A STUDY ON BASE DEFICIT AS A PREDICTOR OF MORTHLITY AND PROGNOSTIC TOOL IN ORGANOPHOSPHATE POISONING

By

DR.SAILEE R BELVI

Dissertation submitted to

BLDE (Deemed to be University)Vijayapur, Karnataka

In partial fulfillment of the requirements for the degree of

DOCTOROFMEDICINE

IN

GENERAL MEDICNE

Under the guidance of

Dr. R.M. HONNUTAGI

PROFESSOR

DEPARTMENTOFGENERAL MEDICNE

BLDE (Deemed to be University)

SHRIB.M.PATILMEDICALCOLLEGE

HOSPITAL & RESEARCH CENTRE, VIJAYAPUR

KARNATAKA

2020

DOCTOR OF MEDICINE IN GENERAL MEDICINE

"A STUDY ON BASE DEFICIT AS A PREDICTOR OF MORTALITY AND PROGNOSTIC TOOL IN ORGANOPHOSPHOROUS POISONING"

LIST OF ABBREVIATIONS

Ach	Acetylcholine
anti-ChE	Anticholincstcrasc
DDT	Dichloro diethyl trichloroethane.
DDT	Dichloro diethyl trichloroethane.
EDRF	Endothelium derived relaxing factor
X’	CHI SQAURE VALUE
IMS	Intermediate syndrome
IV	Intravenous
No	Number
OP	Organophosphorus
OPC	Organophosphorus compound
OPIDP	Organophosphate-induced delayed polyneuropathy
2-PAM	Pralidoxime
PChc	Pscudocholincstcrasc
POP scale	Peradeniya Organophosphorus poisoning scale
S	Significant.
TEPP	Tctracthyl pyrophosphate
TOCP	Organophosphate triorthocrcsyl phosphate
GABA	Gamma-aminobutyric acid
GTP	Guanosine Triphosphate
GDP	Guanosine Diphosphate

TABLE OF CONTENTS

LIST OF TABLES

INTRODUCTION:

Poisoning by organophosphorous compounds is a serious issue for public health in developing nations, particularly in India. About 500,000 people each year in India die from intentional self-harm, with insecticide poisoning accounting for about 60% of these deaths, of which 66% are brought on by poisoning with organophosphorus compounds. 1 Due to the extensive agricultural activity in South Indian states, insecticide poisoning is quite prevalent and contributes significantly to ICU admissions in this area. Organophosphorus chemicals are one of the most often utilised tools for intentional self-harm due to their ease of accessibility and lax rules and restrictions regulating sales. Agricultural labourers and manufacturing workers are both frequently exposed accidentally. The mortality rate of OP poisoning has been recorded in various hospital data to range from 20% to It is thought that respiratory insufficiency brought on by a combination of pulmonary cholinergic effects (bronchoconstriction and massive bronchial secretions), nicotinic effects (weakness of the respiratory muscles), and CNS cholinergic effects (inhibition of the respiratory centres) is the main factor in OP poisoning deaths3

Base deficit (BD) is the quantity of strong acid or base needed to bring the pH of 1 litre of whole blood to 7.4, assuming a temperature of 37 degrees Celsius and a partial pressure of carbon dioxide of 40 mmHg. It is used to describe tissue hypoperfusion and hypoxia. Anderson and Engel created this assay in 1960, and it is being used to assess metabolic acid-base activity today4.

According to numerous publications, OP poisoning causes cardiac toxicity, aberrant ECGs, and respiratory distress. These symptoms can lead to hypotension, hypoperfusion, and electrolyte imbalance. These elements may be the main causes of respiratory and metabolic acidosis in acute OP poisoning. One of the main risk factors

that affects how OP poisoning victims fare in terms of their health is acidosis. Additionally, atropine itself, which is essential in the treatment of OP poisoning6, has the potential to cause deadly arrhythmias.

Sodium bicarbonate infusion is used to treat the metabolic acidosis that results from OPI poisoning, which enhances the protective effects of atropine and oxime treatment. The sodium bicarbonate treatment's elevation in blood pH may also accelerate the hydrolysis of the organophosphate molecule's ester moiety, reducing the toxicity of the compound. 7 A general indicator of disease severity is provided by the APACHE II, which assigns a score based on the initial values of 12 common physiological parameters, such as arterial pH, age, and prior health condition. A higher score (in the range of 0-71) is linked to a higher mortality rate. Additionally, since there is a correlation between BD and APACHE II scores in terms of mortality8, BD may be utilised as a replacement to diagnose metabolic acidosis.

AIMS AND OBJECTIVES

1. To study the correlation between base deficit and APACHE 2 score in organophosphorous poisoning.

REVIEW OF LITERATURE

"Anything in excess is a poison"

Organophosphorus (OPCs) insecticides are one of the most commonly used insecticides in India and Asia reporting annually almost 2,00,000 deaths[9]. Due to their high toxicity, exposure to these pesticides and insecticides, whether intentional or unintentional, frequently poses a risk to human life. Through cutaneous absorption, ingestion, or inhalation, it enters the human body. Tetraethyl pyrophosphate (TEPP), was the first Organophosphorus insecticide to be developed. Organic phosphorus compounds (OPCs) and carbamates are routinely used in India. These insecticides possess anticholinesterase properties which trigger the phosphorylation of acetylcholinesterase at nerve terminals. As acetylcholine and inhibition of acetylcholinesterase play a significant part in the pathophysiology of OP poisoning, it is crucial to review physiology of cholinergic transmission in body. This ultimately results in excessive collection of Ach in nerve endings.

- Ravi et al described the incidence of organophosphorus poisoning as around 1.26 lakhs during the year 2007 in India. According to recent data, prompt and appropriate management improves results. After resuscitation, patients with moderate to severe organophosphorus poisoning should be admitted to an intensive care unit to allow for meticulous antidote titration, intubation, ventilation, and the use of inotropes or vasopressors if necessary10. Acute organophosphorus poisoning can cause multisystem toxicity, which can be fatal. The diagnosis of poisoning is made based on the patient's medical history and physical examination; biochemical tests may also be used to support the diagnosis. Prompt resuscitation, antidotes as needed (especially atropine, oximes, stomach lavage), and selective decontamination make up management. Continuous observation and excellent supportive care are crucial. Standard measures should be taken by healthcare professionals caring for exposed patients.

- Samel Park et al have proposed anion gap as a critical marker for death in patients with acute pesticide intoxication, in correlation with other parameters, in surviving and deceased patients. In 1,058 patients with acute pesticide intoxication: arterial blood gas analysis, electrolytes, pesticide field of use, class, and ingestion amount, clinical outcome (death rate, length of hospital stay, length of intensive care unit stay, and seriousness of toxic symptoms), and the calculated anion gap were assessed. Among the 481 patients with a high anion gap, 52.2% had a blood pH in the physiologic range, 35.8% had metabolic acidosis, and 12.1% had acidemia[11] the patients with metabolic acidosis required swift measures such as mechanical ventilation for survival.
- Asari et al. noted rapid onset metabolic acidosis associated with profound hypotension in 4 organophosphate-poisoned patients[12] The hypotension was

resistant to catecholamine therapy. Zadik et al also described a case of organophosphate poisoning presenting as diabetic ketoacidosis[13] The role of sodium bicarbonate in the treatment of metabolic acidosis remains controversial. However, the patient showed dramatic improvement after sodium bicarbonate therapy. They suggest, pending specific recommendations on the subject, patients with organophosphate poisoning with hypotension should be screened for metabolic acidosis with arterial blood gas analysis. If pH is found <7.20, treatment with sodium bicarbonate should be considered.

- Smith I and Kumar P et al found that both base excess and lactate, or the combination of the two, can be used to predict outcome in patients admitted to the intensive care unit. These variables could be utilized to identify patients who have a high risk for mortality and thus who should be admitted to the intensive care unit[14]

- Liu JH, Chou CY, Liu YL et al. carried out a study that states Acid-base interpretation can be effective in quick diagnosis and prediction of the outcome of patients with acute OP poisoning[15]

- Balali-Mood M, Ayati MH and Ali-Akbarian H. study says that infusion of high doses of bicarbonate appears to be beneficial in treatment of patients with OP poisoning[16]

History of Organophosphate Compounds

Jean Louis Lassaigne and Philippe de Clermont were early innovators in the field (early 19th century) (1854). The earliest description of the cholinergic nervous system effects of organophosphates was made in 1932 by German chemist Willy Lange and his graduate student, Gerde von Krueger. They noted a choking sensation and a darkening of vision following exposure. This discovery eventually motivated German chemist Gerhard Schrader to test these substances as pesticides while working for IG Farben in the 1930s. The Nazi administration tasked Schrader with creating organophosphate (in the broadest sense of the word) nerve gases as soon as their potential for use as chemical warfare agents became clear. Sarin, Tabun, and Soman were among the G series of weapons that Schrader's lab identified. These substances were nevertheless widely developed by the Nazis. British scientists experimented with a cholinergic organophosphate of their own, called diisopropylfluorophosphate (DFP), during the war. The British later produced VX nerve agent, which was many times more potent than the G series, in the early 1950s, almost 20 years. However, nerve agents have rarely been used in warfare; the only notable instance of use being by Iraq against that country's own Kurdish population (le Chˆene, 1989). There have also been allegations of use of OP nerve agents during the Iran/Iraq war. The nerve agent sarin, in an impure form, was used in two terrorist attacks in Japan, respectively, in Matsumoto 1994 andTokyo in 1995 , as was, almost certainly, VX, but

this agent was used for assassination of individuals

CLASSIFICATION

It is of pharmacological and toxicological significance the organophosphorous classification system Holmstedt proposed.

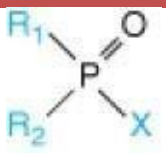
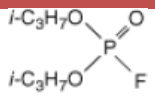
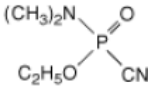
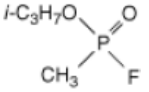
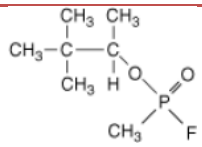
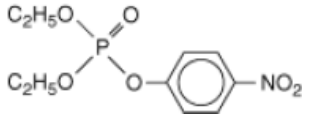
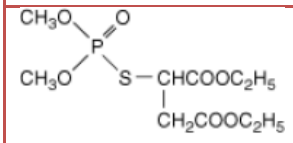
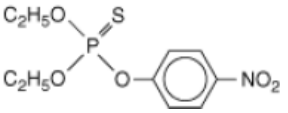
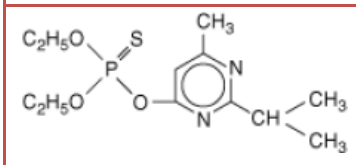
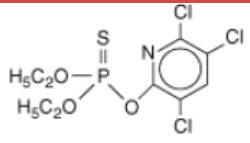
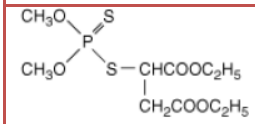
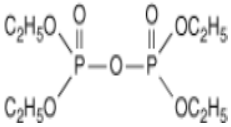
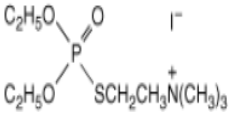
Chemical Classification of Representative Organophosphorus Compounds of Particular Pharmacological or Toxicological Interest	
General formula	
Group A, X = halogen, cyanide, or thiocyanate leaving group; Group B, X = alkylthio, arylthio, alkoxy, or aryloxy leaving group; Group C, thionophosphorus or thio-thionophosphorus compounds; Group D, pyrophosphates and similar compounds; Group E, quaternary ammonium leaving group. R_1 can be an alkyl (phosphonates), alkoxy (phosphorates) or an alkylamino (phosphoramidates) group.	

Table A Chemical classification of OP compounds

GROUP	STRUCTURAL FORMULA	COMMON, CHEMICAL, AND OTHER NAMES	COMMENTS
A		DFP; Isoflurophate; diisopropyl fluorophosphate	Potent, irreversible inactivator
		Tabun	Extremely toxic "nerve gas"
		Ethyl N-dimethylphosphoramidocyanidate	
		Sarin (GB)	Extremely toxic "nerve gas"
		Isopropyl methylphosphonofluoridate	
		Soman (GD)	Extremely toxic "nerve gas"
		Pinacolyl methylphosphonofluoridate	
B		Paraoxon (MINTACOL), E 600	Active metabolite of parathion
		O,*O*-Diethyl *O*-(4-nitrophenyl)-phosphate	
		Malaoxon	Active metabolite of malathion
		O,*O*-Dimethyl *S*-(1,2-dicarboxyethyl)-phosphorothioate	
C		Parathion	Employed as agricultural insecticide, resulting in numerous cases of accidental poisoning
		O,*O*-Diethyl *O*-(4-nitrophenyl)-phosphorothioate	
		Diazinon, Dimpylate	Insecticide in wide use for gardening and agriculture
		O,*O*-Diethyl *O*-(2-isopropyl-6-methyl-4-pyrimidinyl) phosphorothioate	
		Chlorpyrifos	Insecticide with restricted use in consumer products and limited to nonresidential settings
		O,*O*-Diethyl *O*-(3,5,6-trichloro-2-pyridyl) phosphorothioate	

		O,O-Dimethyl *S*-(1,2-dicarbethoxyethyl) phosphorodithioate	
		Malathion	Widely employed insecticide of greater safety than parathion or other agents because of rapid detoxification by higher organisms
		O,O-Dimethyl *S*-(1,2-dicarbethoxyethyl)phosphorodithioate	

GROUP	STRUCTURAL FORMULA	COMMON, CHEMICAL, AND OTHER NAMES	COMMENTS
D		TEPP	Early insecticide
		Tetraethyl pyrophosphate	
E		Echothiophate (PHOSPHOLINE IODIDE), MI-217	Extremely potent choline derivative; employed in treatment of glaucoma; relatively stable in aqueous solution
		Diethoxyphosphinylthiocholine iodide	

CLASSIFICATION ACCORDING TO CLASS OF COMPOUNDS[17]

Table B: Classification according to class of compounds

OrganoChlorine Compounds	OrganoPhosphorus Compounds	Carbamates
Methoxychlor DDT HCH (BHC) Lindane Chlordene Hepatochlor Dieldrin Aldrin	Chlorthion Diazinon Dioxathion Dimethoate EPN Malathion (OMS-1) Fenthion (OMS – 2) Methylparathion, Parathion Ronnel Trichlorfos Dichlorvos, Chlorpyrifos	Carbaryl Pyrolan Dimetilan Propoxur Synthetic Pyrethroids

PHARMACODYNAMICS AND TOXICOKINETICS OF ORGANOPHOSPHOROUS COMPOUNDS

ABSORBTION

These substances are typically spread as aerosols or dusts and are composed of organophosphorous chemicals that have been absorbed into harmless finely dispersed materials. Therefore, almost all pathways, including the gastrointestinal system, skin, and mucous membranes, promptly and effectively absorb these substances after coming into touch with the liquid form. After inhaling the vapours or finely distributed dusts or aerosols, the lungs also absorb them.

The amount of absorption is influenced by the duration of skin contact, the lipophilicity of the agent, and the presence of emulsifiers and solvents in the formulation, such as xylene, which can speed up absorption. Powders absorb into the skin more quickly and completely the finer they are. Other crucial elements include the pesticide's volatility (for example, dichlorvos is substantially more volatile than malathion), the permeability of garments, the degree of surface coverage, and personal hygiene. The damaged area of the skin affects the rate of absorption as well. For instance, parathion is more easily absorbed via the skin of the head, neck, and axillae than it is through the skin of the hands and arms. It is likely that dermatitis or damaged skin allow OP chemicals to be absorbed more readily. In one investigation, just 1.23% of the calculated potential dermal exposure was actually absorbed dermally as liquid parathion on average.

DISTRIBUTION AND STORAGE

After ingestion, OP chemicals quickly build up in the liver, kidneys, fat, and salivary glands. The prolonged intoxication and clinical relapse after apparent recovery that have been observed in poisoning from these OP insecticides may be explained by the fact that phosphorothioates (P=S), such as diazonin, parathion, and bromophos, are more lipophilic than phosphates (P=O), such as dichlorvos, and are therefore extensively stored in fat. Since OP chemicals are often lipophilic, they frequently traverse the blood–brain barrier**.**

Highly lipid-soluble drugs like chlorfenthion can cause prolonged systemic release of stored subcutaneous lipids following redistribution, resulting in symptoms and signs of cholinergic overactivity lasting days to weeks. These substances also result in recurring release even after ostensibly effective management.

The plasma half-life varies depending on the chemicals and delivery method from a few minutes to a few hours18

BIOTRANSFORMATION

Oxidation is the primary mechanism of metabolism.
Phosphorothioates (P=S) require bioactivation to their phosphate counterparts (oxon) to become biologically active, whereas phosphonates (P=O) are physiologically active as acetylcholinesterase (AChE) inhibitors. As a result, unless airborne oxidation has previously taken place to produce residues of oxon, the symptoms of poisoning after exposure to phosphorothioates (P=S) are delayed. Microcosms in the liver change parathion into the physiologically active chemical "Paroxon." In larger animals, malathion is converted more quickly into

an inert molecule, making it less harmful to humans.

The metabolic activation of OP compounds other than phosphates (P=O) occurs by oxidation desulfuration, which is mediated by P450 isoforms, flavin-containing mono-oxygenase enzymes, N-oxidation, and S-oxidation.The oxons which inhibit AChE can be deactivated by hydrolases, such as the carboxylases and by A-esterases, for example paraoxonase[18]

ELIMINATION

Organophosphorous insecticides undergo detoxification either by biochemical change of their structural components or through connection to the binding site without toxicological effect.

Metabolites are primarily excreted in urine, with smaller amounts found in faeces and expired air. The inhibitory oxon of chlorpyrifos or dementon-S-methyl may remain for days as a result of their considerable storage in fat, although some OPs, such as dichlorvos, which is not significantly retained in fat, may be removed in hours. 18

ANATOMY OF AUTONOMIC NERVOUS SYSTEM:

It has two divisons[19]:-

1. **Sympathetic**(Thoracolumbar)
2. **Parasympathetic**(Craniosacral)

divisions originate CNS nuclei and emerge from brain stem, where they give rise to preganglionic efferent fibres that end in motor ganglia.

The thoracic and lumbar spinal nerves are where preganglionic sympathetic fibres escape. These are brief and terminate in paravertebral chain ganglia22.

Third, seventh, ninth, and tenth cranial nerves as well as the Sacral spinal nerve roots two, three, and four. Preganglionic parasympathetic fibres can terminate in ganglions that are positioned external to the organ. a few pelvic ganglia, the iliary, submandibular, and pterygopalatine ganglion, etc. However, the majority of preganglionic parasympathetic fibres result in an organ ganglion.

Postganglionic fibres emerge from ganglions and innervate the destination organsystem.

ENTERIC NERVOUS SYSTEM (ENS) :

It’s vast well-organized cluster of neurons in gastrointestinal system. It is known as the ANS's third division. It runs from the oesophagus to the distal colon and regulates the gut's motor and sensory activities. It contains Auerbach's myentric

plexus and Meissner's Submucous plexus. It regulates mucosal motility and secretory cells. The ENS operates in a semiautonomous mode.

CHOLINOCEPTORS[20]:

Muscarinic and Nicotinic Receptors are the two types of receptors for acetylcholine. Nicotinic receptor is a ligand-gated channel, while the muscarinic receptor is a G protein coupled receptor.

MUSCARINIC RECEPTOR:

Muscarine stimulates them whereas Atropine inhibits them.

The central nervous system, sweat glands, gastrointestinal tract, respiratory system, ocular smooth muscle, and arteries in the heart are the main areas it impacts. Additionally, it can be present in the autonomic ganglia, where it serves as a modulator. Muscarinic auto receptors are found pre junctionally on the postganglionic cholinergic nerve terminals and block Ach release when activated. Muscarinic receptors are found on the endothelium of all blood arteries; however there are no cholinergic innervations.

SUBTYPES OF MUSCARI9NIC RECEPTORS[20]:

M1 M2 M3 are the three main subtypes.

Neurotransmitter release is regulated by M4 and M5, which are mostly found on nerve terminals in the brain

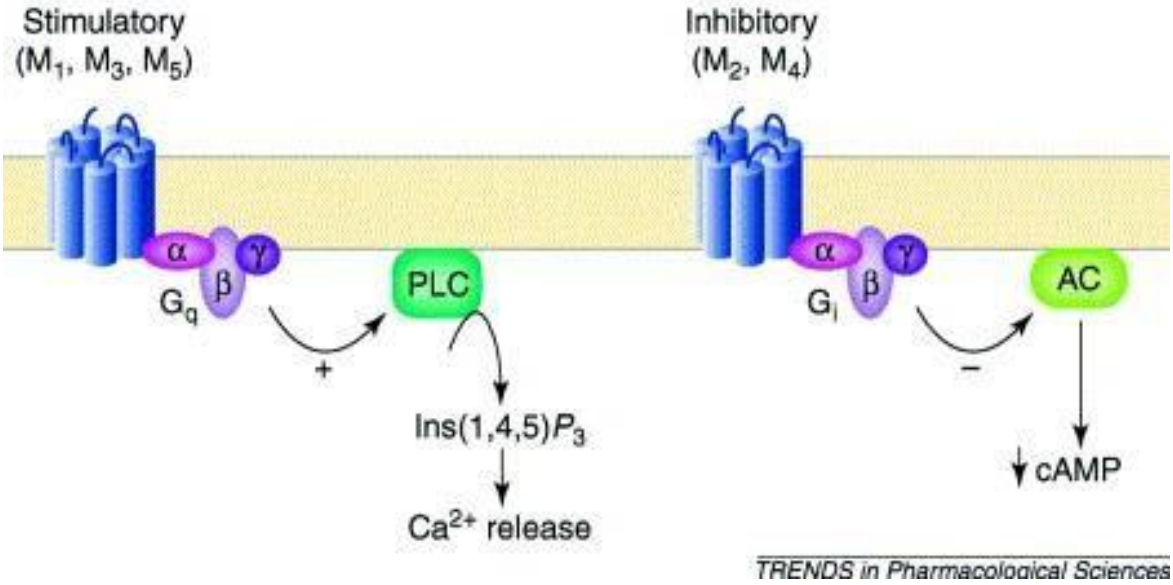


FIGURE 1 MECHAN4ISM OF MUSCARINIC RECEPTORS

M1receptor:

In the CNS, gastric glands, and autonomic ganglia, it is a G protein coupled receptor that promotes depolarization, histamine release, learning, and motor function. Oxotremorine, MCN-34A, and Telenzepin are M1 receptor agonists and antagonists, respectively. It operates through the IP3/DAGl second messenger, which results in increased cytosolic calcium and the activation of phospholipase A2.

M2RECEPTOR:

It is a G protein-coupled receptor as well. through triggering potassium channels, decreases cyclic AMP. Reduced impulse generation due to hyperpolarization caused by SA node activation, lower conduction speed at the AV node, and shortening of the atrium are all effects of this. reduced ventricle contractility, and an analgesic effect in the central nervous system is produced

Methacholin is the antagonist.

M3RECEPTOR:

It also utilises G protein coupled receptors, much like the M1 receptor Locations of it include ocular exocrine glands, ciliary muscle, visceral smooth muscle, and vascular endothelium.. Nitric oxide is released, which promotes vasodilation.

NICOTINICRECEPTOR:

Nicotine selectively activates nicotinic receptors.

Tubocurarine and Hexamethonium antagonistic. Activation results in channel opening and fast cation flow, as well as depolarization and an action potential.

NMreceptor:

Mediates skeletal muscular contraction and is found in the endplate of skeletal muscles. Tubocurarine is an antagonist, while phenyltrimethyl ammonium is an agonist.

NN receptor:

present on some regions like spinal cords, medulla, and ganglionic cells. Agonist: dimethyl phenyl piperazinium.

They are two types Alpha betareceptor.

These G-protein coupled receptors that are membrane-bound control intracellular levels of the second messengers cAMP or IP3/DAGl

ALPHARECEPTOR: It is divided in to 2 types

ALPHA1RECEPTOR:

present in the genitourinary junction, and its presence causes smooth muscle spasm, gland secretion, gut relaxation. It also leads to breakdown of liver liver glycogen stores.

