COMPARISON OF SERUM AMYLASE AND CREATINE PHOSPHOKINASE LEVELS IN ASSESSING THE SEVERITY OF ORGANOPHOSPHATE POISONING

By

Dr. RAKSHA CHANDRAIAH MBBS

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Under the guidance of

Dr. SANJEEVKUMAR N. BENTOOR M.D

PROFESSOR & HOD

DEPARTMENT OF MEDICINE

BLDE DEEMED TO BE UNIVERSITY

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

VIJAYAPURA, KARNATAKA

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Date: **Dr. RAKSHA CHANDRAIAH**

Place: Vijayapura

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Date:

Place: Vijayapura

Dr. SANJEEVKUMAR. N.BENTOOR, M.D

Professor and Head

Department of General Medicine

Shri B.M. Patil Medical College,

Vijayapura

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& RESEARCH CENTRE, VIJAYAPURA

ENDORSEMENT BY THE HOD, PRINCIPAL/HEAD OF THE INSTITUTION

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Seal & Signature of HOD of Medicine

Dr. SANJEEVKUMAR N. BENTOOR
M. D. (Medicine)
BLDEDU's Shri B.M. Patil Medical College, Hospital & Research Centre, Vijayapura

Date:

Place: Vijayapura

Seal and signature of The Principal

Dr. ARAVIND V PATIL
M.S. (General Surgery)
BLDEDU's Shri B.M.Patil Medical College, Hospital & Research Centre, Vijayapura

Date:

Place: Vijayapura

B.L.D.E DEEMED TO BE UNIVERSITY

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Date: **Dr. RAKSHA CHANDRAIAH**

Place: Vijayapura

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Dr. RAKSHA CHANDRAIAH

ABBREVIATIONS

2-PAM - 2-Pralidoxime

ABG - Arterial Blood Gas

ACh - Acetylcholine

AChE - Acetylcholinesterase

ALT - Alanine Aminotransferase

ARDS - Acute Respiratory Distress Syndrome

AST - Aspartate Aminotransferase

BP - Blood Pressure

BUN - Blood Urea Nitrogen

CNS - Central Nervous System

CPK - Creatine Phosphokinase

DUMBBELS - Defecation, Urination, Miosis, Bronchospasm, Bronchorrhea, Emesis, Lacrimation, Salivation

ECG - Electrocardiogram

GCS - Glasgow Coma Scale

GI - Gastrointestinal

HR - Heart Rate

ICU - Intensive Care Unit

IM - Intramuscular

IMS - Intermediate Syndrome

IV - Intravenous

OP - Organophosphate

OPP - Organophosphate Poisoning

PAM - Pralidoxime

PNS - Peripheral Nervous System

POP - Peradeniya Organophosphorus Poisoning

PPS - Peradeniya Organophosphorus Poisoning Scale

RBC - Red Blood Cell

RR - Respiratory Rate

SD - Standard Deviation

SLUDGE - Salivation, Lacrimation, Urination, Defecation, Gastrointestinal distress, Emesis

SpO2 - Oxygen Saturation

WBC - White Blood Cell

WHO - World Health Organization

ABSTRACT

Introduction: Organophosphate compounds are widely used pesticides that cause significant morbidity and mortality worldwide, particularly in developing countries. The inhibition of acetylcholinesterase enzyme leads to accumulation of acetylcholine, resulting in characteristic cholinergic manifestations. While acetylcholinesterase levels are the gold standard for diagnosis and severity assessment, their limited availability in resource-constrained settings necessitates exploration of alternative biomarkers. This study aimed to evaluate serum amylase and creatine phosphokinase (CPK) as potential markers for assessing the severity of organophosphate poisoning and to correlate these findings with clinical severity and outcomes.

Materials and Methods: This prospective study included 73 patients with organophosphate poisoning admitted to a tertiary care center. Clinical severity was assessed using the Peradeniya Organophosphorus Poisoning (POP) scale. Serum acetylcholinesterase, amylase, and CPK levels were measured on days 1, 3, and 5 of hospitalization. Statistical analysis was performed to determine correlations between biochemical parameters and clinical severity, as well as their associations with outcomes.

Results: Among the 73 patients, 67.1% were young adults (21-40 years), with a nearly equal gender distribution. Based on the POP scale, 43.8% had mild poisoning, 39.7% moderate, and 16.4% severe. Elevated serum amylase levels (>110 units) were observed in 63% of patients on day 1, while elevated CPK levels (>200 units) were noted in 16.4%. Strong correlations were found between the POP score and both amylase ($r=0.865$, $p<0.001$) and CPK levels ($r=0.817$, $p<0.001$). Acetylcholinesterase levels on admission were significantly associated with mortality, with lower levels (<5320 units) corresponding to higher mortality rates (34.5% vs. 6.7%,

p=0.034). Ventilatory support was required in 26% of patients, and the overall mortality rate was 15.1%.

Conclusion: Serum amylase and CPK levels demonstrate strong correlations with clinical severity in organophosphate poisoning, with amylase exhibiting a slightly stronger correlation. These readily available biochemical markers can serve as valuable adjuncts to clinical assessment in determining severity and predicting outcomes, particularly in settings where acetylcholinesterase assays are not available. Future research with larger sample sizes is warranted to establish definitive cut-off values for these markers in clinical decision-making.

Keywords: Organophosphate poisoning, Acetylcholinesterase, Serum amylase, Creatine phosphokinase, Peradeniya Organophosphorus Poisoning scale, Severity assessment, Biomarkers, Cholinergic crisis.

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INTRODUCTION

Organophosphate (OP) poisoning represents a significant global health challenge, accounting for approximately 3 million poisoning cases annually and 300,000 deaths, predominantly in developing countries.[1] The World Health Organization estimates that pesticide poisoning contributes to about one-third of global suicides, with organophosphates being the most commonly used agents.[2] This high mortality rate, coupled with the widespread availability of these compounds, makes OP poisoning a critical public health concern requiring prompt diagnosis and accurate severity assessment for optimal management.

Organophosphates exert their toxic effects primarily through the inhibition of acetylcholinesterase (AChE), leading to the accumulation of acetylcholine at synaptic junctions.[3] This accumulation results in the characteristic clinical manifestations of cholinergic excess, affecting multiple organ systems through muscarinic, nicotinic, and central nervous system effects. The complexity of presentation and the variable onset of symptoms make severity assessment particularly challenging, necessitating reliable biochemical markers for accurate prognostication.

The traditional approach to assessing OP poisoning severity has relied heavily on clinical parameters and cholinesterase levels. However, these methods have several limitations:

Clinical Assessment Limitations:

- Subjective nature of symptom evaluation
- Variable presentation patterns

- Delayed onset of certain manifestations
- Influence of pre-hospital interventions
- Inter-observer variability

Cholinesterase Level Limitations:

- Not universally available
- Time-consuming analysis
- Affected by various physiological and pathological conditions
- May not accurately reflect severity in all cases
- Cost considerations

Recent research has focused on identifying alternative biomarkers that could provide more reliable and objective assessment of poisoning severity.[4] Among these, serum amylase and creatine phosphokinase (CPK) have emerged as promising candidates. These enzymes reflect different aspects of organ system involvement in OP poisoning:

Serum Amylase:

- Indicates pancreatic involvement
- May reflect cholinergic overstimulation
- Shows correlation with respiratory failure
- Easy to measure in most healthcare settings
- Relatively cost-effective

Creatine Phosphokinase:

- Reflects muscle injury and rhabdomyolysis
- Indicates severity of nicotinic effects

- Associated with need for ventilatory support
- Widely available test
- Serial measurements possible

The relationship between these enzymatic markers and OP poisoning severity has been documented in various studies. Research by Kumar et al. (2022) demonstrated a significant correlation between elevated serum amylase levels and the need for mechanical ventilation in OP poisoning cases.[5] Similarly, Bhattacharyya et al. (2021) found that CPK levels showed strong association with mortality outcomes in severe poisoning cases.[6]

The pathophysiological basis for these enzymatic elevations is complex and multifactorial:

Amylase Elevation Mechanisms:

- Direct cholinergic stimulation of pancreatic acinar cells
- Pancreatic duct hypertension
- Acute inflammatory response
- Oxidative stress-induced damage
- Potential direct toxic effects on pancreatic tissue

CPK Elevation Mechanisms:

- Excessive muscular activity from fasciculations
- Direct muscle fiber damage
- Rhabdomyolysis
- Prolonged immobilization
- Respiratory muscle fatigue

The timing of these enzymatic changes carries particular significance in the clinical setting. Studies have shown that changes in serum amylase and CPK levels often precede severe clinical manifestations, potentially serving as early warning indicators.[7] This temporal relationship makes these markers especially valuable in resource-limited settings where more sophisticated monitoring tools may not be available.

The severity assessment of OP poisoning has direct implications for patient management:

1. Determining the need for intensive care admission
2. Guiding atropine and oxime therapy
3. Anticipating the need for ventilatory support
4. Predicting complications
5. Estimating prognosis
6. Planning resource allocation
7. Guiding preventive measures for complications

Recent advances in understanding the molecular mechanisms of OP toxicity have highlighted the importance of multi-parameter assessment approaches.[8] The complex interplay between cholinergic effects, inflammatory responses, and oxidative stress suggests that no single marker can fully capture the spectrum of toxicity. This understanding has led to increased interest in combining multiple biochemical markers for more accurate severity assessment.[9]

The cost-effectiveness of using these enzymatic markers is particularly relevant in developing countries, where OP poisoning is most prevalent. Both serum amylase and CPK tests are:

- Widely available
- Relatively inexpensive
- Technically simple to perform
- Reliable and reproducible
- Quick to obtain results

The potential impact of accurate severity assessment extends beyond individual patient care to public health planning and resource allocation. Understanding the epidemiological patterns and severity distributions of OP poisoning cases can help in:

- Developing targeted prevention strategies
- Improving emergency response systems
- Optimizing healthcare resource allocation
- Training healthcare providers
- Formulating evidence-based treatment protocols

However, challenges remain in standardizing the interpretation of these enzymatic markers.[10] Factors that need consideration include:

- Age-related variations
- Gender differences
- Timing of sample collection
- Pre-existing medical conditions

- Concurrent medications
- Laboratory standardization
- Cost-benefit considerations

This study aims to evaluate the comparative utility of serum amylase and CPK levels in assessing OP poisoning severity, potentially establishing more reliable and objective criteria for severity assessment and prognostication.

AIM & OBJECTIVES

Objectives:

1. To estimate and compare the Serum levels of Amylase and Creatine Phosphokinase in Acute Organophosphate poisoning.
2. To correlate the levels of the same with clinical severity using Peradeniya Organophosphorus Poisoning scale (POP scale).
3. To know which is a better biomarker that correlates with the severity of Organophosphate poisoning.

REVIEW OF LITERATURE

CHEMISTRY AND METABOLISM OF OPS

"Figure 1 depicts the overall structure of OPs, which was first suggested by Schrader in 1937. Their chemistry has been extensively studied. X is the so-called "leaving group," which is eliminated when the OP phosphorylates AChE and is the most susceptible to hydrolysis. R1 and R2 are most frequently alkoxy groups (i.e., OCH3 or OC2H5), though isopropyl substitutes are also possible. The pentavalent phosphorus is double-bonded to either an oxygen or a sulfur (in this case, the compound is defined as a phosphorothioate). Phosphonothioates, phosphoramidates, phosphonates, and other chemical subclasses of OPs are also known to exist.[11] While some OPs (such as dichlorvos, methamidophos, or the nerve agents sarin or soman) have a P = O bond and do not require any bioactivation, the majority of OPs used as insecticides are phosphorothioates (i.e., they have a P = S bond) and must be bioactivated in vivo to their oxygen analogs in order to exert their toxic action. An oxidative desulfuration, this bioactivation is facilitated by a number of different cytochrome P450 enzymes. There are other bioactivation processes, such as the creation of a sulfoxide (S = O) and a sulfone (O = S = O), which are both catalyzed by CYPs (e.g., disulfoton). The OPs are detoxified by all other biochemical reactions that are catalyzed by CYPs or hydrolytic esterases (such as carboxylesterase and paraoxonase-1) and result in metabolites that are less toxic or nonexistent".[12]

TYPES OF ORGANOPHOSPHORUS COMPOUNDS

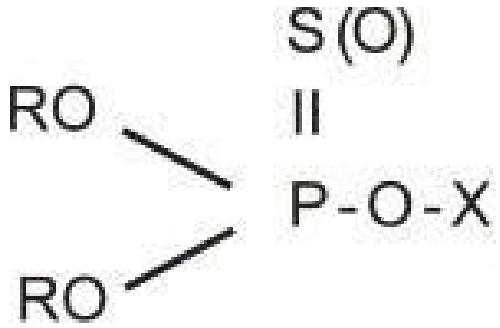
Phosphoric acids and their derivatives are the source of organophosphorus compounds (OPCs), which are organic molecules with "at least one carbon-phosphorus bond. Applications for

pentavalent phosphorus-containing compounds are mostly found in industry and the environment. The toxicity of these phosphoric acid esters is mostly determined by the substituents that are joined to the phosphorus. [13] Thiols, amides, or esters of phosphonic, phosphinic, phosphoric, or thiophosphoric acids with two extra organic side chains of the phenoxy, cyanide, or thiocyanate group are known as organophosphorus insecticides. Certain OPCs are classified as phosphonothioates (S-substituted), and phosphonofluoridates include nerve poisons, also referred to as chemical warfare agents. [14]

These nerve agents fall into four categories: (1) the German-developed G-series agents, which include cyclosarin (GF), sarin (GB), soman (GD), and tabun (GA). (2) V-series agents (V for venomous) include Chinese VX and Russian VX, as well as VE, VG, VM, and VX. (3) GV-series, such as GV, 2-dimethylaminoethyl-(dimethylamido)-fluorophosphate, which combine the characteristics of series G and V. In general, compounds in the G series are less harmful than those in the V series; (4) Novichok series of compounds, such as Novichok-5, Novichok-7, A230, A232, A234, and substance-33. The first individual to describe the creation of the first three compounds—substance-33, A230, and A232—at the GosNIIOKhT facility in Russia was Dr. Mirzayanov. These substances were agents that were unitary. Unitary A232 served as the basis structure for the synthesis of Novichok-5, the first binary agent, later in 1989. Novichok poisons are liquids, however they can be made into dusty formulations by adsorbing liquid droplets onto carriers like talc, pumice, silica gel, or fuller's earth. A230, A232, and A234 were found to hydrolyze more slowly than agents from the G and V classes. Generally speaking, there is a great deal of disagreement on the structures of these compounds because of the secrecy surrounding their development; as a result, numerous structural variations have been

hypothesized". [15]

Figure 1: Structure of OP Compounds



Stereogenic phosphorus atoms are found in the cyanide-releasing tabun, the fluoride-releasing volatiles soman and sarin, and the thiocholine-releasing VX. "With the exception of Soman, which has two chiral atoms—one a carbon center and the other phosphorus—all of these OPCs have two enantiomers, P(−) and P(+). Soman has four enantiomeric forms: C (+)P(+), C (+)P(−), C (−)P(+), and C (−)P(−)."[16] Recent years have seen the compilation and careful evaluation of extensive structural data pertaining to the many types and isomers of OPC nerve agents. Stereoisomers are important when considering the compound's range of toxicity. P(−) enantiomers are typically more hazardous.[17]

HISTORICAL PERSPECTIVES

The French scientist Philippe de Clermont was credited by Swedish pharmacologist Bo Holmstedt in a frequently cited article with synthesizing the first OP (tetraetylpyrophosphate—TEPP) in 1854.[18] However, other people have suggested that some OPs might have been created even earlier. Triethylphosphate (TEP) was created in 1820 by Jean Louis Lassaigne when ethanol and phosphoric acid interacted; nevertheless, Franz Anton Voegeli was later credited with this synthesis in 1848. Jean Pierre Boudet, another Frenchman, is thought

to have created an OP from phosphoric acid and alcohol even earlier, in 1801.[19] Despite being the first OP cholinesterase inhibitor, TEPP was synthesized by a number of other chemists "in addition to de Clermont (with assistance from Russian chemist Wladimir Moschnin, who was also employed at Adolphe Wurtz's laboratory in Paris). In fact, de Clermont sampled the substance and characterized it as a sticky liquid with a burning taste and an odd odor. At the time, neither the toxicity nor the method of action of TEPP were understood. Willy Lange of the University of Berlin created a few compounds with the P-F bond in 1932. He observed the harmful effects of the fumes on himself while working with doctoral student Gerda von Krueger to synthesize dimethyl- and diethyl phosphofluoridate." "The vapours of these compounds have a pleasant and strongly aromatic odor, but a marked pressure develops in the larynx a few minutes after inhaling, along with breathlessness," they noted. Mild consciousness problems then appeared, along with a painful reactivity of the eyes to light and a dazzled sense. The symptoms only go away after a few hours. The effects are produced in very little amounts. Although Lange appeared to be aware that OP chemicals may be used to create insecticides, he quickly departed Germany to relocate to the US, where he worked for Procter & Gamble and the University of Cincinnati before leaving the OP industry.[20]

"Gerhard Schrader, a chemist of the I.G. Farbenindustrie in Germany, is regarded as the father of contemporary OP pesticide toxicity despite all of these earlier attempts and achievements. One day in December 1936, Schrader was working on the synthesis of organic fluorine and sulfur compounds when he realized "that, on my way home, my visual acuity was somewhat reduced." My vision had almost fully recovered by the next day, so I went back to work. It became clear that a new synthetic drug was the cause of more visual problems. It was

discovered that 0-ethyl N, N-dimethyl-phosphoroamido-fluoridate was too poisonous to warm-blooded animals to be utilized in farming. Although it was not stable enough for plant protection, Schrader is credited with developing a novel, straightforward process for synthesizing TEPP, the first OP pesticide to be sold commercially under the trade name Bladan in combination with other hexa-compounds. Schrader is credited with creating thousands of OP chemicals. [21] Although octamethyl-pyrophosphoramide (OMPA) was synthesized in 1942, the real "breakthrough" occurred in 1944 when a novel compound with ideal stability and insecticidal action (code name E605) was created. The Allies took over the synthesis techniques at the end of World War II, and E605 was eventually released into the agricultural market under the trade name parathion, which turned out to be the most popular insecticide in this class. British researchers McCombie and Saunders were also working on OPs concurrently with Schrader; they later patented dimefox and diisopropyl fluorophosphate (DFP). Some of the OPs that Schrader produced during that time proved to be highly hazardous to mammals. The development of OPs followed two parallel strategies, which were declared "secret" by the German government in 1938. The first was the synthesis of chemicals that were less toxic to mammals and effective as insecticides; the second was the development of compounds with high human toxicity and high volatility, which were to be used as poison gases in place of phosgene, mustard gas, or chlorine. Although they weren't employed during World War II, compounds like Tabun, Sarin, and Soman were created during that time with the possibility of being utilized as chemical warfare weapons. [22] Hundreds of OP compounds have been produced and marketed globally as insecticides in a range of formulations since the late 1930s. When the majority of commonly used organochlorine pesticides were phased out or outlawed in the 1970s, their use

peaked. OPs made up about 70% of all insecticides used in the United States until 2000, but in the years that followed, that percentage was cut in half. Nonetheless, the majority of underdeveloped nations continue to use OPs extensively, mostly because to their low cost in comparison to more modern pesticides". [23]

"The mechanism of action of OPs, which is the inhibition of acetylcholinesterase (AChE), was also identified concurrently with their manufacture. German researchers discovered that atropine might act as an antidote to the parasympathomimetic (cholinergic) effects of OPs. These conclusions were undoubtedly made easier by the actions of physostigmine, an alkaloid that was isolated in 1864, whose mode of action as an AChE inhibitor was clarified by Loewi and Navratil in 1926, and whose miotic activity and atropine antagonism were simultaneously identified. [24] In fact, as early as 1939, the mechanism of action of OPs was proposed. Ten years later, Ken Du Bois and John Doull conclusively proved that parathion toxicity resulted from AChE inhibition. The identification of the reactivation and "aging" of the phosphorylated AChE are two other significant turning points in the early history of OPs. Irwin Wilson of Columbia University in New York demonstrated in 1951 that hydroxylamine may restart AChE that had been blocked by OPs. Wilson (in the United States) and Albert Green and Dan Davies (in the United Kingdom) worked together over the course of the following several years to synthesize pralidoxime (2-PAM), which, when combined with atropine, is still the major treatment for OP poisoning today. (The more general term phosphylate/phosphylation may also be used to describe the interaction of OPs with B-esterases.) This positive development in the treatment of OP poisoning was somewhat counteracted by the discovery, also in the mid-1950s, that the ability of oximes to reactivate phosphorylated Since "aging" (the nonenzymatic removal of an

alkyl chain from the phosphate) would change the inhibited enzyme into a nonreactivatable version, AChE declined over time. [25]

Since natural compounds are the source of insecticides like pyrethroids and carbamates, natural OPs have also been discovered, albeit after synthetic OPs were created. After being separated from cultures of the soil microbe Streptomyces antibioticus, two OPs (designated CGA 134735 and CGA 134736) were discovered to be strong AChE activity inhibitors. The freshwater cyanobacterium anabaena flos-aquae strain NRC-525-17 yielded another naturally occurring substance, anatoxin-a, which was discovered to be an irreversible inhibitor of AChE. Therefore, decades of chemical research have ultimately "reinvented" (and improved) what nature had already provided, even for Ops". [26]

OP POISONING

Mechanism of Action of OP Compounds

Otto Loewi proved in 1920 that ACh functions as a chemical bridge that allows nerve impulses to travel between synapses.[27] Acetyl-coenzyme A (acetyl-CoA) is the source of the neurotransmitter sodium chloride (ACA). Choline acetyltransferase catalyzes the production of acetyl-CoA from glucose and choline, which is then converted into the neurotransmitter acetylcholine (ACh). Upon stimulation, vesicles—packages of ACh held within presynaptic membranes—are released.

