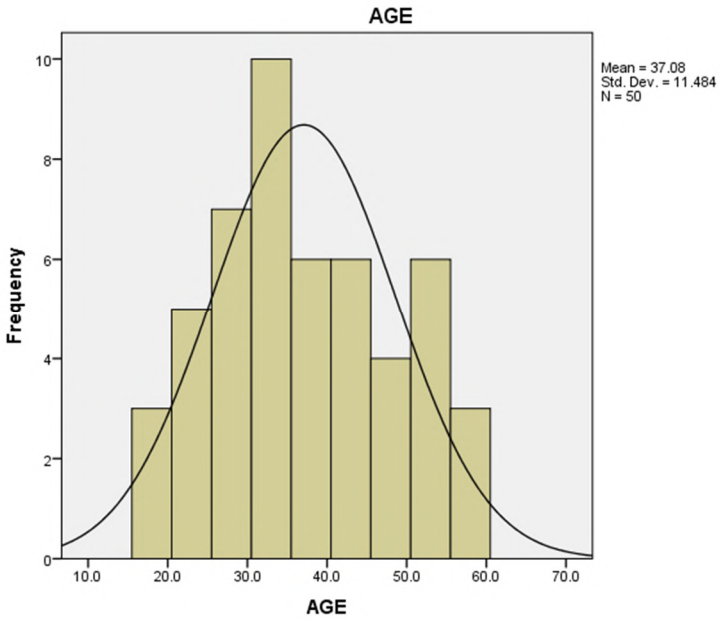


Figure 1: Age distribution of the participants

Gender distribution of the participants

Majority of them were males (n=37, 74%) and the rest were females (n=13, 26%).

SEX		Frequency	Percent
	Female	13	26.0
	Male	37	74.0
	Total	50	100.0

Table 2: Gender distribution of the participants

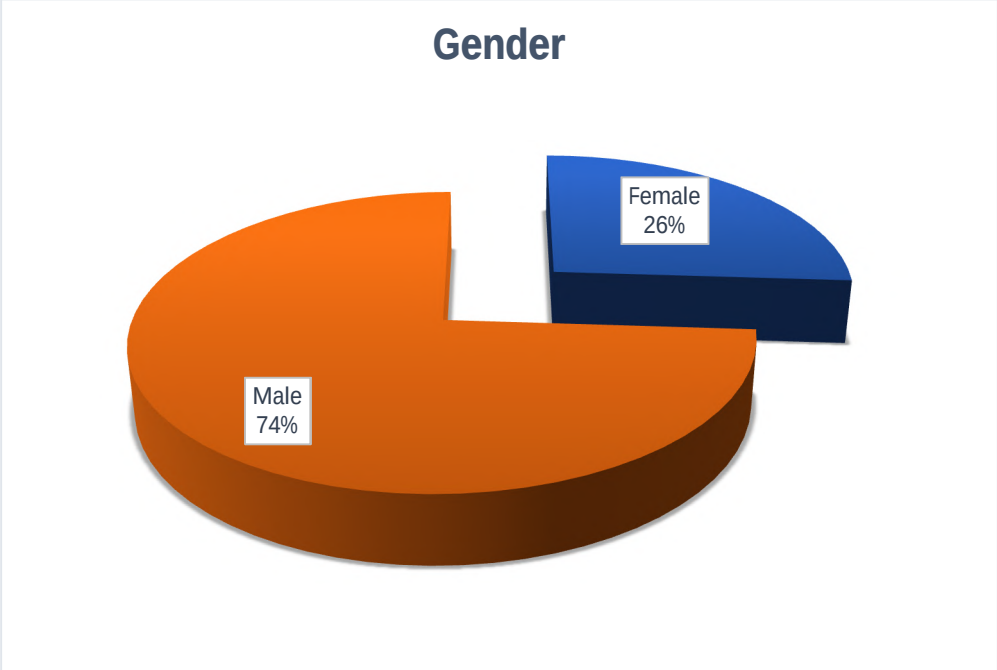


Figure 2: Gender distribution of the participants

Compound ingested

The reason for consumption is suicidal attempt. Majority of them consumed Chlorpyrifos (n=23, 46%) followed by Dimethoate (n=10, 20%).

COMPOUND		Frequency	Percent
	Chlorpyrifos	23	46.0
	Cyclopyrifos	1	2.0
	Dichlorvos	5	10.0
	Dimethoate	10	20.0
	Methyl Parathion	1	2.0
	Monochrotophos	3	6.0
	Parathion	3	6.0
	Phorate	1	2.0
	Quinolphos	3	6.0
	Total	50	100.0