The agonist is methoxamin.

The antagonist, prazosine, is selective.

ALPHA 2 RECEPTOR:

found in nerve endings and beta cells in pancreas. Stimulation of receptor causes transmitter release inhibition decreased sympathetic flow vasoconstriction.

Yohimbine is antagonist,

Clonidine is selective agonist.

BETA ADRENOCEPTORS: There are four different types of beta receptors: beta1, beta2, and beta3.

JG cells in the heart and kidneys express the beta1 receptor.

Dobutamine is an antagonist.

Antagonism exists between metiprolol and atenolol.

uterus, gastrointestinal tract, urinary tract, and eye all contain beta2 receptors.

An exclusive agonist is salbutamol.

Specifically antagonistic, propranolol.

Adipose tissue contains beta3 receptor

ACETYLCHOLINE NEUROTRANSMISSION

Sodium-potassium or sodium-potassium ATPase transports sodium ions into the synaptic space when Ach attaches to the receptor, opening the ion channel. Averaging 10 ions per millisecond, Ach receptor molecules conduct electrical signals. To open an ion channel, at least two Ach molecules are needed at each Ach receptor. 21 The binding sites for agonist activation are found in two alpha subunits that bind Ach. In 0.1–10 ms, each Ach receptor closes.

Ach is hydrolysed by acetylcholinesterase in the synaptic space and loses its effect[22] Agonists that have been present for a while make the receptor more sensitive. Calcium, N-and O-glycosylation, cytoplasmic site phosphorylation, and the presence of fatty acids are all factors that control receptor activation. Non-physiological substances like the muscle relaxant neurotoxic curare and topical anaesthetics can potentially have an impact. ACH is hydrolysed to choline and acetate in the synaptic space by the enzyme acetyl cholinesterase. This enzyme is ubiquitous in neurons through axonal transport.

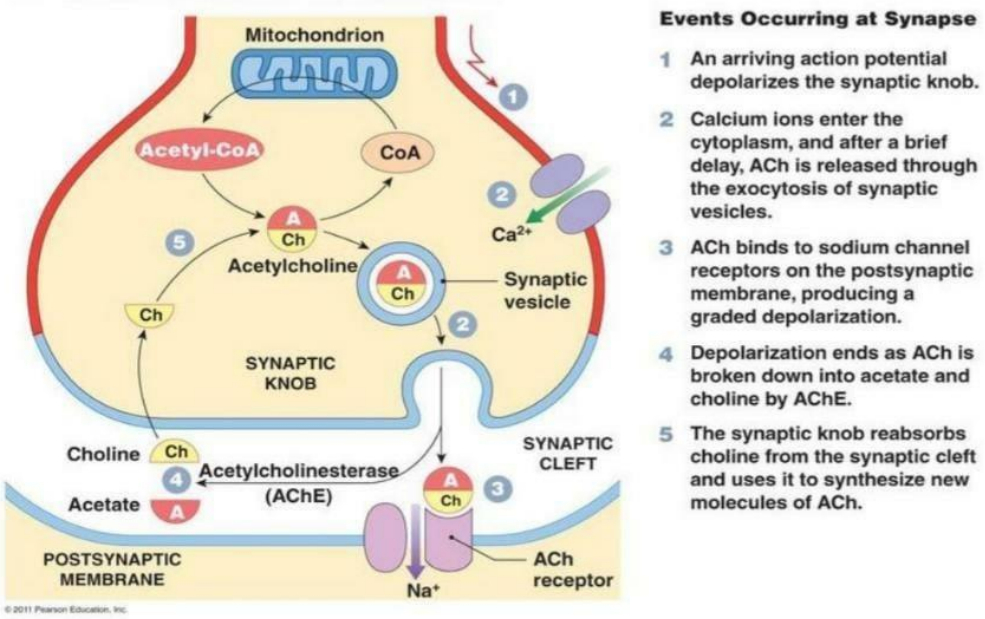


Figure1: Schematic diagram of cholinergic synapse.

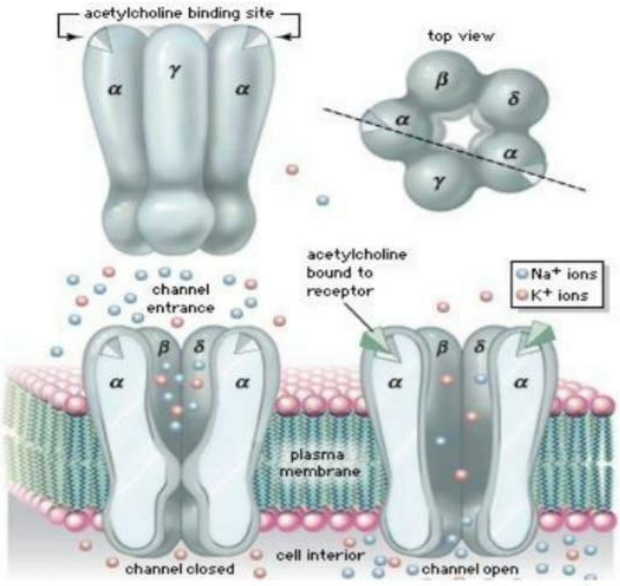


Figure 2: structure of acetylcholine receptor

FIGURE 2 STRUCTURE OF ACH RECEPTOR AND DIAGRAM OF CHOLINERGIC SYNAPSE

Chemical structure of the Ach receptor:

The cytoplasmic side of the membrane of the Ach receptor's pentameric structure, which contains four crucial proteins, is made up of intracellular proteins (Figure 2). Actin-binding activity and phosphatase activity are both displayed by some of the proteins. This molecule is structured like a funnel as it reaches the synapses. The subunits expand into the synaptic space and round the ion channel. Our understanding of these intricate structures is largely based on investigations of the functional and anatomical parallels between Ach receptors at the neuromuscular junction and "electrolytes" discovered in electric fish and torpedoes.

Trypsin can break each subunit by proteolytic means on both sides of the membrane thanks to the subunits' geometric arrangement. receptor has cytoplasmic domains and an extracellular membrane.

One on each of the two high-affinity agonist-binding sites subunit, are among the receptor's most distinctive ligand-binding sites. A conformational shift brought on by antagonist binding to these locations results in channel opening or desensitisation. The subunit domain's glycosylation has an impact on antagonist binding.

Ion channel function-related amino acid residues are mostly found in the membrane domain. Each of its closely spaced amphipathic helices contributes to the formation of a hydrophilic section. Ion channels don't directly interact with cations, therefore their conducting capabilities depend on conformational changes in the side chains.

ACETYL CHOLINESTERASE (AChE)

These enzymes are responsible for converting acetylcholine to acetic acid and choline. Cholinesterase is divided into two types. Acetyl cholinesterase and butyryl cholinesterase.

PROPERTIES	ACETYLCHOLINESTERSE	BUTRYLCHOLINESTERASE
SYNONYMM	Rbc cholinesteras	Plasma/ Pseudocholinesteras
SITE	NM junction	Plasma
SUBTRATE	Acetylcholin	Butrylcholine
AVAILABILITYY	Not available	Betterr
ACCURACY	Greater	Les
ONSET OF DEPRESSION	Laterr	Earrly
DEPRESSION LASTS FOR	Days toweeks	Upto months

This hydrolase-related enzymehas a distinctive ellipsoidal form. It is made up of eight sturdy -strands joined by -helices. The catalytic triad, an area of the enzyme that contains glutamic acid, histidine, and serine, is made up of three amino acids. The active site "GORGE" at its base, which is only partially permeable to the enzyme, forms the catalytic triad. Esteratic site and anion site are the two precise active subsites that make up the active site, or "GORGE." The anion site is used to attach the quaternary group of acetylcholine, and the ester site is used for catalytic action. Ach and other quaternary ligands now have extra binding sites on this

enzyme. Many aromatic amino acid residues, particularly tryptophan, cap the GORGE sites, and these peripheral anionic sites on the pharynx produce substrate inhibition.

Acetyl cholinesterase and butyryl cholinesterase can be distinguished from one another by six conserved aromatic residues that surround the pox site. Glutamate, histidine, and serine form a catalytic trio in which serine is given electrons by glutamate and histidine. With acetylcholine, this active serine residue creates a covalent connection. As a result, a "tetrahedral oxyanion intermediate" that forms an oxyanion hole and is stabilised by interactions with amide groups is created. Acetate and choline are released after the covalent link is dissolved. A two-step process of acylation and deacylation is involved here. Catalysis is also impacted by the substrate's composition. The efficiency of catalysis is determined by substrate binding to an enzyme's active site. The precise compatibility of thioesters and carbaresters makes them excellent substrates for catalysis, whereas organophosphorus compounds irreversibly inhibit enzymes due to their different shapes.

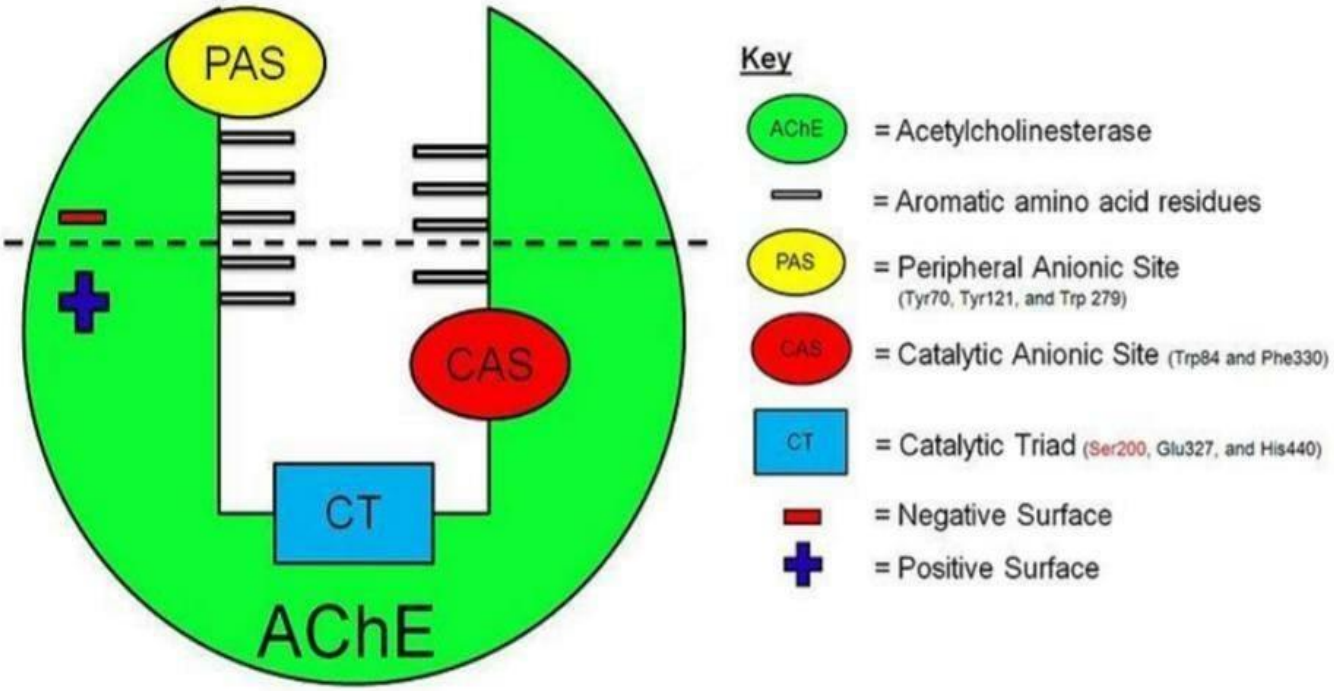


FIGURE 3 REPRESENTING THE ACETYLCHOLINESTERASE ENZYME

MECHANISM OF ACTION OF ORGANOPHOSPHATES

Organophosphate substances bind to the cholinesterase enzyme as a result of their molecular mimicry. They associate with the acetyl and pseudo cholinesterase serine active sites via a covalent connection with phosphate (serum cholinesterase). Ach is hydrolyzed by cholinesterase into choline and acetic acid. Acetylcholine is created when the choline moiety is returned to the presynaptic neuron. When an organophosphate going group departs and substance establishes a covalent link with enzyme, the enzyme is phosphorylated.Highlystable, this phosphorylated enzyme. The phosphoryl group will now inhibit the serine group, preventing it from participating in acetylcholine hydrolysis. The enzyme is finally irreversibly stopped, according to ageing theory, when it blocked by the phosphateof OP molecule. A component of the OPserine combination dealkylated, rendering enzyme resistant to nucleophiliic assault. An inactive enzymee cannot be activated again. The central nervous system's Ach receptor sites, sympathetic ganglia nicotinic receptors, skeletal myoneural junctions, and muscarinic neuroeffector sites are all affected by the accumulation of Ach and overstimulation of Achreceptor sites as a result of cholinesterase inhibition.

PATHOPHYSIOLOGY

Following are some of the harmful impacts of OP chemicals on different bodily systems:

1. Breathing system: OP substances paralyse the respiratory muscles. The patient may have bradypnea, which can lead to apnea, tightness in the chest, wheezing, and a productive cough. The primary cause of mortality is respiratory failure, which can be brought on by bronchoconstriction or respiratory centre inhibition. 26

2. Cardiovascular system: Myocardial cell death brought on by acute OP poisoning can result in elevated blood levels of lactate dehydrogenase and creatinine kinase27. Bradycardia is the traditional indicator. The patient may have arrhythmias, an altered volume status, and an irregular heart rate. ECG alterations can include ST seg elevation, extended QT PR interval, and small Twaves.

3. Central nervous system: Neurone injury that delays the classification of stimuli may last even up to six months. Cerebellar syndromes, Parkinson's symptoms, cognitive impairment, etc.

4. Hepato biliary System: liver is location of OPC biotransformation; congestion, necrosis, hepatocyte inflammation, and sinusoidal cell dilatation29.

5. Renal System: Organophosphate substances can cause glycosuria, renal failure, and occasionally even RCC30

6. EndocrineSystem: The main effect of OP chemicals on sex hormones is hypogonadism.31

SYMPTOMATOLOGY: The fastest mechanism of absorption for OP chemical toxicity is inhalation, followed by oral and finally cutaneous routes, although the clinical presentation varies. Headache, lightheadedness, or nausea are some of early signs. The patient may gradually start to exhibit symptoms of increased secretions, such as perspiration, salivation, rhinorrhea, and lacrimation. Miosis and visual blurring are additional significant warning indicators. Miosis is typically the first clinical sign, followed by GIT symptoms and hypersalivation. The earliest clinical indications are frequently those with muscarinic characteristics. Children that are exposed to OP compounds may experience seizures, lethargy, and weak, flaccid muscles. (27) Table 4 summarises the symptoms.

TABLE 4 SYMPTOMS OF CHOLINERGIC TOXICITY

Cholinergic Toxidrome		
Nicotinic:	**Muscarinic:**	**Central:**
Pupil dilatation	Pupil constriction	Agitation
Tachycardia	Bradycardia	Confusion
Bronchodilatation	Lung mucous production & airway obstruction	Lethargy
Hypertension	Vomiting & diarrhoea	Coma
Sweating +++	Hypersalivation & tearing	Seizure
Muscle weakness (inc respiratory arrest)	Urinary incontinence	Death

INTERMEDIATE SYNDROME:

I Wadia made the initial discovery of it.[33] He described it as paralysis of type 2. Senanayake and Karalliedde were the ones to coin the phrase "intermediate syndrome" in 1987[34].

Incidence - 20 – 70 %[35,36].

Definition: The emergence of symptoms between early cholinergic phase and delayed peripheraal neuropathy. Symptoms usually appear 12 to 96 hours following exposure to an OP substance.

Pathophysiology - Acetylcholine acts on nicotinic receptors over an extended period of time.

Clinical features: Muscular weakness in the ocular, neck, bulbar, and proximal limbs, as well as respiratory muscle weakness, which leads to respiratory failure. Dystonic posture is sometimes seen, which might be the initial sign/symptom of this condition. This condition has no sensory symptoms.

Despite timely care, it will take 4-18 days for a full recovery. During this stage, the enzyme acetyl cholinesterase is suppressed for a long time, and metabolites of the main chemical expelled in urinne.

Electrophysiologicalinvestigations [36]: In early days of intermediate syndrome, low response on low frequencies of 1 to 3 Hz and with normal response on 10 20 or 50 Hz.

It is Post synaptic defect.

OPIDN –Organo phosphorus induced delayed neuropathy/

OPIDP – Organo phosphorus induced delayed polyneuropathy [37]

It is a delayed neurotoxic complication. After 5 weeks of toxic exposure, it usually occurs. The exact cause has yet to be determined.

According to Jokanovic et al.,2002 these effects are not attributable to acetyl cholinesterase alone.

In 2004, ERDMAN supported the same conclusion.

Pesticides include TOCP/TOTP,

the OP chemicals that cause neuropathy include

TOCP Triorthocresylphosphate

TOTP Triorthotolylphosphate

EPN Oethyl Opnitrophenyl phenylphosphonothioate

DFP Di isopropyl phosphorofluoridate

NEUROPATHOLOGY [38]:

Degeneration of the distal sections of big, long myelinated axons is the primary lesion. Later, afflicted fibre areas have Wallerian-like degeneration .

The initial lesion is generally seen in a distant non-terminal axonal area, with subsequent changes to the terminal axonal terminals. Bilateral long peripheral nerves long tracts of the brain spinal cord, such as the fasciculus gracillis, as well as spinocerebelllar spinolivarry and rubrospineal reticulospineal tracts, are involved

MECHANISM OF TOXICITY [39]:

Despite the fact that clinical manifestations emerges after long latent period, the initial event namely NTE inhibition, happens within a few hourss

NTE - neuropathy target esterase. Neurotoxicesteraese is another name for this enzyme. It's a carboxyeseterase enzyme that's present in neuron and normal human cells. PNPLA6 is gene that encodes enzyme Though its specific activities are unknown, it is thought to have a role in neuronal outgrowth and neuritic tissue development. The OP substance in oxon form inhibits this enzyme.

Blocking the NTE alone won't cause irreversible polyneuropathy; a large amount of inhibition is required instead, i.e. .70%.

The exact relation between NTE and OPIDN is unknown. Despite the fact that NTE is found in nonneural cells such as kidney and lymphocytes, no detrimental

consequences of OPC induced NTE inhibition have been seen out of nervous system.

Because continuous NTE suppression is not required for OPIDN, there is no link between NTE levels and clinical features. Before signs of neuropathy appear, activity will return to pre-exposure levels.

An imbalance in calcium homeostasis is another suggested cause for OPIDN. Calcium-activated neutral protease was activated, resulting in an increase in calcium/calmodulin-dependent protein kinases.

It has a role in cytoskeletal protein phosphorylation and protein digestion in terminal axon. As a result, Wallerian degeneration occurs. Replacement of normal calcium homeostasis is presently being studied.

CLINICAL MANIFESTATIONS:

begins typically with sensory signs as tingling or numbness in the distal extremities. begin with the lower limb and work up to uppper limb.

Sensory complaints such as tingling and numbness in the distal extremities are common. Begin with the lowe limb and ascend up to uppper limb.

Muscular flaccidity in the distal extremities is a later sign of motor complaints. Typically, the weakness is symmetrical and bilateral. movement abnormalities, such as a highstepping gait occurs. There have been reports of ataxia. Quadriplegia

with foot and wrist drop, as well as moderate pyramidal symptoms, are found as the disease develops in severe versions. (Jokanovic, Stukalov et al. 2002)

Axonal neuropathy is shown by electrophysiological studies with OPDIP organophosphate, which show a slowing of motor and sensory transmission.

Chronic muscle denervation may be present

PROGNOSIS:

recovery usually occurs exclusively in sensory symptoms. motor signs are still persistent. Sensory complaints disappear during the next 1 2 months. While patients with less severe polyneuropathies recover over several months, those with more severe polyneuropathies experience long-term effects. (van Gemert 1999; Kwong 2002)

amount of pyramidal involvement and ataxia also influence functional recovery (Stukalov et al. 2002).

No particular therapy has been found as of yet. (Dewhurst 2000)

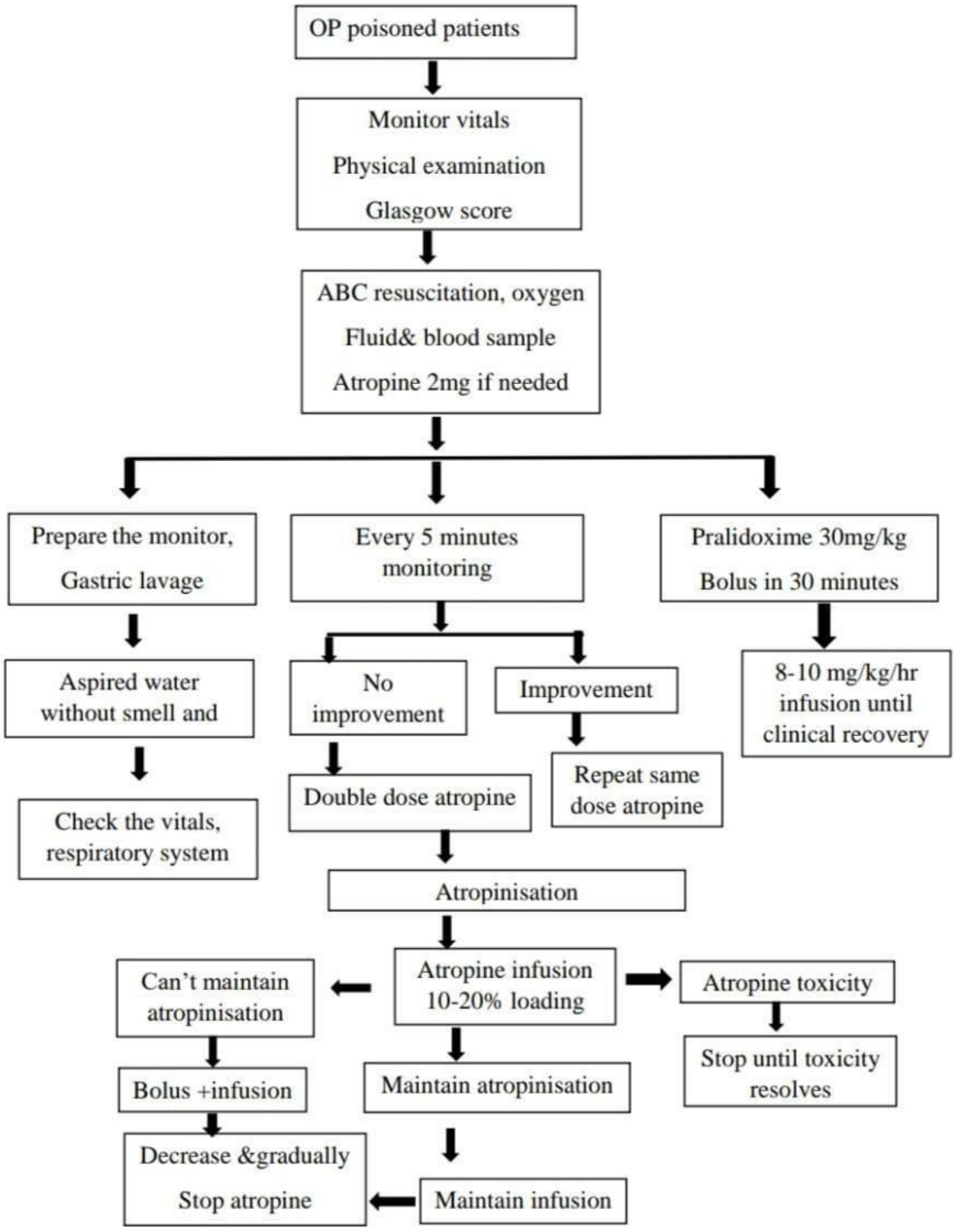
Early administration of pralidoxime with atropine is also not effective in preventing the disease.(Tareg and colleagues, 2001)

MANAGEMENT OF OP POISONING

When patient is brought to hospital with exposure to an organophosphorus compound, care should be taken to prevent further exposure, remove the poison from the body, and neutralise any adverse consequences.