AChE effectively stops the neurotransmitter ACh's action on the muscarinic and nicotinic receptors by hydrolyzing it into choline and acetate. 28 Organophosphates have the ability to permanently bind to AChE and stop ACh from breaking down. Muscarinic and

nicotinic receptors, which are found throughout the body, are overstimulated as a result of this "liberation" of ACh.

Nicotinic Receptors

"Nicotinic receptors are of 2 types—central (neuronal) and peripheral (neuromuscular). Central nicotinic receptors, also known as NN or N2, are located in the central nervous system (CNS). They can also be found in the sympathetic and parasympathetic ganglia of the peripheral nervous system (PNS) and the adrenal medulla. Peripheral nicotinic receptors, or NM or N1, are located at the neuromuscular junctions. The N1 neuromuscular junction can cause fasciculation and muscular weakness, whereas the N2 autonomous nervous system is associated with hypertension and tachycardia".

Muscarinic Receptors

"All 5 subtypes of muscarinic receptors, M1 to M5, are distributed throughout the CNS. Postganglionic muscarinic receptors provide parasympathetic innervation to the heart, exocrine glands, and smooth muscles of the internal organs. Sympathetic postganglionic fibers provide innervation to the sweat glands.[29]

Stimulation of each specific receptor yields distinct clinical signs and symptoms, as mentioned below".[30]

- "M2 receptors in the heart: Hypotension and bradycardia
- M2 and M3 receptors in the eyes: Miosis
- M2 and M3 receptors in the gastrointestinal system: Abdominal cramps, drooling, and salivation

- M2 and M3 receptors in the respiratory system: Bronchospasm, bronchorrhea, and rhinorrhea
- M2 and M3 receptors in the smooth muscles of internal organs: Abdominal cramps and urinary urgency
- M1 to M5 receptors in the CNS: Seizure, anxiety, and agitation"

EPIDEMIOLOGY

Organophosphorus compound (OP) poisoning is a worldwide issue. According to estimates from the World Health Organization, two million people are hospitalized for pesticide-related suicide attempts each year, and one million major unintentional poisonings happen annually. [31] "A study from 1995 to 2004 found that the number of organophosphate exposure incidents peaked in 1997 with 20,135 cases and then decreased in subsequent years, according to the annual reports of the Toxic Exposure Surveillance System (TESS), which is kept up to date by the American Association of Poison Control Centers. [32] The National Poison Data System's 2020 annual report listed 2079 organophosphate exposure instances; no fatalities were reported. [33] The U.S. Environmental Protection Agency's decision to gradually phase out the use of organophosphate pesticides in residential settings is largely responsible for this significant decrease in exposure to these chemicals. This project started in 2000 and ended in 2005.[32] Accurately estimating the overall worldwide exposure rate of organophosphate and the associated toxicity is difficult. According to estimates, 371,594 people worldwide suffered from pesticide self-poisoning in 2007, which accounted for around one-third of all suicides that took place that year. [34] According to WHO estimates, there were about 20,000 fatalities and 1 million unintentional pesticide poisonings in 1990. According to a 2020 study, there were 740,000

unintended pesticide poisonings in 141 nations, which led to 7446 fatalities. [35] Due to insufficient reporting and a lack of statistical data, the true level of exposure and toxicity is probably higher".

INDIAN PERSPECTIVE

India is primarily an agrarian nation, and farming there frequently involves the usage of pesticides. Suicidal poisoning with household agents (OPs, carbamates, pyrethrinoids, etc.) is the most frequent type of poisoning, according to statistics from the National Poison Information Centre India.[36] According to recent data from India's National Crime Bureau, in 2006 and 2007, 19.4% and 19.7% of all cases of suicidal poisoning were caused by pesticide intake.[37] Poisoning has grown in concern during the last ten years, both in India and internationally.[38] Poisoning is only a 1–2% cause of death in developed nations, but it is the fourth leading cause of death in developing nations like India, with rates ranging from 15–30%, particularly in rural areas.[39] According to WHO estimates, pesticides are currently the most popular way for people to commit suicide globally. In 2016, the suicide death rate was 16.5 per 100,000, compared to the global average of 10.5 per 100,000. The elderly, those with special needs, and those aged 15 to 29 are the most at risk.[40] Due to the extensive usage of pesticides for domestic and agricultural purposes, pesticide poisoning is very common in India. The most common cause of suicide in India for both men and women aged 15 and over is pesticide poisoning, primarily from organophosphates, which accounts for over 92,000 fatalities per year.[41]

Pathophysiology

One neurotransmitter that is widely used in the neurological system is acetylcholine. "All postganglionic parasympathetic nerves, the postganglionic sympathetic nerve that innervates sweat glands, parasympathetic and sympathetic ganglia, and skeletal neuromuscular junctions contain acetylcholine". Acetylcholine is released into the synaptic cleft when an axon depolarizes, activating postsynaptic receptors and causing an action potential to propagate. Acetylcholine is hydrolyzed by carboxylic ester hydrolases to produce choline and acetic acid. "Choline is reabsorbed into the presynaptic neuron to be used for the manufacture of more acetylcholine, and this process happens quickly. The primary enzymes in charge of this metabolism are butyrylcholinesterase (BuChE) and AChE. AChE is found on erythrocyte membranes and in skeletal and neurological tissues. Plasma and several organs, including the liver, heart, pancreas, and brain, contain BuChE. The role of BuChE is still not fully known, though".[42]

The ability of organophosphate insecticides to inhibit carboxyl ester hydrolases—with a primary focus on AChE inhibition—is their primary characteristic. By phosphorylating the enzyme's serine hydroxyl group, these pesticides render AChE inactive. Since AChE is necessary for the breakdown of acetylcholine, its inhibition causes acetylcholine to build up in the synapse, which in turn causes both nicotinic and muscarinic receptors to be overstimulated.

"Myoclonic jerks and fasciculations can be caused by overstimulation of nicotinic receptors at the neuromuscular junction, which can ultimately result in depolarizing blocks that cause flaccid paralysis". The adrenal glands also contain nicotinic receptors, which may be the cause of symptoms like perspiration, tachycardia, hypertension, and left-shift leukocytosis.[43–45]

Because organophosphate poisoning acts on muscarinic receptors, it causes symptoms. Through a G-protein–coupled receptor mechanism, these effects usually manifest more slowly than nicotinic receptor actions. Both the parasympathetic and sympathetic nervous systems contain muscarinic receptors. Excessive diaphoresis is caused by the sympathetic nervous system overstimulating the sweat glands. Organophosphate poisoning can have parasympathetic effects on the heart, exocrine glands, and smooth muscles, among other systems. Breathing problems like bradycardia, bronchorrhea, and bronchospasm can result from muscarinic overstimulation, which can create serious, sometimes fatal diseases.[28]

"Excessive acetylcholine in the CNS can cause CNS depression, leading to coma and seizures. In cases where patients ingest agricultural pesticides, the presence of co-formulants and alcohol also poses a concern. Pesticides are frequently combined with solvents and surfactants to form an emulsifiable concentrate rather than being in a pure organophosphate form. The extent of the toxicity associated with co-formulants remains uncertain. Considering that organophosphate toxicity can induce CNS depression and coma, the risk of aspirating these solvents is a considerable concern. Reports of aspiration pneumonitis and adult respiratory distress syndrome (ARDS) have emerged in cases of organophosphate toxicity. However, it remains uncertain whether these conditions are caused by the compound itself or its aspiration".[46]

Toxicokinetics

The fastest absorption of organophosphate pesticides is through inhalation, although they can also be taken through eating, ocular contact, cutaneous exposure, and inhalation.[47] After cutaneous exposure, systemic absorption varies, but it can be accelerated by a number of conditions, including dermatitis, damaged skin, and high ambient temperatures. Both

unintentional exposures in children and deliberate efforts at self-harm in adults are frequently linked to oral intake.

It is uncertain when the plasma concentration peaks following exposure to organophosphates. However, a research conducted on "human volunteers found that the time to peak plasma concentrations was about 6 hours after relatively modest dosages of chlorpyrifos were taken orally.[48] Interestingly, these results might not hold true for other organophosphate substances, particularly when huge volumes are consumed, as occurs in deliberate efforts at self-harm. "Additionally, the study used pure chlorpyrifos, which is different from agricultural pesticides and may have additives that affect the organophosphate's distribution and absorption. In contrast to agricultural pesticides that might contain additives that could affect the organophosphate's absorption and distribution, this study also used pure chlorpyrifos".

The majority of organophosphates have a large volume of distribution and are lipophilic. They spread quickly into the liver, kidneys, and adipose tissue. They offer defense against metabolism due to their wide spread. The result following poisoning may be influenced by the patient's adipose tissue and degree of lipophilicity. A study conducted in Korea in 2014 looked at the results of 112 patients who had been acutely poisoned, 40 of whom were obese. Longer stays in the intensive care unit (ICU), longer duration of hospitalization overall, and lengthier mechanical breathing were all encountered by patients with a body mass index (BMI) of greater than 25.[49]

Cholinergic crises can be brought on by the release of unmetabolized organophosphates from fat reserves. People with low lipophilicity and lower volumes of distribution usually do not

exhibit this behavior, which is linked to highly lipophilic substances. After absorption, organophosphates can directly block the AChE enzyme without requiring first metabolism. These direct-acting substances are known as oxons, and they are distinct from other substances termed thions, which become active only after the body's metabolism is activated. Enzymes called cytochrome P450 (CYP450), which are mostly found in the liver and intestine, activate thion organophosphate molecules. Depending on the organophosphate's kind and quantity, different CYP450 enzymes may be involved.[50]

"When an organophosphate binds to the enzyme AChE, it undergoes cleavage, forming a stable yet reversible bond and rendering the AChE inactive. Although a regeneration process may occur, it proceeds more slowly than the inhibition and may take hours to days to restore AChE function completely. During its inactive state, the enzyme can potentially undergo the aging process, in which the initial reversible bond becomes irreversible, and enzyme regeneration can no longer occur. The time frame of aging varies among different organophosphate compounds. The antidote pralidoxime accelerates acetylcholine regeneration and reduces the number of inactive enzymes available for aging. Pralidoxime is effective only before the aging process, which is time-sensitive and dependent on the specific organophosphate compound involved.[51] Once aging takes place, AChE can no longer be regenerated, thereby necessitating de novo synthesis for enzyme replenishment".

Adverse Effects of Organophosphates[52]

"The adverse effects of exposure to organophosphate pesticides can be categorized based on the duration of exposure, as mentioned below.

- Acute effects: Occur within minutes to 24 hours

- Subacute effects: Occur between 24 hours and 2 weeks
- Chronic effects: Extend beyond weeks to years"

"Since organophosphate pesticides can enter the body through the skin, integumentary system, respiratory system by inhalation, or direct ingestion, poisoning is the main result of acute organophosphate exposure. Inhalation is when organophosphate insecticides show up clinically the quickest. The consequences of acute exposure to organophosphates can also be induced by chronic exposure. Chronic exposure, however, can also cause memory loss, speech problems, poor judgment, and difficulties with coordination. In addition to causing flu-like symptoms such nausea, vomiting, malaise, and weakness, prolonged exposure to organophosphates has also been linked to peripheral polyneuropathy. A possible risk of cancer has been linked to exposure to specific organophosphates. Pesticides including parathion, tetrachlorvinphos, diazinon, and malathion are classified as potential carcinogens, per a report by the International Agency for Research on Cancer. The ability of organophosphate insecticides and nerve gas to block the activity of AChE, the enzyme that breaks down ACh, is a defining characteristic of exposure to these compounds. The function of AChE in plasma, red blood cells, and synapses in the PNS and CNS is impacted by the irreversible bonds that organophosphate pesticides create with it. Nicotinic and muscarinic receptors are overstimulated as a result of the accumulation of Ach".

Complications Related to Organophosphate Exposure

Because they are connected to the impacted systems, the problems brought on by exposure to nerve gas or organophosphate pesticides are system-specific. Both nicotinic and muscarinic receptors are overstimulated, which leads to the clinical signs of these problems.

Clinical manifestations of organophosphates are mostly seen in the cardiovascular, renal, gastrointestinal, CNS, and respiratory systems.

Respiratory System

Exposure to organophosphate pesticides can cause problems in the respiratory system, including severe bronchospasm, noncardiogenic pulmonary edema, "aspiration pneumonia from excessive salivation, and progressive respiratory failure from weakening respiratory muscles, particularly the diaphragm".

"Cardiovascular System"

"In the respiratory system, exposure to organophosphate pesticides may lead to complications such as arrhythmias, especially ventricular tachycardia, bradycardia, hypertension, hypotension, and prolonged QTc".

"Central Nervous System"

"Exposure to organophosphate pesticides in the CNS may lead to complications such as psychosis, seizure, change in mental status, and hallucination".

"Gastrointestinal and Metabolic Systems"

"Exposure to organophosphate pesticides can result in various complications within the gastrointestinal and metabolic systems, including electrolyte imbalances due to fluid and electrolyte losses from the gastrointestinal tract, pancreatitis, hyperglycemia, and reduced bicarbonate levels".

"Renal System"

"Exposure to organophosphate pesticides in the renal system can cause acute kidney injury. Limited case reports have documented acute kidney injury linked to

organophosphate pesticide exposure, typically managed through conservative approaches or hemoperfusion treatment".

History and Physical

The precise substance involved and the period of exposure are crucial components of the patient's medical history when handling possible poisoning instances, particularly when purposeful consumption is involved. "Since the toxicity of various chemicals can vary greatly, an effort should be made to secure the pesticide container, if possible, in order to give this information to the Poison Control Center or a medical toxicologist". The degree of toxicity, the specific organophosphate substance involved, the exposure route, and the dosage all affect when symptoms appear. Furthermore, the compound's toxicokinetics, notably its lipophilicity, affect how long toxicity lasts. As the substance is released from fat reserves, cholinergic effects may occasionally reappear.[53]

Diaphoresis, muscle fasciculations, pinpoint pupils, and unresponsiveness are characteristic symptoms of severe organophosphate exposure. Urinary incontinence, lacrimation, diarrhea, emesis, and excessive salivation are possible further symptoms. The smell of garlic or solvent may linger when organophosphates are purposefully self-poisoned.

"Several helpful mnemonics exist for recalling the signs and symptoms of organophosphate poisoning and the receptor responsible for them.

To remember the nicotinic signs of AChE inhibitor toxicity, the following days of the week can be used:"

- "Monday = Mydriasis

- Tuesday = Tachycardia
- Wednesday = Weakness
- Thursday = Hypertension
- Friday = Fasciculations”

“The frequently used mnemonic that encompasses the muscarinic effects of organophosphate poisoning is DUMBELS, as mentioned below.

- D = Defecation/diaphoresis
- U = Urination
- M = Miosis
- B = Bronchospasm/bronchorrhea
- E = Emesis
- L = Lacrimation
- S = Salivation”

Anxiety, disorientation, fatigue, emotional instability, seizures, hallucinations, migraines, insomnia, memory loss, and circulatory or respiratory depression are some other acute symptoms. The most common cause of mortality in fatal instances is respiratory failure brought on by central respiratory depression, bronchoconstriction, bronchorrhea, and respiratory muscle weakness or paralysis. Patients who survive acute poisoning may be at risk for additional long-term problems.

Evaluation

Since clinical assessment is the primary method of diagnosing organophosphate poisoning, treatment must begin prior to laboratory confirmation. It is essential to have a strong clinical suspicion of organophosphate poisoning, particularly in cases where exposure or ingestion is unknown. Patients with respiratory distress, diaphoresis, and miotic pupils are the most common presentations of poisoning. Certain organophosphates have a characteristic smell, like petroleum or garlic, which might help with diagnosis.

An atropine trial may be used if organophosphate poisoning is suspected but not confirmed. Suspicion of AChE inhibitor poisoning is raised if symptoms improve after taking 0.6–1 mg of atropine. Interpreting the sensitivity and specificity of this experiment, however, might be difficult because of the paucity of data, especially in situations of severe poisoning. Therefore, more research is required to solve this problem. A tiny dose of atropine may not cause any reaction in patients with severe poisoning, which could lead to a false-negative test.

Even though certain labs are capable of measuring cholinesterase activity directly, these tests are frequently contracted out to establishments that might not deliver data quickly enough to inform treatment. Red blood cell AChE (RBC AChE) and BuChE are the two cholinesterase enzymes that are frequently tested. Compared to RBC AChE activity, BuChE activity is less selective. Iron deficiency anemia, chronic sickness, liver disease, malnutrition, and genetic enzyme failure can all be associated with low BuChE activity. Interpreting this test is made more difficult by the fact that the degree of enzyme inhibition varies according on the particular organophosphate that caused the poisoning and that there is little information available for many of these compounds.

The clinical manifestations of organophosphate toxicity are thought to be more strongly correlated with RBC AChE activity. Although this threshold can change depending on the chemical, symptoms usually appear in clinical settings when more than 50% of this enzyme is blocked. [54] Notably, fluoride can deactivate the enzymes, potentially producing erroneously low activity levels, hence it is crucial to collect blood samples in the proper tubes.

A variety of necessary laboratory tests, such as particular diagnostic tests for organophosphate poisoning and additional tests to evaluate the patient's general health, may be ordered by healthcare professionals. A complete blood cell count (CBC), a basic metabolic panel test, tests for kidney and liver function, blood glucose levels, arterial blood gas analysis, and pregnancy testing are a few examples of these. Because of parasympathetic activity, sinus bradycardia is usually shown on the electrocardiogram (ECG).

Assessment of Severity of OP Poisoning

"The severity of organophosphate (OP) poisoning can be assessed using a variety of methods. Serum biomarkers are increasingly used in diagnosing and assessing the severity of organophosphate (OP) poisoning. These biomarkers can help identify the extent of exposure, monitor treatment response, and predict outcomes":[55]

- **"Peradeniya Organophosphorus Poisoning (POP) scale**: A clinical scale that assesses six common clinical features of OP poisoning, such as pupil size, heart rate, and level of consciousness. Each feature is scored on a scale of 0–2, with a score of 0–3 indicating mild poisoning, 4–7 indicating moderate poisoning, and 8–11 indicating severe poisoning.

- **Red blood cell (RBC) cholinesterase level**: A measure of cholinesterase levels in the patient's red blood cells.
- **Pseudocholinesterase (PChE)**: A prognosticator of OP poisoning, with lower levels indicating more severe poisoning.
- **Glasgow coma scale (GCS) score**: A factor that can help assess the severity of OP poisoning.
- **Acute Physiology and Chronic Health Evaluation (APACHE) II score**: A factor that can help assess the severity of OP poisoning.
- **Creatine phosphokinase**: A factor that can help assess the severity of OP poisoning.
- **Leukocyte count**: A marker for the severity of OP poisoning.
- **Troponin and Creatine Kinase (CK):**
- **Troponin I or T and Creatine Kinase (CK):**
    - While primarily used as markers for myocardial injury, elevated troponin or CK levels may occur in OP poisoning, particularly in cases of severe poisoning, where arrhythmias or direct cardiotoxic effects may contribute to heart dysfunction.
    - **Prognostic Value:** Elevated troponin or CK levels may suggest cardiovascular involvement and an increased risk of complications, although these biomarkers are not specific to OP poisoning.

Cytokines (Inflammatory Markers):

- **Cytokines (such as IL-6, TNF-alpha, and IL-1β):**

- Severe OP poisoning can trigger an inflammatory response, resulting in increased levels of pro-inflammatory cytokines. The release of cytokines may reflect systemic inflammation and contribute to organ dysfunction (such as acute respiratory distress syndrome or multi-organ failure).
- **Prognostic Value:** Elevated cytokine levels may be associated with severe outcomes, such as systemic inflammation, respiratory failure, or shock.

Glutathione (GSH) and Other Antioxidants:

- **Glutathione (GSH):**

  OP poisoning can induce oxidative stress by generating reactive oxygen species (ROS), which deplete cellular antioxidants like glutathione. This can lead to cell damage, especially in tissues like the liver and nervous system.

  - **Prognostic Value:** Decreased serum glutathione levels and increased markers of oxidative stress could be indicative of more severe poisoning and may help to assess organ damage, particularly in the liver or nervous system.

AMYLASE[56]

The digesting enzyme amylase is mostly released by the salivary glands and pancreas, with trace amounts found in other organs. One of the first enzymes to be studied scientifically was amylase, which was first characterized in the early 1800s. This enzyme was dubbed "amylase" in the early 20th century, despite its original name being diastaste. Amylases' main function is to break down the glycosidic bonds that hold complex carbohydrates together, converting them into simpler sugars.