Table 3: Compound ingested

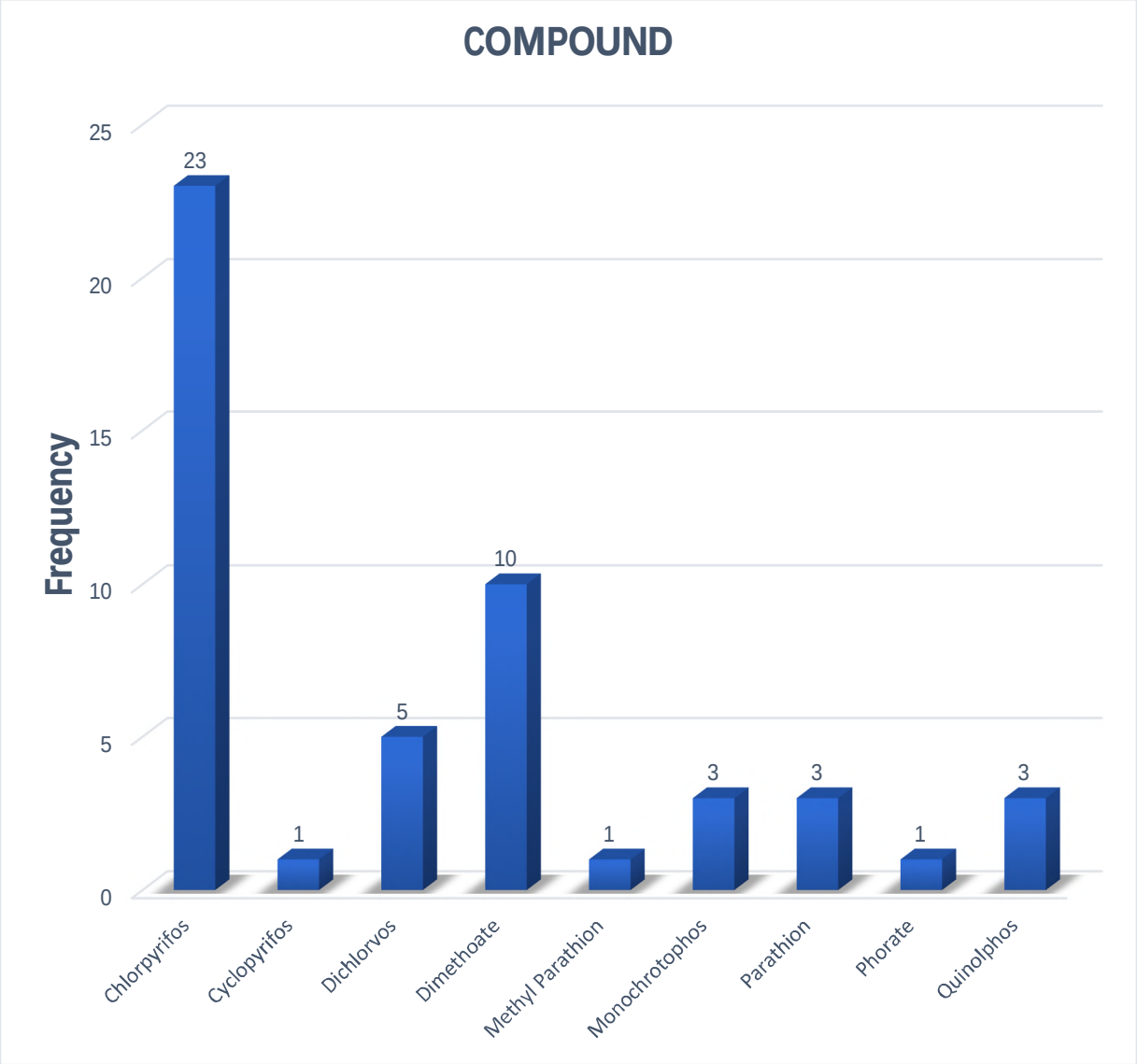


Figure 3: Compound ingested

POP SCORE

Majority of patients had POP score >5 (n=31, 62%).

POP SCORE		Frequency	Percent
	0.0	1	2.0
	2.0	3	6.0
	3.0	7	14.0
	4.0	5	10.0
	5.0	3	6.0
	6.0	7	14.0
	7.0	8	16.0
	8.0	4	8.0
	9.0	6	12.0
	10.0	4	8.0
	11.0	2	4.0
	Total	50	100.0