The first step is to take off contaminated clothing and wash the body to remove pesticides. Gastric lavage is administered if the patient is awake. Endotracheal intubation should be administered to unconscious individuals before gastric lavagee, and it is best if the patient comes immediately after taking OPC. 40 Absorption falls by 42% if completed in 20 minutes and by 16% if completed in 60 minutes. 41 After the patient has been fundamentally stabilised, the WHO suggests stomach lavage; activated charcoal can improve absorption.

FIGURE 5 MANAGEMENT OF OP POISONING



INITIAL PHASE: Monitoring of an adequate airway, breathing, and circulation should be required. To reduce aspiration and absorption, the patient should lie in the left lateral position with a patent airway. If there is respiratory trouble, give oxygen. For 24 hours, the patient should not have any oral fluids because increasing oral fluid can speed up absorption.

MAINTENANCE PHASE: Anticholinergic medications, such as atropine, are used to counteract the excessive accumulation of Ach. Atropine 1–3 mg is injected slowly at a starting dose. OPC poisoning has muscarinic side effects that can be treated with atropine43. Repeat atropine infusions every 3 to 5 minutes, even if the dose is doubled, until signs of atropinization such as clear lung fields, mid-pupil position, heartbeats per minute (bpm) more than 110, SBP above 90 millimetres of mercury, bowel sounds, and dryness of the mouth and nose are attained. (51) Depending on the patient's condition, 0.015to0.05 mg/kg of atropine is infused intravenously (I.V.) every 15 minutes in young children. When poisoning is really severe, a continuous infusion is employed. When the patient has been stable for at least six hours, the dosage can be decreased. The patient should then be watched after over the following 72 hours to look for any indications of a relapse. If symptoms return, atropinization should be administered. Atropine can cause tachycardia, dryness, mydriasis, psychosis, and even paralysis as side effects. If the patient experiences a fever, altered sensorium, or muscular fibrillation, atropine must be withdrawn (52).

When atropine toxicity or severe respiratory distress occur, glycopyrrolate is preferred.Until the patients heart rate is higher thann 60 beats per minute, fasciculations are absent, the mucosal membranne is dry, approximately 7.5 mg of glycopyrrolate is infused into 200ml of NS. (53) To achieve the optimum outcomes, enzyme activity must be restored within 10 minutes. Oximes enable this to happen.

For best results, oximes should be delivered within 48 hours.

ATROPINE:

Organophosphorus poisoning is treated with atropine, a physiological antidote. It blocks muscarinic post synaptic membrane receptor-mediated actions in the CNS (bronchial secretion, salivation, increased sweating, bradycardia, and so on). Prior to administering atropine, the patient should be oxygenated.

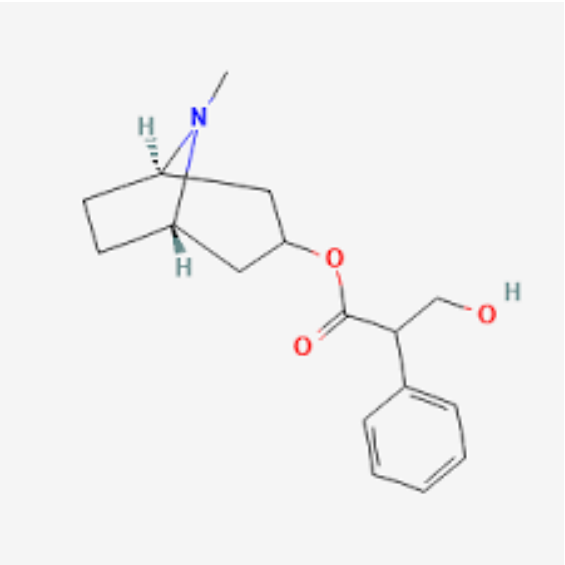


FIGURE 6 : Structure of Atropine

DOSING OF ATROPINE [43]:

There is a lot of information available about the dosage regimen for atropine. There are 38 separate dosage schedules mentioned. All these regimens suggest a bolus must be given until the requirements are met. Then take a maintenance dosage on a regular basis.

Atropine's impact peaks after three minutes. As a result, evaluate the patient every minute until indications of atropinization appear.

Atropine loading doses of 1.8-3 mg IV should be given quickly. Further doses should be given every 5-10 minutes until muscarinic symptoms such as bradycardia, miosis, and bronchorrea have subsided. Other methods of atropine administration include nebulization, which improves oxygenation.

Because of its ability to absorb through mucous membrane, atropine can also be administered via endotracheal tube in an emergency.

The goal of anticholinergic therapy is to dry up tracheobronchial tree secretions and other secretions while also raising heart rate.

Atropine causes pupillary dilation as a first response. Atropine infusions of 0.02-0.08 mg/kg/h are also an approach. When compared to intermittent therapy, this therapeutic strategy has a substantial reduction in mortality.

If atropinization is gone, provide another atropine bolus dosage and speed up the infusion.. If atropine toxicity is suspected, the infusion should be discontinued and the toxicity treated.

Infusion was resumed at a rate that was 70% of the previous rate once toxic effects had dissipated. once the rate of infusion was reduced, the patient was checked hourly, followed by every 2-3 hours.

The atropine infusion should be maintained pour 2to5 days and then reduced over 3to7 days. Atropine must be taken with caution older people with coronary artery disease who are at risk of heart failure due to tachycardia. Tachycardia is not contraindication to taking atropine (however a heartrate of more than 140beats should be avoided).

objectives of therapy with atropine [30]:-

1.80 or more beats per minute for pulse.

2. SBP was kept at 90 mm Hg or higher.

3. There should be no secretions in the lungs; there should be no wheezing.

4. Axillae must not be moist

5. pupil should be enlarged

NATURAL SOURCE OF ATROPINE:

It's plant alkaloid found in Daturastramonium, thornapple, and atropa belladona, or death shadow..

ABSORPTION:

Gut absorption is excellent, absorbed well via conjunctiva and skin.

DISTRIBUTION:

It is dispersed widely throughout the body. Atropine also penetrates the bloodbrain barrier, counteracting acetylcholine's effects in central nervous system. Within 30 minutes to 1 hour, significant amounts were obtained in the CSF.

METABOLISM AND EXCRETION:

Elimination takes place in two stages: fast and slow.

The fast phase has a t1/2 of 2 hours while the slow phase has a t1/2 of 13 hours.

About half of the medication gets eliminated unaltered in the urine.

The parasympathetic action in the eye lasts for more than 72 hours.

PHARMACODYANAMICS:

Atropine is a reversible muscarinic receptor blocker. Atropine inhibits the release of inositoltriphosphate(IP3) and the inhibition of adenylcyclase by binding to the muscarinic receptor. Atropine has a high sensitivity to salivary, bronchial, and sweat glands. The stomach's parietal cells are the least sensitive. The muscarinic receptor is extremely selective for atropine. At the M1,M2,M3 receptors, atropine has no difference.

SYSTEMIC EFFECTS:

CENTRAL NERVOUS SYSTEM:

Has a minor CNS stimulating effect on medulla

EYE:

Cycloplegia and mydriasis both decrease lacrimal secretion. All of these factors contribute to the hazy vision that occurs after atropinization and can persist up to a week.

CARDIOVASCULAR SYSTEM:

By inhibiting the prejunctional M1 receptor at low dosages, it causes bradycardia. Blocking the muscarinic receptor in the A-V node reduces the PR interval on the ECG

By inhibiting vagal slowing, a moderate dosage causes tachycardia. Local anaesthetic effect causes intraventricular conduction abnormalities in hazardous dosages. Atropine inhibits cardiac dilation mediated by the parasympathetic nervous system. Atropine has a little effect on blood pressure.

RESPIRATORY SYSTEM:

Atropine reduces bronchial secretions and causes bronchodilation.

GASTROINTESTINAL TRACT:

Salivary secretion is reduced more than stomach secretion. Smooth muscle motility in the G.I. reduced from the stomach to the colon. The time it takes for the stomach to empty is delayed, and the time it takes for the intestines to transit is extended.

GENITOURINARY TRACT:

By relaxation of muscles of ureters and bladder, it reduces urination

SWEAT GLANDS:

Atropine suppresses thermo regulatory perspiration. Atropine fever is frequent in adults after a big dosage, but it is occurs in children and babies with very low doses.

ATROPINE TOXICITY:

Dry mouth, flushed skin, dilated pupils, excitation, delirium, palpitations, hypotension, cardiovascular collapse, convulsions, and coma are symptoms of an atropine overdose. Most of these signs and symptoms are indicative of organophosphorus poisoning. This condition needs to be identified, and the dosage needs to be changed.

GLYCOPYRROLATE [44]:

If there is no indication of central toxicity, glycopyrolate(0.5mg/kg), a quaternaryammonium molecule, isused instead of atropine It offers a number of potential benefits over atropine. It doesn't pass the blood-brain barrier, therefore it

can't cause any central effects. There's also reduced tachycardia and improved secretion management, reduces the risk of respiratory illnesses.

OXIMES- CHOLINESTERASE REACTIVATORS[45,46,47]:

Pralidoxime (2-Hydroxyiminomethyl-1pyridiniumchloride, 2-PAM;pyridine 2 aldoximemethylchloride)

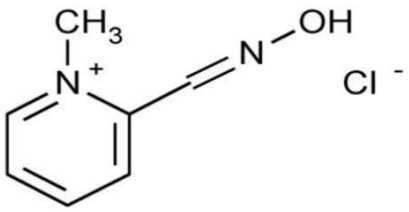


FIGURE 7 : PRALIDOXIME

1. Cholinesteraese reactivation via cleavage of phosphorylated active sitess
2. An unbounded organophosphorus molecule undergoes a direct reaction and is detoxified.
3. Anticholinergic action produced by the body. PAM attaches to the area where the enzyme has connected and prevents cholinesterase from activating causing enzyme to work properly Cholinesterase "regeneration" is the term for this process. By vying for the phosphate portion of the OP molecule, pralidoxime inhibits the acetyl cholinesterase enzyme. This activity happens only after the enzyme has been

damaged and inhibited, following which enzyme “Ages” and alters to irreversibly inactive state.

AGING:- This inhibitor creates strong irreversible connection with the enzyme over a length of time. As a result of this interaction, oximes are unable to bind to the enzyme. The length of time varies depending on the chemical. Beyond that, oximes serve no useful use.

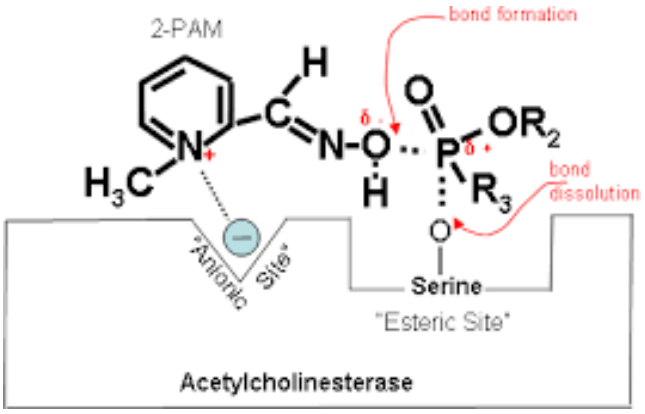


FIGURE 8: ACTION OF PRALIDOXIME

CARBAMATE POISONING AND OXIMES:

Due to the fact that the hazardous substance's link with the enzyme lyses on its own after a few hours, pralidoxime has no effect on carbamate toxicity.

bond does not age with time. Although early in the illness is when pralidoxime is most effective, it has beneficial benefits for a long time following exposure. If

administered within 6 hours following poisoning, the oximes are most likely to be successful.

Certain situations require the use of oximes for an extended period of time, or It may be initiated even after the ageing stage has ended. They are:-

1 Compounds that are fat soluble will stay for a long period and release after the somtime, resulting in clinical symptoms later owing to enzyme re inhibition.

2 A OP substance must produce an active metabolite in order to elicit clinical symptoms. It will take a while.

3 Dermatologic exposure will have delayed manifestations.

Pralidoxime is eliminated in the kidneys, and 80 percent of the dosage is recovered unaltered in the urine within 12 hours.

Plasma half-life is 75 minutes.

Adults are administered 1-2 grams of pralidoxime in 100to150 millilitres of 0.9 percent sodiumchloride intravenously over 30 minutes. If muscular weakness and fasciculations do not improve within an hour, repeat the dose.

This dose should be repeated every 6-12 hours for 24-48hrs Due to the serum concentration's anticipated decrease to below therapeutic levels in a few hours, toxicity might return before the next dosage.

For severe poisoning, a 500mg/hour continuous infusion has been recommended.

The British national formulary recommends a maximum dosage of 12 grams in 24 hours

UNTOWARD EFFECTS:

In humans, adverse effects of 2PAM are limited, and may not appear until extremely high levels (400 mg/ml) are reached.

1. Dizziness for a short period of time, dry mouth
2. Temporary visual problems due to increased intraocular pressure.
3. The rate of infusion may be linked to an increase in diastolic blood pressure.
4. Sudden cardiac arrest has been recorded after rapid IV delivery, even at a normal dosage of 2gms over 10 minutes.
5. Higher dosages can cause neuromuscular blockade on their own.
6. Has an interaction with atropine. Atropine's harmful effects can occasionally be precipitated. Other oximes: Sugar oximes (a chemical mixture of glucose and 2-PAM derivatives) appear to be a potential way to increase CNS penetration.

OBIDOXIME :

Also known as Toxogonin

It is more powerful than 2-PAM since it has two active sites per molecule

To combat nerve gases used in chemical warfare, the H series of oximes (named after Hagedorn) HI-6 and HJ-6 were created..

They have direct central and peripheral anticholinergic actions in addition to reactivating cholinesterase.

Eyer F. et al. investigated the role of obidoxime in organophosphate poisoning in relation to signs, symptoms, and cholinesterase levels. This oxime reacts to parathion differently from other OPCs, according to the research [49.]

PHARMACOKINETICS:

Plasma half life is 6to9 hours

Renal clearance : 69 ml/min

According to renal function, the obidoxime dose should be modified. To assess the therapeutic window of this drug in organophosphate poisoning, more randomised controlled studies are needed.

METABOLIC ACIDOSIS

Acid-base disorders are disturbances in the homeostasis of hydrogen ion concentration in the plasma. Any process that increases the serum hydrogen ion concentration is an acidotic process. The term acidemia is used to describe serum that is abnormally acidic, and this can be due to a respiratory acidosis, which involves changes in carbon dioxide, or a metabolic acidosis which is influenced by decreased serum bicarbonate levels.

Metabolic acidosis is characterized by an increase in the hydrogen ion concentration in the systemic circulation that results in an abnormally low serum bicarbonate level. Metabolic acidosis signifies an underlying disorder that needs to be corrected to minimize morbidity and mortality. According to traditional concepts of acid-base physiology, the [H+] in extracellular fluid is determined by the balance between the partial pressure of carbon dioxide (PCO2) and the concentration of bicarbonate (HCO3) in the fluid. This relationship is expressed as follows:

$$[H+] = 24 \times (PCO2/HCO3)$$

Lactic acidosis, ketoacidosis, renal failure, intoxication with ethylene glycol, methanol, salicylate, and less frequently with pyroglutamic acid (5-oxoproline), propylene glycole, or djenkol bean are the causes of high anion gap metabolic acidosis (gjenkolism). The loss of gastrointestinal bicarbonate, renal tubular acidosis, drug-induced hyperkalemia, early renal failure, and acid administration are the most frequent causes of hyperchloremic metabolic acidosis..

The Anion Gap The anion gap is a rough estimate of the relative abundance of unmea-sured anions, and is used to determine if a metabolic acidosis is due to an

accumulation of non-volatile acids (e.g., lactic acid) or a primary loss of bicarbonate (e.g., diarrhea)

To achieve electrochemical balance, the concentration of negatively charged anions must equal the concentration of positively charged cations.

This electrochemical balance is expressed in the equation shown below using electrolytes that are routinely measured, including sodium (Na), chloride (CL), and bicarbonate (HCO3), as well as the unmeasured cations (UC) and unmeasured anions (UA).

$$Na + UC = (CL + HCO3) + UA$$

Rearranging the terms in this equation yields the following relationships:

$$Na – (CL + HCO3) = UA – UC$$

The difference (UA – UC) is a measure of the relative abundance of unmeasured anions, and is called the anion gap (AG).

The difference (UA – UC) is a measure of the relative abundance of unmeasured anions, and is called the anion gap (AG).

$$AG = Na – (CL + HCO3)$$

A normal anion gap depends on concentration of phosphate and serum albumin in serum and ranges from 4to12 mmol/L. An increased or normal anion gap metabolic acidosis is typically due to excess acid and/or decreased base. A reduction in the anion gap is most commonly due to decreased albumin concentration.

APACHE II SCORE

APACHE-II Score provides an estimate of ICU mortality based on a number of laboratory values and patient signs taking both acute and chronic disease into account.

	+4	+3	+2	+1	0	+1	+2	+3	+4
Rectal temperature (°C)	≥41	39–40.9		38–38.9	36–38.4	34–35.9	32–33.9	30–31.9	≤29.9
MAP (mmHg)	≥160	130–159	110–129		70–109		50–69		≤49
Heart rate (/min)	≥180	140–179	110–139		70–109		55–69	40–54	≤40
Respiratory rate (/min)	≥50	35–49		25–34	12–24	10–11	6–9		≤5
If FiO_2 ≥50%, check A-a gradient; if FiO_2 <50%, PaO_2									
A-a gradient	≥500	350–499	200–349		<200				
PaO_2 (mmHg)					>70	61–70		55–60	<55
Arterial pH	≥7.7	7.6–7.69		7.5–7.59	7.3–7.49		7.25–7.3	7.15–7.2	<7.15
Na (mM)	≥180	160–179	155–159	150–154	130–149		120–129	111–19	≤110
K (mM)	≥7	6–6.9		5–5.9	3.5–4.9	3–3.4	2.5–2.9		<2.5
Creatinine(mg/L)	≥35	20–34	15–19		6.0–14		<6.0		
Hematocrit (%)	≥60		50–59.9	46–49.9	30–45.9		20–29.9		<20
WBC count(10^9/L)	≥40		20–39.9	15–19.9	3–14.9		1–2.9		<1

Glasgow coma score (GCS): 0–12 points = 15–GCS

Age (y)	Points
<44	0
45–54	2
55–64	3
65–74	5
>75	6

Chronic health (history of chronic conditions)[a]	Points
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

FIGURE 9 ACUTE PHYSIOLOGY AND CHRONIC HEALTH EVALUATION SCORE

APACHE II Score	Nonoperative	Postoperative
0-4	4%	1%
5-9	8%	3%
10-14	15%	7%
15-19	25%	12%
20-24	40%	30%
25-29	55%	35%
30-34	73%	73%
>34	85%	88%

FIGURE 10 MORTALITY BASED ON APACHE 2 SCORE

Created by William Knaus, MD

MATERIALS AND METHODS:

It is a cross-sectional study of 94 confirmed cases of organophosphorus poisoning, admitted in the medicine ICU / wards "SHRI B. M PATIL MEDICAL COLLEGE AND RESEARCH CENTRE" , VIJAYAPURA during the period of **January 2021 to June 2022**

INCLUSION CRITERION

Confirmed cases of OPC poisoning confirmed by the PDC report

EXCLUSION CRITERIA

1. 1. Based on their medical histories and clinical characteristics, patients with other pesticide and combined poisoning (such organo-carbamates) have been ruled out.
2. 2. Patients who had consumed alcohol-containing substances have been disqualified eg. Ethylene glycol, methanol, paraldehyde, formaldehyde.
3. Patients with known medical illness such as seizure disorder, renal failure, diabetic ketoacidosis, uraemia, salicylate poisoning etc.
4. Pregnant patients are excluded from the study

STATISTICAL ANALYSIS

SPSS (Statistical Package For Social Sciences) version 20. (IBM SPASS statistics [IBM corp. released 2011] was used to perform the statistical analysis

- Data was entered in the excel spread sheet.
- Descriptive statistics of the explanatory and outcome variables were calculated by mean, standard deviation for quantitative variables, frequency and proportions for qualitative variables.
- Inferential statistics like
    - Chi-square test was applied for qualitative variables
    - ROC curve was computed to find the cut-off values, sensitivity and specificity of BD to predict Outcome and Ventilation.
    - Pearson's correlation was applied to correlate Base deficit and APACHE 2 scores.
- The level of significance is set at 5%
- Categorical variables was compared using the Chi-square test.
- Correlation between variables was calculated by Person's/ Spearman's Correlation.
- $P<0.05$ was assumed statistically significant.

RESULTS

	N	Minimum	Maximum	Mean	S.D
Age	94	16.0	75.0	31.95	13.99

TABLE 1: MEAN AGE DISTRIBUTION OF THE SUBJECTS

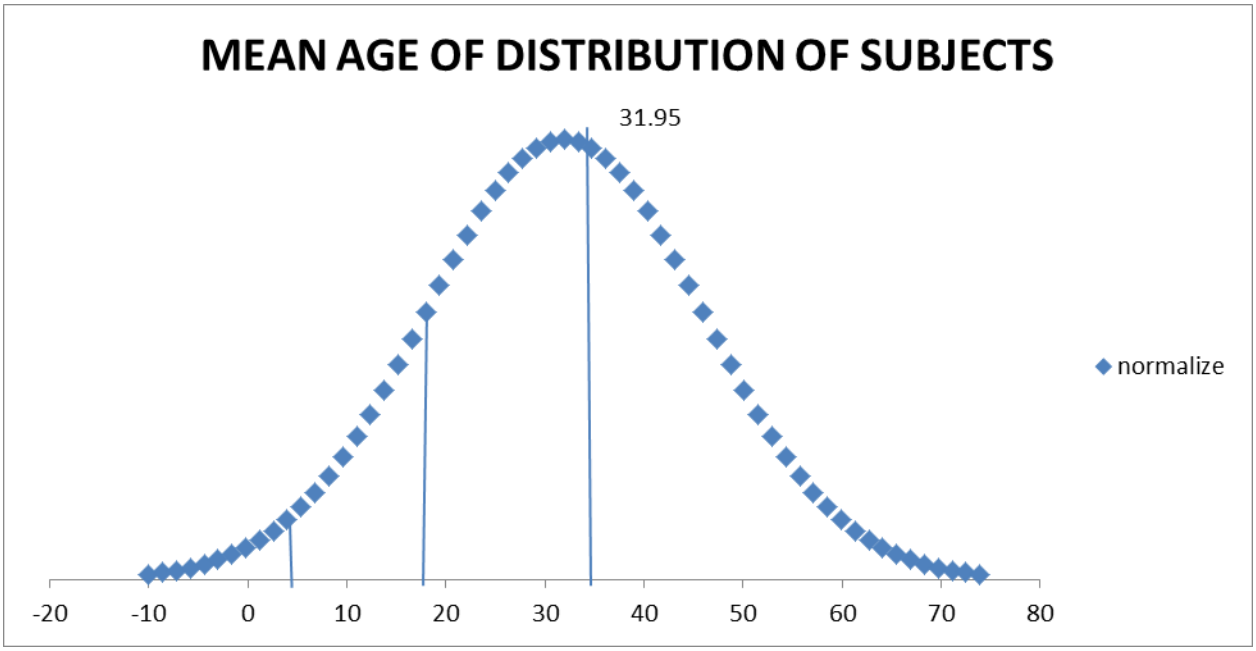


FIGURE 11 MEAN AGE OF DISTRIBUTION OF SUBJECTS

TABLE 2: DISTRIBUTION OF THE SUBJECTS BASED ON AGE GROUPS

Age groups	Frequency	Percent
16 to 25 yrs	42	44.7
26 to 35 yrs	26	27.7
36 to 45 yrs	10	10.6
46 to 55 yrs	8	8.5
> 55 yrs	8	8.5
Total	94	100.0

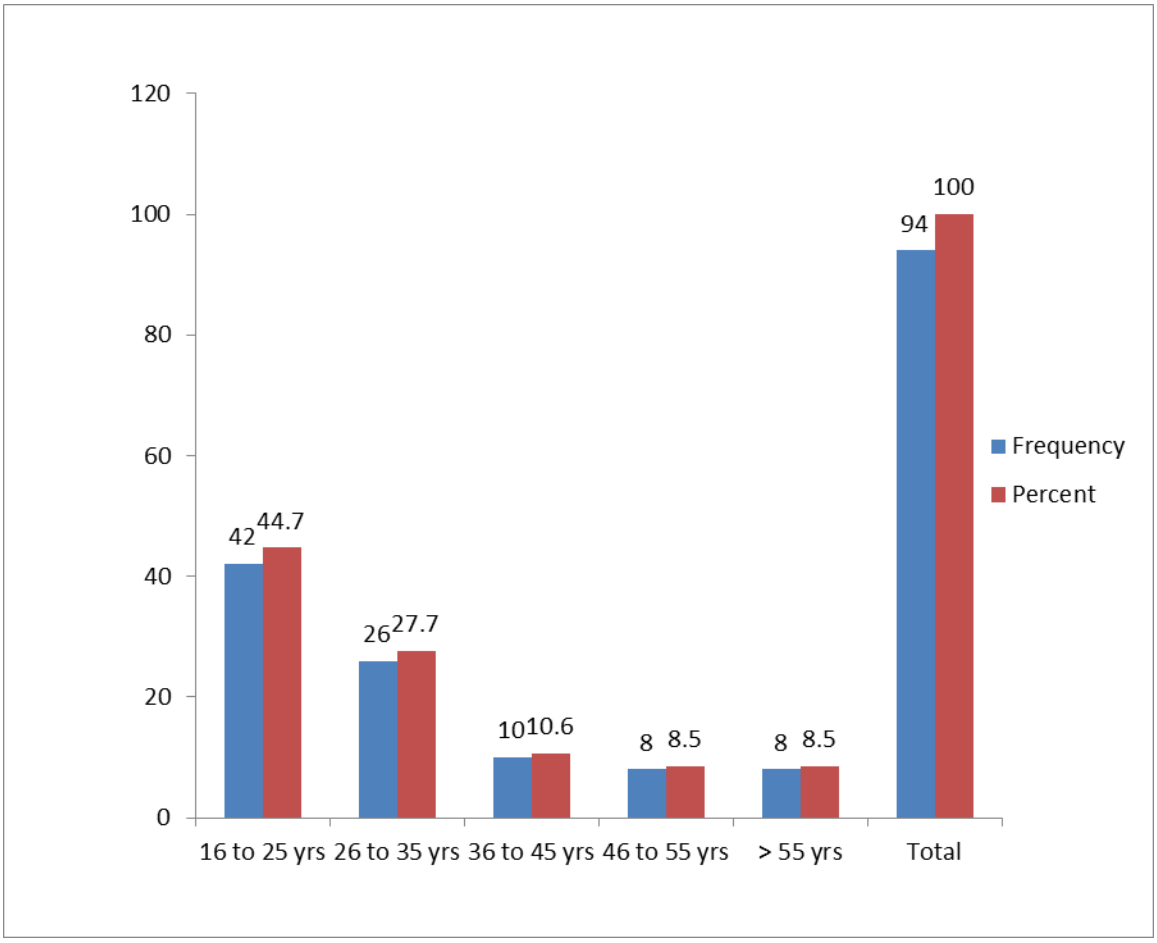


FIGURE 12 DISTRIBUTION OF PATIENTS BASED ON AGE GROUPS.