Alpha-, beta-, and gamma amylases are the three primary kinds of amylase enzymes, and they all target “different parts of the carbohydrate molecule. While beta amylase is mostly found in plants and microorganisms, alpha amylase is found in people, animals, plants, and microbes”. In contrast, gamma amylase is found in both plants and animals. Wohlgemuth's 1908 discovery revealed that urine contained amylase, opening the door for its use as a diagnostic laboratory test. Amylase is a commonly requested standard diagnostic test that is typically used in conjunction with lipase, especially when a patient is suspected of having acute pancreatitis.

Etiology and Epidemiology

Reduced metabolic clearance, macroamylasemia, and intestinal, salivary, and pancreatic disorders are among the illnesses that can cause elevated amylase levels. Elevated pancreatic enzyme levels are present in about 11% to 13% of people with non-pancreatic stomach discomfort. Sixty percent of “asymptomatic HIV-positive patients had abnormal lipase or amylase values at least once”. Serum amylase levels were increased in 26 out of 208 patients (12.5%) who had acute abdominal pain that was not associated with pancreatic problems at the time of admission. Thirty-five percent of liver disease patients had abnormally high amylase levels. Additionally, between 16% and 25% of instances of diabetic ketoacidosis have increased amylase levels. Thirteen patients out of 74 with surgically treatable lung cancer had hyperamylasemia.

Pathophysiology

Usually ranging in molecular weight from 54 to 62 kDa, amylase is a complex calcium-dependent metalloenzyme. Amylase's small size makes it easier for it to filter effectively through the glomeruli. The renal system and the reticuloendothelial system both remove amylase. "The pancreatic (P-type) and nonpancreatic (S-type) isoenzymes of this enzyme are produced by two closely related loci on chromosome 1. Allelic variation leads to additional amylase heterogeneity; the S-type has 12 alleles, while the P-type has 6. Additionally, both forms of amylase experience post-translational" changes that result in different isoforms through deamidation, glycosylation, and deglycosylation. Although amylase is found in many different tissues, the exocrine pancreas and salivary glands have the highest levels of P- and S-type activity, respectively. The pancreatic acinar cells produce P-type amylase, which is then discharged into the intestinal tract via the pancreatic duct system. The duodenum's slightly alkaline environment maximizes P-type amylase's enzymatic activity. The highest S-type amylase activity, on the other hand, is found in the salivary glands, which start the hydrolysis of starch during oral mastication and esophageal passage. However, when exposed to stomach acid, this effect stops. "Additionally, S-type amylase can be found in body fluids such semen, colostrum, tears, and milk, as well as in extracts from the testes, ovaries, fallopian tubes, Mullerian ducts, striated muscle, lungs, and adipose tissue. The majority of plasma amylase is reabsorbed in the proximal tubules, whereas the kidneys expel around 25% of it. With a half-life of roughly ten hours, the liver is thought to be the main organ in charge of amylase removal. The body has a delicate balance between the generation and clearance rates of serum amylase, which is tightly regulated. Increased production, whether from the pancreas or elsewhere, or a

decreased rate of clearance can lead to elevated amylase levels. The initial assessment of salivary amylase is probably heavily influenced by genetic control. The most common amylase isozymes found in babies' urine come from their saliva, and as they develop, both pancreatic and salivary amylase isozymes become more noticeable. The presence of calcium is absolutely necessary for amylase to function properly. However, certain anions, such as monohydrogen phosphate, nitrate, bromide, or chloride, are required for full functionality. The best activators are bromide and chloride. The pH range between 6.9 and 7.0 is ideal for amylase activity. The hydrolysis of 1,4-α-glucosidic bonds between neighboring glucose units in complex carbohydrates is catalyzed by the analyte amylase, an endoglycosidase enzyme that is a member of the hydrolase class. Interestingly, the rates at which branched-chain polyglucans, like amylopectin and glycogen, and straight-chain (linear) polyglucans, like amylose, are hydrolyzed vary. The enzyme breaks down amylose's chains at alternating α-1,4-hemiacetal (-C-O-C-) bonds, producing maltose and a small amount of leftover glucose. The enzyme produces glucose, maltose, and a residue of limit dextrins when it comes to branching polyglucans. Interestingly, the α-1,6-links at the branch points are not targeted by the enzyme".

Interfering Factors

Triglycerides, bilirubin, or hemoglobin usually do not interfere with amylase assays. However, the chelation of essential amylase cofactors may cause results to be mistakenly lowered if specimens are collected in tubes containing oxalate, citrate, or EDTA. Serum amylase levels may be impacted by a number of medications, including morphine, aspirin, antiretrovirals, and medications that include estrogen. A disorder called macroamylasaemia, which is typified by the development of macromolecular complexes, is linked to elevated amylase activity in serum.

Immunoglobulins, mainly IgA or IgG, are usually involved in these complexes, however self-polymerization or protein association are also possible. These complexes usually retain their enzymatic activity, but the renal glomeruli are unable to filter them efficiently. This syndrome consequently causes elevated serum amylase activity and delayed clearance. Up to 1.5% of hospitalized patients have been documented to have this benign illness, which accounts for up to 28% of cases of chronic and otherwise unexplained hyperamylasemia. Autoimmunity, cancer, heart disease, diabetes mellitus, and malabsorptive diseases are all linked to macroamylasemia. When assessing asymptomatic patients with increased blood amylase levels, macroamylasemia should be taken into account. Interestingly, since this illness is usually benign, no particular therapy is required. Compared to female patients with A blood type, whose circulating pancreatic amylase levels are typically lower, those with O blood type have higher levels. Even in healthy people, psychosocial stress raises salivary amylase levels, which may lead to increased levels of "total serum amylase. However, whether psychosocial stress has a lasting impact on blood amylase levels has not been shown by clinical research. Serum amylase levels may inadvertently fall within the normal range in cases of pancreatitis with hypertriglyceridemia". This disparity is linked to an inhibitor that interferes with the enzyme test and is linked to increased triglycerides. Serum amylase levels can be recalculated to determine the true concentration by diluting the serum, which will minimize the inhibiting effect.

SERUM AMYLASE AND OP POISONING[57]

"Serum **amylase** levels can sometimes be elevated in cases of **organophosphate (OP) poisoning**, although it is not a specific marker for OP toxicity. The elevation of amylase in the context of OP poisoning may be linked to various factors, including pancreatic injury,

gastrointestinal distress, and the systemic effects of the poisoning. Here's how **serum amylase** might be relevant in OP poisoning:

1. “Pancreatic Injury:

- **Acute Pancreatitis:** OP poisoning, particularly in severe cases, can cause systemic toxicity that leads to organ damage, including the pancreas. The pancreas can become inflamed, leading to **acute pancreatitis**, which is characterized by elevated serum amylase levels. Although not the most common complication, pancreatitis in the setting of OP poisoning can contribute to elevated amylase levels.
- **Mechanism:** This could be related to **hypoxia**, **systemic inflammation**, or **direct cytotoxic effects** on the pancreatic cells as part of the multi-organ damage seen in severe cases of OP poisoning.

2. Gastrointestinal Distress:

- **Vomiting and Diarrhea:** OP poisoning often leads to **gastrointestinal symptoms**, including nausea, vomiting, and diarrhea. Severe cases of gastrointestinal distress can sometimes lead to dehydration and **gastrointestinal mucosal injury**, which may result in a mild increase in serum amylase levels, as amylase is produced not only by the pancreas but also by the salivary glands and gastrointestinal tract.
- **Gastric or Intestinal Injury:** Mechanical injury to the gastrointestinal tract from excessive vomiting or the direct effects of the toxin might also contribute to elevated amylase levels”.

3. “Muscle Injury (Rhabdomyolysis):

- **Rhabdomyolysis:** In severe OP poisoning, **muscle weakness** and **fasciculations** (muscle twitches) can occur due to excessive cholinergic stimulation. Muscle injury can lead to the release of **muscle enzymes** such as creatine kinase (CK), but in some cases, mild elevation in amylase may also be observed due to **muscle cell stress**. However, creatine kinase (CK) is the more specific marker for rhabdomyolysis.

4. Direct Toxic Effects on the Pancreas or Gastrointestinal System:

- **Cholinergic Effects on the Pancreas and GI Tract:** OPs inhibit acetylcholinesterase, leading to an accumulation of acetylcholine. This excessive cholinergic activity may overstimulate the pancreas or gastrointestinal system, potentially contributing to mild elevations in amylase. However, this mechanism is less well-documented and is not a primary factor in the presentation of OP poisoning.

5. Amylase as a Non-Specific Marker:

- While **serum amylase** can be elevated in OP poisoning, it is **non-specific** and can be increased in many other conditions, such as:
    - **Acute pancreatitis**
    - **Salivary gland inflammation (e.g., mumps)**
    - **Renal failure**
    - **Gastrointestinal obstruction**
    - **Alcohol abuse**

Therefore, an isolated increase in amylase is not diagnostic for OP poisoning and should be considered along with other clinical findings and laboratory markers (such as cholinesterase activity) when assessing for OP toxicity".

Amylase as a Non-Specific Marker:[57]

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    - **Salivary gland inflammation (e.g., mumps)**
    - **Renal failure**
    - **Gastrointestinal obstruction**
    - **Alcohol abuse"**

CREATINE PHOSPHOKINASE (CPK)

The enzyme that catalyzes the conversion of creatine and adenosine triphosphate (ATP) to phosphocreatine (PCr) and adenosine diphosphate (ADP) is called creatine phosphokinase (CPK), sometimes referred to as creatine kinase (CK). ATP can be produced from PCr and ADP in this reversible CK enzyme process. The brain, skeletal muscles, and heart are among the organs and cells that employ phosphocreatine, which is produced by this process, to deliver significant amounts of ATP. A key modulator of cellular energy homeostasis is CK. Derangement in CK levels can be caused by a variety of illnesses, such as medicines, heart disease, renal disease, or rhabdomyolysis. Consequently, it serves as a diagnostic marker for a number of illnesses, including acute myocardial infarction (AMI) and rhabdomyolysis.

Pathophysiology

The compact 82 kDa enzyme known as creatine kinase (CK) is present in the mitochondria and cytoplasm of tissues that require a lot of energy. M (muscle type) and B (brain type) are the two 42 kDa polypeptide subunits that make up CK in the cytosol. These subunits'

genes are found on two distinct chromosomes: M on 19q13 and B on 14q32. "Three tissue-specific isoenzymes—CPK-MB (cardiac muscle), CPK-MM (skeletal muscle), and CPK-BB (brain)—can be formed thanks to these subunits. Generally speaking, the subunit ratio differs depending on the type of muscle: cardiac muscle (70% to 80% MM and 20% to 30% MB), skeletal muscle (98% MM to 2% MB), and the brain, which mostly contains the isoenzyme BB. There are two distinct types of CK found in mitochondria: Mt-CK, a sarcomeric Mt-CK found in cardiac and skeletal muscle, and ubiquitous Mt-CK, a non-sarcomeric version found in many tissues, including the brain, smooth muscle, and sperm. Each of the four dimers that make up the mitochondrial CK isoform is an octamer. Cytosolic CK uses PCr to regenerate ATP from ADP, whereas mitochondrial CK directly contributes to the formation of PCr from mitochondrial ATP. With CK functioning as an in situ ATP regenerator, this occurs at intracellular locations where ATP is used by the cell. A so-called PCr/Cr-shuttle or circuit connects Mt-CK with cytosolic CK. The cytosolic CK that is linked to ATP-dependent activities, such as ATPases, like actomyosin ATPase and calcium ATPase involved in muscle contraction, and sodium/potassium ATPase involved in sodium retention in the kidney, receives PCr produced by Mt-CK in the mitochondria. When PCr is shuttled across the cell, the bound cytosolic CK takes it in and utilizes ADP to regenerate ATP, which the ATPases use as an energy source (CK and the ATPases form a linked microcompartment). Between the subcellular locations of energy production (mitochondria and glycolysis) and energy use (ATPases), PCr acts as a buffer and transporter. CK is normally found in the brain, skeletal muscles, and heart tissue, among other places. On the other hand, CK leaks into the bloodstream when muscles are injured. CK is therefore a sign of muscle injury. Whereas CPK-MM is more suggestive of skeletal muscle

damage, CPK-MB is a more precise biomarker of myocardial muscle damage. Because of the natural turnover of muscle tissue, MM activity accounts for nearly all of the CK activity in the serum of healthy individuals, while trace levels of CPK-MB may also be present. CPK-MM has the closest mobility to the cathode, CPK-MB has an intermediate mobility, and CPK-BB travels the furthest from the point of application to the anode when electrophoresed. In severe anoxic shock and liver illness, Mt-CK, which is more cathodal than the MM fraction, is typically linked to tissue necrosis. Another macromolecular form of CK activity is known as macro-CK. Only a tiny percentage of hospitalized patients have elevated CK activity in their serum, however up to 6% of them have macro-CK in their sera temporarily. There are two types of the enzyme: types 1 and 2. A compound of CK, usually CK-BB, and an immunoglobulin, usually IgG, is known as macro-CK type 1. Women over 50 are typically diagnosed with macro-CK type 1. Children with tissue distress or critically unwell adults with cancers have macro-CK type 2, which is oligomeric Mt-CK".

Although the "C-terminal lysine residue of the M and B subunits is present in both, only the former is digested by blood-borne carboxypeptidases. The two CK-MM isoforms, CK-MM2 (one lysine residue removed) and CK-MM1 (both lysine residues removed), are created when carboxypeptidases B or N hydrolyze the lysine residues from CKMM in a sequential manner. A more negatively charged CK molecule with increased anodic mobility at electrophoresis results from the removal of positively charged lysine. Since CK-MB only contains one M subunit, CK-MB2 is the dimer that the M and B genes code for, and CK-MB1 is the dimer that is lysine-hydrolyzed. Specialized methods like high-voltage electrophoresis (with gel cooling), HPLC, chromatofocusing, or immunoassay are needed for the assay of the CK isoforms".

Interfering Factors

Since erythrocytes do not contain CK activity, a moderate level of hemolysis (up to 0.32 g/dL of hemoglobin) has no discernible effect on the observed CK activity. Severe hemolysis, however, is unacceptable since the lag phase and assay system side reactions may be impacted by the enzymes and intermediates (AK, ATP, and glucose-6-phosphate) released by the erythrocytes. It is possible to evaluate turbid and icteric materials; if the initial absorbance is not too high, the right values are obtained.

RELAVENCE OF CPK IN OP POISONING[58]

1. Muscle Injury and Rhabdomyolysis:

- **Rhabdomyolysis** is a condition where skeletal muscle tissue breaks down, releasing intracellular contents like **myoglobin**, **creatine kinase (CK)**, and **electrolytes** (such as potassium) into the bloodstream. In the context of OP poisoning, **muscle fasciculations (twitching)** and **muscle weakness** can be caused by the excessive cholinergic stimulation due to **acetylcholinesterase inhibition**.
- As a result of this prolonged muscle activity, there can be muscle damage and breakdown, leading to elevated CK levels, particularly **CK-MM** (the muscle isoform of creatine kinase).

2. Mechanism of Muscle Damage in OP Poisoning:

- OPs inhibit acetylcholinesterase, leading to an accumulation of **acetylcholine** at the neuromuscular junction. This overstimulation of muscles results in **fasciculations**, which

are involuntary muscle twitches. These repeated contractions can lead to **muscle fatigue, damage, and necrosis**.

- The muscle injury releases **creatine kinase** (along with myoglobin), which is then detected in the serum. **Elevated CK levels** in the blood are often used as a marker of muscle injury or rhabdomyolysis.

3. Rhabdomyolysis in OP Poisoning:

- **Rhabdomyolysis** can occur in severe OP poisoning, particularly when there is significant neuromuscular involvement due to high-dose exposure or prolonged exposure to OP compounds.
- **Symptoms of rhabdomyolysis** in OP poisoning include **muscle pain, weakness**, and **dark-colored urine** (due to myoglobinuria), which could indicate **renal complications** (such as acute kidney injury) resulting from the release of **myoglobin** into the bloodstream.

4. Prognostic Significance of Elevated CK:

- **Elevated CPK levels** in OP poisoning are typically associated with more severe poisoning and a worse prognosis, especially if there is associated **rhabdomyolysis**.
- Very high levels of CK, particularly in the **thousands to tens of thousands of IU/L**, suggest significant muscle damage. If left untreated, **rhabdomyolysis** can lead to **renal failure**, **electrolyte imbalances**, and **cardiovascular instability**, all of which can worsen the outcome of OP poisoning.

- **Renal involvement**: The release of myoglobin from damaged muscle fibers can precipitate in the kidneys, leading to **acute kidney injury (AKI)**, which is another severe complication of OP poisoning.

5. Diagnostic and Monitoring Role of CK:

- **CK is a useful biomarker** to assess the extent of muscle injury in OP poisoning, particularly when combined with clinical signs such as muscle weakness, fasciculations, or myoglobinuria.
- While **CK alone** is not specific to OP poisoning, its measurement can help in monitoring the severity of muscle damage and the risk of developing complications such as rhabdomyolysis or acute renal failure.

REVIEW OF RELATED ARTICLES

"Subedi B et al (2023)[59] Assessing the type of OP poisoning and establishing the relationship between serum amylase levels and the patient's presentation and outcome were the main goals of this investigation. Metacid was the most prevalent OP toxin (53.5%, 92). Serum amylase levels were substantially greater in deceased subjects than in living ones, either within 12 hours of exposure (468.60 vs. 135.4 IU/ml, P<0.001) or after 12 hours of exposure (152.0 vs. 58.9 IU/ml, P<0.001). The odds of severe/life-threatening severity were more than two times higher for participants with an initial serum amylase level of 100 IU/ml and more than 18 times higher for those with a level of less than 100 IU/ml after 12 hours of exposure (odds ratio=2.40, 95% CI: 1.28–4.52, P=0.007, and odds ratio=18.67, 95% CI: 8.02–43.47, P<0.001), respectively. They came to the conclusion that serum amylase levels are directly correlated with the clinical severity of OP poisoning. Significantly, patients with OP poisoning that resulted in mortality had

higher mean serum amylase level values. Therefore, one of the simple, quantifiable prognostic markers of OP poisonings may be the blood amylase level".

Nimsarkar, A. D et al (2023)[60] The goal of the current investigation was to determine whether serum creatine phosphokinase (CPK) might be utilized as a marker to gauge the severity of OP compound poisoning and track prognosis. One hundred properly screened patients who presented with OP compound were categorized by severity grade using the POP scale in this hospital-based prospective observational study. In accordance with conventional care practice, serum cholinesterase and serum CPK levels were measured twice, on day 1 and day 4, and the results were compared across severity degrees of OP compound poisoning. They came to the conclusion that serum CPK is a useful indicator of prognosis and outcome and can be utilized as an effective indicator of severity in patients with OP compound poisoning.

Serum amylase levels in patients with OPC poisoning were investigated by **Thirunavukkarasu, S. et al. (2022)**[61], who also correlated the levels with the clinical characteristics on the day of presentation. It was a prospective longitudinal research. 157 patients who met our inclusion and exclusion criteria were chosen as our study subjects out of the 278 patients who came to our hospital with a history of OPC poisoning during the specified time period. Using the POP (Peradeniya OP poisoning) scale, the degree of OPC intoxication was assessed and classified as mild, moderate, or severe. On the day of admission, each patient's serum amylase level was tested.

Zobeiri M et al (2021)[62] The purpose of this study is to ascertain how serum amylase levels affect prognostic assessment in patients suffering from acute OP poisoning. 332 consecutive patients with acute OP poisoning participated in this two-year observational

case-control study. Patients with acute OP poisoning had a mean age of 28.9 ± 23.95 years, with a slight female preponderance. The gastrointestinal tract was used to intoxicate each subject. Patients who experienced tachycardia, ICU admission, mental status decline, and mortality had significantly higher mean amylase levels. They came to the conclusion that individuals with OP poisoning who had greater serum amylase levels than usual had a more severe clinical course and a higher chance of dying. Serum amylase measurement can be useful for making fast outcome predictions.

This investigation was carried out by **Paul G. et al. (2021)**[63] "to determine the relationship between the severity of acute OP poisoning and the serum amylase level. The average age of the patients was 23.68±6.80 years, and 65.3% of them were men. Mild, moderate, and severe OP poisoning were found in 56.7%, 34.7%, and 8.7% of patients, respectively, according to the POP scale. 54.7% of the individuals had normal serum amylase levels, whereas 53.3% had increased levels. The median serum amylase level was 103.50 (IQR 73.75-156.0) IU/l. Serum amylase levels increased gradually as the severity of OP poisoning increased; in mild grade, they were 77.0 IU/l (IQR 58.0-97.0), in moderate grade, they were 154.0 IU/l (IQR 125.25-162.5), and in severe grade, they were 298.0 IU/l (IQR 289.5-305.0). The differences in median amylase levels among the three groups were statistically significant ($p < 0.001$). Additionally, a strong positive connection ($r=0.970$; $p<0.01$) was found between the POP scale score and the serum amylase level. They came to the conclusion that, in environments with limited resources, serum amylase levels could be utilized as an easily accessible indicator of the severity of acute OP poising".

Serum levels of lipase, creatine kinase, and amylase were linked to the severity of OP poisoning by **Minz, N. T. et al. (2021)**[64]. They came to the conclusion that serum levels of lipase, creatine kinase, and amylase had a strong correlation with the degree of organophosphorus poisoning and may be used as an additional signal to gauge the severity. Compared to lipase and creatine kinase (CPK), serum amylase is a more accurate measure of severity.