Table 4: POP SCORE

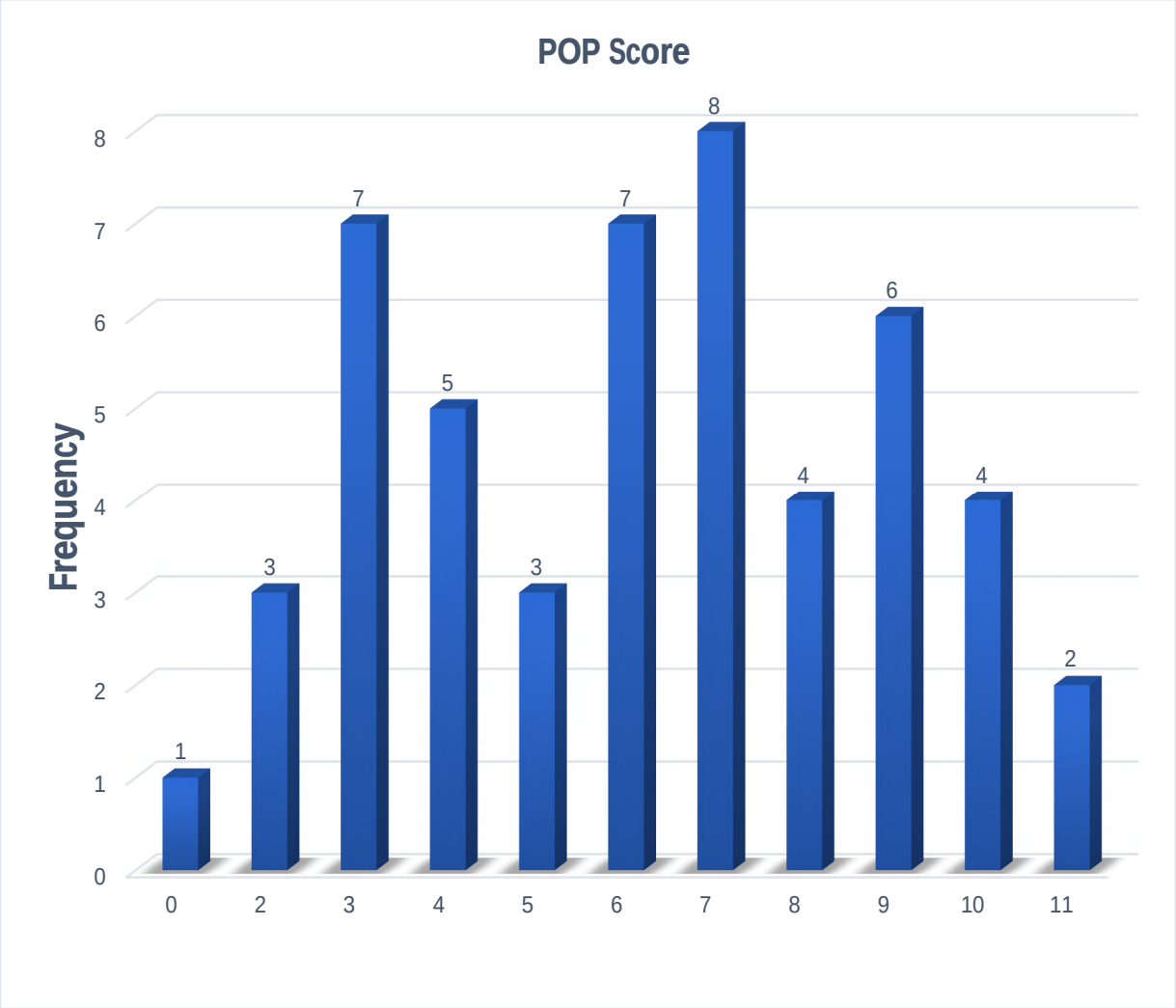


Figure 4: POP SCORE

ECG on admission

Out of 50 patients, ECG on admission was abnormal in 39 patients (78%). QTc prolongation was found in 20% (n=10) of the patients while sinus tachycardia was found in 18% (n=9) and sinus bradycardia was found in 14% (n=7) of the patients.

	ECG on admission	Frequency	Percent
	AV block	1	2.0
	Extrasystole	2	4.0
	Low voltage	2	4.0
	Normal	11	22.0
	PR Prolongation	2	4.0
	QTc prolongation	10	20.0
	Sinus bradycardia	7	14.0
	Sinus tachycardia	9	18.0
	ST Depression	3	6.0
	ST Elevation	2	4.0
	T inversion	1	2.0
	Total	50	100.0