TABLE 3: DISTRIBUTION OF THE SUBJECTS BASED ON GENDER

Gender	Frequency	Percent
Females	27	28.7
Males	67	71.3
Total	94	100.0

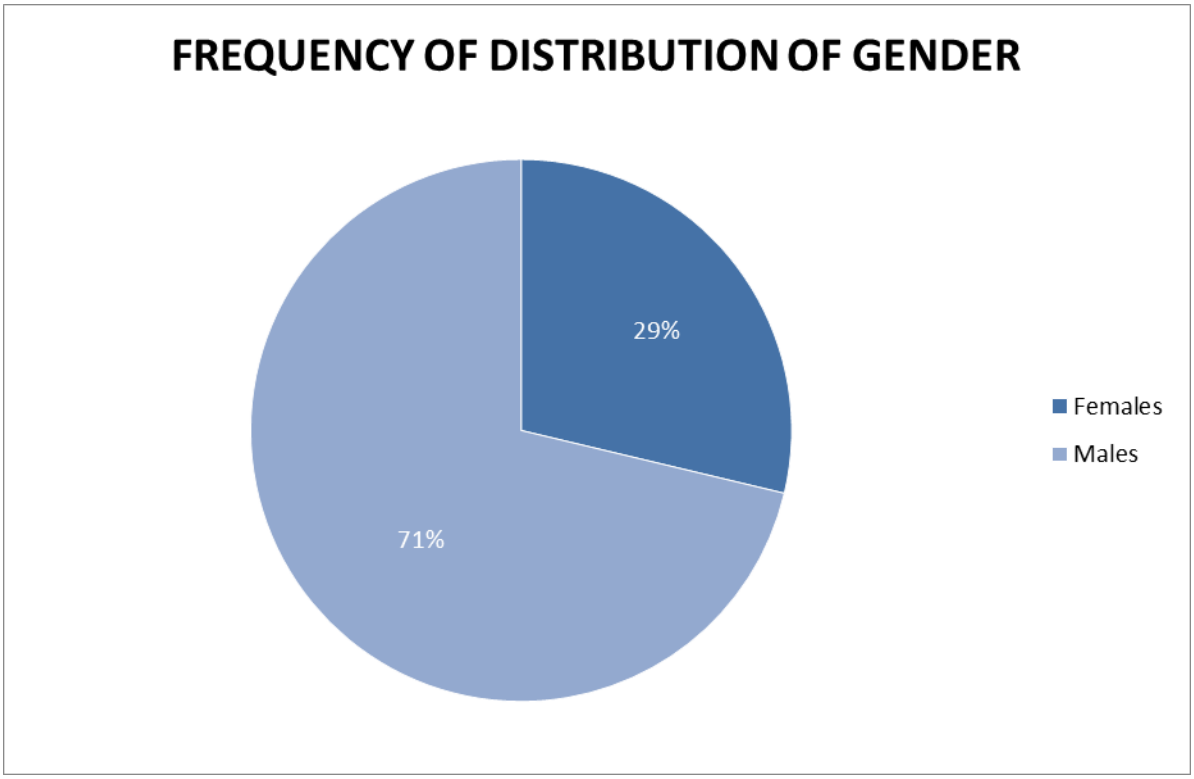


FIGURE 13 FREQUENCY OF DISTRIBUTION OF GENDER

TABLE 4: MEAN VALUES

	N	Minimum	Maximum	Mean	S.D
CBC : TLC	94	4.08	68.00	14.162	8.391
HB	94	5.90	20.50	13.578	2.565
PLT COUNT	94	1.71	585.00	202.890	141.702
RBS	94	72.0	276.0	116.904	32.127
CHOLIN.	94	200.0	10182.1	2988.847	3038.340
ALBUMIN	94	2.0	5.1	3.851	0.602
UREA	94	7.0	90.0	29.883	17.283
NA	94	116.0	168.0	141.096	8.088
K	94	2.6	6.1	4.186	0.868
PH	94	6.90	7.51	7.298	0.134
HCO3	94	3.2	24.0	16.522	4.826
BD	94	0.0	20.8	7.446	4.823
SBP	94	80.0	150.0	108.681	13.696
PR	94	80.0	150.0	123.298	13.061
RR	94	12.0	44.0	22.074	5.927
HEMATOCRIT	94	18.2	67.7	40.856	7.936