Amylase, lipase, and plasma cholinesterase levels in acute OP poisoning were estimated by **Dungdung A et al. (2020)**[65] to use plasma cholinesterase levels and correlate them with two other markers in order to determine the degree of OP poisoning. A statistically significant negative correlation between plasma cholinesterase levels and serum lipase and amylase was observed among 100 individuals. Serum amylase was found to have the highest diagnostic accuracy for determining the severity of poisoning; of the 10 deaths, 6 had plasma cholinesterase activity below 10%, and 8 of the 10 patients had elevated amylase levels. They came to the conclusion that an increased amylase level is linked to OP poisoning. Together with plasma cholinesterase levels, serum lipase and amylase can be employed as supplementary prognostic indicators. Compared to lipase, serum amylase may be a more accurate indicator of severity.

A. Kumar and colleagues (2017)[66] Serum Creatine Phosphokinase (CPK) levels in acute OP poisoning patients were estimated in this study in order to correlate with prognosis. Males made up 78% (n=39) of the 50 patients, while females made up 22% (n=11). The majority of patients were between the ages of 21 and 40. The most often utilized substance was chlorpyrifos. 8% suffered severe poisoning, 20% had moderate poisoning, and 72% had mild poisoning. The severity of acute OP poisoning patients was significantly correlated with serial assessments of serum CPK levels. The CPK levels had a 92% positive predictive value, 74%

sensitivity, and 81% specificity. They came to the conclusion that there is a correlation between CPK levels and severe organophosphorus poisoning. As an alternative marker to choline esterase, this study suggests estimating CPK levels to determine severity and prognosticate patients with organophosphorus compounds.

The goal of the study by **Bhattacharyya K et al. (2011)**[67] was to determine whether CPK could be used to gauge the severity of OP poisoning instead of cholinesterase levels in blood. This study was observational and prospective. The Peradeniya organophosphorus poisoning (POP) scale was used to classify the clinical severity of sixty-three OP poisoning patients who had not had any previous therapy and who had presented within six hours. Serum CPK, blood EchE, and pH levels were assessed after admission, and the total atropine dosage (mg) was determined until the ultimate clinical result (full recovery or death). The statistical significance was evaluated using Pearson's correlation coefficient and the Student's t-test. The POP scale showed that 17 (27%), 32 (50.8%), and 14 (22.2%) patients had mild (score 0–3), moderate (scoring 4–7), and severe (score 8–11) clinical severity. There was a substantial correlation between clinical severity and serum CPK, blood pH, EchE level, and total atropine dose. Serum CPK is suggested by our study as a substitute marker.

MATERIAL AND METHODS

- **Study design:** Prospectus cohort study
- **Study area:** Department of General Medicine, "Shri B M Patil Medical College and Research Centre, Vijayapura, Karnataka, India".
- **Study period:** Research study was conducted from May 2023 to December 2024. Below is the work plan.

Table 1: Work plan of the study with percentage of allocation of study time and duration in months

Work plan	% of allocation of study time	Duration in months
Understanding the problem, preparation of questionnaire.	5-10%	May 2023
Pilot study, Validation of questionnaire, data collection and manipulation	Upto 80%	June 2023 to May 2024
Analysis and interpretation	5-10%	June 2024 to August 2024
Dissertation write-up and submission	5-10%	September 2024 to December 2024

- **Sample size**: According to the analysis of T. N. Dubey et al. the proportion of severity of OP poisoning according to the POP scale is 5%.[68] Considering the confidence limit of these studies to be 95% with a 5% level of significance and a margin of error of 0.05. The sample size is computed using the following formula

  Sample size (n) = (Z2*p*(1-p)) /d2

  Where z is the z score= 1.96

  d is the margin of error= 0.05

  n is the population size

  p is the population proportion =0.05

  The estimated sample size of this study is 73.

- **Inclusion criteria:**
  1. Patients who were admitted with organophosphate poisoning above 18 years.
- **Exclusion criteria:**
  1. Patients with a history of organophosphate compound consumption mixed with alcohol or other poison.
  2. Patients with Comorbid conditions like chronic alcoholism, musculoskeletal, hepatic and renal disease

METHODOLOGY:

This was a prospective cohort study conducted at Shri B M Patil Medical College Hospital and Research Centre, Vijayapura. The study included patients above 18 years of age who were admitted with organophosphate poisoning.

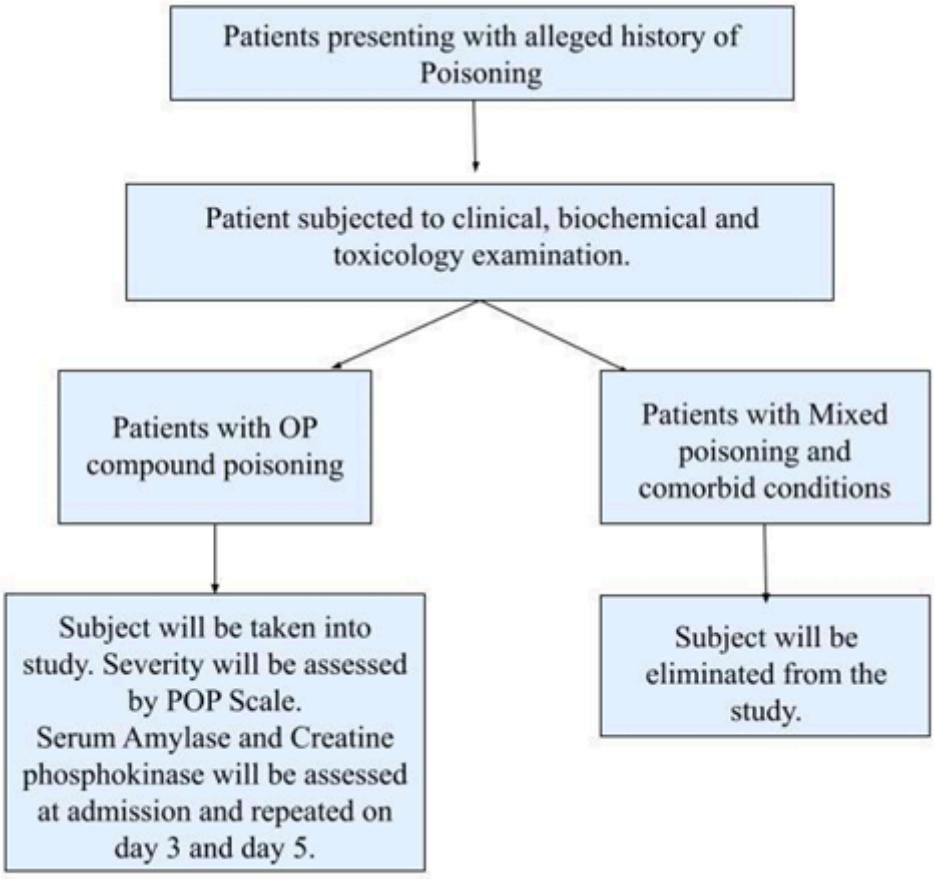
The sample size was calculated to be 73 patients, based on previous studies showing the

proportion of severity of OP poisoning according to the POP scale as 5%. This was computed using a confidence limit of 95%, a 5% level of significance, and a margin of error of 0.05.

At admission, detailed history was collected according to a pre-designed proforma. Clinical examination was performed, and the severity of poisoning was assessed using the Peradeniya Organophosphorus Poisoning (POP) scale. The POP scale evaluated six clinical parameters on a three-point scale (0-2 points each). The total score was calculated by adding individual parameter scores, with severity graded as mild (0-3), moderate (4-7), and severe (8-11).

Blood samples were collected for various investigations including complete blood count, renal function tests, liver function tests, serum cholinesterases, serum amylase, and creatine phosphokinase levels. Additional investigations included ECG, chest X-ray, toxicology report, and urinalysis. The serum amylase and creatine phosphokinase levels were measured on days 1, 3, and 5 of admission along with the POP score assessment.

Written informed consent was obtained from all participants in both English and Kannada languages after explaining the study procedure in detail. The study protocol was approved by the institutional ethics committee of the hospital.



The Peradeniya Organophosphorus Poisoning (POP) scale

The Peradeniya Organophosphorus Poisoning Scale is used to determine the severity of organophosphate poisoning. Six parameters are evaluated for the POP scale, and the results are then given a score of 0, 1, or 2 accordingly. Scores are added up, and severity is determined. A score between 0 and 3 denotes a mild case of poisoning, a score between 4 and 7 indicates a moderate case, and a score between 8 and 11 denotes a severe case.

Parameter	Criteria	Score
Pupil size	≥2 mm	0
	<2 mm	1
	pinpoint	2
Respiratory rate	<20/min	0
	≥20/min	1
	≥20/min with central cyanosis	2
Heart rate	>60/min	0
	41-60/min	1
	<40/min	2
Fasciculation	None	0
	Present, generalized/ continuous	1
	Both generalized and continuous	2
Level of consciousness	Conscious and rationale	0
	Impaired response to verbal command	1
	No response to verbal command	2
Seizures	Absent	0
	present	1
0-3: mild poisoning, 4-7: moderate poisoning, 8-11: severe poisoning		

STATISTICAL ANALYSIS

SPSS version 20 was used to conduct statistical analysis once the data was entered into Microsoft Excel sheets. The mean, standard deviation, counts, and percentages were used to display the results. An independent sample test was employed for continuous variables that were normally distributed between two groups. For variables that weren't normally distributed, the Mann-Whitney U test was used. Fisher's exact test or the Chi-square test were used to compare categorical variables between two groups. ANOVA for normally distributed data and the Kruskal-Wallis H Test for non-normally distributed data were employed for comparisons involving more than two groups. Statistical significance was defined as a p-value of less than 0.05. Every statistical test was run with two tails.

RESULTS

The present study was conducted in the department of General medicine at Shri B M Patil Medical College and Research Centre, Vijayapura, to compare the serum amylase and creatine phosphokinase levels in assessing the severity of organophosphate poisoning. A total of 73 patients were included in the study.

Following were the results of the study:

Table 1: Distribution of patients according to age

Age (in years)	Frequency	Percentage
16-20	16	21.9%
21-40	49	67.1%
41-60	3	4.1%
61-80	5	6.8%
Total	**73**	**100%**

Table 1 and graph 1 shows the age distribution of the 73 patients in the study, with the majority (67.1%) falling in the 21-40 years age group, followed by 16-20 years (21.9%), while only small percentages were in the older age groups of 41-60 years (4.1%) and 61-80 years (6.8%).

Graph 1: Distribution of patients according to age

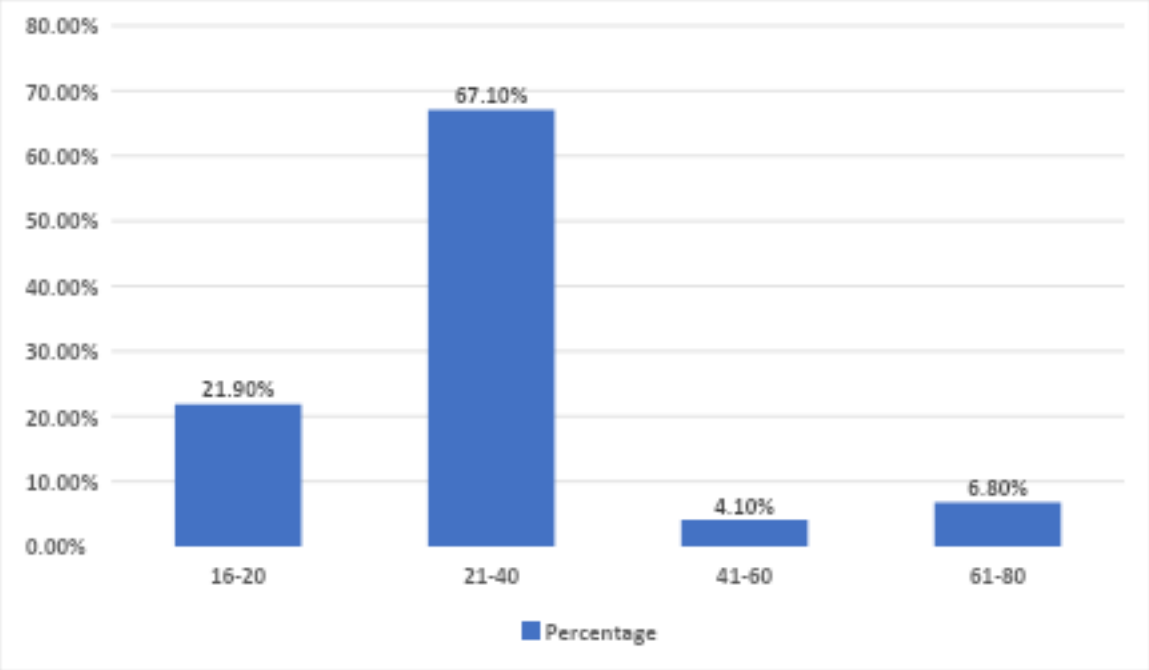


Table 2: Distribution of patients according to gender

Gender	Frequency	Percentage
Female	37	50.7%
Male	36	49.3%
Total	**73**	**100%**

Table 2 and graph 2 indicates an almost equal gender distribution among the study participants with a slight female predominance at 50.7% compared to males at 49.3%.

Graph 2: Distribution of patients according to gender

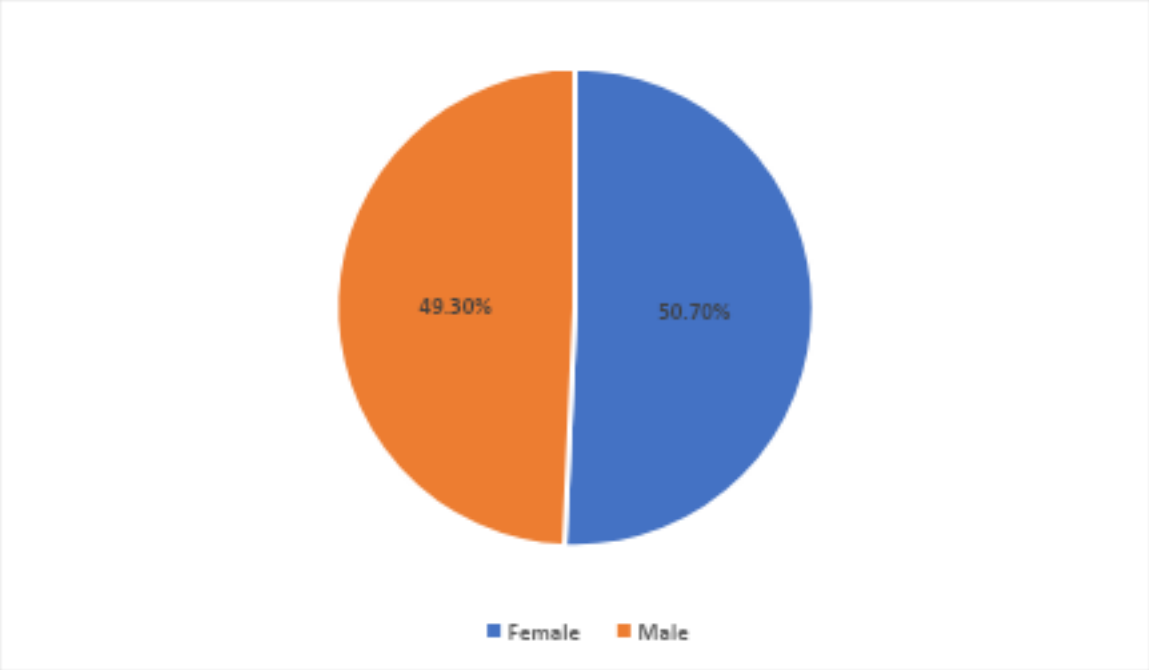


Table 3: Distribution of patients according to time since exposure

Time since exposure (hours)	
Mean	5.9
SD	4.5

Table 3 and graph 3 reveals that patients arrived for treatment at an average of 5.9 hours after exposure to organophosphate poisoning, with a standard deviation of 4.5 hours indicating considerable variation in time to presentation.

Graph 3 : Distribution of patients according to time since exposure

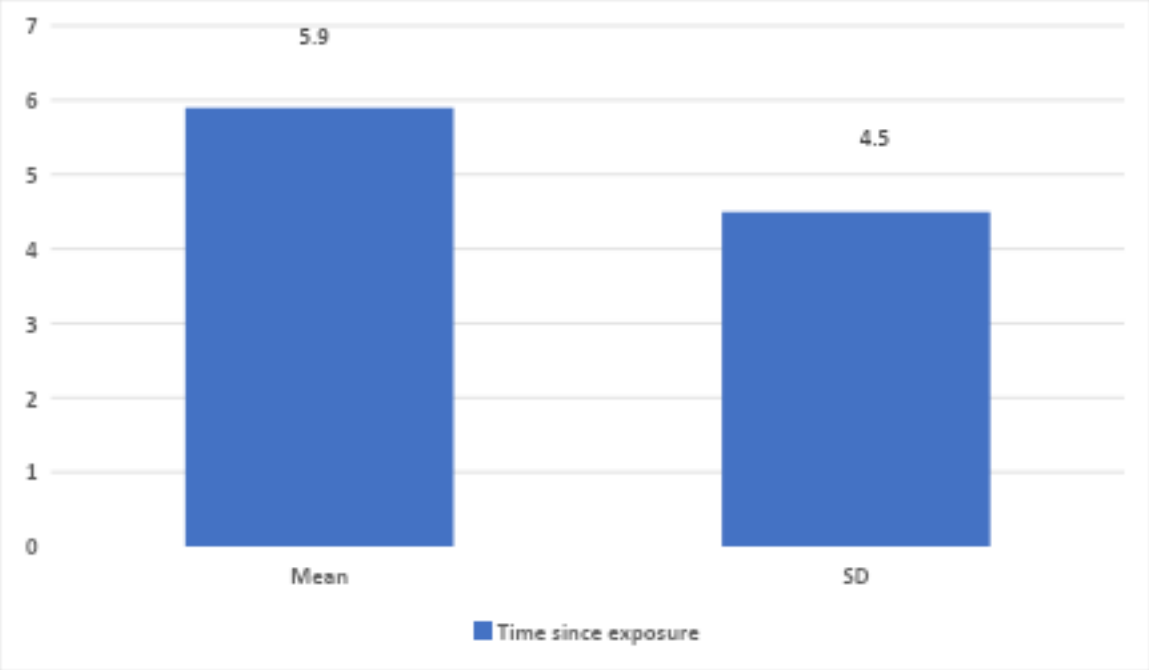


Table 4: Distribution of patients according to clinical presentation

Clinical presentation	Frequency	Percentage
Vomiting	56	76.7%
Abdominal pain	8	11%
Diarrohea	17	23.3%
Salivation	14	19.2%
Lacrimation	1	1.4%
bronchospasm	23	31.5%
Muscle weakness	27	37%
Convulsions	4	5.5%

Table 4 and graph 4 demonstrates the clinical presentation patterns of organophosphate poisoning, with vomiting being the most common symptom (76.7%), followed by muscle weakness (37%), bronchospasm (31.5%), diarrhea (23.3%), salivation (19.2%), abdominal pain (11%), convulsions (5.5%), and lacrimation (1.4%).

Graph 4: Distribution of patients according to clinical presentation

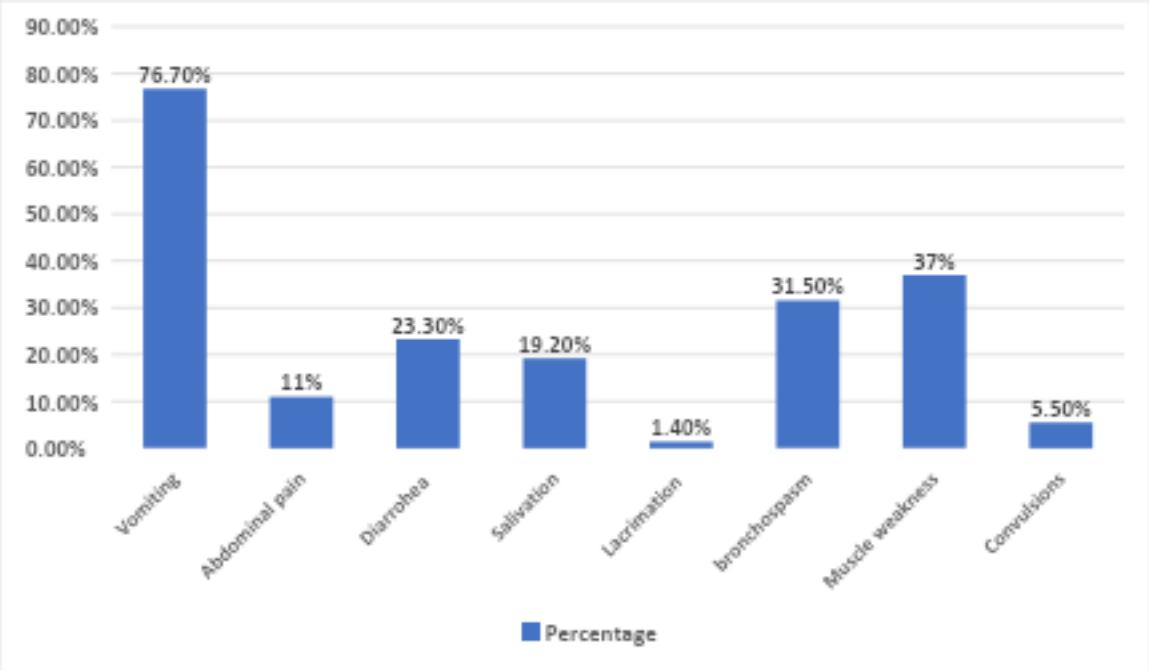


Table 5: Distribution of patients according to severity grading by Peradeniya Organophosphorus Poisoning

POP severity grading	Frequency	Percentage
Mild	32	43.8%
Moderate	29	39.7%
Severe	12	16.4%
Total	**73**	**100%**

Table 5 and graph 5 categorizes patients according to the Peradeniya Organophosphorus Poisoning (POP) severity grading, showing 43.8% with mild poisoning, 39.7% with moderate poisoning, and 16.4% with severe poisoning.