Table 5: ECG on admission

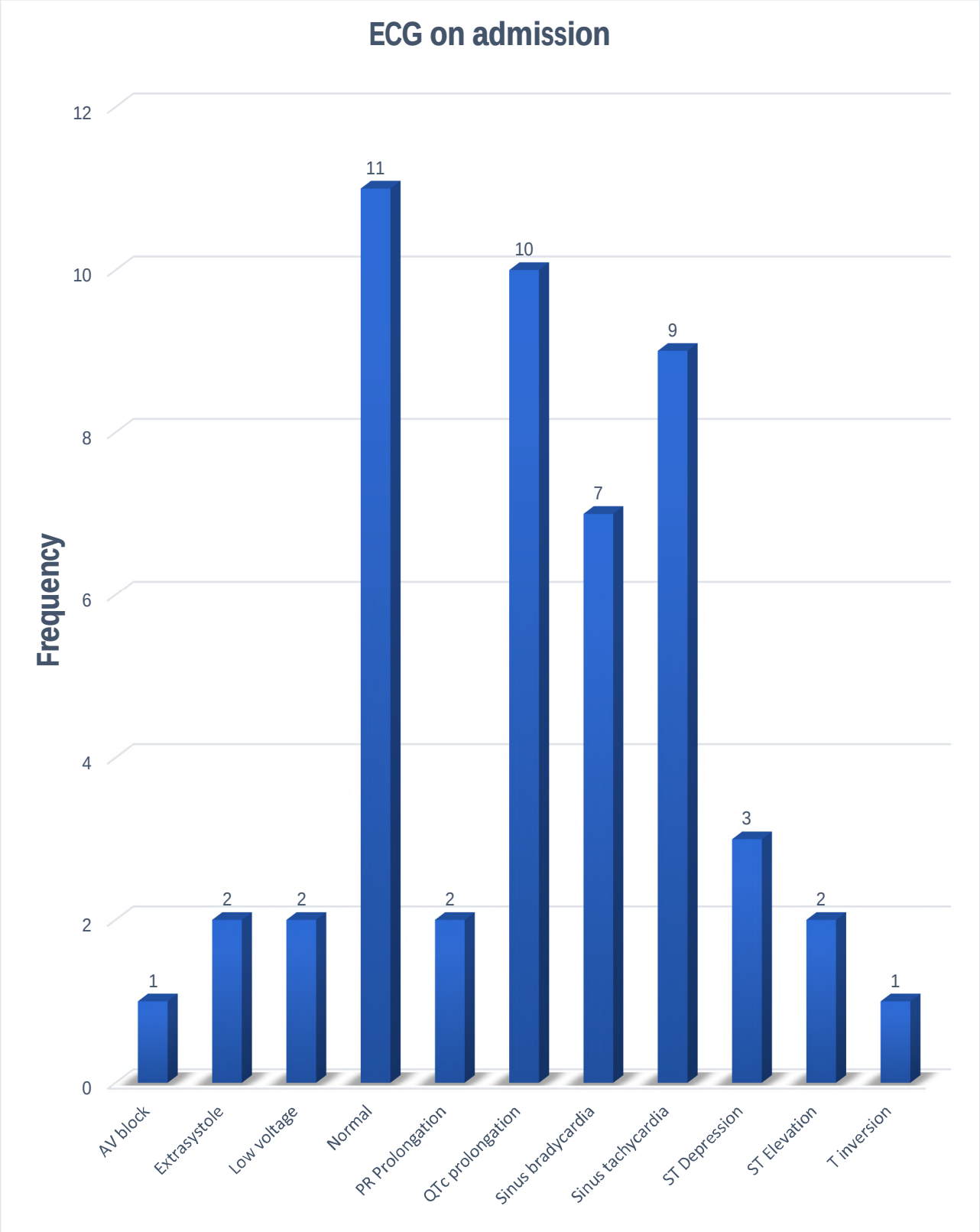


Figure 5: ECG on admission

ECG 12 hours after admission

Out of 50 patients, ECG on admission was abnormal in 37 patients (74%). QTc prolongation was found in 18% (n=9) of the patients while sinus tachycardia was found in 26% (n=13) and sinus bradycardia was found in 2% (n=1) of the patients.

ECG 12 hours after admission	Frequency	Percent
AV Block	1	2
Extrasystole	2	4
Low voltage	2	4
Normal	13	26
PR Prolongation	2	4
pVT	1	2
QTc Prolongation	9	18
Sinus Bradycardia	1	2
Sinus Tachycardia	13	26
ST Depression	3	6
ST Elevation	2	4
T inversion	1	2
Total	50	100

Table 6: ECG 12 hours after admission

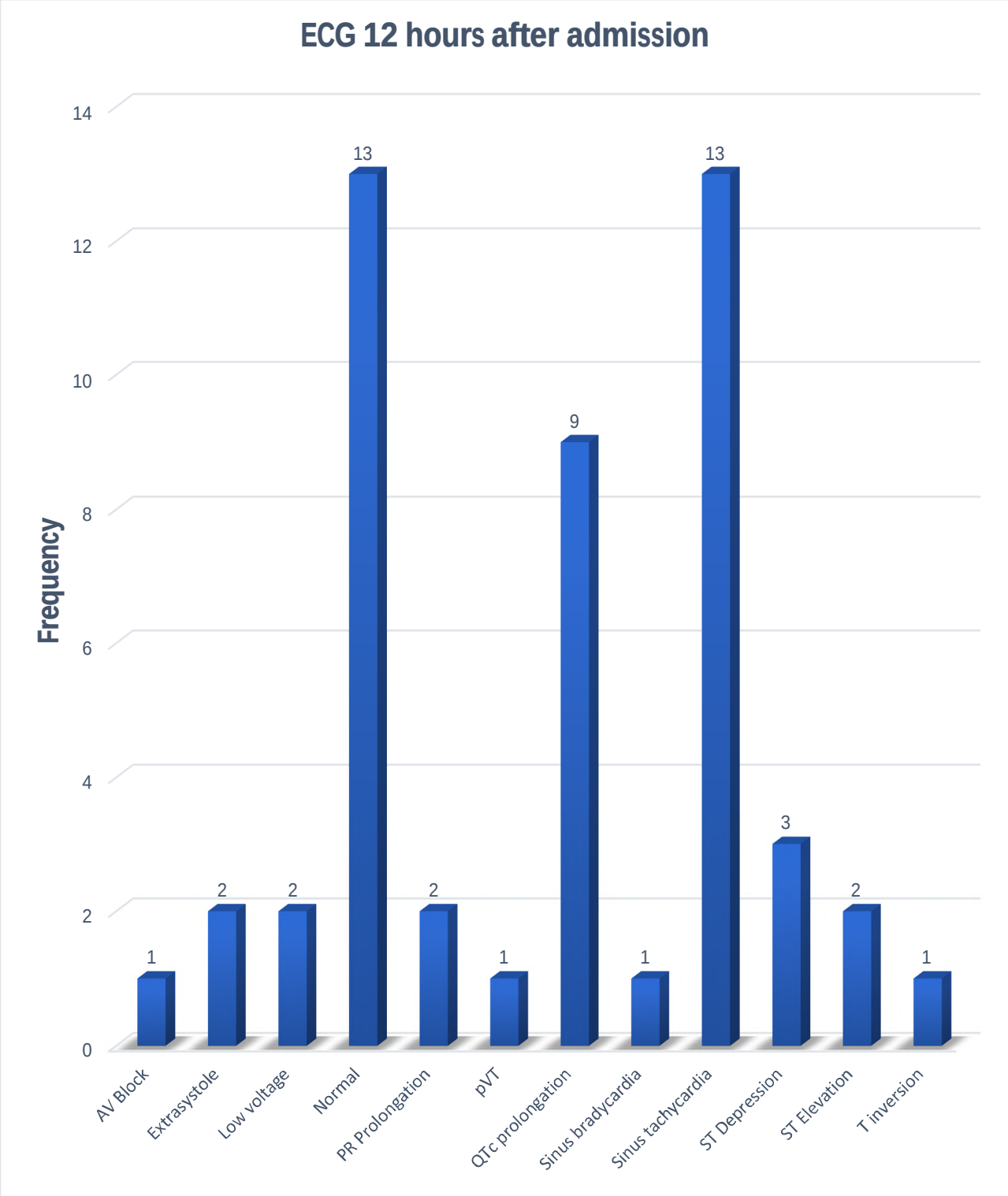


Figure 6: ECG 12 hours after admission

CPK-MB on admission

The mean CPK-MB on admission was 51.1 IU/L.