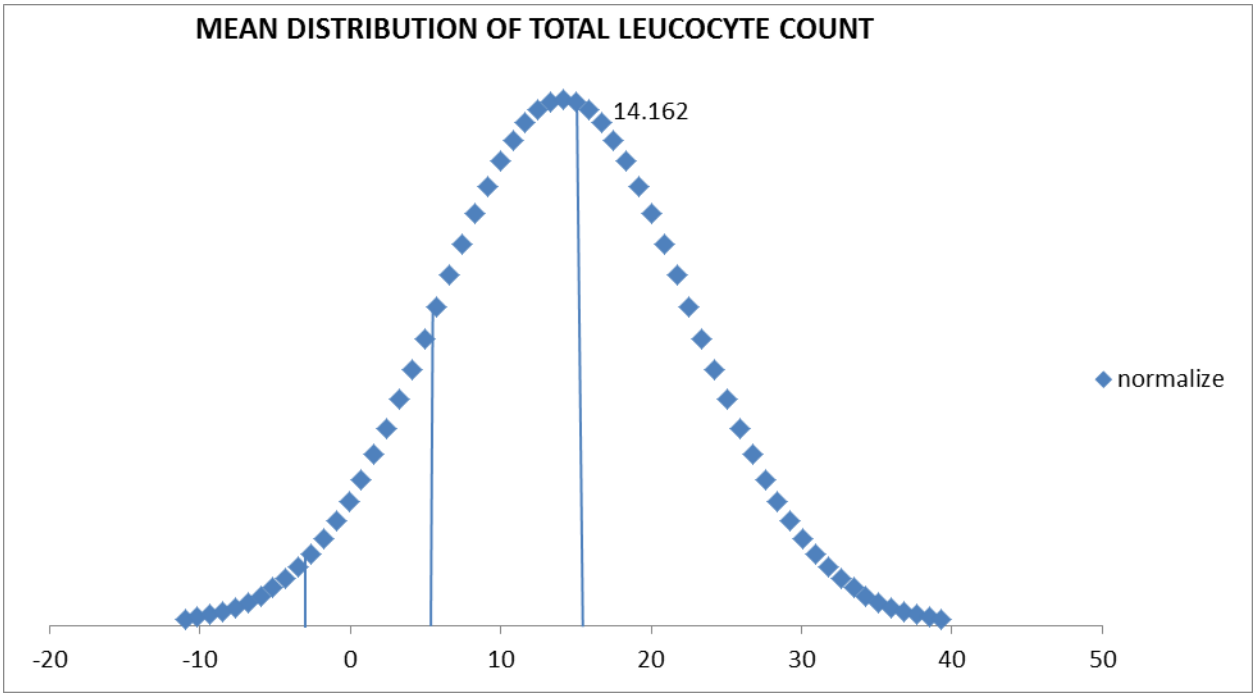


FIGURE 14 DISTRIBUTION OF TOTAL LEUCOCYTE COUNT

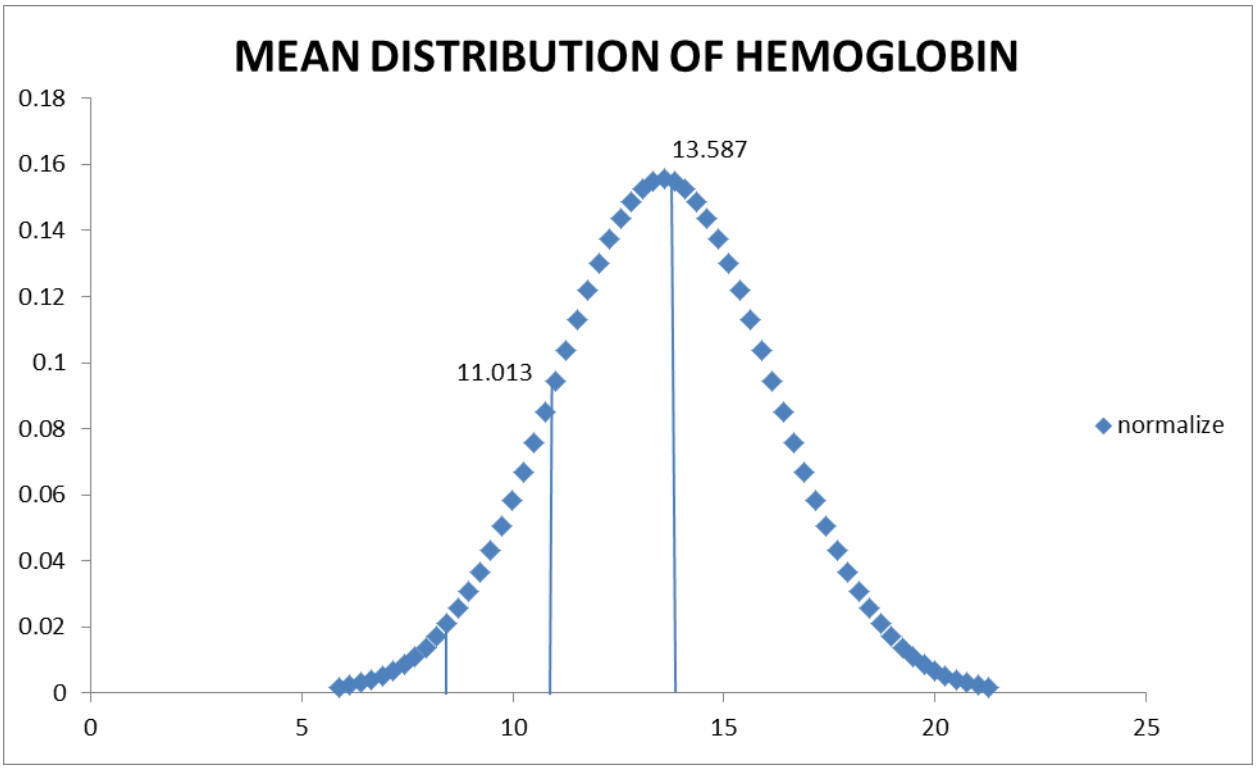


FIGURE 15 DISTRIBUTION OF HEMOGLOBIN

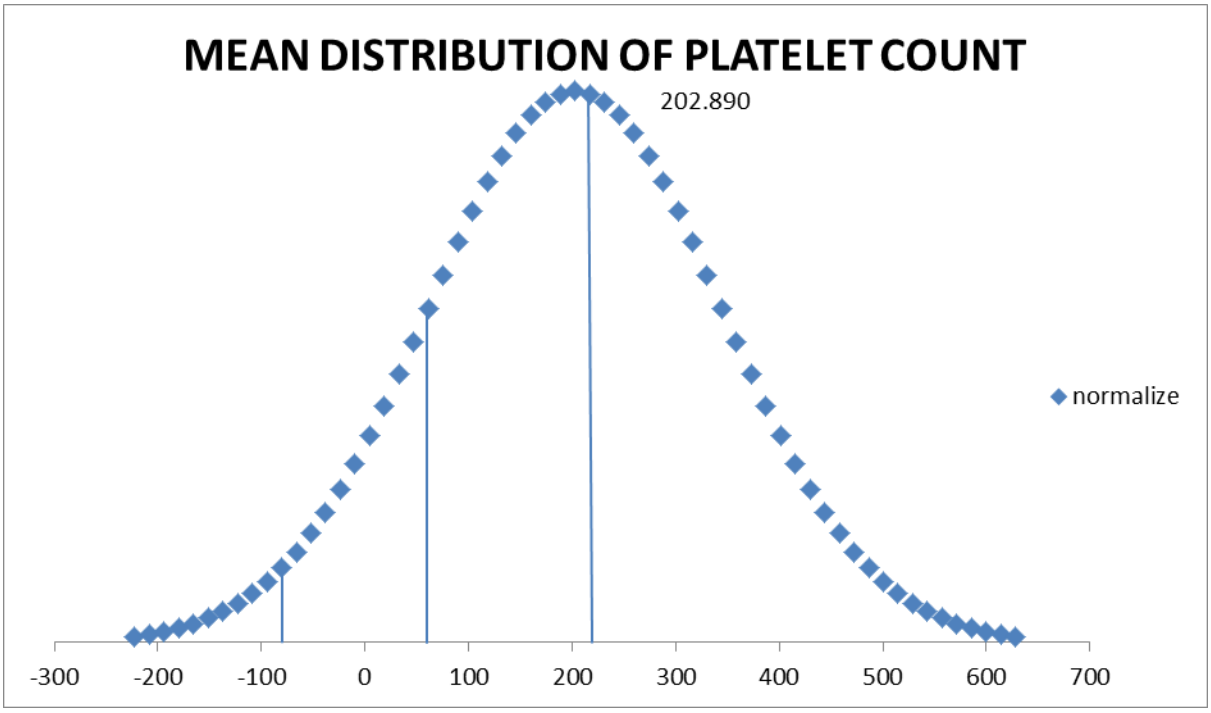


FIGURE 16 DISTRIBUTION OF PLATELET COUNT

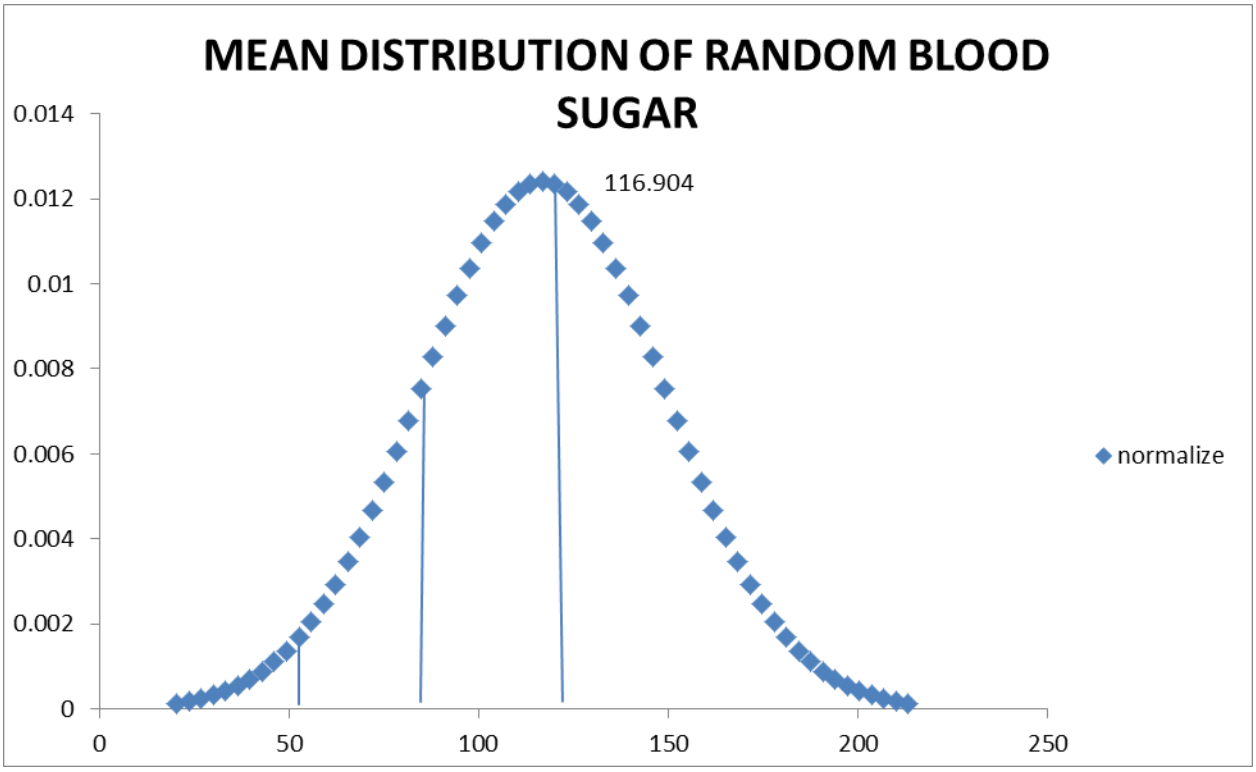


FIGURE 17 DISTRIBUTION OF RANDOM BLOOD SUGAR

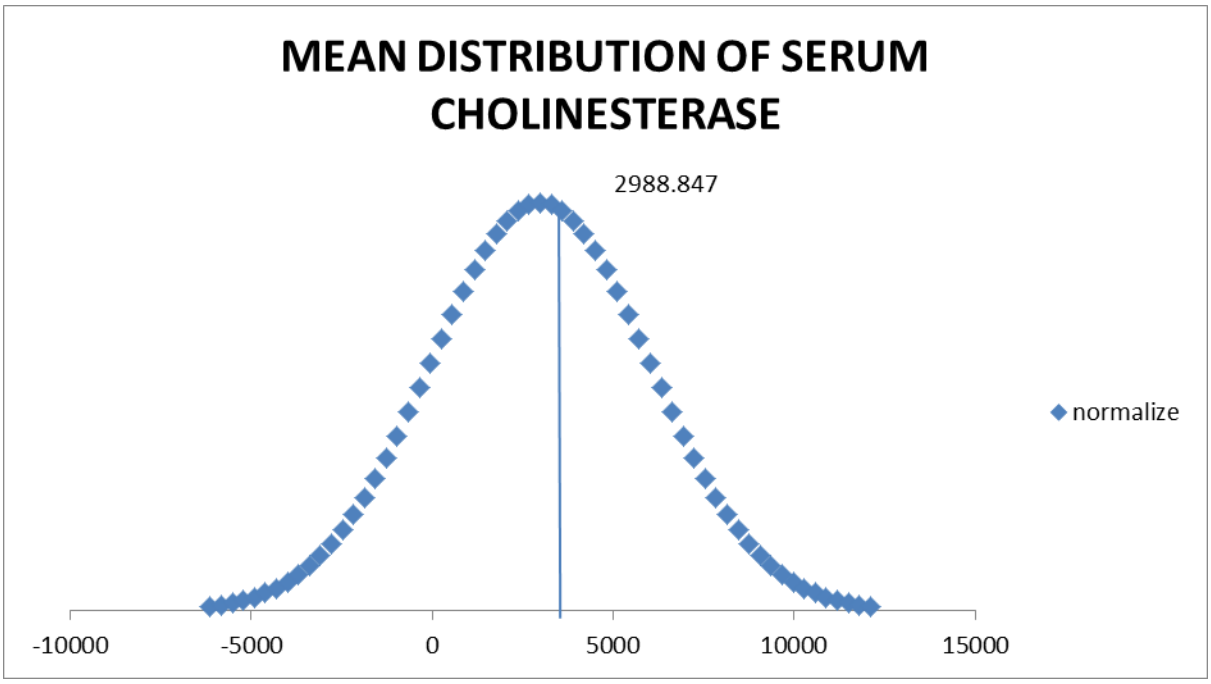


FIGURE 18 DISTRIBUTION OF SERUM CHOLINESTERASE

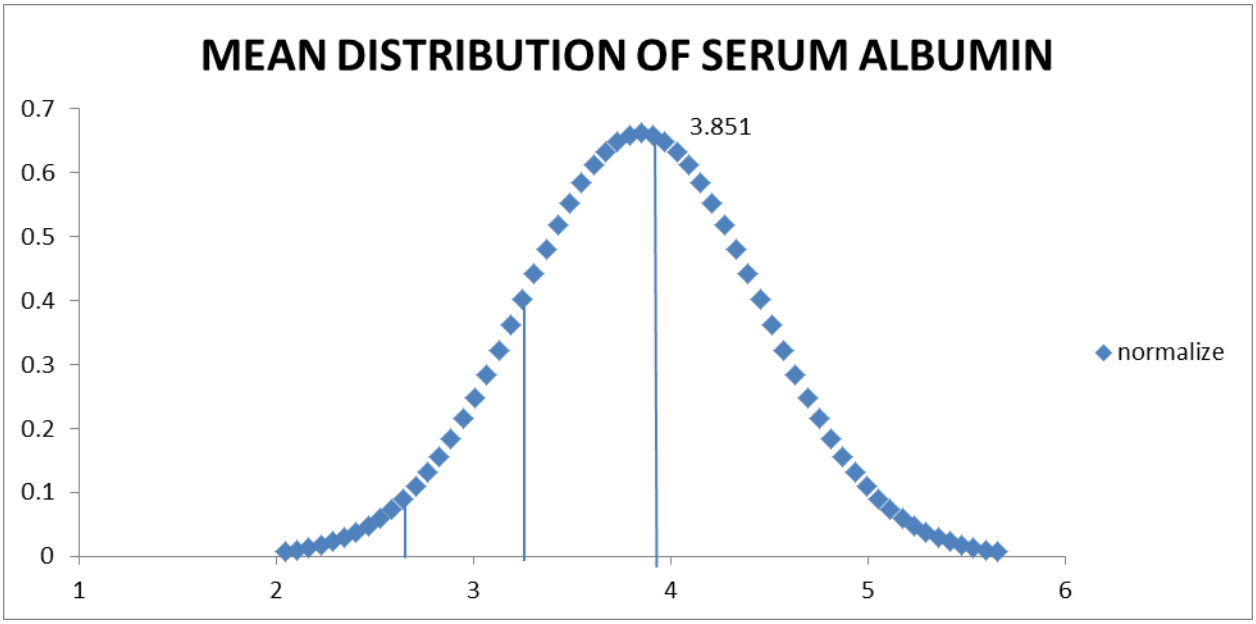


FIGURE 19 DISTRIBUTION OF SERUM ALBUMIN

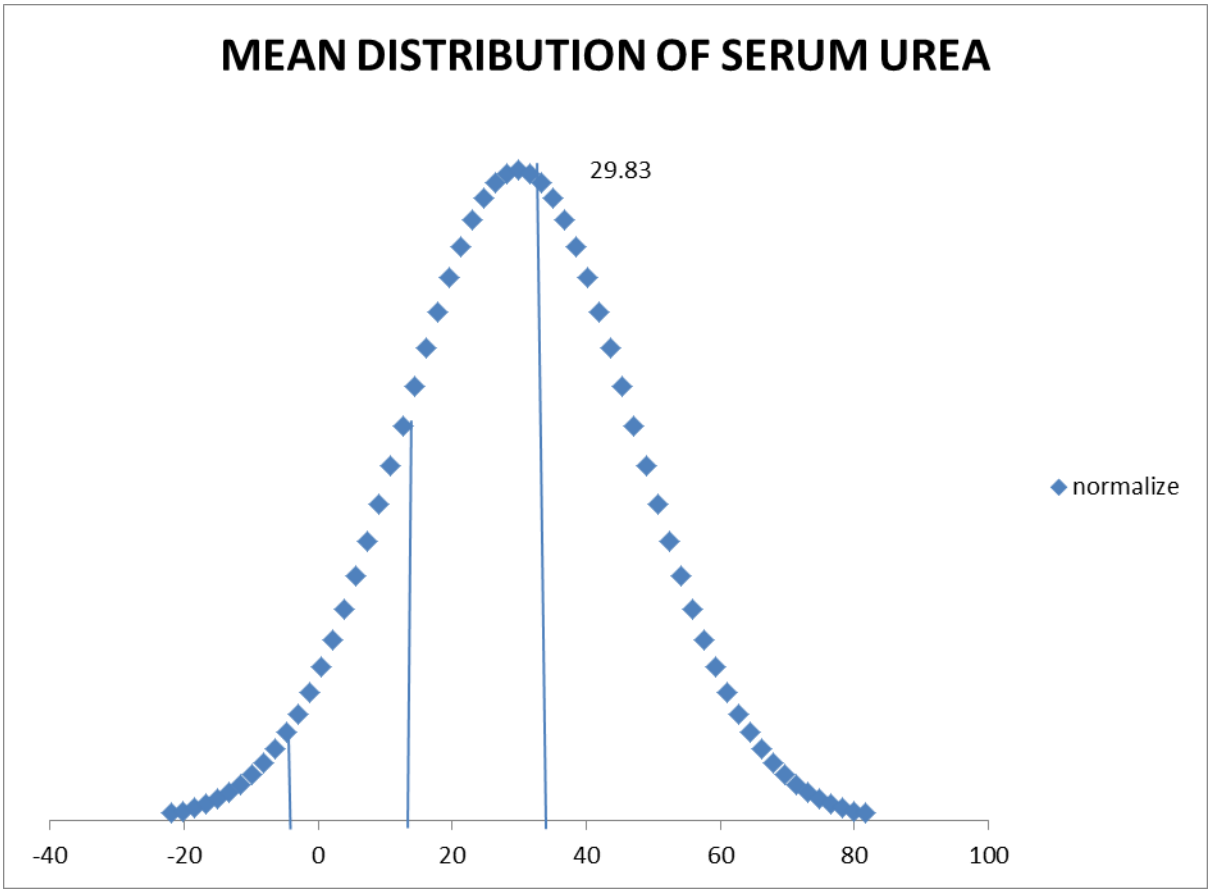


FIGURE 20 DISTRIBUTION OF SERUM UREA

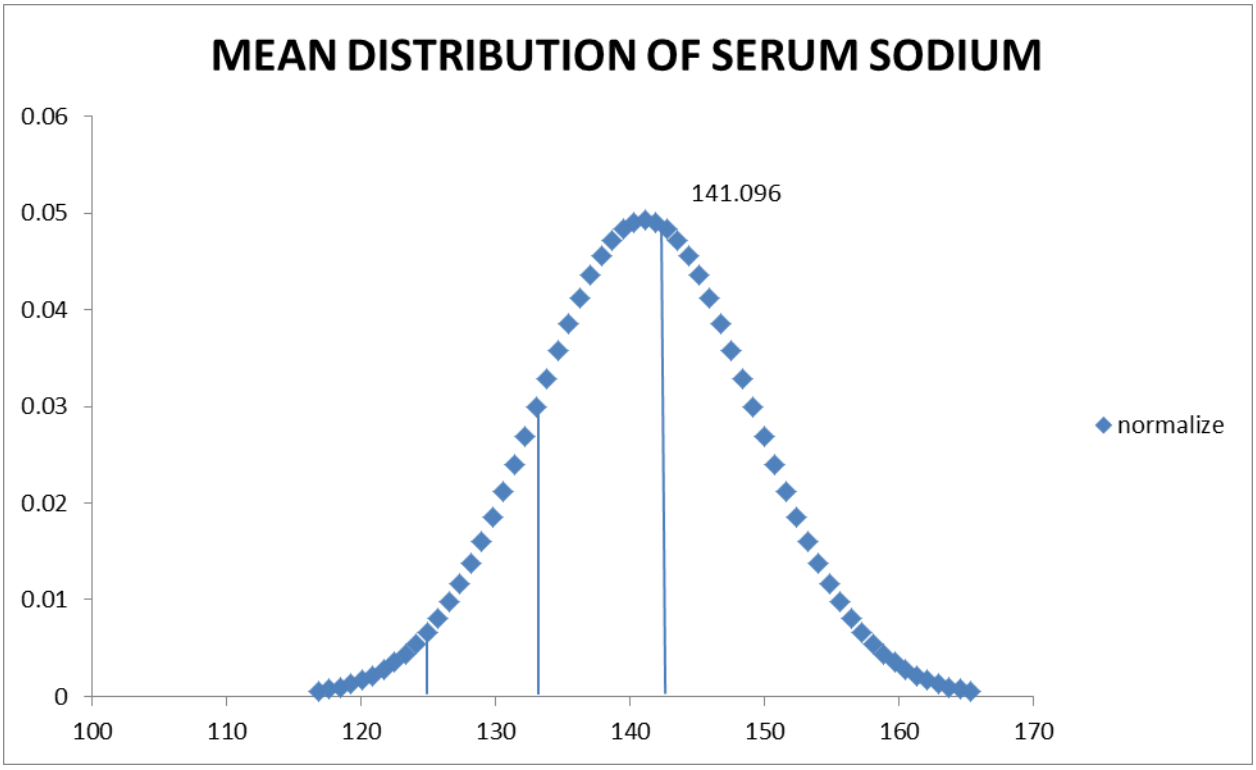


FIGURE 21 DISTRIBUTION OF SERUM SODIUM

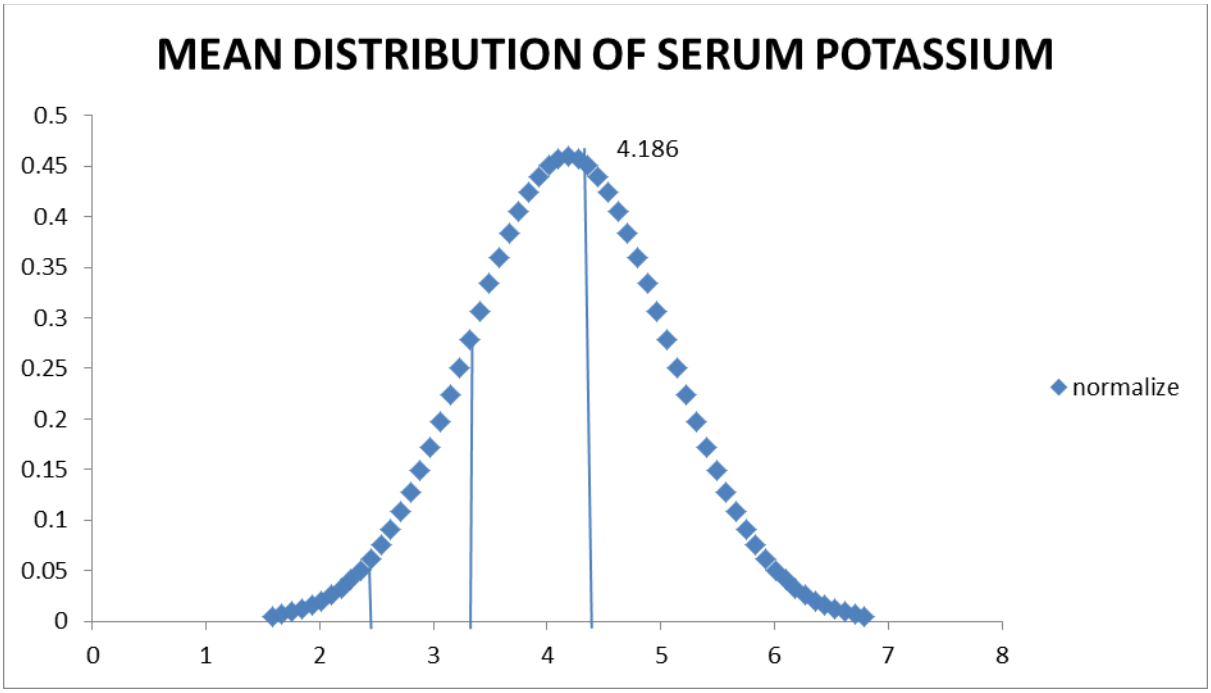


FIGURE 22 DISTRIBUTION OF SERUM POTASSIUM

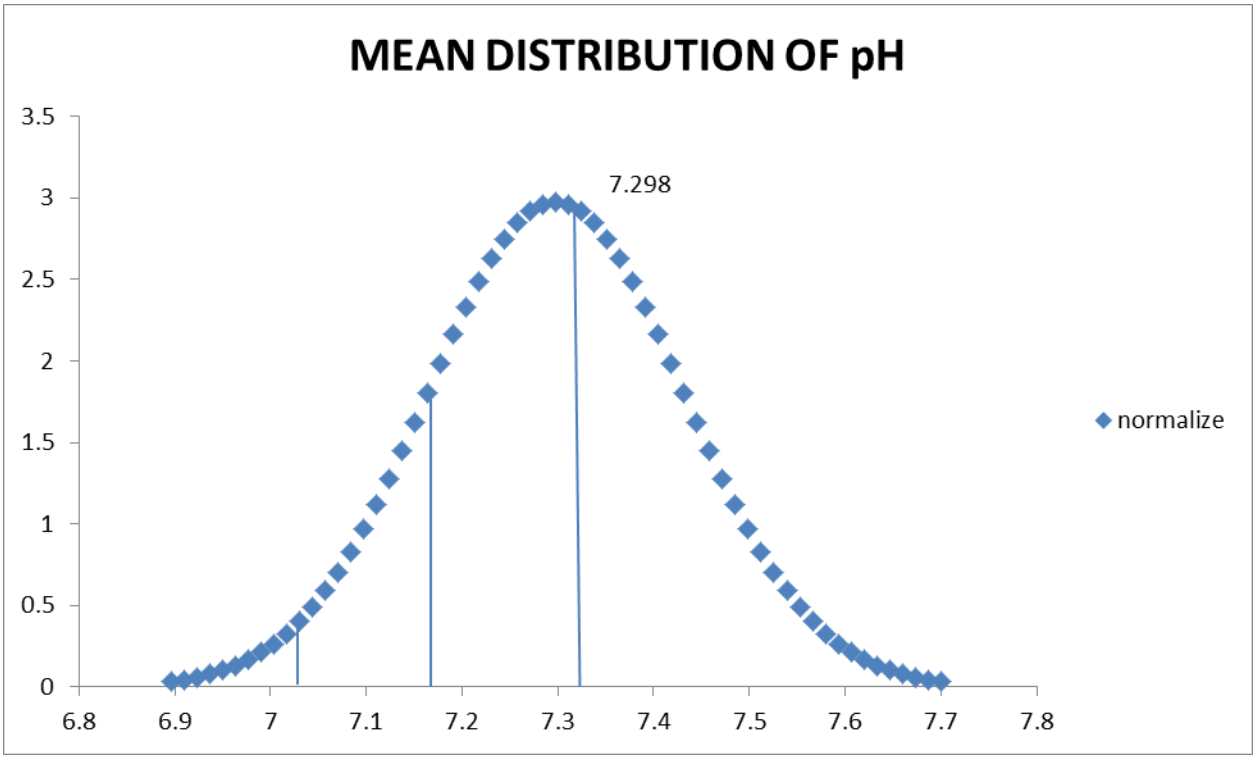


FIGURE 23 DISTRIBUTION OF SERUM Ph

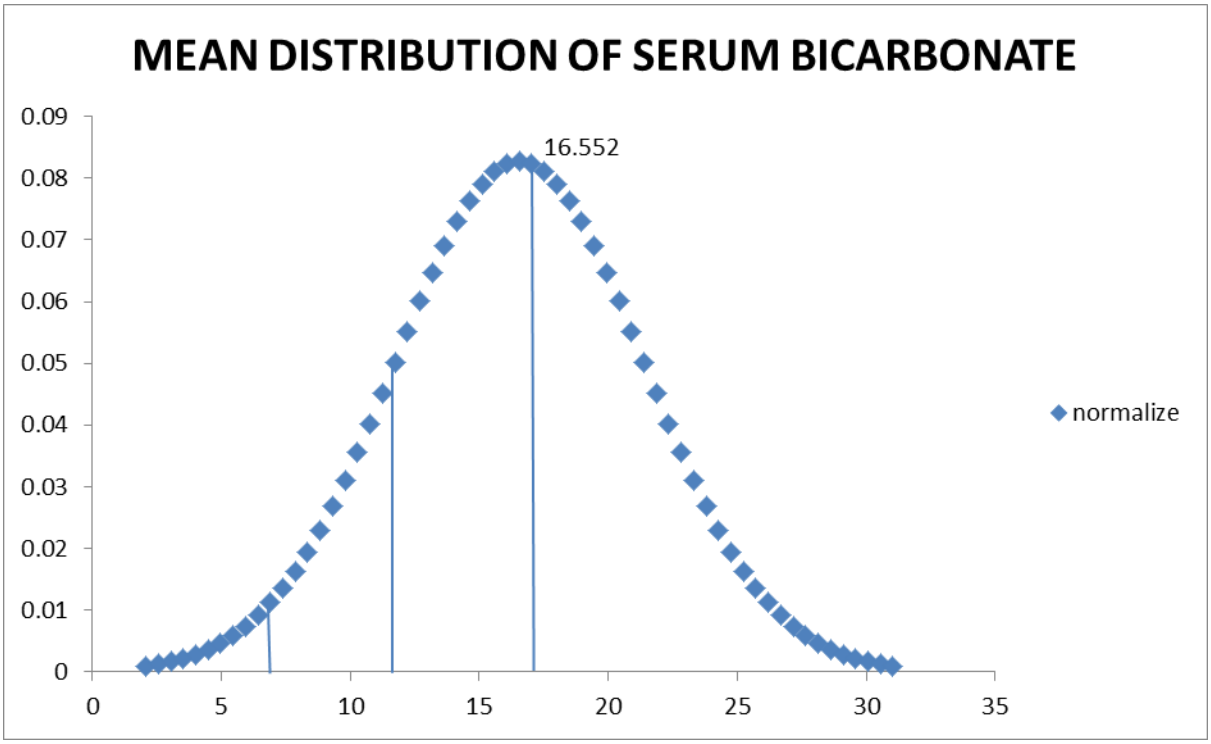


FIGURE 24 DISTRIBUTION OF SERUM BICARBONATE

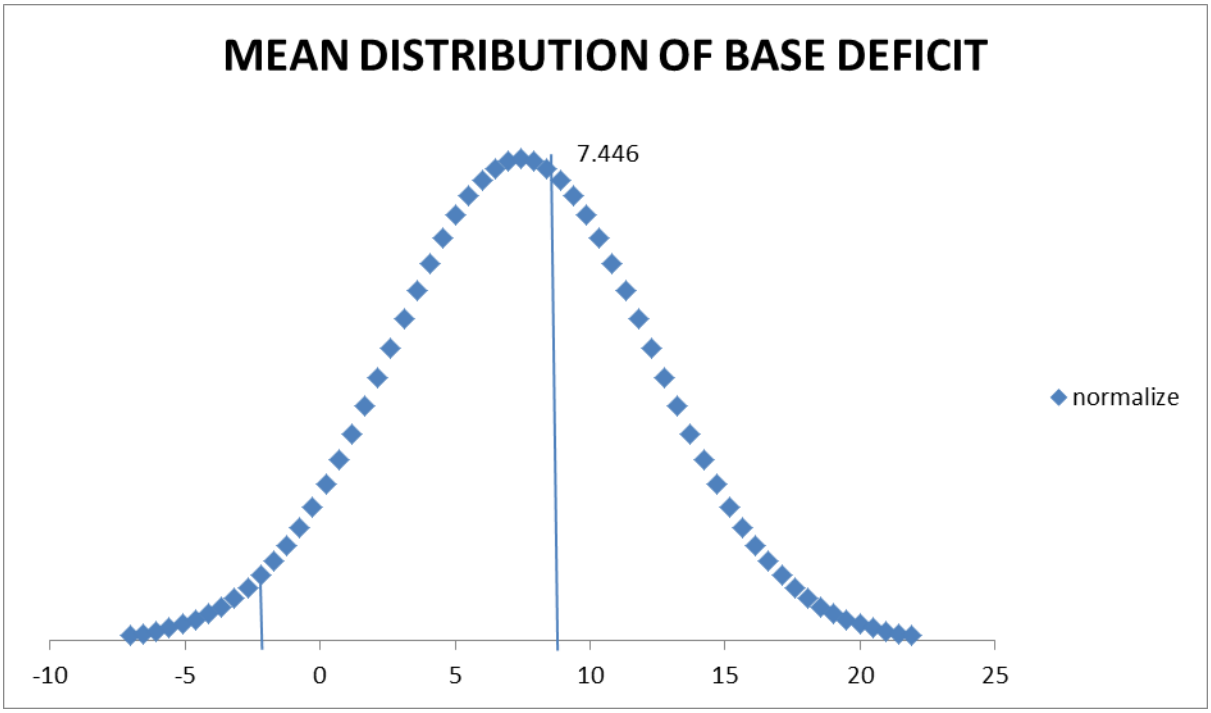
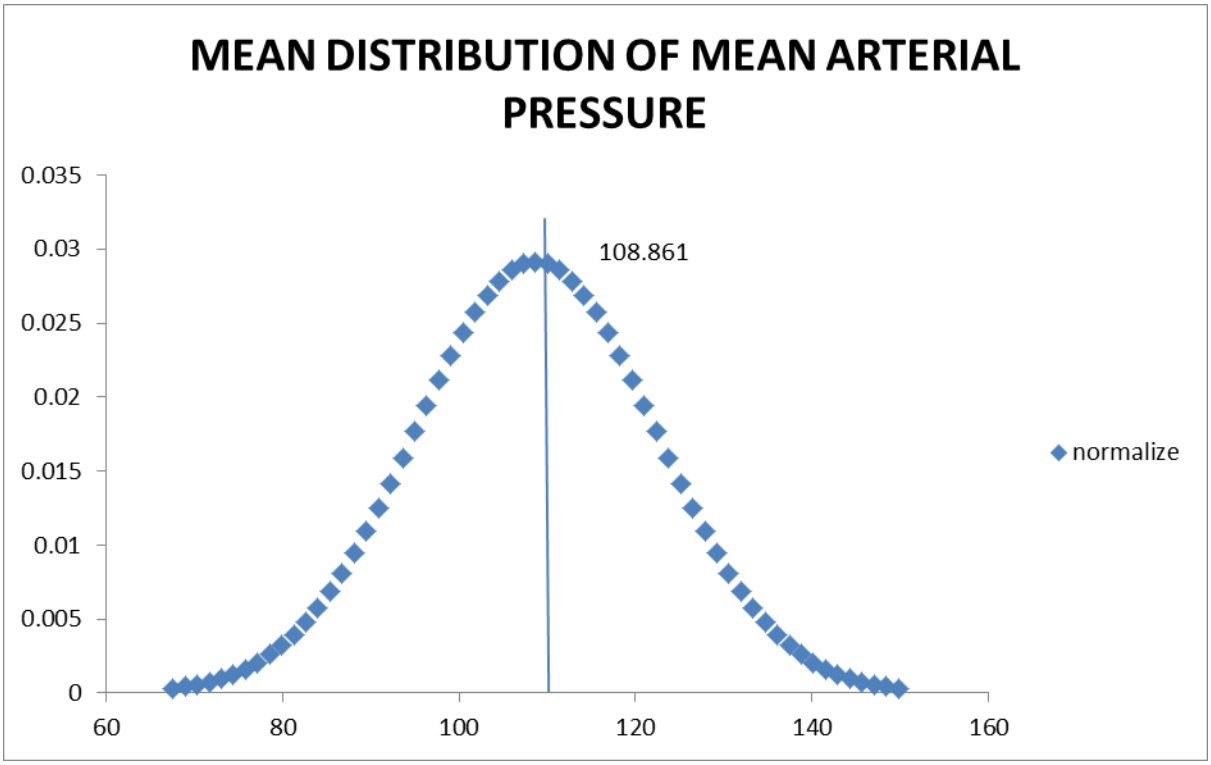