Graph 5: Distribution of patients according to severity grading by Peradeniya Organophosphorus Poisoning

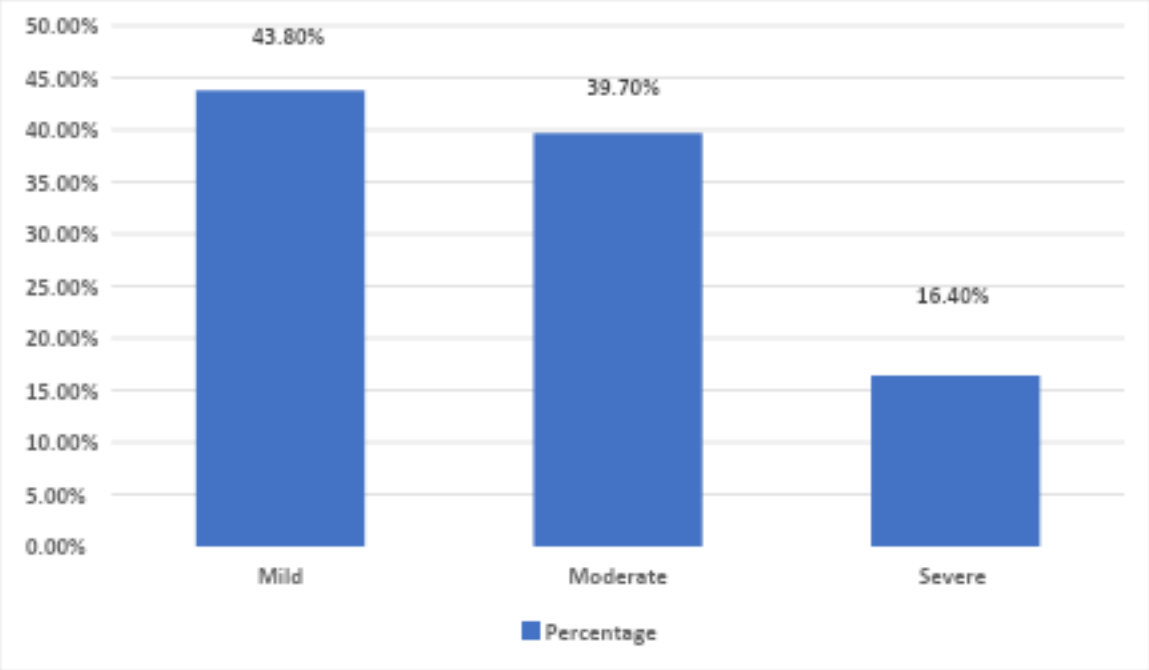


Table 6: Distribution of patients according to acetyl cholinesterase enzyme levels at different intervals

acetyl cholinesterase enzyme levels	Day 1	Day 3	Day 5
<500	29 (39.7%)	29 (39.7%)	28 (38.4%)
500-1000	5 (6.8%)	5 (6.8%)	6 (8.2%)
1000-2499	9 (12.3%)	8 (11%)	8 (11%)
2500-5319	15 (20.5%)	16 (21.9%)	15 (20.5%)
>5320	15 (20.5%)	15 (20.5%)	16 (21.9%)

Table 6 and graph 6 tracks acetylcholinesterase enzyme levels at different intervals (Day 1, 3, and 5), revealing that the distribution of patients across the different enzyme level categories remained relatively stable throughout the observation period, with the highest percentage consistently in the <500 range (around 39%).

Graph 6: Distribution of patients according to acetyl cholinesterase enzyme levels at different intervals

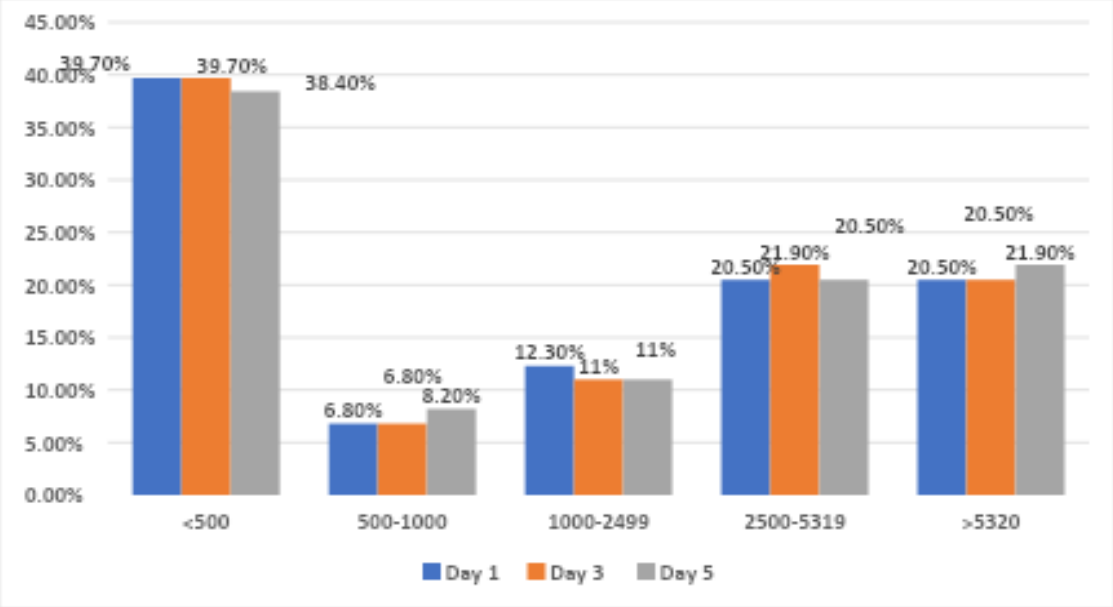
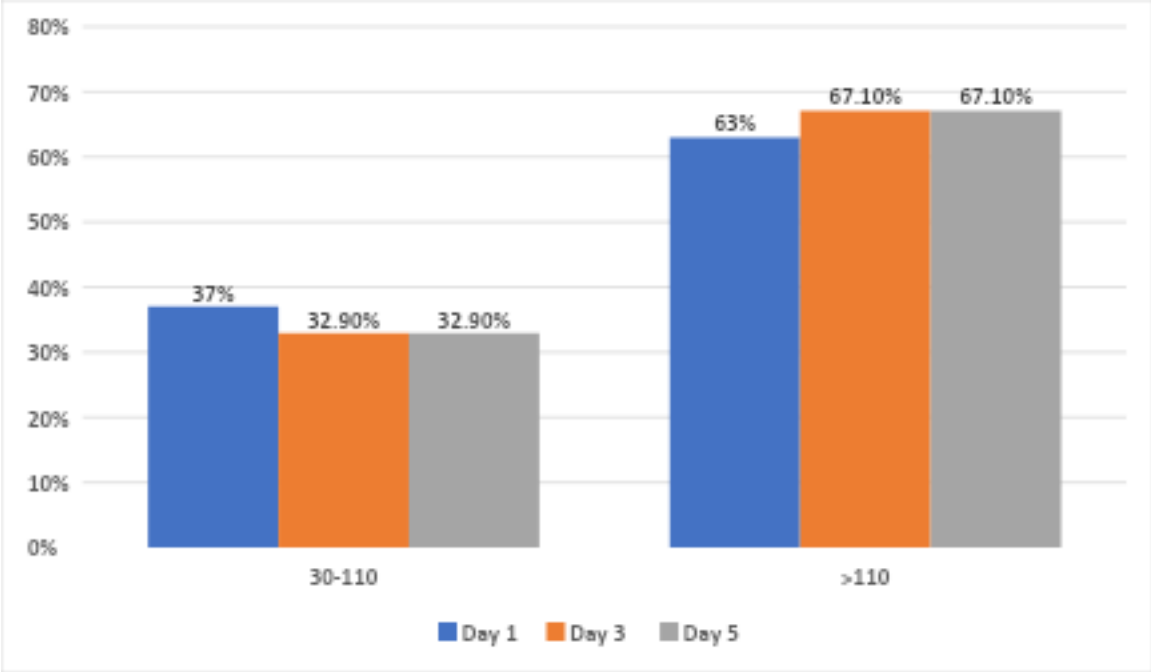


Table 7: Distribution of patients according to investigations at different intervals

Investigations		Day 1	Day 3	Day 5
Amylase	**30-110**	27 (37%)	24 (32.9%)	24 (32.9%)
	>110	46 (63%)	49 (67.1%)	49 (67.1%)
CPK	**20-200**	61 (83.6%)	59 (80.8%)	60 (82.2%)
	>200	12 (16.4%)	14 (19.2%)	13 (17.8%)

Table 7 and graph 7 presents the distribution of amylase and CPK investigations at different intervals, showing that elevated amylase levels (>110) were present in 63% of patients on Day 1, increasing slightly to 67.1% by Days 3 and 5, while elevated CPK levels (>200) were less common, affecting 16.4% of patients on Day 1, 19.2% on Day 3, and 17.8% on Day 5.

Graph 7A: Distribution of patients according to serum amylase at different intervals



Graph 7B: Distribution of patients according to CPK at different intervals

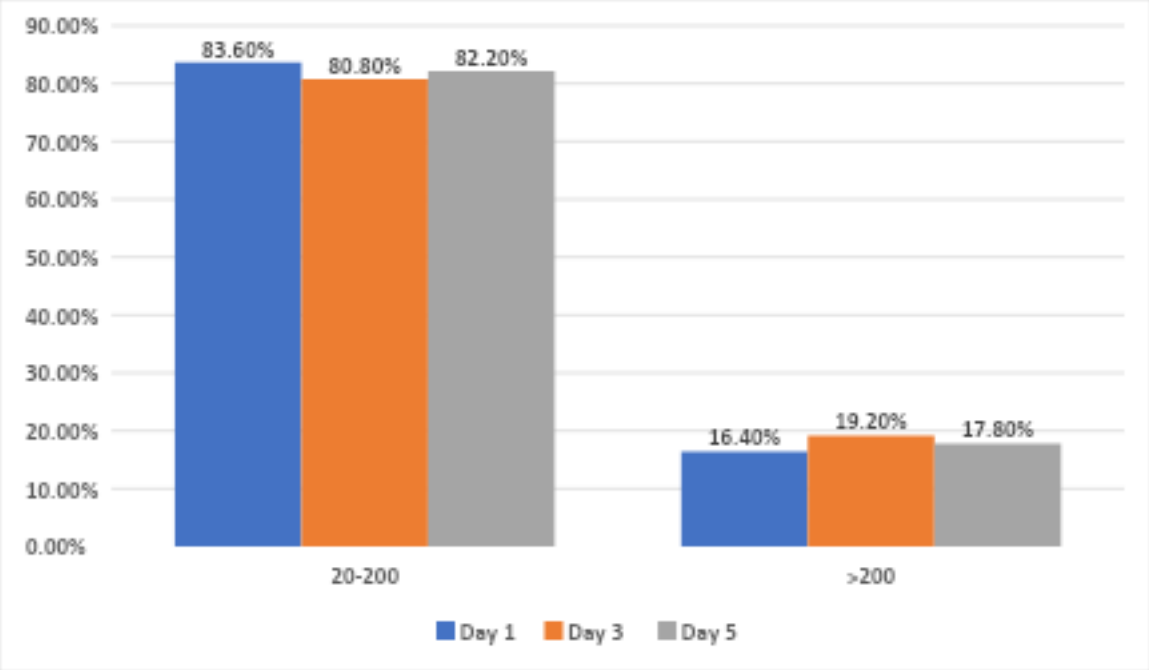


Table 8: Distribution of patients according to requirement of ventilator

requirement of ventilator	Frequency	Percentage
Yes	19	26%
No	54	74%
Total	**73**	100%

Table 8 and graph 8 indicates that 26% of the patients required ventilator support during their treatment, while 74% did not need ventilator assistance.

Graph 8: Distribution of patients according to requirement of ventilator

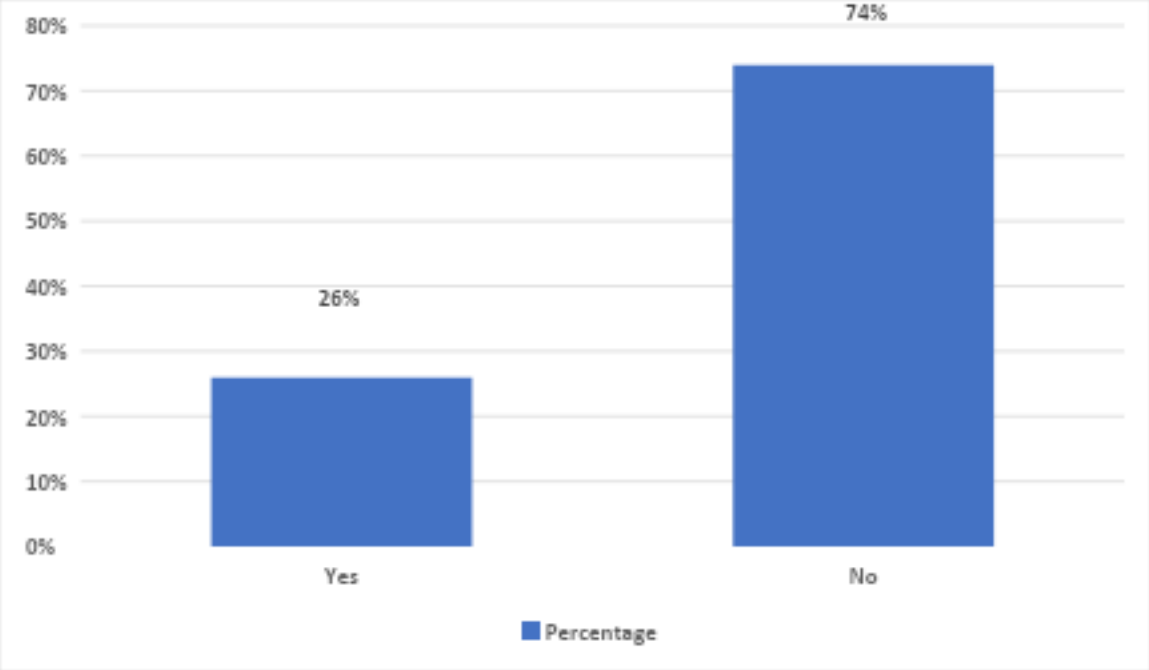


Table 9: Distribution of patients according to outcome

Outcome	Frequency	Percentage
Survivors	62	84.9%
Non-survivors	11	15.1%
Total	**73**	**100%**

Table 9 and graph 9 presents the final outcome of the patients, showing a survival rate of 84.9% and a mortality rate of 15.1% among the 73 study participants.

Graph 9: Distribution of patients according to outcome

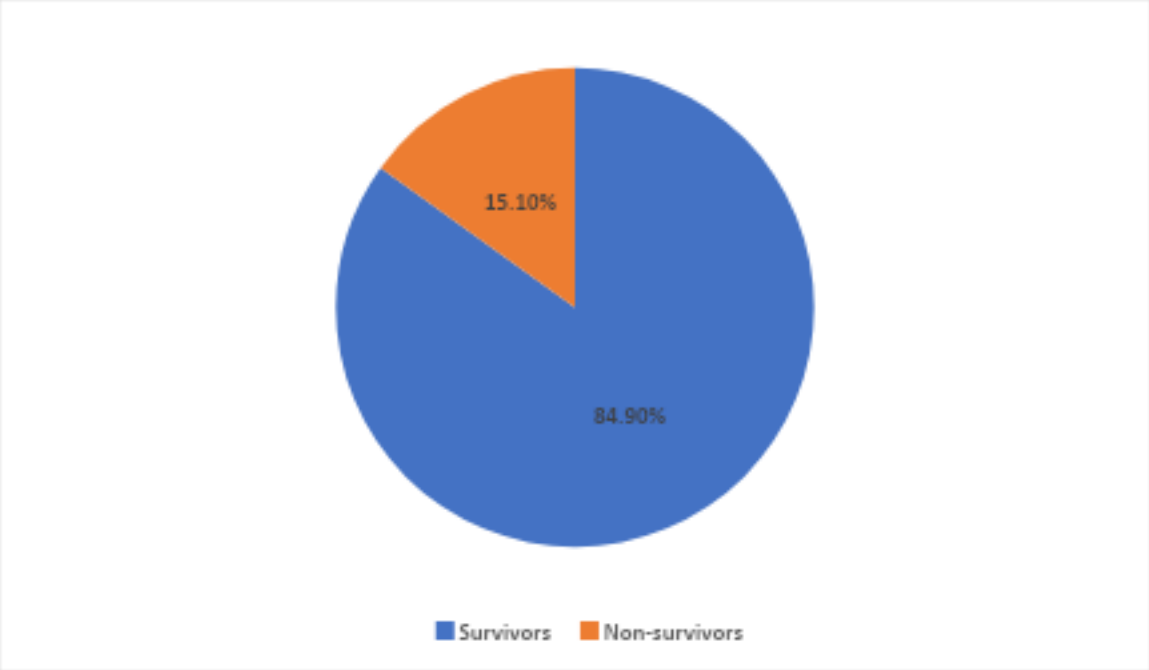


Table 10: Distribution of patients according to pupil size

pupil size (mm)	
Mean	2.1
SD	0.84

Table 10 and graph 10 indicates that the mean pupil size of patients was 2.1 mm with a standard deviation of 0.84 mm, suggesting miosis (pupillary constriction) which is a characteristic sign of organophosphate poisoning.

Graph 10: Distribution of patients according to pupil size

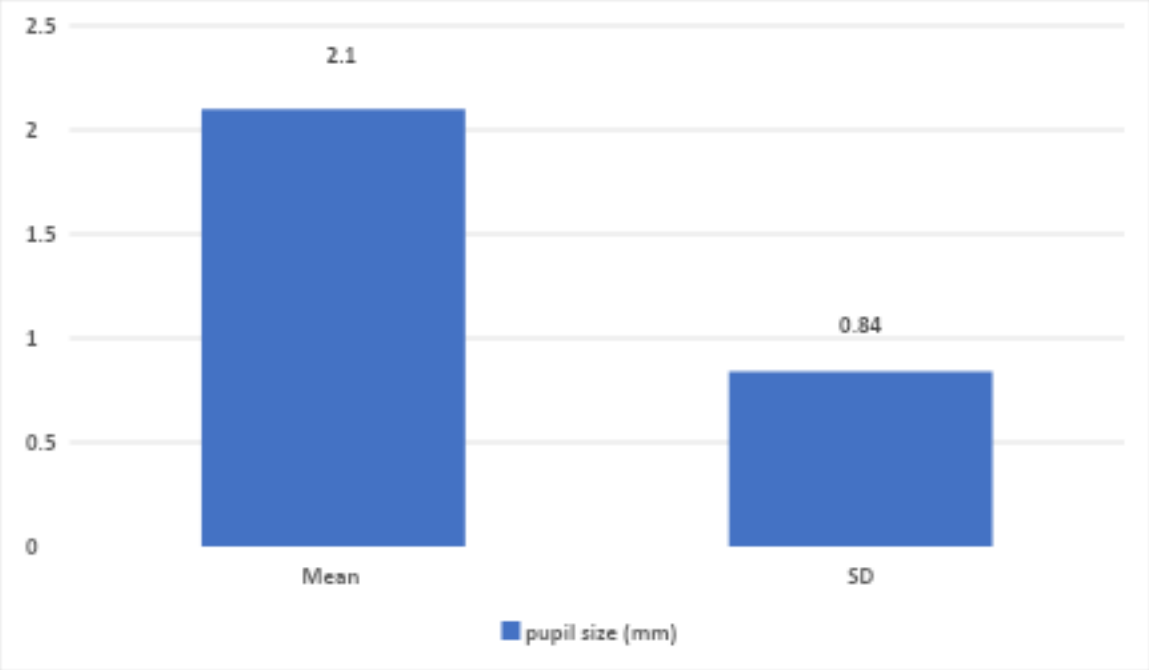


Table 11: Distribution of patients according to length of hospital stay

length of hospital stay (days)	
Mean	5.45
SD	3.2

Table 11 and graph 11 shows that the average length of hospital stay was 5.45 days with a standard deviation of 3.2 days, indicating variability in recovery time among patients.