CPK-MB on admission	Value (IU/L)
Mean	51.060
Median	26.500
Std. Deviation	56.1159
Minimum	9.0
Maximum	239.0

Table 7: CPK-MB on admission

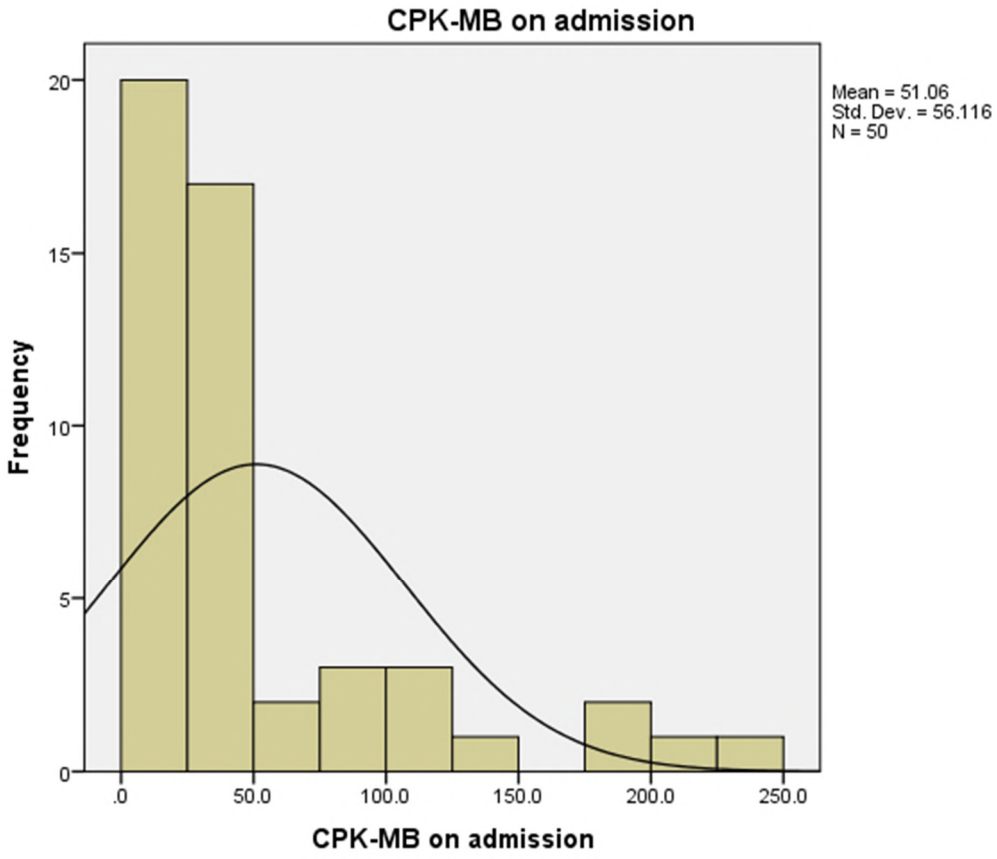


Figure 7: CPK-MB on admission

CPK-MB 12 hours after admission

The mean CPK-MB 12 hours after admission was 61.4 IU/L.

CPK-MB 12 hours after admission	Value (IU/L)
Mean	61.480
Median	26.000
Std. Deviation	71.1165
Minimum	17.0
Maximum	252.0

Table 8: CPK-MB 12 hours after admission

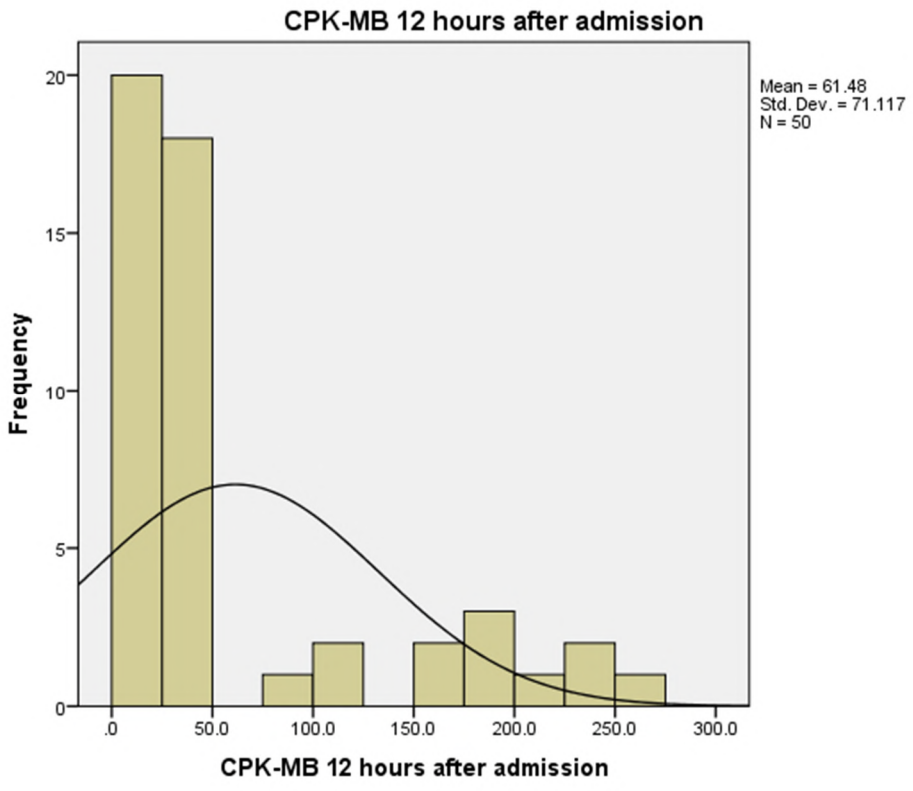


Figure CPK-MB 12 hours after admission

Outcome of the event

Out of the 50 patients,76% (n=38) survived while 24% (n=12) expired.