FIGURE 25 DISTRIBUTION OF BASE DEFICIT



` **FIGURE 26 DISTRIBUTION OF MEAN ARTERIAL PRESSURE**

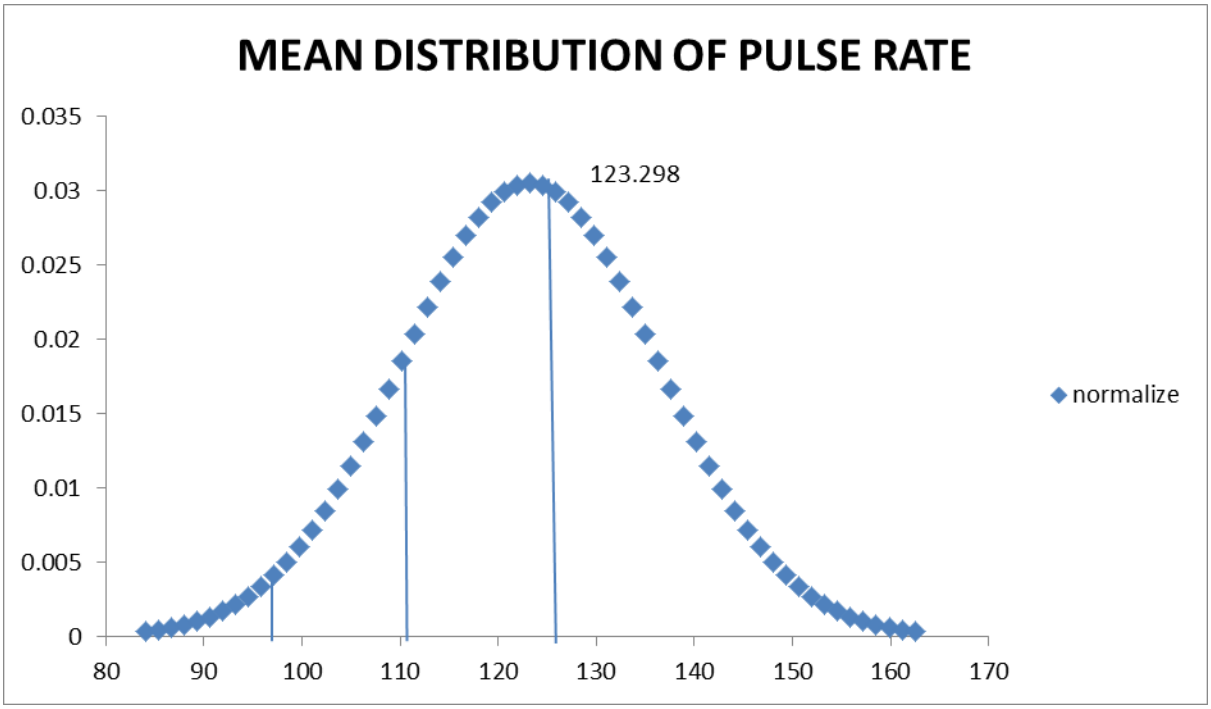


FIGURE 27 DISTRIBUTION OF PULSE RATE

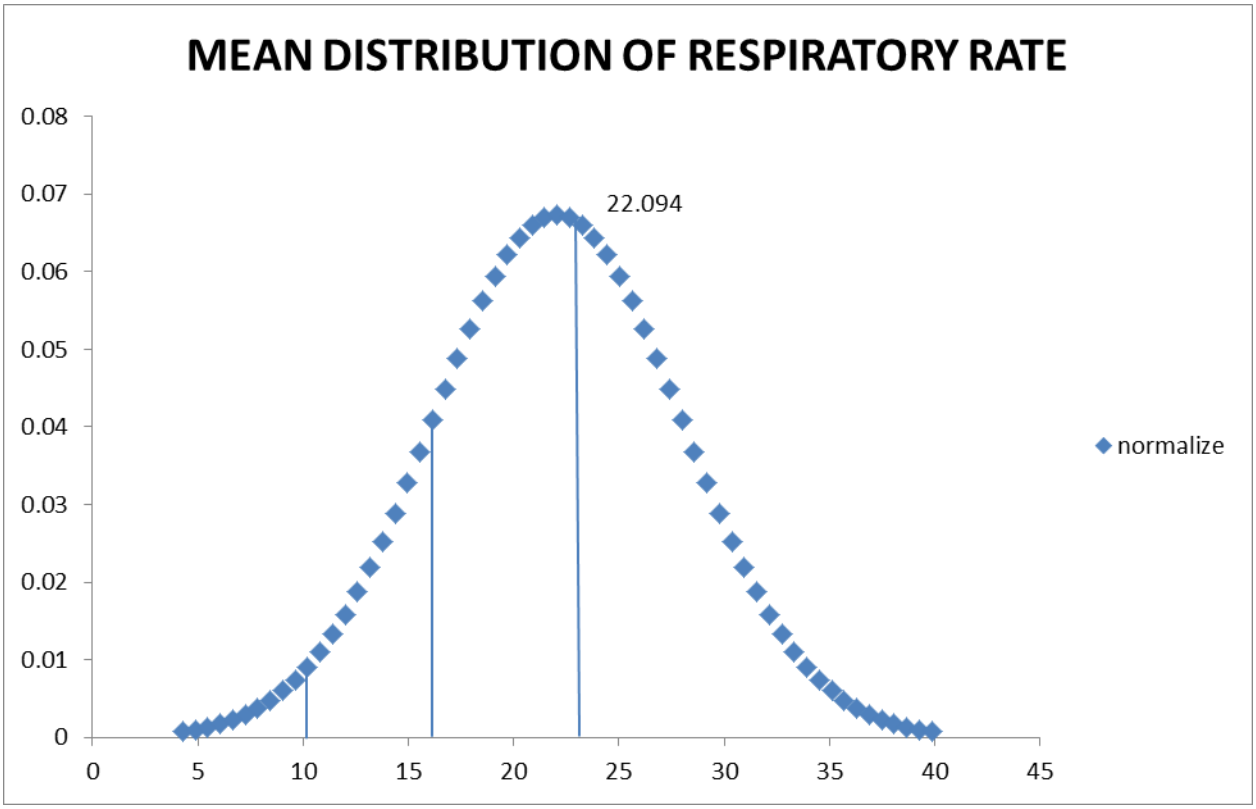


FIGURE 28 DISTRIBUTION OF RESPIRATORY RATE

TABLE 5: DISTRIBUTION OF THE SUBJECTS BASED ON OUTCOME

Outcome	Frequency	Percent
Alive	71	75.5
Dead	23	24.5
Total	94	100.0

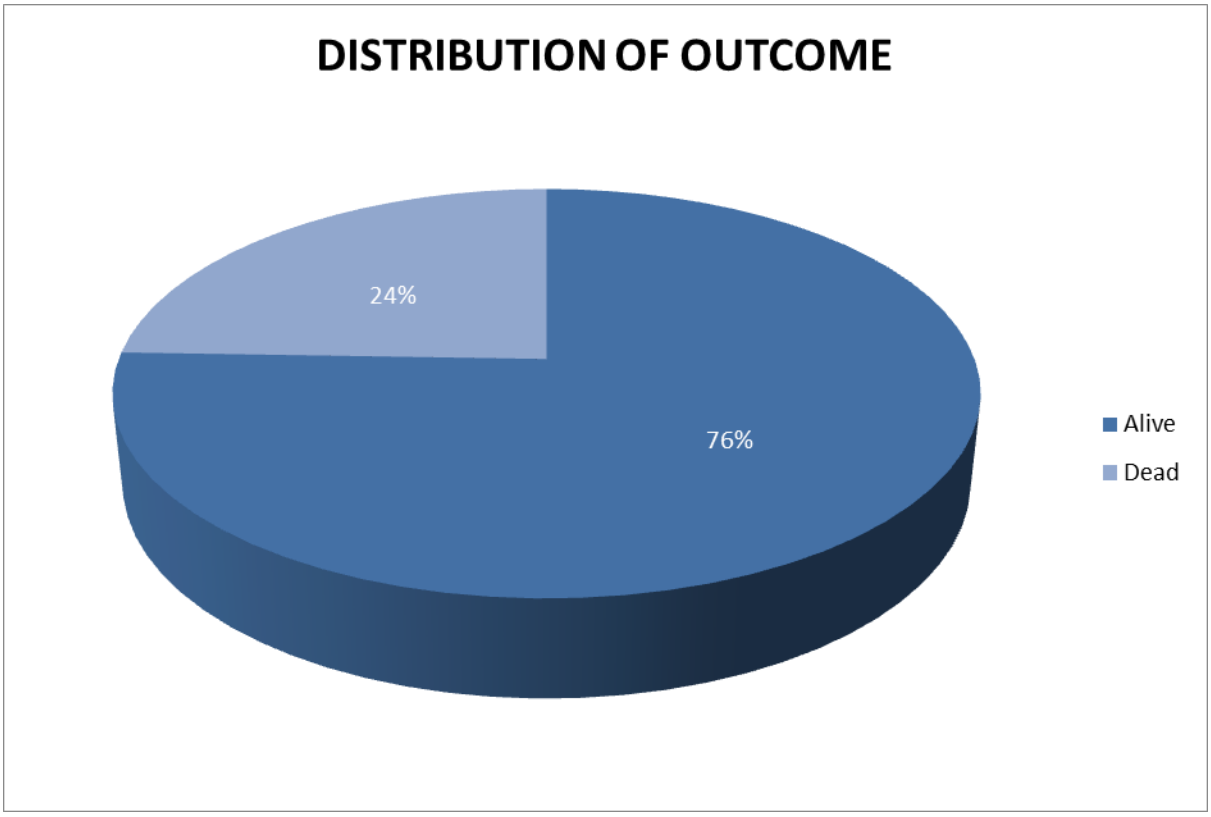


FIGURE 30 DISTRIBUTION OF OUTCOME

TABLE 6: MEAN GCS AND APACHE

	N	Minimum	Maximum	Mean	S.D
GCS	94	3.0	15.0	11.319	3.55
APACHE 2	94	2.0	42.0	12.957	10.61

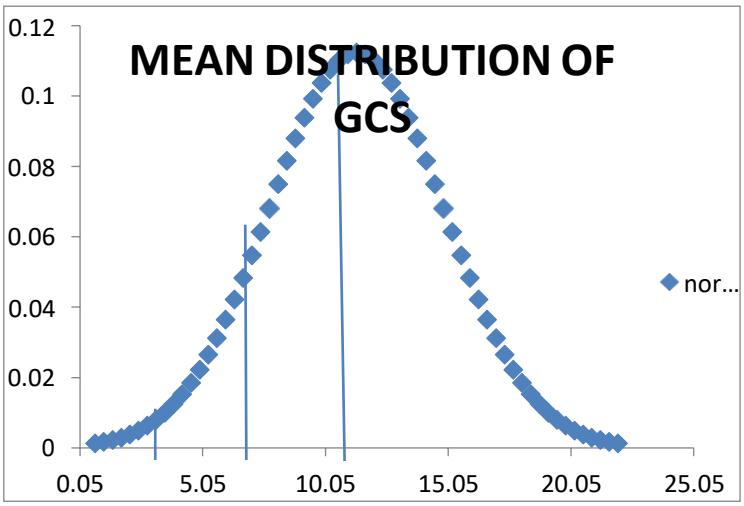


FIGURE 31 DISTRIBUTION OF GLASGOW COMA SCALE

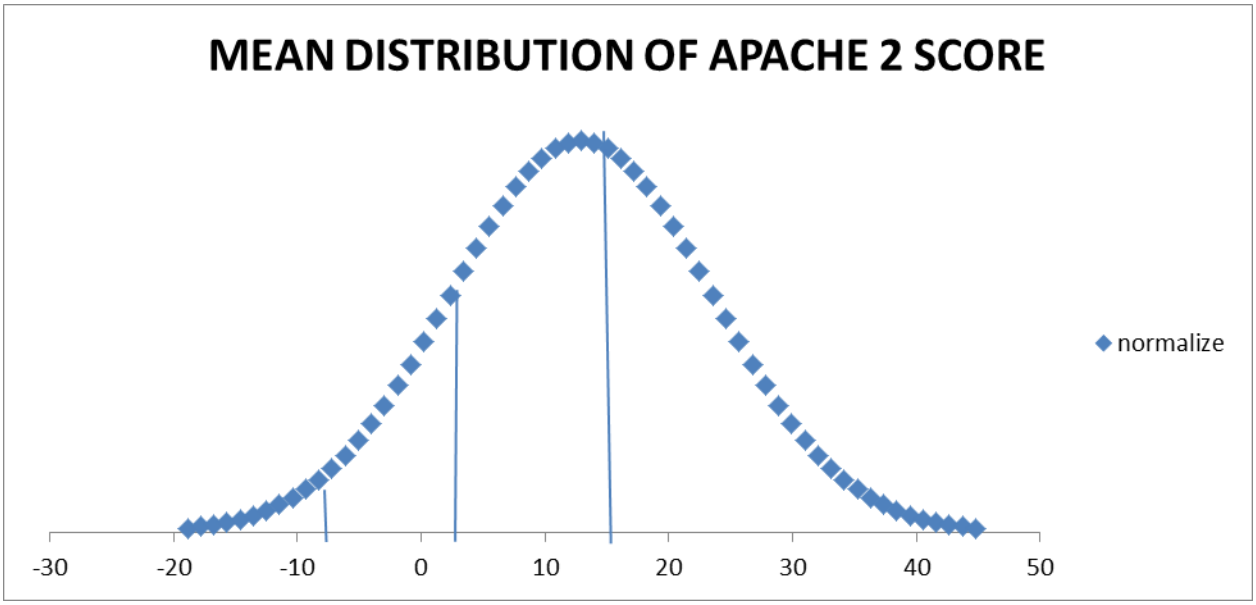


FIGURE 32 DISTRIBUTION OF APACHE 2 SCORE

TABLE 7: DISTRIBUTION OF THE SUBJECTS BASED ON VENTILATION

Ventilation	Frequency	Percent
No	54	57.4
Yes	40	42.6
Total	94	100.0

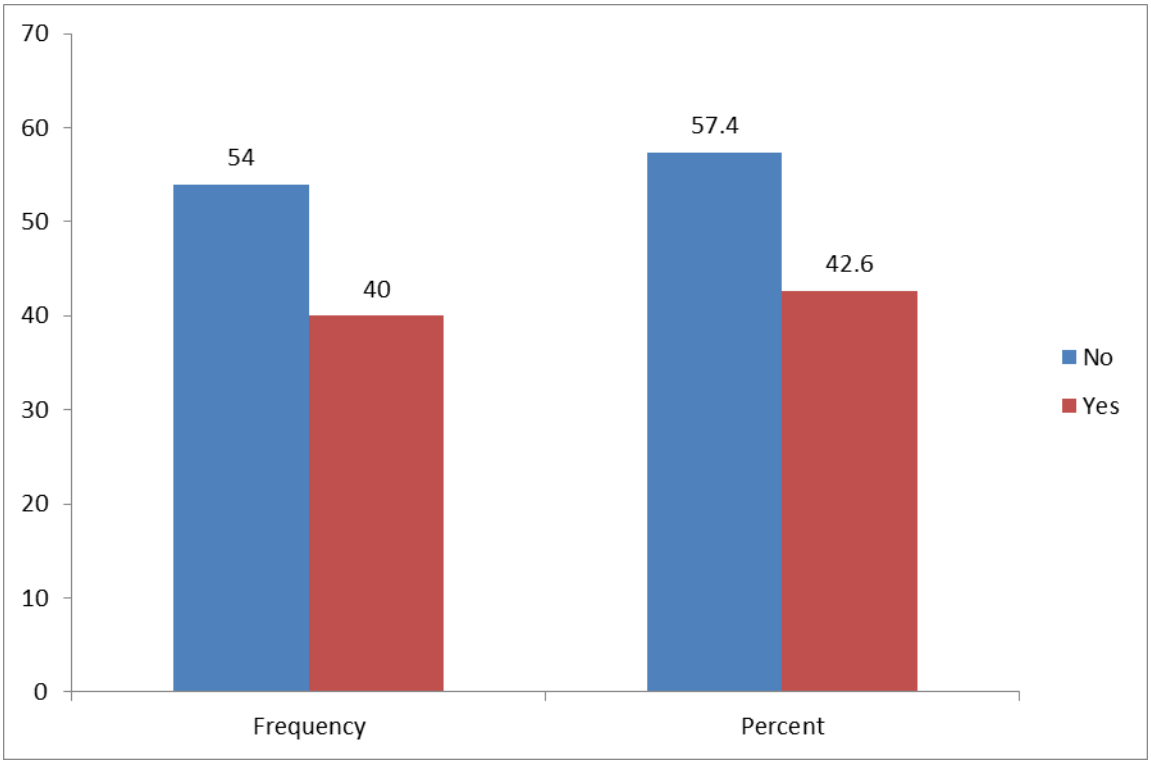


FIGURE 33 FREQEUNCY OF NEED FOR MECHANICAL VENTILATION

TABLE 8: CUT OFF OF BD TO PREDICT VENTILATION

Area Under the Curve				
Test Result Variable(s): NLR				
Area	Std. Error[a]	P value	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.893	.032	.001*	0.830	0.955

The Base Deficit to predict ventilation was 7.15 which had a sensitivity of 80% and specificity of 79.6%. The area under curve was 0.893with SE= 0.032 and 95% CI from 0.830 to 0.955.

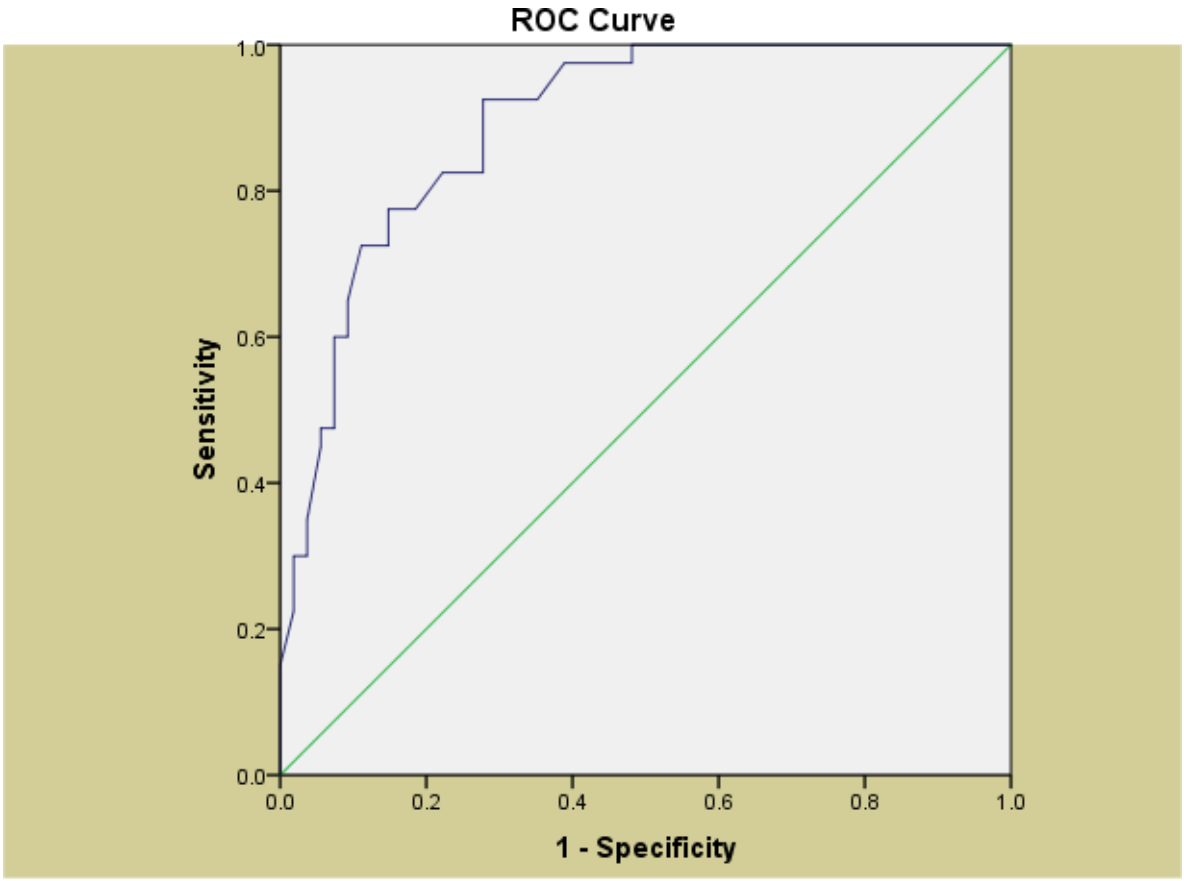


FIGURE 34

TABLE 9: CUT OFF OF BD TO PREDICT OUTCOME

Area Under the Curve				
Test Result Variable(s): NLR				
Area	Std. Error[a]	P value	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.826	0.044	.001*	0.740	0.913

The Base Deficit to predict Outcome was 7.15 which had a sensitivity of 82.6% and specificity of 66.2%. The area under curve was 0.826 with SE= 0.044 and 95% CI from 0.740 to 0.913.

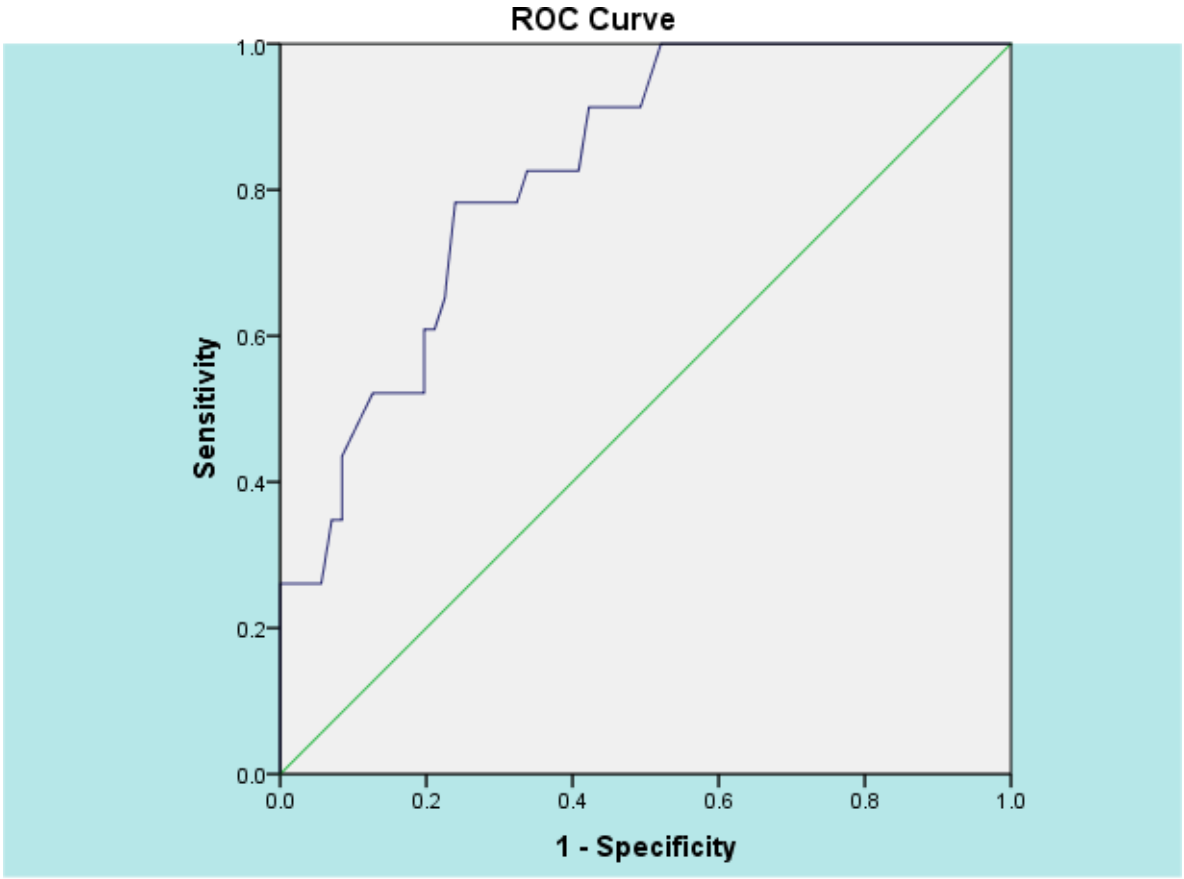


FIGURE 35

TABLE 10: CROSS-TABULATION OF BD WITH VENTILATION

Ventilation		BD		Total
		< 7.15	> 7.15	
Not required	Count	36	18	54
	%	38.3%	19.1%	57.4%
Required	Count	15	25	40
	%	16.0%	26.6%	42.6%
Total	Count	51	43	94
	%	54.3%	45.7%	100.0%
Chi-square value- 7.87				
p value- 0.005*				

	Value	95% CI
Sensitivity	58.14%	42.13% to 72.99%
Specificity	70.59%	56.17% to 82.51%
PPV	62.5%	50.39 % to 73.22%
NPV	66.67%	57.42% to 74.79%
Accuracy	64.89%	54.36% to 74.46%

TABLE 11: CROSS-TABULATION OF BD WITH MORTALITY

Outcome		BD		Total
		< 7.15	> 7.15	
Alive	Count	46	25	71
	%	48.9%	26.6%	75.5%
Dead	Count	5	18	23
	%	5.3%	19.1%	24.5%
Total	Count	51	43	94
	%	54.3%	45.7%	100.0%
Chi-square value- 12.97				
p value- 0.001*				

*significant

	Value	95% CI
Sensitivity	41.86%	27.01% to 57.87%
Specificity	90.2%	78.59% to 96.74%
PPV	78.26%	59.32% to 89.89%
NPV	64.79%	58.43% to 70.66%
Accuracy	68.09%	57.67% to 77.33%