Graph 11: Distribution of patients according to length of hospital stay

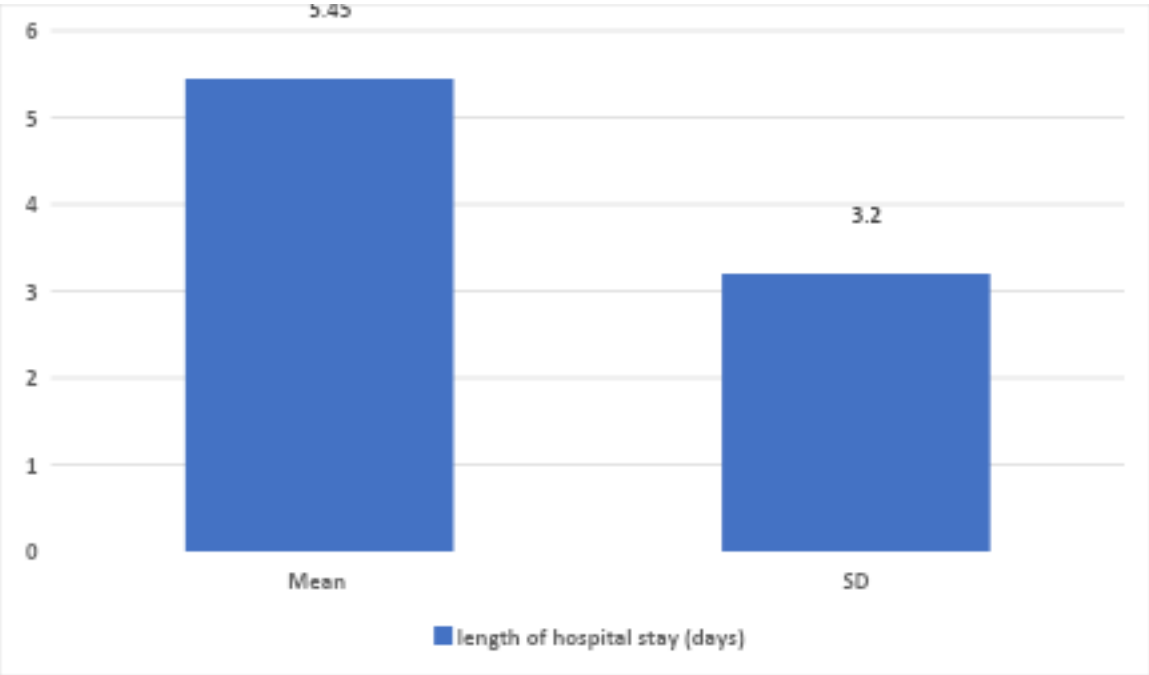


Table 12: Association of severity grading with acetylcholinesterase enzyme levels

acetylcholinesterase enzyme levels	severity grading			p-value
	Mild	Moderate	Severe	
Day 1	4526.1±3396.8	3136.4±2731.6	1671.3±2136.6	**0.005**
Day 3	4243.9±3142.6	3040.6±2681.2	1589.7±1989	**0.005**
Day 5	4248.6±3136.9	3110.2±2746.1	1628.04±2001.4	**0.006**

Table 12 and graph 12 demonstrates a statistically significant association ($p<0.005$) between severity grading and acetylcholinesterase enzyme levels across all three days of measurement, with enzyme levels decreasing as severity increased (mild cases had the highest enzyme levels, while severe cases had the lowest).

Graph 12: Association of severity grading with acetylcholinesterase enzyme levels

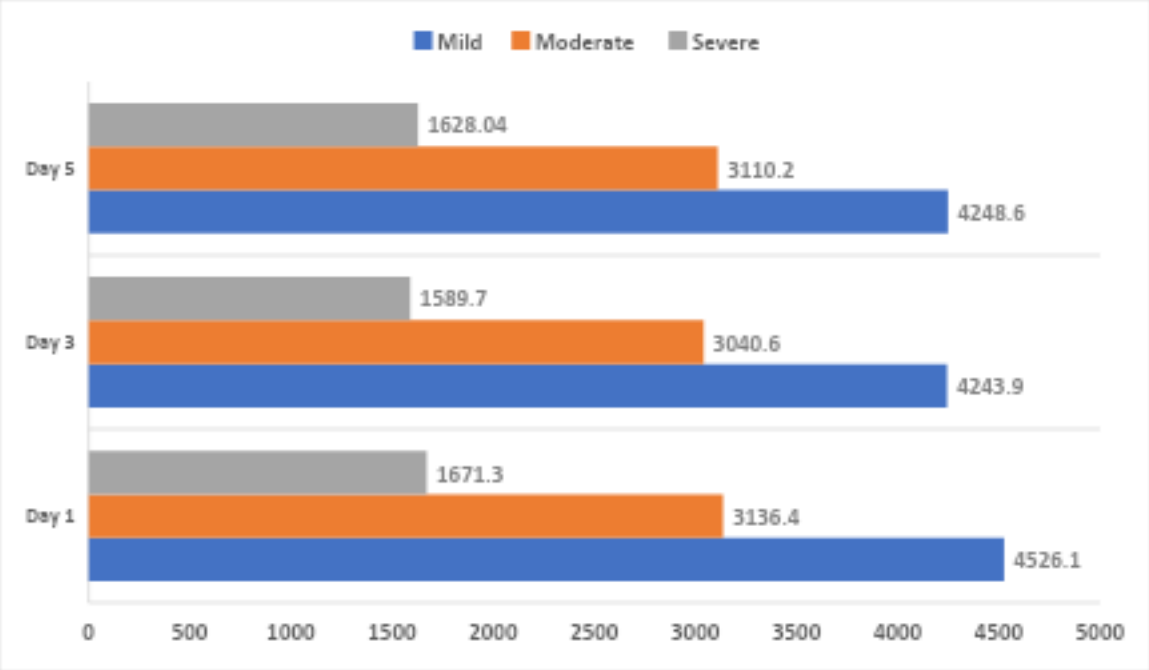


Table 13: Association of severity grading with investigations at day 1

Investigations (mean±SD)	severity grading			p-value
	Mild	Moderate	Severe	
Amylase	92.6±13.8	161.8±24.3	251.7±29.3	**<0.001**
CPK	73.6±13.2	110.6±19.7	308.1±63.1	**<0.001**

Table 13 and graph 13 reveals a highly significant association ($p<0.001$) between severity grading and both amylase and CPK levels on day 1, with both enzyme markers progressively increasing from mild to severe cases, supporting their potential role as severity indicators.

Graph 13: Association of severity grading with investigations at day 1

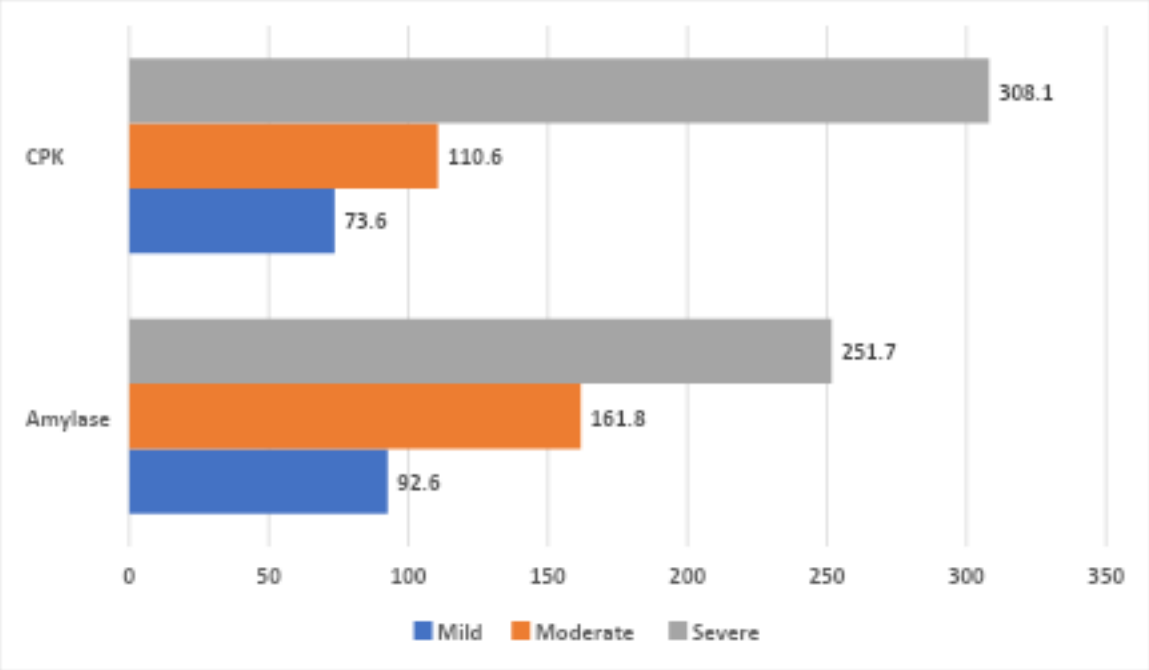


Table 14: Association of acetyl cholinesterase enzyme levels on admission with investigations

Investigations (mean±SD)	acetyl cholinesterase enzyme levels		p-value
	<5320	**>5320**	
Amylase	1.56±0.49	1.86±0.35	**0.03**
CPK	1.08±0.28	1.46±0.51	**<0.001**

Table 14 and graph 14 shows a statistically significant association between acetylcholinesterase enzyme levels and both amylase ($p=0.03$) and CPK ($p<0.001$) levels, with higher amylase and CPK values observed in patients with acetylcholinesterase levels >5320 compared to those with levels <5320.

Graph 14: Association of acetyl cholinesterase enzyme levels on admission with investigations

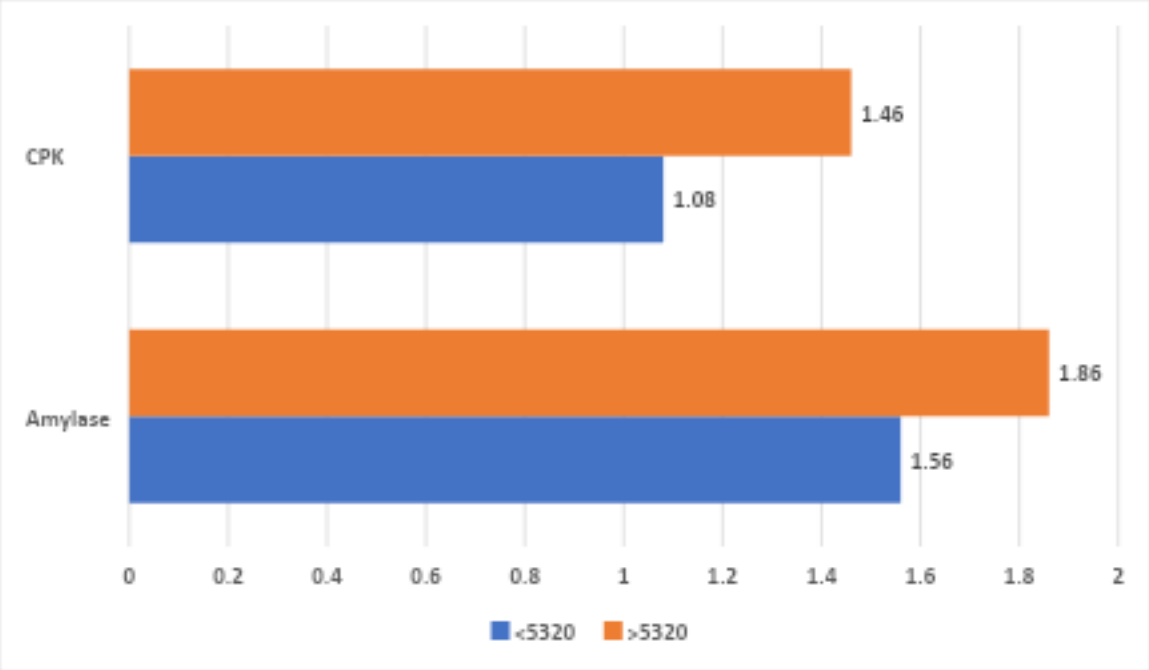


Table 15: Association of acetyl cholinesterase enzyme levels on admission with outcome

Outcome	acetyl cholinesterase enzyme levels		p-value
	<5320	**>5320**	
Non survivors	20 (34.5%)	1 (6.7%)	**0.034**
Survivors	38 (65.5%)	14 (93.3%)	
Total	**58 (100%)**	**15 (100%)**	

Table 15 and graph 15 demonstrates a significant association (p=0.034) between acetylcholinesterase enzyme levels on admission and patient outcomes, with a notably higher survival rate (93.3%) among patients with enzyme levels >5320 compared to those with levels <5320 (65.5% survival rate).

Graph 15: Association of acetyl cholinesterase enzyme levels on admission with outcome

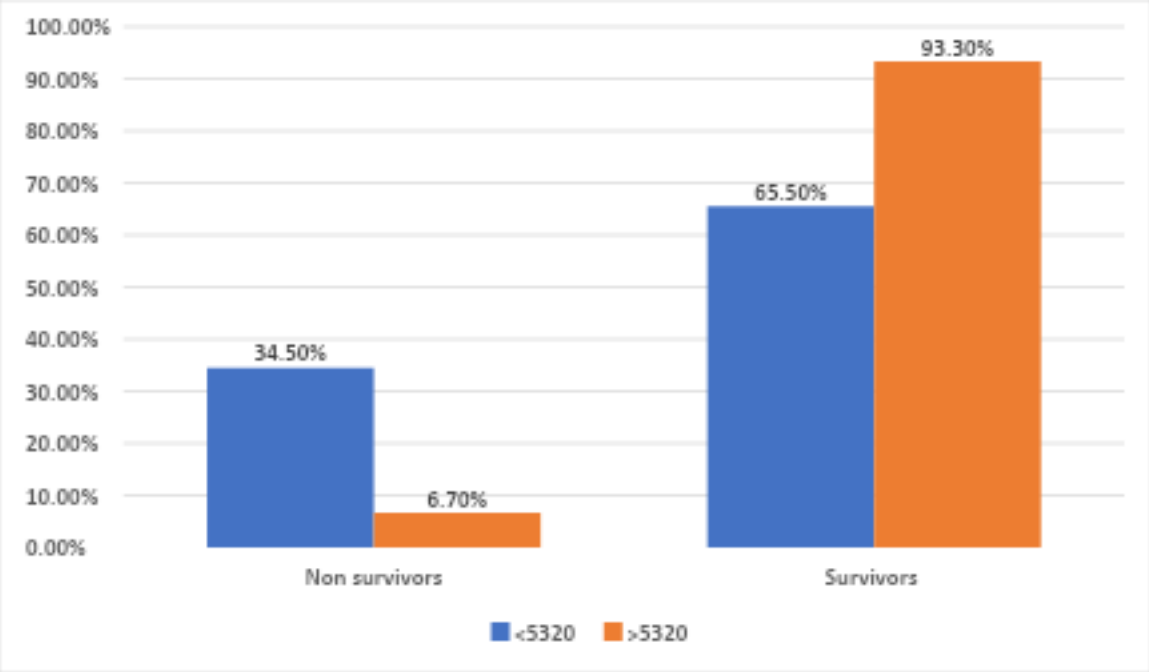


Table 16: Correlation POP score with investigations

POP score	Amylase	CPK	Acetyl cholinesterase
Pearson's correlation	0.865	0.817	0.249
p-value	**<0.001**	**<0.001**	**0.03**

Table 16 shows significant correlations between POP score and laboratory investigations, with strong positive correlations for amylase ($r=0.865$, $p<0.001$) and CPK ($r=0.817$, $p<0.001$), and a weaker but still significant correlation with acetylcholinesterase ($r=0.249$, $p=0.03$), suggesting amylase and CPK could be valuable markers for assessing organophosphate poisoning severity**.**

DISCUSSION

Organophosphate compounds are among the most common pesticides used worldwide, particularly in agricultural regions. Despite their beneficial effects in controlling pests and improving crop yields, these compounds pose significant health risks when humans are exposed to them, either accidentally or intentionally. Organophosphate poisoning (OPP) represents a major public health challenge, especially in developing countries where these compounds are widely available with minimal regulatory oversight. The mechanism of toxicity primarily involves the inhibition of acetylcholinesterase enzyme, leading to the accumulation of acetylcholine at synaptic junctions and resulting in a characteristic cholinergic crisis. This manifests as a spectrum of clinical features ranging from mild symptoms to severe, life-threatening conditions requiring intensive care management. The present study was conducted to evaluate the efficacy of serum amylase and creatine phosphokinase (CPK) levels as biomarkers for assessing the severity of organophosphate poisoning and to correlate these findings with the conventional Peradeniya Organophosphorus Poisoning (POP) scale. This discussion aims to interpret our findings in the context of existing literature and explore their implications for clinical practice and future research.

Demographic Profile of Patients with Organophosphate Poisoning

In our study, we observed that organophosphate poisoning predominantly affected young adults, with 67.1% of cases occurring in the age group of 21-40 years, followed by adolescents and young adults aged 16-20 years (21.9%). Similar age distribution has been reported by Banday et al., who found that 70% of cases in their study were between 21-40 years of age, suggesting that the economically productive age group is most vulnerable to such exposures.[69] The gender distribution in our study was nearly equal, with a slight female predominance (50.7% vs. 49.3%).

This finding differs somewhat from other studies, such as that by Muley et al., who reported a male preponderance (63% males vs. 37% females) in their study of 90 OPP cases.[70]

The almost equal gender distribution in our study could be attributed to regional variations in agricultural practices, socioeconomic factors, and cultural norms that influence access to and handling of pesticides. The slight female predominance might also reflect changing patterns of female involvement in agricultural activities or domestic use of pesticides in our study region.

Clinical Presentation and Time Since Exposure

The mean time since exposure to hospital presentation in our study was 5.9 ± 4.5 hours. This delayed presentation could be attributed to various factors including lack of immediate recognition of poisoning symptoms, transportation delays, initial management at local healthcare facilities before referral, or socio-cultural factors influencing healthcare-seeking behavior. Karki et al. reported a median time of 4 hours from exposure to hospital presentation in their study, slightly shorter than our findings.[71] The delayed presentation observed in both studies highlights the need for improved awareness about the urgency of seeking medical care following pesticide exposure and establishing efficient referral systems.

Regarding clinical presentation, vomiting was the most common symptom (76.7%), followed by muscle weakness (37%), bronchospasm (31.5%), diarrhea (23.3%), salivation (19.2%), abdominal pain (11%), convulsions (5.5%), and lacrimation (1.4%). This constellation of symptoms aligns with the cholinergic excess characteristic of organophosphate poisoning. Similar findings were reported by Banday et al., who observed vomiting in 78% of cases, followed by salivation (65%) and fasciculations (48%).[69] The variations in symptom frequency across studies may reflect differences in the specific organophosphate compounds involved, the severity of

poisoning, time elapsed since exposure, and individual variations in susceptibility and response.

Severity Assessment Using Peradeniya Organophosphorus Poisoning Scale

The Peradeniya Organophosphorus Poisoning (POP) scale is a widely used clinical tool for assessing the severity of organophosphate poisoning. In our study, 43.8% of patients were classified as having mild poisoning, 39.7% as moderate, and 16.4% as severe based on the POP scale. This distribution is comparable to that reported by Rehiman et al., who found 42% mild, 38% moderate, and 20% severe cases in their study of 50 patients.[72] The slightly lower percentage of severe cases in our study might be attributed to regional variations in the types of organophosphate compounds used, differences in the amount ingested, or variations in the time elapsed between exposure and initiation of treatment.

The POP scale's utility in predicting clinical outcomes was evident in our study, as it showed significant correlations with both biochemical markers (amylase and CPK) and acetylcholinesterase levels. This reinforces the findings of Senanayake et al., who originally developed the scale and demonstrated its value in prognostication.[73] However, it is worth noting that while clinical scoring systems like the POP scale are valuable, they have limitations, particularly in settings where patients present with altered consciousness or when symptoms have been modified by pre-hospital interventions such as atropine administration.

Acetylcholinesterase Enzyme Levels and Their Clinical Significance

Acetylcholinesterase enzyme levels are considered the gold standard for diagnosing and monitoring organophosphate poisoning. In our study, 39.7% of patients had severely depressed enzyme levels (<500 units) on day 1, which persisted in a similar proportion of patients on days 3 (39.7%) and 5 (38.4%). This pattern of persistent enzyme inhibition reflects the irreversible nature

of acetylcholinesterase inhibition by organophosphates, which necessitates de novo synthesis of the enzyme for recovery.

We observed a significant association between acetylcholinesterase levels and severity grading based on the POP scale. Mean acetylcholinesterase levels on day 1 were 4526.1 ± 3396.8 units in mild cases, 3136.4 ± 2731.6 units in moderate cases, and 1671.3 ± 2136.6 units in severe cases (p=0.005). This inverse relationship continued on days 3 and 5. These findings align with those reported by Chaudhary et al., who also found a significant correlation between cholinesterase levels and clinical severity.[74]

Furthermore, our study revealed a significant association between acetylcholinesterase levels on admission and patient outcomes. Among patients with enzyme levels <5320 units, 34.5% were non-survivors, compared to only 6.7% among those with levels >5320 units (p=0.034). This finding underscores the prognostic value of acetylcholinesterase levels in predicting mortality, as also reported by Nouira et al. in their study of 60 patients with organophosphate poisoning.[75]

However, it is important to recognize that while acetylcholinesterase levels provide valuable diagnostic and prognostic information, their utility is constrained by several factors. These include the wide normal range of the enzyme, significant inter-individual variations, and more importantly, the limited availability of this test in resource-constrained settings where organophosphate poisoning is most prevalent. This highlights the need for alternative, readily available biomarkers that can complement clinical assessment in determining the severity and prognosis of organophosphate poisoning.