OUTCOME		Frequency	Percent
	Death	12	24.0
	Survived	38	76.0
	Total	50	100.0

Table 9: Outcome of the event

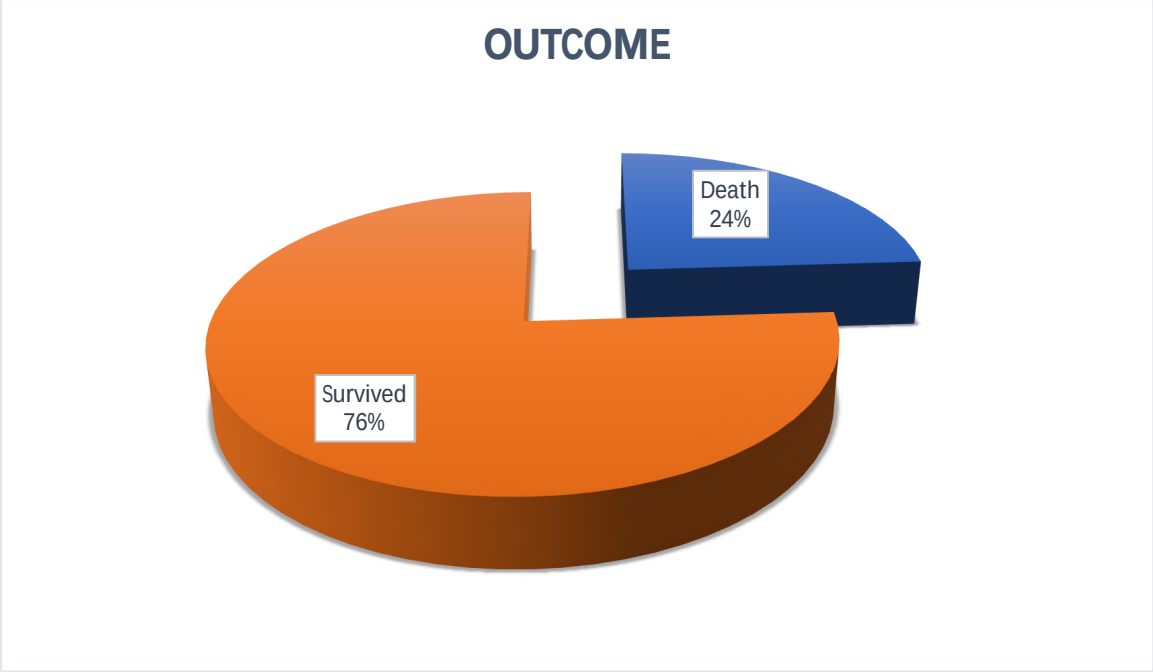


Figure 8: Outcome of the event

Comparison of CPK-MB with ECG on admission

ECG on admission		CPK-MB on admission (IU/L)	CPK-MB 12 hours after admission (IU/L)	Student t-test p-value
AV block	Mean	10.000	22.000	p<0.05 Statistically significant
	Std. Deviation	.	.	
Extrasystole	Mean	18.000	21.000	
	Std. Deviation	11.3137	4.2426	
Low voltage	Mean	69.500	100.500	
	Std. Deviation	45.9619	106.7731	
Normal	Mean	48.727	59.727	
	Std. Deviation	43.3038	62.7504	
PR Prolongation	Mean	18.000	27.500	
	Std. Deviation	4.2426	3.5355	
QTc prolongation	Mean	107.800	128.100	
	Std. Deviation	92.5705	107.0020	
Sinus bradycardia	Mean	25.714	22.000	
	Std. Deviation	3.6384	4.1231	
Sinus tachycardia	Mean	29.333	33.667	
	Std. Deviation	24.3824	27.7534	
ST Depression	Mean	44.000	54.000	
	Std. Deviation	19.9249	38.9358	
ST Elevation	Mean	26.500	21.000	
	Std. Deviation	2.1213	1.4142	
T inversion	Mean	89.000	155.000	
	Std. Deviation	.	.	
Total	Mean	51.060	61.480	
	Std. Deviation	56.1159	71.1165	

Table 10: Comparison of CPK-MB with ECG on admission

Comparison of CPK-MB with ECG on admission

ECG on Admission		CPK-MB on admission (IU/L)	CPK-MB 12 hours after admission (IU/L)
Abnormal	Mean	51.718	61.974
	Std. Deviation	59.7080	74.0556
Normal	Mean	48.727	59.727
	Std. Deviation	43.3038	62.7504
Total	Mean	51.060	61.480
	Std. Deviation	56.1159	71.1165

Table 11: ECG on Admission

Comparison of CPK-MB with ECG 12 hours after admission

ECG 12 hours after admission		CPK-MB on admission (IU/L)	CPK-MB 12 hours after admission (IU/L)	Student t-test p-value
AV Block	Mean	10.000	22.000	p<0.05 Statistically significant
	Std. Deviation	.	.	
Extrasystole	Mean	18.000	21.000	
	Std. Deviation	11.3137	4.2426	
Low voltage	Mean	69.500	100.500	
	Std. Deviation	45.9619	106.7731	
Normal	Mean	35.692	42.923	
	Std. Deviation	31.6764	48.8424	
PR Prolongation	Mean	18.000	27.500	
	Std. Deviation	4.2426	3.5355	
pVT	Mean	239.000	252.000	
	Std. Deviation	.	.	
QTc prolongation	Mean	93.222	114.333	
	Std. Deviation	85.1451	103.6750	
Sinus bradycardia	Mean	27.000	18.000	
	Std. Deviation	.	.	
Sinus tachycardia	Mean	37.615	41.385	
	Std. Deviation	34.5845	44.0673	
ST Depression	Mean	44.000	54.000	
	Std. Deviation	19.9249	38.9358	
ST Elevation	Mean	26.500	21.000	
	Std. Deviation	2.1213	1.4142	
T inversion	Mean	89.000	155.000	
	Std. Deviation	.	.	
Total	Mean	51.060	61.480	
	Std. Deviation	56.1159	71.1165	