TABLE 12: PEARSON'S CORRELATION BETWEEN BD AND APACHE 2

	r value	p value
BD Vs APACHE 2	0.727	0.001*

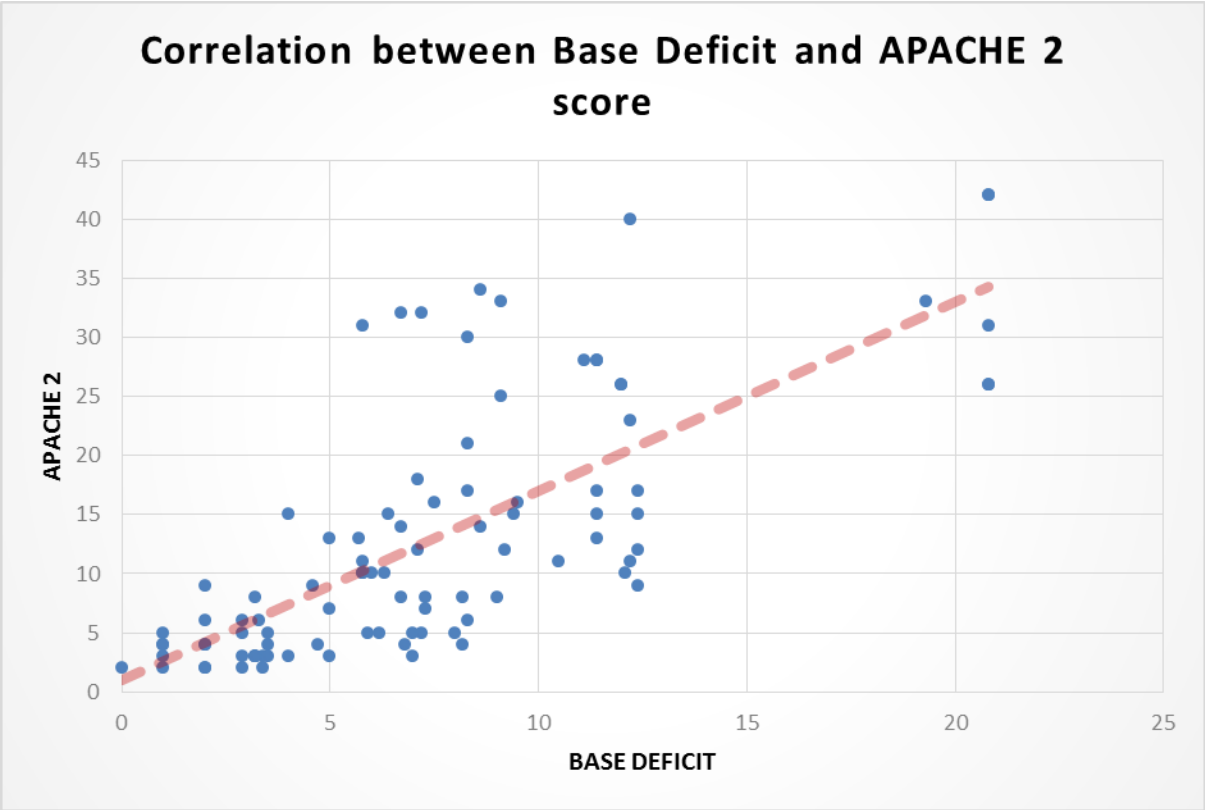


FIGURE 36 CORRELATION BETWEEN BASE DEFICIT AND APACHE 2 SCORE

DISCUSSION

In our study of 94 patients of organophosphorous poisoning, the mean age of distribution of participants was 31.95 with a confidence interval of 95%

Among the 94 patients included in our study, 44.7% were in the age group of 16 to 25 years; 27.7% in the age group of 26 to 35 years; 10.6% in the age group of 36 to 45 years; 8.5% in the age group of 46 to 55 years and 8.5% in greater than 55 years

Among the 94 patients in our study, 71.3% were males and 28.7% were females

In our study, the mean frequency of distribution of total leucocyte count was 14.162 with SD of 8.391

The mean frequency of distribution of haemoglobin was 13.578 with SD of 2.565

The mean frequency of distribution of random blood sugar was 116.904 with SD of 32.127

The mean frequency of distribution of serum cholinesterase was 2988.847 with a SD of 3038.340

The mean frequency of distribution of serum albumin was 3.851 with SD of 0.602

The mean frequency of distribution of serum urea was 39.883 with SD of 17.283

The mean frequency of distribution of serum sodium was 141.096 with SD of 8.088

The mean frequency of distribution of serum potassium was 4.186 with SD of 0.868

The mean frequency of distribution of serum pH was 7.298 with SD of 0.134

The mean frequency of distribution of serum bicarbonate was 16.522 with SD of 4.826

The mean frequency of distribution of base deficit was 7.446 with SD 4.823

The mean frequency of distribution of mean arterial pressure was 108.681 with SD of 13.696

The mean frequency of distribution of pulse rate was 123.298 with SD of 13.061

The mean frequency of distribution of Respiratory rate was 22.074 with SD of 5.927

The mean frequency of distribution of haematocrit was 40.856 with SD of 7.936

Among the 94 patients diagnosed with organophosphorous poisoning, 23 patients died and 71 patients survived; that is 24.5% and 75.5% respectively.

Of the 94 patients, 40 patients required mechanical ventilation and 54 patients did not require mechanical ventilation.

In our study, to identify the cut off values of base deficit, ROC curve analysis was done and 7.15 was determined as the cut off value.

A base deficit of 7.15 was statistically significant in predicting the need for mechanical ventilation, with a sensitivity of 80% and a specificity of 79.6% (p=0.001)

A base deficit of 7.15 was statistically significant in predicting mortality with a sensitivity of 82.6% and a specificity of 66.2% (p=0.001)

There was a positive and statistically significant correlation between base deficit and APACHE 2 score. (r=0.727 ; p=0.001)

A similar study was carried out by S B Lee et. Al in the Republic of South Korea[52]; the sample si

ze they consisted of 154 patients. This study was first of it's kind and no further studies have been carried out to determine the correlation between BD and mortality. In their study, Out of 154 patients, 31 patients died and their base deficits were significantly higher than those who survived. They have considered patients who mainly require mechanical ventilation. by segregating base deficits into quartiles, they could effectively quantify and correlate APACHE II with each base deficit quartile. In our study of 94 patient population, 23 patients died with a similar result of increased base deficit among those who expired as compared to those who were alive. In our study we did not segregate BD into quartiles; thus a single cut off value was determined for BD of 7.15 which made the correlation with APACHE II scores less cumbersome.

The disadvantages that were common to both studies were a smaller sample size. In the future, larger multicentric studies should be carried out to prove the effectiveness of our hypothesis. Also, in both the studies BD was calculated on patient arrival only. Serial estimations of BD and subsequent serial APACHE II scores can more accurately predict the need for ventilatory support.

Asari et al. showed in a case report of a 35 year old male presenting with dichlorvos consumption and respiratory distress[12]; on admission, his bicarbonate was 16, proving severe metabolic acidosis; he also developed profound hypotension and was on inotropes. He benefitted from sodium bicarbonate infusions. Our patients with severe metabolic acidosis benefitted from stat corrections of sodium bicarbonate as well. However, in our study, all patients with

significant base deficit were not administered infusions, rather severe acidemia i.e. pH below 7.02 were only administered sodium infusions.

Liu JH, Chou CY, Liu YL et al[15] carried out a study where they segregated OPC consumption patients into groups having normal blood gas analysis, metabolic acidosis and mixed acidosis. In their study, they realised that patients with severe metabolic acidosis and mixed acidosis (most likely due to hypoperfusion and raised lactate and low bicarbonate levels) did not survive the illness as compared to those patients with no metabolic acidosis. They also hypothesized that oxime and atropine therapy is improved by infusions of sodium bicarbonate. In our study, patients with severe acidaemia needed mechanical ventilation.

Li Tai et al tried to demonstrate that APACHE II score might be used as an alternative severity of index in OPC poisoning[53] They stated that severity of OPC poisoning can be correlated with mortality. However detailed description of APACHE II was not provided; in our study we have calculated the APACHE II score by using 12 parameters which included GCS of the patient; and showed an association between APACHE II and BD.

Balali-Mood M, Ayati MH and Ali-Akbarian H. study say that infusion of high doses of bicarbonate appears to be beneficial in treatment of patients with OP poisoning[16] they realised that higher doses of sodium bicarbonate infusion administered in patients with severe metabolic acidosis and a higher base deficit meant lesser doses of atropine needed for atropinisation and lesser duration of hospital stay and lesser mortality.

CONCLUSION

- In our study, patients with higher values of BD required mechanical ventilation, thus increasing their duration of hospital stay.
- Among the patients of OP poisoning who died, BD values of 7.15 and above were significant.
- APACHE 2 score is accurate in predicting ICU mortality; because of the strong statistical correlation between BD and APACHE 2 score, BD may be used as a tool in predicting ICU mortality in OP poisoning patients
- Acute OP poisoning is a highly fatal condition that requires a rapid and precise diagnosis and adequate support and treatment. Higher numerical values of BD in patients with OP poisoning require fast and precise intensive care

SUMMARY

- 94 patients were included in the sample size for this investigative study. they were referred to our hospital for organophosphate poisoning from January 2021 to June 2022.
- Most of the patients were in the age group of 16 to 25 years and were predominantly male. Most of them were farm workers, and 96% of patients had used poisons with a suicidal intent.
- In patients with a base deficit of 7.1 and above, there was increased duration of hospital stay as evidenced by increased need for mechanical ventilation and increased 30 day mortality.
- A base deficit of 7.1 and above showed a linear positive and statistically significant correlation with increased APACHE 2 scores.
- Such patients might benefit from infusions of sodium bicarbonate. A reduction in base deficit may lead to better outcome and a decreased need for mechanical ventilation, thus effectively reducing hospital stay.

BIBLIOGRAPHY :

1. World Health Organization. WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 2000-2001. WHO/PCS/01.4. Geneva: World Health Organization, 2001

2. Jesslin J, Adepu R, Churi S. Assessment of prevalence and mortality incidences due to poisoning in a South Indian tertiary care teaching hospital. Indian J Pharm Sci 2010;72:587-91.

3. Roberts DM and Aaron CK. Managing acute organo-phosphorus pesticide poisoning. BMJ 2007; 334:629–634.

4. Andersen OS, Engel K. A new acid-base nomogram an improved method for the calculation of the relevant blood acid-base data. Scandinavian Journal of Clinical and Laboratory Investigation. 1960 Jan 1;12(2):177-86.

5. Henzel JH, DeWeese MS, Ridenhour G. Significance of Magnesium and Zinc Metabolism in the Surgical Patient: I. Magnesium. Archives of Surgery. 1967 Dec 1;95(6):974-90.

6. Worek F, Kleine A, Falke K, et al. Arrhythmias in organophosphate poisoning: effect of atropine and bis-pyridinium oximes. Arch Int Pharmacodyn Ther 1994;329: 418–435.

7. Balali-Mood M, Ayati MH and Ali-Akbarian H. Effect of high doses of sodium bicarbonate in acute organo-phosphorous pesticide poisoning. Clin Toxicol 2005;43: 571–574

8. Knaus WA, Draper EA, Wagner DP, et al. APACHE II: a severity of disease classification system. Crit Care Med 1985; 13: 818–829.

9. 1.World Health Organization. WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 2000-2001. WHO/PCS/01.4. Geneva: World Health Organization, 2001

10. Balasubramaniyan S. Creatine Phosphokinase: A Prognostic Marker in Organophosphorus Compound Poisoning.

11. Lee SH, Park S, Lee JW, Hwang IW, Moon HJ, Kim KH, Park SY, Gil HW, Hong SY. The anion gap is a predictive clinical marker for death in patients with acute pesticide intoxication. Journal of Korean medical science. 2016 Jul 1;31(7):1150-9.

12. Asari Y, Kamijyo Y, Soma K. Changes in the hemodynamic state of patients with acute lethal organophosphate poisoning. Veterinary and human toxicology. 2004;46(1):5-9.

13. Zadik Z, Blachar Y, Barak Y, Levin S. Organophosphate poisoning presenting as diabetic

14. Smith I,KumarP,Molloy S, et al.Base excess and lactate as prognostic indicators for patients admitted to intensive care. Intensive Care Med Exp 2001; 27: 74–83.

15. Liu JH, Chou CY, Liu YL, et al. Acid-base interpretation can be the predictor of outcome among patients with acute organophosphate poisoning before hospitalization.Am J Emerg Med 2008; 26: 24–30.

16. Balali-Mood M, Ayati MH and Ali-Akbarian H. Effect of high doses of sodium bicarbonate in acute organophosphorous pesticide poisoning. Clin Toxicol 2005; 43: 571–574

17. John E.Hall Pd. Exitation of skeletal muscle: neuromuscular transmission and exitation-contraction coupling Guyton and hall Text book of medical physiology. 12 ed2011. p. 83-91.

18. Kumar EA. Current review on organophosphorus poisoning. Archives of Applied Science Research. 2010;2(4):199-215.

19. Kinkaid.J.C. The Autonomic Nervous System. Medical Physiology,2nd ed.P.108-118.

20. Katzung.B.G, Masters.S.B, Trevor.A.J, Basic & Clinical Pharmacology, McGraw-Hill Medical; 11 ed

21. Arthur Karlin (2002). Emerging structure of nicotinic acetylcholine receptors.Nature Reviews Neuroscience3,102-114

22. Irwin B.Levitan and Leonard K.Kaczmarek(20020 The Neuron.Oxford University Press

23. P.Taylor(1991) The Cholinesterases. Journal of Biological Chemistry266,4025-4028

24. P.Taylor and Z.Radic(1994) The Cholinesterases:From genes to proteins.Annual Review of Pharmacology and Toxicology34,281-320

25. . Holmstedt B: Pharmacology of Organophosphorus cholinesterase inhibitors. Pharmacol Rev:1986 20. Katzung B G, Masters S B, Trevor A J, Basic and clinical Pharmacology, McGraw – Hill Medical; 11th ed

26. Thomas Chang – Yao Tsao et al. Respiratory failure of acute Organophosphate and carbamate poisoning. CHEST 1990 Sep; 98(3); 631-636

27. Basu A, Das AK, Chandrashekar S: organophosphate poisoning - A clinical profile J. Assoc Physicians India:36;24

28. . Wadia R.S, Saagopal C, Anim R.P. et al. Neurological Manifestation of Organophosphorus Poisoning. Journal of Neurology, neurosurgery, Psychiatry,1974;37:841-847

29. . Kastrup E., ed: Facts and Comparisons, Philadelphia, Lippincott,1983

30. Prakash , Shoba TR, Glycosuria in OP & Carbamate poisoning JAPI 2000 48:1197

31. Guyton Arthur C: Textbook of Medical Physiology. 9th ed

32. 27. Namba T: Nolte CT, Jackrel J et al, Poisoning due to Organophosphate Insecticides. Acute and chronic manifestation - American Journal of Med.1971:50:475-492

33. Wadia R.S, Saagopal C, Anim R.P. et al. Neurological Manifestation of Organophosphorus Poisoning. Journal of Neurology, neurosurgery, Psychiatry,1974;37:841-847

34. Senanayake N, Karaliedde L. Neurotoxic effects of organophosphorus insecticides and intermediate syndrome. N Engl J Med 1987;316:761-3

35. Samuel J, Thomas K, Jeyaseelan L, Peter JV, Cherian AM. Incidence of intermediate syndrome in organophosphorus poisoning. Assoc Physicians India 1995;43:321-3.

36. De Bleecker J, Van Den Neucker K, Colardyn F. Intermediate syndrome in organophosphorus poisoning: a prospective study. Crit Care Med 1993;21:1706-11.

37. Marion Ehrich and Bernard S. Jortner Organophosphate-Induced Delayed Neuropathy From: Handbook of Neurotoxicology, vol. 1 Edited by: E. J. Massaro Totowa, NJ

38. Cavanagh, J. B. (1954) The toxic effects of tri-ortho-cresyl phosphate on the nervous system. An experimental study in hens. J. Neurol. Neurosurg. Psychiatry 17, 163–172.

39. Vilanova, E., Escudero, M. A., and Barril, J. (1999) NTE soluble isoforms: new perspective for targets of neuropathy inducers and promoters. Chem. Biol. Interact. 199-120,525–540.

40. 47. Milby T: Prevention and management of Organophosphate poisoning, JAMA 1971;216:2131-2133

41. 48. Sundaram K, Ratheesh KJ. Organophosphorous poisoning:Current Management guidelines. API update 2010;420-6.

42.. Johnson MK vale JA, clinical management of acute OP poisoning: an overview. In: Ballantyne B mans T.C(eds) clinical and experimental Toxicology of organophosphates and carbamates. Oxford: Butterworth Heinemann ;1992;528-35

43. 50. Christopher H L, Michael J B. Poisoning and drug dosage. Harrison Principle of Internal Medicine 18th ed, Mcgraw Hill – 2011; 261.

44. Darren M Roberts, Cynthia K Aaron. Managing acute Organophosphorus pesticide poisoning. BMJ 2007; 334:629-34

45. Sunder Ram J, Kumar S.S, Jayarajan A et a!: "Continuous doses of high atropine in the treatment of Organophosphorus Poisoning JAPI 1991:39:190-193

46. Singh S, Batra Y.K.: "Is atropine alone sufficient in acute severe Organophosphorus poisoning?: mt. J. Clin. Pharmacol Ther.1995:93(11)

47. Grmec Š, Mally Š, Klemen P. Glasgow Coma Scale score and QTc interval in the prognosis of organophosphate poisoning. Academic emergency medicine. 2004;11(9):925-30.

48. Senanayake N, Sanmuganathan P. Extrapyramidal manifestations complicating organophosphorus insecticide poisoning. Human & experimental toxicology. 1995;14(7):600-4.

49. Anne Kelly C, Upex A, Bateman DN. Comparison of consciousness level assessment in the poisoned patient using the alert/verbal/painful/unresponsive scale and the Glasgow Coma Scale. Annals of emergency medicine. 2004;44(2):108-13.

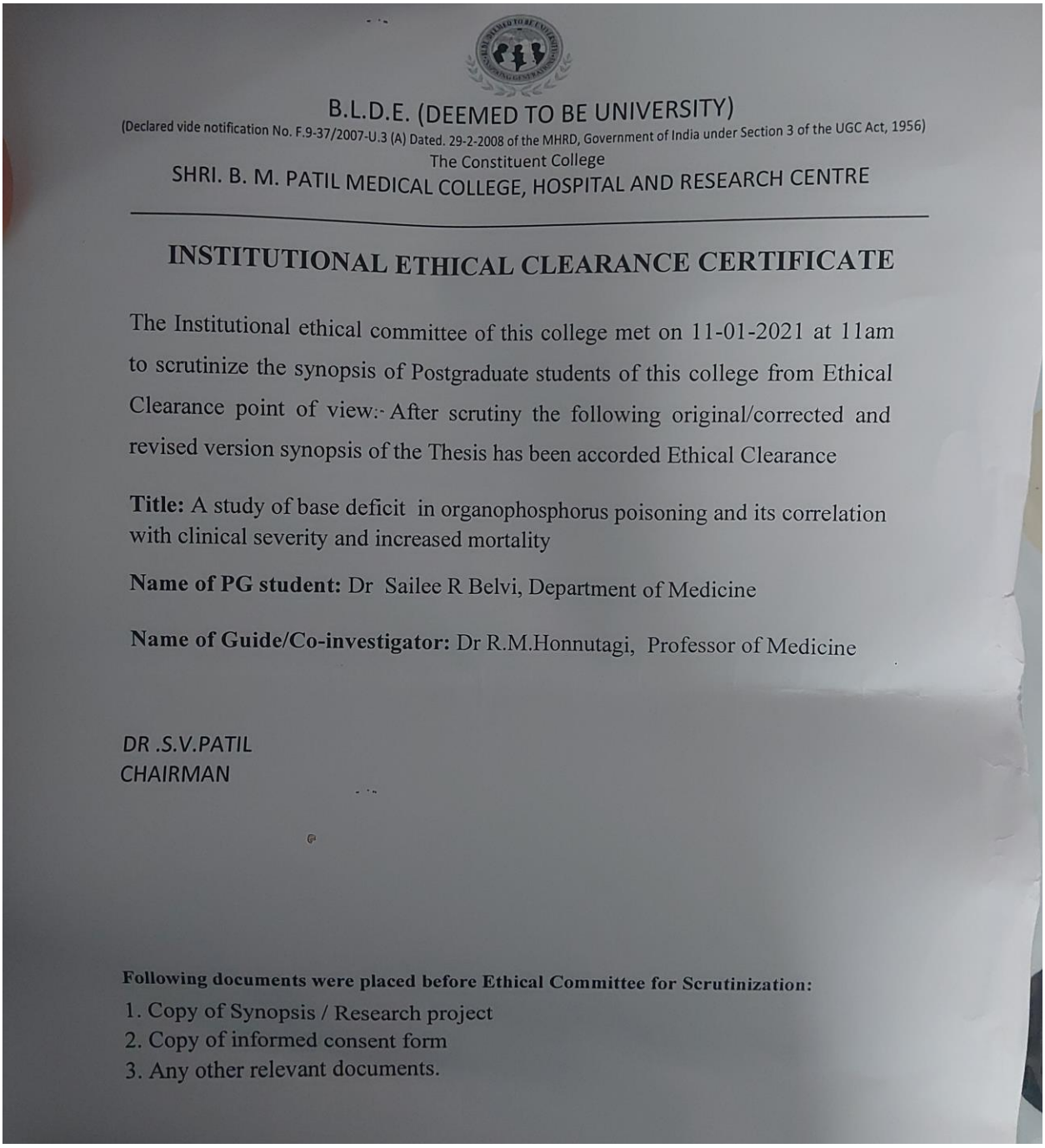
50. Chan B, Gaudry P, Grattan-Smith T, McNeil R. The use of Glasgow Coma Scale in poisoning. The Journal of emergency medicine. 1993;11(5):579-82.

51. Goswamy R, Chaudhuri A, Mahashur A. Study of respiratory failure in organophosphate and carbamate poisoning. Heart & lung: the journal of critical care. 1994;23(6):466.

52. 1.Lee S, Kang C, Kim D, et al. Base deficit is a predictor of mortality in organophosphate insecticide poisoning. Human ExperimentalToxicology.2018;37(2):doi:10.1177/0960327117694

53. Lee P, Tai DY. Clinical features of patients with acute organophosphate poisoning requiring intensive care. Intensive Care Med 2001;27:694 - 9.

ANNEXURE III



B.L.D.E. (DEEMED TO BE UNIVERSITY)

(Declared vide notification No. F.9-37/2007-U.3 (A) Dated. 29-2-2008 of the MHRD, Government of India under Section 3 of the UGC Act, 1956)

The Constituent College

SHRI. B. M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Institutional ethical committee of this college met on 11-01-2021 at 11am to scrutinize the synopsis of Postgraduate students of this college from Ethical Clearance point of view:- After scrutiny the following original/corrected and revised version synopsis of the Thesis has been accorded Ethical Clearance

Title: A study of base deficit in organophosphorus poisoning and its correlation with clinical severity and increased mortality

Name of PG student: Dr Sailee R Belvi, Department of Medicine

Name of Guide/Co-investigator: Dr R.M.Honnutagi, Professor of Medicine

DR .S.V.PATIL
CHAIRMAN

Following documents were placed before Ethical Committee for Scrutinization:

1. Copy of Synopsis / Research project
2. Copy of informed consent form
3. Any other relevant documents.

ANNEXURE IV

CONSENT FORM

TITLE OF STUDY

"A STUDY OF BASE DEFICIT AS A PREDICTOR OF MORTALITY IN ORGANOPHOSPHOROUS POISONING"

NAME OF THE INVESTIGATOR: DR SAILEE BELVI

NAME OF THE GUIDE: DR. R.M. HONNUTAGI

CONFIDENTIALITY OF RECORDS:

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

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

REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at any time, **DR.SAILEE R. BELVI** available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of this study, which might influence my continued participation.

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

REFUSAL OR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital.

I also understand that **DR. SAILEE R. BELVI**, will terminate my participation in this study at any time after he has explained the reasons for doing so and has helped arrange for my continued care by my own physician or therapist, if this is appropriate.