Serum Amylase Levels in Organophosphate Poisoning

Our study found elevated serum amylase levels (>110 units) in 63% of patients on day 1,

which increased to 67.1% on days 3 and 5. This high prevalence of hyperamylasemia in organophosphate poisoning aligns with findings from previous studies. Singh et al. reported elevated serum amylase in 66% of their patients, a figure remarkably similar to our findings.[76]

The mechanism underlying hyperamylasemia in organophosphate poisoning is multifactorial. Direct pancreatic injury due to cholinergic hyperstimulation, ischemic injury to the pancreas due to hypotension, and reduced clearance of serum amylase due to cholinergic effects on renal blood flow are all potential contributors. Matsumiya et al. proposed that the excessive cholinergic stimulation leads to pancreatic hypersecretion and eventual damage to pancreatic acinar cells, resulting in the release of amylase into the circulation.[77]

A significant finding in our study was the strong correlation between serum amylase levels and clinical severity as assessed by the POP scale. Mean amylase levels were 92.6 ± 13.8 units in mild cases, 161.8 ± 24.3 units in moderate cases, and 251.7 ± 29.3 units in severe cases ($p<0.001$). This robust correlation (Pearson's correlation coefficient 0.865, $p<0.001$) suggests that serum amylase could serve as a valuable biochemical marker for severity assessment.

Our findings are in line with those of Lee et al., who also found a significant correlation between serum amylase levels and the severity of organophosphate poisoning in their study of 121 patients.[78] Similarly, Ahmed et al. reported that serum amylase levels were significantly higher in non-survivors compared to survivors in their study, further supporting the prognostic value of this biomarker.[79]

Interestingly, we also observed that patients with acetylcholinesterase levels <5320 units had significantly lower amylase levels compared to those with higher acetylcholinesterase levels (1.56 ± 0.49 vs. 1.86 ± 0.35, $p=0.03$). This inverse relationship might seem counterintuitive given

that lower acetylcholinesterase levels indicate more severe poisoning. However, this could be explained by the complex interplay between cholinergic effects, pancreatic stimulation, and potential protective mechanisms that might be activated in severe poisoning. Alternatively, it could reflect the heterogeneity in individual responses to organophosphate exposure or variations in the specific compounds involved.

Creatine Phosphokinase (CPK) Levels in Organophosphate Poisoning

Creatine phosphokinase (CPK) is an enzyme found predominantly in skeletal muscle, cardiac muscle, and brain tissue. Elevated serum CPK levels indicate damage to these tissues. In our study, 16.4% of patients had elevated CPK levels (>200 units) on day 1, with similar proportions on days 3 (19.2%) and 5 (17.8%). While this prevalence is lower than that of hyperamylasemia, it still represents a significant finding.

The mechanism of CPK elevation in organophosphate poisoning is primarily attributed to muscle injury resulting from fasciculations, tremors, and seizures that occur in severe cases. Additionally, direct toxic effects of organophosphates on muscle tissue and rhabdomyolysis secondary to hypoxia or prolonged immobility might contribute to CPK elevation.

Our study revealed a significant association between CPK levels and clinical severity. Mean CPK levels were 73.6 ± 13.2 units in mild cases, 110.6 ± 19.7 units in moderate cases, and 308.1 ± 63.1 units in severe cases ($p<0.001$). This strong correlation (Pearson's correlation coefficient 0.817, $p<0.001$) suggests that CPK, like amylase, could serve as a useful biochemical marker for severity assessment in organophosphate poisoning.

Similar findings were reported by Bhattacharyya et al., who found significantly higher CPK levels in moderate and severe poisoning compared to mild cases.[80] They also observed that CPK

levels were predictive of the need for mechanical ventilation, a finding that aligns with our observation that 26% of patients in our study required ventilatory support.

Interestingly, we found that patients with acetylcholinesterase levels <5320 units had significantly lower CPK levels compared to those with higher acetylcholinesterase levels (1.08 ± 0.28 vs. 1.46 ± 0.51, $p<0.001$). This pattern mirrors what we observed with amylase levels and warrants further investigation to elucidate the underlying mechanisms.

Comparative Evaluation of Amylase and CPK as Severity Markers

A key objective of our study was to evaluate the relative efficacy of serum amylase and CPK as markers of severity in organophosphate poisoning. While both markers showed significant correlations with clinical severity as assessed by the POP scale, amylase demonstrated a stronger correlation ($r=0.865$) compared to CPK ($r=0.817$). This suggests that serum amylase might be a slightly more reliable marker for severity assessment.

This finding is particularly relevant in the context of resource-constrained settings where acetylcholinesterase assays may not be readily available. Serum amylase is a relatively simple and widely available test that could provide valuable prognostic information to guide clinical management. As Sumathi et al. noted in their study, serum amylase elevation often precedes clinical deterioration, making it a potentially useful early marker for identifying patients at risk of developing complications.[81]

However, it is important to acknowledge that both amylase and CPK have limitations as severity markers. Amylase can be elevated in conditions other than organophosphate poisoning, such as pancreatitis, salivary gland disorders, renal impairment, and various other pathologies. Similarly, CPK elevation can result from numerous causes including muscle trauma, myocardial

infarction, seizures, and certain drugs. Therefore, these markers should be interpreted in the context of clinical presentation and, when available, acetylcholinesterase levels.

Clinical Outcomes and Predictors of Mortality

In our study, the overall mortality rate was 15.1%, with 11 non-survivors among the 73 patients. This figure is comparable to the mortality rates reported in other studies from similar settings. Kang et al. reported a higher mortality rate of 20% in their study from South Korea.[82]

Several factors were associated with mortality in our study. Patients with lower acetylcholinesterase levels (<5320 units) had a significantly higher mortality rate compared to those with higher levels (34.5% vs. 6.7%, p=0.034). This aligns with findings from numerous previous studies that have established the prognostic value of acetylcholinesterase levels in organophosphate poisoning.

The need for mechanical ventilation was another important predictor of outcomes. In our study, 26% of patients required ventilatory support, and this subgroup had a higher mortality rate. This finding is consistent with that of Kang et al., who found that the need for mechanical ventilation was an independent predictor of mortality in their multivariate analysis.[82]

The mean length of hospital stay in our study was 5.45 ± 3.2 days, reflecting the significant healthcare burden imposed by organophosphate poisoning. Factors associated with prolonged hospital stay included the severity of poisoning, development of complications such as respiratory failure, and the need for mechanical ventilation. These findings underscore the importance of early recognition and prompt management of organophosphate poisoning to reduce morbidity, mortality, and healthcare costs.

Strengths and Limitations of the Study

Our study has several strengths, including its prospective design, comprehensive assessment of multiple markers (acetylcholinesterase, amylase, and CPK), and sequential measurements at different time points (days 1, 3, and 5). This allowed us to evaluate not only the diagnostic utility of these markers but also their prognostic value and temporal trends.

However, our study also has certain limitations that should be acknowledged. First, the sample size (n=73) is relatively modest, which may limit the generalizability of our findings. Second, we did not have information on the specific organophosphate compounds involved in each case, which could have influenced the clinical presentation and biochemical changes. Different organophosphate compounds have varying potencies and durations of action, which might affect the severity and persistence of symptoms as well as the pattern of biochemical alterations.

Third, our study did not account for potential confounding factors such as pre-hospital interventions, comorbidities, and concomitant ingestion of other substances, which could have influenced the clinical course and biochemical parameters. Fourth, while we found significant correlations between biochemical markers and clinical severity, we did not establish definitive cut-off values for these markers that could guide clinical decision-making.

Despite these limitations, our study provides valuable insights into the utility of serum amylase and CPK as markers of severity in organophosphate poisoning, particularly in settings where acetylcholinesterase assays may not be readily available.

Clinical Implications and Future Directions

The findings of our study have several important clinical implications. First, they suggest that serum amylase and CPK can serve as useful adjuncts to clinical assessment in determining the

severity of organophosphate poisoning, especially in settings where acetylcholinesterase assays are not available. Given their stronger correlation with clinical severity, these markers might even add value in settings where acetylcholinesterase assays are accessible.

Second, the significant associations between these biochemical markers and outcomes highlight their potential prognostic value. Patients with markedly elevated amylase or CPK levels may warrant closer monitoring and more aggressive management due to their higher risk of developing complications.

Third, the persistent elevation of these markers over the five-day observation period suggests that they might be useful for monitoring the clinical course and response to treatment. Persistently elevated or rising levels might indicate ongoing toxicity or the development of complications, necessitating a reassessment of the management approach.

Future research should focus on several areas. Larger, multicenter studies are needed to validate our findings and establish definitive cut-off values for amylase and CPK that can guide clinical decision-making. Studies incorporating detailed information on the specific organophosphate compounds involved would provide insights into compound-specific effects on these biochemical markers.

Research exploring the mechanisms underlying the elevation of amylase and CPK in organophosphate poisoning would enhance our understanding of the pathophysiology of this condition. Additionally, studies evaluating the cost-effectiveness of incorporating these markers into the routine assessment of organophosphate poisoning would be valuable, particularly for resource-constrained settings.

Long-term follow-up studies are also needed to assess the persistent or delayed effects of organophosphate poisoning and to determine whether early biochemical changes predict long-term outcomes. Finally, research on novel biomarkers and point-of-care testing for organophosphate poisoning could lead to more timely and accurate diagnosis and severity assessment, potentially improving patient outcomes.

Conclusion

In conclusion, our study demonstrates that serum amylase and creatine phosphokinase are valuable biomarkers for assessing the severity of organophosphate poisoning. Both markers showed strong correlations with clinical severity as assessed by the Peradeniya Organophosphorus Poisoning scale, with amylase exhibiting a slightly stronger correlation. These biochemical markers can serve as useful adjuncts to clinical assessment, particularly in settings where acetylcholinesterase assays are not readily available.

The significant associations between these markers and patient outcomes highlight their prognostic value. Patients with markedly elevated amylase or CPK levels may warrant closer monitoring and more aggressive management due to their higher risk of developing complications.

While acetylcholinesterase remains the gold standard for diagnosing and monitoring organophosphate poisoning, our findings suggest that serum amylase and CPK can provide complementary information that enhances severity assessment and prognostication. This is particularly relevant in resource-constrained settings where organophosphate poisoning is most prevalent.

Future research should focus on validating these findings in larger, more diverse populations, establishing definitive cut-off values for clinical decision-making, and exploring the

mechanisms underlying the elevation of these markers in organophosphate poisoning. Such efforts could lead to improved management strategies and better outcomes for patients with this potentially life-threatening condition.

CONCLUSION

Organophosphate poisoning continues to be a significant public health concern, particularly in agricultural regions where these compounds are widely used as pesticides. Our study has demonstrated that both serum amylase and creatine phosphokinase serve as valuable biomarkers in assessing the severity of organophosphate poisoning, with strong correlations to the clinical severity assessed by the Peradeniya Organophosphorus Poisoning scale.

The findings of our study revealed that serum amylase exhibited a stronger correlation with clinical severity compared to creatine phosphokinase, suggesting its superior utility as a severity marker. This is particularly significant in resource-limited settings where acetylcholinesterase assays might not be readily available. The early elevation of these enzymes and their persistent abnormal levels during the five-day observation period highlight their potential value in both initial assessment and monitoring the clinical course of patients with organophosphate poisoning.

Furthermore, our study confirmed that reduced acetylcholinesterase levels on admission were significantly associated with poorer outcomes, with markedly higher mortality rates observed in patients with enzyme levels below 5320 units. This underscores the prognostic value of acetylcholinesterase levels when available. However, the strong correlations between amylase and CPK levels with clinical severity suggest that these more widely available tests can serve as practical alternatives for severity assessment and prognostication.

The demographic profile and clinical presentation patterns observed in our study align with previous research, confirming that organophosphate poisoning predominantly affects

young adults, with vomiting, muscle weakness, and bronchospasm being the most common manifestations. The overall mortality rate of 15.1% reflects the serious nature of this condition and emphasizes the need for prompt recognition and appropriate management.

In conclusion, while acetylcholinesterase measurement remains the gold standard for diagnosing organophosphate poisoning, our study provides compelling evidence that serum amylase and creatine phosphokinase can effectively complement clinical assessment in determining severity and predicting outcomes. Incorporating these readily available biochemical markers into clinical practice could potentially enhance the management of organophosphate poisoning cases, particularly in settings with limited resources. Future research with larger sample sizes across diverse populations would further validate these findings and potentially establish definitive cut-off values for clinical decision-making.

SUMMARY

INTRODUCTION

Organophosphate compounds are widely used pesticides that cause significant morbidity and mortality worldwide, particularly in developing countries. The inhibition of acetylcholinesterase enzyme leads to accumulation of acetylcholine, resulting in characteristic cholinergic manifestations. While acetylcholinesterase levels are the gold standard for diagnosis and severity assessment, their limited availability in resource-constrained settings necessitates exploration of alternative biomarkers. This study aimed to evaluate serum amylase and creatine phosphokinase (CPK) as potential markers for assessing the severity of organophosphate poisoning and to correlate these findings with clinical severity and outcomes.

AIMS AND OBJECTIVES

Objectives:

1. To estimate and compare the Serum levels of Amylase and Creatine Phosphokinase in Acute Organophosphate poisoning.
2. To correlate the levels of the same with clinical severity using Peradeniya Organophosphorus Poisoning scale (POP scale).
3. To know which is a better biomarker that correlates with the severity of Organophosphate poisoning.

MATERIAL AND METHODS

This prospective study included 73 patients with organophosphate poisoning admitted to a tertiary care center. Clinical severity was assessed using the Peradeniya Organophosphorus Poisoning (POP) scale. Serum acetylcholinesterase, amylase, and CPK levels were measured on

days 1, 3, and 5 of hospitalization. Statistical analysis was performed to determine correlations between biochemical parameters and clinical severity, as well as their associations with outcomes.

RESULTS

- This study enrolled 73 patients with organophosphate poisoning to evaluate the efficacy of serum amylase and creatine phosphokinase as markers of severity. The following are the key findings:
- The study population primarily consisted of young adults, with 67.1% of patients falling within the 21-40 years age group, followed by 21.9% in the 16-20 years group. Gender distribution was nearly equal, with a slight female predominance (50.7% females vs. 49.3% males). The mean time from exposure to hospital presentation was 5.9 ± 4.5 hours.
- Clinical presentation was dominated by vomiting (76.7%), followed by muscle weakness (37%), bronchospasm (31.5%), diarrhea (23.3%), salivation (19.2%), abdominal pain (11%), convulsions (5.5%), and lacrimation (1.4%). Based on the Peradeniya Organophosphorus Poisoning scale, 43.8% of patients were classified as having mild poisoning, 39.7% moderate, and 16.4% severe.
- Acetylcholinesterase enzyme levels were severely depressed (<500 units) in 39.7% of patients on day 1, with similar proportions on days 3 and 5. A significant association was observed between acetylcholinesterase levels and clinical severity, with mean levels on day 1 being 4526.1 ± 3396.8 units in mild cases, 3136.4 ± 2731.6 units in moderate cases, and 1671.3 ± 2136.6 units in severe cases ($p=0.005$).

- Serum amylase levels were elevated (>110 units) in 63% of patients on day 1, increasing to 67.1% on days 3 and 5. Mean amylase levels showed a strong correlation with clinical severity: 92.6 ± 13.8 units in mild cases, 161.8 ± 24.3 units in moderate cases, and 251.7 ± 29.3 units in severe cases ($p<0.001$). The correlation coefficient between POP score and amylase was 0.865 ($p<0.001$).
- Elevated creatine phosphokinase levels (>200 units) were observed in 16.4% of patients on day 1, with similar proportions on subsequent days. Mean CPK levels were significantly different across severity categories: 73.6 ± 13.2 units in mild cases, 110.6 ± 19.7 units in moderate cases, and 308.1 ± 63.1 units in severe cases ($p<0.001$). The correlation coefficient between POP score and CPK was 0.817 ($p<0.001$).
- The study revealed a significant association between acetylcholinesterase levels on admission and patient outcomes. Among patients with enzyme levels <5320 units, 34.5% were non-survivors, compared to only 6.7% among those with levels >5320 units ($p=0.034$).
- Ventilatory support was required in 26% of patients, and the overall mortality rate was 15.1%. The mean length of hospital stay was 5.45 ± 3.2 days, and the mean pupil size was 2.1 ± 0.84 mm.
- In summary, both serum amylase and creatine phosphokinase demonstrated strong correlations with clinical severity in organophosphate poisoning, with amylase showing a slightly stronger correlation. These findings suggest that these readily available biochemical markers can serve as valuable adjuncts to clinical assessment in determining

severity and predicting outcomes, particularly in settings where acetylcholinesterase assays may not be available.

CONCLUSION:

Serum amylase and CPK levels demonstrate strong correlations with clinical severity in organophosphate poisoning, with amylase exhibiting a slightly stronger correlation. These readily available biochemical markers can serve as valuable adjuncts to clinical assessment in determining severity and predicting outcomes, particularly in settings where acetylcholinesterase assays are not available. Future research with larger sample sizes is warranted to establish definitive cut-off values for these markers in clinical decision-making.

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Annexure I: Ethical Clearance

BLDE

(DEEMED TO BE UNIVERSITY)

Declared as Deemed to be University u/s 3 of UGC Act, 1956

Accredited with 'A' Grade by NAAC (Cycle-2)

The Constituent College

SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, VIJAYAPURA

BLDE (DU)/IEC/ 879/2022-23 10/4/2023

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this University met on **Saturday, 18th March, 2023 at 11.30 a.m. in the CAL Laboratory, Dept. of Pharmacology,** scrutinized the Synopsis/ Research Projects of Post Graduate Student / Under Graduate Student /Faculty members of this University /Ph.D. Student College from ethical clearance point of view. After scrutiny, the following original/ corrected and revised version synopsis of the thesis/ research projects has been accorded ethical clearance.

TITLE: "CORRELATION OF SERUM AMYLASE AND CREATINE PHOSPHOKINASE LEVELS IN ASSESSING THE SEVERITY OF ORGANOPHOSPATE POISING".

NAME OF THE STUDENT/PRINCIPAL INVESTIGATOR: DR.RAKSHA CHANDRAIAH

NAME OF THE GUIDE: DR.ANAND AMBALI, PROFESSOR, DEPT. OF MEDICINE.

Dr. Santoshkumar Jeevangi
Chairperson
IEC, BLDE (DU),
VIJAYAPURA

Chairman,
Institutional Ethical Committee,
BLDE (Deemed to be University)
Vijayapura

Dr.Akram A. Naikwadi
Member Secretary
IEC, BLDE (DU),
VIJAYAPURA

MEMBER SECRETARY
Institutional Ethics Committee
BLDE (Deemed to be University)
Vijayapura-586103, Karnataka

Following documents were placed before Ethical Committee for Scrutinization:

- Copy of Synopsis/Research Projects
- Copy of inform consent form
- Any other relevant document

Smt. Bangaramma Sajjan Campus, B. M. Patil Road (Sholapur Road), Vijayapura - 586103, Karnataka, India.
BLDE (DU): Phone: +918352-262770, Fax: +918352-263303, Website: www.bldedu.ac.in, E-mail:office@bldedu.ac.in
College: Phone: +918352-262770, Fax: +918352-263019, E-mail: bmpmc.principal@bldedu.ac.in

BLDE

(DEEMED TO BE UNIVERSITY)

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The Constituent College

SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, VIJAYAPURA

Department of Medicine

To
The Registrar
BLDE (Deemed to be University)
Vijayapur

Date: 03.02.2024

Sub: Re-allotment of PG Guides to PGs 2022(March), 2022(Nov) & 2023 batch.

Sir,

Following is the List of re-allotment of PG Guides to PGs of 2022 (March), 2022(Nov) and 2023 batch for information and needful.

Sl. No.	Name of PG	Batch	Name of Previous Guide	Name of Present Guide
1	Dr Somani Gourav	2022(March)	Dr A P Ambali	Dr S T Kalsad
2	Dr Ajaykumar T J	2022(March)	Dr A P Ambali	Dr S T Kalsad
3	Dr Raksha Chandraiah	2022(Nov)	Dr A P Ambali	Dr S N Bentoor
4	Dr Akhil Thati	2022(Nov)	Dr A P Ambali	Dr R M Honnutagi
5	Dr Kommineni Anilkumar	2023	Dr A P Ambali	Dr R C Bidri
6	Dr Ganesh Dad	2023	Dr A P Ambali	Dr V G Warad

Thanking you

Yours sincerely,

Dr S N Bentoor
Professor & Head
Department of Medicine

PROF. & HOD, MEDICINE
BLDE (Deemed to Be University)
Shri B.M.Patil Medical College
Hospital & Research Centre, Vijayapura.

Annexure II : INFORMED CONSENT FORM

BLDE DU'S SHRI B. M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA- 586103

TITLE OF THE PROJECT: Comparison of Serum Amylase and Creatine Phosphokinase Levels in Assessing the Severity of Organophosphate Poisoning.