Table 12: Comparison of CPK-MB with ECG 12 hours after admission

Comparison of CPK-MB with ECG 12 hours after admission

ECG 12 hours after admission		CPK-MB on admission (IU/L)	CPK-MB 12 hours after admission (IU/L)
Abnormal	Mean	56.459	68.000
	Std. Deviation	61.9389	76.9459
Normal	Mean	35.692	42.923
	Std. Deviation	31.6764	48.8424
Total	Mean	51.060	61.480
	Std. Deviation	56.1159	71.1165

Table 13: Comparison of CPK-MB with ECG 12 hours after admission

Comparison of CPK-MB levels shows that there is an elevation of CPK-MB levels at 12 hours after admission than at admission. The difference is noted with every ECG finding. The result is statistically highly significant ($p<0.05$).

Comparison of CPK-MB with outcome of the event

Comparison of CPK-MB levels with outcome shows that there is an elevation of CPK-MB levels in those who died than those who survived. There is a positive correlation between CPK-MB levels and the outcome of the event. The result is statistically highly significant ($p<0.05$).

OUTCOME		CPK-MB on admission (IU/L)	CPK-MB 12 hours after admission (IU/L)	Student t-test p-value
Death	Mean	136.000	178.000	p<0.05 Statistically significant
	Std. Deviation	58.3064	54.3624	
Survival	Mean	24.237	24.684	
	Std. Deviation	8.9848	5.0409	

Table 14: Comparison of CPK-MB with outcome of the event

DISCUSSION

DISCUSSION

- The mean age of the patients in this study is 37.1 years (S.D=11.5 years). In the study conducted by *Shankar Laudari et al and P Karki et al* the mean age was 29.8 ± 13.9 years and 26.85 years respectively.
- Majority of them are males (n=37, 74%) and the rest are females (n=13, 26%). The reason for consumption is suicidal attempt. Majority of them consumed Chlorpyrifos (n=23, 46%) followed by Dimethoate (n=10, 20%). Majority of them had POP score >5 (n=31, 62%).
- Out of 50 patients, ECG on admission was abnormal in 39 patients (78%). QTc prolongation was found in 20% (n=10) of the patients while sinus tachycardia was found in 18% (n=9) and sinus bradycardia was found in 14% (n=7) of the patients. Similarly in study conducted by *Shankar Laudari et al, P Karki et al* and in several other series, the frequency of QTc prolongation was shown to be 20 to 80% depending on the severity of the poisoning and the type of the toxic agent.
- Out of 50 patients, ECG after 12 hrs of admission was abnormal in 37 patients (74%). QTc prolongation was found in 18% (n=9) of the patients while sinus tachycardia was found in 26% (n=13) and sinus bradycardia was found in 2% (n=1) of the patients.
- In the present study we observed that normal ECG parameter was associated with a mortality of 15.38%. It was due to pulmonary edema, one of the fatal complications of OPC poisoning. QT prolongation was associated with a mortality of 44.45%

- The mean CPK-MB on admission was 51.1 IU/L. The mean CPK-MB 12 hours after admission was 61.4 IU/L. In the present study it was observed that the abnormal ECG parameters were associated with significantly high CPK-MB levels, which were mainly due to skeletal muscle and respiratory muscle involvement.
- With normal ECG the levels of CPK-MB were observed as 35.7±31.67 ng/dl. Prolonged QTc interval was the most commonly observed ECG abnormality and the levels of CPK-MB observed were 93.22±85.14 ng/dl. In study conducted by Shou-Hsuan Liu et al, the CPK-MB levels with normal ECG were 11.37±6.75 ng/dl and with prolonged QTc interval the CPK-MB levels were 28.89±60.65 ng/d.
- Out of the 50 patients, 76% (n=38) survived while 24% (n=12) expired.
- Comparison of CPK-MB levels shows that there is an elevation of CPK-MB levels at 12 hours after admission than at admission. The difference is noted with every ECG finding. The result is statistically highly significant ($p<0.05$).
- Comparison of CPK-MB levels with outcome shows that there is an elevation of CPK-MB levels in those who died than those who survived. There is a positive correlation between CPK-MB levels and the outcome of the event. The result is statistically highly significant ($p<0.05$).

CONCLUSIONS

CONCLUSIONS

- This study was done to predict increased mortality rate in OPC poisoning patients based on specific ECG parameter and CPK MB levels.
- In our study mortality was mainly observed in patients whose on admission ECG had QTc prolongation, sinus tachycardia.
- We observed that the CPK-MB levels recorded were frequently high among the OPC poisoning patients. There was significant difference in CPK-MB levels among expired patients and survived patients.
- Within each ECG parameter significant difference was observed in CPK-MB levels among survived and expired patient.

LIMITATIONS

- Echocardiogram was not included in our study.
- Serum or RBC cholinesterase levels couldn’t be analyzed in grading the severity of poisoning due to non availability in our setting.