INJURY STATEMENT:

I understand that in the unlikely event of injury to me/my ward, resulting directly to my participation in this study, if such injury were reported promptly, then medical treatment would be available to me, but no further compensation will be provided.

I understand that by my agreement to participate in this study, I am not waiving any of my legal rights.

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

Date:

Dr. R.M. HONNUTAGI
(Guide)

DR. SAILEE R. BELVI
(Investigator)

Participant's name:

Address:

TITLE OF THE PROJECT:

"A STUDY OF BASE DEFICIT AS A PREDICTOR OF MORTALITY IN ORGANOPHOSPHOROUS POISONING"

The details of the study have been provided to me in writing and explained to me in my own language. I confirm that I have understood the above study and had the opportunity to ask questions. I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without the medical care that will normally be provided by the hospital being affected. 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 have been given an information sheet giving details of the study. I fully consent to participate in the above study.

_____ _____

(Participant) (Date)

_____ _____

(Witness to signature) (Date)

_____ _____

(Investigator to signature) (Date)

ANNEXURE X

OPC POISONING CASE PROFORMA

NAME:

AGE/SEX:

OCCUPATI0
N:

ADDRESS:

RELIGION:

DATE OF
ADMISSION:

I P NO:

CASE NO. :

PLACE:

CHIEF
COMPLAINT
S :

HISTORY OF PRESENTING ILLNESS :

PAST HISTORY:

FAMILY HISTORY :

PERSONAL HISTORY :

1. DIET
2. APPETITE
3. SLEEP
4. BOWEL / BLADDER HABITS
5. HABITS

GENERAL PHYSICAL EXAMINATION :

- LEVEL OF CONSCIOUSNESS -

CONSCIOUS	
ORIENTED	

DROWSY	
STUPOR	
COMATOSE	

- PUPIL SIZE - mm
- FASCICULATION -
- PALLOR - YES / NO
- ICTERUS - YES / NO
- CLUBBING - YES / NO
- LYMPHADENOPATHY - YES / NO
- CYANOSIS - YES / NO
- EDEMA - YES / NO
- WEIGHT - kg
- HEIGHT - cm
- BMI - kg/cm2

VITALS :

PULSE RATE -

BLOOD PRESSURE -

SPO2 -

TEMPERATURE -

HEART RATE –

RESPIRATORY RATE -

SYSTEMIC EXAMINATION :

1. PER ABDOMEN :

2. CARDIOVASCULAR SYSTEM :

3. RESPIRATORY SYSTEM :

4. CENTRAL NERVOUS SYSTEM :

Higher Mental Functions:

Appearance and Behaviour:

Consciousness:

- (If conscious)
  - Oriented
  - Confused
  - Drowsy
  - Stupor
  - Coma
- If consciousness is diminished/ in coma

GCS SCORING:

Eye opening: SCORE:

- Open spontaneously 4
- Open only to verbal stimuli 3
- Open only to pain 2
- Never open 1

Best verbal response: SCORE:

- Oriented and converses 5
- Converses, but disoriented, confused 4
- Uses inappropriate words 3
- Makes incomprehensible sounds 2
- No verbal response 1

Best motor response: SCORE:

- Obeys commands 6
- Localizes pain 5
- Exhibits flexion withdrawal 4
- Decorticate rigidity 3
- Decerebrate rigidity 2
- No motor response 1

TOTAL GCS SCORE:

- FASCICULATION -
- PUPIL SIZE - mm

INVESTIGATIONS :

1.COMPLETE BLOOD COUNT :

TOTAL COUNT	
HAEMOGLOBIN	
PLATELET COUNT	
ESR	
RBC	

2. RANDOM BLOOD SUGAR - mg/dl

3. SERUM CHOLINESTERASE - U / mL

4. LIVER FUNCTION TEST :

TOTAL BILIRUBIN	
DIRECT BILIRUBIN	
INDIRECT BILIRUBIN	
ALBUMIN	
SGOT	
SGPT	
ALP	

5. RENAL FUNCTION TEST :

CREATININE	
UREA	
SODIUM	
POTASSIUM	

6 . ARTERIAL BLOOD GAS ANALYSIS :

BLOOD PH	
PO2	
PCO2	
HCO3	
LACTATE	

7. APACHE 2 SCORE

ANNEXURE IV MASTER CHART

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y
1	NAME	IP NO.	AGE	AGE/SEX	CBC	TLC	HB	PLT COUN	RBS	CHOLIN	ALBUMIN	CREAT	UREA	NA	K	PH	HCO3	BD	SBP	PR	RR	HEMATOCRIT	STATUS	GCS	APACHE2	VENTILATOR
2	VAISHALI YALLAPPA KATNALLI	166277	18	F	13.72	13.1	2.44	99	4231.1	3.8	0.4	12	146	3.3	7.31	16.3	5.7	90	124	26	34.4	ALIVE	9	12	NO
3	BASAWARAJ BHIMAPPA HALLAD	19667	23	M	9.61	13.5	2.49	98	4545.1	3.5	1.3	20	129	3.5	7.2	15	9	100	122	18	44.2	ALIVE	14	8	NO
4	SIDDU AMOGI HANDIGANUR	15725	24	M	8.7	15.4	2.05	124	544.4	3.7	0.7	11	139	3.9	7.34	17	7	110	120	20	38.2	ALIVE	13	5	NO
5	YEENASHRI B HIREMATH	80838	20	F	16.47	13	3.22	84	5633.8	5	0.6	56	143	4	7.34	17	7	110	120	20	38.2	ALIVE	15	3	NO
6	APPASAB SIDDAPPA ADAVI	80884	26	M	8.12	14.1	2.8	76	7124.3	3.7	0.7	19	140	3.5	7.4	20.7	3.3	100	130	16	41.1	ALIVE	12	6	NO
7	ALTAF HUYASAB YALAGAR	166492	21	M	17.83	15	2.91	72	200	4.4	1.4	15	144	3.5	7.24	11.9	12.1	90	134	22	44.4	ALIVE	12	10	NO
8	KAVERI PARAMAND MALI	162251	22	F	17.08	13.9	2.67	157	4270	4	0.5	20	135	3.1	7.45	22	2	110	90	16	35	ALIVE	13	9	NO
9	AMMANGOUDA LAXMANGOUDA	122284	40	M	14.36	15.8	2.67	201	6564.7	4	0.8	15	144	5	7.45	22	2	110	102	16	35	ALIVE	14	2	NO
10	RAVI GODIHAL	141924	20	M	9.1	9.5	3.14	103	804.5	4.2	1.2	15	135	4.1	7.41	15.8	8.2	130	124	18	48.5	ALIVE	14	8	NO
11	BASAWARAJ SHINDE	165727	55	M	9.54	11.7	1.71	97	1862	3.7	0.8	16	150	2.9	7.51	18.2	5.8	140	118	18	31.3	ALIVE	14	10	NO
12	DUNDAVVA SIDARAYA	163093	40	F	10.5	11.6	2.55	163	1812	4.9	0.7	31	149	4	7.39	17.8	6.2	100	116	20	35.8	ALIVE	14	5	NO
13	MADIVALAPPA TELAGANI	178770	35	M	5.62	12.4	2.93	120	200	4.1	0.7	27	132	2.6	7.33	21.1	2.9	110	125	18	40.9	ALIVE	14	5	NO
14	MANGALA H YALAWAR	176863	17	F	10.78	13.4	3.74	80	6205	3.3	0.6	21	141	4.5	7.45	22	2	110	90	16	35	ALIVE	14	2	NO
15	SOMANINGA HUGAR	191392	25	M	9.63	15.9	183	96	200	4.4	0.7	15	143	3.8	7.35	19	5	100	132	18	32	ALIVE	14	7	NO
16	YEERESH CHANDRAYYA	207015	34	M	14.97	14.2	336	142	200	4.1	0.8	19	140	4.7	7.45	20	4	100	132	18	32	ALIVE	14	3	NO
17	SHANKAR SOMA SUL		25	M	6.800	15.4	2.74	100	4327	4.1	0.6	21	141	3.5	7.4	20.6	3.4	120	130	18	42.7	ALIVE	14	3	NO
18	SHIVANAND N PAWAR	226994	28	M	9.98	13.3	2.89	154	1121	4.3	1	21	143	3.7	7.4	20.6	3.4	120	130	22	42.7	ALIVE	15	2	NO
19	DHARMARAJ BIRADAR	229423	20	M	9.95	11.2	2.77	108	6207	3.8	0.7	16	142	3	7.43	21.1	2.9	120	100	14	46.1	ALIVE	15	2	NO
20	NAGARAJ MADARAKI	230847	36	M	13.63	15.7	300	121	200	4.3	0.7	21	141	5.2	7.41	15.8	8.2	130	126	24	48.5	ALIVE	15	4	NO
21	PARASHURAM MAREPPA	236406	35	M	7.39	14.9	302	118	913.2	4.6	1.3	37	155	4.3	7.21	17.7	6.3	120	130	22	48.1	ALIVE	14	10	NO
22	SANTRAM RAM KUMBAR	245464	60	M	13.66	17	243	99	200	4.8	3	28	145	5.4	7.2	11.6	12.4	100	136	32	34	ALIVE	12	15	YES
23	SAVITRI R BOLEGAON	259645	19	F	15.69	9.6	2.43	89	3000	4.1	0.5	16	142	2.7	7.51	20	4	140	110	18	31.3	ALIVE	9	15	NO
24	SANTOSH TODALABAGI	259688	32	M	10.43	14.7	1.99	97	5472	3.9	0.6	15	140	3.8	7.43	21.1	2.9	120	100	14	46.1	ALIVE	14	6	NO
25	JAGADISH HAMADEV JADHAV	266727	52	M	13.22	11.21	3.01	105	5355	3.7	1.1	20	138	3.9	7.44	16.7	7.3	130	111	18	34.7	ALIVE	14	8	NO
26	SHANKARLING TELI	282396	28	M	4.66	13.6	3.45	112	5198	3.3	0.7	31	144	2.7	7.34	19.3	4.7	100	112	16	30.5	ALIVE	15	4	NO
27	SADASHIV MADARKHANDI	289908	30	M	12.4	16.3	2.61	78	8034	4.9	1	18	146	3.6	7.36	16	8	94	130	20	47.1	ALIVE	15	5	YES
28	SHARANAMMA HOONALLI	293122	20	F	12.11	10	3.68	109	345	4.4	2.2	40	144	4.9	7.34	16.9	7.1	96	138	24	31.7	ALIVE	14	12	NO
29	VISHAL RAMESH NAIK	294734	21	M	19.47	14.2	3.56	98	5620	4.1	0.7	22	142	4.2	7.4	23	1	100	114	12	36.2	ALIVE	14	4	NO
30	MOHAN SOMANATH CHAVAN	314535	28	M	7.41	15.7	259	109	9350	4.2	0.6	13	141	4.3	7.34	20.5	3.5	110	121	20	47	ALIVE	15	3	NO
31	SHREEDEVI HIREMATH	28355	25	F	7.13	9.7	296	89	6424.6	3.7	0.5	22	136	3.4	7.33	22	2	110	102	20	30.5	ALIVE	13	6	NO
32	BHARTI B TELLI	164172	22	M	30.9	9.1	585	276	6404.5	4.6	0.6	20	143	4.2	7.2	11.6	12.4	100	126	22	34	ALIVE	14	9	NO
33	BHAGYAVANTI LAYAPPA	155075	19	F	6.52	13.1	203	97	5209	4.4	0.6	7	146	4	7.34	20.5	3.5	110	121	20	47	ALIVE	14	4	NO
34	BANGAMMA WALIKER	104279	25	M	9.51	12.3	254	101	5934	3.6	0.7	21	152	4.5	7.43	21.1	2.9	120	100	14	46.1	ALIVE	14	3	NO
35	BASAPPA B MOOLE	74288	20	M	17.27	16.8	307	110	3642.3	5	0.8	27	140	4.1	7.4	23	1	100	114	12	36.2	ALIVE	15	5	NO
36	AMAR VISHNU MORE	78100	23	M	22	14.6	249	102	200	3.8	2.8	40	144	6.1	6.9	3.2	20.8	100	140	26	45.6	DEAD	3	31	YES
37	GIDDAYYA MATAPATI	81703	35	M	17.31	18.2	406	185	200	4.1	0.7	7	150	3.4	7.41	19.4	4.6	100	122	22	55.5	ALIVE	13	9	YES
38	GIRISH KOLLI	317216	25	M	14.5	15.5	205	123	200	3.7	0.7	18	140	3.2	7.34	20.5	3.5	110	121	20	47	ALIVE	13	5	NO
39	MUTTANNA AURASANG	211048	31	M	15.76	16.6	376	141	1020	4.7	1.1	26	142	4.6	7.2	11.6	12.4	100	126	22	34	ALIVE	12	12	YES
40	LAXMI HATTI	175462	18	F	13.56	14.7	283	97	4172.2	3.9	1.1	24	137	4.3	7.37	16.8	7.2	100	122	22	40.4	ALIVE	13	5	NO
41	HANAMAGOUDA G HADAHALLI	168520	56	M	16.51	20.5	291	88	200	3.9	1.8	50	168	5.5	7.07	12.9	11.1	110	128	24	60.4	ALIVE	10	28	YES
42	JYOTI PRABHULING BIRADAR	166980	24	F	13.81	8.5	401	107	1399.2	4.1	2	54	139	4.9	7.2	11.6	12.4	100	130	24	34	ALIVE	12	17	YES
43	BHARATI B TELLI	164172	24	F	30.94	9.1	585	276	6404.5	4.6	0.6	20	143	4.2	7.3	18	6	110	130	24	34	ALIVE	14	10	NO
44	SUBBARAI AINAPUR	159615	75	M	10.21	13.4	173	86	5665.1	3.4	0.9	27	143	3.7	7.3	19	5	100	130	22	38.6	ALIVE	14	13	NO
45	BHAGYAVANTI LAYAPPA	155075	19	F	6.52	13.1	203	97	5209	4.4	0.6	7	146	4	7.3	20.8	3.2	100	130	22	47.1	ALIVE	15	3	NO
46	SATISH SAJJAN	151766	22	M	5.24	13.7	194	110	6386	3.8	0.8	19	138	4.3	7.3	20.8	3.2	100	130	22	47.1	ALIVE	15	3	NO
47	KANCHANA HOLAGI	146288	18	F	10.9	11	262	109	5557.4	3.1	0.6	21	138	3.6	7.26	18.1	5.9	100	130	22	35.7	ALIVE	14	5	NO
48	NINGARAJ HUGAR	132706	22	M	12.98	15.7	263	94	200	4.1	0.7	17	138	3.6	7.46	11.8	12.2	110	130	22	47.8	ALIVE	8	11	YES
49	RENUKA SONAGAR	127612	27	F	18.18	11	294	157	200	4	0.6	26	137	3.8	7.23	16.5	7.5	100	140	22	35.4	ALIVE	8	16	YES
50	SHILPA S LONI	107852	26	F	18.18	11.7	422	121	4571.6	4.1	1.4	45	144	4.3	7.29	14.6	9.4	100	130	20	36.2	ALIVE	9	15	YES
51	GURULINGAPPA PADASALAGI	108534	55	M	5.43	9.1	248	97	3034	2.9	0.9	22	155	3.8	7.34	13.5	10.5	120	130	22	29.8	ALIVE	14	11	NO
52	RAJU RATHOD	105797	28	M	10.79	13.9	359	132	6251.4	4	1.1	27	145	4.3	7.37	17.2	6.8	100	132	20	42.6	ALIVE	14	4	NO
53	DANAMMA AMBAGI	94456	18	F	11.2	11.6	248	100	2473	3.9	0.5	24	142	3.6	7.36	15.7	8.3	100	132	22	36.2	ALIVE	14	6	NO
54	GANGAMMA WALIKAR	99898	25	F	9.51	12.3	254	88	5934.3	3.6	0.7	24	152	3.5	7.3	20.8	3.2	100	130	22	47.1	ALIVE	14	8	NO
55	SANGANGOUDA S PATL	97109	30	M	7.41	14.9	180	94	5505.2	3.5	0.9	28	116	3.7	7.42	16.7	7.3	100	124	22	47.9	ALIVE	14	7	NO
56	PEERAPP ALONI	97021	26	M	17.75	20	390	102	7704.5	3.3	1.2	15	147	4.6	7.17	12.6	11.4	110	122	22	47.7	ALIVE	10	17	YES
57	BASAMMATARACHAND WASTER	97100	45	F	8.61	5.9	147	108	200	4.7	1.3	45	144	4.8	7.22	16.9	7.1	100	128	22	18.2	ALIVE	10	19	YES
58	PANDIT LAXMAN BIRADAR	87488	55	M	15.38	12.7	224	99	2078.8	3.8	0.8	21	142	3.1	7.17	12.6	11.4	110	122	22	45.5	ALIVE	12	13	NO
59	ARJUN S BHAJANTRI	89389	40	M	10.39	14.9	262	128	10094.7	4.1	0.9	43	142	4.2	6.94	24	0	120	124	16	45.9	ALIVE	14	2	NO
60	SIDDAPPA GOPAL NIMBAL	78462	36	M	10.13	11.8	183	95	200	3.8	0.8	22	154	3.1	7.27	14.6	6.4	130	122	22	45.9	ALIVE	8	15	YES
61	DANAMMA HADAR	73901	18	F	9.36	12.2	258	106	6038.9	3.9	0.6	28	142	3.2	7.34	23	1	120	132	16	49.1	ALIVE	15	2	NO
62	AMINMA A HADAF	61058	20	F	6.38	12.4	398	141	6326.3	4.2	0.6	28	144	4.7	7.32	22	2	110	132	20	39.4	ALIVE	15	4	NO
63	GIRISH KABBIN	59479	22	M	8.37	15.3	309	121	5713.2	3.7	0.9	17	143	2.7	7.34	23	1	120	132	16	49.1	ALIVE	15	4	NO
64	YALLAPPA WALIKAR	49371	40	M	10.36	15.6	371	130	10192.1	4.3	1	27	143	4.1	7.3	20.8	3.2	100	130	22	47.1	ALIVE	15	3	NO
65	BHIRAPPA SIDDAPPA PUJARI	40473	22	M	12.32	16.2	278	127	8503	4.3	0.8	22	142	3.5	7.34	23	1	120	132	16	49.1	ALIVE	15	3	NO
66	SURESH T CDALBAGI	140829	32	M	7.34	12.9	232	129	8510.8	3.6	0.7	21	136	3.8	7.35	22	2	130	115	18	26	ALIVE	14	4	NO
67	KIRAN BABU TIKOTA	131545	28	M	15.16	15.4	145	109	214	5.1	0.8	19	143	3.3	7.32	15.4	8.6	90	136	22	47.7	ALIVE	9	14	YES
68	LAKKAPP A PUJARI	47209	75	M	14.24	17.3	246	132	6585	3.4	1.3	21	148	4.2	7.16	19	5	120	138	22	52.7	ALIVE	13	3	NO
69	GIRISH KOLLI	317216	25	M	14.5	15.5	205	121	200	3.7	0.7	18	140	3.4	7.2	14.5	9.5	100	134	22	47	ALIVE	8	16	YES
70	ANJUTH GOUD	230150	20	F	4.39	10.2	242	110	1065.2	3.6	0.5	22	140	3.5	7.44	14.6	9.4	120	130	20	41.6	ALIVE	9	12	YES
71	SANTOSH P KULAKARNI	130679	40	M	10.13	17.5	162	125	225.6	4.6	1	24	138	4.1	7.17	12.6	11.4	110	122	19	45.5	ALIVE	9	15	YES
72	SURESH MAHADEVAPPA JAINAPUR	226824	17	M	14.12	14.7	326	104	200	3	1.8	40	146	5.1	7.38	17.3	6.7	130	118	20	47.1	ALIVE	9	14	YES
73	bhimappabsaramappa taradoqi	8331	50	M	13.14	14.3	267	108	200	4	2	50	126	5.6	7.3	12	12	90	144	20	33	DEAD	8	26	YES
74	amarsh rupla Rathod 13049		28	M	14.12	14.7	326	104	200	3.8	3.2	45	130	5.4	7.1	12	12	90	132	22	37	DEAD	6	26	YES
75	khajappa yaatti	1753419127	31	M	32.3	17.5	162	125	200	4.2	2.6	50	140	5.6	6.9	3.2	20.8	80	186	22	32	DEAD	8	26	YES
76	rajid mahender	17809	32	M	10	12.9	232	129	200	3.5	3	50	144	5.6	7.1	11.8	12.2	110	130	32	50.2	DEAD	3	40	YES
77	shivalaola sadaqori	4589	23	F	12	15.9	222	130	200	3.7	4	67	122	5.6	7.32	15.4	8.6	90	136	32	54	DEAD	5	34	YES
78	prajual ganahol	33990	22	M	15.33	12.9	232	129	200	4	5.1	72	150	6.1	6.9	3.2	20.8	150	30	40	43	DEAD	3	42	YES
79	zubair dadappa nadagauda	16572	25	M	12.81	9.5	401	120	200	2.8	1.2	45	129	4.8	7.36	15.7	8.3	100	130	20	30	DEAD	7	17	YES
80	Kaveri manahar jadhav	143991	19	F	14.12	14.7	326	104	200	3	0.5	22	135	4.5	7.29	18.2	5.8	120	110	22	32	DEAD	12	11	YES
81	Shantamma Krishnaappa dadmani	19970	46	F	7.34	12.9	232	129	200	3	1	18	122	4.7	6.9	3.2	20.8	120	110	20	33.4	DEAD	8	26	YES
82	zaubaqyairanqaudakava	14874	22	F	15.16	15.4	145	109	214	3	3.3	60	154	5.5	7.16	14.9	9.1	120	138	22	35.5	DEAD	6	25	YES
83	barappajambaqizhivappa		56	M	21.1	12.7	224	99	200	4	2.2	45	140	4.9	7.46	11.8	12.2	110	118	33	36.7	DEAD	6	23	YES
84	zudkar Mallikarjun naik		40	M	9.51	12.3	254	101	200	4	1.2	18	132	3.2	7.38	17.3	6.7	130	114	20	38.2	DEAD	12	8	YES
85	anantzhivappahaaratti	43004	42	M	13.12	11.21	3.01	105	200	4.1	1.8	15	140	5.2	7.36	15.7	8.3	90	180	33	40	DEAD	8	21	YES
86	ranjiramanagarathad	15476	30	M	8.37	15.3	309	121	200	2.8	3.3	50	156	5.2	7.17	12.6	11.4	110	134	40	30	DEAD	8	28	YES
87	mallappayamanti	19916	34	M	12.2	12.5	232	129	200	2.9	2.2	60	135	5	7.16	14.9	9.1	120	138	44	29.1	DEAD	6	33	YES
88	shankarlingbhoorappanallabadi	18849	32	M	16.3	12.9	232	129	200	3.2	3.3	62	135	5.5	7.37	16.8	7.2	90	130	30	31.3	DEAD	5	32	YES
89	mallappaniyappazujja	11994	45	M	19	12.9	232	129	200	2.7	4	48	122	5.5	7.3	4.7	19.3	100	180	32	34.3	DEAD	6	33	YES
90	naqavenizidappakadagatti	27635	21	F	15.33	12.9	232	129	200	4	5.1	72	150	6.1	6.9	3.2	20.8	80	190	40	47.1	DEAD	4	42	YES
91	Basavaraj mallappa bellaki	28142	56	M	21.12	12.9	232	129	200	3	3	50	133	4.8	7.36	15.7	8.3	100	132	22	49.1	DEAD	5	30	YES
92	linappakulal	18536	65	M	12	12.9	232	129	200	2	2.6	45	129	4	7.38	17.3	6.7	110	114	20	44.1	DEAD	8	32	YES
93	maharh makadevkali	35667	48	M	17	12.9	232	129	200	2.2	5.2	90	131	5.2	7.17	12.6	11.4	100	122	22	46.1	DEAD	8	28	YES
94	mallappaqurriddappabudani	31407	72	M	14.1	9.1	248	97	200	3	3.3	80	128	3.7	7.29	18.2	5.8	120	130	24	44.2	DEAD	6	31	YES
95																									