PRINCIPAL INVESTIGATOR - Dr. Raksha Chandraiah

P. G. GUIDE NAME - Dr. SANJEEVKUMAR N. BENTOOR M.D

PROFESSOR & HOD

DEPARTMENT OF MEDICINE

CHAIRMAN ETHICAL COMMITTEE

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

1) PURPOSE OF RESEARCH:

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

2) PROCEDURE:

I am aware that in addition to routine care received I will be asked a series of questions by the

investigator. I have been asked to undergo the necessary investigations and treatment to help to investigator in this study.

3) RISK AND DISCOMFORTS:

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

4) BENEFITS:

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

5) CONFIDENTIALITY:

I understand that the medical information produced by this study will become a part of Hospital records and will be subject to confidentiality and privacy regulation. Information of a sensitive personal nature will not be a part of the medical records but will be stored in the investigator's research file and identified only by a code number. The code key connecting name to numbers will be kept in a separate location. If the data are used for publication in the medical literature or teaching purposes, no name will be used, and other identifiers such as photographs and audio or videotapes will be used only with my special written permission. I understand that I may see the photographs and videotapes and hear the audiotapes before giving this permission.

6) REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at any time. Dr. RAKSHA CHANDRAIAH is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the study, which might influence my continued participation. If during the study, or later, I wish to discuss my participation in or

concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me. I will be given a copy of this consent form to keep for careful reading.

7) REFUSAL OR WITHDRAWAL OF PARTICIPATION:

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

8) INJURY STATEMENT:

I understand that in the unlikely event of injury to me resulting directly from my participation in this study, if such injury were reported promptly, the appropriate treatment would be available to me, but no further compensation would be provided. I understand that by my agreement to participate in this study, I am not waiving any of my legal rights. I have explained the purpose of the research, the procedures required, and the possible risks and benefits to the best of my ability in the patient's language.

II) STUDY SUBJECT CONSENT STATEMENT:

I confirm that Dr. Raksha Chandraiah has explained to me the purpose of the research, the study procedures that I will undergo, and the possible risks and discomforts as well as benefits that I may experience in my language. I have read and understand this consent form. Therefore, I agree to give consent to participate as a subject in this research project.

Participant or Guardian Date:

Witness to signature Date:

Annexure III : Proforma

Comparison of Serum amylase and Creatine phosphokinase levels in assessing the severity of organophosphate poisoning

SHRI BM PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE

VIJAYAPURA, KARNATAKA 586103

SCHEME OF CASE TAKING

Informant :

Name: CASE NO:

Age: IP NO:

Sex: DOA:

Religion: DOD:

Present Occupation:

Residence:

Chief complaints:

History of present illness:

Past History:

Personal History:

Family History:

Treatment History:

General Physical Examination Height:

Weight:

Body Mass Index:

Vitals: PR:

BP:

RR:

Temperature:

Head to toe examination:

SYSTEMIC EXAMINATION

CENTRAL NERVOUS SYSTEM:

RESPIRATORY SYSTEM:

CARDIOVASCULAR SYSTEM:

PER ABDOMEN:

POP SCORE:

INVESTIGATIONS

1. HAEMATOLOGY

Hemoglobin	gm. %
WBC	Cells/ mm^3

Count	
Platelet count	

2. Radiological investigations:

CHEST X-RAY

3. OTHERS

● SERUM CHOLINESTERASE

● RENAL FUNCTION TEST

● LIVER FUNCTION TEST

● CREATININE PHOSPHOKINASE

● SERUM AMYLASE

● URINE ANALYSIS

● **ECG**

	POP score	**Serum Amylase**	**Creatine phosphokinase**
Day 1			
Day 3			
Day 5			

Date:

Signature:

Annexure IV : Master chart

Patient ID	NAME	IP NO	Age	Sex	Time since poisoning (HRS)	POP score	Severity Category	Ventilator Required	Intermediate syndrome	Outcome (1=DEAD, 2=SURVIVED)	Cholinesterase D1	Cholinesterase D3	Cholinesterase D5	Amylase D1	Amylase D3	Amylase D5	CPK D1	CPK D3	CPK D5	Vomiting	Abd pain	Diarrohea	Salivation	Lacrimation	Bronchospasm	Muscle Weakness	Convulsions	GCS score	RR	HR	pupil size	Length of ICU stay (days)
1	roopa shrishail banikol	169791	19.00	F	11.5	1	1	0	0	2	4382	4,057.4	4,057.4	102	102.05	102.05	64	81.81	81.81	1	0	0	0	0	0	0	0	15	18	98	3	2
2	ishwar pandu bandagar	217010	65.00	M	3	1	1	0	0	2	206.8	191.55	191.55	111	130.75	130.75	51	66.67	66.67	0	0	1	0	0	0	0	0	14	18	78	3.5	5
3	savithri prashant biradar	216953	30.00	F	3.5	5	2	0	0	2	5145.4	5,128.1	5,128.1	180	200.13	200.13	93	131.23	131.23	1	0	0	0	0	0	0	0	15	16	78	1.5	3
4	ashwini irayya mathapati	222088	22.00	F	unknov	3	1	0	0	2	287.7	261.87	261.87	77	86.33	86.33	76	87.61	87.61	1	0	0	0	0	0	1	0	15	16	76	2	6
5	siddappa parasappa talawar	234925	26.00	F	24	6	2	1	1	1	367.6	408.31	450.64	197	191.77	169.62	102	218.52	174.86	1	0	0	0	0	1	0	0	13	20	144	1.5	2
6	rukmini danasingh pujari	245066	16.00	M	7	1	1	0	0	2	200	197.43	197.43	89	90.61	90.61	73	102.64	102.64	1	1	0	0	0	0	0	0	15	16	120	3.5	6
7	shanubhai yuvaraj naik	247449	28.00	F	4	6	2	0	0	2	4570.4	4,504.6	4,504.6	147	162.95	162.95	83	87.54	87.54	1	1	0	0	0	0	0	0	15	16	74	2.5	4
8	geeta nana jadhav	250421	23.00	F	11.5	6	2	0	0	2	200	198.54	198.54	135	150.48	150.48	120	172.63	172.63	0	0	0	1	0	0	1	0	15	18	120	2	5
9	vachu meghu rathod	252360	60.00	M	11.5	0	1	0	0	2	269.1	268.16	268.16	100	103.83	103.83	95	138.04	138.04	1	0	1	0	0	0	1	0	15	16	68	3.5	4
10	prahalad shivappa kattimani	255424	26.00	M	8	5	2	1	0	1	4223	4,535.9	6,179.2	170	165.41	127.00	136	124.13	84.81	1	0	1	0	0	1	0	0	3	36	140	1	1
11	manjunath siddaray kadimani	259855	29.00	M	3.5	4	2	1	0	1	7898.2	8,692.6	8,953.1	195	156.13	136.40	120	115.84	68.52	1	0	0	0	0	0	1	0	12	19	84	2.5	4
12	parashuram raju kattimani	259948	24.00	M	2	3	1	0	0	2	255.1	237.74	237.74	118	125.09	125.09	82	92.08	92.08	0	0	1	0	0	0	0	0	15	20	96	2	4
13	roopa tiretappa hirekurabar	260663	21.00	F	4	7	2	0	0	2	5888.4	5,684.0	5,684.0	120	140.10	140.10	109	141.52	141.52	1	0	0	0	0	0	0	0	15	18	98	4	2
14	aisha davalasab kalegar	261648	22.00	F	2.5	0	1	0	0	2	3727.6	3,492.4	3,492.4	106	115.34	115.34	93	132.77	132.77	0	0	0	1	0	0	0	0	15	16	98	3	1
15	sachin b naykodi	265336	17.00	M	3	3	1	0	0	2	236.4	234.20	234.20	96	107.29	107.29	78	116.10	116.10	1	0	0	0	0	0	0	0	15	16	102	3	5
16	paramanand basappa hadapad	278468	38.00	M	0.5	0	1	0	0	2	200	191.53	191.53	80	83.86	83.86	54	58.36	58.36	0	0	0	0	0	0	0	0	15	18	96	2	4
17	kiratiashok bistagond	285163	26.00	F	2	4	2	0	0	2	4006.6	3,784.9	3,784.9	183	195.65	195.65	90	94.61	94.61	1	0	0	0	0	0	0	0	15	16	112	3	4
18	muttappa ashok biradar	299267	30.00	M	3	3	1	0	0	2	2195.5	1,992.3	1,992.3	72	80.91	80.91	96	101.22	101.22	1	0	0	0	0	0	1	0	15	24	112	2	5
19	savithri jagadevappa biradar	310434	23.00	F	5	7	2	1	0	2	200	182.32	182.32	123	133.18	133.18	128	189.00	189.00	1	0	0	0	0	1	1	1	4	36	108	1	7
20	yallappa l madar	311540	45.00	M	10	10	3	1	1	1	593.9	755.44	812.35	200	196.61	160.64	306	362.79	247.08	1	0	0	1	0	1	1	0	9	30	118	2	2

21	manjula mallikarjun babaleshw	333652	35.00	F	0.5	1	1	0	0	2	2221.2	2,001.(	2,001.0	81	95.22	95.22	83	87.43	87.43	0	0	0	0	0	0	1	0	15	16	120	3	3
22	mallikarjun kallappa kudari	334976	80.00	M	4	6	2	0	0	2	7911.4	7,516.4	7,516.4	182	196.16	196.16	90	115.77	115.77	1	0	0	0	0	0	0	0	15	16	88	3	2
23	mallappa s hittanalli	347372	25.00	M	5.5	5	2	0	0	2	7569.4	7,189.5	7,189.5	155	168.97	168.97	116	128.86	128.86	0	1	0	0	0	0	0	0	15	16	88	3	3
24	kallappa vittal naikodi	347905	65.00	M	5.5	7	2	1	0	2	200	197.14	197.14	159	181.25	181.25	118	121.85	121.85	1	0	1	0	0	1	1	0	7	22	102	2	3
25	saibanna jateppa kambar	348268	24.00	M	7	10	3	0	1	2	1031.5	1,011.9	1,011.9	264	311.77	311.77	350	520.07	520.07	1	0	0	0	0	1	1	0	15	22	98	1	8
26	rakmaji laxman lokhande	349160	80.00	F	21.5	0	1	1	0	1	458.7	497.60	583.72	103	92.97	75.11	98	90.60	50.22	0	0	0	1	0	1	0	0	7	24	120	1	2
27	mallappa lagamappa naikodi	350411	35.00	M	7	1	1	0	0	2	200	188.36	188.36	83	98.64	98.64	67	88.63	88.63	0	0	0	0	0	0	0	0	15	20	70	2	3
28	akshay kumar shivaray dalawai	369470	25.00	M	5	7	2	1	0	2	200	189.07	189.07	177	197.84	197.84	110	154.41	154.41	1	0	1	0	0	1	0	0	3	36	106	1.5	14
29	basavantrayagouda s patil	379227	17.00	M	11	5	2	0	1	2	2762.2	2,510.3	2,510.3	129	129.85	129.85	91	132.26	132.26	1	0	0	0	0	1	1	0	11	36	96	1.5	4
30	Raghavendra sadashiva balochi	388252	28.00	M	0.5	4	2	0	0	2	7898.2	7,412.7	7,412.7	183	208.69	208.69	146	187.47	187.47	1	0	0	0	0	0	0	1	12	18	88	3	5
31	kavitha rajendra bagali	390778	29.00	F	6	11	3	0	1	2	7248	6,544.5	6,544.5	272	310.60	310.60	251	380.05	380.05	1	0	0	0	0	0	0	0	15	18	114	3.5	5
32	megha hanamanth mashyalkar	3874	18.00	F	4.5	11	3	0	1	2	990.9	895.23	895.23	267	312.85	312.85	389	851.26	851.26	0	0	1	1	0	0	0	0	15	20	96	2	5
33	roopa shivarudra shivanagi	6535	25.00	F	5	7	2	0	0	2	200	193.66	193.66	146	147.25	147.25	128	154.19	154.19	1	0	1	1	0	0	1	1	11	18	126	1	8
34	karishma irappa yaranal	9106	25.00	F	5	3	1	1	0	2	975.4	897.53	897.53	114	129.04	129.04	100	102.87	102.87	1	0	0	0	0	1	1	0	3	18	100	1	9
35	reshma dastagiri dhaded	15013	28.00	F	3.5	1	1	0	0	2	962.3	954.35	954.35	105	116.87	116.87	72	85.65	85.65	0	1	0	0	0	0	0	0	15	18	102	3	6
36	irappa g belavaddagi	34785	22.00	M	4	0	1	1	0	2	200	187.64	187.64	119	138.28	138.28	79	87.33	87.33	0	0	1	1	0	1	1	1	10	28	132	1	18
37	anand rajshekar pujari	33745	30.00	M	unkno	9	3	0	1	2	6234.3	5,674.1	5,674.1	254	269.06	269.06	320	850.98	850.98	0	1	0	0	0	1	0	0	3	28	58	1.5	8
38	ashwini channu chavan	49032	19.00	F	4	0	1	0	0	2	4045	3,785.5	3,785.5	85	89.22	89.22	75	92.43	92.43	1	0	0	0	0	0	0	0	15	18	102	2.5	4
39	bhagyashree shivaraj alamatti	55284	21.00	F	2	10	3	0	0	2	6584.6	6,226.4	6,226.4	238	248.99	248.99	229	251.64	251.64	1	0	0	0	0	0	0	0	15	18	120	4	4
40	archana basavaraj hosamani	57293	16.00	F	unkno	10	3	0	0	2	7112.2	6,732.3	6,732.3	288	296.39	296.39	221	230.17	230.17	1	0	0	0	0	0	0	0	15	18	120	3	1
41	kashinath laxman betagoudar	100240	26.00	M	17	11	3	0	1	2	1064	1,042.4	1,042.4	289	327.78	327.78	368	386.27	386.27	1	0	0	0	0	1	1	0	15	36	136	1	5
42	deepa mallikarjun dolli	112229	34.00	F	3	5	2	0	0	2	4110.5	3,768.(	3,768.0	164	176.69	176.69	101	103.17	103.17	1	0	0	0	0	0	1	0	15	20	62	1.5	5
43	ambika mahantesh chavan	11223	38.00	F	4	4	2	0	0	2	4267.7	4,134.1	4,134.1	188	217.06	217.06	113	128.97	128.97	1	0	0	0	0	0	0	0	15	18	120	2	2
44	tanuja karan logavi	120577	18.00	F	2	2	1	0	0	2	7781.3	7,009.2	7,009.2	93	94.83	94.83	70	74.66	74.66	1	0	1	0	0	0	1	0	15	18	120	2	5
45	bharat kumar p meti	138722	20.00	M	6	5	2	0	0	2	4456.5	4,402.(	4,402.0	170	189.61	189.61	142	176.37	176.37	0	0	0	1	0	1	0	0	10	28	130	2.5	3

46	savithri revansidda managuli	140405	25.00	F	2	3	1	0	0	2	359	355.73	355.73	71	73.23	73.23	59	83.24	83.24	1	0	0	0	0	0	0	0	15	18	90	2.5	6
47	girish shankareppa masuti	143084	28.00	M	3	3	1	1	0	1	1961	2,538.2	3,420.7	95	82.51	79.96	56	52.74	40.24	1	0	0	0	0	1	1	0	7	28	102	1	2
48	sanjana suresh rathod	224626	19.00	F	11.5	5	2	0	0	2	5176	4,666.7	4,666.7	131	139.82	139.82	113	164.12	164.12	0	0	0	0	0	0	0	0	15	16	96	2.5	5
49	allisab md sab mulla	155117	52.00	M	12	1	1	0	0	2	1520	1,474.4	1,474.4	75	86.37	86.37	68	71.12	71.12	1	0	0	0	0	0	0	0	15	18	94	2.5	4
50	shrikant dharma raj hasanapur	162460	35.00	M	3	3	1	1	0	1	200	214.43	263.84	92	85.52	72.11	79	78.11	46.84	1	0	1	0	0	1	1	0	8	24	130	1	8
51	renuka pujari	175303	25.00	F	6	2	1	0	0	2	200	197.19	197.19	103	117.30	117.30	69	76.47	76.47	1	0	0	0	0	0	0	0	15	18	124	2.5	6
52	malingray m yaladagi	175292	32.00	M	6	3	1	1	0	2	351	325.72	325.72	80	93.24	93.24	74	95.33	95.33	1	0	1	0	0	1	1	0	10	20	116	2	10
53	laxman guranna	189796	24.00	M	9.5	6	2	0	0	2	2827	2,649.6	2,649.6	136	141.49	141.49	86	116.34	116.34	1	0	1	0	0	0	1	0	12	24	130	2	8
54	praveen anil rathod	230759	20.00	M	3	2	1	0	0	2	6002	5,590.8	5,590.8	88	105.33	105.33	57	83.12	83.12	1	1	0	0	0	0	0	0	15	20	86	3	6
55	akshay bharat salunke	241312	25.00	M	8	4	2	0	0	2	5210	4,781.5	4,781.5	140	152.09	152.09	141	158.25	158.25	1	0	0	0	0	0	0	0	15	16	98	2.5	3
56	nana jadhav	258356	29.00	M	4	4	2	0	0	2	200	199.38	199.38	131	155.72	155.72	121	173.22	173.22	1	0	0	0	0	0	0	0	15	18	72	3	9
57	kaveri bhimaray pujari	269269	19.00	F	11.5	5	2	0	1	2	200	185.42	185.42	194	212.49	212.49	147	233.00	233.00	1	1	0	0	0	0	0	0	15	16	130	1.5	18
58	mallamma suresh kenganal	272364	32.00	F	16	6	2	0	1	2	1000	975.36	975.36	192	215.60	215.60	86	101.80	101.80	1	0	0	0	0	0	0	0	15	18	86	3	6
59	deepa namadev shinge	276797	24.00	F	4	6	2	0	0	2	1674	1,644.3	1,644.3	143	145.59	145.59	84	90.06	90.06	1	0	1	0	0	0	0	0	15	18	84	2.5	5
60	vidya shree s mamadapur	291951	18.00	F	8	2	1	0	0	2	4992	4,708.6	4,708.6	92	109.50	109.50	66	79.62	79.62	1	1	0	0	0	0	0	0	15	18	98	3	5
61	amasiddh dhondappa gheradi	1026	65.00	M	3	3	1	1	0	2	200	191.99	191.99	74	82.68	82.68	73	89.71	89.71	1	0	0	0	0	1	1	0	3	34	66	1.5	8
62	ashwini sambaji pawar	2048	28.00	F	2	11	3	0	0	2	6989	6,410.0	6,410.0	267	288.58	288.58	383	454.08	454.08	0	0	0	0	0	0	0	0	15	18	116	2.5	9
63	arun gangayya hiremath	3216	26.00	M	5	4	2	1	0	1	200	231.61	303.58	165	153.04	124.41	99	94.63	68.69	1	0	1	1	0	1	1	0	9	28	120	1	9
64	sharanappa bhimanna agasar	3910	35.00	M	4	3	1	1	0	1	200	200.88	246.99	82	69.67	52.44	71	64.97	46.37	1	0	0	0	0	1	1	0	3	36	98	1	3
65	preethi iranna hatti	5944	20.00	F	4	0	1	0	0	2	2338	2,149.7	2,149.7	85	98.72	98.72	55	65.35	65.35	1	0	0	1	0	0	0	0	15	24	106	2	9
66	aishwarya anand badiger	10714	18.00	F	3	3	1	1	0	1	200	233.39	308.04	90	88.01	68.56	86	79.58	54.16	1	0	0	1	0	1	1	0	3	24	86	1	5
67	lakshmibai bhirappa jambagi	11346	25.00	F	2	2	1	1	0	1	200	226.72	312.81	91	77.36	74.28	76	73.98	70.22	0	0	0	1	0	1	1	0	7	24	80	1	7
68	supiya sadiq mulla	11339	21.00	F	2	6	2	0	0	2	200	183.96	183.96	177	193.84	193.84	102	125.41	125.41	1	0	1	0	0	0	0	0	15	18	102	2	6
69	ravi mannur rathod	11733	40.00	M	7	0	1	0	0	2	5955.3	5,818.5	5,818.5	114	128.38	128.38	63	83.85	83.85	1	0	0	0	0	0	0	0	13	20	70	3	5
70	prakash mallappa methi	12147	28.00	M	3	10	3	0	1	2	6966	6,824.9	6,824.9	251	277.87	277.87	285	767.98	767.98	1	0	0	0	0	0	0	0	15	18	80	3	6
71	ravi kumar galave	12312	24.00	M	6	8	3	0	0	2	9299	8,629.3	8,629.3	204	220.36	220.36	363	390.45	390.45	1	0	0	1	0	0	0	0	15	18	78	3	7
72	baby santhosh chavan	14661	32.00	F	7	11	3	1	0	2	200	180.23	180.23	227	262.90	262.90	233	274.18	274.18	1	0	1	1	1	1	1	0	3	24	100	1	7
73	sanika rathod	15511	18.00	F	4.5	4	2	0	0	2	2195.7	2,028.3	2,028.3	182	209.10	209.10	95	127.23	127.23	1	0	0	0	0	0	0	0	15	16	102	3	5