MASTER CHART

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SNO	AGE	SEX	COMPOUND	REASON	POP SCORE	CPK-MB on admission	CPK-MB 12 hours after admission	ECG on admission	ECG 12 hours after admission	OUTCOME
1	33	F	Quinolphos	Suicidal	3	20	22	Sinus tachycardia	Sinus tachycardia	Survival
2	18	M	Chlorpyrifos	Suicidal	7	23	20	Normal	Normal	Survival
3	32	F	Dimethoate	Suicidal	9	30	28	QTc prolongation	QTc prolongation	Survival
4	43	M	Chlorpyrifos	Suicidal	9	85	103	Normal	Normal	Death
5	45	M	Chlorpyrifos	Suicidal	6	10	22	AV block	AV Block	Survival
6	38	F	Monochrotophos	Suicidal	7	100	196	QTc prolongation	QTc prolongation	Death
7	23	M	Chlorpyrifos	Suicidal	7	15	25	PR Prolongation	PR Prolongation	Survival
8	54	M	Cyclopyrifos	Suicidal	3	18	20	QTc prolongation	QTc prolongation	Survival
9	48	M	Chlorpyrifos	Suicidal	5	31	25	Sinus tachycardia	Sinus tachycardia	Survival
10	29	F	Chlorpyrifos	Suicidal	8	21	20	Sinus tachycardia	Sinus tachycardia	Survival
11	42	M	Dimethoate	Suicidal	9	37	25	Low voltage	Low voltage	Survival
12	31	M	Monochrotophos	Suicidal	11	92	107	Sinus tachycardia	Sinus tachycardia	Death
13	37	M	Quinolphos	Suicidal	8	23	29	Normal	Normal	Survival
14	54	M	Chlorpyrifos	Suicidal	7	11	20	Sinus tachycardia	Normal	Survival
15	19	M	Methyl Parathion	Suicidal	6	196	243	QTc prolongation	QTc prolongation	Death
16	49	M	Chlorpyrifos	Suicidal	7	9	24	QTc prolongation	QTc prolongation	Survival
17	48	M	Phorate	Suicidal	3	22	27	Normal	Normal	Survival
18	31	F	Chlorpyrifos	Suicidal	5	25	22	ST Elevation	ST Elevation	Survival
19	33	M	Dichlorvos	Suicidal	8	27	18	Sinus bradycardia	Sinus bradycardia	Survival
20	45	M	Quinolphos	Suicidal	4	29	17	Sinus bradycardia	Sinus tachycardia	Survival
21	48	M	Chlorpyrifos	Suicidal	3	25	27	Normal	Normal	Survival
22	31	F	Dimethoate	Suicidal	10	20	26	Sinus bradycardia	Normal	Survival
23	51	M	Dichlorvos	Suicidal	8	209	230	QTc prolongation	QTc prolongation	Death
24	27	M	Chlorpyrifos	Suicidal	2	32	40	ST Depression	ST Depression	Survival
25	19	M	Dichlorvos	Suicidal	0	32	22	Normal	Normal	Survival
26	21	F	Dimethoate	Suicidal	4	22	28	Sinus bradycardia	Sinus tachycardia	Survival
27	21	M	Dimethoate	Suicidal	3	13	24	Sinus tachycardia	Sinus tachycardia	Survival
28	56	F	Monochrotophos	Suicidal	6	28	20	ST Elevation	ST Elevation	Survival
29	21	F	Dimethoate	Suicidal	11	197	222	QTc prolongation	QTc prolongation	Death

30	39	M	Chlorpyrifos	Suicidal	10	60	38	QTc prolongation	QTc prolongation	Survival
31	21	M	Chlorpyrifos	Suicidal	6	89	155	T inversion	T inversion	Death
32	36	F	Chlorpyrifos	Suicidal	5	30	21	Sinus bradycardia	Normal	Survival
33	29	M	Dichlorvos	Suicidal	2	22	25	Normal	Normal	Survival
34	30	M	Dimethoate	Suicidal	6	26	27	Sinus tachycardia	Sinus tachycardia	Survival
35	60	M	Chlorpyrifos	Suicidal	9	123	188	Normal	Normal	Death
36	56	M	Dimethoate	Suicidal	2	26	18	Extrasystole	Extrasystole	Survival
37	55	M	Dimethoate	Suicidal	7	28	26	Sinus tachycardia	Sinus tachycardia	Survival
38	52	M	Chlorpyrifos	Suicidal	6	20	28	QTc prolongation	QTc prolongation	Survival
39	33	M	Dichlorvos	Suicidal	9	67	98	ST Depression	ST Depression	Death
40	31	M	Chlorpyrifos	Suicidal	4	21	30	PR Prolongation	PR Prolongation	Survival
41	29	F	Parathion	Suicidal	4	33	24	ST Depression	ST Depression	Survival
42	37	M	Chlorpyrifos	Suicidal	3	27	24	Sinus bradycardia	Sinus tachycardia	Survival
43	41	M	Parathion	Suicidal	7	25	20	Sinus bradycardia	Sinus tachycardia	Survival
44	29	M	Chlorpyrifos	Suicidal	4	24	30	Normal	Normal	Survival
45	28	F	Chlorpyrifos	Suicidal	7	22	32	Sinus tachycardia	Sinus tachycardia	Survival
46	51	M	Chlorpyrifos	Suicidal	10	239	252	QTc prolongation	pVT	Death
47	34	F	Chlorpyrifos	Suicidal	10	102	176	Low voltage	Low voltage	Death
48	39	M	Parathion	Suicidal	3	10	24	Extrasystole	Extrasystole	Survival
49	35	M	Chlorpyrifos	Suicidal	6	24	20	Normal	Normal	Survival
50	42	M	Dimethoate	Suicidal	9	133	166	Normal	Sinus tachycardia	Death